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Original Article

Effect of ultrasound-guided stellate ganglion block on lung protection for patients undergoing one-lung ventilation

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Abstract: Objective: To explore the potential effect of ultrasound-guided stellate ganglion block (SGB) on lung protection for patients undergoing one-lung ventilation (OLV). Methods: A total of 123 patients undergoing elective one-lung ventilation surgery were selected as research subjects in this prospective study. These patients were randomly divided into the SGB group, control group and blank group on average. Stellate ganglion block was carried out in the SGB and control groups. Patients in the SGB group were injected with 6 ml mixture of 0.25% ropivacaine hydrochloride and 1% lidocaine hydrochloride, while those in the control group were injected with 6 mL of 0.9% saline. Punctures weren't performed for patients in the blank group. The same induction and maintenance of general anesthesia was adopted for all three groups. Hemodynamics, respiratory parameters and arterial blood gas analysis were recorded after entering the operation room (T0), pre-OLV (T1), 30 min after OLV (T2), 60 min after OLV (T3), at the end of surgery (T4), and 30 min after extubation (T5). Oxygenation index (OI), pulmonary shunt fraction (Qs/Qt) and pH value were compared at different time points. Intravenous serum was collected at T0, T3 and T5 for the detection of surfactant proteins A (SP-A), superoxide dismutase (SOD), malondialdehyde (MDA), interleukin-6 (IL-6) and interleukin-10 (IL-10) levels, respectively. The complications related to SGB after surgery and the postoperative pulmonary complications within 72 h were recorded. Results: At T1, T2, and T3, MAP level in SGB group was lower than that in blank and control groups ($P<0.05$). At T2, and T3, SGB group had lower hear rate (HR), peak airway pressure (P_{peak}) and tidal volume (TV) than blank and control groups (all $P<0.05$). From T2 to T5, SGB group had higher OI but lower Qs/Qt than blank and control groups (both $P<0.05$). At T3 and T5, SGB group had lower SP-A, IL-6, and MDA levels but higher IL-10 and SOD levels than blank and control groups (all $P<0.05$). There was one case of hypoxemia in the blank group within 72 h after surgery. Conclusion: Ultrasound-guided SGB has lung-protective effects on patients undergoing OLV, which significantly improves patients' OI, reduces intrapulmonary shunts, declines ventilator-induced lung damage, and inhibits inflammatory response as well as oxidative stress (China Clinical Trial Registry, registration number ChiCTR2000033385, https://www.chictr.org.cn).

Keywords: Stellate ganglion block, one-lung ventilation, lung protection, inflammatory response, oxidative stress

Introduction

With the development of thoracoscopic surgery with a minimally invasive approach to the chest, the application of one-lung ventilation (OLV) technology is increasingly frequent in thoracoscopic surgery. OLV, a significant part of modern anesthesia, is widely used in clinical practice [1]. The use of OLV during anesthesia provides the surgeon with a clearer surgical field of vision, a broader operating space, and reduces the damage caused by the traction compression of lung tissue. Besides, effective OLV management isolates the affected lung from the healthy lung and prevents the spread of polluted lesions to the healthy lungs [2]. Thus, in thoracic surgery, OLV has become the most important anesthesia management. However, OLV can easily cause lung tissue cells to release inflammatory mediators, proinflammatory cytokines and anti-inflammatory cytokines, resulting in an imbalance of lung tissue oxidation and

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anti-oxidation, thereby causing mechanical ventilator-related lung injuries and increasing the incidence of postoperative pulmonary complications [3-5]. Changes in the interstitium, alveolar epithelium, capillary endothelium, and extracellular matrix induced by OLV lasting more than 2 h results in acute lung injury (ALI) [6]. How to minimize lung injury caused by OLV has always been the focus of clinical anesthesiologists. The stellate ganglion (SG) is the largest sympathetic ganglion formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion. The main postganglionic fibers from the SG are distributed in the upper limbs, head and neck blood vessels, glands and muscles, etc. The sympathetic nerve fibers are involved in forming the heart plexus and regulating the activity of the heart and blood vessels. In recent years, stellate ganglion block (SGB) has been used in the treatment of a variety of clinical diseases, including chronic pain, neurological, endocrine and immunological disorders. SGB can protect the lungs through many mechanisms. SGB regulates the body's immune function by acting on the hypothalamic-pituitary-epinephrine axis, thereby inhibiting the activity of monocyte-macrophages, epithelial cells and mesenchymal cells, reducing the synthesis of pro-inflammatory factors, and increasing the number and activity of T cells, increasing the release of anti-inflammatory factors and exerting a certain anti-inflammatory effect [7]. SGB effectively inhibits the oxidation reaction, reduces malondialdehyde (MDA) level, increases superoxide dismutase (SOD) activity, enhances the body's ability to scavenge free radicals, reduces free radical damage, and plays an antioxidant role. All these may be related to the fact that after SGB, blood vessels dilate, blood flow increases, and tissue metabolites are easily and quickly transported, reducing tissue damage caused by inflammatory responses and oxidative stress [8]. SGB reduces nerve apoptosis by upregulating Bcl-2, which appears to be associated with inhibition of hypothalamic-pituitary-adrenal overactivity and reduced catecholamine release by inhibiting sympathetic nervous system overactivity [9]. SGB regulates the vasomotion of pulmonary blood vessels by regulating the content of vasomotor factor nitric oxide (NO), reducing the decrease of Oxygenation index (OI), and exerting a certain lung protective effect [10]. SGB is effective in improving lung function by regulating autonomic homeostasis via inhibiting excessive sympathetic nervous system activity, which may be related to SGB decreasing norepinephrine plasma concentrations [11, 12]. However, the current study of the lung-protective effect of SGB in OLV mainly relies on animal experiments [13]. More clinical evidence is needed to be confirmed whether SGB plays a lung-protective role in patients receiving OLV through the above mechanisms in the process of clinical anesthesia and surgery.

Therefore, by observing the changes in hemodynamics, blood gas analysis, inflammatory response and oxidative stress, this study explored the lung protective effect of ultrasound-guided SGB on patients with OLV, with a view to providing a useful reference for the lung protection of patients undergoing OLV.

Materials and methods

General data

This prospective, single-center, and single-blind randomized controlled study had been reviewed and approved by the Ethics Committee of Suzhou Hospital Affiliated to Nanjing Medical University (No. SZSLYY-2021-01-006). A total of 123 patients undergoing elective surgery with OLV in Suzhou Hospital Affiliated to Nanjing Medical University from January 2021 to April 2022, were randomly enrolled in this study. All included patients and their families voluntarily signed informed consent forms and gave informed consent for anesthesia.

Inclusion criteria: (1) Patients aged from 18 to 75 years old. (2) Patients' body mass index was between 18.0 and 25.0 kg/m^2. (3) Patients were classified in the American Society of Anesthesiologists I-III. (4) Patients had 2-4 h OLV time during surgery.

Exclusion criteria: (1) Patients who had contraindications to SGB punctures, such as infection, scarring, or a history of traumatic surgery at the site of the puncture. (2) Patients who had bleeding tendency, myasthenia gravis, hyperthyroidism, hypothyroidism, emphysema, or atelectasis before surgery. (3) Patients who had preoperative anemia, fever, lung infection, etc. (4) Patients who had tumors in other areas and had a history of radiotherapy, chemotherapy, and open chest surgery before surgery. (5)

Patients who had liver and renal insufficiency before surgery.

Exemption criteria: (1) Patients who had bad SGB effects. (2) Patients who had massive intraoperative bleeding. (3) Patients who had OLV time <2 h or >4 h during surgery. (4) Serious adverse events occurred during the trial. (5) Patients who had hospital stays after surgery <3 d. (6) Patients requested to withdraw from the research. (7) Other unforeseen circumstances.

Methods

Grouping

All included participants were divided into the SGB, control and blank groups according to a random number table, with 41 cases in each group.

Ten minutes before induction of anesthesia, ultrasound-guided SGB was performed on the ipsilateral side of the operated lung under sufficient sedation. A mixture of 6 mL of 0.25% ropivacaine hydrochloride plus 1% lidocaine hydrochloride was injected for patients in the SGB group. Before the induction of anesthesia, ultrasound-guided puncture was performed on the ipsilateral side of the operated lung under sufficient sedation, and 6 ml of 0.9% saline (to exclude false positive results due to puncture needle stimulation of SG) was injected for patients in the control group. Puncture wasn't performed for patients in the blank group. The same induction and maintenance of general anesthesia was adopted for all three groups. OLV was carried out after induction of anesthesia and intubation. In addition, lung-protective ventilation strategies were used to maintain anesthesia ventilation during surgery.

Anesthesia methods

Patients were given a preoperative visit 1 d before surgery. The basic information and previous relevant medical history of the patients were recorded in detail. Whether they met the above inclusion criteria was carefully checked, and the patients who failed to meet the requirements were excluded. Patients were asked to abstain from food and drink for 6 h before surgery.

After the patients entered the operation room, intravenous access was established in the upper extremity on the non-surgical side. Ringer's solution (10 mL/kg/h) was adopted for intravenous infusion. In addition to routine monitoring (electrocardiogram, blood oxygen, noninvasive blood pressure, and bispectral index (BIS)), 2 L of oxygen flow was given through the patient's nose within 1 minute via face mask. After 5 min, the patients were intravenously given dexmedetomidine (20041731, Yangtze River Pharmaceutical Group Co., Ltd.) at a loading dose of 1.0 μg/kg for over 10 min, and then were continuously given 0.5 μg/kg/h of dexmedetomidine.

After the patients were fully sedated, an ultrasound scan of the neck was performed to confirm if there was a safe operating area for SGB, to decide whether to perform ultrasound-guided SGB puncture or not. The same anesthesiologist would judge the effect of the block, and observe the postoperative puncture complications.

Induction of anesthesia started after confirmation of the effect and exclusion of serious complications. After oxygen inhalation via face mask for 3-5 min, patients were intravenously injected with 0.1 mg/kg of Midazolam (MS210612, Jiangsu Enhua Pharmaceutical Co., Ltd., China), 2.0 mg/kg of 1% Propophenol (20102243, Yangtze River Pharmaceutical Group Co., Ltd., China), 0.5 μg/kg of Sufentanil citrate (01A06293, Yichang Renfu Pharmaceutical Co., Ltd., China) and 0.15 mg/kg of Atricuronium cisbenzenesulfonate (21062403, Jiangsu Hengrui Pharmaceutical Co., Ltd., China). Double-lumen endobronchial cannula was performed. Catheter type was selected based on the patient's height, weight, and surgical site. The bronchial catheter was properly fixed under the guidance of a fiber branch and connected to anesthesia machines for temporary double lung ventilation to control breathing, tidal volume (TV) within the range of 6-8 mL/kg, and respiratory rate (RR) of 12-15 time/min. Patients adjusted to lateral recumbent position according to the surgical site, and OLV was implemented. TV was set at 4-6 mL/kg, inhaled oxygen concentration was maintained at 60-80%, RR was set at 16-18 time/min, and positive end expiratory pressure (PEEP) was set at 4-6 cmH_2O. Manual pulmonary rehabili-

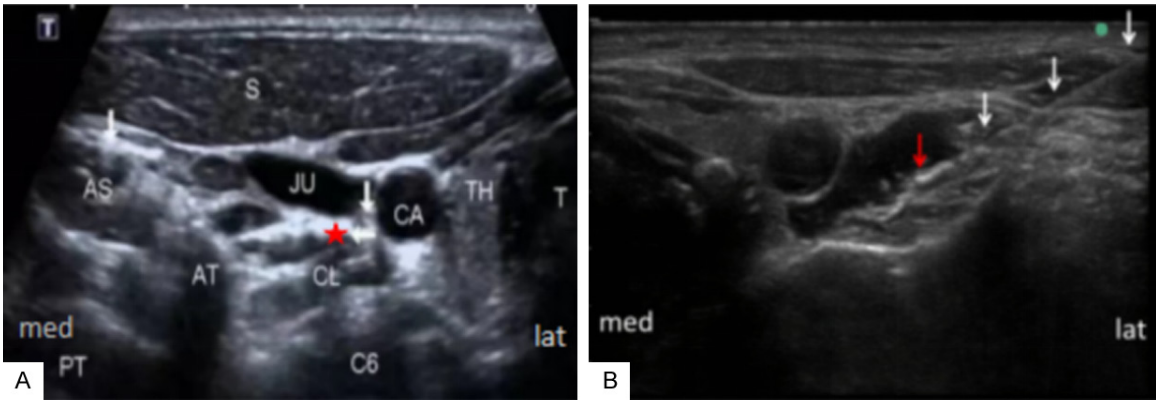

Figure 1. Anatomy on horizontal ultrasound image of the neck 6 transverse process and SGB puncture path. A: Anatomy on ultrasound images; B: The white line pointed by the arrow is the puncture path. SGB, stellate ganglion block; TH, thyroid gland; CL, collilongus; JU, jugular vein; CA, carotid artery; T, trachea; AT, anterior tubercle; PT, posterior tubercle; S, sternocleidomastoid; AS, anterior scalene muscle; C6, 6th cervical vertebra; lat, lateral side; med, medial side.

tation was performed every 30 min, with 30 cmH_2O of the continuous pressure of pulmonary rehabilitation for 60 s [14]. At the beginning of the operation, the inhaled oxygen concentration and ventilator parameters were adjusted appropriately according to oxygen saturation, airway pressure, and end-tidal carbon dioxide ($EtCO_2$). Patients' vital signs were monitored continuously. The intraoperative BIS was maintained between 40 and 60, and the range of changes in blood pressure and heart rate (HR) was ±20% of the base value. After surgery, patients were transferred to the resuscitation room for anesthesia resuscitation until the patient recovered spontaneous breathing. When patients' BIS≥80 and the patients could perform post-directive actions, the tracheal catheter was removed, and patients were observed for 30 min after extubation.

Ultrasound-guided SGB

Patients took a supine position without a pillow. A uniform coupling agent applicator was applied to a 13-6 MHz high frequency linear ultrasound probe (Sonosite, USA). The probe was attached to the neck, forming an angle of 30°-45° to the sagittal section of the neck and was slowly moved along the surface. SGB was performed on the anterior tubercle of the transverse process of the sixth cervical spine (C6; **Figure 1A**). Planar stitch method was adopted. Ultrasound dynamic monitoring ensured that the needle avoided the vascular nerve and reached the deep side of the prevertebral fascia. After the assistant repeatedly drew back the syringe to confirm that there was no blood, patients in the SGB group were injected with a mixture of 6 ml of 0.25% ropivacaine hydrochloride (PS16131, AstraZeneca, Sweden) and 1% lidocaine hydrochloride (1B200829102, Hebei Tiancheng Pharmaceutical Co., Ltd., China) [15]; while those in the control group were injected with 6 mL of 0.9% saline (1G90A1, China Otsuka Pharmaceutical Co., Ltd., China). After the injection was completed, local anesthesia or saline may be seen to spread evenly between the transverse and carotid arteries (**Figure 1B**). Horner syndrome would occur on the blocked side after successful block [16]. The symptoms included microscopic pupils, narrow eye clefts, inverted eyeballs, conjunctival congestion, facial flushing, and increased facial skin temperature. More than three of the above symptoms were identified as positive Horner syndrome.

Outcome measures

The general information and surgical data in the 3 groups were recorded. The general information covered age, gender, height, weight, and ASA classification. Anesthesia time, duration of surgery, OLV time, fluid intake, bleeding volume, as well as urine volume were included in surgical data.

Hemodynamics (mean arterial pressure (MAP), HR, saturation of pulse oxygen (SPO_2)), and respiratory parameters (peak airway pressure (P_{peak}), TV, RR, $EtCO_2$) were recorded after entering the operation room (T0), pre-OLV (T1), 30 min after OLV (T2), 60 min after OLV (T3), at the end of surgery (T4), and 30 min after extubation (T5). Oxygenation index (OI), pulmonary shunt fraction (Qs/Qt) and pH value were compared at different time points. All data was obtained from the PHILIPS IntelliVue MP30 monitor.

Arterial blood gas analysis was carried out from T0 to T5, OI, Qs/Qt and pH value were compared among groups. Five mL venous blood from the elbow was collected at T0, T3 and T5 for the detection of surfactant proteins A (SP-A, SP-A BeyotELI kit, P0013S, Beyotime Biotechnology, China), superoxide dismutase (SOD, SOD BeyotELI kit, P0045D, Beyotime Biotechnology, China), malondialdehyde (MDA, MDA BeyotELI kit, P0024M, Beyotime Biotechnology, China), interleukin-6 (IL-6, IL-6 ELISA kit, U01233W, R&D Systems, USA) and interleukin-10 (IL-10, IL-10 ELISA kit, U01365P, R&D Systems, USA) levels by enzyme-linked immunosorbent assay (ELISA), respectively. The steps of ELISA detection method were as follows. Five mL of blood from the patient's non-infusion elbow vein was collected and placed at room temperature for 20 min. After the blood naturally coagulated, it was centrifuged at the speed of 3,000 rpm for 20 min. The upper layer of the serum was collected and placed in a freezer at -80°C for later use. Then the procedures were performed following the ELISA instructions.

The complications related to SGB (local anesthetic intoxication, trachea, bronchus, and esophagus injuries, local hematoma, recurrent laryngeal nerve block, phrenic nerve block, brachial plexus nerve block, total spinal anesthesia) after surgery and the postoperative pulmonary complications (hypoxemia, dyspnea, pulmonary infection, atelectasis, pneumothorax, pulmonary edema) within 72 hours were recorded.

Statistical analysis

PASS 15.0 was used for sample size estimation. According to the results of the pre-experiment, the mean and standard deviation of OI in SGB and blank groups were obtained. A 20% increase in the mean and standard deviation was considered as significant difference. One-sided variable inspection plan was applied and the efficient inspector was set as 0.9. An alpha of 0.05 was used as the cutoff for significance. The ratio of the two sample sizes was 1:1. Finally, we concluded that the required sample size for each group was at least 40 cases.

SPSS 24.0 software was adopted for statistical analyses. Measurement data with normal distribution was expressed as mean ± standard deviation ($\bar{x}$ ± sd). One-way ANOVA was used for comparison among groups. The two-by-two pairwise comparisons were carried out using LSD method and analyzed by repeated measures analysis of variance. If there was an error, the Bonferroni method was further used for pairwise comparisons. Measurement data with non-normal distribution was expressed as M (P25, P75) and analyzed using the Wilcoxon rank sum test. Count data was expressed as percentage (%) and tested by Pearson's chi-square test or Fisher's exact test. $\alpha=0.05$ and $P<0.05$ were considered statistically significant. Data was input into Graphpad Prism 9.20 software, and graphs were generated.

Results

Comparison of general data and surgery data

A total of 130 patients were included in the trial, 7 cases were excluded (4 cases of poor blocking effect, 2 cases of OLV time less than 2 h, and 1 case of postoperative hospital stays less than 3 d), and 123 patients finally completed the trial. There were no cases of withdrawal or dropping out during follow-up. Among all patients who completed the trial, there were no statistically significant differences in general data such as age, gender, height, weight, and ASA classification (all P>0.05). All patients received thoracoscopic lobectomy. No significant differences were found in anesthesia time, surgery time, and OLV time (all P>0.05). See **Table 1**.

Comparison of hemodynamic and respiratory parameters at different time points

Compared with T0, MAP level and HR at T1, T2 and T3 were significantly reduced in the three groups (both P<0.05), while those at T4 and T5 had no significant difference (both P>0.05). At T1, T2 and T3, MAP level in the SGB group was lower than that in blank and control groups (P<0.05). At T2 and T3, the SGB group had

Table 1. Comparison of general data and surgical data

	Blank group (n=41)	Control group (n=41)	SGB group (n=41)	X^2/F	P
Age (years)	57.6±9.7	58.5±11.2	59.4±10.6	0.3	0.741
Sex				0.457	0.796
Male	23	20	22		
Female	18	21	19		
Height (cm)	172.13±10.54	169.32±11.24	171.19±9.69	0.759	0.47
Weight (kg)	68.52±11.82	67.64±13.40	66.76±12.47	0.201	0.819
ASA				0.875	0.928
I	8	9	6		
II	30	29	31		
III	3	3	4		
Anesthesia time (min)	209.63±25.26	204.89±23.36	205.37±19.55	0.625	0.537
Duration of surgery (min)	193.56±15.28	192.81±16.50	189.45±17.36	0.73	0.484
OLV time (min)	176.41±11.43	178.62±12.21	175.84±13.32	0.58	0.561
Fluid intake (mL)	793.72±68.22	798.84±70,68	800.36±72.75	0.099	0.905
Bleeding volume (mL)	113.96±47.84	118.43±50.11	115.82±49.04	0.087	0.918
Urine volume (mL)	278.93±36.76	281.44±38.97	283.27±41.02	0.128	0.879

Note: SGB, stellate ganglion block; ASA, American Society of Anesthesiologists; OLV, one-lung ventilation. Compared among groups, P>0.05.

Table 2. Comparison of hemodynamic parameters at different time points (n=41)

Parameter	T0	T1	T2	T3	T4	T5	F	P
MAP (mmHg)								
Blank group	93.23±5.65	82.21±5.25^{a}	84.34±5.31^{a}	83.63±4.56^{a}	91.39±4.45	93.63±4.87	44.19	<0.001
Control group	94.42±5.87	84.42±6.41^{a}	81.46±7.47^{a}	82.38±6.16^{a}	90.50±4.19	91.51±5.81	32.37	<0.001
SGB group	92.74±6.52	76.45±7.32^{a,b,c}	73.87±6.36^{a,b,c}	72.51±5.26^{a,b,c}	90.24±5.23	92.33±4.96	107.1	<0.001
F	0.843	17.04	28.91	52.82	0.691	1.713		
P	0.433	<0.001	<0.001	<0.001	0.503	0.185		
HR (time/min)								
Blank group	76.27±4.72	69.63±5.46^{a}	67.84±5.42^{a}	68.36±4.33^{a}	75.38±5.76	74.16±4.33	21.62	<0.001
Control group	77.58±5.24	66.78±4.28^{a}	67.90±3.46^{a}	68.43±5.09^{a}	76.69±6.94	75.23±6.12	34.97	<0.001
SGB group	75.62±4.56	67.59±6.83^{a}	62.62±5.21^{a,b,c}	63.55±3.65^{a,b,c}	74.07±5.83	76.21±4.58	61	<0.001
F	1.738	2.799	16.53	16.6	1.83	1.675		
P	0.18	0.065	<0.001	<0.001	0.165	0.192		
SPO$_2$ (%)								
Blank group	98.51±1.22	98.23±1.93	97.61±3.21	97.68±3.81	97.91±3.21	97.62±2.37	0.736	0.597
Control group	98.67±1.26	97.72±1.82	97.11±3.03	97.72±2.44	97.29±3.87	97.20±2.40	2.013	0.078
SGB group	98.30±1.17	98.46±1.45	98.30±1.62	97.48±2.63	98.54±1.19	98.11±1.30	2.227	0.052
F	0.953	1.93	1.193	1.332	1.223	1.953		
P	0.389	0.15	0.474	0.268	0.317	0.146		

Note: Compared with T0, ^{a}P<0.05; compared with blank group, ^{b}P<0.05; compared with control group, ^{c}P<0.05. SGB, stellate ganglion block; MAP, mean arterial pressure; HR, heart rate; SPO$_2$, saturation of pulse oxygen; OLV, one-lung ventilation; T0, after entering the operation room; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery; T5, 30 min after extubation.

lower HR than blank and control groups (P< 0.05). There were no significant differences in MAP level and HR in the three groups at other time points (both P>0.05). From T0 to T5, no difference was found in SPO$_2$ level among the three groups (P>0.05). See **Table 2** and **Figure 2**.

Compared with T1 and T4, P$_{peak}$ and RR were higher and TV was lower in the three groups at

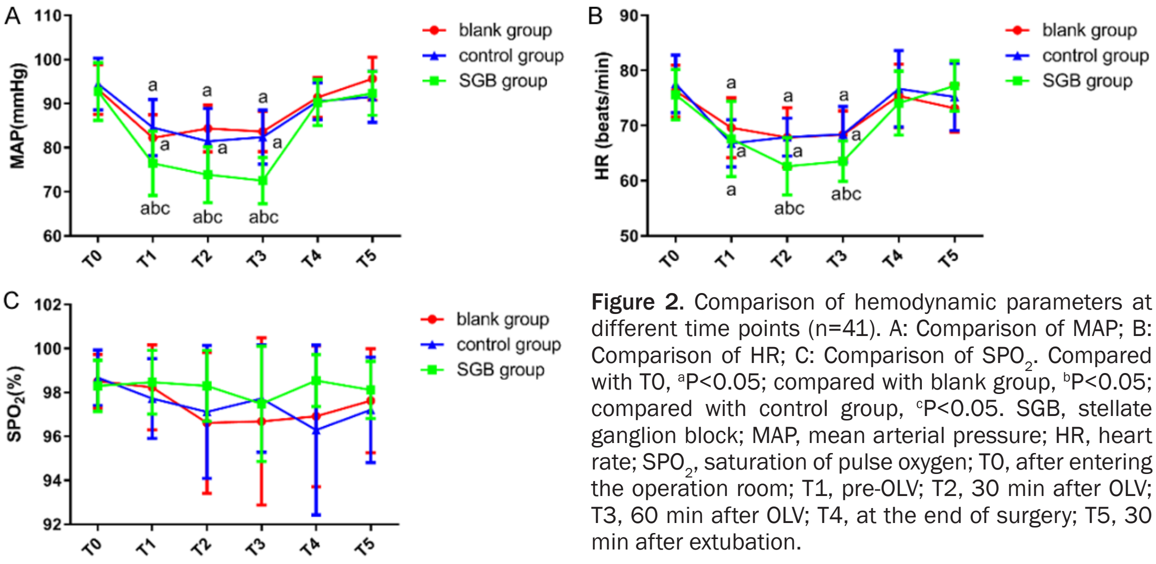

Figure 2. Comparison of hemodynamic parameters at different time points (n=41). A: Comparison of MAP; B: Comparison of HR; C: Comparison of SPO_2. Compared with T0, $^aP<0.05$; compared with blank group, $^bP<0.05$; compared with control group, $^cP<0.05$. SGB, stellate ganglion block; MAP, mean arterial pressure; HR, heart rate; SPO_2, saturation of pulse oxygen; T0, after entering the operation room; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery; T5, 30 min after extubation.

T2 and T3 (all P<0.05). At T2 and T3, the SGB group had lower P_{peak} and TV than blank and control groups (both P<0.05). There were no differences in P_{peak} and TV between blank and control groups at T2 and T3 (both P>0.05). At T1 and T4, no differences were observed in P_{peak} and TV among three groups (both P>0.05). From T1 to T4, there were no significant differences in RR and $ETCO_2$ (both P>0.05). See **Table 3** and **Figure 3**.

Comparison of arterial blood gas analysis, serum SP-A, inflammatory factors, and oxidative stress markers at different time points

From T0 to T5, the pH value of three groups was within the normal range, and there was no significant difference (P>0.05). Compared with T0, all the groups had significantly higher OI at T1; however, there was no significant difference among groups (P>0.05), while lower OI was observed from T2 to T5, and the SGB group had the highest OI compated to the other two groups (P<0.05). The Qs/Qt was increased at T2 and T3 and was significantly higher than that at T0 (P<0.05) in all three groups. It was decreased at T4 and T5 but was still higher than that at T0 and T1 (P<0.05). From T2 to T5, the SGB group had lower Qs/Qt than the blank and control groups (P<0.05). See **Table 4** and **Figure 4**.

At T3 and T5, SP-A and IL-6 levels in all three groups were increased significantly compared with T0 (both P<0.05), and SGB group had lower SP-A and IL-6 levels than blank and control groups (both P<0.05). Compared with T0, IL-10 and SOD levels were lower at T3 and T5 in blank and control groups (both P<0.05), while they were higher in the SGB group (P<0.05). The SGB group had higher IL-10 and SOD levels than the blank and control groups (both P<0.05). At T3 and T5, MDA level in the blank and control groups was increased significantly compared with T0 (P<0.05), while there was no difference in the SGB group (P>0.05), and the SGB group had lower MDA level than the blank and control groups (P<0.05). See **Table 5** and **Figure 5**.

Complications associated with SGB within 24 h after surgery

None of the subjects experienced serious puncture complications such as vessel injury, local anesthetic intoxication, trachea, bronchus, and esophagus injuries, and total spinal anesthesia during the course of the study. In the control group, 3 patients had local hematomas after puncture, but hematomas did not increase after compression. There were no symptoms such as tracheal compression and dyspnea. In the SGB group, 4 patients developed symptoms of unilateral recurrent laryngeal nerve block, which was characterized by hoarseness for 2-3 min after local anesthesia injection. Additionally, 1 patient suffered from brachial plexus block, which showed numbness in the upper extremities and hands, five min after the block. The above patients were not treated spe-

Table 3. Comparison of respiratory parameters at different time points (n=41)

Parameter	T0	T1	T2	T3	T4	T5	F	P
P_{peak} (cmH_2O)								
Blank group		15.67±4.11	25.67±4.42^{a}	28.39±3.55^{a}	16.22±5.22		90.82	<0.001
Control group		14.81±3.98	24.34±5.41^{a}	29.20±4.37^{a}	14.57±3.87		108.9	<0.001
SGB group		14.38±3.87	18.67±3.54^{a,b,c}	19.45±3.20^{a,b,c}	15.49±4.28		17.49	<0.001
F		1.112	27.71	85.85	1.389			
P		0.332	<0.001	<0.001	0.253			
TV (mL/kg)								
Blank group		7.31±1.42	6.61±2.21^{a}	6.53±2.22^{a}	7.51±1.68		4.301	0.006
Control group		7.52±1.57	6.78±2.43^{a}	6.67±1.86^{a}	7.78±2.21		4.875	0.003
SGB group		7.47±1.52	5.29±2.25^{a,b,c}	5.33±2.79^{a,b,c}	7.41±1.51		14.23	<0.001
F		0.218	3.368	4.126	0.451			
P		0.805	0.028	0.019	0.638			
RR (time/min)								
Blank group		12.62±1.39	19.24±2.25^{a}	18.64±2.26^{a}	12.67±1.56		167.8	<0.001
Control group		12.74±1.56	18.67±2.19^{a}	18.93±3.11^{a}	12.39±2.12		99.57	<0.001
SGB group		12.31±1.49	18.65±3.21^{a}	18.40±2.89^{a}	12.33±2.31		80.36	<0.001
F		0.919	0.685	0.375	0.33			
P		0.402	0.506	0.688	0.715			
$EtCO_2$ (mmHg)								
Blank group		39.43±4.42	40.21±3.32	41.21±2.10	41.02±2.52		1.463	0.227
Control group		39.20±3.67	41.61±2.87	40.53±3.39	40.11±2.92		1.644	0.182
SGB group		39.62±4.11	40.82±3.14	41.24±3.51	40.25±2.77		1.578	0.201
F		0.898	0.659	2.475	1.31			
P	-	0.41	0.519	0.088	0.274			

Note: Compared with T1, $^{a}P<0.05$; compared with blank group, $^{b}P<0.05$; compared with control group, $^{c}P<0.05$. SGB, stellate ganglion block; P_{peak}, peak airway pressure; TV, tidal volume; RR, respiratory rate; $EtCO_2$, end-tidal carbon dioxide; OLV, one-lung ventilation; T0, after entering the operation room; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery; T5, 30 min after extubation.

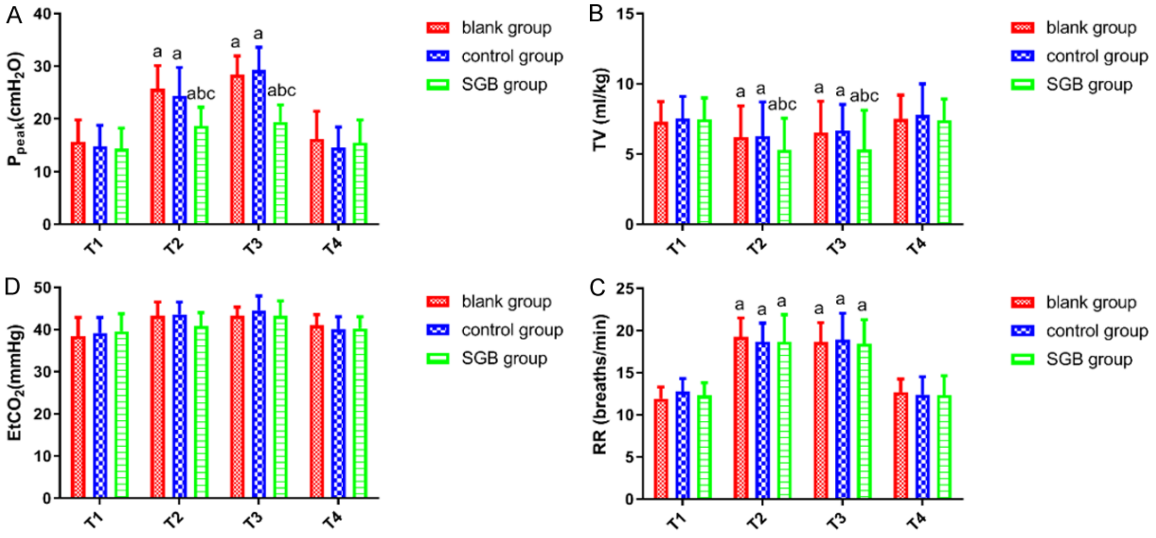

Figure 3. Comparison of respiratory parameters at different time points. A: Comparison of P_{peak}; B: Comparison of TV; C: Comparison of RR; D: Comparison of $ETCO_2$. Compared with T1, $^{a}P<0.05$; compared with blank group, $^{b}P<0.05$; compared with control group, $^{c}P<0.05$. SGB, stellate ganglion block; P_{peak}, peak airway pressure; TV, tidal volume; RR, respiratory rate; $EtCO_2$, end-tidal carbon dioxide; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery.

Table 4. Comparison of arterial blood gas analysis at different time points (n=41)

Parameter	T0	T1	T2	T3	T4	T5	F	P
pH value								
Blank group	7.37±0.71	7.39±0.51	7.41±0.42	7.42±0.54	7.39±0.42	7.40±0.50	0.045	0.999
Control group	7.38±0.82	7.39±0.30	7.42±0.61	7.40±0.37	7.40±0.39	7.39±0.49	0.038	0.992
SGB group	7.36±0.81	7.37±0.43	7.39±0.53	7.38±0.44	7.41±0.37	7.38±0.36	0.046	0.999
F	0.007	0.031	0.035	0.079	0.026	0.02		
P	0.993	0.97	0.966	0.924	0.974	0.98		
OI (mmHg)								
Blank group	424.23±72.25	568.61±65.62^{a}	205.43±35.41^{a}	188.32±33.42^{a}	352.45±47.43^{a}	383.22±33.28^{a}	327	<0.001
Control group	427.28±73.56	565.79±74.78^{a}	207.30±33.13^{a}	192.14±32.91^{a}	345.51±46.81^{a}	372.24±36.42^{a}	289.6	<0.001
SGB group	423.47±66.32	566.91±67.33^{a}	268.22±35.25^{a,b,c}	255.73±24.36^{a,b,c}	414.08±43.60^{a,b,c}	477.39±33.80^{a,b,c}	259.2	<0.001
F	0.033	0.017	43.68	63.13	27.63	114.9		
P	0.967	0.983	<0.001	<0.001	<0.001	<0.001		
Qs/Qt (%)								
Blank group	1.44±0.34	1.33±0.51	25.66±5.63^{a}	28.32±4.90^{a}	16.90±3.11^{a}	17.63±4.43^{a}	387.3	<0.001
Control group	1.54±0.32	1.35±0.53	26.72±5.67^{a}	29.20±3.56^{a}	15.23±4.86^{a}	18.27±5.10^{a}	371.6	<0.001
SGB group	1.57±0.36	1.41±0.49	18.94±4.57^{a,b,c}	18.31±4.18^{a,b,c}	8.51±4.11^{a,b,c}	7.19±4.32^{a,b,c}	199.5	<0.001
F	1.64	0.273	25.84	83.11	48.34	74.02		
P	0.198	0.762	<0.001	<0.001	<0.001	<0.001		

Note: Compared with T0, ^{a}P<0.05; compared with blank group, ^{b}P<0.05; compared with control group, ^{c}P<0.05. SGB, stellate ganglion block; OI, oxygenation index; Qs/Qt, the pulmonary shunt fraction; OLV, one-lung ventilation; T0, after entering the operation room; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery; T5, 30 min after extubation.

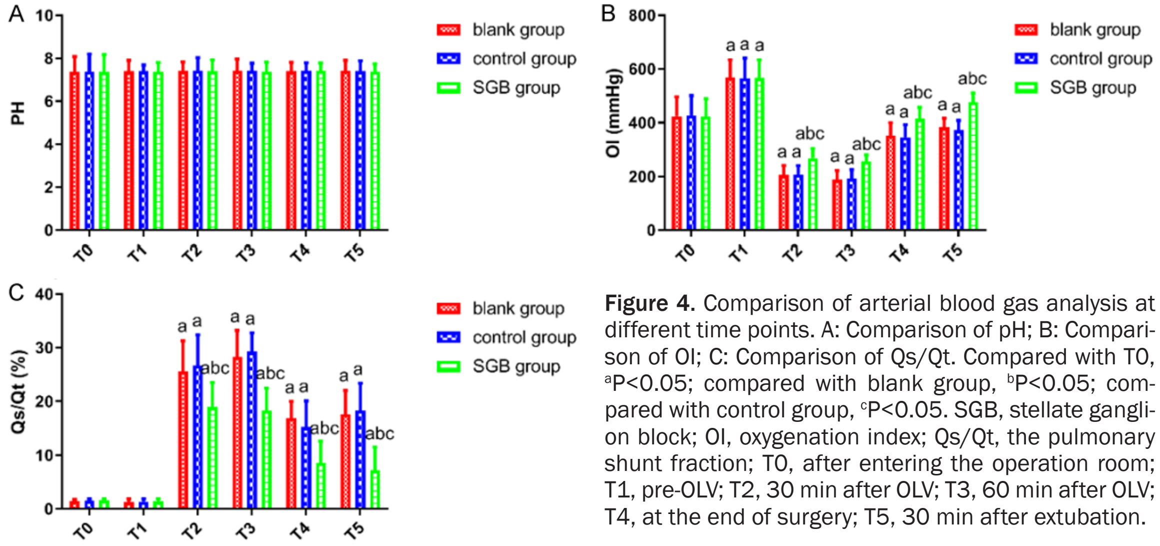

Figure 4. Comparison of arterial blood gas analysis at different time points. A: Comparison of pH; B: Comparison of OI; C: Comparison of Qs/Qt. Compared with T0, ^{a}P<0.05; compared with blank group, ^{b}P<0.05; compared with control group, ^{c}P<0.05. SGB, stellate ganglion block; OI, oxygenation index; Qs/Qt, the pulmonary shunt fraction; T0, after entering the operation room; T1, pre-OLV; T2, 30 min after OLV; T3, 60 min after OLV; T4, at the end of surgery; T5, 30 min after extubation.

cially. All of their symptoms were improved within 24 h after surgery, and no other adverse reactions were found in postoperative follow-up. See **Table 6**.

Pulmonary complications within 72 h after surgery and length of hospital stay

All patients were followed up within 72 h after surgery. There were no serious pulmonary complications. In the blank group, 1 patient had hypoxemia 12 h after surgery, with a constant SPO_2 level below 90%. Lung infection, atelectasis, pneumothorax, and heart failure were excluded after CT chest and electrocardiogram. The patient got better after oxygen therapy via low-flow nasal cannula, combined with sedation and analgesic therapy. No significant difference was found in the length of hospital stay among SGB (8.71±2.10 d), blank (8.83±2.53 d) and control (9.30±2.43 d) groups (P>0.05).

Discussion

OLV is a necessary ventilation method for minimally invasive surgery in thoracic surgery, and

Table 5. Comparison of serum SP-A, inflammatory factors, and oxidative stress markers at different time points (n=41)

Parameter	T0	T3	T5	F	P
SP-A (mg/L)					
Blank group	18.69±2.49	37.68±5.22[a]	51.32±10.23[a]	239.2	<0.001
Control group	18.41±3.20	39.26±4.85[a]	46.93±8.81[a]	240.6	<0.001
SGB group	19.23±2.89	25.57±3.19[a,b,c]	29.28±6.72[a,b,c]	49.88	<0.001
F	0.862	113.2	73.6		
P	0.425	<0.001	<0.001		
IL-6 (pg/mL)					
Blank group	8.79±3.41	15.38±4.34[a]	24.42±4.51[a]	149.1	<0.001
Control group	9.21±3.60	15.75±5.01[a]	23.39±4.54[a]	105.6	<0.001
SGB group	8.56±3.55	12.63±2.23[a,b,c]	13.83±3.32[a,b,c]	32.82	<0.001
F	0.359	7.307	80.7		
P	0.699	<0.001	<0.001		
IL-10 (pg/mL)					
Blank group	38.66±6.62	23.14±9.73[a]	27.32±8.55[a]	123.421	<0.001
Control group	36.71±7.82	22.32±8.01[a]	30.19±6.70[a]	121.5	<0.001
SGB group	38.90±6.23	46.54±5.72[a,b,c]	49.12±4.91[a,b,c]	121.4	<0.001
F	1.234	121.5	121.4		
P	0.295	<0.001	<0.001		
MDA (nmol/L)					
Blank group	4.62±3.29	8.34±2.28[a]	9.21±3.22[a]	27.7	<0.001
Control group	5.17±2.42	8.65±1.79[a]	9.27±3.64[a]	26.93	<0.001
SGB group	4.32±2.76	4.56±2.63[b,c]	4.74±1.83[b,c]	0.305	0.737
F	0.941	41.631	30.79		
P	0.393	<0.001	<0.001		
SOD (ng/L)					
Blank group	110.16±10.33	76.43±13.81[a]	87.61±24.35[a]	40.78	<0.001
Control group	113.42±11.27	85.27±13.76[a]	88.25±15.20[a]	53.74	<0.001
SGB group	112.24±11.82	152.35±10.57[a,b,c]	177.14±11.33[a,b,c]	347.3	<0.001
F	0.897	431.1	342.6		
P	0.41	<0.001	<0.001		

Note: Compared with T0, [a]P<0.05; compared with blank group, [b]P<0.05; compared with control group, [c]P<0.05. SGB, stellate ganglion block; SP-A, surfactant proteins A; MDA, malondialdehyde; SOD, superoxide dismutase; IL-6, interleukin-6; IL-10, interleukin-10; OLV, one-lung ventilation; T0, after entering the operation room; T3, 60 min after OLV; T5, 30 min after extubation.

an important part of modern anesthesiological techniques [17]. The application of lung isolation has greatly improved the conditions of thoracic surgery and promoted the development of thoracic surgery to refine minimally invasive.

OLV itself is prone to biological lung damage caused by the release of inflammatory mediators, oxidation, and antioxidant imbalances in lung tissues [18, 19]. It has been reported that approximately 3% of patients undergo lobectomy with OLV suffer from ALI, while rate for those who receive total lung resection reaches 8% [20]. Therefore, reducing OLV-related complications has always been a hot spot for clinical anesthesiologists. With the continuous deepening of research, protective lung ventilation strategies have emerged, mainly in the areas of small TV, appropriate application of PEEP, permissible hypercapnia, regular pulmonary rehabilitation, and control of FiO_2. Protective lung ventilation strategies have been shown to reduce the incidence and case fatality of postoperative pulmonary complications [21, 22]. However, in the clinic, it is not enough to control OLV induced lung damage through protective lung ventilation strategies. Dexmedetomidine plays a role in lung protection by inhibiting

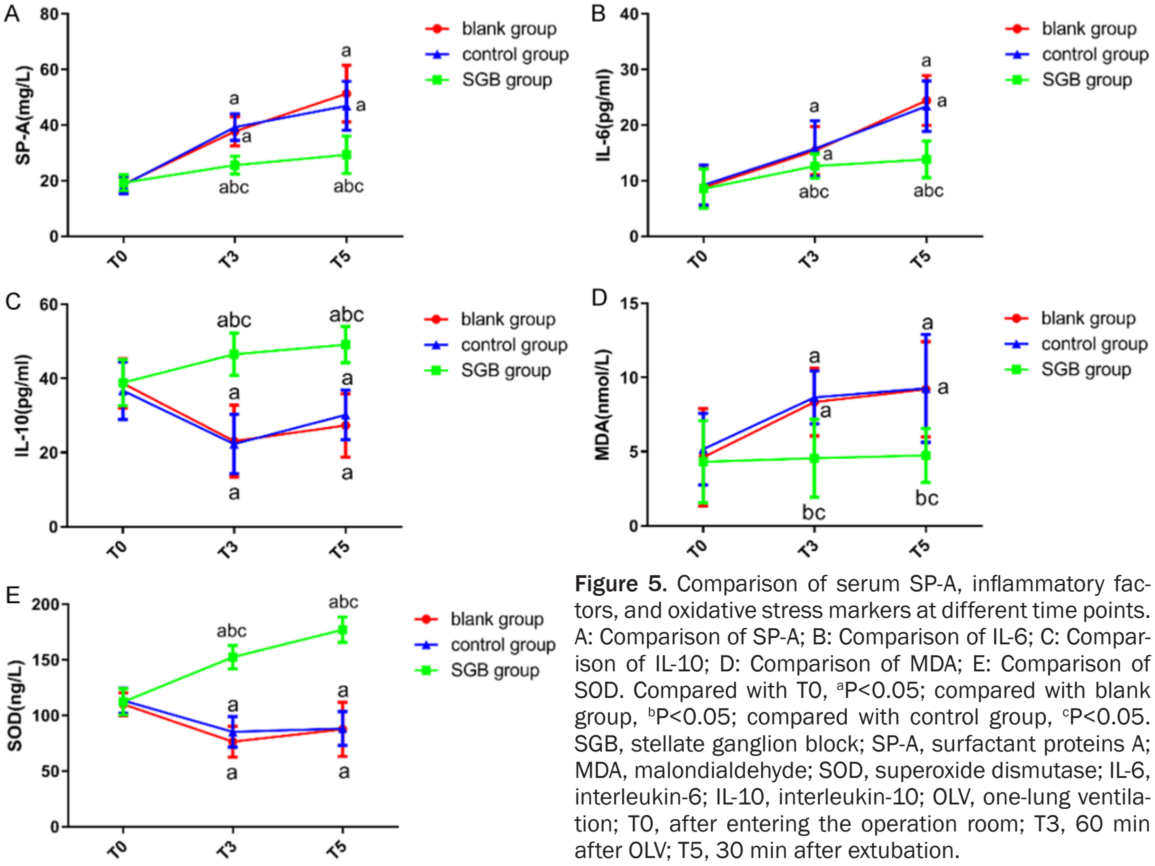

Figure 5. Comparison of serum SP-A, inflammatory factors, and oxidative stress markers at different time points. A: Comparison of SP-A; B: Comparison of IL-6; C: Comparison of IL-10; D: Comparison of MDA; E: Comparison of SOD. Compared with T0, $^aP<0.05$; compared with blank group, $^bP<0.05$; compared with control group, $^cP<0.05$. SGB, stellate ganglion block; SP-A, surfactant proteins A; MDA, malondialdehyde; SOD, superoxide dismutase; IL-6, interleukin-6; IL-10, interleukin-10; OLV, one-lung ventilation; T0, after entering the operation room; T3, 60 min after OLV; T5, 30 min after extubation.

Table 6. Complications associated with stellate ganglion block (n=41)

Group	Local anesthetic intoxication	Trachea, bronchus, and esophagus injuries	Local hematoma	Recurrent laryngeal nerve block	Phrenic nerve block	Brachial plexus nerve block	Total spinal anesthesia
Blank group	-	-	-	-	-	-	-
Control group	0	0	3	0	0	0	0
SGB group	0	0	0	4	0	1	0

Note: SGB, stellate ganglion block.

inflammatory response and controlling oxidative stress [23]. Sevoflurane reduces the production of arachidonic acid by inhibiting phospholipase A2 expression, mitigating pathological changes in lung injury induced by OLV [24]. Some scholars believe that propofol performs better than sevoflurane in alleviating inflammatory response and oxidative stress in patients with OLV, and has a greater protective effect on lung damage caused by OLV [25]. Thus, the protection strategy for OLV induced lung injury mainly focuses on ventilation mode and related drug application [26, 27]. The SGB is also known as the cervicothoracic ganglion, which inhibits the excitement of the sympathetic nervous system when blocked. Studies have pointed out that the SGB plays an active role in the treatment of neurogenic pulmonary edema through a variety of mechanisms [28-33]. It suggests that SGB may also have some preventive and protective effects on clinical OLV-induced lung injury [34]. In recent years, with the continuous development of ultrasound-guided nerve blocks, visualization greatly improves the safety and accuracy of SGB punctures [35]. In this study, the results showed that SGB was effective in reducing MAP level during OLV in patients with thoracoscopic lobectomy without affecting HR and SPO_2. During OLV, lower P_{peak}, and RR were observed, but after

SGB, OI was higher and Qs/Qt was lower. These findings suggested that SGB achieved lung protection by improving hemodynamics and respiratory mechanics in patients with OLV.

SP-A, expressed in lung tissues, plays a physiological role in maintaining the surface tension of alveoli. Normally, SP-A is rarely expressed extrapulmonary, so there is very little SP-A in the serum of normal humans. Only when the lung tissue is damaged by some adverse factors, the pulmonary vascular endothelial cells are destroyed, and the SP-A within the pulmonary epithelial cells enters the blood circulation, making it possible to monitor changes in their concentration in plasma or serum [36]. Therefore, the change in SP-A is an important indicator for observing lung damage. Tajima et al. pointed out that serum SP-A levels accurately reflected the extent of lung tissue damage and played an important role in the pathogenesis and diagnosis of noninfectious lung injury [37]. The results in this study demonstrated that the SP-A of the three groups were increased to varying degrees after OLV, indicating OLV caused damage to the lung tissue, and that there was a synergistic correlation between lung injury and inflammatory response and oxidative stress reaction. SGB had lower serum SP-A level than that in the blank and control groups during and after surgery, indicating that ultrasound-guided SGB mitigated lung damage during OLV. The cause may be that SGB inhibits the release of SP-A factor when patients undergo OLV, which is conducive to maintaining the surface tension of alveoli, reducing postoperative alveolar collapse, and protecting lung function.

IL-6 is one of the most important pro-inflammatory cytokines, and changes in serum content are sensitive indicators that reflect the inflammatory response and the severity of tissue damage [38, 39]. In animal models of lipopolysaccharide-induced acute lung injury, significantly elevated serum IL-10 levels can be detected to inhibit overactivation of certain pro-inflammatory factors such as IL-6, and IL-8, thereby preventing lung tissue damage [40, 41]. Studies have revealed that the mechanisms of lung injury induced by mechanical ventilation including biological damage caused by inflammatory processes in the lungs, and that an imbalance of pro-inflammatory and anti-inflammatory cytokines is one of the mechanisms by which OLV-associated lung injury occurs [42, 43]. In this study, compared with T0, IL-6 level was increased while IL-10 level was decreased in three groups at T3 and T5, suggesting that OLV caused increased production of pro-inflammatory factors while inhibiting the production of anti-inflammatory factors. In the same time, IL-6 level in the SGB group was lower, while IL-10 level was higher than that in the other two groups, indicating that SGB reduced the production of pro-inflammatory factors during OLV, increased the production of anti-inflammatory factors, inhibited inflammatory response, and played a lung-protective role by regulating the pro-inflammatory or anti-inflammatory balance [44]. The oxidative stress is an imbalance of the redox process when the body is stimulated, and oxidation plays a major role [45]. When oxidative stress occurs, oxidative intermediates such as free radicals destroy invading pathogens, but free radicals cause harm if their levels become too high in the body.

SOD has antioxidant effects, whose activity can evaluate the body's ability to reduce and repair. MDA is a marker of lipid peroxidation, whose concentration reflects the degree of oxidative stress in the body. In this study, compared with T0, the blank and control groups had significantly higher MDA level, while there was no difference in the SGB group at T3 and T5. At the same time point, MDA in the SGB group was lower than that in the other two groups. Compared with T0, the SOD was significantly lower in blank and control groups while it was higher in the SGB group at T3 and T5. At the same time point, the SGB group had higher SOD than the other two groups. This indicated that OLV caused enhanced oxidation reaction. In addition, SGB significantly reduced the content of neutrophils and hypersensitivity C-reactive protein 24 h after surgery, which further shows that SGB inhibits the inflammatory response of human beings after OLV.

None of the subjects experienced serious puncture complications such as vessel injury, local anesthetic intoxication, trachea, bronchus, and esophagus injuries, and total spinal anesthesia during the course of the study. All patients were followed up within 72 h after surgery. There were no serious pulmonary complications, which showed that the clinical application of ultrasound-guided was accurate and safe.

However, this study being from a single center and having a small sample size cannot fully reflect the overall characteristics of SGB, and can only preliminarily characterize the lung protective effect of SGB on patients undergoing lung cancer surgery with OLV. Thus, the sample size should be expanded to reduce the error. Besides, SGB was only used for the surgical side only once in this study. Local anesthesia dosage and concentrations will play different roles and SGB for different sides will also have various effects on the cardiovascular system. Hence, whether SGB can be widely used in the clinic as a lung protection measure requires further studies on drug dosage, concentrations, and anesthesia methods.

In conclusion, ultrasound-guided SGB has lung-protective effects on patients undergoing OLV, which significantly improves patients' OI, reduces intrapulmonary shunts, declines ventilator-induced lung damage, and inhibits inflammatory response as well as oxidative stress.

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Disclosure of conflict of interest

None.

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