

Original Article

Impact of propofol epidural anesthesia on immune function and inflammatory factors in patients undergoing gastric cancer surgery

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Received December 9, 2020; Accepted January 21, 2021; Epub April 15, 2021; Published April 30, 2021

Abstract: Objective: To investigate the impact of propofol epidural anesthesia on indexes such as T lymphocytes, NK cells and inflammatory factors in patients undergoing gastric cancer surgery. Methods: Eighty patients undergoing laparoscopic radical gastrectomy were randomly divided into the control group and the observation group, with 40 cases in each group. The control group was given propofol intravenous anesthesia, while the observation group was given propofol epidural anesthesia. The anesthetic indexes, mean arterial pressure (MAP), bispectral index (BIS), level of serum inflammatory mediators, level of T lymphocytes, level of NK cells and safety analysis were observed during anesthesia. Results: The anesthesia onset time, complete block time, time to resume spontaneous breathing and orientation recovery time in the observation group were reduced, and there was a difference compared with the control group ($P < 0.05$). MAP before anesthesia (T0), after tracheal intubation (T1), at 30 min during operation (T2), at 60 min during operation (T3) and at the end of the operation (T4) all had a relatively small overall fluctuation. MAP at T2 and T3 in the observation group was lower than that in the control group ($P < 0.05$). BIS value at T2 and T3 in the observation group was lower than that in the control group ($P < 0.05$). Compared with the control group, the expression of IL-6 and TNF- α in the observation group decreased after tracheal intubation (S1), 1 d after the operation (S2), 3 d after the operation (S3), 5 min after extubation (S4) ($P < 0.05$), while there was no significant difference at other time points ($P > 0.05$). For pairwise comparison within each group, IL-1 β , IL-6 and TNF- α level at S1 and S2 were upregulated compared with those at S0, and IL-1 β , IL-6 and TNF- α level at S3 and S4 were downregulated compared with those at S2 ($P < 0.05$). CD3+ T cells levels at S1, S2, S3 showed a downward trend compared to S0 ($P < 0.05$). Compared with the control group, CD4+ T cells level at S4 increased ($P < 0.05$). CD4+ T cells levels at S3 in the two groups both increased compared with those at S1 and S2, and CD4+ T cells levels at S4 in the two groups both increased compared with those at S1, S2 and S3 ($P < 0.05$). Compared with the control group, CD8+ T cells levels at S3 and S4 in the observation group decreased. CD8+ T cells levels at S1, S2, S3 showed a downward trend compared to S0 ($P < 0.05$), while those at S4 showed an upward trend compared to S1 ($P < 0.05$). Compared with the control group, the CD4+/CD8+ at S4 in the observation group increased ($P < 0.05$). Compared with the control group, NK cells levels at S1-S4 increased ($P < 0.05$), and NK cells levels at S1, S2, S3 showed a downward trend compared to S0 ($P < 0.05$). The incidence of adverse reactions in the observation group was lower than that in the control group ($P < 0.05$). Conclusion: The anesthetic effect of propofol epidural anesthesia was better than that of intravenous anesthesia in patients undergoing gastric cancer surgery. The main performance was that the expression of inflammatory mediators such as IL-1 β , IL-6, TNF- α decreased at different time points before and after anesthesia, the proportion of CD4+ T cells, CD4+/CD8+ and NK cells increased, and the adverse reactions were less, which makes propofol epidural anesthesia worthy of clinical promotion.

Keywords: Gastric cancer, propofol, immune function, inflammatory factors, epidural anesthesia, intravenous anesthesia

Introduction

Gastric cancer is a disease of the digestive system. The pathogenesis is that superficial gastritis

and atrophic gastritis occur in the stomach, and then the lesions metastasize to the intestine and produce epithelial metaplasia, which finally becomes heterogeneous hyperplasia

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and induces cancer [1]. According to epidemiological surveys, gastric cancer is a global disease. In China, the incidence and mortality of gastric cancer continue to increase, with gender and age gaps. Men aged 40 to 60 are the high-risk population [2]. Surgical stress leads to the activation of the immune system, and the secretion of inflammatory cytokines can affect the body's recovery after the operation. Therefore, narcotic drugs and methods should be scientifically selected following the characteristics of the surgery and the patient's own immune function [3]. For patients with autoimmune suppression, narcotic drugs can aggravate the immunosuppressive reaction, resulting in a poor prognosis. Opioids can strongly inhibit cellular and humoral immune function, but local anesthesia can reduce the neuroimmune response and tumor recurrence [4].

Anesthesia is an indispensable part of the surgical treatment of gastric cancer. Intravenous anesthesia acts on nerves through the blood, which makes the patient lose consciousness and the body remain relaxed, ensuring the smooth progress of the operation [5, 6]. Epidural anesthesia is a common anesthesia method, which can block spinal cord nerve transmission, has less influence on hemodynamics and has a long anesthesia duration [7]. Propofol has the characteristics of a quick effect, quick recovery and high safety [8]. Propofol epidural anesthesia suppresses nerve excitation and reduces the vasoconstriction and myocardial excitation by interactive inhibition. Patients can wake up quickly after using propofol as narcotic drugs. Propofol is suitable for use in combination with other anesthetics [9]. Olesen et al. confirmed that propofol epidural anesthesia could accelerate the patients' recovery time after the operation and reduce the dosage of auxiliary anesthesia drugs, which is similar to the conclusion of Li et al. research [10, 11]. However, there is little literature about the impact of propofol epidural anesthesia on immune function and inflammatory factors in patients undergoing gastric cancer surgery. Therefore, the following research is carried out in this paper.

Materials and methods

General information

Eighty patients undergoing laparoscopic radical gastrectomy in our hospital from June 2017 to

June 2019 were enrolled in this study, with a male to female ratio of 52:28 and ages ranging from 50 to 75 years old. The inclusion criteria were: patients' condition was in accordance with the 2013 standardized diagnosis and treatment guidelines for gastric cancer [5]; all patients underwent laparoscopic radical gastrectomy; the subjects were diagnosed by gastroscopy; patients had no cognitive dysfunction and language disability; patients had normal coagulation function. The exclusion criteria were: patients with metabolic diseases; patients with immune system dysfunction or coagulation dysfunction; patients without contraindications for the operation; patients taking sedatives; patients with hypoglycemia; patients disobeying medical orders. The patients were randomly divided into the control group and the observation group, with 40 cases in each group. The control group was given propofol intravenous anesthesia, and the observation group was given propofol epidural anesthesia. All patients and their family members understood the content of this study and had signed the consent form. This study was in line with the ethical provisions of our hospital.

Methods

Thirty minutes before anesthesia, 0.3 mg of atropine (China Resources Double Crane Pharmaceutical Co., Ltd., China) was injected intramuscularly. The venous passage was opened after the MY002-B gas monitor detected the vital signs. A mixture of sodium lactate Ringer's solution (Qingdao Jieshikang Biotechnology Co., Ltd., China) and 6% hydroxyethyl starch (Shanghai Huayasichuang Biotechnology, China) was injected during the operation, with a dose of 10-12 ml/kg/h. Once decreased blood pressure occurred during the operation, 2 mg of dopamine (Shanghai Hefeng Pharmaceutical Co., Ltd., China) was injected. The central venous pressure was measured, according to which the infusion flow rate was controlled. Patients were sent back to the ward after recovery of consciousness.

The anesthesia induction method of the control group. The upper limb vein was opened, and mask oxygen-inspiration for 3 min was conducted. Four minutes after anesthesia with fentanyl (Yichang Renfu Pharmaceutical Co., Ltd., China) (3 µg/kg), midazolam (Yichang Renfu Pharmaceutical Co., Ltd., China) (0.15 mg/kg), atracurium (GlaxoSmithKline Manu-

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facturing S.p.A., Italy) (0.5 mg/kg) and isopropyl chloride (Xi'an Libang Pharmaceutical Co., Ltd., China) (1.5 mg/kg), the intubation was performed. After the position of the endotracheal tube was determined, mechanical ventilation was performed with an anesthesia machine. The oxygen flow was monitored. When the ratio of breath to time reached 1:2, and the partial pressure of carbon dioxide reached 30-35 mmHg, a mini-dose of propofol (3-5 mg/kg/h) was infused to maintain anesthesia. The patient's condition situation was observed, and fentanyl (2 µg/kg) was added if needed.

The anesthesia induction method of the observation group. Patients took a right decubitus position. The epidural puncture was performed between T8 and T9, with a depth of 4 cm, and 1.5% lidocaine (Xi'an Disai Biopharmaceutical Co., Ltd., China) was injected. Tracheal intubation was performed as the control group. A mini-dose of propofol (3-5 mg/kg/h) was infused to maintain anesthesia. Fentanyl (Yichang Renfu Pharmaceutical Co., Ltd., China) (2 µg/kg) was added if needed. After the operation, the tracheal catheter and epidural catheter were pulled out.

Outcome measures

Primary outcome measures: (1) Comparison of the anesthesia effect. The anesthesia onset time, complete block time, time to resume spontaneous breathing and orientation recovery time of the two groups were recorded.

(2) Comparison of the mean arterial pressure (MAP) and bispectral index (BIS). MAP level and BIS scores of the two groups were recorded before anesthesia (T0), after tracheal intubation (T1), at 30 min during operation (T2), at 60 min during operation (T3) and at the end of the operation (T4). After disinfecting the patient's forehead and connecting the BIS motor, BIS was detected by the BIS detector (model: BIS EEG-VISTA, Shanghai Jumu Medical Equipment Co., Ltd., China), and the value was recorded when it became stable.

(3) Analysis of IL-1β, IL-6 and TNF-α level in serum. Two milliliters of venous blood from the elbow were collected from the two groups before anesthesia (S0), after tracheal intubation (S1), 1 d after the operation (S2), 3 d after the operation (S3) and 5 min after extubation

(S4). The blood samples were centrifuged by a high-speed centrifuge (model: AVanti JXN-30/26, Beckman Coulter, USA) with a condition of 4000 r for 10 min. The levels of IL-6, IL-1β and TNF-α were detected by ELISA.

(4) Comparison of the levels of T lymphocytes and NK cells. Two milliliters of peripheral blood from the elbow of the two groups were collected before anesthesia (S0), after tracheal intubation (S1), 1 d after the operation (S2), 3 d after the operation (S3) and 5 min after extubation (S4). The blood samples were anticoagulated and put into sterile EP tubes, and one volume of PBS was added to dilute the blood. The lymphocyte concentration was adjusted to 2×10^6 in DMEM medium (Youkang Hengye Biotechnology (Beijing) Co., Ltd., China). After standing for 30 min, anti-CD3+, CD4+, CD8+, CD4/CD8+ antibodies (Abcam, China) and anti-killer cells (NK cells) antibodies (Shanghai Jingkang Bioengineering Co., Ltd., China) were added, and the samples were left to stand for 20 min. The samples were then centrifuged, washed twice with PBS buffer and analyzed by flow cytometry (Navios, Beckman Coulter, USA).

Secondary outcome measures: Adverse reactions after anesthesia. The occurrence of shivering, nausea, vomiting and other adverse reactions were monitored after the operation, and the incidence was calculated.

Statistical analysis

All data were analyzed by SPSS 23.0 software. The enumeration data were expressed as (n (%)) and analyzed by the χ^2 test. The measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm sd$). Comparison between multiple time points was conducted by the repeated measurement ANOVA. Comparison between the two groups was conducted by independent-samples t-test. $P < 0.05$ was considered significantly different.

Results

Comparison of general information between the two groups

Gender, average age, average weight, pathological type (signet ring cell carcinoma and mucinous adenocarcinoma), degree of differen-

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Table 1. General information (n, $\bar{x} \pm sd$)

Factor	Observation group (n=40)	Control group (n=40)	χ^2/t	P
Gender			0.897	0.644
Male	28	24		
Female	12	16		
Average age (year)	65.4 \pm 7.2	66.3 \pm 6.9	0.539	0.595
Average weight (kg)	58.5 \pm 9.0	58.0 \pm 10.2	0.218	0.829
Pathological type			0.208	0.901
Signet ring cell carcinoma	25	23		
Mucinous adenocarcinoma	15	17		
Degree of differentiation			0.739	0.691
Well differentiated	22	20		
Moderately differentiated	12	11		
Poorly differentiated	6	9		
Lesion site			0.251	0.882
Stomach	30	28		
Fundus of stomach	10	12		

Table 2. Comparison of the anesthesia effect between the two groups ($\bar{x} \pm sd$)

Group	n	Anesthesia onset time (min)	Complete block time (min)	Time to resume spontaneous breathing (min)	Orientation recovery time (min)
Observation group	40	1.86 \pm 0.50	1.30 \pm 0.45	5.05 \pm 2.11	15.60 \pm 4.55
Control group	40	2.45 \pm 1.05	1.69 \pm 0.62	6.20 \pm 2.10	20.30 \pm 2.14
T		3.001	3.012	2.280	5.530
P		0.004	0.003	0.025	0.001

tiation (well differentiated, moderately differentiated and poorly differentiated) and lesion site (gastric body and gastric fundus) of the two groups had no significant difference ($P>0.05$). See **Table 1**.

Comparison of the anesthesia effect between the two groups

Compared with the control group, the anesthesia onset time, complete block time, time to resume spontaneous breathing and orientation recovery time of the observation group were significantly shorter ($P<0.05$). See **Table 2**.

Comparison of MAP and BIS between the two groups

Compared with the control group, the MAP levels of the observation group at T2 and T3 decreased ($P<0.05$), and there were significant differences between T1 and T0, T2 and T1, T3 and T2, T4 and T3 within each group ($P<0.05$). Compared with the control group, the BIS values of the observation group at T2 and T3 were

lower ($P<0.05$), and there were significant differences between T1, T2, T3, T4 and T0 within each group ($P<0.05$). See **Table 3** and **Figure 1**.

Comparison of the levels of IL-1 β , IL-6, TNF- α in serum between the two groups

Compared with the control group, the expression of IL-1 β at S1, S2, S3 and S4 in the observation group was significantly decreased, and the expression of IL-6 and TNF- α at S1, S2, S3 and S4 was downregulated (all $P<0.05$), and there was no difference at other time points ($P>0.05$). For comparison within each group, IL-1 β , IL-6, TNF- α at S1 and S2 were upregulated compared with S0, and IL-1 β , IL-6, TNF- α at S3 and S4 were downregulated compared with S2 ($P<0.05$). See **Table 4** and **Figure 2**.

Comparison of the levels of T lymphocytes and NK cells in serum between the two groups

In the level of CD3+ T cells, there was no difference at S0~S4 between the two groups ($P>0.05$). For comparison within each group,

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Table 3. Comparison of MAP and BIS during anesthesia ($\bar{x} \pm sd$)

Time	MAP (mmHg)		BIS	
	Observation group	Control group	Observation group	Control group
T0	90.50±8.90	89.60±9.11	92.30±2.11	93.10±1.90
T1	80.51±7.20 ^Δ	78.64±8.42 ^{Δ,a}	47.61±3.12 ^Δ	48.61±2.42 ^Δ
T2	80.10±8.81 ^{Δ,#,*}	83.20±9.21 ^{Δ,#}	46.23±3.11 ^{Δ,***}	54.14±2.23 ^Δ
T3	84.24±9.23 ^{Δ,#,a,*}	88.60±9.40 ^{Δ,#,a}	47.20±2.70 ^{Δ,***}	52.10±2.40 ^Δ
T4	81.22±7.70 ^{Δ,#,a,b}	81.00±8.10 ^{Δ,#,a,b}	51.30±3.20 ^Δ	50.60±3.50 ^Δ
F	9.202	10.160	157.800	191.600
P	<0.001	<0.001	<0.001	<0.001

Note: Compared with the control group, *P<0.05, ***P<0.001. For comparison within each group: compared with T0, ^ΔP<0.05; compared with T1, [#]P<0.05; compared with T2, ^aP<0.05; compared with T3, ^bP<0.05. MAP: mean arterial pressure; BIS: bispectral index.

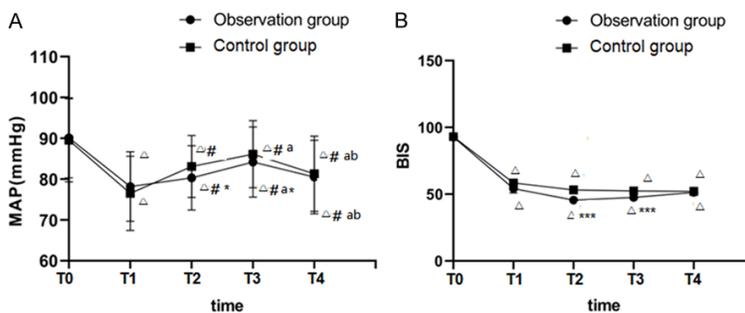


Figure 1. Comparison of MAP and BIS during anesthesia. A: Comparison of MAP; B: Comparison of BIS. Compared with the control group, *P<0.05, ***P<0.001. For comparison within each group: compared with T0, ^ΔP<0.05; compared with T1, [#]P<0.05; compared with T2, ^aP<0.05; compared with T3, ^bP<0.05. T0, before anesthesia; T1, after tracheal intubation; T2, at 30 min during operation; T3, at 60 min during operation; T4, at the end of operation. MAP: mean arterial pressure; BIS: bispectral index.

the levels at S1~S3 showed a downward trend compared to S0 (P<0.05), and there was no difference between S4 and S0 (P>0.05). In the level of CD4+ T cells, there was no difference at S0~S3 between the two groups (P>0.05). Compared with the control group, the level at S4 increased in the observation group (P<0.05). For comparison within each group, the levels at S3 were higher than those at S1 and S2, and the levels at S4 were higher than those at S1~S3 (P<0.05). In the level of CD8+ T cells, compared with the control group, the levels at S3 and S4 were lower in the observation group (P<0.05). For comparison within each group, the levels at S1~S3 showed a downward trend compared to S0 (P<0.05), and the levels at S4 showed an upward trend compared to S1 (P<0.05). In the CD4+/CD8+ ratio, there was no difference at S0~S3 between the two groups (P>0.05). Compared with the control group, the

ratio at S4 increased in the observation group (P<0.05). For the level of NK cells, there was no difference at S0 between the two groups (P>0.05). Compared with the control group, the levels at S1~S4 increased in the observation group (P<0.05). For comparison within each group, the levels at S1~S3 showed a downward trend compared to S0 (P<0.05), and there was a difference between the levels at S4 and S0 (P<0.05). See **Tables 5, 6** and **Figure 3**.

Safety analysis of the two groups of patients

The incidence of shivering, respiratory depression and other events in the observation group was 11 cases (27.50%), which was lower than that of the control group (40.00%). There was a significant difference between the two groups (P<0.05). See **Table 7**.

Discussion

Blood pressure changes in patients with gastric cancer during surgery. The increase of blood pressure in patients using intravenous general anesthesia is related to the blood flow limitation in the distal abdominal aorta. The rise of blood pressure in patients with gastric cancer can be accelerated 5 minutes after the start of surgery [11]. MAP refers to the body's average arterial pressure. After epidural anesthesia, the

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Table 4. Analysis of levels of IL-1 β , IL-6, TNF- α in serum ($\bar{x} \pm sd$)

Time	IL-1 β (pg/mL)		IL-6 (pg/mL)		TNF- α (pg/mL)	
	Observation group	Control group	Observation group	Control group	Observation group	Control group
S0	10.66 \pm 5.68	10.25 \pm 6.18	45.50 \pm 10.23	46.30 \pm 10.14	14.22 \pm 3.36	13.60 \pm 4.01
S1	17.21 \pm 5.14 ^{Δ,*}	21.05 \pm 8.14 ^Δ	118.60 \pm 20.15 ^{Δ,***}	175.67 \pm 21.56 ^Δ	20.33 \pm 7.17 ^{Δ,***}	30.51 \pm 8.14 ^Δ
S2	16.20 \pm 5.56 ^{Δ,***}	19.32 \pm 6.02 ^Δ	65.23 \pm 11.20 ^{Δ,#,***}	89.63 \pm 15.30 ^{Δ,#}	17.22 \pm 5.41 ^{Δ,***}	25.87 \pm 6.22 ^{Δ,#}
S3	11.23 \pm 3.35 ^{#,a,***}	14.36 \pm 4.25 ^{#,a}	35.20 \pm 8.02 ^{#,a,***}	66.33 \pm 9.20 ^{#,a}	16.21 \pm 5.05 ^{#,a,***}	23.20 \pm 6.14 ^{#,a}
S4	10.70 \pm 3.15 ^{#,a,***}	13.20 \pm 3.80 ^{#,a}	21.35 \pm 6.16 ^{#,a,**,b}	50.14 \pm 7.21 ^{a,b}	14.33 \pm 4.11 ^{#,a,**,b}	17.04 \pm 3.69 ^{#,a}
F	19.770	22.940	388.700	602.200	9.367	53.380
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: Before anesthesia (S0), after tracheal intubation (S1), 1 d after operation (S2), 3 d after operation (S3), 5 min after extubation (S4). Compared with the control group, *P<0.05, **P<0.01, ***P<0.001. For comparison within each group: compared with S0, ^ΔP<0.05; compared with S1, [#]P<0.05; compared with S2, ^aP<0.05; compared with S3, ^bP<0.05.

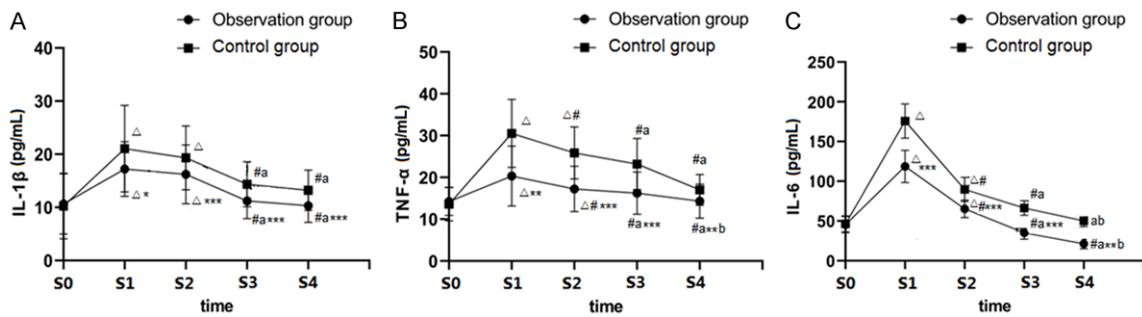


Figure 2. Comparison of levels of IL-1 β , IL-6, TNF- α in serum between the two groups. A: Comparison of IL-1 β ; B: Comparison of TNF- α ; C: Comparison of IL-6. Compared with the control group, *P<0.05, **P<0.01, ***P<0.001. For comparison within each group: compared with S0, ^ΔP<0.05; compared with S1, [#]P<0.05; compared with S2, ^aP<0.05; compared with S3, ^bP<0.05. S0, before anesthesia; S1, after tracheal intubation; S2, 1 d after operation; S3, 3 d after operation; S4, 5 min after extubation.

Table 5. Comparison of levels of CD3+ and CD4+ T cells in serum ($\bar{x} \pm sd$)

Time	CD3+		CD4+	
	Observation group	Control group	Observation group	Control group
S0	61.05 \pm 5.44	60.85 \pm 5.67	39.22 \pm 3.78	38.95 \pm 4.11
S1	48.15 \pm 5.40 ^Δ	47.69 \pm 5.51 ^Δ	29.01 \pm 4.11 ^Δ	28.47 \pm 4.60 ^Δ
S2	50.11 \pm 5.23 ^Δ	49.62 \pm 7.63 ^Δ	31.66 \pm 4.33 ^Δ	30.75 \pm 5.14 ^Δ
S3	52.63 \pm 3.61 ^{Δ,#}	51.39 \pm 6.35 ^{Δ,#}	35.20 \pm 3.78 ^{Δ,#,a}	32.96 \pm 5.60 ^{Δ,#,a}
S4	60.10 \pm 3.81 ^{#,a}	60.48 \pm 4.02 ^{#,a,b}	39.20 \pm 3.35 ^{#,a,b,*}	35.63 \pm 4.06 ^{#,a,b}
F	60.410	44.620	54.630	29.950
P	<0.001	<0.001	<0.001	<0.001

Note: Before anesthesia (S0), after tracheal intubation (S1), 1 d after operation (S2), 3 d after operation (S3), 5 min after extubation (S4). Compared with the control group, *P<0.05. For comparison within each group: compared with S0, ^ΔP<0.05; compared with S1, [#]P<0.05; compared with S2, ^aP<0.05; compared with S3, ^bP<0.05.

sympathetic nerve block leads to a decrease of myocardial blood volume and blood pressure [12]. This study confirmed that propofol epidural anesthesia can stabilize the level of MAP in patients. The mechanism may be related to reduced cardiac stress and decreased blood

pressure caused by epidural block. BIS is an important index to evaluate the cerebral cortex's function by using the digital processing results of EEG. BIS can directly and accurately reflect the depth of anesthesia in patients undergoing gastric cancer surgery, which helps

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Table 6. Comparison of levels of CD8+ T cells, CD4+/CD8+ and NK cells in serum ($\bar{x} \pm sd$)

Time	CD8+		CD4+/CD8+		NK cells	
	Observation group	Control group	Observation group	Control group	Observation group	Control group
S0	24.80±2.02	25.10±1.95	1.52±0.35	1.57±0.30	20.14±5.68	19.41±6.60
S1	20.66±1.58 ^Δ	20.93±1.44 ^Δ	1.36±0.28	1.44±0.30	17.02±6.55 ^{Δ,**}	13.02±6.14 ^Δ
S2	21.50±0.98 ^{Δ,*}	21.06±0.87 ^Δ	1.47±0.21	1.43±0.35	16.11±6.20 ^{Δ,**}	12.70±5.51 ^Δ
S3	22.51±0.56 ^{Δ,***}	23.17±0.61 ^Δ	1.52±0.22	1.49±0.31	18.20±6.11 ^{Δ,**}	15.71±6.22 ^Δ
S4	24.17±1.25 ^{Δ,*,#}	25.10±1.60 [#]	1.65±0.28 ^{**}	1.48±0.31	19.77±6.50 ^{Δ,*}	17.25±5.10 ^Δ
F	64.830	88.190	5.880	1.241	3.100	10.090
P	<0.001	<0.001	<0.001	0.295	0.017	<0.001

Note: Before anesthesia (S0), after tracheal intubation (S1), 1 d after operation (S2), 3 d after operation (S3), 5 min after extubation (S4). Compared with the control group, *P<0.05, **P<0.01, ***P<0.001. For comparison within each group: compared with S0, ^ΔP<0.05; compared with S1, [#]P<0.05.

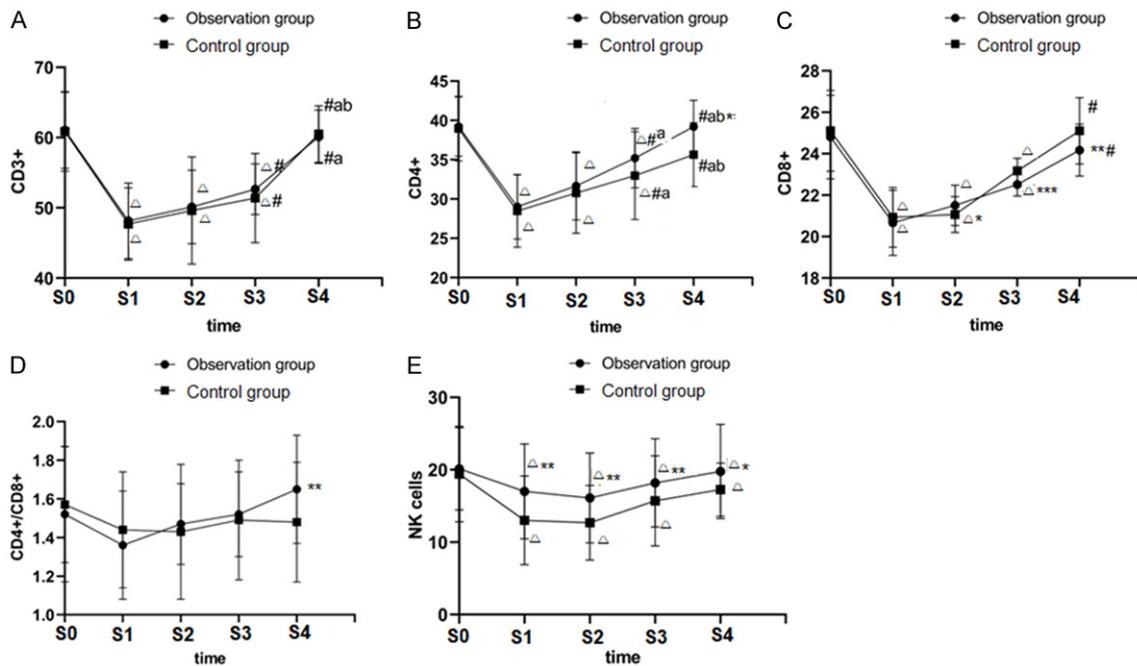


Figure 3. Comparison of levels T lymphocytes and NK cells in serum between the two groups. A: Comparison of CD3+ T cells; B: Comparison of CD4+ T cells; C: Comparison of CD8+ T cells; D: Comparison of CD4+/CD8+; E: Comparison of NK cells. Compared with the control group, *P<0.05, **P<0.01, ***P<0.001. For comparison within each group: compared with S0, ^ΔP<0.05; compared with S1, [#]P<0.05; compared with S2, ^ΔP<0.05; compared with S3, ^ΔP<0.05. S0, before anesthesia; S1, after tracheal intubation; S2, 1 d after operation; S3, 3 d after operation; S4, 5 min after extubation.

control the dosage of narcotic drugs and accelerate postoperative recovery of patients [13]. Propofol can reduce the BIS scores and has a certain degree of sedative effect [14]. Xia Z et al. confirmed that propofol epidural anesthesia can promote patients to quickly enter the anesthesia state, which showed a concentration-dependent effect, and it had a good anesthetic effect similar to intravenous anesthesia [15]. Epidural anesthesia can effectively control the depth of anesthesia, promote the rapid onset

of propofol anesthesia and, at the same time, stabilize blood pressure [16]. In this study, after epidural anesthesia with propofol, the BIS at T2 and T3 in the observation group was lower than that in the control group, indicating that propofol epidural anesthesia has a fast sedative speed.

The expression of IL-1 β and IL-6 was upregulated after surgical trauma. A stress reaction occurs in postoperative gastric cancer patients,

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Table 7. Safety analysis of the two groups of patients (n (%))

Group	n	Chills	Respiratory depression	Feeling sick and vomit	Incidence rate (%)
Observation group	40	4 (10.00)	1 (2.50)	6 (15.00)	11 (27.50)
Control group	40	6 (15.00)	3 (7.50)	7 (17.50)	16 (40.00)
χ^2			0.571		4.512
P			0.752		0.030

which can accelerate the expression of serum IL-1 β and IL-6. TNF- α is an inflammatory mediator that can regulate immune function. The expression of TNF- α is upregulated in perioperative period, resulting in the secretion of a variety of inflammatory mediators to infiltrate gastric tissues and induce injury. Propofol has an effect of inhibiting the release of inflammatory mediators, reducing inflammatory cells and mediating the chemotaxis of granulocytes [17]. Epidural anesthesia can effectively reduce the stress response of patients with gastric cancer during perioperative period and reduce the expression of serum TNF- α in postoperative patients [18]. Yan et al. found that the expression of IL-1 β and IL-6 was downregulated after epidural anesthesia with propofol, which was related to the upregulation of NK cellular activity [19]. In this study, the expression of serum inflammatory mediators in the observation group was lower than that in the control group, indicating that propofol epidural anesthesia can reduce the reaction of serum inflammatory mediators and accelerate recovery.

Patients with gastric cancer have low immune function and disorders of inflammatory mediators. Surgical trauma will increase the body's excessive stress, reduce the patient's immune function, and accelerate the reaction of inflammatory mediators [20]. T lymphocytes mainly include CD3+, CD4+, CD8+ T cells. CD3+ T cells are all mature T cells in the peripheral system. CD4+ T cells activate B cells, and B cells can regulate the body's anti-injury effect in many ways [21]. When an immune response occurs, CD8+ T cells will play a toxic role in target cells, promote the increase of immunosuppressive factors, weaken the level of immune response and have an effect of blocking CD4+ T cells. The CD4+/CD8+ ratio directly reflects the body's ability to regulate the immune response. When the immune balance is destroyed, the ratio of CD4+/CD8+ decreases. NK cells are cells in the immune system that have the effect

of destroying pathogens and have anti-tumor effects [22]. In the serum of patients with gastric cancer, the number of B cells and NK cells decreases, and the body's immune system is damaged [23]. Compared with general anesthesia, epidural anesthesia can

effectively reduce the perioperative immune suppression and reduce the body stress response. Meanwhile, deep anesthesia has less impact on patients' immune function, and the stress response is lighter [24]. Epidural anesthesia can block the noxious stimulation input during operation, while intravenous anesthesia can only inhibit the signal input from the hypothalamus to the cerebral cortex, reducing patients' immune function [25]. Yuan et al. confirmed that intravenous anesthesia could decrease the number of NK cells, which was conducive to the spread of cancer cells after surgery, while epidural anesthesia could effectively upregulate the activity of NK cells [26]. In this study, the levels of T lymphocytes and NK cells in the observation group were higher than those in the control group, indicating that propofol epidural anesthesia can reduce the damage of anesthetic drugs on immune function. The adverse reactions of the two groups were analyzed. Patients in the observation group, who were given propofol epidural anesthesia, maintained a better sedative effect, and the occurrence of shivering was reduced.

Due to the limited time, the sample size in this study is small, and the experimental results are unitary. In the later stage, our research group will strengthen the cooperation with other related research units, increase the sample size, refine the experimental content, and provide a reference for the clinical perioperative anesthesia effect of gastric cancer.

In conclusion, the anesthetic effect of propofol epidural anesthesia is better than that of intravenous anesthesia in patients undergoing gastric cancer surgery, which is mainly manifested by the decreased expression of inflammatory mediators IL-1 β , IL-6 and TNF- α , the increased proportion of CD4+ T cells and NK cells, and a high ratio of CD4+/CD8+ at different time points before and after anesthesia. Propofol epidural anesthesia has high safety and is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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References

- [1] Miyauchi W, Shishido Y, Kono Y, Murakami Y, Kuroda H, Fukumoto Y, Osaki T, Sakamoto T, Honjo S, Ashida K, Saito H and Fujiwara Y. Less invasive surgery for remnant stomach cancer after esophago-proximal gastrectomy with ICG-guided blood flow evaluation: a case report. *Yonago Acta Med* 2018; 61: 187-191.
- [2] Wang Y, Li Z, Jin C, Ying X, Gao C, Wang Y, Xiao Q, Zhang Y, Chen Y, Zhang L and Ji J. Clinicopathological characteristics and prognostic factor analysis of carcinoma in remnant stomach cancer at Peking University Cancer Hospital. *Zhonghua Wei Chang Wai Ke Za Zhi* 2018; 21: 522-528.
- [3] Lin JX, Huang YQ, Xie JW, Wang JB, Lu J, Chen QY, Cao LL, Lin M, Tu R, Huang ZN, Lin JL, Zheng CH, Huang CM and Li P. Association of the age-adjusted charlson comorbidity index and systemic inflammation with survival in gastric cancer patients after radical gastrectomy. *Eur J Surg Oncol* 2019; 45: 2465-2472.
- [4] Elgebaly AS and Sabry M. Sedation effects by dexmedetomidine versus propofol in decreasing duration of mechanical ventilation after open heart surgery. *Ann Card Anaesth* 2018; 21: 235-242.
- [5] Liu L, Yang B, Zhang H, Yang W and Zhang F. Evaluation of propofol and sevoflurane in early post-operative cognitive function and memory in patients undergoing laparoscopic cholecystectomy. *J Kunming Med Univ* 2019; 40: 96-100.
- [6] Videnovic N, Mladenovic J, Pavlovic A, Trpkovic S, Filipovic M, Markovic N and Stojkovic M. Analysis of the applied technique of intravenous anesthesia for in vitro fertilization in obese and patients with normal body mass index. *Srp Arh Celok Lek* 2019; 147: 588-594.
- [7] Fukumoto K, Jo T, Yasunaga H and Nakajima J. P1.17-38 does use of epidural anesthesia affects survival of resectable NSCLC? Analysis from a Japanese nationwide database. *J Thorac Oncol* 2019; 14: S622-S623.
- [8] Li M, Qu L, Chen F and Zhu X. Propofol upregulates miR-320a and reduces HMGB1 by down-regulating ANRIL to inhibit PTC cell malignant behaviors. *Pathol Res Pract* 2020; 216: 152856.
- [9] Guan J and Chang W. Application effects of propofol combined with lidocaine for intravenous anesthesia in neurosurgery and its influences on hemodynamics. *Eval Anal Drug Use Hosp Chin* 2018; 18: 910-912, 914.
- [10] Olesen ND, Frederiksen HJ, Storkholm JH, Hansen CP, Svendsen LB, Olsen NV and Secher NH. Internal carotid artery blood flow is enhanced by elevating blood pressure during combined propofol-remifentanyl and thoracic epidural anaesthesia: a randomised crossover trial. *Eur J Anaesthesiol* 2020; 37: 482-490.
- [11] Li X and Wang L. Effect of external abdominal aorta compression on circulation during anesthesia induction in elderly patients. *Chin Crit Care Med* 2017; 29: 629-632.
- [12] Liu B and Jia K. Effect of propofol on lower respiratory tract infection and immune function after radical gastrectomy for gastric cancer. *Chin J Curr Adv Gen Surg* 2020; 23: 237-239.
- [13] Dang X, He Y and Lai B. Efficacy of bispectral index-monitored closed-loop targeted-controlled infusion of propofol for laparoscopic radical operation for gastric cancer. *J Hainan Med Univ* 2019; 25: 54-57.
- [14] Liu C, Mou J, Qin A, Wu S and Tan Z. Observe epidural anesthesia blocks the composite rachel fentanyl and propofol used for cutting chest operation is fast channel anesthesia clinical application effect. *Chin J Med Guide* 2012; 14: 1771-1772.
- [15] Zheng X, Lv Z, Yin K and Peng M. Effects of epidural anesthesia combined with inhalation anesthesia or intravenous anesthesia on intrapulmonary shunt and oxygenation in patients undergoing long term single lung ventilation. *Pak J Med Sci* 2018; 34: 799-803.
- [16] Liu P. Effect of epidural anesthesia combined with tracheal intubation general anesthesia on postoperative extubation blood pressure and heart rate in elderly patients with rectal cancer. *Henan Med Res* 2020; 29: 70-71.
- [17] Lu Y, Atkins SJ, Fernando R, Trierweiler A, Messter T, Grisolia ABD, Mou P, Novaes P and Smith TJ. CD34+ orbital fibroblasts from patients with thyroid-associated ophthalmopathy modulate TNF- α expression in CD34+ fibroblasts and fibrocytes. *Invest Ophthalmol Vis Sci* 2018; 59: 2615-2622.
- [18] Yi S, Zhang X, Zhou Y, Wang Y and You X. Effect of general anesthesia combined with epidural anesthesia on stress response, inflammatory reaction and coagulation in patients with colon cancer. *J Hainan Med Univ* 2018; 24: 1678-1682.

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- [19] Yan J, Yu J and Zhao S. Effects of epidural anesthesia combined with general anesthesia on inflammation, stress response and complications in patients undergoing radical gastrectomy for gastric cancer. *Mod Dig Interv* 2018; 23: 615-617.
- [20] Zhao J and Mo H. The Impact of different anesthesia methods on stress reaction and immune function of the patients with gastric cancer during peri-operative period. *J Med Assoc Thai* 2015; 98: 568-573.
- [21] Jiang C, Cai X, Zhang H, Xia X, Zhang B and Xia L. Activity and immune correlates of a programmed death-1 blockade antibody in the treatment of refractory solid tumors. *J Cancer* 2018; 9: 205-212.
- [22] Zhang H, Dai X, Guo W and Zeng S. Analyze the changes of lymphocyte subgroups and expression of cytokines in gastric cancer tissues. *Anat Res* 2018; 40: 100-103.
- [23] Liu H, Zhang N, Song X, LI Y and Ma X. Effects of epidural anesthesia, general anesthesia and depth of anesthesia on the immune function and stress response of patients with cervical cancer during perioperative period. *Chin J Hum Sex* 2020; 29: 33-37.
- [24] Goh M, Lim ZM, Koh V, Lum J, Zhang X, McGovern N, Msallam R, Larbi A, Poidinger M, Ginhoux F, Ng MCH, Tan P, Yong WP, So JBY and Chen J. Single-cell analysis of immune-microenvironment and immune-tumor interaction in human gastric cancers. *J Clin Oncol* 2019; 37: 29.
- [25] Sun L. Effects of different analgesia methods on the visual analog scale of patients with esophageal cancer. *Hebei Med J* 2008; 30: 204-205.
- [26] Yuan X, Qu P, Fang J, Cai S and Fu S. Effect of epidural anesthesia on the immune function of patients with non-small cell lung cancer. *Int J Pharmacol* 2018; 14: 826-834.