

Clinical impact of early enteral nutrition on postoperative pain, gastrointestinal function and nutritional status in colorectal cancer patients.

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Keywords: colorectal cancer; early enteral nutrition; postoperative pain; analgesic pump.

Abstract. This research aimed to clarify the clinical impact of early enteral nutrition (EN) on postoperative pain, gastrointestinal function and nutritional status of colorectal cancer (CRC) patients. Eighty rectal cancer patients undergoing surgery in our hospital from October 2021 to October 2023 were selected as research subjects and divided into an experimental group (EG) and a control group (CG) using a random number table method, with 40 cases each. Both groups received conventional nursing, including preoperative, intraoperative, and postoperative nursing. The CG received a traditional preoperative routine diet and postoperative EN support. The EG received five-day preoperative EN support and postoperative parenteral nutrition support based on a traditional preoperative routine diet. The analgesic effect indicators, pain scores, gastrointestinal function recovery indicators, adverse reactions and nutritional indicators in both groups received measurement and comparison. The Average additional amount of flurbiprofen axetil in the EG decreased relative to those in the CG ($p < 0.05$). At six h and 12 h after surgery, VAS scores in the EG were lower than those in the CG during the same period; at 24 h and 48 h after surgery, no statistical significance in VAS scores was shown between both groups ($p > 0.05$). The bowel sound recovery time, first defecating time, first exhaust time, and first getting-out-of-bed time in EG were inferior relative to those in the CG ($p < 0.05$). The incidence of adverse reactions in the EG was reduced relative to that in the CG ($p < 0.05$). Before surgery and one day after surgery, no statistically significant differences in total protein (TP) and serum albumin (ALB) levels were shown between both groups ($p > 0.05$); three days and seven days after surgery, TP and ALB levels in the EG exhibited an elevation relative to those in CG during the same period ($p < 0.05$). In conclusion, early EN can improve not only postoperative gastrointestinal function and nutritional status of patients but also mitigate postoperative pain and facilitate postoperative recovery with high safety, which is worthy of further clinical promotion.

Impacto clínico de la nutrición enteral temprana sobre el dolor post-quirúrgico, función gastrointestinal y estado nutricional de pacientes con cáncer colorrectal.

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Palabras clave: cáncer colorrectal; nutrición enteral temprana; dolor postoperatorio; bomba analgésica.

Resumen. Esta investigación tuvo como objetivo aclarar el impacto clínico de la nutrición enteral temprana (EN) en el dolor posoperatorio, la función gastrointestinal y el estado nutricional de los pacientes con cáncer colorrectal (CCR). Se seleccionaron ochenta pacientes con cáncer de recto sometidos a cirugía en nuestro hospital desde octubre de 2021 hasta octubre de 2023 como sujetos de investigación y se dividieron en un grupo experimental (GE) y un grupo de control (GC) utilizando un método de tabla de números aleatorios, con 40 casos cada uno. Ambos grupos recibieron enfermería convencional, incluida enfermería preoperatoria, intraoperatoria y posoperatoria. El GC recibió una dieta de rutina preoperatoria tradicional y apoyo de EN posoperatorio. El GE recibió apoyo de EN preoperatoria durante cinco días y apoyo de nutrición parenteral posoperatoria basado en una dieta de rutina preoperatoria tradicional. Los indicadores de efecto analgésico, las puntuaciones de dolor, los indicadores de recuperación de la función gastrointestinal, las reacciones adversas y los indicadores nutricionales en ambos grupos recibieron medición y comparación. La cantidad adicional promedio de flurbiprofeno axetilo en el GE mostró un descenso en relación con los del GC ($p < 0,05$). A las seis y 12 h después de la cirugía, las puntuaciones VAS en el GE fueron inferiores a las del GC durante el mismo período; a las 24 y 48 h después de la cirugía, no hubo significación estadística en las puntuaciones VAS entre ambos grupos ($p > 0,05$). El tiempo de recuperación del sonido intestinal, el tiempo de la primera defecación, el tiempo del primer escape y el tiempo del primer levantamiento de la cama en el GE fueron inferiores en relación con los del GC ($p < 0,05$). La incidencia de reacciones adversas en el GE se redujo en relación con la del GC ($p < 0,05$). Antes de la cirugía y un día después de la cirugía, no se mostraron diferencias estadísticamente significativas en los niveles de proteína total (TP) y albúmina sérica (ALB) entre ambos grupos ($p > 0,05$); tres y siete días después de la cirugía, los niveles de TP y ALB en el GE exhibieron una elevación en relación con los del GC durante el mismo período ($p < 0,05$). En conclusión, la EN temprana puede mejorar no solo la función gastrointestinal posoperatoria y el estado nutricional de los pacientes, sino también mitigar el dolor posoperatorio y facilitar la recuperación posoperatoria con alta seguridad, lo que merece una mayor promoción clínica.

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INTRODUCTION

Colorectal cancer (CRC) is a prevalent malignant gastrointestinal tumor in clinical practice, and CRC patients all suffer from varying degrees of malnutrition¹. Tumor cachexia, the primary reason for malnutrition in tumor patients, often results from metabolic abnormalities and reduced food intake, characterized by a negative balance between energy and protein metabolism^{2,3}. Malnutrition can attenuate patients' immune systems and quality of life, elevate surgery-related complications, and even enhance the mortality rate⁴. The nutritional metabolism of CRC patients has common characteristics in most malignancies, such as insulin resistance, lipid peroxidation, accelerated protein conversion, and elevated acute phase protein synthesis, among others⁵. On the other hand, gastrointestinal dysfunction is a unique cause of malnutrition in CRC patients⁶. Thus, CRC patients are more likely to suffer from malnutrition and weakened immune function. Furthermore, high metabolic status, prolonged fasting, and impaired intestinal mucosal barrier and immune function due to surgical treatment further deteriorate the nutritional status of CRC patients, thereby affecting postoperative recovery and reducing their quality of life^{7,8}. Thus, adequate and reasonable nutritional interventions during the perioperative period have become a crucial component of comprehensive treatment for CRC.

For patients who plan to undergo therapeutic surgery but have preoperative malnutrition or nutritional risks, enteral nutrition (EN) support or combined enteral and parenteral nutrition (PN) support treatment is preferred^{9,10}. The therapeutic effect of nutrition support should be directly reflected in improving postoperative gastrointestinal function and elevation of the nutritional status. In clinical practice, open surgery is usually applied to treat CRC patients, whereas surgery takes quite a long time and can

result in remarkable trauma to patients; patients often have to endure pain, especially during bowel movements, which often makes them hesitant to undergo surgery^{11,12}. Thus, effective nutritional intervention remains necessary to control postoperative pain.

This research aimed to clarify the clinical impact of early EN on postoperative pain, gastrointestinal function and nutritional status of CRC patients, which may guide postoperative nursing work for gastrointestinal tumors.

MATERIALS AND METHODS

General data

Eighty rectal cancer patients undergoing surgery in our hospital from October 2021 to October 2023 were selected as research subjects and divided into an experimental group (EG) and a control group (CG) using a random number table method, with 40 cases each. **Inclusion criteria:** 1) Age ranging from 50-70 years old; 2) major clinical manifestations including changes in bowel habits and stool characteristics, abdominal discomfort, abdominal masses, intestinal obstruction, anemia, etc.; 3) diagnosed as rectal cancer through colonoscopy and histopathological examination, and all underwent anterior resection of the rectum as clinical therapy; 4) the patient's condition was stable, conscious, and had good communication and expression abilities; 5) all were informed of this research and signed an informed consent. **Exclusion criteria:** 1) Those with advanced rectal cancer, severe liver and kidney dysfunction, and intestinal inflammation; 2) emergency surgery, conversion to laparotomy, and inability to establish pneumoperitoneum during surgery; 3) patients with blurred consciousness, cognitive and communication barriers, mental illness; and 4) female patients during pregnancy and childbirth. This research received approval from our hospital's ethics committee.

METHODS

Both groups received conventional nursing, including preoperative, intraoperative, and postoperative nursing.

Preoperative nursing: (1) Preoperative education: After patients were admitted, nursing staff informed the patients of the approximate stage and time of treatment and explained the importance of early postoperative activities. They were provided timely guidance for different psychological problems, patiently answered patients' doubts about treatment, and helped patients smoothly pass through the perioperative period. (2) Preoperative intestinal preparation: A semi-liquid or low-residue diet was administered one day before surgery. Then, 750 mL of glucose water was administered to patients ten and two hours before surgery. Fasting and water deprivation occurred six and two hours before surgery, and no gastrointestinal decompression tube was placed.

Intraoperative nursing: The Dixon surgery procedure (transabdominal radical resection of the rectum) was used as a surgical method performed under general anesthesia. An intraoperative insulation blanket was used during surgery to prevent hypothermia. Infusion and flushing liquids received appropriate warming.

Postoperative nursing: (1) Analgesia: Postoperative patients received patient-controlled intravenous analgesia (PCA) intervention. The analgesic pump formula was: Flurbiprofen axetil (150 mg) + Dezocine (50 mg) + Tropisetron (8 mg) + Dexmedetomidine (60 µg) + normal saline (100 mL). The analgesic pump speed was 1.2-1.5 mL/h, with patient-controlled speed at around 1.5 mL/h, with a locking time of 15 min. When the patient's pain index was relatively high, and PCA was inadequate to mitigate it, flurbiprofen axetil could be added each time additionally.

Nursing staff created an analgesic pump usage card, and after patients returned to the ward, provided a detailed introduction to

the working principle, usage method, and adverse reactions of the analgesic pump to patients and their family members, improving patients and their family members' predictability of adverse reactions and preventing severe complications that might endanger patients' life safety. Nursing staff improved acute pain work mode. All nursing staff regularly inquired about and evaluated patients' postoperative pain, responded promptly to patients' pain, provided timely feedback to ensure that doctors administered expedient treatment and analgesic intervention, and summarized clinical medication effects to improve medication plans continuously. (2) Tube management: antibiotics were administered 2-3 days after surgery to shorten the retention time of drainage tubes and related catheters. According to wound healing, urinary catheters and nasogastric tubes were removed within 24-48 hours after surgery, and drainage tubes were removed on the fifth day after surgery. (3) Postoperative activities: 12 hours after surgery, patients engaged in bed activities such as turning over and sitting under a doctor's or nurse's guidance. The next day after surgery, nursing staff encouraged and guided patients to engage in getting-out-of-bed activities.

Nutrition intervention: The Experimental Group (EG) received postoperative early enteral nutrition (EN) based on a standard preoperative routine diet. In contrast, the Control Group (CG) received standard total parenteral nutrition (TPN) support for seven days following surgery. The total liquid intake for both groups was 50 mL·kg⁻¹·d⁻¹, with energy provided at a rate of 105 kJ·kg⁻¹·d⁻¹ and nitrogen intake at 0.2 g·kg⁻¹·d⁻¹. The nitrogen-to-calorie ratio was 1:552 kJ. Nutritional support was provided as a "fully-integrated" solution administered via peripheral veins. The EG received the same caloric and nitrogen intake as the control group. 500 mL of Nutrison Fibre (NUTRICIA) was administered on the first day after surgery. On the second day, the volume increased to 1000 mL; from the third to the

seventh day, 1500 mL of Nutrison Fibre was given daily. Nutrison Fibre supplied 4180 kJ of calories, 40 g of protein, and 6.4 g of nitrogen per 1000 mL, and it also contained vitamins, dietary fiber, and microelements. After recovery of gastrointestinal function, the diet should gradually transition from liquid or semi-liquid to general.

Observation indicators

1. Analgesic effect indicators: The average additional amount of Flurbiprofen axetil in both groups was recorded.
2. Pain scores: The pain degree in both groups at six, 12, 24, and 48 hours after surgery received evaluation with the Visual Analog Pain Scale (VAS) ¹³. Patients' pain scores during rest and activity (coughing, turning over, deep breathing, etc.) were recorded, with a score range of 0-10 points. A score of 0-3 points indicated mild pain, 4-6 points indicated moderate pain, and 7-10 points indicated severe pain.
3. Gastrointestinal function recovery indicators: The bowel sound recovery time, first defecating time, first exhaust time, and first getting-out-of-bed time in both groups were recorded.
4. Adverse reactions: Both groups' adverse reactions (majorly vomiting and nausea) received recording.
5. Nutritional indicators: The total protein (TP) and serum albumin (ALB) levels in both groups before surgery and 1, 3, and 7 days after surgery were measured with a colorimetric method.

STATISTICAL ANALYSIS

Statistical analysis of data of this research was performed with the SPSS 27.0® software. Counting data were expressed as %, followed by the χ^2 test for intergroup comparisons. Measurement data conforming to a normal distribution were expressed as mean $\pm$ standard deviation ($\bar{x} \pm SD$), followed by t-tests for intergroup comparisons. The difference was statistically significant when $p < 0.05$.

RESULTS

Comparison of general data between both groups

The CG included 25 (62.50%) males and 15 (37.50%) females with a mean age of 58.84 ± 4.47 years. Based on TNM staging, 17 (42.50%) cases were in stage I, 13 (32.50%) were in stage II, and 10 (25.00%) were in stage III. The examination of comorbidities in CG patients showed that seven (17.50%) patients had hypertension and nine (22.50%) patients had diabetes. EG included 22 (55.00%) males and 18 (45.00%) females with a mean age of 59.24 ± 4.40 years. Based on TNM staging, 18 (45.00%) cases were in stage I, 14 (35.00%) were in stage II, and eight (20.00%) were in stage III, and the examination of co-morbidities in EG patients showed that five (12.50%) patients had hypertension and 10 (25.00%) patients had diabetes. No statistical significance in gender, age, TNM staging, and comorbidities was found in the two groups (Table 1).

Table 1
General data in both groups.

Groups	N	Gender [n (%)]		Age (years)	TNM staging [n (%)]			Comorbidities [n (%)]	
		Male	Female		I	II	III	Hypertension	Diabetes
CG	40	25 (62.50)	15 (37.50)	58.84 ± 4.47	17 (42.50)	13 (32.50)	10 (25.00)	7 (17.50)	9 (22.50)
EG	40	22 (55.00)	18 (45.00)	59.24 ± 4.40	18 (45.00)	14 (35.00)	8 (20.00)	5 (12.50)	10 (25.00)
χ^2/t		0.464		0.896		0.288		0.406	
p		0.496		0.373		0.866		0.816	

Comparison of analgesic effect indicators between both groups

The average additional amount of Flurbiprofen axetil in EG was lower than in the CG, and there was a significant statistical difference between the two groups ($p < 0.0001$) (Fig. 1).

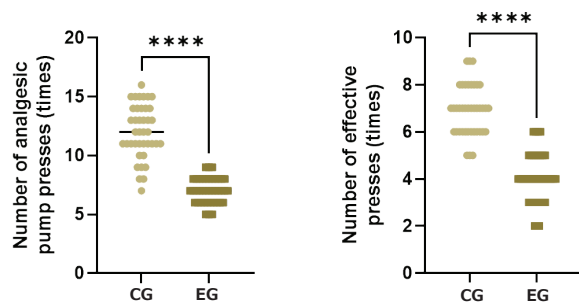


Fig. 1. Analgesic effect indicators in both groups. Note: EG versus CG, **** $P < 0.0001$.

Comparison of pain scores between both groups

At six hours and 12 hours after surgery, VAS scores in the EG were inferior to those in CG during the same period, indicating a statistical significance difference ($p < 0.001$). At 24 h and 48 h after surgery, neither group exhibited statistically different significance in VAS scores (Fig. 2).

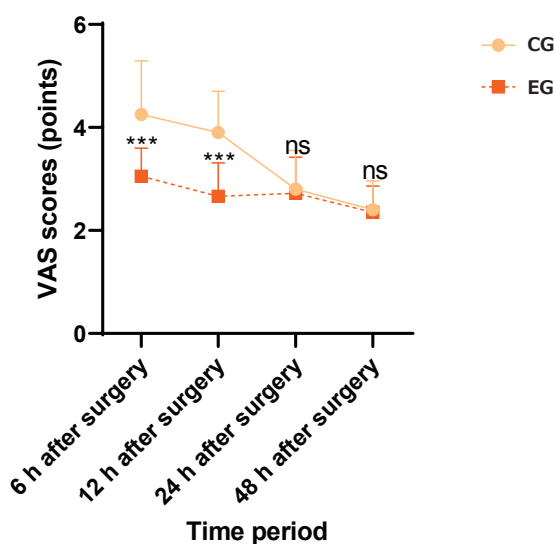


Fig. 2. Pain scores in both groups of patients. Note: EG versus CG, ns=no significance. *** $p < 0.001$.

Comparison of gastrointestinal function recovery indicators between both groups

The bowel sound recovery time, first defecating time, first exhaust time, and first getting-out-of-bed time in the EG were reduced relative to those in CG, indicating a statistical significance difference ($p < 0.0001$) (Fig. 3).

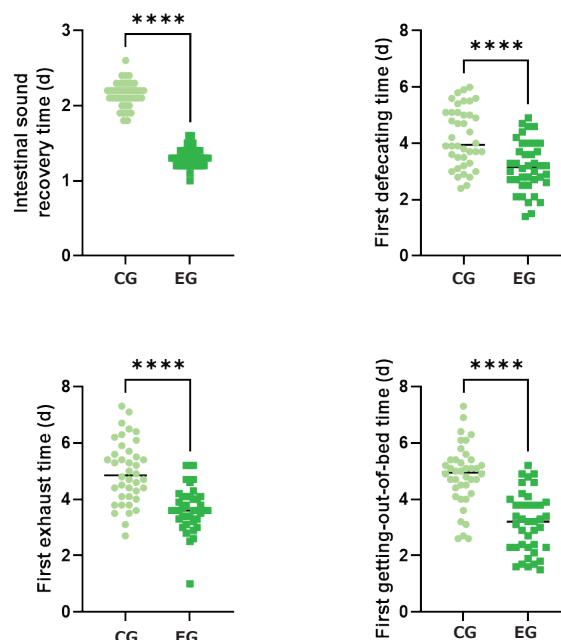


Fig. 3. Gastrointestinal function recovery indicators in both groups. Note: EG versus CG, **** $p < 0.0001$.

Comparison of incidence of adverse reactions between both groups

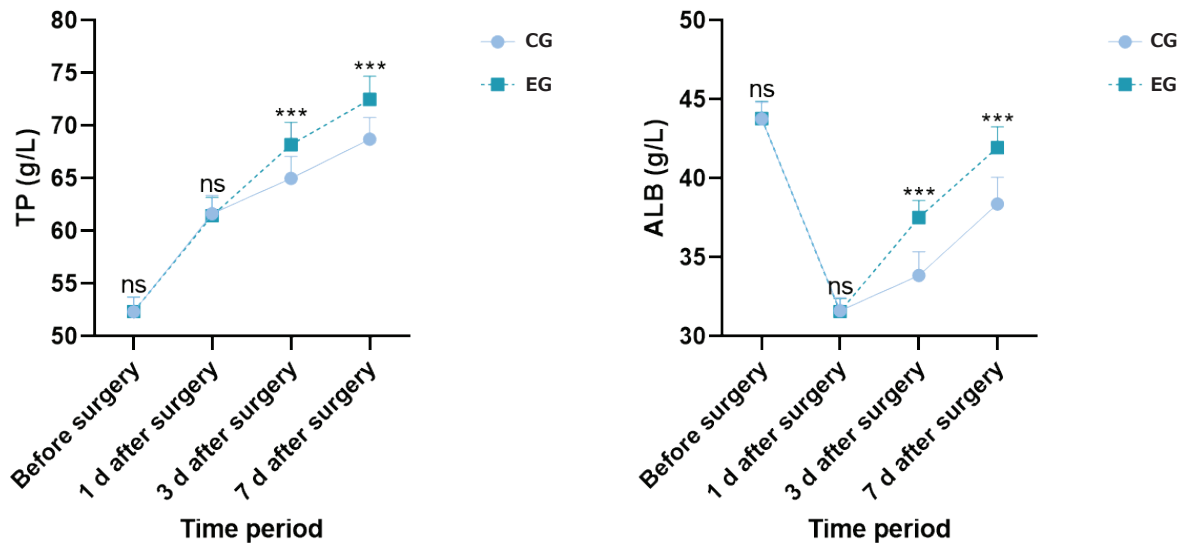
The incidence of adverse reactions in EG was lower than in the CG, indicating a statistical significance difference ($p < 0.043$) (Table 2).

Comparison of nutritional indicators between both groups

Before surgery and one day after surgery, no statistically significant difference in TP and ALB (borrowed protein) levels was exhibited between both groups. At three days and seven days after surgery, TP and ALB levels in EG were elevated relative to those in the CG during the same period, indicating statistical significance ($p < 0.001$) (Fig. 4).

Table 2. Incidence of adverse reactions in both groups.

Groups	N	Nausea	Vomiting	Others	Total incidence of adverse reactions [n (%)]
CG	40	5	3	0	8 (20.00)
EG	40	1	1	0	2 (5.00)
χ^2		/	/	/	4.114
p		/	/	/	0.043

**Fig. 4.** Nutritional indicators in both groups.

Note: EG versus CG, ns=no significance, *** $p < 0.001$.

DISCUSSION

CRC patients often have varying degrees of malnutrition or risk of malnutrition before surgery. Currently, tumor cachexia, the primary reason for malnutrition in tumor patients, often results from metabolic abnormalities and reduced food intake; its primary feature is the negative balance between energy and protein metabolism. Research has depicted that symptoms and signs such as anorexia, emaciation, and weight loss due to imbalanced nutritional needs and intake by metabolic abnormalities and reduced food intake in patients often cannot be wholly reversed through individual nutritional interventions¹⁴.

CRC patients often experience abnormal intestinal function¹⁵. Before providing

nutrition support to patients, appropriate nutrition support pathways should be selected based on their intestinal function. Nutrition support therapy majorly includes EN and PN. PN is the major nutrition support pathway, which can keep the intestine in a relatively static state of function and provide timely supplement nutrients needed by the body, which is beneficial for the recovery of damaged intestines^{16,17}. Nevertheless, long-term total PN support can lead to intestinal mucosal atrophy, weakened mucosal barrier function, and translocation of intestinal microbiota, inducing complications such as enterogenous infections¹⁸. Thus, EN is preferred for patients who require nutrition support for therapy. EN support is inexpensive and more in line with physiology, which can stimulate secretion of digestive

fluids and gastrointestinal hormones, facilitate gastrointestinal peristalsis and gallbladder contraction, elevate intestinal blood flow, maintain normal growth of mucosal cells and gut microbiota, help maintain the integrity of chemical, mechanical, and immune barriers of the intestinal mucosa, and reduce complications, which is conducive to improving the overall state of patients^{19,20}. Herein, the CG only received TPN after surgery, while the EG received early EN before and after surgery. The results depicted that bowel sound recovery time, first defecating time, first exhaust time, and first getting-out-of-bed time in the EG were diminished relative to those in the CG, indicating that early EN probably can facilitate the recovery of gastrointestinal function of patients and further ameliorate their nutritional status, which better meets the nutritional and gastrointestinal needs of CRC patients.

Surgery is a major treatment for non-terminal stage CRC, and comprehensive treatments such as surgery and psychological elements can lead to a high metabolic stress state in the body after surgery, which can further worsen malnutrition. Research has demonstrated that tumor patients with preoperative malnutrition have remarkably higher incidence and mortality rates of postoperative complications relative to those with good nutritional status^{21,22}. Serum protein levels are the most commonly applied indicators reflecting the nutritional status of patients, including TP and ALB. In this regard, no statistically significant differences in TP and ALB levels were observed between both groups before and one day after surgery. Three and seven days after surgery, TP and ALB levels in EG were elevated relative to those in the CG during the same period, indicating that early EN probably can facilitate visceral protein synthesis and enhance the overall nutritional status of patients.

Postoperative pain, as a complication of surgery, has always been a hot research topic that needs urgently to be solved in clinical, surgical patients after surgery, and

also a vital factor affecting the degree of postoperative recovery and psychological stress state of patients²³. Common Western medicine pain relief methods after surgery include epidural analgesia, patient-controlled analgesia, and oral opioid analgesics, among others. Herein, both groups received PCA intervention, and in addition, Nutrison Fibre was chosen for the EG as an alternative diet for early nutritional intervention. The results showed that the average additional amount of flurbiprofen axetil in the EG was lower relative to those in CG. Within 24 hours after surgery, VAS scores in the EG were lower than those in the CG during the same period. No statistically significant difference in VAS scores was shown between both groups 24 hours later, indicating that early EN probably reduces the additional amounts of analgesics and mitigates patients' pain levels. Moreover, the incidence of adverse reactions in the EG was reduced relative to that in the CG, indicating that early EN probably can attenuate adverse gastrointestinal events in patients, improve the safety of postoperative use of analgesic pumps, and thereby enhance the prognosis of patients.

In conclusion, early EN can improve patients' postoperative gastrointestinal function and nutritional status, mitigate postoperative pain, and facilitate postoperative recovery with high safety, which is worthy of further clinical promotion.

Limitation

The subjective method using the nutritional screens (GLIM, MUST, NSR) was impossible due to the time limit.

Conflict of interest

The authors declare no conflict of interest.

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Contribution of authors

All authors have been contributed equally to this research article.

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