Am J Transl Res 2026;18(4):3309-3321
www.ajtr.org /ISSN:1943-8141/AJTR0171269

Original Article

Effect of intravenous infusion of remimazolam versus propofol on intraoperative neurophysiological monitoring stability and postoperative neurological function in patients undergoing spinal surgery

Jing Cui*, Baolong Zhou*, Junjie Wang, Lan Yao

*Department of Anesthesiology, Peking University International Hospital, Beijing 102206, China. *Equal contributors and co-first authors.*

Received January 5, 2026; Accepted March 25, 2026; Epub April 15, 2026; Published April 30, 2026

Abstract: Objectives: Intraoperative neurophysiological monitoring (IONM) plays a critical role in spinal surgery by reducing the risk of nerve injury; however, its quality can be significantly influenced by anesthetic agents. This study aimed to compare the effects of remimazolam and propofol on IONM performance and postoperative recovery. Methods: This retrospective analysis included patients who underwent prone-position spinal surgery with IONM between January 2021 and June 2025. Patients were divided into either a remimazolam group or a propofol group according to the primary sedative administered. The outcomes assessed included IONM parameters [somatosensory evoked potentials (SEP)/motor evoked potentials (MEP) amplitude/latency] after intubation (T1) and at 30 min (T3) and 50 min (T4) following recovery from neuromuscular blockade. Additional outcomes included hemodynamics, remifentanil consumption, recovery time, and cognitive function scores. Results: A total of 204 patients included in the analysis (Remimazolam group: 101 cases, Propofol group: 103 cases). Compared to the propofol group, the remimazolam group demonstrated significantly improved IONM signals, higher SEP amplitude at T4 (2.16 vs. 1.97 μV, P<0.001), and higher MEP amplitude at T4 (1680.73 vs. 1500.64 μV, P<0.001). The incidence of hypotension (6.93% vs. 19.42%, P=0.009) and bradycardia (5.94% vs. 14.56%, P=0.043) were significantly lower, while remifentanil consumption was significantly higher (2005.64 vs. 1425.44 ug, P<0.001) in the remimazolam group. In addition, patients in the remimazolam group exhibited shorter recovery times (awakening time: 18.91 vs. 24.25 min, P<0.001) and better cognitive function (MoCA score on postoperative Day 3: 24.41 vs. 23.54, P<0.001). Conclusions: Remimazolam provides superior IONM conditions, a lower incidence of intraoperative hypotension and bradycardia, and faster postoperative recovery compared to propofol in patients undergoing spinal surgery.

Keywords: Remimazolam, propofol, intraoperative neurophysiological monitoring, spinal surgery, postoperative recovery, cognitive function

Introduction

Spinal diseases, including spinal degeneration disorders and spinal deformities, are often managed by surgical intervention, which inevitably increases the risk of intraoperative nerve injury [1, 2]. Intraoperative neurophysiological monitoring (IONM) is considered the gold standard for detecting and preventing such injuries by enabling real-time assessment of neural pathway integrity [3]. The effectiveness of IONM is closely associated with anesthetic management, as most anesthetics cause dose-dependent effects on both neuronal activity and signal quality [4]. IONM typically involves somatosensory and motor evoked potentials (SEP/MEP), both of which are highly sensitive to the depth of anesthesia and to anesthetic drugs with electrophysiologic inhibitory properties [5].

Propofol, a widely used intravenous anesthetic, provides reliable hypnotic effects; however, it has been reported to suppress SEP and MEP signals and is associated with a higher incidence of intraoperative hypotension and brady-

https://doi.org/10.62347/QLLI7857

cardia, possibly compromising the reliability of continuous monitoring [6, 7]. Remimazolam, a newly introduced ultra-short-acting benzodiazepine, exhibits favorable pharmacokinetic properties and may offer superior hemodynamic stability. Nevertheless, its effect on IONM stability remains incompletely determined [8, 9].

The influence of anesthetics on IONM is primarily mediated through their actions on γ-aminobutyric acid type A (GABA_A) receptors. Propofol exerts its anesthetic effects by potentiating GABA_A receptor activity, thereby enhancing inhibitory synaptic transmission, reducing signal amplitude, and prolonging the latency of evoked potentials [10, 11]. Benzodiazepines such as remimazolam also act on GABA_A receptors but bind to distinct allosteric sites, which may result in comparatively less inhibitory effects on cortical and spinal motor neurons involved in MEP generation [12, 13]. Therefore, identifying an anesthetic regimen that maintains IONM signal fidelity while facilitating rapid postoperative neurological recovery remains a clinical priority.

This study aimed to evaluate whether remimazolam provides greater stability for IONM parameters compared to propofol in patients undergoing spinal surgeries. The novelty of this study lies in its thorough comparison of novel anesthetics with established standards, with particular focus on neurophysiological outcomes essential for surgical safety. These findings are expected to provide valuable evidence for optimizing anesthetic strategies, and improve the safety and efficacy of complex spinal procedures.

Materials and methods

Study population and ethical statement

This retrospective cohort study included 204 patients admitted to Peking University International Hospital between January 2021 and June 2025. Patients who received anesthesia induction and maintenance with propofol were assigned to the propofol group, whereas patients who received remimazolam were assigned to the remimazolam group. As this study used de-identified patient data, the requirement for informed consent was waived due to the absence of potential harm to participants. This study was approved by the Ethics Review Committee of Peking University International Hospital, and all procedures were conducted in accordance with relevant regulatory and ethical standards, including the Declaration of Helsinki.

Inclusion criteria: age ≥18 years; ability to understand and accurately respond to questions; American Society of Anesthesiologists (ASA) physical status classification of I-III [14]; undergoing scheduled prone-position spinal surgery under IONM at Peking University International Hospital; preoperative American Spinal Injury Association (ASIA) Impairment Scale scores of B-E [15]; and absence of severe cardiopulmonary dysfunction or cerebrovascular diseases.

Exclusion criteria: (1) Congenital or acquired neurological disorders (e.g., epilepsy and other neuropsychiatric disorders); (2) Preoperative use of antidepressants, sedatives, analgesics, or a history of alcohol abuse; (3) Presence of a cardiac pacemakers or intracranial devices; (4) Poor compliance or difficulty in communication; (5) Known tolerance or hypersensitivity to benzodiazepines; (6) Body Mass Index (BMI) <15 kg/m^2 or >35 kg/m^2 [16]; (7) Skull defects or a history of previous neurosurgical operations; (8) Preoperative ASIA grade A or inability to elicit IONM signals.

Treatment methods

Anesthesia monitoring: All patients were instructed to fast for 8-12 hours before surgery. Upon arrival in the operation room, standard monitoring was established, including electrocardiography, heart rate (HR), bispectral index (BIS), and other routine measurements. Under local anesthesia, ultrasound-guided radial artery catheterization was performed for continuous invasive arterial blood pressure monitoring.

Anesthesia induction: After the establishment of peripheral intravenous access, oxygen was administered via face mask for preoxygenation. In the propofol group, anesthesia was induced with intravenous injection of propofol (Approval No. 16UC3373, Beijing Fresenius Kabi Pharmaceutical Co., Ltd., China) at 2 mg/kg, sufentanil (Approval No. AB50602111, Yichang Renfu Pharmaceutical Co., Ltd., China) at 0.3 μg/kg, and rocuronium (Approval No. EA2512, Zhejiang Xianju Pharmaceutical Co., Ltd., China) at 0.6

mg/kg. In the remimazolam group, anesthesia was induced with intravenous injection of remimazolam (Approval No. AC5070151, Yichang Renfu Pharmaceutical Co., Ltd., China) at 0.3 mg/kg, combined with sufentanil at 0.3 μg/kg, and rocuronium at 0.6 mg/kg.

After achieving an adequate anesthesia depth (BIS <60), endotracheal intubation was performed, followed by initiation of mechanical ventilation. Ventilation parameters were set as follows: air flow rate of 1-2 L/min, respiratory rate of 12 breaths/min, tidal volume of 8-10 ml/kg, and an inspiratory-to-expiratory ratio (I:E) of 1:2. Minute ventilation was adjusted based on arterial partial pressure of CO_2 ($PaCO_2$) to maintain intraoperative $PaCO_2$ between 35-40 mmHg (1 mmHg = 0.133 kPa). A bite block was used to prevent dental and oral soft tissue injury caused by masseter muscle contractions during neurophysiologic stimulation.

Anesthesia maintenance: Anesthesia was maintained using total intravenous anesthesia (TIVA). In the remimazolam group, remimazolam was administered via continuous intravenous infusion at a rate of 0.4-1.2 mg/kg/h. In the propofol group, propofol was administered at a rate of 4-12 mg/kg/h. Infusion rates in both groups were adjusted in real-time based on BIS monitoring values (COVIDIEN, USA) to maintain a target range of 45-60. Both groups received continuous intravenous infusion of remifentanil (Approval No.: H20143315, Jiangsu Nhwa Pharmaceutical Co., Ltd., China) at a rate of 0.05-0.20 μg/kg/min. The infusion rate was adjusted based on intraoperative analgesic needs, including hemodynamic fluctuations (blood pressure or heart rate exceeding ± 20% of baseline), patient movement, signs of spontaneous breathing, and changes in BIS values.

During surgery, rocuronium and sufentanil were administered as needed to maintain adequate muscle relaxation and analgesia. Mean arterial pressure was maintained within ± 20% of baseline levels. If necessary, appropriate vasoactive drugs were administered. Intraoperative fluid management was guided by pulse pressure variation (PPV). Measures such as warming blankets, fluid warmers, and surface warming devices, were applied to maintain core body temperature between 36°C and 37°C.

Neurophysiological monitoring: Neurophysiological monitoring was performed using a combination of SEP and MEP with an intraoperative electroencephalography/electromyography/evoked potential monitoring system, (Cascade Pro, Cadwell Laboratories, Inc., USA). For SEP monitoring, stimulation electrodes for the upper limbs were placed over the median nerve at the wrist (2 cm proximal to the wrist crease) with a stimulation intensity of 25 mA and a frequency of 4.7 Hz; for the lower limbs, stimulation electrodes were placed over the posterior tibial nerve, located posterior to the medial malleolus (midline between the posterior edge of the Achilles tendon and the medial malleolus). The stimulation intensity was adjusted to produce visible toe movement within a range of 1-2 cm at a stimulation frequency of 5.3 Hz. Recording electrodes for SEP were placed at the Cz point on the scalp, with reference electrodes at the Fz point on the forehead. The band-pass filter was set to 30-3000 Hz, and responses were averaged over 100 trials.

For MEP monitoring, transcranial electrical stimulation was applied with the anode positioned at Cz' and the cathodes at C3 and C4. Compound muscle action potentials were recorded from the abductor pollicis brevis muscle in the upper limbs and from the tibialis anterior or extensor digitorum longus muscles in the lower limbs. MEPs were elicited using a train of five pulses, with a stimulation intensity of 400 V (fixed intensity, based on pre-stimulation to achieve a stable supramaximal baseline), a pulse width of 0.1 ms, and an interstimulus interval of 2 ms. The recording sensitivity was set at 50-100 μV/div, with a band-pass filter of 20-3000 Hz.

Abnormal intraoperative neurophysiological monitoring signals were defined as follows: for SEP, a decrease in amplitude of more than 50% or an increase in latency of more than 10% at T3 or T4 compared with baseline (T1); for MEP, a decrease in amplitude of more than 80% at T4 compared with T3.

Neuromuscular transmission was monitored using train-of-four (TOF) stimulation. Stimulating electrodes were placed on the ulnar nerve at the wrist, delivering supramaximal stimulation (30-50 mA) at 2 Hz with a 15-second inter-train interval. Recording electrodes were placed on the ipsilateral abductor pollicis brevis muscle, and TOF ratios were recorded using acceleromyography (AMG). The TOF ratio was defined as T4/T1. All TOF data were synchronized with IONM recordings and collected at T1 (immediately after intubation), T3 (30 min after recovery from neuromuscular blockade), and T4 (50 min after recovery from neuromuscular blockade).

Data collection and outcome measures

Baseline demographic and clinical characteristics of all patients were collected from the hospital's case management system. The primary outcomes included intraoperation SEP and MEP data (amplitude and latency), and postoperative cognitive recovery. Data were collected at the following predefined time points: upon entry into the operating room (T0), immediately after intubation (T1), 1 min after recovery of neuromuscular function (T2), 30 min after recovery from neuromuscular blockade (T3), and 50 min after recovery from neuromuscular blockade (T4).

The selection of T4 was based on the pharmacokinetic profile of rocuronium (0.6 mg/kg), for which previous studies have reported a median time of approximately 50 min for complete recovery (TOF ratio reaching ≥0.9) [17]. Therefore, T4 was considered the time point at which neuromuscular transmission had fully recovered, minimizing the influence of residual neuromuscular blockade on MEP recordings. Intraoperative neurophysiological data included the included SEP and MEP amplitudes and latencies recorded at T1, T3, T4, and at the end of surgery. Due to the pharmacodynamic effects of rocuronium [18], reliable MEP data were only obtained at T3 and T4.

Arterial blood samples (3 mL) were obtained and analyzed using a blood gas analyzer (Nova STAT Profile pH Ox Ultra, NOVA Biomedical, USA) for the measurement of PaO_2, $PaCO_2$, arterial pH, and hematocrit (Hct). These measurements were used to guide intraoperative ventilatory management, with adjustments made to maintain $PaCO_2$ within the target range.

Hemodynamic data were continuously monitored using electrocardiography and invasive arterial blood pressure monitoring. A disposable pressure transducer system (B. Braun Medical, Suzhou, China) was connected to the arterial catheter for real-time measurement of mean arterial pressure (MAP).

Intraoperative hypotension was defined as a MAP <65 mmHg or a reduction of >30% from baseline lasting for ≥1 minute [19]. Bradycardia was defined as a heart rate <50 beats per minute (bpm), requiring pharmacologic intervention (atropine/ephedrine) or persisting for >1 minute [20].

Neurological function was evaluated using the Japanese Orthopedic Association (JOA) score before and after surgery. The JOA score ranges from 0 to 17, with higher JOA scores indicating better neurological function (intraclass correlation coefficient [ICC] = 0.813) [21].

Cognitive function was evaluated at baseline and on postoperative days 3 to 7 using the Mini-Mental State Examination (MMSE), which assesses orientation, memory, attention, calculation, recall, and language abilities, with a total score of 30 points (Cronbach's α = 0.83-0.87) [22]. The Montreal Cognitive Assessment (MoCA) was also used, evaluating visuospatial ability, executive function, naming, memory, attention, language, delayed recall, and orientation, with a total score of 30 points (Cronbach's α = 0.85) [22]. Higher MMSE and MoCA scores reflect better cognitive function.

Postoperative pain at rest within 24 hours was assessed using the Visual Analog Scale (VAS). Patients marked their pain intensity on a 10-cm linear scale ranging from 0 (no pain) to 10 (worst imaginable pain). The distance (to the nearest 0.1 cm) was recorded. All assessments were performed with patients in a resting supine position.

Statistical method

Statistical analyses were performed using R 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were expressed as frequencies (percentages) [n (%)] and compared between groups using the chi-square test (χ^2). Continuous variables were first evaluated for normality using the Shapiro-Wilk test. All data followed a normal distribution and were expressed as means ± standard deviations (mean ± SD). Comparisons between two groups were performed using the independent samples t-test. Multivariate logistic regression analysis was per-

Table 1. Comparison of baseline characteristics between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t/χ^2	*P* value
Age (year)	58.06 ± 6.21	58.58 ± 6.12	0.594	0.553
Sex (Male/Female) [n (%)]	57 (55.34%)/46 (44.66%)	53 (52.48%)/48 (47.52%)	0.168	0.682
BMI (kg/m^2)	23.41 ± 1.94	23.49 ± 1.72	0.287	0.774
ASA Physical Status (I/II/III) [n (%)]	19 (18.45%)/67 (65.05%)/17 (16.5%)	16 (15.84%)/69 (68.32%)/16 (15.84%)	0.297	0.862
JOA Score, Preoperative (point)	14.57 ± 0.51	14.54 ± 0.60	0.298	0.766
Smoking Status [n (%)]			0.300	0.861
Does not Smoke	55 (53.40%)	51 (50.50%)		
Smoked Previously	31 (30.10%)	34 (33.66%)		
Smokes Currently	17 (16.50%)	16 (15.84%)		
Comorbidities [n (%)]				
Hypertension	32 (31.07%)	30 (29.70%)	0.045	0.832
Diabetes	15 (14.56%)	17 (16.83%)	0.198	0.656
Cardiac	12 (11.65%)	12 (11.88%)	0.003	0.959
Respiratory	9 (8.74%)	10 (9.90%)	0.082	0.775
Hepatologic	9 (8.74%)	10 (9.90%)	0.082	0.775
Renal	3 (2.91%)	3 (2.97%)	0.152	0.697
Education [n (%)]			0.011	0.917
High School and Below	82 (79.61%)	81 (80.20%)		
Above High School	21 (20.39%)	20 (19.80%)		

Note: BMI: Body Mass Index; ASA: American Society of Anesthesiologists; JOA: Japanese Orthopedic Association.

Table 2. Comparison of intraoperative surgical findings and anesthesia depth between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t	*P* value
Duration				
Duration of Anesthesia (min)	174.19 ± 43.44	176.57 ± 48.68	0.370	0.712
Duration of Operation (min)	117.64 ± 36.04	118.26 ± 41.44	0.114	0.909
Time to Loss of Consciousness (s)	45.17 ± 12.54	44.86 ± 11.98	0.182	0.856
BIS				
T0	95.22 ± 1.17	95.43 ± 1.20	1.314	0.190
T1	51.42 ± 2.24	51.70 ± 2.44	0.843	0.400
T2	51.30 ± 2.45	51.62 ± 2.34	0.955	0.341
T3	51.41 ± 2.39	51.72 ± 2.22	0.964	0.336
T4	51.47 ± 2.58	51.24 ± 2.59	0.629	0.530

Note: BIS: Bispectral Index.

formed to identify independent protective factors for early postoperative cognitive dysfunction. Results were presented as adjusted odds ratios (OR) and their 95% confidence intervals (CI) and *P*-values. A *P*-value <0.05 was considered significant.

Results

Baseline demographics and clinical characteristics

As shown in **Table 1**, no significant differences were observed between the two groups in baseline characteristics, including age, sex distribution, BMI, ASA classification, preoperative JOA score, the prevalence of comorbidities, smoking status, and education level (all P>0.05), indicating adequate baseline comparability.

IONM, surgical findings, and anesthesia management

No significant differences were observed between the two groups in anesthesia duration, operation time, or anesthesia depth (BIS across T0-T4) (all P>0.05; **Table 2**).

Table 3. Comparison of intraoperative anesthesia management and blood gas analysis between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t/χ^2	*P* value
Arterial Blood Gas Analysis				
pH	7.32 ± 0.03	7.31 ± 0.03	1.114	0.267
PaO_2 (mmHg)	216.76 ± 23.31	214.48 ± 24.58	0.679	0.498
$PaCO_2$ (mmHg)	35.17 ± 2.24	35.46 ± 2.35	0.906	0.366
Hematocrit (%)	35.54 ± 3.47	35.59 ± 3.44	0.099	0.921
Administered Agents				
Additional Rocuronium [n (%)]	3 (2.91%)	3 (2.97%)	0.152	0.697
Total Consumption of Remifentanil (μg)	1425.44 ± 410.42	2005.64 ± 680.84	7.354	<0.001

Note: PaO_2: Partial Pressure of Oxygen; $PaCO_2$: Partial Pressure of Carbon Dioxide.

Table 4. Comparison of intraoperative neurophysiological monitoring (IONM) data between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t	*P* value
Latency of SEP (ms)				
T1	38.54 ± 3.14	39.06 ± 2.85	1.240	0.217
T3	42.52 ± 4.04	41.04 ± 3.54	2.781	0.006
T4	41.03 ± 3.24	39.75 ± 2.86	2.987	0.003
Amplitude of SEP (μV)				
T1	2.12 ± 0.42	2.13 ± 0.36	0.288	0.773
T3	1.26 ± 0.30	1.52 ± 0.42	5.072	<0.001
T4	1.97 ± 0.16	2.16 ± 0.13	9.746	<0.001
Latency of MEP (ms)				
T3	33.02 ± 3.23	31.54 ± 3.25	3.256	0.001
T4	35.03 ± 3.55	33.57 ± 3.45	2.974	0.003
Amplitude of MEP (μV)				
T3	1300.01 ± 148.37	1530.42 ± 147.36	11.127	<0.001
T4	1500.64 ± 149.16	1680.73 ± 148.19	8.649	<0.001
Abnormal SEP signals	29 (28.16%)	14 (13.86%)	6.263	0.012
Abnormal MEP signals	0 (0.00%)	0 (0.00%)	None	1.000
TOF ratio				
T3	0.77 ± 0.11	0.78 ± 0.10	0.451	0.653
T4	0.94 ± 0.06	0.95 ± 0.05	1.142	0.255

Note: MEP: Transcranial Motor Evoked Potential; SEP: Somatosensory Evoked Potential; TOF ratio: Train-of-Four Ratio.

Arterial blood gas analysis revealed no significant between the two groups in pH, PaO_2, $PaCO_2$, or Hct (all P>0.05; **Table 3**). Additionally, the proportion of patients requiring additional rocuronium was also similar between groups (P=0.697). However, total remifentanil consumption was significantly higher in the remimazolam group compared to the propofol group (P<0.001).

Regarding IONM data (**Table 4**), no significant differences were observed in SEP latency (P=0.217) or amplitude (P=0.773) at baseline (T1). However, at T3 and T4, compared with the propofol group, SEP latency was significantly shorter in the remimazolam group (T3: P=0.006; T4: P=0.003), while SEP amplitude was significantly higher (both P<0.001). Similarly, MEP latency at T3 and T4 was significantly shorter in the remimazolam group (T3: P=0.001; T4: P=0.003), and MEP amplitude was significantly higher at both time points (both P<0.001). Furthermore, analysis of IONM signal abnormalities revealed a significantly

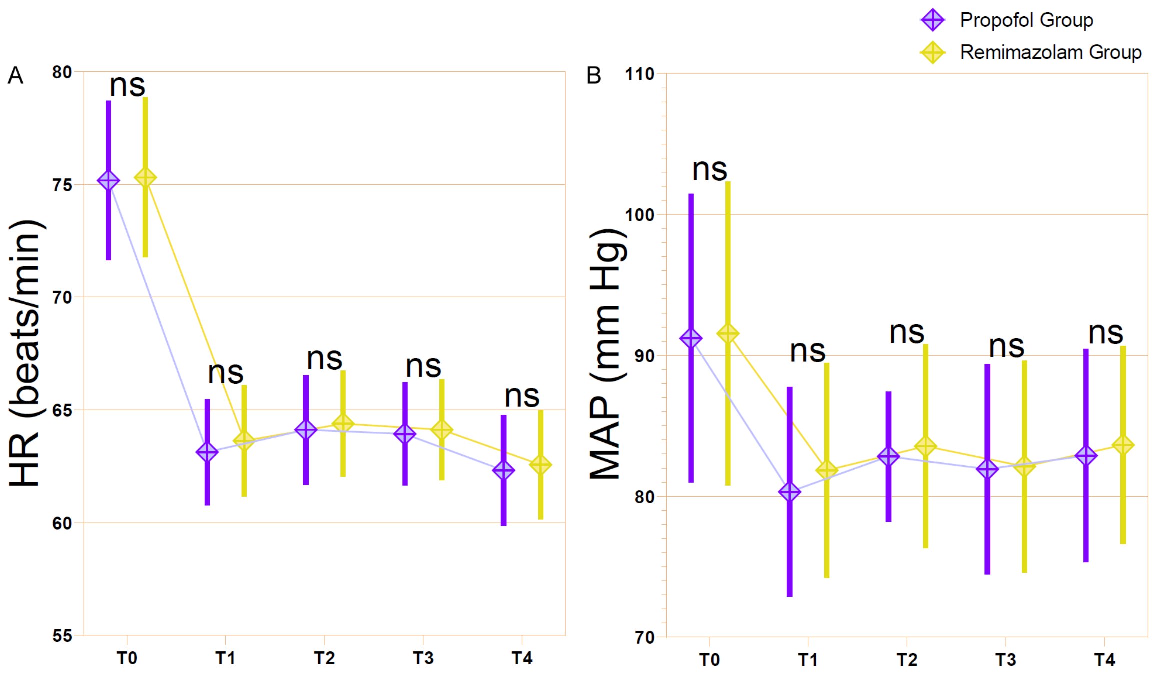

Figure 1. Intraoperative hemodynamic changes in both groups. Note: (A) HR (beats/min); (B) MAP (mm Hg); ns, no significant; HR, Heart Rate; MAP, Mean Arterial Pressure. T0: upon entering the operating room, T1: immediately after endotracheal intubation, T2: one minute after cessation of muscle relaxants, T3: 30 minutes after cessation of muscle relaxants, T4: 50 minutes after cessation of muscle relaxants.

lower incidence of abnormal SEP signals in the remimazolam group (P=0.012), while no MEP signal abnormalities were observed in either group (P=1.000). In contrast, the TOF ratio did not show significant differences between groups at either T3 (P=0.653) or T4 (P=0.255), indicating comparable recovery of neuromuscular function.

Hemodynamic measurements, including HR and MAP, did not show significant differences between the two groups at all measured time points (all P>0.05; **Figure 1**).

In terms of intraoperative complications, the incidence of bradycardia and hypotension was significantly higher in the propofol group compared to the remimazolam group (bradycardia: P=0.043; hypotension: P=0.009; **Figure 2**). Although the use of vasoactive drugs (ephedrine and norepinephrine) was more frequent in the propofol group, these differences did not reach statistical significance (ephedrine: P=0.080; norepinephrine: P=0.130).

Postoperative recovery status and multivariate regression analysis

The awakening time, extubation time, and time to follow commands were significantly longer in the propofol group compared to the remimazolam group (all P<0.001; **Table 5**). No significant differences were found in the incidence of extubation-related adverse events in the post-anesthesia care unit (PACU) (P=0.697) or in PACU length of stay (P=0.861).

Postoperative JOA scores were comparable between the two groups (P=0.944; **Table 6**). Baseline cognitive function, assessed on preoperative day 1, showed no significant differences between the two groups in MMSE or MoCA scores (P=0.837; P=0.145). On postoperative days 3 and 7, MMSE scores were significantly higher in the remimazolam group compared to the propofol group (day 3: P<0.001, day 7: P=0.008). Similarly, MoCA scores on postoperative days 3 and 7 were significantly higher in the remimazolam group compared to the propofol group (day 3: P<0.001, day 7: P<0.001). No significant differences were observed between the two groups in other postoperative outcomes, including patient-controlled analgesia (PCA) withdrawal, postoperative nausea and vomiting, overall postoperative adverse events, 24-hour postoperative VAS scores, or length of hospital stay (all *P*>0.05).

In the multivariate logistic regression analysis of early postoperative cognitive dysfunction

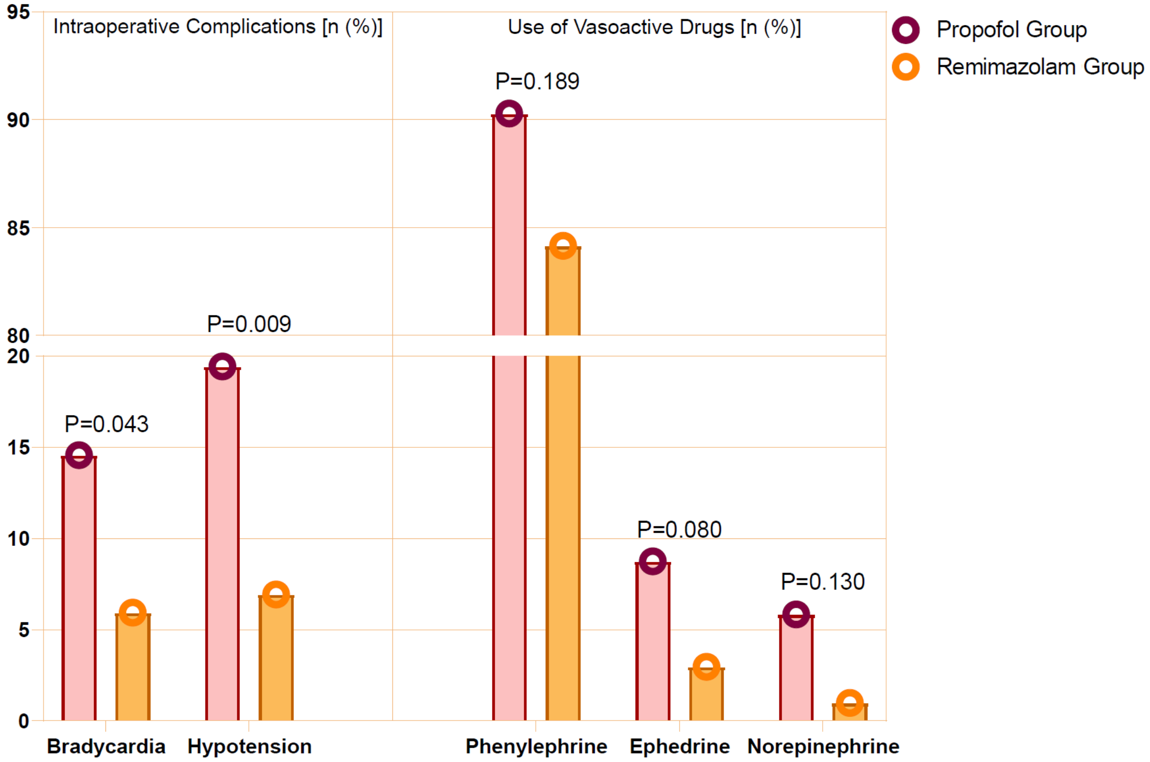

Figure 2. Comparison of intraoperative complications and use of vasopressor agents between the two groups.

Table 5. Comparison of postoperative awakening and early recovery between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t/χ^2	*P* value
Time to Awakening (min)	24.25 ± 4.01	18.91 ± 3.90	9.647	<0.001
Time to Extubation (min)	36.44 ± 4.64	30.15 ± 4.34	9.996	<0.001
Time to Obey Command (min)	26.07 ± 5.05	20.04 ± 4.05	9.403	<0.001
Adverse Events Related Extubation in PACU [n (%)]	3 (2.91%)	5 (4.95%)	0.151	0.697
Duration of PACU Stay (min)	43.17 ± 7.54	43.36 ± 7.92	0.175	0.861

Note: PACU, Post-anesthesia Care Unit.

(**Table 7**), remimazolam was associated with a significantly lower risk, compared to propofol (P<0.001, OR=0.250). Both advanced age (P=0.006, OR=1.096) and higher ASA classification (P=0.009, OR=3.210) were associated with increased risk of postoperative cognitive dysfunction. In addition, longer anesthesia duration was also associated with a modest increase in risk (P=0.020, OR=1.015). However, total remifentanil consumption was not significantly associated with postoperative cognitive dysfunction (P=0.158, OR=1.001).

Discussion

This retrospective analysis demonstrated that the choice of intravenous anesthetics has profound implications for the quality of IONM and early postoperative neurological recovery in patients undergoing prone-position spinal surgery. While both anesthetic regimens achieved comparable depths of anesthesia, remimazolam was associated with superior IONM signal characteristics, fewer episodes of intraoperative hypotension and bradycardia, and improved early postoperative recovery profiles, including

Table 6. Comparison of postoperative neurological function, cognitive function, and complications between the two groups

Item	Propofol Group (n=103)	Remimazolam Group (n=101)	t/χ^2	*P* value
JOA Score, Postoperative (point)	15.18 ± 0.79	15.19 ± 0.82	0.070	0.944
MMSE Score (point)				
Preoperative Day 1	28.32 ± 0.90	28.34 ± 0.79	0.206	0.837
Postoperative Day 3	22.72 ± 1.30	23.34 ± 1.19	3.560	<0.001
Postoperative Day 7	25.69 ± 1.80	26.34 ± 1.64	2.697	0.008
MoCA Score (point)				
Preoperative Day 1	27.41 ± 0.76	27.61 ± 1.10	1.466	0.145
Postoperative Day 3	23.54 ± 0.98	24.41 ± 0.92	6.519	<0.001
Postoperative Day 7	25.64 ± 0.77	26.04 ± 0.91	3.344	<0.001
Postoperative 24-hour VAS score	2.11 ± 0.33	2.04 ± 0.29	1.513	0.132
Other				
PCA Withdrawal Due to PONV [n (%)]	34 (33.01%)	36 (35.64%)	0.157	0.692
Postoperative Adverse Events [n (%)]	3 (2.91%)	1 (0.99%)	0.235	0.628
Postoperative Hospital Stay Duration (d)	4.41 ± 2.41	4.24 ± 1.94	0.543	0.588

Note: JOA: Japanese Orthopedic Association; MMSE: Mini-mental State Examination; MoCA: Montreal Cognitive Assessment; PCA: Patient-controlled Analgesia; PONV: Postoperative Nausea and Vomiting; VAS: Visual Analog Scale.

Table 7. Multivariable logistic regression analysis for early postoperative cognitive impairment (MoCA <24 on Postoperative Day 3)

Item	Coefficient	P	OR	CI Lower	CI Upper
Remimazolam vs. Propofol	-1.387	<0.001	0.250	0.121	0.515
Age	0.092	0.006	1.096	1.027	1.171
ASA Physical Status (I and II/III)	1.166	0.009	3.210	1.336	7.716
Duration of Anesthesia	0.014	0.020	1.015	1.002	1.027
Total Consumption of Remifentanil (μg)	0.001	0.158	1.001	1.000	1.002

faster awakening and better early cognitive function. These findings suggest that remimazolam may be a suitable alternative in surgical settings where preservation of neurophysiological signal fidelity and rapid postoperative recovery are essential.

The most striking observations concerned the intraoperative behavior of SEP and MEP. The remimazolam group exhibited shorter latencies and higher amplitudes at later intraoperative time points, indicating a relatively reduced suppressive effect on neural pathways essential for generating these evoked potentials. This is clinically relevant, as the effectiveness of IONM depends on the acquisition of stable and interpretable signals to enable timely detection of neurological compromise [23]. Both propofol and remimazolam are GABA-A receptor agonists; however, their differential effects on MEP and SEP may stem from their distinct receptor binding kinetics and subunit specificity [24]. Propofol exerts a strong dose-dependent inhibitory effect on cortical and spinal motor neurons, which can attenuate signal amplitudes [25]. In contrast, the pharmacokinetic profile of remimazolam, characterized by a short context-sensitive half-time and potentially milder modulation of neuronal circuits responsible for motor evoked potentials, may contribute to better preservation of signals [26]. Previous experimental work has shown that benzodiazepine-mediated enhancement of inhibitory signaling has a less pronounced effect on synaptic transmission pathways responsible for generating evoked potentials, whereas the stronger GABAergic potentiation induced by propofol may inhibit corticocortical and subcortical signal propagation [27]. Clinical studies in cranial neurosurgery have similarly reported that propofol can reduce MEP amplitudes, leading some centers to optimize anesthetic protocols to mitigate its suppressive effects [28]. Consistent with these observations, the present study observed a lower incidence of SEP signal abnormalities in the remimazolam group, further supporting its potential advantage in preserving IONM signal integrity. Our findings extend these observations to the spinal domain, highlighting that remimazolam may be particularly advantageous in procedures requiring continuous monitoring of both sensory and motor pathways.

The lower incidence of intraoperative bradycardia and hypotension observed in the remimazolam group suggests a more favorable cardiovascular profile. Propofol is known to exert myocardial depressant effects. For example, a previous clinical study comparing propofol with sevoflurane in patients undergoing esophagectomy reported that propofol was associated with greater reductions in cardiac index and right ventricular ejection fraction, as well as higher systemic vascular resistance index [29]. Such hemodynamic effects may necessitate more frequent use of vasoactive drugs may during surgery, which may affect spinal cord perfusion [16]. In contrast, recent pharmacokinetic studies suggest that ultra-short acting benzodiazepines, such as remimazolam, exert minimal effects on systemic vascular resistance and heart rate, likely due to rapid metabolism with limited receptor accumulation [29]. This reduced frequency of hemodynamic adverse events not only benefits overall patient management but also indirectly supports IONM reliability, as severe hypotension itself can lead to signal degradation and complicate the interpretation of IONM changes indicative of surgical injury [30]. In addition, minimizing the need for vasoactive agents may be advantageous, as these drugs can exert variable and sometimes unpredictable effects on neurophysiological signals. Current data align with emerging evidence supporting the use of anesthetics that maintain autonomic stability in high-risk spinal surgeries [31].

Another discovery was that remimazolam was associated with faster postoperative recovery, as reflected by shorter times to awakening, extubation, and response to verbal commands. This observation is consistent with its pharmacokinetic characteristics, characterized by rapid hydrolysis through tissue esterases and organ-independent elimination [32]. Accelerated recovery may facilitate earlier neurological assessment and reduce time spent in PACU, potentially lowering risk of airway issues.

Furthermore, patients in the remimazolam group demonstrated higher cognitive function scores in the early postoperative period. Cognitive performance, assessed using standardized screening tools, was better on postoperative days 3 and 7. The early postoperative period is a vulnerable period for subtle neurocognitive impairment, and higher scores during this stage may suggest a more favorable recovery trajectory. Potential mechanisms may involve reduced inhibition of cortical activity during surgery and avoidance of propofol-associated changes in cerebral autoregulation and metabolic homeostasis [33]. This aligns with preclinical findings associating propofol with alterations in cerebral blood flow and neuronal activity, which may contribute to transient cognitive impairment [35]. It is therefore plausible that the improved early cognitive outcomes observed with remimazolam in our study might be related to reduced disruption of neurophysiological and neuroplastic processes. Early studies in cardiac and orthopedic surgery have reported similar trends, where drugs with minimal effect on neurophysiological monitoring also yielded better early cognitive outcomes [34]. The consistency of these observations across different surgical specialties strengthens the argument for prioritizing anesthetic strategies that preserve cortical excitability when perioperative neurocognitive protection is a priority.

Notably, patients receiving remimazolam required higher total doses of opioids to maintain a comparable anesthesia depth. This finding is biologically plausible, as benzodiazepines, while effective for hypnosis, may provide less suppression of nociceptive transmission compared to propofol, thereby necessitating increased opioid administration [35, 36]. However, this did not translate into a higher incidence of adverse outcomes, such as respiratory depression or prolonged PACU stay in our study. These findings underscore the importance of balanced anesthetic strategies, in which hypnotic and analgesic components are titrated appropriately to achieve optimal intraoperative conditions.

The incidence of other postoperative complications was comparable between the two groups, further supporting the safety profile of remimazolam in this setting. Additionally, the final JOA score was comparable between groups, suggesting that the choice of anesthetic regimen did not adversely affect surgical efficacy or neurologic recovery. This observation aligns with previous reports that most patients experience neurological improvement over time following significant IONM events and that timely intervention is key [37]. Furthermore, the cellular mechanisms underlying organ protection during anesthesia are complex. While our study focuses on neurocognitive outcomes, research into other organ systems, such as the heart [38], has shown that propofol may exert cardioprotective effects. These findings suggest that anesthetic selection involves a balance of multiple physiological considerations, and the superior early cognitive outcomes with remimazolam in our study should therefore be interpreted within the broader context of these multifaceted pharmacologic effects.

Despite these promising results, several limitations should be acknowledged. First, the retrospective, single-center design may have introduced selection bias and limited the generalizability of the findings. Second, the follow-up period was relatively short and primarily focused on early postoperative recovery and cognitive function within the first postoperative week. Long-term neurological and cognitive outcomes remain unclear and warrant further investigation. Additionally, while the sample size was sufficient to observe differences in primary IONM data, it may have been underpowered to identify rare adverse events.

Future studies should aim to address these gaps through prospective, randomized, multicenter trials. Furthermore, the general applicability of our findings to all types of spinal surgeries, particularly complex deformity surgeries, requires further validation. As the utility of IONM may vary depending on surgical setting, the relative advantages of specific anesthetic agents may also differ across procedures. Moreover, future studies could incorporate quantitative TOF analysis to precisely assess the independent contribution of neuromuscular blockade recovery to MEP signals, and further validate the true effect size of drug choice on differences in IONM data. Studies should also aim to clarify the specific pharmacodynamic mechanisms underlying the differential effects of remimazolam and propofol on motor and sensory pathways.

Conclusion

In patients undergoing prone-position spinal surgery, remimazolam is associated with improved preservation of intraoperative neurophysiological monitoring signals, a lower incidence of intraoperative hypotension and bradycardia, and improved early postoperative cognitive outcomes, compared to propofol.

Acknowledgements

This study was supported by the Hubei Chen Xiaoping Science and Technology Development Foundation (No. CXPJJH123001-2324).

Disclosure of conflict of interest

None.

Address correspondence to: Lan Yao, Department of Anesthesiology, Peking University International Hospital, No. 1 Life Park Road, Zhongguancun Life Science Park, Changping District, Beijing 102206, China. E-mail: 1508yaolan@sina.com

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