# Propofol and sevoflurane combined with remifentanil on the pain index, inflammatory factors and postoperative cognitive function of spine fracture patients

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**Abstract.** The effects of propofol vs. sevoflurane combined with remifentanil on the pain index, inflammatory factors and postoperative cognitive function in spine fracture patients were studied and analyzed. A total of 62 patients with vertebral fracture were randomly divided into the propofol group (P group, n=41) and the sevoflurane group (S group, n=41). P group used induction anesthesia with propofol, and maintained anesthesia via intravenous injection of remifentanil. While patients in S group received induction anesthesia with sevoflurane, and also remifentanil as the maintained anesthesia. Results showed that extubation time, eye-opening time and response time of P group were lower than S group ($p<0.05$). The VAS score 48 h after surgery in P group was significantly lower than the S group ($p<0.05$). Levels of IL-6, IL-1β, ICAM-1 and MMP-9 in serum in P group were lower than those in S group ($p<0.05$). Mini-mental state examination (MMSE) score 24 h after surgery in P group was higher than that in S group ($p<0.01$). Compared with sevoflurane anesthesia, propofol combined with remifentanil anesthesia on spine fracture patients can significantly decrease the pain index and inflammatory reaction, shorten the postoperative recovery time.

## Introduction

Spinal fracture is a clinical disease that frequently occurs, characterized by a wide range of incidence and wide population distribution, which has the highest incidence rate in the elderly (1,2). Spinal fractures caused by osteoporosis and trauma can generally be diagnosed by clinical medical history combined with imaging examination, and surgery dominates in its treatment (3). The occurrence site of spinal fracture is closely related to the operation difficulty, so the operation should be performed as soon as possible under the anesthesia of patients using rapid-onset anesthetics with good effects, reducing the pain and anxiety of patients, and increasing the success rate of the operation (4). Sevoflurane and propofol are two most commonly-used anesthetics. Cao *et al* (5) found that sevoflurane has a small blood-gas partition coefficient, its concentration in blood is easy to be controlled and it, as a new anesthetic, can exert an anesthetic effect through inhibition of N-methyl-D-aspartate (NMDA) receptors, with higher safety, which can provide effective anesthesia for the elderly and children; at the same time, its poor solubility of blood tissues leads to rapid onset of induced anesthesia. Propofol, as a potent general anesthetic, has the advantages of rapid onset, short recovery time and few side-effects, and is widely used in preoperative sedation anesthesia of clinical patients (6). De Conno *et al* (7) found that anesthetics can reduce the patient's pain index and inflammatory response, so the choice of appropriate anesthetics is essential. The study of Visvabharathy *et al* (8) found that propofol can reduce the impact of operation on patients' cognitive function, but there has been no research on the differences in effects of propofol and sevoflurane anesthesia on pain index, inflammatory factors and cognitive function of patients during operation. In this study, the effects of propofol and sevoflurane anesthesia on pain index, inflammatory response and cognitive function of patients with spinal fractures were analyzed, and the anesthetic effects of propofol and sevoflurane on patients with spinal fractures were evaluated.

## Patients and methods

*Patients*. A total of 82 patients with spinal fractures treated in the Orthopedics Department of Jining First People's Hospital (Jining, China) from January 2015 to January 2017 were selected, and all patients were diagnosed with spinal compression fractures [American Society of Anesthesiologists (ASA) grade I-II] via spinal magnetic resonance (MR) conventional scan. The above eligible patients were randomly divided into two groups, the propofol group (Group P, n=41) and the sevoflurane group (Group S, n=41). In Group P, there were 22 males and 19 females aged (53.7±18.9) years. In Group S, there were 23 males and 18 females aged (52.1±19.8) years. The patients enrolled had basically normal liver and kidney functions, and had no serious auditory, visual or central nervous system diseases before operation. Patients with mini-mental

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state examination (MMSE) score <24 points, other wasting diseases, chronic inflammation or inadaptation to sevoflurane and propofol were eliminated. The groups of patients enrolled were given the same preoperative and postoperative nursing and treatment measures. The operation was performed by the same physician. Patients signed the informed consent, and all clinical and pathological data of patients during hospitalization were retained. The differences in age, sex and course of disease were not statistically significant between the groups of patients. This study was approved by the ethics committee of Jining First People's Hospital. Signed written informed consents were obtained from all participants before the study.

*Anesthesia process*. Before anesthesia, all patients received intramuscular injection of 0.1 mg/kg midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., Xuzhou, China), and intravenous injection of 0.5 mg/kg atropine (Dongying Tiandong Pharmaceutical Co., Ltd., Dongying, China) and 0.1 g/kg dilantin (New Asiatic Pharmaceutical, Dongguan, China) and a multi-function monitor (GE Healthcare, Buckinghamshire, UK) was connected during operation to monitor physiological indexes of all patients, followed by tracheal intubation. The anesthesia for patients in Group P was induced with 1 mg/kg propofol (Xi'an Libang Pharmaceutical Co., Ltd., Xi'an, China) and maintained at a dose of 6 mg/kg/h. Before induced anesthesia in patients in Group S, the air storage bag was emptied and the oxygen flow rate was adjusted to 8 l/min, sevoflurane was filled for 1 min, and patients were asked to take a deep breath, fasten the mask and keep a deep breath until the disappearance of eyelash reflex in patients, indicating the successful induced anesthesia. At 3 min after ventilation, tracheal intubation was performed and anesthesia machine was connected for mechanical ventilation for patients. Two groups of patients were treated with continuous intravenous pumping of 0.2 $\mu$g/kg/min remifentanil (Yichang Humanwell Healthcare, Yichang, China) for induced anesthesia. During operation, patients in both groups were intravenously injected with 0.15 mg/kg cisatracurium (Dongying Tiandong Pharmaceutical) intermittently to maintain muscle relaxation. The injection of muscle relaxant was terminated half an hour before the end of the operation, and anesthetics were withdrawn during suture. During the operation, the depth of anesthesia of patients was monitored using bispectral index (BIS); the cannula could be removed when patients could hear and respond to the doctor's instructions and the spontaneous respiratory rate had reached 16-22 times/min; patients were sent back to the ward when they met the requirements of recovery room.

*Pain index evaluation in perioperative period*. Visual analogue scale (VAS) was used to evaluate the degree of pain in patients at 24 and 48 h after operation. VAS score: 0 point, no pain; 10 points, intense pain; 0-2 points, good analgesic effect; 2-4 points, better analgesic effect; and more than 4 points, poor analgesic effect. The extubation time, eye-opening time and response time of patients in two groups after operation were recorded in detail used for evaluation of patients' recovery after anesthesia. Extubation time: duration from using anesthetics to removing the tracheal cannula out of the mouth of patients; eye-opening time: duration from withdrawing anesthetics to the time when patients responded to external stimulus and instructions with eyes opened; response time: duration from withdrawing anesthetics to the time when patients could clearly answer the physician's questions.

*Monitoring of inflammatory response*. The expression of inflammatory factors in serum of patients in each group after operation were detected using enzyme-linked immunosorbent assay (ELISA) kits. Arterial blood was drawn from patients in both groups before operation and at 30 min and 24 h after operation, placed into the anticoagulant tube, and centrifuged at 2,400 x g for 20 min at 4˚C. Then the supernatant was collected for the serum. The levels of corresponding inflammatory factors in serum of patients in each group were detected using interleukin-6 (IL-6), IL-10β, intercellular adhesion molecule-1 (ICAM-1) and matrix metalloproteinase-9 (MMP-9) kits, respectively: The standard substances in kits were added into the sample plate to prepare the standard curve, and Curve Expert was used to fit and prepare the standard curve, used as a quantitative criterion; the serum sample was diluted 10 times with diluent in the kit, and added into each sample well; the operation was repeated 3 times for each sample. After the plate was sealed with sealing membrane, the serum sample was incubated at 37˚C for 60 min. The liquid in the well was patted dry, the corresponding biotin-labeled antibodies were added, and the plate was sealed, followed by incubation at 37˚C for 90 min. The liquid in the well was patted dry, and each well was washed with 300 $\mu$l washing liquid for 3 min; then the washing liquid was discarded, 100 $\mu$l avidin-peroxidase complex was added, and the plate was sealed, followed by incubation at 37˚C for 30 min; the waste liquid was discarded and 200 $\mu$l of washing liquid was added. After that, 50 $\mu$l of stop buffer was added to terminate the reaction. The optical density value of sample in each group was measured at 465 nm, and the levels of serum IL-6, IL-1β, ICAM-1 and MMP-9 in each group were calculated using standard curves.

*Evaluation of cognitive function*. The cognitive functions of patients in the groups were evaluated using MMSE scale. Before anesthesia, and at 24 and 48 h after operation, the cognitive functions of patients in the groups were evaluated, and the scores were analyzed. Compared with that before operation, MMSE score was decreased, and the difference of more than 2 points indicated that the cognitive function of patients had declined. The serum S100β concentration in patients in each group was detected using the ELISA kit, as above. The serum S100β level was used to evaluate the cognitive function of patients in each group.

*Postoperative evaluation of physiological indexes*. The physiological indexes of patients at 24 and 48 h after operation were recorded, including mean arterial pressure (MAP) and heart rate (HR). Changes in physiological indexes of patients in the two groups after operation were evaluated.

*Statistical analysis*. Data in the present study are expressed as mean ± standard deviation, and analyzed using Statistical Product and Service Solutions 19.0 software (SPSS, Inc., Chicago, IL, USA). Comparison between groups was done using one-way ANOVA test followed by post hoc test (least

Table I. General data of patients in each group (mean ± SD).

| Group | Sex (male/female) | Age (years) | Years of education (years) | BMI (kg/m$^2$) | ASA grade (I/II) |
|---|---|---|---|---|---|
| Group P | (22/19) | 53.7±18.9 | 7.5±3.8 | 24.8±2.3 | (28/13) |
| Group S | (23/18) | 52.1±19.8 | 7.3±4.2 | 24.9±2.7 | (30/11) |
| P-value | >0.05 | >0.05 | >0.05 | >0.05 | >0.05 |
| t-test | 0.624 | 0.653 | 0.937 | 0.824 | 0.532 |

Table II. Operation conditions (mean ± SD).

| Group | Operation time (min) | Amount of intraoperative bleeding (ml) | Anesthesia time (min) |
|---|---|---|---|
| Group P | 123.6±15.6 | 352.3±73.5 | 159.6±18.8 |
| Group S | 118.9±22.8 | 361.9±50.6 | 155.3±24.2 |
| P-value | >0.05 | >0.05 | >0.05 |
| t-test | 0.530 | 0.852 | 0.735 |

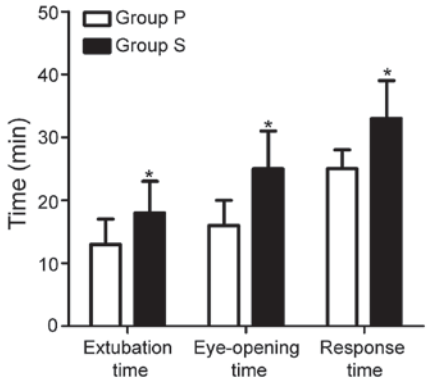


Figure 1. Evaluation of recovery time after operation. The extubation time, eye-opening time and response time of patients in Group P are significantly shorter than those in Group S. *p<0.05 vs. Group P.

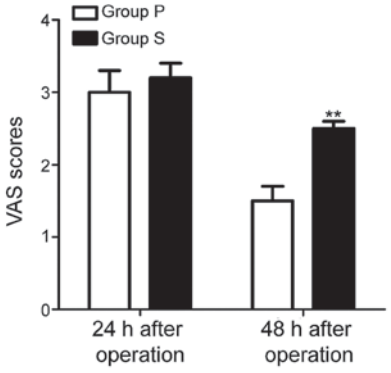


Figure 2. VAS scores of patients in two groups. There is no statistically significant difference in VAS score between the groups of patients at 24 h after operation, and the VAS score of patients in Group P at 48 h after operation is significantly lower than that in Group S. **p<0.01.

significant difference). Percentage (%) was used to express the enumeration data and Chi-square test was used for data analysis. The non-parametric total rank of independent samples of grade data was used to test. A value of P<0.05 was considered to indicate a statistically significant difference.

## Results

*General data*. Each examination was finished for patients in Group P and Group S within 24 h after admission, and data of patients in the groups were analyzed. The general data of patients in both groups are shown in Table I. There were no statistically significant differences in the sex, age, years of education, body mass index (BMI) and ASA grade between the groups of patients (p>0.05). The operations for two groups of patients were performed by the same doctor, and the operation time, amount of intraoperative bleeding and anesthesia time of patients in both groups were recorded in detail. The results showed that the operation time, amount of intraoperative bleeding and anesthesia time had no statistically significant difference between the groups of patients (p>0.05) (Table II).

*Comparison of recovery time after operation between two groups of patients*. The extubation time, eye-opening time and response time of patients in the groups after operation were recorded and analyzed. The results showed that the extubation time, eye-opening time and response time of patients in Group P were significantly shorter than those in Group S, and the differences were statistically significant (p<0.05) (Fig. 1).

*Comparison of pain index between two groups of patients*. VAS was used to evaluate the pain indexes of patients in both groups at 24 and 48 h after operation. The results revealed that there was no statistically significant difference in VAS score between two groups of patients at 24 h after operation (p>0.05), and the VAS score of patients in Group P at 48 h after operation was significantly lower than that in Group S (p<0.05) (Fig. 2).

*Comparison of inflammatory response*. The expression levels of serum inflammatory factors in patients in the groups were detected before operation and at 30 min and 24 h after operation, respectively. The results revealed that the levels of serum

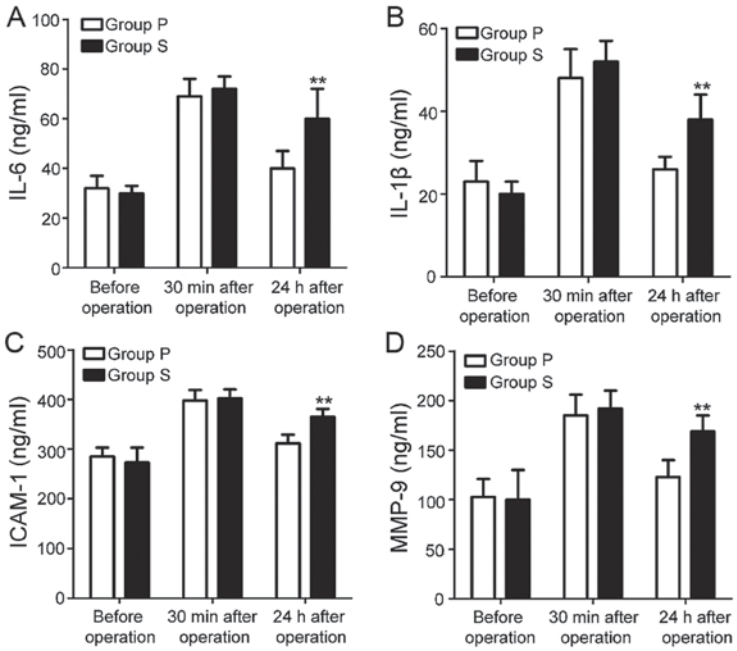


Figure 3. Comparison of inflammatory response. (A) Serum IL-6 concentration; (B) serum IL-1β concentration; (C) serum ICAM-1 concentration; (D) serum MMP-9 concentration. The levels of serum IL-6, IL-1β, ICAM-1 and MMP-9 in patients in the groups have no statistically significant differences before and after operation; the levels of serum IL-6, IL-1β, ICAM-1 and MMP-9 in patients in Group P at 24 h after operation are significantly lower than those in Group S. $^{**}p<0.01$ vs. Group P.

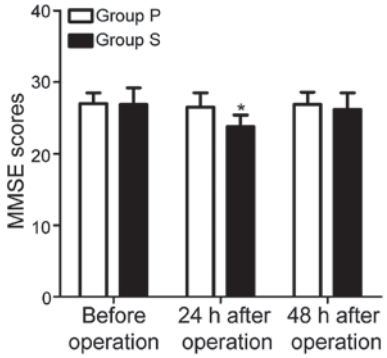


Figure 4. MMSE scores. There are no statistically significant differences in the MMSE scores between two groups of patients before operation and at 48 h after operation; at 24 h after operation, the MMSE score of patients in Group P is significantly higher than that in Group S. $^{*}p<0.05$ vs. Group P.

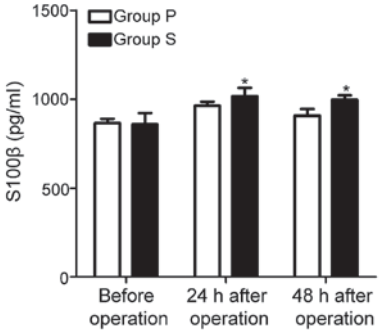


Figure 5. Serum S100β concentrations. There is no statistically significant difference in the serum S100β concentration between two groups of patients before operation; at 24 and 48 h after operation, the serum S100β concentrations of patients in Group P are significantly lower than those in Group S. $^{*}p<0.05$ vs. Group P.

IL-6, IL-1β, ICAM-1 and MMP-9 in patients in the groups had no statistically significant differences before operation and at 30 min after operation ($p>0.05$); the levels of serum IL-6, IL-1β, ICAM-1 and MMP-9 in patients in Group P at 24 h after operation were significantly lower than those in Group S, and the differences were statistically significant ($p<0.01$) (Fig. 3).

*Comparison of cognitive function and serum S100β concentration after operation*. The cognitive functions of patients in two groups before operation and at 24 and 48 h after operation were evaluated using MMSE scale. As shown in Fig. 4, there was no statistically significant difference in the MMSE score between two groups of patients before the operation ($p>0.05$); at 24 h after operation, the MMSE score of patients in Group S was lower than that in Group P ($p<0.05$), and the difference was more than 2 points compared with that after operation; the MMSE scores of patients in Group P and Group S at 48 h after operation had no statistically significant difference ($p>0.05$); the serum S100β concentrations in patients in the groups before operation and at 24 and 48 h after operation were detected using ELISA kit. The results showed that there was no statistically significant difference in the serum S100β concentration between two groups of patients before operation; the serum S100β concentrations of patients in Group S at 24 and 48 h after operation were significantly lower than those in Group P ($p<0.05$) (Fig. 5).

*Postoperative evaluation of physiological indexes*. The physiological indexes of patients in the groups were recorded at 24 and 48 h after operation, respectively. The results showed that there were no statistically significant differences in MAP

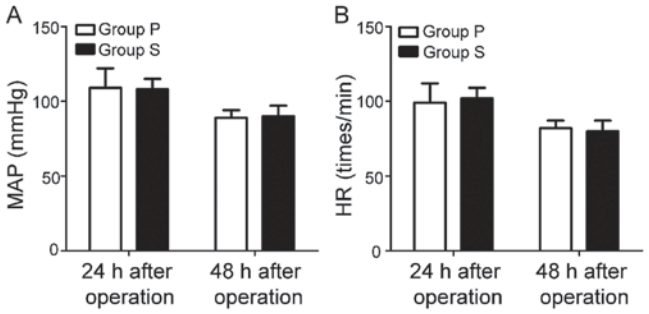


Figure 6. Postoperative evaluation of physiological indexes. There are no statistically significant differences in MAP and HR at 24 and 48 h after operation between the two groups of patients.

and HR at 24 and 48 h after operation between two groups of patients ($p>0.05$) (Fig. 6).

## Discussion

Surgical operation has become the most common and effective treatment for spinal fracture, which can significantly reduce the trauma and pain in patients due to fracture. However, patients often have different degrees of cognitive impairment after operation (9). Waterloo *et al* (10) found that choosing the appropriate anesthetics during operation can effectively reduce the pain index in patients after operation, and benefit the recovery of patients' cognitive function after operation. Waterloo *et al* (11) found that fracture orthopedic surgery can cause damage to some soft tissues, leading to endothelial cell infiltration, producing inflammatory response; reducing the inflammatory response during operation can significantly increase the success rate of operation and improve the prognosis of patients. Zhang *et al* (12) showed that the propofol-induced anesthesia can significantly reduce the inflammatory response of patients during operation, obviously inhibiting the release of inflammatory factors and reducing the infiltration of neutrophils and eosinophils. Postoperative cognitive impairment is a common neurological complication of patients after operation, which often occurs in elderly patients, causing serious damage to the memory, attention and orientation of patients, and even affecting the life quality of patients after operation (13). Wang *et al* (14) found that the incidence rate of postoperative cognitive dysfunction in patients undergoing thoracic surgery under general anesthesia is over 10%.

In this study, the effects of propofol and sevoflurane anesthesia, combined with remifentanil, were compared on the pain index, inflammatory factors and cognitive function of patients with spinal fractures, and it was found that both propofol and sevoflurane had good effects of induced anesthesia, which could make patients enter the anesthesia state quickly, and reduce the pain of patients caused by fracture; besides, there was no effect on physiological indexes of patients after operation with a high safety factor; however, the VAS score of patients after operation showed that propofol had a better analgesic effect. Sevoflurane is characterized by no stimulation against upper respiratory tract as well as stable and safe anesthetic effect, and propofol has the advantages of rapid onset of action and good analgesic effect (15). Moreover, remifentanil combined with sevoflurane or propofol can significantly reduce the drug concentration in anesthesia and the incidence rate of adverse reactions, which can also obtain a good anesthetic effect with rapid recovery (16). Compared with sevoflurane, propofol has a strong inhibitory effect on inflammatory response, which can significantly reduce the levels of serum inflammatory factors (IL-6 and IL-1β). MMP-9, through increasing the activity of elastase, can promote the adhesion of neutrophils and vascular endothelium, and hydrolyze the adhesion protein and connexin, causing damage to the lung tissues (17). ICAM-1, an intercellular adhesion molecule, exerts its biological activity by binding to specific receptors on the surface of vascular endothelial cells, which plays an important role in promoting the endothelial cell migration. The study of Zhu *et al* (18) found that the serum ICAM-1 and MMP-9 levels in patients with pneumonia are significantly increased. It was found in this experiment that the serum ICAM-1 and MMP-9 levels in patients in Group P were significantly lower than those in Group S, indicating that propofol can significantly reduce the inflammatory response caused by the operation. Moreover, this study found that MMSE scores of patients in both groups were decreased to some degree after operation, and the concentration of S100β was increased. The above results suggested that both sevoflurane and propofol anesthesia can cause a certain degree of cognitive impairment. Fracture surgery will lead to decreased ratio of ventilation volume to blood flow in the body of patients to some extent, resulting in hypoxemia and certain damage to cognitive function in patients; sevoflurane will block the synaptic transmission of postsynaptic cholinergic neuron and inhibits the long-term potentiation of hippocampal synapses, further impairing the cognitive function in patients (19). Propofol can directly activate γ-aminobutyric acid receptors, weaken the synaptic activity, and reduce the cerebrovascular blood flow, thus causing some damage to cognitive function (20). It was found in this evaluation that the MMSE score of patients in Group P was significantly higher than that in Group S, indicating that propofol anesthesia causes less damage to the cognitive function in patients after operation.

In conclusion, compared with sevoflurane, propofol has a better analgesic effect used in the induced anesthesia in operation of patients with spinal fractures, which can effectively reduce the inflammatory response of patients during operation with little damage to the cognitive function, so its safety is significantly higher than that of sevoflurane, and propofol is worthy of extensive promotion in clinical operation.

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article.

## Authors' contributions

YZ designed the study, collected the data and prepared the manuscript. HZ analysed the data and revised the study. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of Jining First People's Hospital (Jining, China). Signed written informed consents were obtained from all participants before the study.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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