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# Effects of dexmedetomidine combined with dezocine on T lymphocytes, NK cells and cognitive function in elderly patients with gastrointestinal cancer after radical surgery

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#### **ABSTRACT**

This study aimed to determine how dexmedetomidine and dezocine interact on T lymphocytes, NK cells and cognitive function in elderly individuals with gastrointestinal cancer after radical surgery. 104 elderly individuals with gastrointestinal cancer after radical surgery who visited our hospital from January 2020 to April 2022 were chosen. The patients were randomly divided into the Control Group (Group C) and Observation Group (Group O) with 52 cases each. Group C was anesthetized with sufentanil, while Group O was anesthetized with dexmedetomidine combined with dezocine. The changes in T lymphocytes, NK cells and their cognitive function were compared before the operation, 1 day after the operation and 3 days after the operation. In the experiment, the cognitive function of the individuals after the operation was evaluated with the Mini-Mental State Examination (MMSE). The overall comparison results indicated that among CD3+, CD4+, CD8+, and CD4+/CD8+, there were statistically significant variations in the interplay between groups over time (P<0.05). Before anesthesia, the two categories did not vary significantly from one another in the percentage of T lymphocytes, the percentage of NK cells and the score of the MESS scale (P>0.05). At 1 day and 3 days after the operation, the CD3+, CD4+, and CD4+/CD8+ in Group O were remarkably higher than those in Group C (P<0.05). At 1 day and 3 days after the operation, the CD8+in Group O was significantly lower than that in Group C (P<0.05). Overall comparison results: There was a variation that is numerically meaningful in the percentage of NK cells over time, groups and time interactions (P<0.05). One day after surgery, there was no discernible change in the proportion of NK cells between the two groups (P>0.05). Three days after the operation, the NK cells in Group O were higher than those in Group C, and the difference was statistically significant (P<0.05). The scores of the MMSE scale in both groups decreased 3 days after the operation compared with those before anesthesia. However, the score of MMSE in Group O was superior to Group C 3 days after the operation, and the difference between the two groups was statistically significant (P<0.05). The application of dexmedetomidine combined with dezocine in elderly individuals with gastrointestinal cancer after radical surgery can increase the percentage of T lymphocytes and NK cells after surgery and promote faster recovery of cognitive function.

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#### Introduction

More than half of the world's new gastric cancer occur in China and Japan, and its incidence rate increases with the increasing trend of population aging (1). Gastrointestinal tumors in the elderly are often associated with cardiovascular diseases, leading to a further increase in the risk of mortality (2). Radical resection of gastrointestinal tumors is the main treatment for gastric cancer or intestinal tumors. Severe hemodynamic fluctuations will occur during the anesthesia of gastrointestinal cancer radical surgery, resulting in insufficient oxygen supply to important organs and surrounding tissues. This situation will aggravate the anesthesia risk of patients (3). Tumor patients are often accompanied by low immune function. Among them, T lymphocytes and NK cells are the main immune factors of the body. After radical resection of gastrointestinal tumors, the change in immune function directly determines the recovery of the prognosis of patients. This research believes that different anesthetic methods can have different effects on the immune function of tumor patients (4,5). In addition, cognitive dysfunction (POCD) is prone to occur in the elderly after radical resection of gastrointestinal tumors, and it is mainly concentrated in the first to third days after the operation (5). The anesthesia mode can affect the POCD of elderly patients after an operation (6-7). Sufentanil is a commonly used intravenous general anesthesia drug, which is characterized by high safety, fast analgesia and good analgesic effect. It is a commonly used anesthetic for gastrointestinal tumor surgery. Dezocine is a bi-directional opioid receptor drug that can inhibit the release pathway of inflammatory mediators produced by the body (8,9). In individuals with tumors, dexmedetomidine can decrease the body's stress reaction and alleviate the suppression of cellular immunological function. In addition, dexmedetomidine has good sedative and hypnotic effects, which can effectively relieve pain, inhibit sympathetic activity and improve cardiovascular stability (10,11). However, whether the combination of the two can improve the postoperative T lymphocytes, NK cells and cognitive function of individuals with gastrointestinal cancer needs further verification.

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#### **Materials and Methods**

#### **General information**

A random number matrix was used to split the 104 senior patients with stomach cancer having major surgery at our institution between January 2020 and April 2022 into Groups C and O, each with 52 instances. Inclusion criteria:(1) patients with gastric cancer, colon cancer and rectal cancer undergoing radical surgery on a selective basis; (2) Age: 65~75; (3) Those diagnosed as gastric cancer, colon cancer and rectal cancer by postoperative pathology; (4) Sane person; (5) The cardiac, hepatic and pulmonary functions of all patients were normal before operation; (6) None of them had received chemotherapy or radiotherapy before the operation, and no history of immune disease and drug allergy; (7) According to the surgery categorization of grade I to III patients by the American Society of Anesthesiologists (ASA); (8) Patients with TNM stage 1-4; (9) Standard informed consent for participants in this study. Exclusion criteria:(1) patients with immune function defect or cognitive impairment before operation; (2) Expected survival time<6 months; (3) Those who are allergic to experimental anesthetics; (4) Those who are accompanied by a serious visual and audio impairment that affect the filling of the questionnaire or cannot communicate normally; (5) Those who were treated with analgesics before operation; (6) Have a history of dependence on psychotropic drugs or alcohol; (7) Refuse to participate in the study. Group C consisted of 29 males and 23 females. The people's ages varied from 65 to 75, with an average age of (68.  $79 \pm 2$ . 95) years. Among them, there were 15 cases of gastric cancer, 16 cases of colon cancer and 21 cases of rectal cancer. There were 25 cases of ASA grade II and 27 cases of ASA grade III. TNM stage 1~2 stage 23 cases, 3~4 stage 29 cases. BMI is 16. 65~34. 23 kg/m2, and the average BMI is (25.  $06 \pm 3.26$ ) kg/m2. Group O included 36 males and 16 females. The age ranged from 65 to 75 years, with an average age of (69.  $31 \pm 3.04$ ) years. Among them, there were 17 cases of gastric cancer, 12 cases of colon cancer and 23 cases of rectal cancer. ASA grade II in 30 cases and grade III in 22 cases. TNM stage 1~2 in 25 cases, 3~4 in 27 cases. BMI is 18. 17~32. 06 kg/m2, with an average BMI of (24.  $11 \pm 2.87$ ) kg/m2. The groups' extremely similar characteristics of sex, age, tumor location, ASA grade, TNM stage, and Weight did not vary significantly (P>0. 05).

#### Anesthesia method

Both groups of patients were not given preoperative medication and were routinely fasting for 8 to 12 hours. The vital signs such as ECG, blood pressure and blood oxygen were dynamically monitored after the patient entered the room. The vascular entry was set up regularly as soon as the patient entered the surgery area. The patient was given continuous ECG monitoring. Monitor the patient's heart rate (HR) and mean arterial pressure (MAP). The individuals in both groups were treated with general anesthesia with combined intubation and inhalation. Anesthesia induction: propofol [(Jiangsu Yingke Biopharmaceutical Co., Ltd., approval number: H20203504, specification: 20ml: 200mg) (1. 5~3. 0 mg/kg)] + sufentanil [(Yichang Humanwell Pharmaceutical Co., Ltd., approval number: H20054171, specification: 1ml: 50µg/kg) (0. 3μg/kg)] + cisatracurium besylate (Hangzhou Hongyou Pharmaceutical Technology Co., Ltd., approval number: H20213438, specification: 10mg) (0. 2 mg/kg), tracheal intubation will be started after successful induction. Intraoperative anesthesia maintenance: propofol [0. 10~0. 25ug/(kg·min)]+remifentanil (Yichang Humanwell Pharmaceutical Co., Ltd., approval number: H20030197, specification: 1mg) [0. 10~0. 25ug/(kg • min)] was used, and cisatracurium besylate was added intermittently. During the operation, maintain the patient's heart rate between  $60\sim100$  beats/min, control the NIBP within  $\pm$  15% of the base value, BIS40~60, SPO2 98%~100%, P<sub>ET</sub>CO<sub>2</sub>35~45 mmHg. Before skin cutting, 4 mg of ondansetron was injected intravenously for 10 min, and 0. 3 sufentanil was added µg/kg. Cisatracurium besylate was terminated within 30 minutes before the end of surgery. Within 24 hours of surgery, patient-controlled injectable analgesics were

### **Group C**

Apply sufentanil injection 1. 0µg/kg 30min before the operation, intravenous drip. Cisatracurium besylate was stopped 30 minutes before the end of the operation. 30ml 0. 9% sodium chloride injection was selected, and the same amount of normal saline was infused 10~15 minutes later. Propofol and remifentanil were stopped 20 minutes before the end of the surgery. When the patient's Steward recovery score was more than 6 points and the patient recovered from spontaneous breathing, the patient was routinely transferred to PACU for observation. After 90 minutes, the patient's vital signs stabilized and were sent back to the main hospital without incident.

### **Group O**

Dexmedetomidine [(Yangzijiang Pharmaceutical Group Co., Ltd., approval No.: H20183220, specification: 2ml: 2000µg) (0. 5µg/kg)] was applied 20 minutes before anesthesia induction. The anesthesia induction method and intraoperative anesthesia maintenance were the same as those in Group C. Cisatracurium besylate was stopped 30 minutes before the end of the operation, and dextrometomidine (0. 5µg/kg), the solution is 0. 9% sodium chloride injection 30ml, and the infusion is completed within 10-15min. After the infusion, Dezocine injection [(Yangzijiang Pharmaceutical Group Co., Ltd. , approval number: H20184150, specification: 1ml) (0. 1mg/kg)] 0. 1mg/kg is applied. Propofol and remifentanil were stopped 20 minutes before the end of the surgery. The remaining anesthetic drugs and anesthetic methods of the two groups were the same. After the routine operation is completed, the patient will pull out the endotracheal tube and turn out of the operating room after Steward's recovery score>6 points, and then turn back to the general ward after the PACU observation.

## Observation indicators Tlymphocytes and NK cells

NK cells exist in the human body. They are a kind of heterogeneous multifunctional immune cells and natural killer cells. NK is mainly responsible for the regulation of various cells in the body, including T lymphocytes and B lymphocytes. In addition, NK has a strong scavenging effect on cancer cells, viruses and parasitic bacteria in the bag. The normal value of NK cells is generally 7-40%, and the reference value is 47. 6%-76. 8%. If the NK cell

value is too high, it will mean that there may be immune diseases, tumor diseases, organ transplantation and other conditions in the body. If the NK cell value is too low, it indicates that the body may have weakened immunity due to acute and chronic diseases. Multipotent stem cells produced from bone marrow are T lymphocytes. They are dispersed to the immunological organs and tissues of the entire body through lymphatic and blood circulation after differentiating and maturing in the thymus, where they perform immune tasks. Therefore, it has immune activity. The body can come into touch with antigens more frequently when T cells are recycled, which strengthens the immune reaction and helps sustain immunological memory over time. The normal range of T lymphocyte value of blood routine tests is between 20% and 40%. The change of T lymphocyte value is correlated with the immune function of the body. If the T cell value is too high, the body may have a viral infection. To determine the value of T lymphocytes and NK cells, 5ml of fasting elbow vein blood was drawn from patients before anesthesia, at the end of the surgery, 1 day and 3 days after surgery. Blood glucose and C-reactive protein (CRP) were measured before anesthesia and at the end of surgery. The CD3+, CD4+, CD8+ and NK in whole blood at each time point were measured by FACSCALIBUR3. 0 flow cytometry of BD Company in the United States, and the CD4/CD8 values were calculated at the same time. The plasma concentrations of IL-2, IL-4, IFN-7 and other cytokines were determined by ELISA (the kit was provided by Shanghai Yanji Biotechnology Co., Ltd.).

#### Cognitive function

The Mini-Mental State Examination (MMSE) is one of the most influential standardized mental state examination tools. As a cognitive impairment test method, MMSE can be used to assess various neuropsychiatric symptoms, behavioral disorders and cognitive functions, and its operation is simple and easy. There are five questions in the scale, including orientation, memory, attention (computational power), memory, and language ability. One point is given for each correct answer; 0 points will be given if you are wrong or don't know; Not suitable for 9 points; 8 points for refusing to answer or not understanding. In total, 8 points and 9 points are calculated as 0 points. The total score is between 0 and 30; 27~30 minutes is regarded as normal; 21~26 scores were considered as mild brain dysfunction; 10-20 scores were considered as moderate brain dysfunction; 0-9 points were considered as severe brain dysfunction. The greater the number, the better the patient's brain performance. During the evaluation, the subject is only allowed to speak once; Subjects are not required to answer in the order of items; If there are errors in the first pass, score first; Then tell the patient where the mistake was and ask him to recall; Until correct; But you can only "learn" five times at most. In this experiment, MMSE was used to assess the cognitive function of patients before anesthesia and 3 days after surgery.

### Hemodynamic indexes and pain degree

(I) Hemodynamic indexes: Compare the heart rate (HR) and mean arterial pressure (MAP) of the two groups before and at 6h, 12h and 24h after the operation. (II) Pain degree: At 6h and 12h 24h after operation, the pain degree was assessed by visual analogue scale (VAS), with a score of 0 to 10 points. The score was positively correlated with the pain degree.

#### Statistical methods

SPSS version 22. 0 statistical software was applied for data processing, and the measurement data was expressed by  $(\bar{x}\pm s)$ , and the comparison between groups in line with normal distribution was conducted by T-test; The counting data is expressed in cases (%);  $\chi^2$  test was used to compare groups; M ( $P_{25}$ ,  $P_{75}$ ) denotes non-normal distribution measurement data; Mann-Whitney test is used for inter-group comparison and correction level  $\alpha$ =0. 05. If P<0. 05, it denotes a numerically meaningful variation, and vice versa.

### Results

## Comparison of general data of two groups of patients

None of the patients selected in this experiment were exfoliated. Table 1 shows their baseline data. There was no remarkable variation between the two groups in general data such as gender, age, tumor site, ASA grade, TNM stage, and BMI index (P>0. 05). Therefore, the follow-up experimental results of the two groups of patients are highly comparable.

# Comparison of T lymphocyte changes between two groups of patients

Overall comparison: There were remarkable variations among CD3+, CD4+, CD8+, and CD4+/CD8+ among groups, time, interaction between groups and time (P<0. 05). Before anesthesia, there was no discernible change in the percentage of T lymphocytes between the two groups (P>0. 05). At 1 day and 3 days after operation, the CD3+, CD4+, and CD4+/CD8+ in Group O were significantly superior to Group C (P<0. 05). At 1 day and 3 days after the operation, the CD8+ in Group O was remarkably inferior to Group C (P<0. 05) (Table 2).

# Comparison of NK cell changes between two groups of patients

Overall comparison: The percentage of NK cells varied statistically significantly across time, groups, and time in-

**Table 1.** Comparison of general data of two groups of patients (N=52).

Group	Gender		Year	Tumor site		ASA classification		TNM classification		BMI	
	Male	Female	(years old)	stomach	colon	rectum	II	III	Phase 2	Phase 3	$(Kg/M^2)$
Control group	29	23	68. 79±2. 95	15	16	21	25	27	23	29	25. 06±3. 26
Group O	36	16	69. 31±3. 04	17	12	23	30	22	25	27	24. 11±2. 87
$X^2/T$	1.	991	-0. 885		0. 787		0.	955	0.	153	1. 565
P	0.	158	0.378		0. 675		0	328	0.	695	0. 121

**Table 2.** Comparison of T lymphocyte changes between two groups of patients  $(\bar{x} \pm s)$ .

Group	Time	CD <sup>3+</sup> (%)	CD <sup>4+</sup> (%)	CD <sup>8+</sup> (%)	CD <sup>4+</sup> /CD <sup>8+</sup>
	Before anesthesia	71. 59±3. 78	41. 35±3. 34	$31.\ 08 \pm 1.\ 72$	1. 33 $\pm 0$ . 13
Group C (N=52	) 1dafter operation	64. 69±2. 59	34. 97±1. 84	30. 51±1. 60	1. 15±0. 08
	3dafter operation	67. 34±2. 60	37. 33±1. 73	30. 83±2. 13	1. 22±0. 11
	Before anesthesia	71. 16±4. 07	41. 08±3. 50	$30.~93 \pm 1.~57$	1. $33 \pm 0. 12$
Group O ( <i>N</i> =52	) 1dafter operation	68. 51±2. 84	40. 67±2. 62	28. 71±1. 17	1. 42±0. 11
	3dafter operation	69. 93±2. 19	43. 67±1. 92	27. 10±1. 06	1. 61±0. 09
$T_{g}/P_{g}$		0. 559/0. 577	-0. 396/0. 693	0. 471/0. 638	0. 094/0. 925
$T_I/P_I$		-7. 162/<0. 001	-12. 851/<0. 001	6. 546/<0. 001	14. 333/<0. 001
$T_2/P_2$		-5. 504/<0. 001	-17. 690/<0. 001	11. 302/<0. 001	20. 099/<0. 001
$F_{\rm interblock}/P_{\rm interblock}$		25. 499/<0. 001	159. 263/<0. 001	95. 001/<0. 001	337. 061/<0. 001
$F_{ m time}/\!P_{ m time}$		72. 771/<0. 001	52. 989/<0. 001	49. 673/<0. 001	39. 062/<0. 001
$F_{ m interactive}/P_{ m interactive}$		15. 144/<0. 001	54. 748/<0. 001	36. 672/<0. 001	91. 583/<0. 001

Note:  $t_0/P_0$  is the comparison between groups before anesthesia;  $t_1/P_1$  is the inter-group comparison 1 day after operation;  $t_2/P_2$  is the comparison between groups 3 days after operation;  $F_{\text{interblock}}/P_{\text{interblock}}$  is the inter-group effect;  $F_{\text{time}}/P_{\text{time}}$  is the time effect;  $F_{\text{interactive}}/P_{\text{interactive}}$  is the interaction between groups and time effect.

**Table 3.** Comparison of NK cell changes between the two groups (%,  $\bar{x} \pm s$ ).

Group	Before anesthesia	1d after operation	3d after operation	F	P
Group C ( <i>N</i> =52)	17. 96 $\pm 2.85$	14. 76±2. 70	16. 88±3. 28	$F_{\text{interblock}} = 2.582$	P <sub>interblock</sub> =0. 111
Group O ( <i>N</i> =52)	17. 33 $\pm$ 3. 11	15. 70±2. 94	18. 21±2. 36	$F_{\text{time}} = 24.394$	$P_{\text{time}} < 0.001$
T	1. 709	-1. 703	-2. 368	$F_{\text{interactive}}=3.501$	$P_{\text{interactive}} = 0.032$
P	0. 283	0. 092	0. 020		

Note:  $F_{\text{interblock}}/P_{\text{interblock}}$  is the inter-group effect;  $F_{\text{time}}/P_{\text{time}}$  is the time effect;  $F_{\text{interactive}}/P_{\text{interactive}}$  is the interaction between groups and time effect.

teractions (P<0.05). There was no meaningful variation in the percentage of NK cells between the two groups before anesthesia and 1 day after the operation (P>0.05). 3 days after the operation, the NK cells in Group O were remarkably superior to Group C (P<0.05) (Table 3).

Figure 1 shows the average trend of the change in NK cell values in the two groups of patients. It is obvious from the figure that both groups showed a trend of decreasing first and then increasing, but the percentage change curve of NK cells in Group O was straight. During the period from pre-anesthesia to 1 day after the operation, the level of NK cells in both groups decreased, and there were no statistically remarkably variations in the two groups at this stage; Between 1 and 3 days after the procedure, the NK cells in both groups increased, and the variation at this stage was statistically remarkable. Finally, the increase of NK cell level in Group O was superior to Group C.

# Comparison of cognitive function changes between the two groups

Before anesthetic, there was no substantial change in MMSE ratings between the two groups (P>0. 05); The scores of MMSE in the two groups were lower than those before anesthesia 3 days after the operation, but the scores of MMSE in Group O were superior to Group C at 3 days after the operation, with a statistically significant difference (P<0. 05) (Table 4).

# Comparison of changes in blood glucose and CRP levels between the two groups

Table 5 demonstrates the contrast of blood glucose and CRP values before and after the operation in the two groups. The data in the table shows that the blood glucose

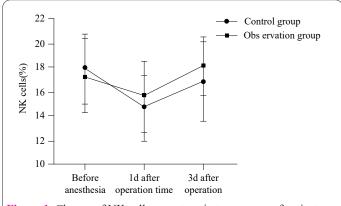


Figure 1. Change of NK cell percentage in two groups of patients.

and CRP levels of participants have increased to different degrees. The comparison results of the variations between the two groups were statistically remarkable. Wherein the increase in Group O was higher than that in Group C.

# Comparison of anesthetic dosage between two groups of patients

The comparison of the anesthetic dosage of the two groups is shown in Table 6. After adding dexmedetomidine, the dosage of the other three drugs in Group O was less than Group C, and the variation was significant.

# Comparison of hemodynamic indexes between the two groups

Table 7 demonstrates a study of cardiac indicators between the two groups. Before surgery, there was no significant variation in HR and MAP between the two groups. At 6h, 12h and 24h after the operation, the HR and

**Table 4.** Comparison of mess scores between two groups of patients (Score,  $\bar{x} \pm s$ ).

Group	Before anesthesia	3d after operation	T	P
Group C ( <i>N</i> =52)	28. 65±0. 65	26. 09±1. 94	-8. 746	< 0.001
Group O ( <i>N</i> =52)	28. $56 \pm 0.57$	27. 19±1. 91	-4. 851	< 0.001
T	0. 797	-2. 901	/	/
P	0. 427	0. 005	/	/

**Table 5.** Comparison of changes in blood glucose and CRP levels between the two groups  $(\bar{x}\pm s)$ .

Comme	Blood suga	ar (mmol/L)	CRP (mg/dL)		
Group	Preoperative	Postoperative	Preoperative	Postoperative	
Group C ( <i>n</i> =52)	4. 97 $\pm$ 0. 52	$8.32 \pm 1.48$	1. $02 \pm 0.22$	1. $88 \pm 0.17$	
Group O ( <i>n</i> =52)	5. $32 \pm 0.48$	6. $43 \pm 1.23$	1. $32 \pm 0. 16$	1. 43±0. 17	
t	1. 709	1. 643	-1. 703	1. 623	
P	0. 283	0. 023	0.092	0.003	

**Table 6.** Comparison of the dosage of narcotic drugs between the two groups (mg,  $\bar{x} \pm s$ ).

Group	Propofol	Fentanyl	Isoflurane
Group C ( <i>n</i> =52)	110. 23±37. 26	0. 18±0. 07	26. 73±5. 16
Group O ( <i>n</i> =52)	62. 94±30. 48	0. 17±0. 06	24. 63±5. 06
t	9. 456	2. 123	2. 036
p	0.000	0. 032	0. 041

**Table 7.** Comparison of hemodynamic indexes between the two groups  $(\bar{x} \pm s)$ .

Target	Group	Preoperative	6h after operation	12h after operation	n 24h after operation
HR (order /min)	Group C ( <i>N</i> =52)	77. 48±3. 23	86. 13±4. 05*	85. 23±4. 71*	82. 14±4. 31*
	Group $O(N=52)$	77. 42±3. 45	78. 39±4. 08#	77. 97±4. 06 <sup>#</sup>	77. 33±4. 26 <sup>#</sup>
MAD ( II.)	Group C ( <i>N</i> =52)	89. 73±4. 16	97. 99±4. 05*	97. 31±3. 71*	96. 54±3. 31*
MAP (mm Hg)	Group O ( <i>N</i> =52)	89. 91±3. 45	91. 24±4. 25#	90. 13±3. 06 <sup>#</sup>	89. 78±3. 26 <sup>#</sup>

Note: \* P<0. 05 compared with the group before operation; Compared with Group C, #P<0. 05.

**Table 8.** Comparison of pain degree between the two groups (Score,  $\bar{x} \pm s$ ).

Group	Preoperative	6h after operation	12h after operation	24h after operation
Group C ( <i>N</i> =52)	2. 72±0. 51	2. 48±0. 36	1. 81±0. 35	1. 37±0. 33
Group O ( <i>N</i> =52)	2. 57±0. 48	1. 96±0. 38	1. 46±0. 40	1. 17±0. 23
t	0.886	4. 537	3. 453	2. 338
p	0. 416	0. 001	0. 003	0. 025

MAP values of patients in Group O were inferior to Group C, and the difference was remarkable.

### Comparison of pain degree between the two groups

Table 8 demonstrates the comparison of pain degrees between the two groups. There was no statistically meaningful variation in VAS scores between the two groups before surgery. At 6h, 12h and 24h after the operation, the VAS score of patients in Group O was inferior to Group C, and the variation between the groups was remarkable.

## Discussion

Tumor metastasis and recurrence during the perioperative period of radical resection of gastrointestinal tumors will be affected by many factors, among which anesthesia is the most important factor. Intravenous anesthesia is a common method of general anesthesia. After intravenous injection of anesthetic drugs, the body's pain sensation disappears, and skeletal muscle relaxation and other anesthetic effects form. In the process of general anesthesia,

anesthetics will lead to increased mitosis and angiogenesis of cells, and promote the distant metastasis of tumors. At the same time, anesthetic drugs will also inhibit NK cells and T lymphocytes, and promote Th1 cells to drift to Th2 cells. However, elderly patients have poor tolerance, decreased immune function, and are prone to cognitive dysfunction after surgery. Therefore, it is necessary to further optimize the anesthesia scheme for elderly patients undergoing radical resection of gastrointestinal tumors.

Frid et al. (12) found that different anesthesia methods have different effects on the long-term efficacy of patients undergoing gastric cancer surgery. Studies have shown that immune function impairment after radical resection of gastric cancer will increase the risk of early recurrence in patients, and peripheral lymphocyte subsets are independent predictors of postoperative recurrence of gastric cancer (13). Simultaneously, general anesthetic coupled with spinal anesthesia and patient-controlled analgesics can successfully suppress cognitive impairment in senior patients following surgery, and will not have abnormal effects on hemodynamic indexes. It can be seen that finding

more rational anesthetic drugs is an important research direction to improve the immune function and cognitive function of elderly participants with gastrointestinal cancer after surgery. The results of animal experiments show that dexmedetomidine can help colon cancer development inhibition, promote tumor cell apoptosis, and has an indirect anti-tumor effect. Dexmedetomidine can regulate CD4+ and CD8+ cells and form a specific inhibitory effect on colorectal cancer (14,15). Dezocine and dexmedetomidine have been used in combination with lung cancer surgery patients. After surgery, the inflammatory factors of patients decreased and their cognitive function improved (16,17). Dezocine can up-regulate PD-L1 and activate the NF-κB pathway, promoting immune escape and glucose metabolism of LC. PD-L1 is linked to the incidence and progression of GI cancers (18). It is speculated that dexmedetomidine combined with dezocine can significantly enhance patients' immunological and brain functions.

This study shows that compared with sufentanil, dexmedetomidine combined with dezocine anesthesia can increase the level of CD3+, CD4+, CD4+/CD8+, and NK cells faster and decrease the CD8+ in participants with gastrointestinal cancer undergoing radical surgery. The Tcell immune response will change under the stimulation of the expression of new antigens generated by tumors in somatic mutation channels. T-cell receptor changes in peripheral hematoma can be used to analyze the prognosis of patients with gastric cancer, and even provide guidance for immunotherapy (13). When the body is exposed to surgical trauma, tumor stimulation and other environments, the number of T lymphocytes will undergo a series of pathological changes. The increase of CD4+/CD8+ratio suggests that the patient's immune function is approaching normal. Kim et al. (19) found that the use of dexmedetomidine in participants undergoing laparoscopic cholecystectomy would promote the transfer of the balance of Th1/ Th2 to Th1 and reduce the level of immune suppression. Dezocine can significantly improve CD4+, CD4+/CD8+ and other indicators in patients with colorectal cancer undergoing radical surgery. The decrease of NK cells marks the decline of the body's innate immune level, which will promote tumor recurrence and metastasis. Dexmedetomidine can not only have a direct effect on NK cells but also promote the killing activity of NK cells by using the norepinephrine release process of nerve endings. There are few studies on the effect of dezocine on NK cells, and no clear mechanism has been formed yet. Consider the influence of T lymphocytes on NK cells at the same time as dezocine. Therefore, compared with fentanyl, dexmedetomidine combined with dezocine can enhance immune function. In addition, the experiment compared the hemodynamic indexes and found that the HR and MAP values of the patients in Group O were superior to Group C at 6h, 12h and 24h after the operation, and the variation was remarkable. The experiment compared the pain degree of participants. The VAS score of patients in Group O was superior to Group C at 6h, 12h and 24h after operation, and the variation between the two groups was remarkable.

Meanwhile, this study found that the use of dexmedetomidine combined with dezocine anesthesia can promote a faster recovery of cognitive function after surgery. This result is similar to that of Ren et al. (20) as an important intelligent process for the body to acquire knowledge and form knowledge, cognitive function is related to the normal physiology of the cerebral cortex. When the structure and function of the cerebral cortex change, the cognitive function of the body will change. For elderly patients, the application of anesthesia technology has the risk of inducing nerve function decline. According to a longitudinal study report, the incidence of cognitive impairment among colorectal cancer survivors is 43%. This study believes that narcotic drugs can induce apoptosis and degeneration of nerve cells, and even cause damage to the nervous system. Dexmedetomidine has been proven to improve postoperative cognitive dysfunction in clinical and animal studies. As an opioid agonist, the mechanism of action of dezocine is similar to that of morphine. It is dose-dependent and can produce pleasant subjective feelings. Animal experiments show that surgery and anesthesia affect the cognitive ability of rats to a certain extent. Dextretomidine plus dezocine can improve memory decline induced by operation and anesthetic, which may be due to a rise in defensive neuroglobulin and norepinephrine in the hippocampus (21). Based on the fact that this research is a clinically controlled study and a single-center study, it is difficult to avoid data bias. In the future, we will further explore the analgesic mechanism and pathway of dexmedetomidine combined with dezocine in elderly cancer patients.

In summary, dexmedetomidine combined with dezocine can enhance the percentage of T lymphocytes and NK cells in elderly participants with gastrointestinal cancer after radical surgery, and also promote the faster recovery of patients' cognitive function.

#### References

- Li Y, Ren N, Zhang B, Yang C, Li A, Li X, Lei Z, Fei L, Fan S, Zhang J. Gastric cancer incidence trends in China and Japan from 1990 to 2019: disentangling age-period-cohort patterns. Cancer 2023; 129(1): 98-106. https://doi. org/10. 1002/cncr. 34511
- Nso N, Nyabera A, Nassar M, Mbome Y, Emmanuel K, Alshamam M, Sumbly V, Guzman L, Shaukat T, Bhangal R, Ojong GA, Radparvar F, Rizzo V, Munira MS. Incidence and risk factors of cardiovascular mortality in patients with gastrointestinal adenocarcinoma. PLoS One 2023; 18(1): e0262013. https://doi. org/10.1371/journal.pone. 0262013
- Sugawara K, Yamashita H, Urabe M, Okumura Y, Yagi K, Aikou S, Seto Y. Geriatric Nutrition Index Influences Survival Outcomes in Gastric Carcinoma Patients Undergoing Radical Surgery. JPEN J Parenter Enteral Nutr 2021; 45(5): 1042-1051. https://doi.org/10.1002/jpen.1978
- Shoka M, Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, Murai T, Asada T, Ishiyama A, Matsushita H, Tanaka C, Kobayashi D, Fujiwara M, Murotani K, Kodera Y. Systemic Inflammation Score as a Predictor of Pneumonia after Radical Resection of Gastric Cancer: Analysis of a Multi-Institutional Dataset. Dig Surg 2020; 37(5): 401-410. https://doi. org/10. 1159/000506940
- Rohan D, Buggy DJ, Crowley S, Ling FK, Gallagher H, Regan C, Moriarty DC. Increased incidence of postoperative cognitive dysfunction 24 hr after minor surgery in the elderly. Can J Anaesth 2005; 52(2): 137-142. https://doi. org/10. 1007/BF03027718
- Sugawara K, Yamashita H, Yajima S, Uemura Y, Okumura Y, Nishida M, Yagi K, Aikou S, Seto Y. Preoperative restrictive pulmonary dysfunction influences the survival after gastrectomy for elderly patients with gastric carcinoma. Surg Today 2020; 50(9): 1065-1073. https://doi. org/10. 1007/s00595-020-01983-y
- 7. Gao C, Tong YX, Zhu L, Dan Zeng CD, Zhang S. Short-term prognostic role of peripheral lymphocyte subsets in patients with

- gastric cancer. Int Immunopharmacol 2023; 115: 109641. https://doi. org/10. 1016/j. intimp. 2022. 109641
- Wang Y, Liu X, Li H. [Incidence of the post-operative cognitive dysfunction in elderly patients with general anesthesia combined with epidural anesthesia and patient-controlled epidural analgesia]. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2016; 41(8): 846-851. Chinese. https://doi. org/10. 11817/j. issn. 1672-7347. 2016.
- Chen W, Qi Z, Fan P, Zhang N, Qian L, Chen C, Huang Y, Jin S. Dexmedetomidine provides type-specific tumour suppression without tumour-enhancing effects in syngeneic murine models. Br J Anaesth 2023; 130(2): 142-153. https://doi. org/10. 1016/j. bja. 2022. 10. 036
- Ding J, Zhu M, Lv H, Zhang J, Chen W. Application Effect of Dexmedetomidine and Dezocine in Patients Undergoing Lung Cancer Surgery under General Anesthesia and Analysis of Their Roles in Recovery Time and Cognitive Function. Comput Math Methods Med 2022; 2022: 9889534. https://doi. org/10. 1155/2022/9889534
- Liu X, Zhang J, Jiang L. Effects of dezocine combined with proposed on cognitive function and complement levels of patients with hysteromyoma undergoing laparoscopic surgery. IJCEM 2020; 13(11): 8746-8755.
- Frid IA, Bershtein MI, Aleksandrin GP, Simonov NN. Vid narkoza i otdalennye rezul'taty khirurgicheskogo lecheniia bol'nykh rakom zheludka [Anesthesia and distant results of surgical treatment in patients with stomach cancer]. Vestn Khir Im I I Grek 1977; 119(12): 95-99. Russian.
- 13. Wang M, Gao P, Ren L, Duan J, Yang S, Wang H, Wang H, Sun J, Gao X, Li B, Li S, Su W. Profiling the peripheral blood T cell receptor repertoires of gastric cancer patients. Front Immunol 2022; 13: 848113. https://doi.org/10.3389/fimmu.2022.848113
- Yuki K. The immunomodulatory mechanism of dexmedetomidine. Int Immunopharmacol 2021; 97: 107709. https://doi.org/10.

- 1016/j. intimp. 2021. 107709
- Wu RS, Wu KC, Huang CC, Chiang YY, Chen CC, Liao CL, Chu CN, Chung JG. Different cellular responses of dexmedetomidine at infected site and peripheral blood of emdotoxemic BALB/c mice. Environ Toxicol 2015; 30(12): 1416-1422. https://doi.org/10.1002/tox.22011
- Zhou ZG, Liu R, Tan HL, Ji XY, Yi XL, Song JF. The application of dexmedetomidine combined with dezocine in thoracoscopic radical resection of lung cancer and its effect on awakening quality of patients. Eur Rev Med Pharmacol Sci 2019; 23(17): 7694-7702. https://doi.org/10.26355/eurrev 201909 18893
- Yu S, Leng Y, Wang Y, Zhao G. A Review of the Biological Mechanisms of Dexmedetomidine for Postoperative Neurocognitive Disorders. Med Sci Monit 2022; 28: e937862. https://doi. org/10. 12659/MSM. 937862
- Dong W, Zhang D, Zhu A, Hu Y, Li W. High Concentration of Dezocine Induces Immune Escape of Lung Cancer and Promotes Glucose Metabolism through Up-Regulating PD-L1 and Activating the NF-κB Pathway. Curr Mol Med 2022; 22(10): 919-928. https://doi. org/10. 2174/1566524022666211222155118
- Kim Y, Kang SH, Hong TH, Cho ML, Han HJ, Kwon SJ, Lee J. Effects of dexmedetomidine on the ratio of T helper 1 to T helper 2 cytokines in patients undergoing laparoscopic cholecystectomy. J Clin Anesth 2014; 26(4): 281-285. https://doi. org/10. 1016/j. jclinane. 2013. 11. 018
- Ren BX, Zong J, Tang JC, Sun DP, Hui X, Li RQ, Zhang JL, Ji Y. Effects of intravenous analgesia with combined dezocine and butorphanol on postoperative cognitive function in elderly patients. Genet Mol Res 2015; 14(2): 5571-5576. https://doi.org/10.4238/2015. May. 25. 8
- Wan Q, Xu L, Bo Y. Effects of Dexmedetomidine combined with Dezocine on cognition function and hippocampal microglia activation of rats. Int J Clin Exp Med 2014; 7(9): 2787-2792.