

## Effects of Ulinastatin Combined with Dexmedetomidine on Postoperative Cognitive Function and Central Nerve Specific Protein Level in Elderly Colorectal Cancer Patients after Laparoscopic

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**Abstract:** Ulinastatin combined with dexmedetomidine can improve postoperative cognitive function and central nerve specific protein (S-100 $\beta$ ) level in elderly colorectal cancer (CC) patients after laparoscopic. Altogether 178 elderly patients who underwent laparoscopic colorectal cancer surgery in our hospital from February 2018 to August 2019 were selected and divided into two groups according to the treatment methods. Those anesthetized by dexmedetomidine were regarded as the routine group (RG, 83 cases), and those anesthetized by ulinastatin and dexmedetomidine were considered as the combined group (CG, 95 cases). The operation conditions of the two groups, the pain scores (VAS) at 4 h, 24 h and 48 h after surgery, and the MMSE scores before, 1 d and 3 d after surgery were recorded. The incidence of cognitive dysfunction and adverse reactions were compared between both groups. The serum S-100 $\beta$  protein (S-100 $\beta$ ) and inflammatory factors were detected by enzyme-linked immunosorbent assay (ELISA). The risk factors of postoperative cognitive dysfunction (POCD) were analyzed. The eye-opening time of clinical indexes in the CG was dramatically lower than in the RG, while other indexes had no marked difference. The VAS scores of the CG were lower than those of the RG at 4 h, 24 h and 48 h after operation. The MMSE scores of patients in the CG were dramatically higher than those in the RG at 1 d and 3 d after surgery. The total incidence of POCD in the CG was lower than that in the RG. There was no remarkable difference in the total incidence of adverse reactions between both groups. The S-100 $\beta$  expression level in the CG was dramatically lower than in the RG at 1 d and 3 d after surgery. The improvement level of inflammatory factors in the CG was dramatically better than that in the RG. Multivariate Logistic regression analysis identified that the eye-opening time, VAS score, IL-10, TNF- $\alpha$ , CRP, and S-100 $\beta$  were independent risk factors for POCD occurrence in elderly CC patients after surgery. Ulinastatin combined with dexmedetomidine anesthesia induction can improve the prognosis of elderly CC patients after laparoscopic and it also reduces postoperative pain and serum inflammatory factors. S-100 $\beta$  concentration can improve the POCD occurrence after surgery.

**Keywords:** Ulinastatin; dexmedetomidine; laparoscopic; elderly colorectal cancer; cognitive function; S-100 $\beta$



## 1 Introduction

Colorectal cancer (CC) is the most common heterogeneous malignancy with the highest mortality in clinical practice in the whole world. It can spread to other tissues of the body of patients (mainly to the lung and liver) [1,2]. Clinically, CC mainly comes from the combination of genetic susceptibility and mitigating factors, and it shows that some personal factors are related to the increase of disease risk, such as CC family history, inflammatory intestinal sickness history, etc. [3,4]. It is mostly treated by surgery [5,6]. However, most patients have obvious postoperative pain. Studies show that anesthesia management and postoperative analgesia are tied to the prognosis of patients [7].

Ulinastatin is a bird trypsin inhibitor derived from human urine, which can inhibit enzyme activity and reduce the occurrence of the systemic inflammatory response in patients [8]. It can also reduce postoperative bleeding and blood transfusion requirements of patients undergoing surgery, inhibit the release of inflammatory mediators caused by surgery, and provide organ protection [9]. If there are studies that show that ulinastatin can improve the cognitive function of elderly patients after hip replacement and reduce the inflammatory reaction, it can better promote their postoperative recovery [10]. Dexmedetomidine has sedative, analgesic, and inhibitory effects on the sympathetic nervous system. It can reduce the dosage of anesthetic during the surgery, improve the stability of hemodynamics during surgery, and reduce the incidence of myocardial ischemia [11]. Some studies also show that it is used more and more in elderly patients. It can reduce the neurotoxicity of general anesthesia patients, improve postoperative analgesia, and effectively reduce the occurrence of postoperative delirium in elderly patients [12]. Wang et al. [13] pointed out that ulinastatin combined with dexmedetomidine could be used to induce anesthesia for acute lung injury after hepatic ischemia-reperfusion in rats reduce inflammatory reaction and inhibit lipid peroxidation. However, some studies have shown that overexposure of anesthetic will have side effects on patients, which will increase POCD risk after surgery [14]. The brain is the organ most sensitive to ability metabolism, and S-100 $\beta$  is a commonly used non-specific marker for brain injury. S-100 $\beta$  is secreted by astrocytes in the central nervous system and is abnormally expressed in various types of trauma (such as major surgery, head injury, etc.) [15].

At the moment, there is little research on ulinastatin combined with dexmedetomidine in laparoscopic elderly CC. This study observes the effects of ulinastatin combined with dexmedetomidine on cognitive function, S-100 $\beta$  expression and anesthetic efficacy of elderly CC patients after laparoscopic, all of which provide a better reference basis for treatment.

## 2 Patients and Methods

### 2.1 General Information

Altogether 178 elderly patients who underwent laparoscopic CC surgery in our hospital from February 2018 to August 2019 were selected as research participants. The routine group (RG) received dexmedetomidine (83 cases) and the combined group (CG) received ulinastatin combined with dexmedetomidine (95 cases). This study was approved by the Ethics Committee of our hospital (Wuhan mental health center, Wuhan, China) and it gave a detailed description of the subjects' experimental contents. The subjects agreed and signed a complete informed consent form. Inclusion criteria were as follows: those in line with the national comprehensive cancer network (NCCN) oncology clinical practice guidelines [16], there was no previous chemical or radiation therapy, no major organ dysfunction, and those had complete clinical general data. Exclusion criteria were as follows: those who quitted the experiment midway, did not cooperate with the treatment, and suffered from severe mental diseases that led to poor treatment compliance, those had infection history before operation, and those who had taken drugs that affected the indicators of this study orally in the past six months, and those who lost to be followed up.

### 2.2 Data and Methods

Anesthesia induction for surgery: all patients received intravenous injection of midazolam 0.02–0.04 mg/kg (Enhua Pharmaceutical Co., Ltd., Jiangsu, China, H20031037), etomidate 0.1–0.3 mg/kg (Shifeng

Biotechnology Co., Ltd., Shanghai, China, EB03700), sufentanil 0.2–0.3  $\mu\text{g}/\text{kg}$  (Renfu Pharmaceutical Co., Ltd., Yichang, China, H20054172) and vecuronium bromide 0.1  $\text{mg}/\text{kg}$  (Welman Pharmaceutical Co., Ltd., Anhui, China, H20084539). We connected an anesthesia machine for mechanical ventilation after tracheal intubation. The oxygen flow rate should be maintained at 1.5 L/min, the respiratory frequency should be 12–15 times/min, the tidal volume should be maintained at 6–8 ml/kg, the respiratory ratio should be 1:2, the fraction of inspired oxygen ( $\text{FiO}_2$ ) should be 100%, and the  $\text{PETCO}_2$  should be maintained at 35–45 mmHg. To maintain anesthesia, remifentanil and propofol were injected intravenously and vecuronium was injected intermittently. Patients in the RG were given dexmedetomidine 0.5  $\mu\text{g}/\text{kg}$  (Yangtze River Pharmaceutical Group Co., Ltd., Jiangsu, China, H20183220) before anesthesia induction for surgery, and were continuously pumped at a speed of 0.3  $\mu\text{g}/(\text{kg}\cdot\text{h})$ . The pumping of dexmedetomidine should be stopped about 30 min before the end of surgery. Altogether 2 kU/kg ulinastatin (Tianpu Biochemical Medicine Co., Ltd., Guangdong, China, H19990134) was infused into the CG on the basis of the RG, and intravenous infusion was continued at a rate of 1 kU/(kg·h) until the end of the operation.

### 2.3 Outcome Measures

(1) The operation clinical indexes of patients in the two groups (operation time, intraoperative blood loss, time to recover spontaneous respiration, eye-opening time after surgery and time of tracheal extubation) were observed and recorded.

(2) The pain degree of patients in the two groups at 4 h, 24 h and 48 h after surgery was evaluated by VAS score [17]. The scoring criteria: the score was recorded by a movable scale with a length of 10 cm; the scale was divided into 10 scales, 0 was painless, and the slide to 10 was aggravated pain.

(3) The cognitive function of patients in the two groups before, 1 d and 3 d after surgery was evaluated by MMSE score [18]. The score was 30 points totally; the lower the scores of patients were, the more serious the cognitive dysfunction was.

(4) The POCD incidence on the 1st and 3rd day after surgery was recorded in both groups.

(5) The incidence of adverse reactions after surgery was recorded in the two groups.

(6) Altogether 5 mL venous blood was drawn from patients in the two groups before, 1 d and 3 d after surgery. And then it was centrifuged 10 min at 1500Xg, 4°C, and placed in  $-70^\circ\text{C}$  low temperature refrigerator for later use. The S-100 $\beta$  expression levels of patients before, 1 d and 3 d after surgery were detected by enzyme-linked immunosorbent assay (ELISA) [19], and interleukin-10 (IL-10), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and C-reactive protein (CRP) before, 1 d and 3 d after surgery were detected. The test was in line with the operation instructions of human S-100 $\beta$  (Xiyuan Biotechnology Co., Ltd., Shanghai, China, XY-KT-435), IL-10 (Hengfei Biotechnology Co., Ltd., Shanghai, China, K003274P), TNF- $\alpha$  (Yanke Biotechnology Co., Ltd., Xiamen, China, iqp-163R), and CRP (Yiyuan Biotechnology Co., Ltd., Shanghai, China, EY-D9154).

### 2.4 Statistical Methods

The data were statistically analyzed by SPSS20.0 (IBM Corp, Armonk, NY, USA), and the pictures were drawn by Graphpad Prism6 (Graphpad, San Diego, CA, USA). The measurement data conforming to normal distribution were expressed by mean  $\pm$  SD. The comparison of inter-group measurement data adopted independent-samples *T* test, the multi-group comparison adopted *F* test of one-way analysis of variance, and the comparison before and after treatment adopted paired *T* test. The counting data were expressed by the number of cases/percentage [n (%)], and the comparison between groups was analyzed through chi-square test. The risk factors of POCD in elderly CC patients after surgery were assessed via multivariate Logistic regression analysis.  $p < 0.05$  was considered to be statistically remarkable.

### 3 Results

#### 3.1 General Information

There was no marked difference in gender, age, place of residence, smoking history, drinking history, exercise history, lymph node metastasis, TNM staging between the CG and the RG ( $p > 0.05$ ). (Tab. 1).

**Table 1:** General data of patients in the two groups [n (%)]/(mean  $\pm$  SD)

| Classification        | CG (n = 95)      | RG (n = 83)      | $t/\chi^2$ | $p$   |
|-----------------------|------------------|------------------|------------|-------|
| Gender                |                  |                  | 0.172      | 0.678 |
| Male                  | 52 (54.74)       | 48 (57.83)       |            |       |
| Female                | 43 (45.26)       | 35 (42.17)       |            |       |
| Age (years)           | 65.34 $\pm$ 5.68 | 64.93 $\pm$ 5.73 | 0.479      | 0.633 |
| Place of residence    |                  |                  | 2.388      | 0.122 |
| Countryside           | 59 (62.11)       | 42 (50.60)       |            |       |
| Cities and towns      | 36 (37.89)       | 41 (49.40)       |            |       |
| Smoking history       |                  |                  | 0.208      | 0.649 |
| Yes                   | 57 (60.00)       | 47 (56.63)       |            |       |
| No                    | 38 (40.00)       | 36 (43.37)       |            |       |
| Drinking history      |                  |                  | 0.195      | 0.676 |
| Yes                   | 59 (62.11)       | 49 (59.04)       |            |       |
| No                    | 36 (37.89)       | 34 (40.96)       |            |       |
| Sports history        |                  |                  | 0.138      | 0.711 |
| Yes                   | 42 (44.21)       | 39 (46.99)       |            |       |
| No                    | 53 (55.79)       | 44 (53.01)       |            |       |
| Lymph node metastasis |                  |                  | 0.087      | 0.767 |
| Yes                   | 41 (43.16)       | 34 (40.96)       |            |       |
| No                    | 54 (56.84)       | 49 (59.04)       |            |       |
| TNM staging           |                  |                  | 0.689      | 0.406 |
| Stages I + II         | 33 (34.74)       | 24 (28.92)       |            |       |
| Stage III             | 62 (65.26)       | 59 (71.08)       |            |       |

#### 3.2 Clinical Indicators

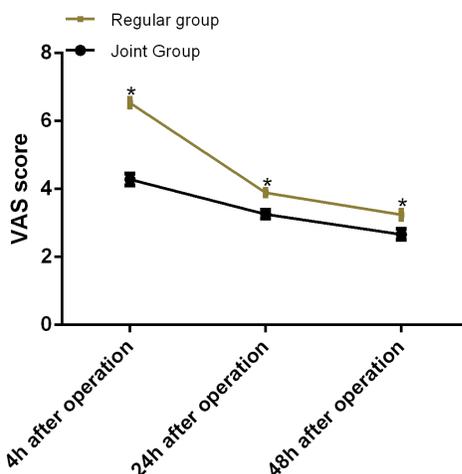
The CG had less eye-opening time than the RG ( $p < 0.05$ ), while there was no marked difference between the two other indexes ( $p > 0.05$ ). (Tab. 2).

**Table 2:** Comparison of clinical indexes of patients in the two groups (mean  $\pm$  SD)

| Group       | Time of operation (min) | Intraoperative hemorrhage (mL) | Time to recover spontaneous respiration (min) | Eye-opening time (min) | Time of tracheal extubation (min) |
|-------------|-------------------------|--------------------------------|---|------------------------|-----------------------------------|
| CG (n = 95) | 254.32 $\pm$ 40.08      | 170.64 $\pm$ 25.34             | 12.39 $\pm$ 2.03                              | 6.02 $\pm$ 1.67        | 1.52 $\pm$ 0.23                   |
| RG (n = 83) | 248.73 $\pm$ 40.02      | 173.28 $\pm$ 25.12             | 11.89 $\pm$ 2.05                              | 7.84 $\pm$ 1.69        | 1.47 $\pm$ 0.26                   |
| $t$         | 0.929                   | 0.696                          | 1.632   | 7.213                  | 1.361                             |
| $p$         | 0.354                   | 0.487                          | 0.105   | <0.001                 | 0.175                             |

### 3.3 Comparison of VAS Scores between the Two Groups in Different Time Periods before and after Surgery

The VSA scores of the two groups decreased dramatically with time ( $p < 0.05$ ), and the scores of the CG were lower than those of the RG at 4 h, 24 h and 48 h after surgery ( $p < 0.05$ ). (Fig. 1).



**Figure 1:** comparison of VAS scores of patients in the two groups at different time periods before and after surgery

The VAS scores of the CG were lower than those of the RG at 4 h, 24 h and 48 h after surgery. Note: compared with RG after treatment, \*  $p < 0.05$ .

### 3.4 Expression of Inflammatory Factors of Patients before and after Surgery in Both Groups

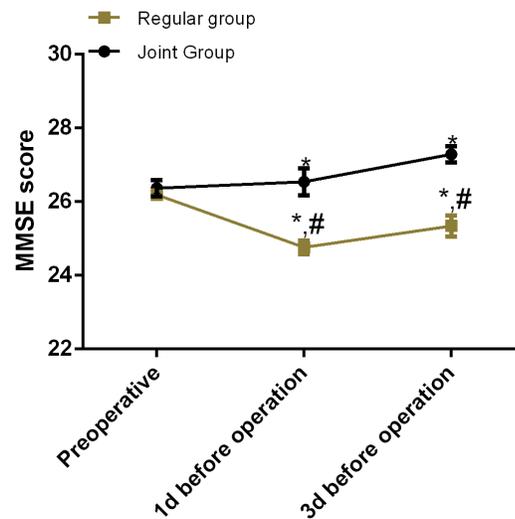
The expression levels of IL-10, TNF- $\alpha$  and CRP before surgery were not dramatically different between the two groups ( $p < 0.05$ ). The IL-10 expression after surgery in the CG was higher than that in the RG ( $p < 0.05$ ), while the TNF- $\alpha$  and CRP expression levels were dramatically lower than those in the RG ( $p < 0.05$ ). (Tab. 3).

**Table 3:** Expression of inflammatory factors (mean  $\pm$  SD) of patients before and after surgery in both groups

| Group       | IL-10 (pg/L)     |                  | TNF- $\alpha$ (pg/L) |                  | CRP (mg/L)       |                  |
|-------------|------------------|------------------|----------------------|------------------|------------------|------------------|
|             | Before surgery   | After surgery    | Before surgery       | After surgery    | Before surgery   | After surgery    |
| CG (n = 95) | 12.47 $\pm$ 2.21 | 24.72 $\pm$ 3.02 | 18.94 $\pm$ 2.74     | 23.17 $\pm$ 4.21 | 11.28 $\pm$ 1.45 | 40.16 $\pm$ 3.27 |
| RG (n = 83) | 12.39 $\pm$ 2.20 | 18.39 $\pm$ 2.78 | 18.59 $\pm$ 2.76     | 33.29 $\pm$ 4.56 | 11.54 $\pm$ 1.47 | 62.76 $\pm$ 5.87 |
| <i>t</i>    | 0.241            | 14.470           | 0.847                | 15.390           | 1.186            | 32.240           |
| <i>p</i>    | 0.809            | <0.001           | 0.398                | <0.001           | 0.237            | <0.001           |

### 3.5 Comparison of MMSE Scores of Patients between the Two Groups in Different Time Periods before and after Surgery

There was no obvious difference in MMSE scores between the two groups ( $p > 0.05$ ). The MMSE scores of patients in the CG increased dramatically with time and were higher than the preoperative scores ( $p < 0.05$ ), while the scores of patients in the RG decreased dramatically with time and were lower than the preoperative scores ( $p < 0.05$ ), and the scores of patients in the CG were dramatically higher than those in the RG ( $p < 0.05$ ) at 1 d and 3 d after surgery. (Fig. 2).



**Figure 2:** Comparison of MMSE scores of patients in the two groups in different time periods before and after surgery

There was no obvious difference in MMSE scores between the two groups before surgery ( $p > 0.05$ ), and the scores in the CG were dramatically higher than those in the RG on the 1st and 3rd day after surgery ( $p < 0.05$ ). Note: compared with before treatment, \*  $p < 0.05$ ; compared with RG after treatment, #  $p < 0.05$ .

### 3.6 Comparison of POCD of Patients between Both Groups

The total incidence of POCD was 8.42% in the CG and 22.89% in the RG at 1 d and 3 d after surgery, and the total incidence in the CG was dramatically lower than that in the RG ( $p < 0.05$ ). (Tab. 4).

**Table 4:** Comparison of cognitive dysfunction of patients between both groups [n (%)]

| Group    | n  | One day after surgery | Three days after surgery | Total incidence |
|----------|----|-----------------------|--------------------------|-----------------|
| CG       | 95 | 7 (7.37)              | 1 (1.05)                 | 8 (8.42)        |
| RG       | 83 | 14 (16.87)            | 5 (6.02)                 | 19 (22.89)      |
| $\chi^2$ | –  | 3.841                 | 3.361                    | 7.209           |
| P        | –  | 0.050                 | 0.067                    | 0.007           |

### 3.7 Total Incidence of Postoperative Adverse Reactions of Patients in the Two Groups

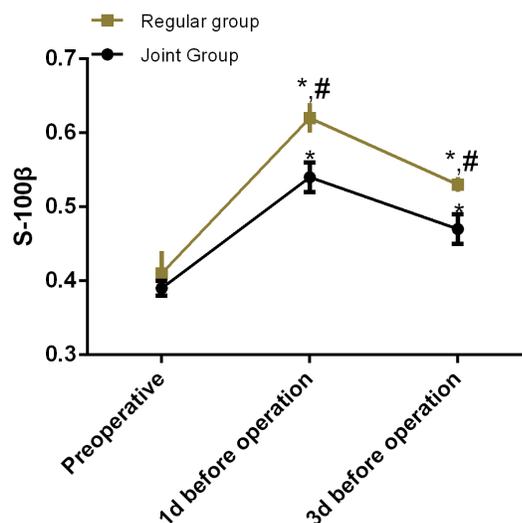
The total incidence of postoperative adverse reactions was 7.37% in the CG and 15.66% in the RG, and there was no marked difference between both groups ( $p > 0.05$ ). (Tab. 5).

**Table 5:** Total incidence of postoperative adverse reactions of patients in the two groups [n (%)]

| Group       | Nausea   | Vomiting | Hypertension | Tachycardia | Dysphoria | Total incidence of adverse reactions |
|-------------|----------|----------|--------------|-------------|-----------|--------------------------------------|
| CG (n = 95) | 1 (1.05) | 0 (0.00) | 3 (3.16)     | 2 (2.11)    | 1 (1.05)  | 7 (7.37)                             |
| RG (n = 83) | 2 (2.41) | 1 (1.20) | 4 (4.82)     | 5 (6.02)    | 1 (1.20)  | 13 (15.66)                           |
| $\chi^2$    | 0.492    | 1.151    | 0.324        | 1.801       | 0.009     | 3.056                                |
| p           | 0.483    | 0.283    | 0.569        | 0.179       | 0.923     | 0.081                                |

### 3.8 Comparison of S-100β Concentration of Patients from Both Groups in Different Periods before and after Surgery

There was no obvious difference in S-100β concentration between the two groups before surgery ( $p > 0.05$ ). The S-100β concentration in the two groups increased on the 1st day after surgery and decreased on the 3rd day after surgery ( $p < 0.05$ ), while the S-100β concentration in the CG was dramatically lower than that in the RG on the 1st day and 3rd day after surgery ( $p < 0.05$ ). (Fig. 3).



**Figure 3:** Comparison of S-100β concentration of patients in both groups at different time periods before and after surgery

There was no remarkable difference in S-100β concentration between the two groups before surgery ( $p > 0.05$ ), and the S-100β concentration in the CG was dramatically lower than that in the RG at 1d and 3d after surgery ( $p < 0.05$ ). Note: compared with before treatment, \*  $p < 0.05$ ; compared with RG after treatment, #  $p < 0.05$ .

### 3.9 Logistic Regression Analysis on POCD Occurrence of Elderly CC Patients after Surgery

There were 27 patients with postoperative POCD and 151 patients with non-POCD. Comparing the differences of clinical parameters and related indexes between postoperative POCD and non-POCD, we discovered that there was no marked difference between them in gender, age, place of residence, smoking history, drinking history, exercise history, lymph node metastasis and TNM staging ( $p > 0.05$ ). However, there was a statistical difference ( $p < 0.05$ ) with eye-opening time, VAS score, IL-10, TNF-α, CRP, and S-100β. The factors with differences were assessed through multivariate Logistic regression analysis. And the results showed that eye-opening time ( $p = 0.023$ ), VAS score ( $p = 0.001$ ), IL-10 ( $p = 0.003$ ), TNF-α ( $p = 0.005$ ), CRP ( $p = 0.003$ ), and S-100β ( $p = 0.001$ ) were independent risk factors affecting POCD occurrence in elderly CC patients after surgery. (Tabs. 6–8).

**Table 6:** Relationship between clinical parameters and various indexes of elderly CC patients and POCD occurrence after surgery

| Classification | n    | POCD group (n = 27) | Non-POCD group (n = 151) | $t/\chi^2$ | $p$   |
|----------------|------|---------------------|--------------------------|------------|-------|
| Gender         |      |                     |                          | 0.834      | 0.361 |
| Male           | 1100 | 13 (48.15)          | 87 (57.62)               |            |       |
| Female         | 778  | 14 (51.85)          | 64 (42.38)               |            |       |
| Age (years)    |      |                     |                          | 0.364      | 0.547 |

|                        |      |              |              |        |        |
|------------------------|------|--------------|--------------|--------|--------|
| <60                    | 882  | 11 (40.74)   | 71 (47.02)   |        |        |
| ≥60                    | 996  | 16 (59.26)   | 80 (52.98)   |        |        |
| Place of residence     |      |              |              | 0.018  | 0.893  |
| Countryside            | 1101 | 15 (55.56)   | 86 (56.95)   |        |        |
| Cities and towns       | 777  | 12 (44.44)   | 65 (43.05)   |        |        |
| Smoking history        |      |              |              | 0.889  | 0.346  |
| Yes                    | 1104 | 18 (66.67)   | 86 (56.95)   |        |        |
| No                     | 774  | 9 (33.33)    | 65 (43.05)   |        |        |
| Drinking history       |      |              |              | 1.254  | 0.263  |
| Yes                    | 1108 | 19 (70.37)   | 89 (58.94)   |        |        |
| No                     | 770  | 8 (29.63)    | 62 (41.06)   |        |        |
| Sports history         |      |              |              | 0.291  | 0.589  |
| Yes                    | 881  | 11 (40.74)   | 70 (46.36)   |        |        |
| No                     | 997  | 16 (59.26)   | 81 (53.64)   |        |        |
| Lymph node metastasis  |      |              |              | 0.472  | 0.492  |
| Yes                    | 775  | 13 (48.15)   | 62 (41.06)   |        |        |
| No                     | 1103 | 14 (51.85)   | 89 (58.94)   |        |        |
| TNM staging            |      |              |              | 2.256  | 0.133  |
| Stages I + II          | 557  | 12 (44.44)   | 45 (29.80)   |        |        |
| Stage III              | 1121 | 15 (55.56)   | 106 (70.20)  |        |        |
| Eye-opening time (min) |      |              |              | 4.844  | 0.028  |
| ≤6 min                 | 994  | 9 (33.33)    | 85 (56.29)   |        |        |
| >6 min                 | 884  | 18 (66.67)   | 66 (43.71)   |        |        |
| VAS scores             |      |              |              | 4.080  | <0.001 |
|                        | 1178 | 3.11 ± 0.56  | 2.69 ± 0.48  |        |        |
| IL-10 (pg/L)           |      |              |              | 6.912  | <0.001 |
|                        | 1178 | 19.47 ± 2.56 | 23.98 ± 3.21 |        |        |
| TNF-α (pg/L)           |      |              |              | 12.840 | <0.001 |
|                        | 1178 | 34.03 ± 5.29 | 24.08 ± 3.36 |        |        |
| CRP (mg/L)             |      |              |              | 17.410 | <0.001 |
|                        | 1178 | 59.78 ± 6.89 | 39.78 ± 5.22 |        |        |
| S-100β                 |      |              |              | 11.620 | <0.001 |
|                        | 1178 | 0.57 ± 0.09  | 0.43 ± 0.05  |        |        |

**Table 7:** Logistic multivariate regression analysis assignment

| Factor           | Variable | Assignment          |
|------------------|----------|---------------------|
| Eye-opening time | X1       | <60 = 0, ≥60 = 1    |
| VAS scores       | X2       | Continuous variable |
| IL-10            | X3       | Continuous variable |
| TNF-α            | X4       | Continuous variable |
| CRP              | X5       | Continuous variable |
| S-100β           | X6       | Continuous variable |

**Table 8:** Multivariate Logistic regression analysis on POCD occurrence in elderly CC patients after surgery

| Variable         | B     | S. E  | Wals   | <i>p</i> | OR    | 95% CI       |
|------------------|-------|-------|--------|----------|-------|--------------|
| Eye-opening time | 0.328 | 0.198 | 5.367  | 0.023    | 1.218 | 0.609–2.436  |
| VAS scores       | 1.108 | 0.027 | 9.479  | 0.001    | 5.389 | 2.695–10.778 |
| IL-10            | 1.085 | 0.048 | 7.178  | 0.003    | 2.673 | 1.337–5.346  |
| TNF- $\alpha$    | 1.937 | 0.574 | 9.371  | 0.005    | 4.792 | 2.396–9.584  |
| CRP              | 1.728 | 0.472 | 8.093  | 0.003    | 4.972 | 2.486–9.944  |
| S-100 $\beta$    | 0.983 | 0.089 | 10.972 | 0.001    | 6.098 | 3.049–12.196 |

#### 4 Discussion

CC is the most common cancer among adult patients in the world [20], which develops continuously, resulting in the transformation of healthy colon epithelial cells into benign growth (e.g., polyps). Then, it develops into a benign tumor and finally develops into an invasive cancer focus [21]. CC is usually treated by surgical resection in clinical practice [22]. However, postoperative pain and patients' cognitive function decline have always been familiar with complications after surgery. Therefore, giving reasonable anesthesia in patients' surgery is of considerable significance to improve the efficacy of CC patients after surgery and promote their recovery [23,24].

In this study, we used ulinastatin combined with dexmedetomidine to intervene in elderly CC patients after laparoscopic, and found that their prognosis has been dramatically improved. For example, Li et al. [25] pointed out that dexmedetomidine could reduce postoperative stress response and chronic pain caused by surgery for esophageal cancer patients. Shan et al. [26] reported that ulinastatin could reduce the level of postoperative inflammatory factors and POCD incidence in elderly fracture patients during surgery. This study's results manifested that the eye-opening time of clinical indicators in the CG was dramatically lower than in the RG. At the same time, there was no marked difference in other indicators, indicating that ulinastatin combined with dexmedetomidine could not prolong the wake-up time when reaching the appropriate sedation depth. The VAS scores of the CG were lower than those of the RG at 4 h, 24 h, and 48 h after surgery, indicating that the combination could better reduce postoperative pain of patients, and the analgesic effect of the CG was better. There was no remarkable difference in the total incidence of postoperative adverse reactions between the two groups, indicating that the two different anesthesia methods' safety was higher.

Some studies have shown that peripheral inflammatory mediators can cross the blood-brain barrier to regulate the process of central inflammation, leading to neurodegeneration and impairing the cognitive function of patients [27]. This study observed the expression of inflammatory factors of patients in the two groups after surgery. It was found that the IL-10 expression in the CG was dramatically higher than that in the RG. In contrast, the TNF- $\alpha$  and CRP expression levels were dramatically lower than those in the RG, indicating that ulinastatin combined with dexmedetomidine could improve the body trauma caused by surgery, thus increasing the level of inflammatory factors in patients. The MMSE scores of patients in the CG were higher than those in the RG on the 1st and 3rd day after surgery, indicating that ulinastatin combined with dexmedetomidine could improve the cognitive function of patients after surgery. Zhou et al. [28] clarified that ulinastatin combined with dexmedetomidine could reduce the postoperative inflammatory response and POCD incidence in heart valve patients. We observed the total incidence of POCD on the 1st and 3rd day of patients from the two groups after surgery. We found that the total incidence in the CG was dramatically lower than in the RG, indicating that ulinastatin combined with dexmedetomidine had an inhibitory effect on the stress response, secretion, and release of inflammatory factors in postoperative patients, thus improving POCD occurrence.

Some studies have shown that S-100 $\beta$  can act as a survival and differentiation factor of neurons, promote neurite extension, and protect neurons from cell stress during development [29]. Moreover, other studies have also shown that S-100 $\beta$  can be used as a specific neurobiochemical marker for brain injury

after surgery in patients with head trauma and cardiac diseases [30]. Rasmussen et al. [31] pointed out that the increased concentration of S-100 $\beta$  in patients' serum after abdominal surgery would lead to postoperative cognitive dysfunction. The results of this study showed that the S-100 $\beta$  concentration in the CG was dramatically lower than that in the RG at 1 d and 3 d after surgery, indicating that ulinastatin combined with dexmedetomidine could reduce the influence of laparoscopic on S-100 $\beta$  level and improve POCD possibility after surgery. Clinical studies show that many factors lead to POCD after surgery, such as anesthesia induction mode of surgery, postoperative infection, etc., that may be related to postoperative cognitive dysfunction [32]. As a result, this carried out a multi-factor Logistic regression analysis on POCD occurrence in elderly CC patients after surgery. This study showed that eye-opening time, VAS score, IL-10, TNF- $\alpha$ , CRP, and S-100 $\beta$  were independent risk factors for POCD occurrence in elderly CC patients after surgery.

Although this study has confirmed that ulinastatin combined with dexmedetomidine is a feasible anesthesia scheme for elderly CC patients after laparoscopic, there is still room for improvement. First of all, it can increase the analysis of patients' quality of life, expand the sample range, and supplement the diagnostic value of S-100 $\beta$  for patients. These improvement spaces need to be further supplemented in future studies.

## 5 Conclusion

To sum up, ulinastatin combined with dexmedetomidine anesthesia induction can improve the prognosis of elderly CC patients after laparoscopic, and it reduces postoperative pain and serum inflammatory factors. S-100 $\beta$  concentration can improve POCD occurrence after surgery.

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