

# Application of dexmedetomidine combined with sufentanil in colon cancer resection and its effect on immune and coagulation function of patients

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**Abstract.** Application of dexmedetomidine combined with sufentanil in colon cancer resection and its effect on immune and coagulation function of patients was studied. Colon cancer cases (n=176) admitted to Xiangya Hospital Central South University were selected into the study. They were divided into group A (n=92) and group B (n=84). In group A, patients underwent surgery anesthesia with dexmedetomidine combined with sufentanil. In group B, patients underwent surgery anesthesia only with sufentanil. The anesthesia induced intubation, operation time and incidence of postoperative adverse reaction of patients were compared between the two groups. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were observed and recorded before induction, before intubation and after intubation. Blood coagulation analyzer was used to detect four items of coagulation before and after operation. FACSCalibur flow cytometry was used to detect T lymphocyte subsets in peripheral blood of patients in the two groups. The pain scores (VAS) of patients in the two groups were measured and recorded after surgery at 4, 24 and 48 h. There was a difference in anesthesia induced intubation and operation time of patients in both groups ( $P<0.05$ ). There were differences in HR, SBP and DBP of patients in both groups after intubation ( $P<0.05$ ), in postoperative coagulation function ( $P<0.05$ ), and in postoperative immune function of patients in both groups ( $P<0.05$ ). The VAS scores of patients in both groups were different at different time-points after operation ( $P<0.05$ ). There were differences in postoperative adverse reactions of patients in both groups ( $P<0.05$ ). Dexmedetomidine combined with sufentanil is a viable anesthetic regimen for colon cancer

resection. The coagulation function and immune function have certain improvement effect for patients.

## Introduction

Colon cancer is the third most common cancer in men and the second most common cancer in women (1). It is a heterogeneous disease (2). The annual incidence rate is approximately 1.2 million and more than 600 patients die each year from the colon cancer (3). Surgical resection is an early method for the clinical treatment of colon cancer. The surgical wound area is large and the patient's postoperative pain is obvious. So the anesthetic management and postoperative analgesia during surgery are important factors for patients to recover quickly after surgery.

Dexmedetomidine is a selective adrenergic agonist that has less effect on respiratory function, has anti-anxiety, anti-sympathetic nerve and analgesic and sedative properties (4). It is an important option for short-term or long-term sedation in intensive care units (5). Previous studies have shown that dexmedetomidine has good analgesic sedative effect, and also significantly reduces the dose of anesthetic drugs required, reduces the duration of coma and shorten duration of mechanical ventilation (6). Sufentanil is an effective analgesic that rapidly crosses the blood-brain barrier and selectively activates central  $\mu$ -opioid receptors (7), with a very high therapeutic index in clinical studies. There is no active metabolite, but there is a high degree of lipophilic property (8). Studies have shown that sufentanil is commonly used in intravenous and intrathecal routes to treat acute pain and can also be used for postoperative analgesia (9,10). In a study on laryngectomy by Qin *et al* (11), dexmedetomidine combined with sufentanil improved postoperative sleep quality, had good analgesic effect and reduced the number of coughs in patients after operation.

At present, there is scarce research on dexmedetomidine combined with sufentanil in colon cancer resection and on the immune function and coagulation function of patients. This study provides more references for the treatment of patients with colon cancer resection by observing the application and anesthetic effect of dexmedetomidine combined with sufentanil in colon cancer resection.

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**Key words:** dexmedetomidine combined with sufentanil, colon cancer resection, coagulation function, immune function

## Materials and methods

**Baseline data.** Cancer patients (n=176) admitted to Xiangya Hospital of Central South University, were selected for study. They were divided into group A (92 cases) and group B (84 cases). There were 42 males and 50 females in group A, aged 29-66 years. The average age was  $52.51 \pm 6.11$  years. TNM stage was 48 cases in I+II stage and 44 cases in stage III. There were 47 males and 37 females in group B, aged 27-64 years. The average age was  $53.13 \pm 6.05$  years. TNM staging was 43 cases in stages I+II and 41 cases in stage III. The study was approved by the Ethics Committee of Xiangya Hospital Central South University (Changsha, China). The patients or their guardians sign a full informed consent.

**Inclusion and exclusion criteria.** Inclusion criteria: In line with the National Comprehensive Cancer Network (NCCN) oncology clinical practice guidelines (12); CT, color doppler ultrasound, MRI and other tests to exclude distant metastases, TNM staging criteria for stage I to III; no previous treatment or radiation therapy, and this is the first diagnosis; no major organ dysfunction, with detailed clinical and pathological data. Exclusion criteria: Patients who were unwilling to participate in this study; patients with other malignant tumors, those who did not cooperate with follow-up and who were lost to follow-up; patients with blood system diseases, comorbid with serious complications and immune system diseases; patients with severe mental illness that led to poor treatment compliance.

**Operative methods.** In both groups, patients underwent general anesthesia intratracheal intubation. In the two groups, patients routinely fasted before surgery, but did not receive preoperative medication. After entering the operating room, venous transfusion was opened routinely to closely monitor non-invasive arterial blood pressure, blood oxygen saturation, end tidal carbon dioxide tension, bispectral index and electrocardiogram. Then patients received sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd.; item no. H20054256) of  $0.5 \mu\text{g}/\text{kg}$ , etomidate (Shanghai Shifeng Biotechnology Co., Ltd.; item no. EB03700) of  $0.3 \text{ mg}/\text{kg}$  and atracurium (Jiangsu Hengrui Pharmaceutical Co., Ltd.; item no. H20060869) of  $0.15 \text{ mg}/\text{kg}$ . After successful anesthesia induction, an appropriate laryngeal mask was placed after the patient's muscles were relaxed and they were unconscious. Then the anesthesia was applied. The tidal volume was 8-10 ml/kg. The respiratory rate was adjusted to 12 times/min. During operation, micro-pump continued to inject remifentanyl (Yichang Humanwell Pharmaceutical Co., Ltd.; item no. H20030197) of 5-6  $\mu\text{g}/(\text{mg}\cdot\text{h})$  and propofol (Sichuan Guorui Pharmaceutical Co., Ltd.; item no. H20030115) of 3-6 mg/kg intravenous pumping. Atracurium of 0.25-0.5 mg/kg was added to maintain anesthesia. After completion of the operation, the tube was extubated after the patient regained spontaneous breathing, cough and swallowing reflex. During analgesia, patients received 200  $\mu\text{g}$  of dexmedetomidine, sufentanil of  $2.0 \mu\text{g}/\text{kg}$  and ramosetron hydrochloride of 0.3 mg (Shanghai Yuanye Biotechnology Co., Ltd.; item no. S61106) for analgesia in group A. Patients were given analgesia with sufentanil of

$2.0 \mu\text{g}/\text{kg}$  and ramosetron hydrochloride of 0.3 mg in group B. In the two groups, analgesic drugs were diluted in normal saline and to a dose of 100 ml.

**Observation indexes.** The time to effect of anesthetics, operation time, awakening time, extubation time and recovery time of patients in the two groups were recorded. Before induction, before and after intubation, the MAP, CVP, HR levels and the incidence of postoperative adverse reactions were measured and recorded in patients of the two groups.

Five milliliters of venous blood was taken before anesthesia induction and 30 min after surgery for 1 day. Blood coagulation analyzer HF-6000 (Hunan Hukang Centrifuge Co., Ltd.; item no. HF-6000) was used to detect four items of coagulation (PT, APTT, TT, FIB).

Five milliliters of venous blood was taken before anesthesia induction for 30 min and after surgery for 1 day. FACSCalibur flow cytometry (BD Biosciences) was used to detect T lymphocyte subsets in peripheral blood. Anticoagulated whole blood of 100  $\mu\text{l}$  was placed in a TruCOUNT tube. Twenty microliters each of CD3-FITC, CD4-PE and CD8-PE (BD Biosciences) antibody was added, mixed and allowed to stand at room temperature for 15 min. Hemolysin of 370  $\mu\text{l}$  was added (BD Biosciences), mixed and allowed to stand at room temperature for 15 min. Samples were tested on a flow cytometer and the peripheral blood CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> values were read.

The pain scores of patients in the two groups were measured and recorded after operation at 4, 24 and 48 h. The visual analogue scale (VAS) was used. The scoring standard: the score was recorded by using a slidable swimming ruler with a length of 10 cm. The scale was: 0, painless and 10 points aggravated by pain.

**Statistical analysis.** The analysis was performed by using SPSS 21.0 statistical software (Easybio). Enumeration data were expressed as cases/percentage [n(%)] within groups. Chi-square test was used to compare the enumeration data between groups. In Chi-square test, when the theoretical frequency was less than 5, continuity correction Chi-square test was adopted. Measurement data were expressed as mean number  $\pm$  standard deviation (mean  $\pm$  SD). The t-test of independent samples was used to compare the measurement data between groups. Paired t-test was used for sequential comparisons within the group. Multiple time-points were observed and compared by using repetitive measurement and analysis of variance. The Bonferroni method was used for pairwise comparison between different time-points in the group. The difference was statistically significant at  $P < 0.05$ .

## Results

**Baseline data.** There were no significant differences in patients regarding sex, age, body mass index, place of residence, nation, educational background, smoking history, drinking history, movement history, diabetes history, obesity status, TNM stage, or other clinical baseline data between the two groups ( $P > 0.05$ ) (Table I).

Table I. Baseline data of patients in both groups [n(%)] (mean  $\pm$  SD).

Classification	Group A (n=92)	Group B (n=84)	t/ $\chi^2$ value	P-value
Sex			1.864	0.172
Male	42 (45.65)	47 (55.95)		
Female	50 (54.35)	37 (44.05)		
Age/years	52.51 $\pm$ 6.11	53.13 $\pm$ 6.05	0.676	0.500
BMI (kg/m <sup>2</sup> )	22.84 $\pm$ 2.15	22.42 $\pm$ 1.71	1.425	0.156
Place of residence			2.582	0.108
City	56 (60.87)	41 (48.81)		
Rural	36 (39.13)	43 (51.19)		
Ethnicity			0.001	0.978
Han	48 (52.17)	44 (52.38)		
Minority	44 (47.83)	40 (47.62)		
Educational background			0.046	0.831
$\geq$ High school	42 (45.65)	37 (44.05)		
< High school	50 (54.35)	47 (55.95)		
Smoking history			2.366	0.124
Yes	43 (46.74)	49 (58.33)		
No	49 (53.26)	35 (41.67)		
Drinking history			0.175	0.676
Yes	53 (57.61)	51 (60.71)		
No	39 (42.39)	33 (39.29)		
Movement history			1.547	0.214
Yes	62 (67.39)	49 (58.33)		
No	30 (32.61)	35 (41.67)		
Diabetes history			0.039	0.842
Yes	49 (53.26)	46 (54.76)		
No	43 (46.74)	38 (45.24)		
Obesity status			0.007	0.934
Yes	52 (56.52)	48 (57.14)		
No	40 (43.48)	36 (42.86)		
TNM stage			0.017	0.896
Stage I+II	48 (52.17)	43 (51.19)		
Stage III	44 (47.83)	41 (48.81)		

*Comparison of anesthesia induced intubation time of patients in the two groups.* There was no significant difference in the time of anesthesia taking effect of patients in the two groups ( $P>0.05$ ). The awakening time, extubation time and recovery time of group A were lower than those of group B ( $P<0.05$ ) (Table II).

*Comparison of HR, SBP and DBP in each period of operation of patients in the two groups.* The expression of HR, SBP and DBP in each time period in patients of both groups were statistically significant ( $P<0.05$ ). There was no significant difference in HR, SBP and DBP of patients in the two groups before induction ( $P>0.05$ ). Before and after intubation, HR, SBP and DBP of patients in the two groups were lower than before induction ( $P<0.05$ ). HR, SBP and DBP before intubation were significantly lower than those after intubation ( $P>0.05$ ). Moreover, HR, SBP and DBP in group A before and

after intubation were significantly lower than those in group B ( $P<0.05$ ) (Fig. 1).

*Comparison of preoperative and postoperative coagulation functions of patients in two groups.* There was no difference in the expression levels of PT, APTT, TT and FIB in coagulation function of patients in two groups before operation ( $P>0.05$ ), but the expression levels of coagulation function PT, APTT, TT and FIB in group A after operation were lower than that in group B ( $P<0.05$ ) (Table III).

*Comparison of immune function of patients in the two groups before and after surgery.* There were no significant differences in the expression of CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup> of patients in the two groups before surgery ( $P>0.05$ ), but the expression of CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup> in group A after surgery was higher than that in group B ( $P<0.05$ ) (Table IV).

Table II. Comparison of anesthesia induced intubation time of patients in the two groups (mean  $\pm$  SD, min).

Items	Group A (n=92)	Group B (n=84)	t value	P-value
Time of anesthesia taking effect	4.78 $\pm$ 1.04	5.02 $\pm$ 1.13	1.467	0.144
Awakening time	13.48 $\pm$ 2.53	14.89 $\pm$ 2.96	3.406	0.001
Extubation time	11.26 $\pm$ 3.12	12.56 $\pm$ 3.45	2.625	0.009
Recovery time	10.46 $\pm$ 2.78	11.56 $\pm$ 2.83	2.600	0.010

Table III. Comparison of preoperative and postoperative coagulation functions of patients in the two groups (mean  $\pm$  SD).

Grouping	PT (sec)		APTT (sec)		TT (sec)		FIB (g/l)	
	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery
Group A (n=92)	15.8 $\pm$ 4.6	11.3 $\pm$ 4.3	35.9 $\pm$ 12.4	26.5 $\pm$ 11.9	15.9 $\pm$ 5.2	12.3 $\pm$ 5.1	4.2 $\pm$ 0.2	2.3 $\pm$ 0.2
Group B (n=84)	15.9 $\pm$ 4.5	13.2 $\pm$ 4.2	36.2 $\pm$ 12.1	31.3 $\pm$ 12.0	16.7 $\pm$ 5.3	14.2 $\pm$ 5.0	4.3 $\pm$ 0.6	3.1 $\pm$ 0.3
t value	0.146	2.961	0.162	2.662	1.010	2.492	1.510	20.980
P-value	0.884	0.004	0.871	0.009	0.314	0.014	0.133	<0.001

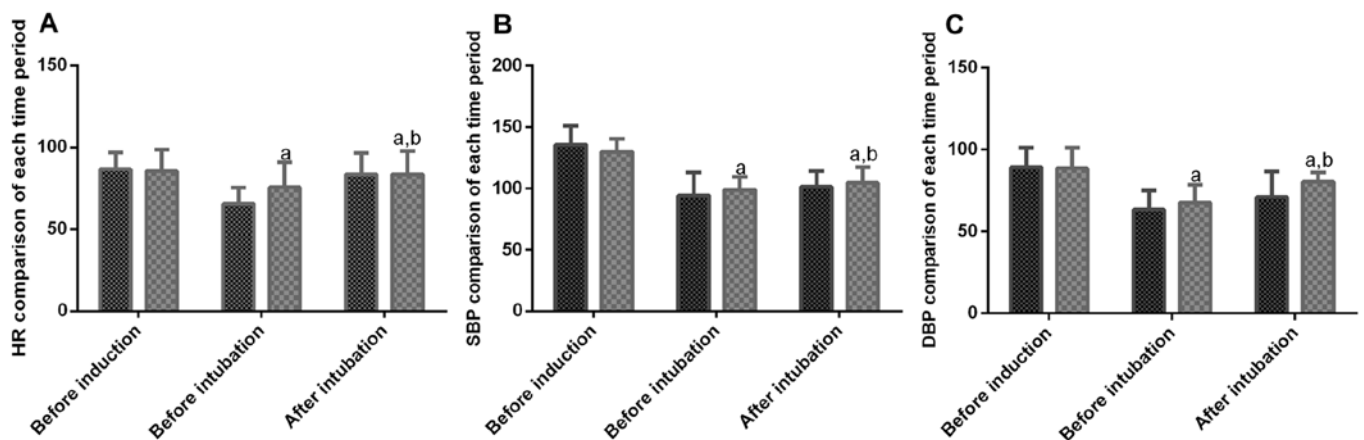


Figure 1. Comparison of (A) HR, (B) SBP and (C) DBP in each period of operation in the two groups. The expression of HR, SBP and DBP in each time period in patients of both groups were statistically significant ( $P < 0.05$ ). There was no significant difference in HR, SBP and DBP of patients in the two groups before induction ( $P < 0.05$ ). Before and after intubation, HR, SBP and DBP of patients in the two groups were lower than before induction ( $P < 0.05$ ). HR, SBP and DBP before intubation were significantly lower than those after intubation ( $P < 0.05$ ). Moreover, HR, SBP and DBP in group A before and after intubation were significantly lower than those in group B ( $P < 0.05$ ). <sup>a</sup> $P < 0.05$  compared with group B before induction; <sup>b</sup> $P < 0.05$  compared with group B before intubation.

*Comparison of VAS scores of patients in the two groups after operation.* The VSA scores of patients in the two groups were significantly decreased with time, with statistical significance ( $P < 0.05$ ). The VAS scores of the patients in group A were lower than those in group B after operation at 4, 24 and 48 h ( $P < 0.05$ ) (Table V).

*Incidence of adverse reactions of patients in the two groups after operation.* In group A, there was 1 case with shivering (1.09%), 2 cases with nausea, vomiting and headache (2.17%) and 1 case with respiratory depression (1.09%). The incidence of total adverse reactions was 4.35%. In group B, there were 2 cases with shivering (2.38%), 4 cases with nausea and vomiting (4.76%), 5 cases with headache (5.95%), 5 cases

with respiratory depression (5.95%). The incidence of total adverse reactions was 19.05%. The total adverse reaction rate of patients in group A was significantly lower than that of patients in group B ( $P < 0.05$ ) (Table VI).

## Discussion

Colon cancer is common (13). Most of the pathogenesis is slow and occult and early symptoms are not obvious (14). Colon cancer is clinically treated with surgical resection (15), but postoperative pain is a common complication after surgery. It is of great significance to improve the therapeutic effect of colon cancer surgery and patient's postoperative recovery by applying reasonable anesthesia in the surgical treatment (16).

Table IV. Comparison of immune function of patients in the two groups before and after surgery (mean  $\pm$  SD).

Grouping	CD3 <sup>+</sup> (%)		CD4 <sup>+</sup> (%)		CD8 <sup>+</sup> (%)		CD4 <sup>+</sup> /CD8 <sup>+</sup>	
	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery
Group A (n=92)	55.88 $\pm$ 9.29	45.74 $\pm$ 7.47	33.49 $\pm$ 5.71	24.11 $\pm$ 5.89	21.44 $\pm$ 4.11	20.99 $\pm$ 3.71	1.57 $\pm$ 0.24	1.19 $\pm$ 0.26
Group B (n=84)	54.91 $\pm$ 8.69	48.62 $\pm$ 6.62	32.46 $\pm$ 5.57	22.33 $\pm$ 4.10	21.05 $\pm$ 3.72	19.78 $\pm$ 3.85	1.56 $\pm$ 0.20	1.11 $\pm$ 0.27
t value	0.714	2.697	1.209	2.306	0.658	2.123	0.299	2.002
P-value	0.477	0.008	0.228	0.022	0.512	0.035	0.766	0.046

Table V. Comparison of VAS scores in each period in the two groups after operation (mean  $\pm$  SD).

Time	Group A (n=92)	Group B (n=84)	t value	P-value
After operation for 4 h	4.27 $\pm$ 0.52	6.32 $\pm$ 1.12	15.790	<0.001
After operation for 24 h	3.45 $\pm$ 0.44	3.87 $\pm$ 0.62	5.217	<0.001
After operation for 48 h	2.78 $\pm$ 0.35	3.12 $\pm$ 0.41	5.932	<0.001
F-value	262.100	390.600	-	-
P-value	<0.001	<0.001	-	-

Table VI. Incidence of total adverse reactions of patients in the two groups after operation [n(%)].

Category	Group A (n=92)	Group B (n=84)	$\chi^2$ value	P-value
Shivering	1 (1.09)	2 (2.38)	0.439	0.508
Nausea and vomiting	0 (0.00)	4 (4.76)	4.483	0.034
Headache	2 (2.17)	5 (5.95)	1.641	0.200
Respiratory depression	1 (1.09)	5 (5.95)	3.157	0.076
Incidence of total adverse reactions	4 (4.35)	16 (19.05)	9.420	0.002

Dexmedetomidine reduces the sympathetic nerves of the heart and surrounding vasculature or enhances the tension of parasympathetic nerve to alter hemodynamics (17). Previous studies have shown that (18) dexmedetomidine can also improve postoperative cellular immune function of patients with malignant tumors. Sufentanil is a widely used analgesic that improves the analgesic effect with a longer duration and a lighter respiratory inhibition (19). It also has a strong opioid receptor activation effect. Its obvious analgesic effect and the possibility of cardiovascular events are low (20). In this study, there was no significant difference in the time of anesthesia taking effect of patients in group A and group B. However, the awakening time, extubation time and recovery time after anesthesia in group A was lower than group B. MAP and CVP were significantly decreased before intubation and HR was significantly slowed. However, after intubation, it recovered to before induction level and group A was lower than group B, indicating that dexmedetomidine combined with sufentanil can provide more stable hemodynamics for patients with colon cancer resection. The VAS scores of patients in group A were significantly lower than those of patients in group B after surgery for 4, 24 and 48 h, indicating that the awakening time language statement and awakening time of dexmedetomidine

combined with sufentanil were faster in colon cancer resection, and the postoperative analgesic effect was better. In the study of Dong *et al* (21), the use of dexmedetomidine and sufentanil in thoracotomy was shown to successfully treat severe pain of patients after thoracotomy and to maintain good hemodynamic stability, similarly to this study. We observed the adverse reactions of patients after surgery and the results showed that the incidence of total adverse reactions in group A was significantly lower than that in group B, indicating that dexmedetomidine and sufentanil were safer.

Blood coagulation of perioperative patients is affected by various factors such as the size of the operation, blood loss, anesthesia and blood transfusion (22). In the study of Chen *et al* (23), the combination of anesthesia and dexmedetomidine also improved the postoperative coagulation status of patients. The results of the present study showed that the expression levels of coagulation function PT, APTT, TT and FIB in group A were lower than those in group B, indicating that dexmedetomidine combined with sufentanil can effectively improve postoperative coagulation function in patients with colon cancer resection. Dexmedetomidine inhibits sympathetic nerve activity, while sufentanil combined with dexmedetomidine can inhibit sympathetic nerve activity and

play the role of inhibiting stress response, thereby preventing blood from becoming hypercoagulated and accelerating blood flow.

Changes of T lymphocyte subsets can assess the immune function of the body. CD3<sup>+</sup>, CD4<sup>+</sup> and CD8<sup>+</sup> T cells can be classified according to their different functions and surface markers. The changes in the ratio of the three are important markers reflecting the immune dysfunction of the body (24). The results of this study showed that the ratio of CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> in peripheral blood of group A and group B after operation was significantly lower than that before operation. The ratio of CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup> and CD4<sup>+</sup>/CD8<sup>+</sup> in group A was significantly higher than that in group B, indicating that anesthesia may have an impact on the immune function of patients with colon cancer resection, while dexmedetomidine combined with sufentanil have less effect on the immune function of patients. In the study of Yang *et al* (25), dexmedetomidine, sufentanil and other anesthesia were applied to patients receiving radical mastectomy, which could effectively improve the immune function of patients. This indicated that dexmedetomidine and sufentanil can improve the immune function of patients.

This study confirmed that dexmedetomidine combined with sufentanil is a viable anesthesia program in colon cancer resection. However, further study is necessary to extend the study time and add follow-up to further confirm the results.

In conclusion, dexmedetomidine combined with sufentanil is a viable anesthetic regimen for colon cancer resection, which can maintain good hemodynamic stability, effectively relieve postoperative pain of patients and has fewer postoperative complications. The coagulation function and immune function also have a certain improvement effect in patients.

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### Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

### Authors' contributions

LZ wrote the manuscript, interpreted and analyzed the patient data. YL designed the study, performed the experiment, and was responsible for the analysis and discussion of the data. Both authors read and approved the final manuscript.

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Xiangya Hospital Central South University (Changsha, China). Patients who participated in this research had complete clinical data. Signed informed consents were obtained from the patients and/or the guardians.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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