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Original Article

Propofol and remifentanil anesthesia improves cerebral oxygen balance and accelerates recovery in patients undergoing craniotomy for traumatic brain injury

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Abstract: Objective: To evaluate the effect of propofol combined with remifentanil anesthesia on the cerebral oxygen supply-demand balance during craniotomy in patients with traumatic brain injury (TBI). Methods: A total of 180 patients who underwent craniotomy for TBI from January 2020 to December 2024 were retrospectively included and divided into two groups according to the intraoperative anesthesia regimen: a control group (n=88, sevoflurane and remifentanil) and a study group (n=92, propofol and remifentanil). Results: The times to spontaneous respiration recovery, orientation recovery, eye opening upon verbal command, tracheal extubation, and exit from the operating room were significantly shorter in the study group than in the control group ($P < 0.05$). During tracheal intubation (T1), debridement (T2), and after surgery (T3), the serum levels of myelin basic protein (MBP), neuron-specific enolase (NSE), inducible nitric oxide synthase (iNOS), norepinephrine (NE), and cortisol (Cor) were significantly lower in the study group than in the control group ($P < 0.05$), whereas the concentration of superoxide dismutase (SOD) was higher ($P < 0.05$). Compared to pre-anesthesia value, jugular venous oxygen saturation ($SjvO_2$) increased and the cerebral oxygen extraction rate ($CERO_2$) decreased at 6 h and 12 h after anesthesia ($P < 0.05$). Compared to the control group at 6 h and 12 h after anesthesia, $SjvO_2$ was higher and $CERO_2$ was lower in the study group ($P < 0.05$). Conclusions: Propofol combined with remifentanil anesthesia may accelerate the postoperative recovery in TBI patients undergoing craniotomy, reduce oxidative stress and cerebral reperfusion injury, and improve cerebral oxygen supply-demand balance, with fewer adverse reactions.

Keywords: Propofol, remifentanil, cerebral oxygen balance, craniotomy, traumatic brain injury

Introduction

Craniotomy is a primary surgical approach for managing traumatic brain injury (TBI). It helps improve cerebral cellular metabolism, reduces secondary brain damage, and rapidly alleviates intracranial hypertension caused by cerebral edema [1]. However, elevated intracranial pressure, commonly observed in patients with TBI, significantly affects cerebral blood flow and oxygen metabolism. Therefore, anesthetic management during craniotomy should focus on maintaining cerebral perfusion and controlling intracranial pressure to prevent aggravation of cerebral hypoxia and secondary brain damage. Anesthesia, surgery, and extubation may induce stress responses that elevate intracranial pressure, cause cerebral hypoxia and ischemia, and further impair neuronal function, exacerbating neuronal damage and postoperative cognitive dysfunction [2, 3]. Therefore, preserving neuronal function, alleviating pain, and minimizing stress response during craniotomy has become a critical clinical challenge. Patients with TBI are at high risk of perioperative cerebral hypoxia, particularly under anesthesia. Most patients with brain death experience varying degrees of cerebral hypoxia and ischemia [4]. In patients with TBI, cerebral hypoxia and ischemia are the predominant contributors to secondary brain damage. Therefore, anesthetic drugs should provide adequate analgesia and sedation while avoiding excessive suppression of cerebral metabolism, which could exacerbate hypoxia and ischemia. Maintaining an optimal balance between brain oxygen supply and demand is essential to avoid secondary brain damage. Therefore, selecting a suitable anes-

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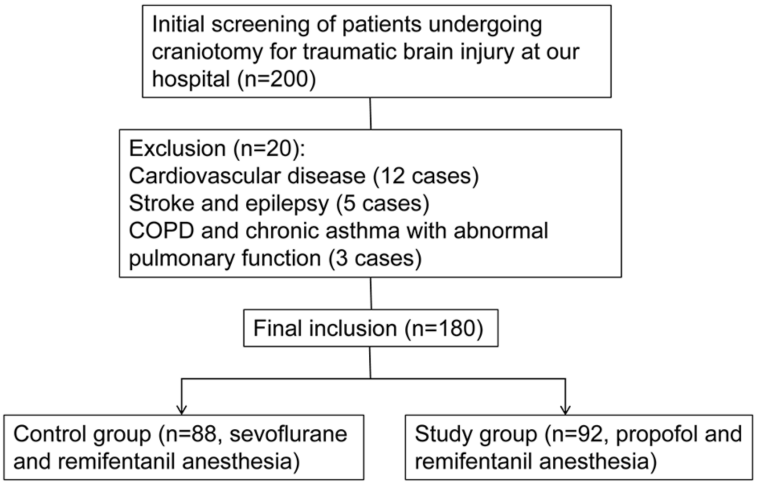

Figure 1. Flow chart for case selection.

thesia regimen is crucial for protecting brain function and promoting recovery.

Propofol is a widely used intravenous anesthetic with notable brain-protective effects. It exerts neuroprotection by reducing cerebral blood flow, cerebral blood volume, and the cerebral metabolic rate of oxygen consumption ($CMRO_2$) [5]. In contrast, inhalational agents such as sevoflurane, due to their vasodilatory properties, may lower $CMRO_2$ while simultaneously increasing cerebral blood flow and cerebral blood volume [6]. Therefore, intravenous anesthetics like propofol are often considered optimal for neurosurgical anesthesia, particularly when maintaining the balance between cerebral oxygen supply and demand is essential. However, Liu et al. [7] reported that compared with single volatile anesthetics, propofol did not significantly reduce the risk of cerebral edema. After stratification by indications for craniotomy, propofol was associated with less cerebral edema in elective craniotomies compared with volatile anesthetics, but no such benefit was observed in emergency craniotomies (e.g., traumatic brain injury). This may be related to the limited sample size and it requires further validation in large-scale studies. Although the influences of various anesthetic agents in intracranial pressure and cerebral blood flow have been explored, few studies have systematically compared their specific roles in maintaining cerebral oxygen supply-demand balance.

Based on these considerations, we hypothesized that propofol combined with remifentanil for anesthesia would be more effective than sevoflurane combined with remifentanil in maintaining cerebral oxygen supply-demand balance in patients with TBI undergoing craniotomy. This hypothesis is theoretically grounded in the evidence that propofol confers neuroprotection by improving cerebral blood flow regulation and oxygen metabolism [8], while sevoflurane may increase cerebral oxygen consumption owing to its pharmacologic properties. Therefore, this study compared the two anesthetic regimens to evaluate their intraoperative and postoperative effects on cerebral oxygen metabolism in TBI patients, aiming to provide new evidence for optimizing anesthesia strategies.

Materials and methods

Study design

The clinical data of 180 patients who underwent craniotomy for TBI at Ganzhou People's Hospital from January 2020 to December 2024 were retrospectively collected. According to the intraoperative anesthetic regimen, patients were divided into two groups: the control group (n=88; sevoflurane and remifentanil anesthesia) and the study group (n=92; propofol and remifentanil anesthesia). The case selection process is shown in **Figure 1**.

All clinical data were retrieved from the hospital's electronic medical record system and anonymized prior to analysis. The study protocol was approved by the Ethics Committee of Ganzhou People's Hospital. Given the retrospective nature of the study, the requirement for additional informed consent was waived. Throughout the research process, all procedures complied with institutional ethical standards.

Eligible patients with TBI were screened based on predefined inclusion and exclusion criteria. Extracted clinical information included demographic characteristics, comorbidities, surgical details, anesthesia regimens, and perioperative monitoring data. All data were extracted by

two researchers and double-checked to ensure data accuracy.

Sample size estimation

The sample size was estimated based on the expected effect size, statistical power, and significance level. Assuming moderate effect size of 0.5 for the primary outcomes (e.g., recovery time and neurological function recovery), a statistical power of 80% and a two-tailed significance level of 0.05 were set. Based on these parameters, sample size calculations were performed using G*Power software, yielding a required sample size of 180 participants (88 in the control group and 92 in the study group). This sample size ensured adequate power to detect clinically meaningful differences between groups.

Inclusion criteria: (1) Patients aged 18 to 65 years; (2) Diagnosis of TBI [9]: a documented history of TBI in their medical records, and imaging examinations (such as head computed tomography or magnetic resonance imaging) confirmed the presence of TBI, such as cerebral contusion, intracranial hematoma, subdural or epidural hematoma, or concussion; (3) Surgical treatment: patients underwent craniotomy during hospitalization (e.g., decompressive craniectomy or intracranial hematoma evacuation), and complete surgical and anesthetic records were available; (4) Preoperative stability: vital signs were stable prior to surgery, defined as systolic blood pressure of 90-140 mmHg, diastolic blood pressure of 60-90 mmHg, heart rate of 60-100 beats/min, blood oxygen saturation > 90%, with no evidence of acute heart failure or respiratory failure.

Exclusion criteria: (1) Severe cardiovascular diseases: Patients with documented heart failure [New York Heart Association (NYHA) Class III-IV] or uncorrectable arrhythmias (e.g., complete atrioventricular block) were excluded; Patients with well-controlled hypertension or mild arrhythmias were eligible for inclusion based on clinical assessment; (2) Preoperative electrocardiogram (ECG) abnormalities: Patients with preoperative ECG abnormalities recorded in medical history, including severe conduction block or acute myocardial infarction, which could interfere with anesthesia management or postoperative recovery were excluded; (3) Severe neurological disorders: Patients with a history of chronic neurological disorders (e.g., stroke, epilepsy) or those presenting with significant baseline neurological impairment were excluded. Significant baseline neurological impairment was defined as persistent cognitive impairment or substantial motor deficits; (4) Chronic respiratory diseases: Patients with chronic obstructive pulmonary disease (COPD) or chronic asthma accompanied by abnormal pulmonary function tests were excluded. Patients with mild chronic respiratory diseases and near-normal pulmonary function could be included following clinical assessment; (5) Nasal conditions: Patients with documented severe nasal polyps, sinusitis, a history of nasal surgery, or recurrent epistaxis, which could compromise airway management during anesthesia, were excluded. Patients with mild nasal conditions were eligible based on clinical assessment; (6) Substance abuse: Patients with a documented history of opioid dependence, such as long-term opioid use, or illicit drug abuse that could compromise anesthetic efficacy were excluded; (7) Pregnant or breastfeeding women, as identified from their medical records, were excluded; (8) Patients with documented inability to tolerate anesthesia or surgery, or other conditions deemed incompatible with the objectives of the study were excluded.

Standard induction

Upon arrival in the operating room, an intravenous access was established. Patients received routine oxygen inhalation along with continuous ECG monitoring. Anesthesia was induced with 3-4 ng/ml remifentanil (Yichang Humanwell Pharmaceutical Co., Ltd.), 0.15 mg/kg cisatracurium (Sinbiopharma, Inc.), and 0.05 mg/kg midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd.).

Control group protocol

Following standard induction, patients in the control group received 7% sevoflurane inhalation (Hebei Sams Pharmaceutical Co., Ltd.). Anesthesia was maintained with sevoflurane at 0.75-1.25 times the minimum alveolar concentration (MAC; equivalent to 0.86%-1.44%), remifentanil at a target plasma concentration of 3-5 ng/ml, and 0.075 mg/(kg·h) cisatracurium.

Study group protocol

Following standard induction, patients in the study group received intravenous anesthesia

with 3-4 μg/ml propofol (Xi'an Libang Pharmaceutical Co., Ltd.). Anesthesia was maintained with 3-5 μg/ml propofol, 3-5 ng/ml remifentanil, and 0.075 mg/(kg·h) cisatracurium. Patients' vital signs were continuously monitored during anesthesia. Infusions were discontinued at the end of the surgical procedure.

Anesthesia protocols and monitoring methods

All patients received standardized anesthesia protocols, including propofol or sevoflurane combined with remifentanil. Bispectral Index (BIS) was used to monitor the depth of anesthesia. The balance of cerebral oxygen supply and demand was monitored in real time using the Near-Infrared Spectroscopy (NIRS), including jugular venous oxygen saturation ($SjvO_2$) and cerebral oxygen extraction ratio ($CERO_2$). Intraoperative hemodynamic and respiratory statuses were monitored via invasive or non-invasive blood pressure measurement, arterial blood gas (ABG) analysis, and peripheral capillary oxygen saturation (SpO_2). Vasoactive agents were used as needed according to the patient's hemodynamic stability, and fluid therapy was adjusted according to standard fluid management protocols.

Monitoring of cerebral oxygen supply-demand balance

To optimize cerebral oxygen metabolism, intraoperative $SjvO_2$ and $CERO_2$ were continuously monitored in both groups, as these indices reliably reflect the cerebral oxygen supply-demand status [6]. To ensure that these indicators remained within normal ranges, the depth of anesthesia and hemodynamic values were adjusted based on real-time monitoring data, thereby maintaining a balanced supply and demand of cerebral oxygen.

Blood gas analysis and other monitoring

ABG values, electrolytes, and lactate levels were monitored using a blood gas analyzer. The anesthesia workstation was used to regulate inhaled anesthetic concentration and ventilation settings, while infusion pumps ensured accurate and continuous delivery of remifentanil, propofol, and other medications. All drugs were prepared in advance to ensure standardized procedures.

Data collection

The primary outcomes of this study included postoperative recovery time, neurological function scores, and cerebral oxygen metabolism indicators, specifically $SjvO_2$ and $CERO_2$. These variables were selected based on their clinical relevance and their value in assessing postoperative neurological recovery and cerebral oxygen balance in patients with TBI.

(1) Post-anesthesia recovery indicators: Indices included time to spontaneous respiration recovery, time to orientation recovery, time to eye opening on verbal command, time to tracheal extubation, and time to exit from the operating room.

(2) Serum markers of neuronal injury and oxidative stress: For each patient, 3 ml of venous blood was collected at four time points: pre-anesthesia (T0), during tracheal intubation (T1), during debridement (T2), and after surgery (T3). After centrifugation (radius of 6 cm, speed of 2500 r/min) for 10 min, the supernatant was collected and stored at -20°C for subsequent analysis. Serum levels of inducible nitric oxide synthase (iNOS), myelin basic protein (MBP), and neuron-specific enolase (NSE) were measured using a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA; Shanghai Yuduo Biotechnology Co., Ltd.). The levels of superoxide dismutase (SOD), norepinephrine (NE), and cortisol (Cor) were determined using radioimmunoassay (kit purchased from Shanghai Daweiq Biological Technology Co., Ltd.).

(3) Cerebral oxygen supply and demand related indicators: Before anesthesia, 6 h and 12 h after the onset of anesthesia, peripheral ABG analysis was performed in both groups. $SjvO_2$ was measured, and $CERO_2$ was calculated to evaluate cerebral oxygen metabolism.

(4) Adverse reactions: Intraoperative adverse outcomes, such as hypertension (defined as blood pressure exceeding 20% of pre-anesthetic levels or ≥ 160/95 mmHg) and hypotension (defined as blood pressure dropping below 20% of pre-anesthetic levels or a systolic pressure < 80 mmHg), as well as postoperative complications including chills, nausea, vomiting, and convulsions, were monitored.

This retrospective analysis was based on clinical records from patients undergoing routine treatment at our hospital. For patients with TBI, postoperative monitoring included measurement of biomarkers such as MBP, NSE, iNOS, NE, and Cor. These biomarkers are part of the routine monitoring during traumatic brain surgery in our hospital, as they reflect postoperative neuronal injury, alterations in oxygen metabolism, and recovery progress.

All biomarker tests were performed using blood samples collected during the patients' routine treatment processes, and the corresponding data were extracted from the hospital's electronic medical record system. These tests did not influence any clinical treatment decisions but provided essential biomarker data for this study, facilitating evaluation of the effects of different anesthesia regimens on cerebral oxygen metabolism and neuroprotection.

Statistical methods

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) 24.0 software. Continuous data were expressed as mean ± standard deviation (mean ± SD). Inter-group comparisons were conducted using the independent-samples t-test, whereas intra-group differences were evaluated using the paired t-test. For multiple time-point comparisons of a single indicator between the two groups, a general linear model for repeated-measures analysis of variance (ANOVA) was employed. Mauchly's test of sphericity was performed. When the sphericity assumption was violated, the Greenhouse-Geisser correction was applied. For multiple comparisons of time points (T0-T3), Bonferroni correction was applied to reduce the risk of type I error. Categorical data were presented as percentages and analyzed using the χ^2 test. Ranked data were evaluated using the rank-sum test. A two-tailed $P < 0.05$ was considered significant.

Results

Demographic and clinical data

The study and control groups were comparable in baseline characteristics, with no significant differences in sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, or trauma etiology ($P > 0.05$) (**Table 1**).

Post-anesthesia recovery indicators

All post-anesthesia recovery indicators, including times to spontaneous respiration (12.7±8.3 vs. 25.3±6.6 min), orientation recovery (14.0±3.3 vs. 20.3±5.6 min), eye opening upon verbal command (11.0±2.3 vs. 14.2±3.7 min), tracheal extubation (12.4±3.4 vs. 18.7±5.2 min), and exit from the operating room (19.7±5.6 vs. 24.6±7.0 min), were significantly shorter in the study group compared to the control group ($P < 0.05$) (**Figure 2**).

Hemodynamic indices

In the control group, heart rate (HR) at T1, T2, and T3 showed significant increases from baseline (T0) ($P < 0.001$; differences remained statistically significant after Bonferroni correction). Similarly, significant differences were noted for SpO_2 at T1 and T2, and MAP at T1 and T3 compared to T0 ($P < 0.001$; differences remained statistically significant after Bonferroni correction). Mauchly's test confirmed that the sphericity assumption was met; therefore, repeated-measures ANOVA was applied.

In contrast, the study group exhibited no significant differences in HR, SpO_2, or MAP across T1, T2, and T3 compared to T0 ($P > 0.05$), except for a notable change in HR at T1 (**Figure 3**).

Cerebral oxygen supply-demand indicators

Compared to pre-anesthesia values, both groups exhibited significantly increased $SjvO_2$ and decreased $CERO_2$ at 6 h and 12 h after anesthesia (all $P < 0.05$; differences remained statistically significant after Bonferroni correction). Moreover, at both 6 h and 12 h after anesthesia, the study group exhibited higher $SjvO_2$ levels and lower $CERO_2$ levels compared with the control group ($P < 0.05$, **Table 2**).

Serum neuronal injury markers

Significant intergroup differences were observed in serum levels of MBP, NSE, and iNOS (all $P < 0.001$, Bonferroni corrected), with the study group demonstrating lower levels at T1, T2, and T3 compared to the control group. Variations in the trend of these markers were also observed between the two groups (**Figure 4**).

Table 1. Comparison of baseline information between the two groups (n, mean ± SD)

Group	Number of cases	Male/ Female	Age (years)	BMI (kg/m^2)	GCS score	ASA classification	Cause of trauma	Surgical time (min)	Intraoperative blood loss (mL)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)
						I/II/III	A/B/C/D				
Control group	88	45/43	52.9±8.5	23.15±3.37	5.62±0.71	30/34/18	40/23/20/5	184.47±31.05	369.77±162.58	180.58±36.94	38.17±4.71
Study group	92	46/46	51.7±7.9	22.81±2.66	5.54±0.82	32/38/22	35/23/21/13	180.67±26.60	364.68±131.55	183.92±33.61	37.65±3.66
χ^2/t/Z		0.023	0.982	0.753	0.698	0.112	3.823	0.883	0.231	0.635	0.829
P		0.879	0.328	0.452	0.486	0.486	0.281	0.378	0.817	0.526	0.408

Note: BMI: body mass index; GCS: Glasgow Coma Scale; ASA: American Society of Anesthesiologists; A: traffic accident; B: fall from height; C: violent trauma; D: others.

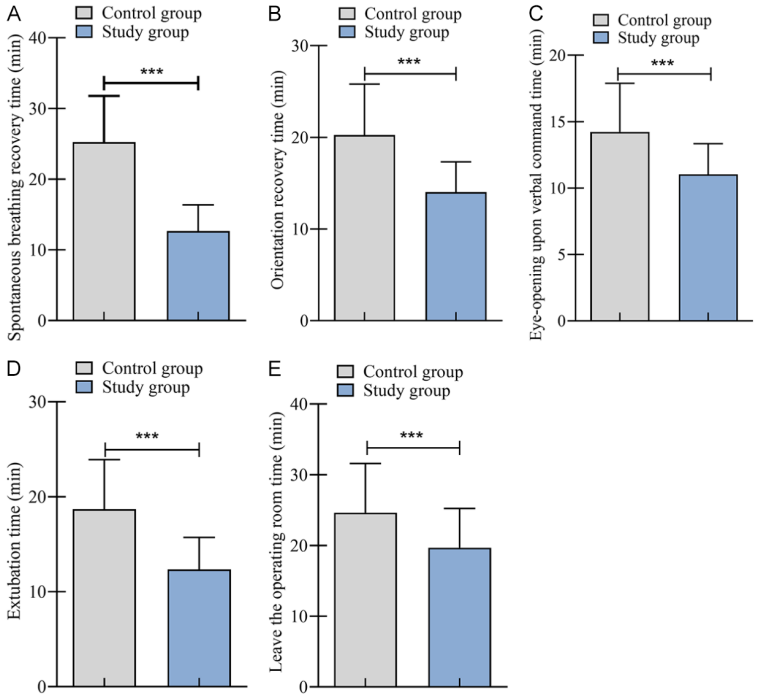

Figure 2. Comparison of postoperative recovery between the two groups. A: Time to spontaneous respiration recovery; B: Time to orientation recovery; C: Time to eye-opening upon verbal command; D: Time to tracheal extubation; E: Time to exist from the operating room. Note: Compared to the control group, $^{***}P < 0.001$. Control group: sevoflurane combined with remifentanil; Study group: propofol combined with remifentanil.

Oxidative stress markers

Significant differences were observed in SOD, NE, and Cor levels between the two groups (all $P < 0.001$). Specifically, SOD levels were elevated, while NE and Cor levels were decreased in the study group compared to the control group at T1, T2, and T3 (all $P < 0.001$, Bonferroni corrected). A divergent progression trend for these markers was observed between the two groups (**Figure 5**).

Adverse events

There was no significant difference in the incidence of intraoperative adverse events between the two groups ($P > 0.05$). However, the incidence of postoperative adverse events in the study group was significantly lower than that in the control group ($P < 0.05$) (**Table 3**).

Discussion

Craniotomy, a common neurosurgical procedure, often provokes significant physiological stress responses arising from sympathetic excitation and endocrine disturbances [10]. These reactions impede postoperative recovery and aggregate secondary brain injury [11, 12]. Therefore, an appropriate anesthesia regimen is important for protecting patients' brain function during surgery and promoting postoperative recovery [13]. The findings of this study revealed that propofol-based anesthesia regimen effectively reduced inflammatory response, enhanced cerebral oxygen supply-demand balance, and decreased cerebral hypoxia in patients undergoing craniotomy, exerting a neuroprotective effect.

In this study, patients receiving propofol-remifentanil anesthesia exhibited faster postoperative recovery and greater intraoperative hemodynamic stability compared with those receiving sevoflurane-remifentanil anesthesia. Specifically, variations in HR, SpO_2, and MAP were smaller, while SOD levels were higher and NE and Cor levels lower in the study group. These results indicate that propofol-remifentanil anesthesia may alleviate surgical stress response, stabilize hemodynamics, and facilitate postoperative recovery. Propofol, as a GABA_A receptor agonist, exerts its anesthetic effects by reducing central nervous system excitability and promoting inhibitory neurotransmission [14, 15]. It can also modulate the hypothalamic-pituitary-adrenal axis by inhibiting the expression of hypothalamic c-fos gene, thereby reducing stress response [14]. Remifentanil, an ultra-short-acting analgesic, further suppresses intraoperative stress responses, minimizes hemodynamic fluctuations, and reduces oxidative stress [16-18].

Cerebral hypoxia following TBI is a major cause of secondary brain damage. Maintaining cerebral oxygen supply-demand balance is therefore essential to improving patient prognosis [19, 20]. In this study, cerebral oxygen metabolism indicators (e.g., $SjvO_2$ and $CERO_2$) were significantly improved in the study group com-

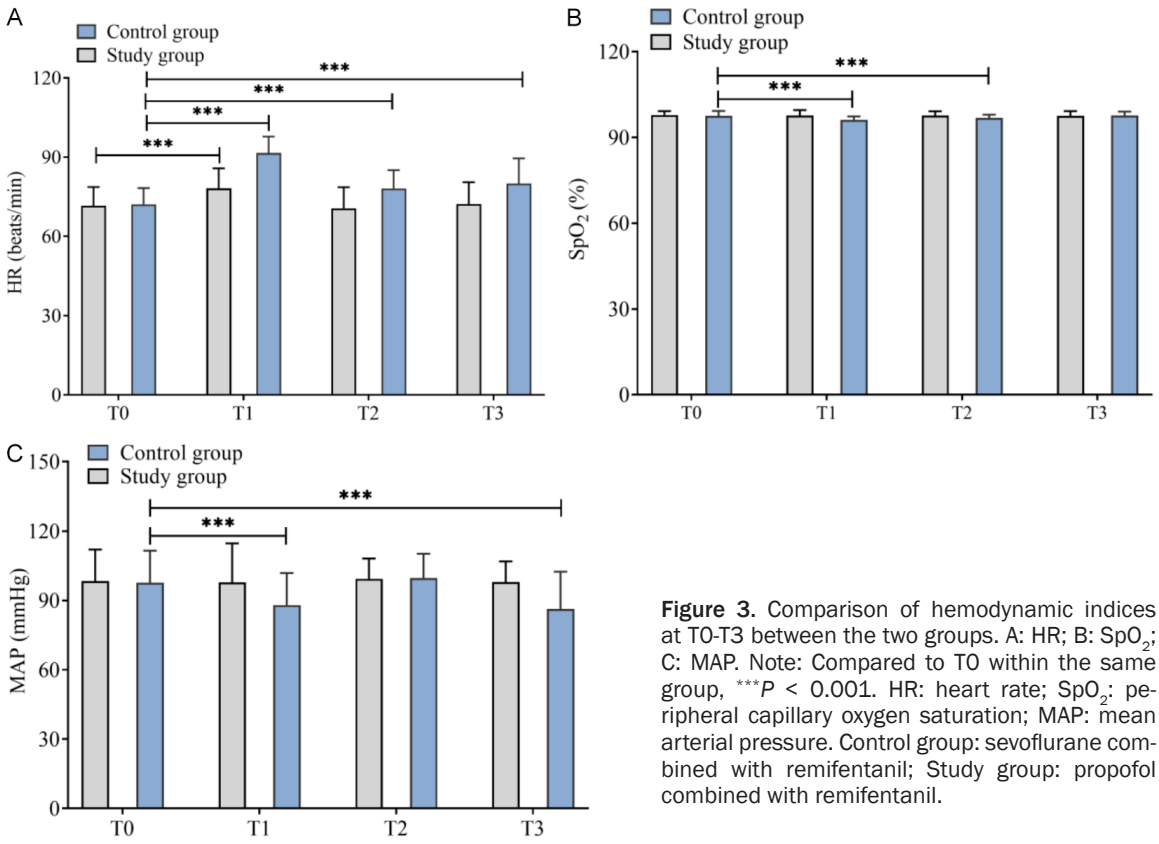

Figure 3. Comparison of hemodynamic indices at T0-T3 between the two groups. A: HR; B: SpO_2; C: MAP. Note: Compared to T0 within the same group, $^{***}P < 0.001$. HR: heart rate; SpO_2: peripheral capillary oxygen saturation; MAP: mean arterial pressure. Control group: sevoflurane combined with remifentanil; Study group: propofol combined with remifentanil.

Table 2. Comparison of cerebral oxygen supply and demand related values between the two groups at various time points (mean ± SD)

Group	Number of cases	Indicator	Before anesthesia	Six hours after anesthesia	Twelve hours after anesthesia
Control group	88	$SjvO_2$	58.77±5.38	63.11±4.99***	63.32±5.81***
		$CERO_2$	41.29±3.84	38.11±2.39***	37.85±3.03***
Study group	92	$SjvO_2$	58.23±5.12	68.81±5.49$^{***,\#\#\#}$	69.03±5.74$^{***,\#\#\#}$
		$CERO_2$	41.57±3.71	33.48±2.38$^{***,\#\#\#}$	33.25±2.36$^{***,\#\#\#}$

Note: Compared to pre-anesthesia level within the same group, $^{***}P < 0.001$; compared to the control group at the same time point, $^{\#\#\#}P < 0.001$. $SjvO_2$: jugular venous oxygen saturation; $CERO_2$: cerebral oxygen extraction ratio.

pared to the control group, especially at 6 h and 12 h after anesthesia, where $SjvO_2$ increased and $CERO_2$ decreased. These findings suggest that propofol-remifentanil anesthesia effectively improves cerebral oxygen supply-demand balance and alleviates cerebral hypoxia. This effect may be partly attributed to the vasodilatory properties of remifentanil. Previous studies have shown that remifentanil can dilate cerebral blood vessels, increase cerebral blood flow, and reduce the cerebral metabolic rate, thereby lowering cerebral oxygen consumption [21, 22]. In addition, propofol can decrease cerebral oxygen consumption by suppressing neuronal excitability and reducing metabolic demand, which contributes to improved cerebral oxygen utilization. This study investigated the effects of different anesthetic agents on the balance between cerebral oxygen supply and demand using both direct and indirect measures. Direct indicators ($SjvO_2$ and $CERO_2$) were complemented by biochemical markers associated with neuronal injury and oxidative stress, including NSE, MBP, iNOS, NE, Cor, and SOD. Although these markers are not direct measures of cerebral oxygen metabolism, they reflect the extent of cerebral hypoxia and reperfusion injury. For example, elevated NSE and

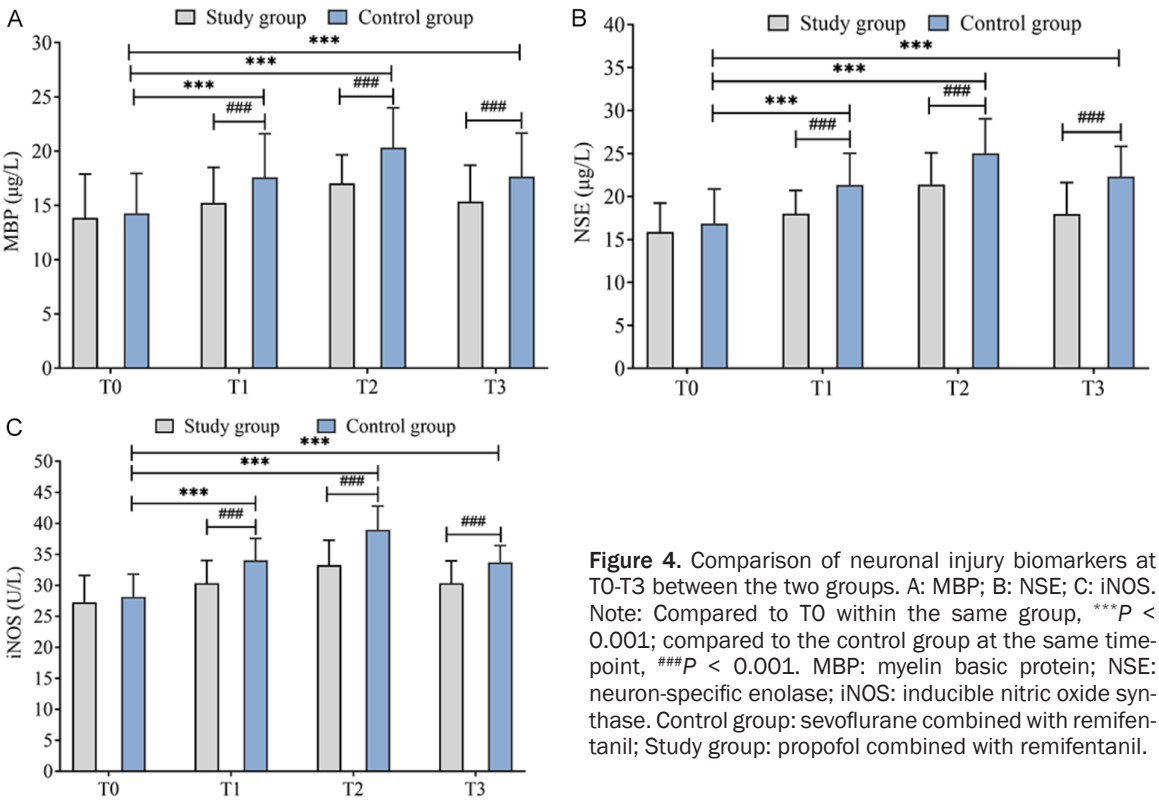

Figure 4. Comparison of neuronal injury biomarkers at T0-T3 between the two groups. A: MBP; B: NSE; C: iNOS. Note: Compared to T0 within the same group, $^{***}P < 0.001$; compared to the control group at the same time-point, $^{###}P < 0.001$. MBP: myelin basic protein; NSE: neuron-specific enolase; iNOS: inducible nitric oxide synthase. Control group: sevoflurane combined with remifentanil; Study group: propofol combined with remifentanil.

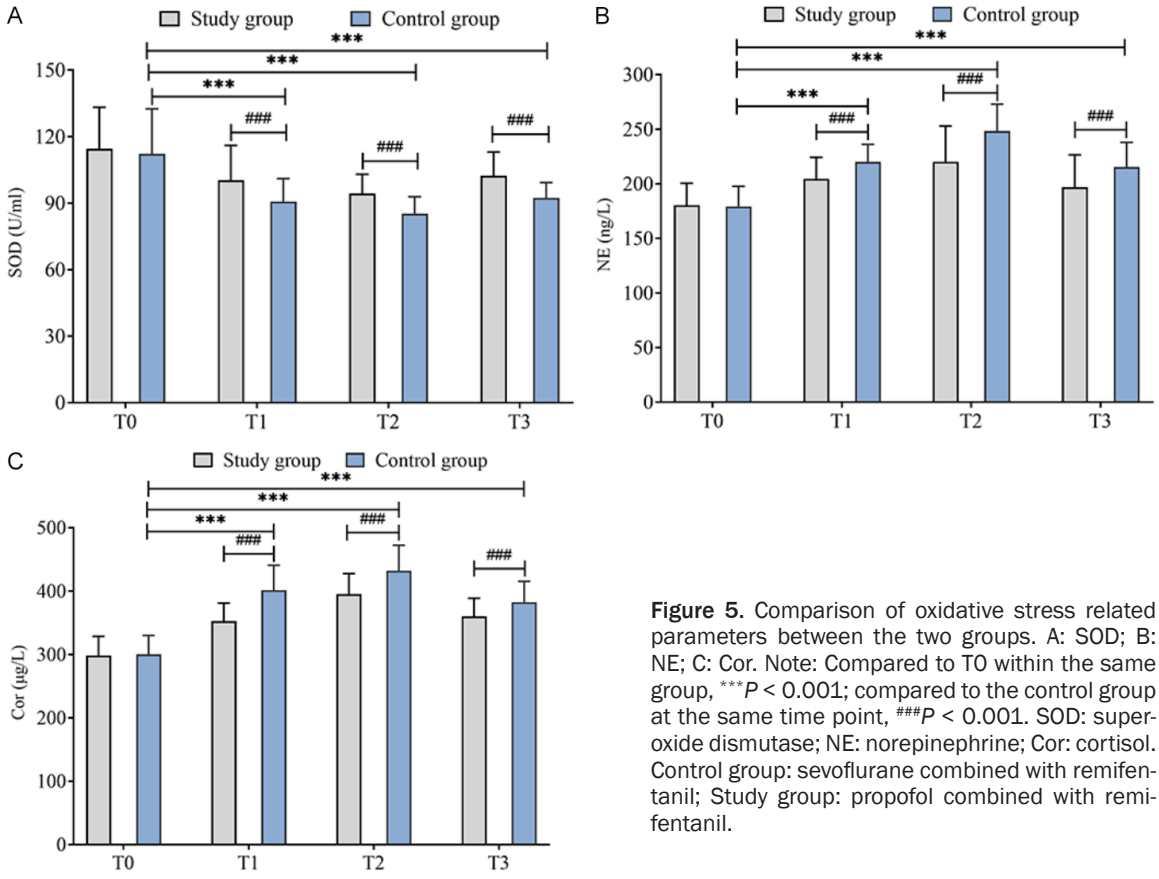

Figure 5. Comparison of oxidative stress related parameters between the two groups. A: SOD; B: NE; C: Cor. Note: Compared to T0 within the same group, $^{***}P < 0.001$; compared to the control group at the same time point, $^{###}P < 0.001$. SOD: superoxide dismutase; NE: norepinephrine; Cor: cortisol. Control group: sevoflurane combined with remifentanil; Study group: propofol combined with remifentanil.

Table 3. Comparison of adverse reactions between the two groups n (%)

Group	Number of cases	Intraoperative adverse reactions			Postoperative adverse reactions			
		Hypertension	Hypotension	Total	Chills	Nausea and vomiting	Convulsions	Total
Control group	88	6 (6.82)	9 (10.23)	15 (17.05)	6 (6.82)	9 (10.23)	2 (2.27)	17 (19.32)
Study group	92	4 (4.35)	6 (6.52)	10 (10.87)	2 (2.27)	5 (5.43)	0 (0.00)	7 (7.70)
χ^2	-	-	-	1.434	-	-	-	5.337
P	-	-	-	0.231	-	-	-	0.021

MBP levels indicate neuronal cell injury commonly associated with cerebral hypoxia, while increased iNOS expression promotes excessive free radical generation, disrupting brain oxygen metabolism homeostasis. Conversely, SOD activity reflects the body's antioxidant capacity and the efficiency of cerebral oxygen utilization.

Taken together, the changes in these indicators collectively demonstrate that propofol combined with remifentanil exerts a regulatory effect on cerebral oxygen balance. Mechanistically, propofol improves cerebral oxygen utilization by reducing cerebral metabolic rate, alleviating inflammatory responses, and mitigating oxidative stress, while remifentanil increases cerebral blood flow by inhibiting sympathetic nerve excitation and dilating cerebral blood vessels. The combined effect of the two anesthetics helps reduce hypoxia-reperfusion injury and preserve neuronal integrity. Consistent with this interpretation, MBP and NSE - key markers of cerebral hypoxia and ischemia - were significantly lower at multiple intraoperative and postoperative time points (T1, T2, T3) in the propofol-remifentanil group compared to the sevoflurane-remifentanil group. This finding suggests that propofol combined with remifentanil provides neuroprotection by mitigating hypoxia-induced neuropathological injury.

Moreover, this study also examined the changes in serum markers of neuronal injury. The results indicated that propofol-based anesthesia significantly reduced the serum concentrations of neuronal injury markers, suggesting its potential to reduce inflammatory response and cerebral hypoxia. Neuronal injury markers, including NSE and S100β, are well-established indicators of cerebral hypoxia and brain tissue damage [23]. Propofol, through its anti-inflammatory effects, may reduce brain injury by alleviating inflammatory response and reducing the postoperative release of these markers. The analgesic effects of remifentanil may also reduce nociceptive and stress responses during and after surgery, thereby further reducing systemic inflammation and the release of injury-related biomarkers [24-26].

Although this study yielded favorable preliminary results, several limitations should be acknowledged. First, the single-center, retrospective design, and relatively small sample size may introduce risks of missing data, selection bias, and information bias, thereby limiting the generalizability of the results. Second, the study did not assess long-term clinical outcomes or the effects of different anesthetic regimens on overall prognosis. Future studies with multicenter, large-sample, prospective designs are required to further assess the long-term effect of various anesthetic strategies on patient outcomes and to explore the mechanisms underlying the combined use of propofol and remifentanil. Third, although key variables, including anesthesia method, comorbidities, and postoperative recovery data, were comprehensively extracted from the hospital's electronic medical record system, residual confounding factors cannot be fully excluded. The inability to achieve the level of control provided by randomized, prospective studies restricted the feasibility of robust multivariate regression analysis. Moreover, certain confounding variables, such as preoperative health status, surgical complexity, and intraoperative anesthetic dosage, could not be adjusted with the same precision as in a controlled trial, thereby affecting internal validity. Future prospective studies with rigorous study design, appropriate sample size calculations, and stricter control of confounding factors are necessary to validate the causal relationship between anesthetic regimens and postoperative outcomes.

Conclusions

Propofol combined with remifentanil anesthesia could significantly mitigate inflammatory and oxidative stress responses in patients undergoing craniotomy. This regimen improved the balance between cerebral oxygen supply and demand, alleviates cerebral hypoxia, and reduced the release of neuroinflammatory biomarkers. Clinically, this contributes to faster postoperative recovery and fewer adverse reactions, providing evidence for optimizing anesthetic strategies in neurosurgical practice.

Disclosure of conflict of interest

None.

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