Am J Transl Res 2026;18(8):6901-6915
www.ajtr.org /ISSN:1943-8141/AJTR0174126

Original Article

Comparison of analgesic and sedative effects of dexmedetomidine and propofol in patients with traumatic brain injury

Xiaoping Shen, Jie Wang, Chao Zhang, Hui Cao, Baoqin Xu

Department of Anesthesiology, Suzhou Ninth Hospital Affiliated to Soochow University, Suzhou 215200, Jiangsu, China

Received May 18, 2026; Accepted June 26, 2026; Epub August 15, 2026; Published August 30, 2026

Abstract: Objective: To assess the analgesic and sedative efficacy of dexmedetomidine (DEX) compared with propofol in individuals suffering from traumatic brain injury (TBI). Methods: A total of 126 participants with TBI and agitation, who were admitted to Suzhou Ninth Hospital Affiliated to Soochow University from January 2023 to January 2025, were enrolled in this study. According to the sedative agent assigned, these participants were categorized either into Group A (DEX) or Group B (propofol). Vital signs and blood gas measurements of the two cohorts were documented and contrasted before and after treatment. The Behavioral Pain Scale (BPS) and the Richmond Agitation-Sedation Scale (RASS) were employed for evaluation and comparison purposes. The frequencies of adverse reactions, including delirium, elevated blood pressure (BP), reduced BP, and bradycardia (slowed heart rate, HR), were monitored and contrasted between the two cohorts. The analgesic effectiveness of DEX was appraised in traumatic brain injury patients, alongside an evaluation of its consequences on vital signs, blood gas parameters, and safety profile. Records were kept regarding sedative and analgesic maintenance outcomes, sedation-linked adverse occurrences, and cerebral oxygen metabolism indices. Spearman correlation and logistic regression analyses were applied to determine factors influencing adverse events. Results: At three hours following drug delivery, measurements of heart rate, mean arterial pressure, respiratory rate, and blood gas parameters in Group A were more favorable than those in Group B ($P<0.05$). The proportion achieving target sedation and analgesic maintenance between 12 and 24 hours was elevated in Group A, whereas the numbers of analgesic rescue events and sedation modifications, together with the risks of patient-ventilator asynchrony, unplanned extubation, and excessive sedation, were diminished in Group A relative to Group B ($P<0.05$). Cerebral oxygen metabolism remained more stable in Group A, accompanied by reduced concentrations of inflammatory cytokines and brain injury indicators, but elevated amounts of brain-derived neurotrophic factor (BDNF) ($P<0.05$). Correlation analyses indicated that pain scores were linked to indicators of inflammation and neural injury. Regression analysis identified propofol, inadequate pain management, and sedation variability as independent risk determinants for adverse events. The overall incidence of adverse events in Group A was 9.30%, which was markedly lower than the 65.00% observed in Group B ($P<0.001$). Conclusion: In agitated patients with TBI, dexmedetomidine was associated with improved sedative and analgesic effects, more stable sedation maintenance, reduced need for additional clinical interventions, and better preservation of respiratory and hemodynamic stability, as well as cerebral oxygen metabolic balance. Propofol, inadequate analgesia, and sedation fluctuations were independent risk factors for adverse events, and dexmedetomidine specifically reduced these risks with a higher safety profile.

Keywords: Traumatic brain injury, dexmedetomidine, propofol, sedative and analgesic effects, vital signs, blood gas parameters

Introduction

Traumatic brain injury is a common type of traumatic disease, encompassing various afflictions such as concussion, diffuse axonal injury, cerebral contusion, and brainstem injury. Its clinical manifestations include impaired consciousness, headache, vomiting, pupil changes, and abnormal vital signs. The condition is complex and variable, prone to inducing severe complications, and poses a serious threat to patients' life and health [1, 2]. Current major

https://doi.org/10.62347/DRCZ2185

therapeutic measures in clinical practice include monitoring vital signs, stabilizing internal circulation, multidimensional brain function monitoring, correcting hemoglobin levels, and removing intracranial space-occupying lesions [3].

In the treatment of patients with traumatic brain injury, the value of sedative and analgesic interventions has been widely recognized for alleviating patient stress responses, protecting brain function, improve quality of life, and improving treatment adherence, thereby enhancing therapeutic outcomes [4]. Commonly used sedatives in current clinical practice include propofol, fentanyl, and morphine, among which propofol is widely used but has issues such as suboptimal analgesic effects, high incidence of complications, poor safety, and more severe pain in patients [5, 6]. Dexmedetomidine (DEX), as a novel sedative and analgesic agent, has been shown in studies to effectively relieve patient stress responses, reduce pain, and increase comfort, with broad potential for clinical application [7, 8]. However, a systematic comparison has remained unclear regarding the sedative and analgesic efficacies, fluctuations in vital signs and blood gas parameters, as well as the safety profiles of dexmedetomidine (DEX) versus propofol in individuals suffering from traumatic brain injury (TBI) accompanied by restlessness. Moreover, the disparity in their clinical value in this specific population remains to be elucidated. This existing gap in knowledge results in an insufficient foundation for making informed clinical decisions when selecting sedative and analgesic protocols, potentially compromising therapeutic outcomes and the prognosis of affected patients.

The present investigation enrolled 126 patients diagnosed with TBI and concurrent restlessness as the study cohort. By evaluating the administration of DEX and propofol, the distinctions between the two agents in terms of sedative and analgesic effects, their influence on vital signs and blood gas parameters, and their respective safety profiles were clarified. The findings derived from this research are expected to offer guidance for clinicians in identifying a superior sedative and analgesic strategy for individuals suffering from TBI with restlessness, thereby aiding in the reduction of adverse reactions, mitigating patient distress, and enhancing therapeutic outcomes. These insights carry significant practical implications for advancing the standard of clinical care delivered to patients afflicted with TBI.

Materials and methods

General information

This study included 126 patients with TBI and restlessness admitted to Suzhou Ninth Hospital Affiliated to Soochow University between 2023 and January 2025. Patients were divided into Group A (n=86, DEX) or Group B (N=40, propofol), according to the sedative used. This study was approved by the Ethics Committee of Suzhou Ninth Hospital Affiliated to Soochow University.

Inclusion criteria: Patients with trauma-induced craniocerebral injury; age between 20 and 65 years; and presence of agitation requiring sedation and analgesia. Exclusion criteria: (1) Severe dysfunction of major organs, including the heart, liver, or kidneys; (2) Pre-existing neurological or psychiatric disorders, such as dementia or epilepsy; (3) Malignant tumors; (4) Severe shock or other serious systemic complications; (5) Known allergy to study-related medications; (6) Unstable traumatic brain injury or requirement for surgical intervention; and (7) Abnormal Glasgow Coma Scale (GCS) scores, long-term use of sedatives, or history of alcohol abuse, in order to minimize the influence of key confounding factors on study outcomes.

Dexmedetomidine injection (Jiangsu Hengrui Pharmaceutical Co., Ltd., China; approval No. H20090248; concentration: 100 μg/mL) and propofol injection (Hebei Yipin Pharmaceutical Co., Ltd., China; approval No. H20093542; specification: 100 mg/unit) were used in this study.

Propofol is a short-acting intravenous anesthetic primarily used for sedation. It provides mild adjunctive analgesic effects in clinical practice, and its analgesic potency is significantly lower than that of dedicated analgesics.

Sample size calculation

Referring to the study by Yang *et al*. (2020) on patients with acute brain injury, the incidence of adverse events in patients receiving early goal-directed sedation (EGDS) with dexmedeto-

midine was approximately 30.36% (including bradycardia 10.71%, tachycardia 14.29%, and hypotension 5.36%) [9]. In contrast, the incidence in patients receiving standard sedation with propofol was approximately 48.98% (including bradycardia 6.12%, tachycardia 38.78%, hypotension 4.08%, and accidental extubation 4.08%). Additionally, based on the study by Deng *et al*. (2024) on patients after craniotomy for severe traumatic brain injury, the incidence of adverse events (primarily bradycardia) in the dexmedetomidine group was approximately 11.32%, compared to 15.94% in the control group (without dexmedetomidine) [10]. Based on the synthesis of the two studies, a lower estimate was used in this study: it was assumed that the incidence of adverse events in the dexmedetomidine group (Group A) was 15% and in the propofol group (Group B) was 45%. With α=0.05 (two-sided test) and a statistical power of (1-β=80%, according to PASS 15.0), a minimum of 34 patients per group would be needed in the sample size calculation. Considering a possible dropout rate of 15 per cent (due to reasons such as patient transfer or family withdrawal of support), the original plan was to enroll 40 patients in the dexmedetomidine group and 40 patients in the propofol group. During actual recruitment, an adequate number of eligible cases allowed the dexmedetomidine group to include 86 patients, while the propofol group included 40 patients. This discrepancy in sample size arose from the actual distribution of clinical cases. To address the unequal group sizes, Welch's corrected t-test was applied in subsequent statistical analyses to compare intergroup differences.

Methods

Upon ICU admission, both groups received standardized treatment. Vital signs were continuously monitored using a monitor, including hemodynamic support, neuromonitoring, hemoglobin optimization, and fluid resuscitation. In this study, an optimized standardized sedation protocol was adopted, with strictly defined dose ranges to reduce bias.

Group A received dexmedetomidine for sedation: an intravenous loading infusion of 0.5-1.0 μg/kg was administered over 10-60 minutes. After reaching the loading dose, the maintenance dose was adjusted to 0.2-1.0 μg/(kg·h), with a maximum not exceeding 1.0 μg/(kg·h).

Group B received propofol for sedation: an intravenous loading infusion of 1-2.4 mg/kg was administered over 15-60 minutes. After reaching the loading dose, the maintenance dose was adjusted to 0.3-4 mg/(kg·h), with a maximum not exceeding 4 mg/(kg·h).

The protocol was based on the drug instructions and clinical routine practice for the dose range, with the target sedation depth set to avoid excessive sedation affecting neurological function assessment.

Observation indicators

Vital indicators: a thorough monitoring was conducted on each patient's vital signs both preceding and subsequent to the therapeutic intervention, with principal focus placed on variations in HR, MAP, and RR.

Blood gas indicators: a detailed assessment was performed regarding the fluctuations in blood gas parameters prior to and following the treatment course, especially emphasizing the alterations in $PaCO_2$, PaO_2, and SaO_2 (**Table 1**).

Pain assessment (BPS) score: It is mainly evaluated by four components: facial expression, ventilation compliance, vocalization, and upper limb movement. Each score is 1-4, and the score is between 4 and 16. The higher the scores, the higher the pain level of the patient.

Adverse reactions: The incidences of adverse reactions such as delirium, hypertension, hypotension, and bradycardia were observed and compared between the two groups.

Respiratory drive parameters: respiratory rate variability (RRv) and tidal volume to inspiratory time ratio (Vt/Ti) were monitored. RRv was assessed by continuously recording the respiratory rate over 5 minutes using a patient monitor. A parameter is chosen for the coefficient of variation, which is calculated as (Standard deviation of respiratory rate during that period/Mean respiratory rate) × 100; this value reflects the regularity of respiration. Vt/Ti was derived from synchronous measurements of tidal volume (Vt) and inspiratory time (Ti) obtained via the monitor, and then this ratio was automatically calculated (unit: mL/s). This value quantifies the patient's inspiratory effort and serves as an indirect measure of central respiratory drive. Both respiratory drive parameters were

Table 1. The score indicators

RASS scoring:	
+4 points	Aggressive and violent behavior
+3 points	Very irritable, trying to get IV, nasogastric, and breathing tubes out
+2 points	Restlessness, anxiety, vigorous body movement, and inability to cooperate with the respirator
+1 point	Restlessness, nervousness, slight body movement
0	Natural state, calm and sober
-1 point	Drowsy, unable to stay awake, staying awake for more than 10 seconds
-2 points	Mild sedation, awake time less than 10s
-3 points	Moderate sedation, but responsive to sound
-4 points	Moderate sedation, responsive to physical stimuli
-5 points	Coma, inability to respond to physical and sound stimuli

Note: RASS, Richmond Agitation-Sedation Scale.

recorded before drug administration and 3 hours after drug infusion. All measurements were performed under stable conditions, free from confounding factors such as changes in body position or airway suctioning during the monitoring period.

Venous blood specimens (4 mL) were collected from each patient prior to and 48 hours following the administration of the drug. Using ELISA, the serum concentrations of inflammatory cytokines [tumor necrosis factor (TNF-α, IL-1β, and IL-6] as well as brain injury markers NSE, S100 calcium-binding protein β (S100β), and BDNF] were measured.

The maintenance indicators for sedation and analgesia were as follows: the achievement of adequate sedation and analgesia was assessed between 12 and 24 hours after medication administration, the number of cases meeting the criteria was recorded, and the achievement rate was calculated. The number of analgesic rescue events requiring additional analgesic medication within 12 to 24 hours after medication was recorded, along with the number of sedation depth adjustments requiring changes in sedative dosage or infusion rate.

Sedation-related adverse events were continuously monitored and recorded during the treatment period for both groups, including the number and incidence rate of patient-ventilator asynchrony, events at risk of unplanned extubation, and oversedation. All the above indicators were assessed and recorded once per hour by designated personnel.

Cerebral oxygen metabolism indicators were measured 48 hours after medication administration. Specimens were drawn from the jugular bulb, and the $SjvO_2$, along with the SaO_2, which were determined using a blood gas analyzer. The cerebral oxygen extraction rate was calculated according to the standard formula. The jugular venous oxygen saturation values were recorded synchronously.

Statistical methods

Data were analyzed using SPSS 20.0 software. All measurement data were first tested for normality. Data conforming to a normal distribution were analyzed using Welch's t-test, while data not conforming to a normal distribution were analyzed using nonparametric tests. Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$). Owing to the disparity in sample sizes across the two groups, between-group comparisons were conducted using the Welch-corrected t-test. Categorical data were expressed as percentages and examined with the χ^2 test. Spearman correlation analysis was utilized to assess relationships among the main parameters. To determine the variables associated with the development of adverse events, variables with $P<0.05$ in the univariate analysis were first screened using the stepwise method and then entered into the multivariable logistic regression model to avoid model redundancy and improve the robustness of the regression results.

Both univariate and multivariate logistic regression analyses were carried out. A threshold of

Table 2. Baseline data

Baseline data	Group A (n=86)	Group B (n=40)	Statistic	*P*
Gender (male/female, cases)	52/34	21/19	χ^2=0.12	0.728
Age (years)	44.82±10.15	45.06±9.78	t=0.12	0.904
BMI (kg/m^2)	20.12±1.03	20.05±0.98	t=0.36	0.719
Type of injury (cases)			χ^2=0.25	0.968
Cerebral contusion	38	17	-	-
Intracranial hematoma	26	12	-	-
Brainstem injury	10	5	-	-
Other	12	6	-	-
Time from injury to admission (h)	3.25±1.56	3.42±1.68	t=0.53	0.597
Comorbidities (cases)			χ^2=0.31	0.956
Hypertension	18	8	-	-
Diabetes	12	5	-	-
Coronary heart disease	9	4	-	-

Note: BMI, body mass index.

Table 3. Changes in vital signs before and after the treatment of patients

Groups	Cases	HR (time/min)		MAP (mmHg)		RR (time/min)	
		Before medication	3 hours of medication	Before medication	3 hours of medication	Before medication	3 hours of medication
Group B	40	92.16±12.52	84.29±6.14	92.56±13.84	78.65±7.05	25.16±2.01	20.31±1.05
Group A	86	93.86±13.58	93.26±6.45	92.85±12.05	88.39±7.45	26.37±2.15	24.56±1.06
T		0.591	7.376	0.119	6.939	0.520	21.506
P		0.555	<0.001	0.905	<0.001	0.603	<0.001

Note: HR, heart rate; MAP, mean arterial pressure; RR, respiratory rate.

P<0.05 was regarded as denoting statistical significance.

Results

Presentation of baseline data

In **Table 2**, no significant differences were observed between group A and group B in sex, age, BMI, injury category, interval from injury to hospital arrival, and comorbid conditions (e.g., hypertension, diabetes, and coronary heart disease), (all *P*>0.05), indicating comparable baseline characteristics between the two groups.

Changes in vital signs before and after the treatment of patients

The HR, MAP, and RR showed no significant difference between the two groups before treatment. At three hours following drug administration, these parameters in group A were more favorable than those observed in group B (**Table 3**).

Comparison of respiratory function parameters between the two groups before and after drug administration

Before drug administration, no marked intergroup disparities were detected regarding PaO_2, $PaCO_2$, SaO_2, RR, MV, RRv, or Vt/Ti (all *P*>0.05). At three hours following drug administration, the dexmedetomidine group showed notably elevated levels of PaO_2, $PaCO_2$, RR, MV, RRv, and Vt/Ti relative to the propofol group (all *P*<0.001). Concerning SaO_2, no significant differences were identified either within each group when comparing pre- and post-treatment measurements or when contrasting the two groups against each other (*P*>0.05). Detailed data are presented in **Table 4**.

Comparison of the RASS score and the BPS score of patients between the two groups

The comparison of the time required to reach the targeted sedation level between the two groups revealed no statistically meaningful dif-

Table 4. Comparison of blood gas indicators and detailed respiratory function indicators of the two groups of patients before and after medication

Indexes	Groups	Cases	Before drug administration	Three hours after drug administration	t	*P*
PaO_2 (mmHg)	Dexmedetomidine group	86	94.23±7.12	92.64±3.45	2.158	0.032
	Propofol group	40	94.16±7.15	85.06±3.41	11.479	<0.001
$PaCO_2$, (mmHg)	Dexmedetomidine group	86	42.18±6.31	48.26±1.26	10.152	<0.001
	Propofol group	40	42.16±6.25	44.75±2.06	3.258	0.002
SaO_2 (%)	Dexmedetomidine group	86	94.61±4.15	92.35±4.15	4.025	<0.001
	Propofol group	40	95.34±4.13	92.86±4.25	3.861	<0.001
RR, (Times/minute)	Dexmedetomidine group	86	26.37±2.15	24.56±1.06	7.892	<0.001
	Propofol group	40	25.16±2.01	20.31±1.05	14.265	<0.001
MV, (L/min)	Dexmedetomidine group	86	7.92±0.98	7.86±0.95	0.458	0.648
	Propofol group	40	7.85±0.92	6.25±0.82	8.963	<0.001
RRv, (%)	Dexmedetomidine group	86	12.45±1.58	12.38±1.52	0.321	0.748
	Propofol group	40	12.32±1.49	8.15±1.26	14.257	<0.001
Vt/Ti, (mL/s)	Dexmedetomidine group	86	48.65±5.31	48.59±5.23	0.078	0.938
	Propofol group	40	48.52±5.28	35.26±4.18	13.682	<0.001

Note: PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide; SaO_2, arterial oxygen saturation; RR, respiratory rate; MV, minute ventilation; RRv, respiratory rate variability; Vt/Ti, tidal volume to inspiratory time ratio.

Table 5. RASS score and BPS score of patients

Groups	Cases	RASS scoring(points)			BPS scoring (points)
		Time to reach the target analgesic index	Wake-up time after drug withdrawal	Interventions within 1-12 hours of medication Number	
Group B	40	30.56±4.25	10.04±1.78	5.00±2.00	6.23±1.42
Group A	86	29.84±4.52	14.56±2.35	2.00±1.00	4.12±0.89
T		0.847	10.800	11.243	10.161
P		0.398	<0.001	<0.001	<0.001

Note: Propofol primarily induces sedation with comparatively limited analgesic properties; thus, the variations in BPS scores documented in this investigation mainly reflected the analgesic superiority of DEX rather than a direct contrast of the analgesic efficacy of propofol. RASS, Richmond Agitation-Sedation Scale; BPS, Behavioral Pain Scale.

ference (*P*>0.05). Following cessation of drug administration, the duration until the patient regained consciousness was extended in group A relative to group B. Meanwhile, across the interval of 1 to 12 hours after drug delivery, both the frequency of sedative rescue interventions and the BPS scores (reflecting pain intensity) were observed to be reduced in group A when compared with group B (*P*<0.001) (**Table 5**).

Inflammatory factor

No significant differences were observed in the concentrations of IL-1β, TNF-α, and IL-6 between group B and group A before drug administration (*P*=0.719, 0.057, 0.440). At 48 hours following drug administration, the levels of IL-1β, TNF-α, and IL-6 in group A were markedly lower than those recorded in group B (t=10.025, 8.740, 11.906; all *P*<0.001), suggesting that DEX effectively attenuated the severity of early inflammatory response.

Brain injury indicators

There were no significant differences in the levels of NSE, S100β, or BDNF between group B and group A before medication (*P*=0.338, 0.412, 0.594). At 48 hours following drug administration, the concentrations of NSE and S100β in both groups exhibited a marked elevation relative to their baseline values, whereas the concentrations of BDNF showed a notable

Table 6. Comparison of inflammatory factor indicators

Groups	n	IL-1β (μg/L)		TNF-α (ng/mL)		IL-6 (ng/L)	
		Before drug administration	48 h after drug administration	Before drug administration	48 h after drug administration	Before drug administration	48 h after drug administration
Group B	40	29.06±4.31	52.06±5.42	4.98±0.79	12.33±2.79	17.38±2.37	41.85±4.02
Group A	86	28.78±3.39	41.84±5.12	4.70±0.67	8.29±1.28	16.98±3.29	32.46±4.33
t		0.362	10.025	1.94	8.74	0.775	11.906
P		0.719	<0.001	0.057	<0.001	0.44	<0.001

Note: IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6.

Table 7. Comparison of Brain Injury Indicators

Groups	n	NSE (μg/L)		S100β (μg/L)		BDNF (ng/L)	
		Before drug administration	48 h after drug administration	Before drug administration	48 h after drug administration	Before drug administration	48 h after drug administration
Group B	40	49.94±5.79	63.2±4.82	0.87±0.06	1.02±0.06	14.30±2.29	7.22±1.07
Group A	86	48.93±4.68	54.9±4.58	0.86±0.07	0.95±0.08	14.05±2.74	8.92±1.83
t		0.966	9.107	0.825	5.459	0.535	-6.54
P		0.338	<0.001	0.412	<0.001	0.594	<0.001

Note: NSE, neuron-specific enolase; S100β, S100 calcium-binding protein β; BDNF, brain-derived neurotrophic factor.

Table 8. Adverse reactions of patients

Groups	Cases	Slow HR	Increased BP	Decreased BP	Delirium	Total
The control group	40	5	6	10	5	26
Group A	86	1	3	2	2	8
χ^2						42.987
P						<0.001

Note: Bradycardia caused by DEX is mostly related to vagal nerve excitation mediated by α_2 receptors. The low incidence of bradycardia in group A (1.16%) in this study may be associated with dose adjustment (maintenance dose ≤1.0 μg/(kg. h)). The bradycardia in group B may be related to the circulatory system depression caused by propofol (dose-dependent myocardial depression). HR, heart rate; BP, blood pressure.

reduction (*P*<0.05). The concentrations of NSE and S100β in group A were significantly lower compared to those in group B (t=9.107 and 5.459, respectively). The concentrations of BDNF in group A were significantly higher than those detected in group B (t=-6.540, *P*< 0.001), while the concentrations of IL-1β, TNF-α, and IL-6 in group A were significantly lower than those in group B (t=10.025, 8.740, 11.906; all *P*<0.001) (**Tables 6**, **7**).

Adverse reactions of patients

The rate of adverse events observed in group A was 9.30%, which was markedly reduced relative to that in group B (65.00%) (*P*<0.001). There was 1 case of bradycardia in group A and 5 cases of bradycardia in group B (**Table 8**).

Further observation of sedation-related detailed adverse events revealed statistically significant discrepancies when comparing the two groups regarding the incidence rates of patient-ventilator asynchrony, unplanned extubation risk events, and oversedation (*P*<0.05) (**Table 9**).

Sedation and analgesia maintenance effects and additional intervention indicators

Significant discrepancies were found when comparing the two groups regarding the 12-24 h sedation and analgesia maintenance target achievement rate, number of analgesic rescue doses, and number of sedation depth adjustments (*P*<0.001) (**Table 10**).

Cerebral oxygen metabolism indicators

At 48 hours after medication administration, the two groups exhibited marked disparities with respect to cerebral oxygen extraction rate

Table 9. Detailed comparison of sedation-related adverse events between the two groups

Indicator	Group A (n=86)	Group B (n=40)	χ^2 value	*P* value
Patient-ventilator asynchrony incidence [n (%)]	3 (3.49)	11 (27.50)	15.432	<0.001
Unplanned extubation risk events [n (%)]	1 (1.16)	6 (15.00)	8.927	0.003
Oversedation incidence [n (%)]	2 (2.33)	9 (22.50)	13.891	<0.001

Table 10. Sedation and analgesia maintenance effects and additional interventions between the two groups

Indicator	Group A (n=86)	Group B (n=40)	Statistical value	*P* value
12-24 h sedation and analgesia maintenance target achievement rate [n (%)]	79 (91.86)	25 (62.50)	χ^2=18.654	<0.001
Number of analgesic rescue doses (times)	0.42±0.20	1.56±0.43	t=16.328	<0.001
Number of sedation depth adjustments (times)	0.51±0.23	1.82±0.51	t=17.105	<0.001

Table 11. Comparison of cerebral oxygen metabolism indicators at 48 hours after medication between the two groups

Indicator	Group A (n=86)	Group B (n=40)	*t* value	*P* value
Cerebral oxygen extraction rate (%)	31.26±2.15	35.79±2.42	9.862	<0.001
Jugular bulb oxygen saturation (%)	68.53±3.26	62.17±3.51	8.753	<0.001

Table 12. Spearman correlation analysis of primary indicators

Indicator Pair	r value	*P* value
BPS score vs IL-1β	0.584	<0.001
BPS score vs TNF-α	0.561	<0.001
BPS score vs IL-6	0.602	<0.001
BPS score vs NSE	0.537	<0.001
BPS score vs S100β	0.512	<0.001
BPS score vs BDNF	-0.526	<0.001
MAP vs HR	0.415	<0.001
PaO_2 vs $PaCO_2$	0.372	0.002

Note: BPS, Behavioral Pain Scale; IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; NSE, neuron-specific enolase; S100β, S100 calcium-binding protein β; BDNF, brain-derived neurotrophic factor; MAP, mean arterial pressure; HR, heart rate; PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide.

and jugular bulb oxygen saturation (*P*<0.001) (**Table 11**).

Correlation analysis

Spearman correlation analysis revealed that the BPS score exhibited a positive association with IL-1β, TNF-α, IL-6, NSE, and S100β (all *P*<0.001); conversely, the BPS score demonstrated a negative relationship with BDNF (*P*<0.001); meanwhile, MAP displayed a positive correlation with HR (*P*<0.001); and PaO_2 was found to be positively linked to $PaCO_2$ (*P*<0.01) (**Table 12** and **Figures 1**, **2**).

Regression analysis of factors influencing adverse events

With the occurrence of adverse events designated as the dependent variable, various factors, including medication regimen, age, sex, BMI, BPS score, number of sedation interventions, patient-ventilator asynchrony, unplanned extubation risk, oversedation, PaO_2, RR, IL-6, NSE, and S100β, were incorporated into univariate and multivariate logistic regression models.

Univariate analysis revealed that medication regimen, BPS score, number of sedation interventions, patient-ventilator asynchrony, unplanned extubation risk, oversedation, and NSE showed associations with the presence of adverse events (all *P*<0.05); in contrast, age, sex, BMI, PaO_2, RR, IL-6, and S100β did not demonstrate significant correlations with the presence of adverse events (all *P*>0.05) (**Table 13**).

Factors that achieved *P*<0.05 in the univariate analysis were subsequently entered into multi-

Figure 1. Correlation heatmap of BPS score with inflammatory/neurological markers. Note: BPS, Behavioral Pain Scale; IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; NSE, neuron-specific enolase; S100β, S100 calcium-binding protein β; BDNF, brain-derived neurotrophic factor. Values in the heatmap represent Spearman correlation coefficients (r). Color intensity indicates the strength of correlation, with red representing positive correlation and blue representing negative correlation. Correlations with $P<0.05$ were considered statistically significant; non-significant correlations were not specially marked in the heatmap.

Figure 2. Spearman correlation heatmap of vital signs and blood gas parameters. Note: MAP, mean arterial pressure; HR, heart rate; PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide. Values in the heatmap represent Spearman correlation coefficients (r). Color intensity indicates the strength of correlation, with red representing positive correlation. Correlations with $P<0.05$ were considered statistically significant; non-significant correlations were not specially marked in the heatmap.

variate logistic regression analysis. The findings indicated that propofol administration, higher BPS score, a greater number of sedation interventions, patient-ventilator asynchrony, oversedation, and elevated NSE constituted independent risk factors for the presence of adverse events (all $P<0.05$) (**Table 14** and **Figure 3**).

Discussion

Patients with traumatic brain injury often present with agitation/restlessness due to factors such as traumatic stress, pain, and intracranial hypertension, which not only increases the risk of secondary injury but also interferes with treatment and monitoring. Therefore, the rational selection of sedative and analgesic drugs is crucial for improving patient prognosis [11, 12]. In everyday clinical practice, propofol is commonly used in these patients due to its rapid onset and easily titratable sedation level. Nevertheless, given its comparatively limited analgesic potency, propofol is frequently combined with opioid medications, and its suppressive effects on both circulation and respiration may further aggravate the instability of a patient's clinical condition [13, 14]. DEX, which functions as a highly selective α_2-adrenergic receptor agonist, provides both hypnotic and antinociceptive effects while exerting only minor influence on respiratory function; consequently, it has drawn growing attention in recent years. Through a comparison of the two drugs' clinical per-

Table 13. Univariate analysis of factors influencing adverse events

Factor	χ^2/t value	*P* value
Medication regimen (propofol vs dexmedetomidine)	42.987	<0.001
Age	0.915	0.339
Sex	0.326	0.568
BMI	0.632	0.427
BPS score	10.161	<0.001
Number of sedation interventions	11.243	<0.001
Patient-ventilator asynchrony	15.432	<0.001
Unplanned extubation risk	8.927	0.003
Oversedation	13.891	<0.001
PaO_2	1.152	0.250
Respiratory rate (RR)	1.014	0.312
IL-6	0.876	0.381
NSE	9.107	<0.001
S100β	0.725	0.468

Note: BMI, body mass index; BPS, Behavioral Pain Scale; PaO_2, partial pressure of arterial oxygen; RR, respiratory rate; IL-6, interleukin-6; NSE, neuron-specific enolase; S100β, S100 calcium-binding protein β.

Table 14. Multivariate analysis of factors influencing adverse events

Factor	OR value	95% CI	*P* value
Propofol (vs dexmedetomidine)	5.261	3.142-8.810	<0.001
BPS score	1.628	1.273-2.084	<0.001
Number of sedation interventions	1.874	1.326-2.647	<0.001
Patient-ventilator asynchrony	3.126	1.682-5.814	0.001
Unplanned extubation risk	1.342	0.815-2.210	0.247
Oversedation	2.753	1.419-5.342	0.003
NSE	1.135	1.042-1.236	0.004

Note: OR, odds ratio; CI, confidence interval; BPS, Behavioral Pain Scale; NSE, neuron-specific enolase.

formances in individuals with traumatic brain injury accompanied by agitation, the present investigation revealed that DEX exhibited superior sedative and analgesic efficacy, more favorable impacts on vital signs and blood gas parameters, and a better safety profile. These observations align with conventional clinical knowledge, yet they also contain certain nuanced details that warrant deeper exploration [15]. According to standard clinical understanding, the primary strength of propofol lies in its robust sedative action and rapid onset. However, because its analgesic effect is weak, pain management in trauma patients often necessitates the co-administration of opioid analgesics such as fentanyl, a strategy that increase the risk of adverse events, such as respiratory depression. By contrast, DEX is characterized by its ability to deliver meaningful pain relief alongside sedation, thereby reducing the requirement for supplemental analgesic agents [16, 17]. The findings of the current investigation strongly echo this concept: between 1 and 12 hours after drug administration, the BPS scores (pain scores) recorded in the DEX group (group A) were markedly lower than those observed in the propofol group (group B), and the frequency of sedation-related interventions was also lower in group A, indicating that DEX more effectively alleviates patient discomfort and minimizes repeated dose adjustments prompted by pain or agitation.

Concerning the regulation of sedation depth, no meaningful difference was detected between the two study arms regarding the time required to achieve the target sedation index, suggesting that the sedative onset of DEX is comparable to that of propofol. This is somewhat different from the traditional clinical impression that DEX has a slightly slower onset, which may be related to the use of a loading dose (0.5-1.0 μg/kg) for rapid infusion of DEX in this study [18]. Additionally, the longer awakening time after drug discontinuation in the DEX group is consistent with its pharmacokinetic characteristics (a half-life of about 2 hours, longer than the 10-15 minutes of propofol). However, the clinical significance needs to be viewed dialectically: for patients requiring frequent neurological assessments, a prolonged awakening period might interfere with the evaluation of their clinical status; conversely, for patients at high risk of agitation who require sustained sedation, an extended emergence time may paradoxically mitigate rebound agitation and diminish the likelihood of addi-

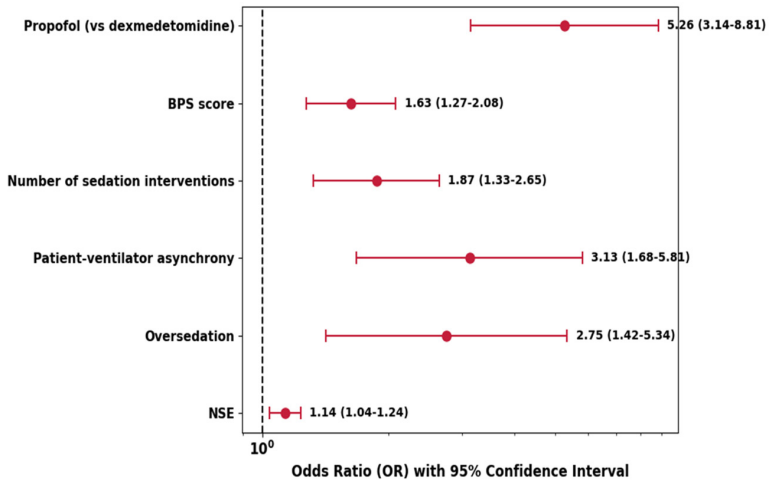

Figure 3. Forest plot of independent risk factors for adverse events. Note: Multivariable logistic regression analysis identified propofol administration, elevated BPS score, frequent sedation adjustments, patient-ventilator asynchrony, oversedation, and increased NSE as independent risk factors for adverse events (all $P<0.05$). In this forest plot, red circles stand for odds ratios (ORs), and horizontal error bars represent 95% confidence intervals (95% CIs). The vertical dashed line at OR=1 is the null-effect reference line; all risk factors presented statistically significant correlations since their 95% CIs did not cross the line of OR=1. Abbreviations: BPS, Behavioral Pain Scale; NSE, neuron-specific enolase.

tional harm [19, 20]. The stability of hemodynamic and ventilatory functions was preserved to maintain adequate cerebral perfusion pressure and avert cerebral hypoxic insults in individuals with traumatic brain injury (TBI). Propofol is recognized to produce more pronounced suppressive effects on systemic circulation when administered at elevated doses; consequently, it may induce bradycardia and hypotension, exacerbating the preexisting conditions of patients already experiencing low blood pressure or reduced intravascular volume. Impairment of ventilatory drive also constitutes a form of adverse effect. Propofol diminishes the function of the medullary respiratory center and attenuates its responsiveness to carbon dioxide, leading to decreased respiratory frequency and minute volume, thereby heightening the risk of hypoxemia. Hence, simultaneous monitoring of the patient's breathing pattern is required during its administration [21]. Dexmedetomidine serves as a highly selective α_2-adrenergic receptor agonist that exerts its sedative effects through action on the locus coeruleus. It exerts only minimal direct suppression on the respiratory center and does not alter respiratory rate or tidal volume. Only with administration of substantial doses may mild irregularities in breathing rhythm emerge because of indirect vagal activation. Therefore, this agent is more appropriate for utilization within the neurocritical care setting. Drawing from the aforementioned observations, it can be inferred that these two categories of pharmaceuticals exert divergent influences on the respiratory system and blood gas profiles. Although baseline measurements of PaO_2, $PaCO_2$, SaO_2, and various other ventilatory indices (including RR, MV, RRv, and Vt/Ti) showed no notable intergroup differences initially, at three hours following drug administration, the propofol-treated cohort displayed a marked decline in PaO_2 as well as pronounced reductions in RR, MV, RRv, and Vt/Ti compared to the dexmedetomidine-treated cohort. RR and MV were substantially decreased in the propofol group, yet $PaCO_2$ rose only modestly; no pronounced elevation occurred as a result of severe respiratory depression. Given the above results, the relationship between the refined respiratory index and typical blood-gas indicators were also explored [22]. The coordinated changes in blood gases and respiratory function indicate that the decline in PaO_2 in the propofol group is directly related to reduced efficiency of pulmonary ventilation caused by decreased RR and MV, and thus, respiratory depression impairs oxygenation. There was no substantial increase in $PaCO_2$; this lack of a significant increase may be attributed to clinical management and respiratory compensation for all patients in the ICU under standardized care, such as baseline oxygen therapy at 30%-40% and continuous respiratory monitoring. As MV decreased, oxygen concentration adjustments and optimizations of patient position (e.g., 30° head-up tilt) were made to maintain gas exchange and partially offset the hypoventilation effect on $PaCO_2$. It has also been proposed that some patients in the propofol group may have shown compensatory increases in tidal volume, thus

improving per-breath gas exchange to offset the lower respiratory rate and maintain $PaCO_2$ within a normal range [23].

Analysis of the parameters of respiratory drive (RRv and Vt/Ti) showed that both were significantly lower in the propofol group after drug administration compared with the dexmedetomidine group; thus, respiratory depression in the propofol group was due to a reduction in ventilation as well as a weakening of the central respiratory drive. This resulted in a reduction of respiratory rhythm variability (a loss of regulatory capacity of the respiratory center to physiological stimuli) and a decrease in inspiratory effort (reduced Vt/Ti). On the other hand, the dexmedetomidine group showed a stable respiratory drive parameter, indicating that the respiratory center was functioning normally, and demonstrated enhanced autonomy and regularity of spontaneous respiration, and thus fewer clinical interventions were needed to maintain PaO_2 and $PaCO_2$. People with traumatic brain injuries are more likely to have an irregular respiratory rhythm; this may result in ventilation-perfusion mismatch and cerebral hypoxia, thus exacerbating the injury. The relatively weak effect of dexmedetomidine on respiratory drive is more consistent with the aim of reducing the risk of organ damage during anesthesia. The results are in line with those reported by Conti *et al*. (2016) in a prospective, open-label, multicenter randomized controlled trial conducted at three Italian university hospitals' ICUs involving 20 difficult-to-wean patients who had failed spontaneous breathing trials and were on pressure support ventilation. At comparable depth of sedation, dexmedetomidine demonstrated better patient-ventilator synchrony than propofol. The asynchrony index (AI) began to diverge between groups at 2 hours after administration and reached statistical significance by 12 hours [24]. Although our study focused on agitated TBI patients rather than difficult-to-wean mechanically ventilated participants, both studies have shown that dexmedetomidine interferes less with respiratory drive and rhythm, thereby improving the coordination of spontaneous breathing and external support (e.g., basic oxygen therapy in our ICU setting or pressure support in Conti's study). This advantage is further reinforced by a retrospective cohort investigation carried out by Liu *et al*. (2024), which included 19,751 individuals with moderate-to-severe TBI (msTBI) who required mechanical ventilation, based on data from the Premier Database (2016-2020). Their findings indicated that the early administration of dexmedetomidine (within the first two days following ICU admission) corresponded to lower in-hospital mortality rates and shorter lengths of hospitalization, while not elevating the incidence of dialysis, vasopressor requirements, or overall treatment expenses [25]. Although the study designs differ (prospective controlled trial vs. retrospective cohort), both converge on core benefits in msTBI patients: our study demonstrates dexmedetomidine's stability in respiratory (RR, MV, drive parameters) and circulatory (MAP, HR) function, with an adverse event rate of only 9.30% (significantly lower than propofol's 65.00%); Lu *et al*. further confirm that this organ-protective effect translates into longer-term clinical benefits such as reduced mortality and facilitated weaning. Together, they indicate that dexmedetomidine's advantages in msTBI management extend beyond short-term stability in vital signs and blood gases to include reduced cardiopulmonary suppression and adverse events, thereby laying a foundation for improved prognosis [26]. In short, the lack of a significant increase in $PaCO_2$ in the propofol group despite a reduced respiratory rate and tidal volume is due to a combination of active ICU interventions and compensatory physiological mechanisms, not a lack of respiratory depression. Based on all the evaluations of blood gases and refined respiratory parameters, dexmedetomidine can maintain respiratory stability and oxygenation in the face of TBI more effectively than other options, and is thus a good choice when needing to balance the requirements of sedation with safety for the cardio-respiratory system.

The present investigation revealed that at 48 hours following surgery, both patient cohorts with traumatic brain injury exhibited marked elevations in serum concentrations of IL-1β, TNF-α, and IL-6; consequently, an evident early-phase inflammatory response attributable to surgical trauma superimposed on the primary brain injury had taken place. Of note, the post-operative measurements of those inflammatory cytokines were markedly reduced in the dexmedetomidine-treated cohort relative to the propofol-treated group; therefore, it could be

inferred that dexmedetomidine attenuates perioperative amplification of inflammation. Earlier reports have documented that secondary damage to the brain following traumatic brain injury is strongly associated with neuroinflammation, and sustained high levels of proinflammatory mediators including IL-1β, TNF-α, and IL-6 can exacerbate disruption of the blood-brain barrier, cerebral edema, oxidative stress, and apoptotic death of neurons; hence, they are capable of impairing neurological recovery as well as clinical prognosis. Accordingly, the inflammatory pattern observed in the current study suggests that dexmedetomidine might confer a neuroprotective benefit by suppressing the cascade of secondary inflammatory injury.

Further analysis of brain injury-related biomarkers showed that NSE and S100β levels were elevated, whereas BDNF levels were reduced at 48 h after surgery in both groups, indicating the presence of early neuronal/glial injury and insufficient neurotrophic support in the postoperative period. However, compared with propofol, dexmedetomidine was associated with lower NSE and S100β levels and a higher BDNF level, suggesting a potential alleviation of early brain injury and preserving the neurotrophic microenvironment. Available evidence indicates that S100β and NSE are widely used circulating biomarkers in traumatic brain injury and have diagnostic and prognostic value, whereas BDNF is involved in neuronal survival, synaptic plasticity, and functional recovery [27, 28]. Clinical and experimental studies have also suggested that dexmedetomidine may modulate BDNF expression under anesthetic or brain injury conditions and may attenuate early neuroinflammation and cellular injury through inflammation- and stress-related pathways, including TLR4/NF-κB and ROS/Nrf2 signaling [29-31]. These earlier observations align broadly with the current data. In the dexmedetomidine group, more stable maintenance of sedation and analgesia was achieved, fewer rescue interventions were required, and the frequencies of patient-ventilator asynchrony, unplanned extubation risk, and oversedation were significantly lower than those recorded in the propofol group; moreover, more stable parameters of cerebral oxygen metabolism were also exhibited in the dexmedetomidine group. Correlation analysis revealed that pain scores were closely associated with inflammatory responses and nerve injury markers, and logistic regression analysis confirmed that propofol use, poor pain control, sedation fluctuations, and an increased degree of brain injury were independent risk factors for adverse events. Based on the cumulative evidence from the experiments described above, dexmedetomidine, owing to its stable sedative and analgesic effects, induce only mild suppression of respiratory and cardiovascular function, and demonstrate a pronounced capacity for cerebral protection, yielded favorable results across multiple clinical trials; consequently, it was adopted as a sedation and analgesia option for the management of acutely unsettled pediatric patients who had sustained TBI, to diminish the likelihood of severe adverse events while concurrently improving both clinical safety and overall patient outcomes.

In the short term, dexmedetomidine (DEX) demonstrates clear advantages in patients with agitation following traumatic brain injury, providing a reference for clinical selection of sedation and analgesia regimens. In situations where both sedation and analgesia are required along with organ protection, especially in patients with poor respiratory reserve or those prone to circulatory depression, dexmedetomidine is a more reasonable choice. In contrast, propofol can be used when rapid awakening or only short-acting sedation is needed, but close monitoring of respiratory and hemodynamic parameters and timely co-administration of analgesics are essential. In summary, the available data indicate that dexmedetomidine offers a better balance between efficacy and safety for sedation and analgesia in agitated patients with traumatic brain injury, has a smaller impact on vital signs and blood gas parameters, and is associated with a lower incidence of adverse effects, thus better meeting the clinical needs of neurocritical care patients.

This study does have some limitations. The number of enrolled participants is limited, and all procedures were conducted at a single institution, which may introduce selection bias. In addition, this was a non-randomized retrospective study without randomization or blinding, potentially leading to selection and detection bias. Moreover, the severe imbalance in sample sizes between the two groups (86 vs. 40

cases) may affect the reliability of the results. This study conducted only a 48-hour observation and did not collect or analyze follow-up data on long-term neurological outcomes, such as changes in intracranial pressure, total hospital stay, or survival rate. Therefore, higher-quality studies are needed to validate the conclusions of this paper further.

Conclusion

Dexmedetomidine provides excellent sedation and analgesia in patients with agitation secondary to TBI, accompanied by a favorable safety profile. It has provided stable maintenance for sedation and analgesia, reduced the number of analgesic rescue doses and adjustments to sedation depth, and lowered the incidence of patient-ventilator asynchrony, unplanned extubation risk, and oversedation. Dexmedetomidine also exerted a diminished influence on both respiratory and circulatory function, demonstrated more consistent cerebral oxygenation parameters, and was linked to a reduced occurrence of undesirable post-treatment events.

Disclosure of conflict of interest

None.

Address correspondence to: Baoqin Xu, Department of Anesthesiology, Suzhou Ninth Hospital Affiliated to Soochow University, No. 2666 Ludang Road, the Taihu Lake New Town, Wujiang District, Suzhou 215200, Jiangsu, China. Tel: +86-0512-82881332; E-mail: baoqinxu0bqx@163.com

References

[1] Karaboue MAA, Ministeri F, Sessa F, Nannola C, Chisari MG, Cocimano G, Di Mauro L, Salerno M and Esposito M. Traumatic brain injury as a public health issue: epidemiology, prognostic factors and useful data from forensic practice. Healthcare (Basel) 2024; 12: 2266.

[2] Pinggera D, Geiger P and Thomé C. Schädel-Hirn-Trauma Traumatic brain injury. Nervenarzt 2023; 94: 960-972.

[3] Ritter M. Evidence-based pearls: traumatic brain injury. Crit Care Nurs Clin North Am 2023; 35: 171-178.

[4] Ceric A and Wise MP. Optimal sedation and analgesia for critical care patients with acute brain injury including post-cardiac arrest. Crit Care Clin 2025; 41: 821-831.

[5] Choo YH, Seo Y and Oh HJ. Deep sedation in traumatic brain injury patients. Korean J Neurotrauma 2023; 19: 185-194.

[6] Williamson DR, Dryden L, Cheng W, Hutton B, Skidmore B, Mehta S, Golan E, Turgeon AF, Adhikari NK, Rose L and Burry L. Sedation for moderate-to-severe traumatic brain injury in adults. Cochrane Database Syst Rev 2025; 5: CD012639.

[7] Laws JC, Vance EH, Betters KA, Anderson JJ, Fleishman S, Bonfield CM, Wellons JC 3rd, Xu M, Slaughter JC, Giuse DA, Patel N, Jordan LC and Wolf MS. Acute effects of ketamine on intracranial pressure in children with severe traumatic brain injury. Crit Care Med 2023; 51: 563-572.

[8] Hatfield J, Soto AL, Kelly-Hedrick M, Kaplan S, Komisarow JM, Ohnuma T and Krishnamoorthy V. Safety, efficacy, and clinical outcomes of dexmedetomidine for sedation in traumatic brain injury: a scoping review. J Neurosurg Anesthesiol 2024; 36: 101-108.

[9] Yang G, Guo X, Mao G, Zhang J, Wang Y and Yang C. Clinical research of early goal directed sedation applying in acute brain injury. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2020; 32: 345-349.

[10] Deng Z, Gu Y, Luo L, Deng L, Li Y and Huang W. The effect of dexmedetomidine on the postoperative recovery of patients with severe traumatic brain injury undergoing craniotomy treatment: a retrospective study. Eur J Med Res 2024; 29: 256.

[11] Zhuang S, Xu Q, Li Y, Hu K, Xia Z and Zhang L. Serum TBK1 levels are correlated with inflammation, optic nerve sheath diameter and intracranial pressure in severe traumatic brain injury patients under deep sedation. Adv Clin Exp Med 2023; 32: 415-422.

[12] Payen JF, Schilte C, Bertrand B and Behouche A. Toward individualized sedation in patients with acute brain damage. Anaesth Crit Care Pain Med 2023; 42: 101219.

[13] Dolmans RGF, Barber J, Foreman B, Temkin NR, Okonkwo DO, Robertson CS, Manley GT, Rosenthal ES. Sedation intensity in patients with moderate to severe traumatic brain injury in the intensive care unit: a TRACK-TBI cohort study. Neurocrit Care 2025; 42: 551-561.

[14] Everson CA, Szabo A, Plyer C, Hammeke TA, Stemper BD and Budde MD. Sleep loss, caffeine, sleep aids and sedation modify brain abnormalities of mild traumatic brain injury. Exp Neurol 2024; 372: 114620.

[15] Wang X, Wang Z, Sun C and Cui Z. Clinical study of dexmedetomidine in combination with butorphanol for the treatment of traumatic

brain injury (TBI). Turk Neurosurg 2024; 34: 14-19.
[16] Inoue G, Ohtaki Y, Satoh K, Odanaka Y, Katoh A, Suzuki K, Tomita Y, Eiraku M, Kikuchi K, Harano K, Yagi M, Uchida N and Dohi K. Sedation therapy in intensive care units: harnessing the power of antioxidants to combat oxidative stress. Biomedicines 2023; 11: 2129.
[17] Suresh V and Magoon R. Comment on "dexmedetomidine sedation in traumatic brain injury: a transforming clinical research and knowledge in traumatic brain injury study". Crit Care Med 2024; 52: e248-e249.
[18] Kurni M, Kaloria N, Hazarika A, Jain K, Gupta SK and Walia R. Comparison of midazolam and propofol infusion to suppress stress response in patients with severe traumatic brain injury: a prospective, randomized controlled trial. Korean J Neurotrauma 2023; 19: 70-81.
[19] Khalili H, Niakan A, Rajabpour-Sanati A, Shaghaghian E, Hesam Alavi M, Dehghankhalili M and Ghaffarpasand F. Effect of Dexmedotomdine hydrochloride (Percedex®) on functional outcome of patients with moderate and severe traumatic brain injury. J Clin Neurosci 2023; 114: 146-150.
[20] Kölbel B, Novotny A, Willms A, Kehl V, Meyer B, Mauer UM and Krieg SM. Study protocol for a multicenter randomized controlled pilot study on decompressive laparotomy vs. decompressive craniectomy for intractable intracranial pressure after traumatic brain injury: the SCALPEL study. Brain Spine 2023; 3: 102677.
[21] Jeffcote T, Weir T, Anstey J, Mcnamara R, Bellomo R and Udy A. The impact of sedative choice on intracranial and systemic physiology in moderate to severe traumatic brain injury: a scoping review. J Neurosurg Anesthesiol 2023; 35: 265-273.
[22] Alaifan T, Sakhakhni A, Khojah A, Alraddadi EA, Alkhaibary A and Alqahtani AM. Impact of dexmedetomidine on hospital and intensive care unit stay duration in adult traumatic brain injury patients: a systematic review. Drug Healthc Patient Saf 2025; 17: 157-171.
[23] Robbins EM, Jaquins-Gerstl AS, Okonkwo DO, Boutelle MG and Michael AC. Dexamethasone-enhanced continuous online microdialysis for neuromonitoring of O_2 after brain injury. ACS Chem Neurosci 2023; 14: 2476-2486.
[24] Conti G, Ranieri VM, Costa R, Garratt C, Wighton A, Spinazzola G, Urbino R, Mascia L, Ferrone G, Pohjanjousi P, Ferreyra G and Antonelli M. Effects of dexmedetomidine and propofol on patient-ventilator interaction in difficult-to-wean, mechanically ventilated patients: a prospective, open-label, randomised, multicentre study. Crit Care 2016; 20: 206
[25] Liu SY, Kelly-Hedrick M, Komisarow J, Hatfield J, Ohnuma T, Treggiari MM, Colton K, Arulraja E, Vavilala MS, Laskowitz DT, Mathew JP, Hernandez A, James ML, Raghunathan K and Krishnamoorthy V. Association of early dexmedetomidine utilization with clinical outcomes after moderate-severe traumatic brain injury: a retrospective cohort study. Anesth Analg 2024; 139: 366-374.
[26] Lu S, Song H, Lin Y, Song B and Lin S. A randomized controlled trial investigating the impact of early goal-directed sedation dominated by dexmedetomidine on cerebral oxygen metabolism and inflammatory mediators in patients with severe brain injury. Neurol Sci 2025; 46: 1741-1750.
[27] Godeiro Coelho LM, Teixeira FJP, Koru-Sengul T, Manolovitz B, Taylor RR, Massad N, Kottapally M, Merenda A, Munoz Pareja JC, de Rivero Vaccari JP, Keane RW, Dietrich WD, O'Phelan KH and Alkhachroum A. Predictive value of nervous cell injury biomarkers in moderate-to-severe traumatic brain injury: a network meta-analysis. Neurology 2025; 105: e213997.
[28] Zekry R, Werida RH, Hegazy ES and Mostafa TM. Role of dexmedetomidine in brain injury: a systematic review. Inflammopharmacology 2025; 33: 5745-5756.
[29] Mavroudis I, Ciobica A, Balmus IM, Burlui V, Romila L and Iordache A. A systematic review and meta-analysis of the inflammatory biomarkers in mild traumatic brain injury. Biomedicines 2024; 12: 293.
[30] Piancone F, La Rosa F, Hernis A, Marventano I, Arcuri P, Rabuffetti M, Navarro J, Saresella M, Clerici M and Comanducci A. Neuroinflammatory signature of post-traumatic confusional state: the role of cytokines in moderate-to-severe traumatic brain injury. Int J Mol Sci 2025; 26: 8593.
[31] Treble-Barna A, Petersen BA, Stec Z, Conley YP, Fink EL and Kochanek PM. Brain-derived neurotrophic factor in pediatric acquired brain injury and recovery. Biomolecules 2024; 14: 191.