


# Comparative Sedative Effects of Esketamine and Dexmedetomidine Versus Dexmedetomidine Alone in Patients Undergoing Spinal Tumor Surgery

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**Objective:** Esketamine and dexmedetomidine are commonly used sedatives in surgery, which can result in minimal respiratory depression and analgesic activity. This study investigated the sedative effect of esketamine combined with dexmedetomidine on patients undergoing spinal tumor (ST) surgery.

**Methods:** We did a retrospective analysis at the Anesthesiology Department of Ningbo City's the sixth Hospital. They studied 75 ST surgery patients who got esketamine in combination with dexmedetomidine (Group ED) between April 2022 and June 2024. In a 1:1 cohort, compare these individuals to those who only received dexmedetomidine at the same time period (Group D). The primary outcome is perioperative hemodynamic status. The secondary outcomes were pain intensity, intraoperative neurophysiological monitoring (IONM), and the occurrence of adverse responses.

**Results:** Compared with group E, the group ED had lower mean arterial pressure (MAP), heart rate (HR), and visual-analogue scale (VAS) scores after the start of surgery (all  $P < 0.05$ ). There was no significant difference in the waiting time for perioperative motor evoked potential (MEP) and the intensity of the first induced MEP current between the two groups (all  $P > 0.05$ ); The Group ED first induced MEP amplitude, somatosensory evoked potential (SEP) amplitude, and MEP amplitude greater than the Group D, while SEP latency and MEP latency were smaller than the Group D (all  $P < 0.05$ ). There was no significant difference in the incidence of perioperative adverse events between the two groups ( $P > 0.05$ ).

**Conclusion:** Compared with dexmedetomidine alone, the combination of esketamine and dexmedetomidine during ST surgery can demonstrated superior sedation and pain control without increasing adverse event risk, making it a viable alternative for ST surgery anesthesia.

**Keywords:** esketamine, dexmedetomidine, spinal tumor, sedative effect

## Introduction

In recent years, affected by many factors such as the aging of the population and the formation of bad living habits, the incidence rate of malignant tumors has continued to increase.<sup>1</sup> As a clinical multiple malignant tumor type, the incidence rate of spinal tumor (ST) also increases.<sup>2</sup> STs pose a great threat to the physical and mental health as well as the quality of life of patients, therefore, early implementation of safe and effective treatment is necessary.<sup>2,3</sup> Surgery is an important measure for clinical treatment of ST.<sup>2-4</sup> But ST surgery is more complex, with a large number of sensitive nerves distributed in the joint capsule and periosteum, which can easily cause severe pain due to invasive surgical procedures. This can easily cause inflammatory stress reactions and hemodynamic fluctuations, which is not conducive to the smooth progress of surgery.<sup>3-5</sup>

Effective anesthesia management during ST surgery plays an important role in improving the effectiveness and safety of surgical treatment.<sup>5,6</sup> As is well known, the spine's special position and intricate functions make spinal surgery challenging and increase the risk of serious bodily trauma. Additionally, once the effects of postoperative anesthesia medications wear off,

the pain becomes worse, which negatively impacts the recovery process following surgery. Dexmedetomidine is a general anesthesia drug that is an alpha 2 receptor agonist. It has hypnotic, analgesic, and sedative effects, can alleviate pain, and has little impact on respiratory function.<sup>7,8</sup> Esketamine is a new type of anesthetic drug, which is the dextrorotatory form of esketamine. It has a strong affinity with N-methyl-D-aspartate (NMDA) receptors, which can reduce adverse cardiovascular reactions and alleviate discomfort.<sup>9,10</sup> At present, relevant evidence has shown the sedative effect of esketamine combined with dexmedetomidine in orthopedic and thoracic surgery.<sup>10,11</sup> Zhang et al discovered in 2023 that people with chronic pain after scoliosis correction surgery experienced considerably better analgesia and subjective sleep quality when the mini-dose esketamine–dexmedetomidine combination was given to sufentanil PCIA, without seeing an increase in adverse effects.<sup>10</sup> However, its sedative effect in specific populations undergoing ST surgery has not been confirmed. The aim of this study is to investigate whether the combination of esketamine and dexmedetomidine can further improve the perioperative sedative effect in patients undergoing ST surgery.

## Materials And Methods

### Research Design and Participants

This study is a retrospective study conducted in the Anesthesiology Department of the Sixth Hospital of Ningbo City. They included a cohort of 75 ST surgery patients who received esketamine combined with dexmedetomidine (Group ED) from April 2022 to June 2024. Match these patients with patients who received dexmedetomidine alone during the same period (Group E) in a 1:1 cohort.

#### Inclusion Criteria

- Meets the diagnostic criteria for ST;<sup>1</sup>
- Accept surgical treatment;
- ASA classification falls between I–II;
- Complete clinical data.

#### Exclusion Criteria

- Electrolyte disorders (such as hypokalemia and hypocalcemia);
- Individuals with coagulation dysfunction;
- Having serious cardiovascular, lung, kidney, or liver diseases;
- Serious respiratory or circulatory system diseases;
- Pregnant or lactating women;
- Long term use of analgesics and sedatives;
- Preoperative bradycardia.

### Sedation Protocol

#### Group D

Dexmedetomidine alone was used (China National Pharmaceutical Group Industrial Langfang Branch, China). Intravenous injection of sufentanil (Yichang Renfu Pharmaceutical Co., Ltd., China) at a dose of 5 µg/kg for anesthesia induction; Administer ropivacaine (0.375%) (AstraZeneca AB, Sweden) for local infiltration anesthesia; Intraoperative infusion of dexmedetomidine 0.5 µg/(kg h) was administered to maintain sedation.

#### Group ED

The combination of esketamine (Jiangsu Hengrui Pharmaceutical Co., Ltd., China) and dexmedetomidine was administered. Intravenous injection of 0.25 mg/kg esketamine for anesthesia induction; The rest of the operations are the same as Group D.

## Outcome

### Main outcome

The main outcome of this study is the intraoperative hemodynamic status. Mean arterial pressure (MAP) and heart rate (HR) were measured at preoperatively (T0), before skin incision (T1), 30 minutes during surgery (T2), and immediately after closure (T3). The multifunctional monitoring device (B40I; GE Healthcare Finland Oy; USA) recorded MAP and HR at different time points.

### Secondary Outcomes

Visual Analog Scale (VAS) was used to assess the degree of pain before surgery, at 6, 12, 24, and 48 hours after surgery; A total of 10 points, the higher the score, the stronger the pain. Record the waiting time, current intensity, amplitude, somatosensory evoked potential (SEP) amplitude, SEP latency, MEP amplitude, and MEP latency of the first motor evoked potential (MEP) during surgery (using the Nicolet Endeavor intraoperative neurophysiological monitoring system from the United States). Sedative adverse events include tachycardia, respiratory depression, hypertension, and post-operative nausea and vomiting (PONV). Surgical related adverse events include pneumothorax, asphyxia and cough, pulmonary hemorrhage, chest pain, heat absorption, and pulmonary infection.

## Statistical Analysis

Statistical software SPSS 26.0 (IBM SPSS Inc., Armonk, United States) and GraphPad Prism 8.0 were used for data processing. Use Shapiro Wilk test to evaluate normal distribution. The continuous data of normal distribution and the data of non normal distribution are represented as mean  $\pm$  standard deviation (SD) and median (interquartile range), respectively. Classification data is represented as frequency and percentage. Use independent sample *t*-test to evaluate continuous data with normal distribution, such as age and body mass index (BMI). Mann–Whitney *U*-test is used for data with non normal distribution. Chi square test is used for classifying data.  $P < 0.05$  is considered statistically significant.

## Results

### Selection and Basic Characteristics of Participants

This study included a total of 150 patients, including 94 males and 56 females; Age range: 39–78 years old,  $59.2 \pm 8.1$  years old; 75 patients in the Group ED were matched with the E group in a 1:1 ratio (Figure 1). There were no significant differences in age, gender, tumor type, BMI, American Society of Anesthesiologists (ASA) grading, and surgical site between the two groups of patients (all  $P > 0.05$ ) (Table 1).

### Hemodynamic State

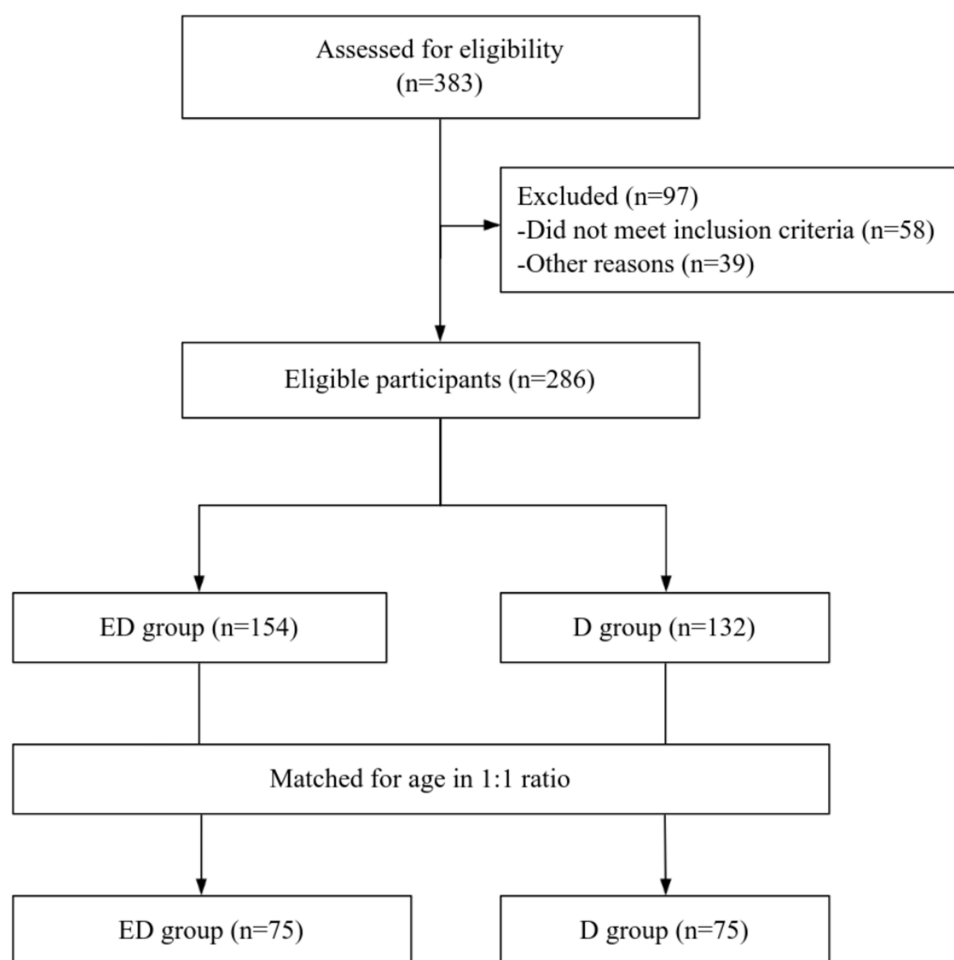
At T0, there was no significant difference in MAP and HR levels between the two groups (all  $P > 0.05$ ); At T1, T2, and T3, the MAP and HR of the Group ED were significantly lower than those of the Group D (all  $P < 0.05$ ) (Figure 2 and Table 2).

### Pain Level

Before surgery, there was no significant difference in VAS scores between the two groups ( $P > 0.05$ ); At 6, 12, 24, and 48 hours postoperatively, the VAS scores in the Group ED were significantly lower than those in the Group D (all  $P < 0.05$ ) (Figure 3 and Table 3).

### Ionm

There was no significant difference in the waiting time and current intensity for the first induction of MEP between the two groups (all  $P > 0.05$ ); The Group ED first induced MEP amplitude ( $1554 \pm 178$ ), SEP amplitude ( $1.85 \pm 0.24$ ), and MEP amplitude ( $1597 \pm 17$ ) were greater than those in MEP amplitude ( $1488 \pm 173$ ), SEP amplitude ( $1.73 \pm 0.29$ ), and MEP amplitude ( $1514 \pm 230$ ) of the Group D, while the SEP latency ( $18.3 \pm 2.9$ ) and MEP latency ( $21(18-23)$ ) were lower than those in SEP latency ( $20.7 \pm 3$ ) and MEP latency ( $23(20-25)$ ) of the Group D (all  $P < 0.05$ ) (Table 4).



**Figure 1** Patient flowchart.

## Perioperative Adverse Events

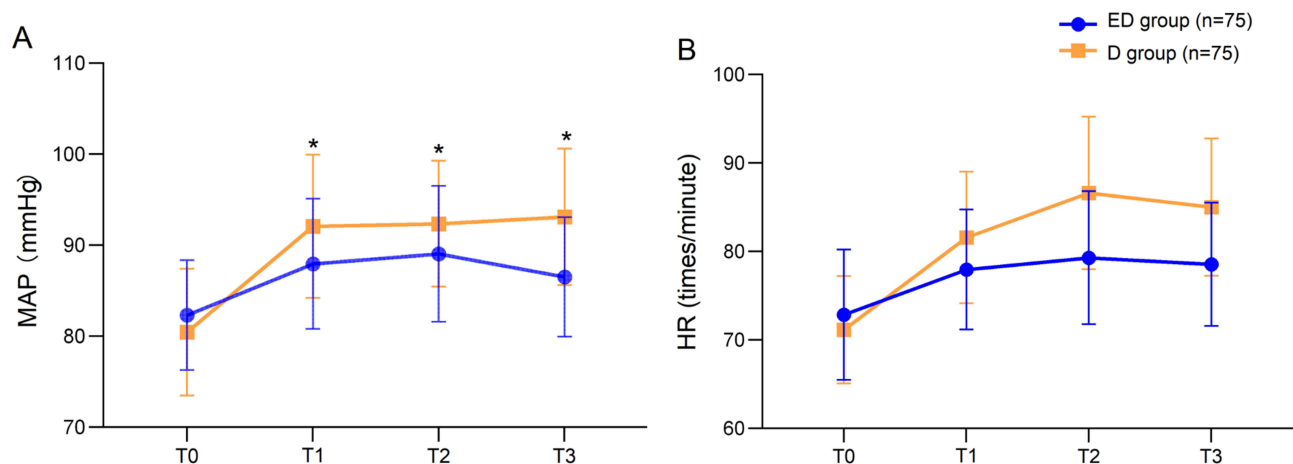
The incidence of sedation-related adverse events in this study was 20.67% (31/150); Among them, the incidence rate of Group ED was 16.00% (12/75), and the incidence rate of Group D was 25.33% (19/75), with no significant difference between the two groups ( $P>0.05$ ). The incidence of surgery related adverse events was 22.67% (34/150); Among them,

**Table 1** Comparison of Basic Characteristics Between Two Groups

Characteristics	Group ED (n=75)	Group D (n=75)	$t/\chi^2$	P
Male/Female	45/30	49/26	0.456	0.500
Age (years)	58.3±8.1	60.1±8.0	-1.388	0.167
BMI (kg/m <sup>2</sup> )	22.1±2.5	22.8±3.1	-1.666	0.098
Tumor type, n (%)				
Primary tumor of vertebral body	9 (12.0)	6 (8.0)	2.049	0.562
Vertebral Metastases	49 (65.3)	52 (69.3)		
Sacral tumor	14 (18.7)	11 (14.7)		
Other	3 (4.0)	6 (8.0)		
ASA Classification (I/II)	39/36	42/33	0.242	0.623
Surgical site (thoracic/lumbar spine)	39/36	48/27	2.217	0.137

**Notes:** Data are expressed as mean (SD), median (25<sup>th</sup> to 75<sup>th</sup> percentiles), or number of patients (%).

**Abbreviations:** ED, esketamine combined with dexmedetomidine; D, dexmedetomidine; BMI, body mass index; ASA, American Society of Anaesthesiologists.



**Figure 2** Perioperative hemodynamic curves ((A) mean arterial pressure, and (B) heart rate). Comparing two groups, \* $P<0.05$ ; T0, preoperatively; T1, before skin incision; T2, 30 minutes during surgery; T3, immediately after closure.

**Abbreviations:** MAP, mean arterial pressure; HR, heart rate; ED, esketamine combined with dexmedetomidine; D, dexmedetomidine; MAP, mean arterial pressure; HR, heart rate.

the incidence rate of Group ED was 18.67% (14/75), and the incidence rate of Group D was 20.67% (20/75); There was no significant difference between the two groups ( $P>0.05$ ) (Table 5).

## Discussion

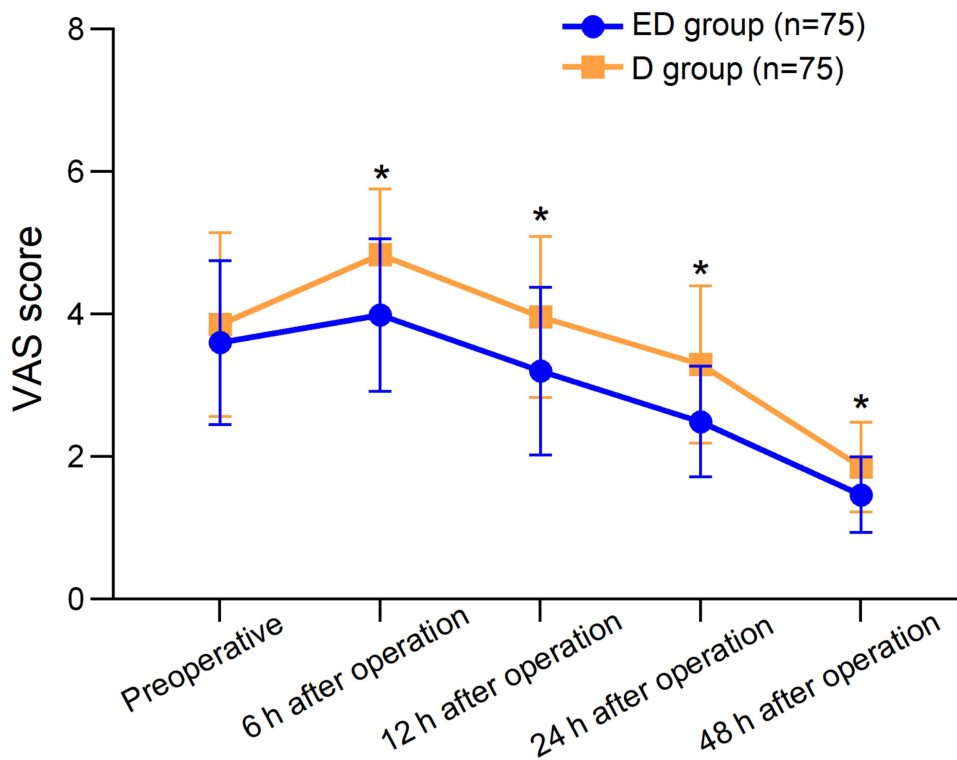
The results of this study indicate that the combination of esketamine and dexmedetomidine is more effective in inhibiting hemodynamic status and reducing postoperative pain in ST surgery compared to using dexmedetomidine alone; It has little effect on MEP and SEP, and does not increase the incidence of adverse events.

Surgery is an important treatment for ST.<sup>3-5,12</sup> Zheng et al<sup>12</sup> found that the spine has a unique position and complex functions, which makes spinal surgery difficult and can easily cause significant trauma to the body; And after the efficacy of postoperative anesthesia drugs subsides, the pain is stronger, which has an adverse effect on postoperative recovery. Therefore, anesthesia management for spinal surgery should be strengthened.<sup>5-10,12</sup> Dexmedetomidine is a commonly used analgesic drug for ST surgery.<sup>7,8,13</sup> Wu et al<sup>13</sup> found that dexmedetomidine can block the sympathetic nervous system, inhibit sympathetic nerve activity, and thus exert stress relief and sedative effects. Esketamine is also a commonly used anesthetic in clinical practice.<sup>9,10</sup> It has both analgesic and sedative effects. Compared to esketamine, its potency is stronger, and its site of action is similar to esketamine; But its affinity with N-methyl-D-aspartate is about twice that of esketamine.<sup>9,10,14</sup>

Based on the above background, some clinical studies attempt to use dexmedetomidine combined with esketamine for spinal surgery treatment.<sup>10,15</sup> Zhang et al<sup>10</sup> applied dexmedetomidine and esketamine in scoliosis correction surgery, and the results showed that a combination intervention of low-dose esketamine and dexmedetomidine could effectively improve postoperative analgesia and subjective sleep quality. The results of this study also showed that the VAS scores of the Group ED were lower than those of the Group D at different time points after surgery, which is consistent with the research results of the aforementioned scholars. This confirms that the combined anesthesia regimen of dexmedetomidine

**Table 2** MAP and HR Comparison Between the Two Groups ( $\bar{x} \pm SD$ )

Group	MAP (mmHg)				HR (times/min)			
	T0	T1	T2	T3	T0	T1	T2	T3
Group E	82.32±6.02	87.96±7.14	89.04±7.47	86.52±6.56	72.85±7.37	77.96±6.78	79.29±7.53	78.55±6.96
Group ED	80.45±6.98	92.08±7.86	92.36±6.91	93.11±7.50	71.15±6.06	81.59±7.42	86.63±8.63	85.01±7.78



**Figure 3** VAS score curve. Comparing two groups, \* $P < 0.05$ .  
**Abbreviations:** ED, esketamine combined with dexmedetomidine; D, dexmedetomidine; VAS, visual-analogue scale.

and esketamine can help alleviate postoperative pain in patients undergoing ST surgery. Mainly due to the sedative, analgesic, anti anxiety, and stress reducing effects of dexmedetomidine.<sup>7,8,15</sup> It can reduce pain by acting on alpha 2 receptors in the central nervous system, downregulating sympathetic nervous activity. Esketamine acts on NMDA receptors and opioid receptors, inhibiting the transmission of pain signals and thereby reducing pain.<sup>9,10,14–16</sup> The combination of the two can play a role in different pain transmission pathways and mechanisms, enhancing the analgesic effect. Lu et al<sup>16</sup> applied a combined anesthesia regimen of dexmedetomidine and esketamine in lung cancer surgery patients, and the results showed that the VAS scores of patients were lower than those who only received sufentanil. This is consistent with the conclusion of this study.

Hemodynamic stability is an important prerequisite for ensuring the effectiveness and safety of surgical treatment. The results of this study showed that the MAP and HR of the Group ED were significantly lower than those of the Group D during surgery. This confirms that the combination of dexmedetomidine and esketamine can also help suppress intraoperative blood pressure and heart rate fluctuations in patients undergoing ST surgery, and maintain hemodynamic stability. This is consistent with the research results of Lin et al<sup>11</sup> and Liu et al.<sup>17</sup> The main reason for this is that esketamine and dexmedetomidine can act on the sympathetic nervous system, reducing the activity of the sympathetic nervous system, thereby reducing the release of catecholamines in children, lowering blood pressure and heart rate.<sup>11,17,18</sup>

In addition, there is a risk of new neurological deficits during the postoperative period of ST surgery. Therefore, intraoperative neurophysiological monitoring and mapping (IONM) is highly necessary.<sup>19,20</sup> Li et al<sup>21</sup> found that SEP

**Table 3** Comparison of VAS Scores at Different Time Points Between the Two Groups ( $\bar{x} \pm SD$ )

Group	Preoperative	6h	12h	24h	48h
Group E	3.60 ± 1.15	3.99 ± 1.07	3.20 ± 1.17	2.49 ± 0.78	1.47 ± 0.53
Group ED	3.85 ± 1.29	4.84 ± 0.92	3.96 ± 1.13	3.29 ± 1.10	1.85 ± 0.63

**Table 4** Comparison of IONM Between Two Groups

Variables	Group ED (n=75)	Group D (n=75)	t/Z	P
First induction of MEP waiting time (min)	28.6±4.7	27.6±6	1.188	0.237
First induced MEP current intensity (mA)	7.76±4.67	7.51±5.97	1.521	0.130
First induction of MEP wave amplitude (uV)	1554±178	1488±173	2.291	0.023
SEP wave amplitude (uV)	1.85±0.24	1.73±0.29	2.752	0.007
MEP wave amplitude (uV)	1597±17	1514±230	2.506	0.013
SEP latency period (ms)	18.3±2.9	20.7±3	-4.99	<0.001
MEP latency period (ms)	21 (18–23)	23 (20–25)	-3.474	0.001

**Notes:** Data are expressed as mean (SD), median (25<sup>th</sup> to 75<sup>th</sup> percentiles).

**Abbreviations:** IONM, intraoperative neurophysiological monitoring; ED, esketamine combined with dexmedetomidine; D, dexmedetomidine; MEP, motor evoked potential; SEP, somatosensory evoked potential.

**Table 5** Incidence of Adverse Reactions in Two Groups, n (%)

Perioperative Adverse Events	Group ED (n=75)	Group D (n=75)	$\chi^2$	P
<b>Sedation-related adverse events</b>				
Tachycardia	1 (1.33)	2 (2.67)	1.992	0.158
Respiratory depression	2 (2.67)	3 (6.00)		
Hypertension	2 (2.67)	4 (5.33)		
PONV	7 (9.33)	10 (13.33)		
Total incidence rate	12 (16.00)	19 (25.33)		
<b>Surgery-related adverse events</b>				
Pneumothorax	9 (12.00)	11 (14.67)	1.369	0.242
Suffocation and cough	1 (1.33)	2 (2.67))		
Pulmonary hemorrhage	1 (1.33)	2 (2.67)		
Chest pain	0 (0)	1 (1.33)		
Postoperative fever	0 (0)	0 (0)		
Pulmonary infection	3 (4.00)	5 (6.67)		
Total incidence rate	14 (18.67)	20 (26.67)		

**Abbreviations:** ED, esketamine combined with dexmedetomidine; D, dexmedetomidine; PONV, postoperative nausea and vomiting.

refers to the electrical activity recorded by sensory nerve fibers that stimulate the skin or peripheral nerves in the corresponding sensory transmission pathways/cortical sensory projection areas on the scalp; MEP is the electrical/magnetic stimulation of the brain motor area/efferent pathway, which records the electrical response of the efferent pathway/muscle at the stimulation point. Both play an important role in the evaluation of anesthesia status. The results of this study showed that the Group ED first induced MEP amplitude, SEP amplitude, and MEP amplitude greater than the Group D, while the SEP latency and MEP latency were significantly lower than the Group D. This indicates that the combined anesthesia regimen of esketamine and dexmedetomidine can also reduce the impact on MEP and SEP, ensuring the effectiveness of anesthesia.<sup>19–21</sup>

Various adverse events often occur during the perioperative period.<sup>22</sup> This study observed sedation related adverse events and surgery related adverse events separately. Among them, vomiting and nausea were the main sedation related adverse events, with an incidence rate of 11.33% (17/150), followed by hypertension (4.0%, 6/150) and respiratory depression (3.33%, 5/150). Opioids are a key trigger factor for PONV, and there is evidence to suggest that intravenous injection of dexmedetomidine or esketamine can reduce the need for opioid drugs during surgery.<sup>19–22</sup> Pneumothorax is the main surgical related adverse event, with an incidence rate of 13.33% (20/150), followed by pulmonary infection (5.33%, 8/150). Stable MAP and HR are more beneficial for elderly patients with lower heart rates or more fragile cardiovascular systems.<sup>22,23</sup> However, regardless of whether it was sedation or surgery related adverse events, although



the incidence rate was lower in the Group ED, there was no statistically significant difference between the two groups. Additionally, we found no discernible difference between the two groups in terms of side effects associated with either dexmedetomidine (such as bradycardia and hypotension) or esketamine (such as mental symptoms). No psychological signs appeared in any of our individuals. This is inconsistent with previous research results, and we believe this may be due to the nature of the study and the small sample size. As a result, this patient population can safely employ our dosage schedule. However, this result is unique to this study, and further patient data is required to validate it.

This study has the following obvious shortcomings. Firstly, this is a retrospective analysis conducted at a tertiary center, and only a sample size of 150 was matched. Secondly, we only evaluated pain scores within the first 48 hours after surgery, which does not reflect long-term outcomes; Postoperative chronic pain can affect patient satisfaction and quality of life. Thirdly, we only used a single dose of esketamine and dexmedetomidine, which may not be the most appropriate dosage. The findings of this study should be supported by future research, including more centers and broader patient participation.

## Conclusion

The combination of esketamine and dexmedetomidine during ST surgery can suppress hemodynamic status, reduce postoperative pain, have minimal impact on MEP and SEP, and do not increase the risk of adverse events. Esketamine may still have certain drawbacks when used in surgery, though, thus further research is required to support this study in subsequent investigations.

## Abbreviations

E, Esketamine; ED, Esketamine and dexmedetomidine; ST, spinal tumor; IONM, intraoperative neurophysiological monitoring; MAP, mean arterial pressure; HR, heart rate; VAS, visual-analogue scale; MEP, motor evoked potential; SEP, somatosensory evoked potential; PONV, postoperative nausea and vomiting; SD, standard deviation; BMI, body mass index.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethics Approval and Consent to Participate

The ethics committee of Ningbo Sixth Hospital approved this study with the number L2021075, Date: November 15th 2021. All procedures involving human subjects adhered to the 1964 Declaration of Helsinki and its subsequent amendments or equivalent ethical standards. Given the retrospective nature of the study, informed consent was waived by the Ethical Committee of Ningbo Sixth Hospital. All data were stored securely, and confidentiality was maintained throughout the study.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests in this work.



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