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Value of narcotrend anesthesia depth monitoring in predicting POCD in gastrointestinal tumor anesthesia block patients

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Abstract

Background The purpose of this research was to evaluate the efficacy of Narcotrend (NT) monitoring on cognitive dysfunction in patients undergoing anesthesia blockade for gastrointestinal tumors and its effect on cerebral oxygen metabolism and inflammatory response.

Methods Patients preparing to undergo resection of gastrointestinal tumor resection were included and randomly divided into a control group (depth of anesthesia assessed by physician experience) and a research group (depth of anesthesia monitored by NT). HR and MAP were monitored at the preoperatively (T_0), 12 h postoperative (T_1), 24 h postoperative (T_2), and 48 h postoperative (T_3) stages. MMSE score was recorded to assess changes in cognitive function. Intracerebral oxygenation indicators ($CjvO_2$, $CERO_2$, and rSO_2) were assessed by a blood gas analyzer. ELISA assay was conducted to explore the serum inflammatory indexes (CRP, IL-1β, and TNF-α) and neurological function indicators (NSE and MBP).

Results MAP was higher in the research group than in the control group at T_1 and T_2 ($P<0.05$). MMSE scores at T1, T2, and T3 stages were higher in the research group than in the control ($P<0.05$). The incidence of POCD was also lower in the research group compared with the control ($P<0.05$). $CjvO_2$, $CERO_2$, and rSO_2 were significantly higher ($P<0.05$) and were positively correlated with the MMSE scores. Postoperative serum inflammatory indexes were significantly elevated in both groups, but more significantly in the control group ($P<0.05$). Both neurological function indicators were usually reduced after surgery, but the reduction was more significant in the research group ($P<0.05$).

Conclusion NT monitoring of anesthetic depth has a less physical impact on patients with gastrointestinal tumor anesthetic block, reduces the degree of postoperative POCD, and has significant clinical value.

Keywords NT, POCD, Anesthesia, Cognitive dysfunction, Intracerebral oxygenation, Inflammation, Narco trend

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Background

Postoperative cognitive dysfunction (POCD) is a phenomenon in which patients experience memory loss and slow cognitive recovery after surgery [1]. The incidence of POCD is 41–75% at 7 days postoperatively and up to 18–45% at three months [2], mostly in elderly postoperative patients. Untreated POCD will lead to the development of Alzheimer's disease and Parkinson's disease [3]. Therefore, the prevention of POCD has become a research hotspot [4]. Established findings indicate that depth of anesthesia is a potential hazard factor for the increasing incidence of postoperative POCD [5] and that lower depths of anesthesia (DOA) are more favorable for recovery from postoperative POCD [6].

General anesthesia (GA) is currently the most commonly used form of anesthesia for clinical surgical treatment with the best results, especially for oncology patients. However, patients are prone to symptoms such as dizziness, transient memory loss, and vomiting, and even adverse complications such as deep vein thrombosis and neurological dysfunction, with POCD being the most common [7]. Previously, anesthesiologists determined the anesthetic dose and depth of anesthesia by clinical signs, which is highly objective and less accurate, and had a greater risk of adverse postoperative prognosis [7]. Several studies have reported the feasibility and accuracy of NT in monitoring the depth of anesthesia, and it is gradually becoming more widely used in clinical applications [8]. NT monitoring based on electroencephalogram (EEG) signal analysis is a new anesthesia monitoring device to assess the depth of anesthesia or consciousness of patients and to guide the rational use of anesthetic drugs [7]. However, its predictive value for postoperative POCD damage was concluded to be inconsistent.

In this study, we hypothesized that NT monitoring of anesthesia depth has some clinical value for anesthesia blockade of gastrointestinal tumors. To confirm this hypothesis, the current research investigated the predictive value of NT anesthesia depth monitoring for POCD in patients undergoing anesthesia block for gastrointestinal tumors, and further analyzed the effects of NT anesthesia on patients' cerebral oxygen metabolism and inflammatory response, in an attempt to propose a novel approach for the prevention of POCD in patients with gastrointestinal tumors patients in the further.

Methods

Participants in this research

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Research Ethics Committee of The First Hospital of Xingtai. Furthermore, the study was successfully registered at the Chinese Clinicial Trial Center (clinical trial number: ChiCTR2400087688, date of the registration: 2024-08-05).

The study sample size was calculated using the sample size formula of Schoenfeld for randomized clinical trials [9]. A parallel experiment design was used and continuous dependent variables, setting the one-tailed significance level at 5% and the testing power at 80%. The estimated sample size was 96. In total, 108 participants were included, exceeding the threshold.

108 patients who underwent laparoscopic gastrointestinal tumor resection between January 2020 and January 2022 in the First Hospital of Xingtai were accepted for the present investigation. To explore the effect of different anesthetic monitoring modalities on a patient's postoperative period, two days before surgery, patients were equally allocated to the control group ($n=54$) and research group ($n=54$) using random numbers generated by SPSS (supplementary material). The inclusion criteria were (a) selection of laparoscopic gastrointestinal tumor resection; (b) Age 18–70 years; (c) American Society of Anesthesiologists class I-III; (d) patients cooperating in completing the mini-mental state examination (MMSE) scale assessment. Exclusion criteria: (a) Intolerance to GA or allergy to anesthetic drugs; (b) Presence of preoperative disorders of consciousness or mental illness; (c) Presence of ulcers and wounds on the head and face that prevent proper placement of equipment such as monitoring electrode pads; (d) Patients with severe liver and kidney insufficiency or serious diseases of a vital organ such as heart and lungs; (e) patients transferred to the ICU postoperatively.

Anesthesia and monitoring

The control group underwent conventional anesthesia, while the research group underwent anesthesia under NT monitoring. After admission to the operating room, routine oxygenation, establishment of peripheral intravenous fluid access, ECG, and noninvasive blood pressure were given. For patients in the research group, after cleaning the forehead skin, Narcotrend (Chindex Medical Limited, China) electrodes with 3 anesthesia Narcotrend indices (NTI) with a spacing greater than 8 cm and a resistance less than 6 $K\Omega$.

Patients were intubated with general anesthesia, and midazolam (0.05–0.1 mg/kg), sufentanil (0.3–0.4 μg/kg), and directed infusion of isoproterenol (2.0 μg/ml) were selected sequentially. Subsequently, the anesthesia was adjusted depending on the patient's condition, and rocuronium bromide 0.6–0.8 mg/kg was injected after the coma. Breathing is controlled with an anesthesia machine while the patient's muscles are relaxed. After successful general anesthesia, the control group determined the depth of anesthesia based on the clinical

experience of the anesthesiologist, while the research group assessed the depth of anesthesia concerning NT monitoring data (the duration of NTI < 35 was considered deep anesthesia), and adjusted the anesthetic dose based on this basis and controlled within the range of D2-E1. Intraoperatively, depending on the patient's status, intermittent infusion of sufentanil and cisatracurium, reasonable control of isoproterenol concentration, to ensure the depth of anesthesia and avoid over-anesthesia. Isoproterenol infusion was stopped at the time of skin suturing. Postoperative intravenous analgesia was administered using a patient-controlled analgesia device with 100 μg sufentanil and 4 mg bupropion at a total dose of 150 ml.

Basic clinical information

Basic clinical information including age, sex, BMI, and duration of operation was collected from patients and recorded in Table 1. The mean arterial pressure (MAP) and heart rate (HR) were recorded preoperatively (T_0), 12 h postoperatively (T_1), 24 h postoperatively (T_2), and 48 h postoperatively (T_3), respectively.

MMSE scores were assessed

MMSE scores in both groups were analyzed to assess patients' postoperative cognitive impairment. Patients were assessed by the MMSE rating scale in the above 4 stages including orientation, attention, computational ability to ask time and place, immediate recall ability, and graphic reproduction ability. The scale was coded in the range of 0–30, with 27–30 being normal cognitive function and scores less than 27 being cognitive impairment.

Cerebral oxygen metabolism indexes

Cerebral oxygen metabolism indexes were examined. When the intraoperative anesthesia depth was appropriate, 5 ml blood was collected from the radial artery and internal jugular vein of the patient. The GEM3000 blood gas analysis pair was used for blood oxygen index analysis, followed by calculation to assess and measure the internal jugular venous bulb oxygen content ($CjvO_2$) and cerebral oxygen uptake rate ($CERO_2$). The patient's venous cerebral oxygen saturation (rSO_2) level was also monitored using a non-destructive near-infrared tissue oxygen monitor the TSAH-100.

Table 1 Basic clinical information statistics of subjects ($\bar{x} \pm s$)

Indicators	Control group ($n=54$)	Research group($n=54$)	t/χ2	*P*
Age	69.22 ± 4.85	68.83 ± 4.27	0.44	0.66
Sex (male/female)	34/20	26/28	2.40	0.12
BMI (kg/m^2)	23.92 ± 2.84	23.76 ± 3.03	0.29	0.77
duration of operation (h)	3.05 ± 0.46	3.10 ± 0.41	-0.66	0.51
Extubation time (h)	23.91 ± 2.02	9.99 ± 1.03	-45.28	< 0.01
Awake time (h)	21.40 ± 2.06	13.19 ± 1.05	-26.05	< 0.01

Acronyms: BMI, Body Mass Index

Serum inflammatory and neurological markers

Serum inflammatory and neurological markers of the T_0 and T_1 stages were also assessed. Commercially available ELISA kits detect serum levels of inflammatory factors IL-1β and TNF-α as well as neurological markers myelin basic protein (MBP) and neuron-specific enolase (NSE). Briefly, the upper serum was collected from the blood. Subsequently, after diluting the sample and standard reaction, the reaction was carried out after adding the enzyme standard reagent. The color development solution was added, and the OD value was read after adding the termination solution for calculation.

Statistical analysis

SPSS 23.0 and GraphPad Prism 9.0 were performed for database analysis. Count data were reported as percentages and analyzed by chi-square test, and measurement data were compared within groups by paired T-test and between groups by independent sample T-test and expressed as mean ± SD. Correlation tests were performed using Pearson's test. $P<0.05$ in the two-sided indicates a statistical difference.

Results

Clinicopathological data of the subjects

As illustrated in Table 1, the research group had 26 males and 28 females with a mean age of 68.83 ± 4.27 years and a BMI was 23.76 ± 3.03 kg/m^2, while the control group had 34 males and 20 females with a mean age of 69.22 ± 4.85 years and BMI was 23.92 ± 2.84 kg/m^2. There were no statistical differences between the two groups in terms of general information ($P>0.05$). Additionally, their duration of operation was no-statistically significant ($P>0.05$). They suggest that the intraoperative and postoperative indices are comparable between them. Furthermore, the time to extubate and the time to wakefulness in the research group were usually less than those in the control group ($P<0.05$, Table 1).

MAP and HR fluctuations in different periods

As indicated in Table 2, there was no statistically significant difference in HR between the two groups at stages T_0, T_2, and T_3 ($P>0.05$). HR was significantly lower in the control group (79.59 ± 9.03 times/min) compared to the research group (82.89 ± 7.62 times/min) at stage T_1. Additionally, there was no statistically significant difference in MAP between the two groups at T0 and T3 stages ($P>0.05$). Similarly, MAP decreased significantly in the control group at T_1 and T_2 stages compared to the research group ($P<0.05$). The results suggest that NT monitoring of deep anesthesia has no significant

Table 2 Comparison of MAP and HR levels between the two groups in different time periods ($\bar{x} \pm s$)

Indicators	Control group($n=54$)	Research group($n=54$)	t	*P*
HR (times/min)				
T_0	80.78±8.18	83.13±7.15	-1.59	0.11
T_1	79.59±9.03	82.89±7.62	-2.05	0.04
T_2	80.70±6.26	79.65±7.43	0.10	0.43
T_3	80.31±8.45	80.89±7.75	0.28	0.71
MAP (mmHg)				
T_0	94.26±9.61	93.06±10.34	0.63	0.53
T_1	77.31±7.78	82.54±8.86	-3.26	<0.01
T_2	77.67±9.18	82.85±8.32	-3.08	<0.01
T_3	90.96±6.72	91.80±7.43	0.46	0.54

Note: T_0, preoperatively; T_1, 12 h postoperatively; T_2, 24 h postoperatively; T_3, 48 h postoperatively

Table 3 Comparison of MMSE score and POCD between the two groups (n/%,$\bar{x} \pm s$)

Indicators	Control group($n=54$)	Research group($n=54$)	t/χ2	*P*
MMSE (score)				
T_0	28.30±2.20	27.80±1.92	1.26	0.21
T_1	21.19±1.88	24.31±2.03	-8.31	<0.01
T_2	23.61±3.64	25.74±1.89	-3.82	<0.01
T_3	26.07±2.95	27.19±1.03	-2.62	0.01
Incidence of POCD(n/%)	9 (16.67)	2 (3.70)	4.96	0.026

Note: T_0, preoperatively; T_1, 12 h postoperatively; T_2, 24 h postoperatively; T_3, 48 h postoperatively

fluctuation in the MAP and HR of patients compared to the control group.

Effect of NT monitoring of anesthesia depth on patients' cognitive function

Preoperatively, the MMSE score of the research group was 27.80±1.92, which was not statistically different from the control group's 28.30±2.20 ($P>0.05$, Table 3). At stage T_1, the MMSE score of the research group was 24.31±2.03, while that of the control group was 21.19±1.88, and the MMSE score of the control group decreased more significantly than that of the research group ($P<0.05$). Then, the same results were observed in the T_2 stages. Although there was a partial improvement in the MMSE score of both groups at stage T_3, the improvement was more significant in the research group than in the control group ($P<0.05$). What's more, the incidence of POCD in the research group (3.70%) was significantly lower than that in the control group (16.67%, $P<0.05$).

Comparison of intraoperative cerebral oxygen metabolism indexes

The intraoperative cerebral oxygen metabolism indexes were subsequently analyzed in both groups. As shown in Table 4, the rSO_2 of the research group was 76.37±3.37%, while that of the control group was 66.74±2.80%, which was significantly lower than that of the research group ($P<0.05$). Moreover, the same results were observed in $CERO_2$ and $CjvO_2$, whose levels were significantly higher in the research group than in the control group ($P<0.05$). Additionally, MMSE scores at postoperative 12 h were positively correlated with rSO_2 ($r=0.646$), $CERO_2$ ($r=0.600$), and $CJVO_2$ ($r=0.624$, $P<0.05$, Table 5).

Table 4 Comparison of cerebral oxygen metabolism indexes between the two groups during operation ($\bar{x} \pm s$)

Indicators	Control group ($n=54$)	Research group ($n=54$)	χ2	*P*
rSO_2 (%)	66.74±2.80	76.37±3.37	-16.14	<0.01
$CERO_2$ (%)	32.56±3.77	40.83±3.40	-11.08	<0.01
$CjvO_2$ (ml/l)	90.91±3.77	97.22±3.60	-8.90	<0.01

Table 5 Correlation between each index and MMSE

Indicators	MMSE score (Pearson)	*P*-value
rSO_2 (%)	0.646	<0.001
$CERO_2$ (%)	0.600	<0.001
$CjvO_2$ (ml/l)	0.624	<0.001

Comparison of serum neurological function and serum inflammatory factors

As presented in Fig. 1A, the preoperative inflammatory indicators CRP, IL-1β and TNF-α levels were not statistically different between the two groups of patients ($P>0.05$). Compared with the preoperative period, CRP, IL-1β, and TNF-α were significantly higher in the research groups and control groups at 12 h postoperatively ($P<0.05$, Table 6). What's more, the elevated levels of CRP, IL-1β, and TNF-α were more significant in the control group than in the research group at 12 h postoperatively ($P<0.05$, Fig. 1B).

Finally, there was no statistical difference in the preoperative MBP and NSE levels between the two groups ($P>0.05$, Fig. 1C). Compared with the preoperative period, the postoperative MBP and NSE levels were significantly lower in both groups ($P<0.05$, Table 6), but to a greater extent in the research groups than in the control group ($P<0.05$, Fig. 1D).

Discussion

With the increasing trend of an aging society, the number of elderly patients undergoing various types of general anesthesia procedures has increased significantly [10]. Due to the decrease in various physiological reserve capacities of the elderly, it is difficult for anesthesiologists to control the dosage of various anesthetics during general anesthesia surgery, which eventually leads to the occurrence of surgical treatment risks and postoperative

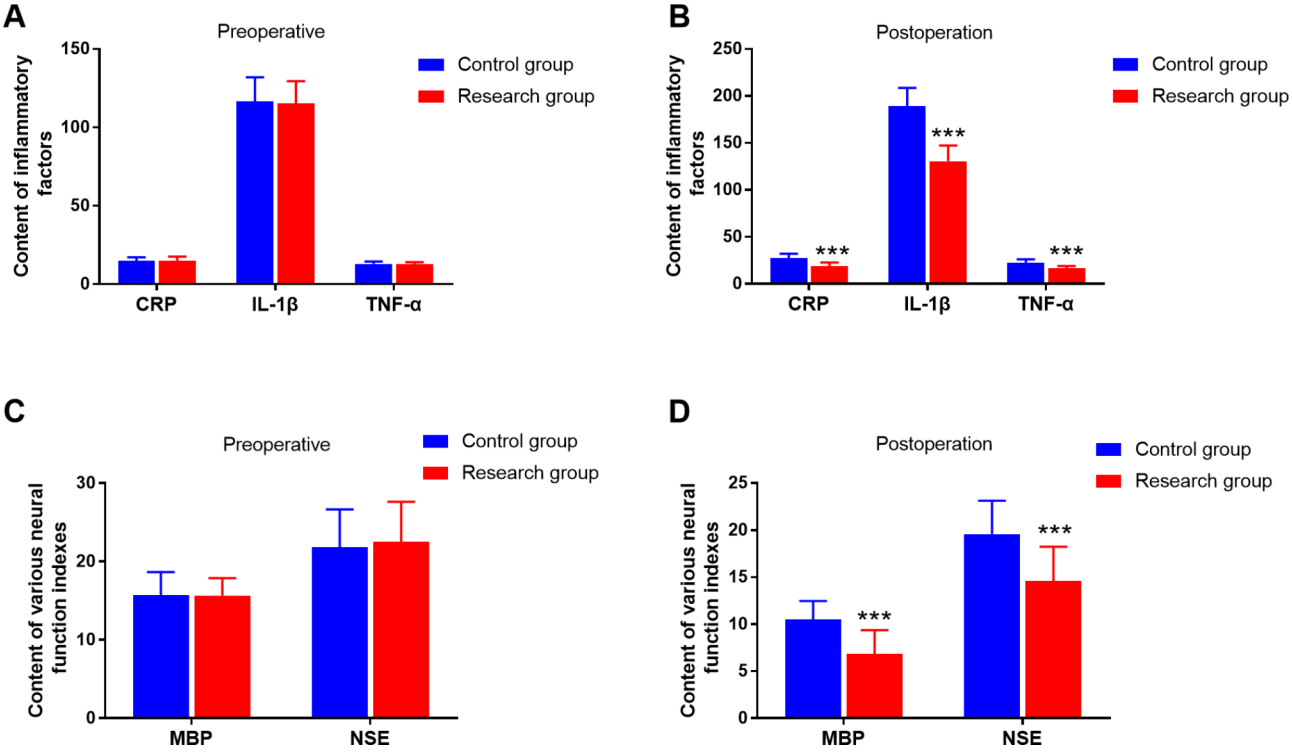

Fig. 1 Comparison of preoperative and postoperative serum inflammatory indexes and neurological function index levels. Analysis of CRP, IL-1β, and TNF-α levels in two groups of patients in preoperative (**A**) and postoperative (**B**). Analysis of MBP and NSE levels in two groups of patients in preoperative (**C**) and postoperative (**D**). *** $P < 0.001$, compared with the Control group

Table 6 Comparison of the levels of inflammatory cytokines between the two groups ($\bar{x} \pm s$)

Indicators	Control group ($n=54$)		t	*P*	Research group ($n=54$)		t	*P*
	Preoperative	Post operation 12 h			Preoperative	Post operation 12 h		
CRP (mg/ml)	14.80 ± 2.33	27.11 ± 4.81	-17.36	< 0.01	14.91 ± 2.71	18.94 ± 3.56	-6.29	< 0.01
IL-1β (ng/ml)	116.63 ± 15.33	188.89 ± 19.65	-22.98	< 0.01	115.17 ± 14.22	130.50 ± 16.61	-5.14	< 0.01
TNF-α (ng/ml)	12.98 ± 1.50	22.44 ± 3.80	-16.84	< 0.01	12.83 ± 1.19	16.48 ± 2.31	-10.55	< 0.01
MBP (μg/ml)	15.69 ± 2.98	10.48 ± 1.98	10.73	< 0.01	15.65 ± 2.23	6.87 ± 2.49	17.81	< 0.01
NSE (ng/ml)	21.80 ± 4.86	19.59 ± 3.55	2.67	< 0.01	22.52 ± 5.12	14.57 ± 3.66	9.80	< 0.01

complications [11]. POCD, as a common complication after anesthesia surgery, is a higher risk in elderly patients, directly affecting the surgical outcome and even presenting a life-threatening condition [12, 13]. The depth of anesthesia may reflect the state of cerebral perfusion, and the depth of anesthesia may result in inadequate cerebral perfusion and thus affect the metabolism and function of nerve cells [14]. Targeted reduction of depth of anesthesia in geriatric surgery can effectively prevent or manage the occurrence of POCD in patients [15]. Currently, the patient's depth of anesthesia is assessed by HR, blood pressure, and personal experience [16]; however, each patient's psychological state and physical function vary greatly, so it is necessary to choose a more accurate way to monitor the patient's depth of anesthesia.

Various anesthesia depth monitors have been developed, and they are monitored by detecting the Bispectral index (BIS) [17], EEG entropy index, NTI, and auditory evoked potential index, respectively. Although BIS is most widely used, it cannot monitor postoperative blood flow changes and accurately predict the time to recovery of consciousness in patients after surgery. In elderly patients who underwent coronary artery bypass grafting, there was no significant change in cognitive function at 6 weeks with and without BIS monitoring [18]. NT is an automatic EEG recording system, by monitors the patient's raw EEG and automatically converts it to visual indicators, its indicator NTI is comparable to BIS in monitoring the depth of anesthesia and assessing sedation [19]. NT also has the point of real-time, fast response, and strong anti-interference ability. Elderly patients undergoing gastrointestinal surgery were selected for this study, and the inclusion and exclusion criteria were strictly enforced for comparability of the patient's general data. The MMSE is one of the most widely used scales for

assessing cognitive function [20]. In the present research, there was no significant difference in the MMSE scores between the two groups, confirming that the cognitive function of the two groups was comparable. Further analysis also revealed that only two patients with NT monitoring of deep anesthesia developed POCD, compared with nine in the control group. The finding suggests that NT monitoring of deep anesthesia may be effective in reducing the occurrence of POCD.

To analyze the underlying mechanisms of the two different anesthetic depth monitoring modalities, we first analyzed the cerebral oxygen metabolism index $CjvO_2$, rSO_2, and $CERO_2$, which are considered to be important factors in causing POCD [21]. As one of the indicators of brain metabolism, rSO_2 is a good indicator of the local blood flow status and the balance of oxygen supply and demand in brain tissue, and its low level can indicate an imbalance of brain perfusion/oxygen supply and oxygen consumption in patients. Previous studies have confirmed that rSO_2 monitoring may influence the development of POCD and is an independent risk factor for the development of POCD in patients [22]. Its reduction was significantly associated with a decrease in POCD after abdominal and cardiac surgery under general anesthesia [23]. Intraoperative monitoring of rSO_2 downregulation predicts POCD and can be used as a routine monitoring program for elderly surgical patients [24]. In this study, $CjvO_2$, rSO_2, and $CERO_2$ levels were found to be significantly higher in the study group than in the control group and showed a significant positive correlation with MMSE scores. The findings suggest that Intraoperative NT monitoring of patients can regulate metabolic levels promptly and reduce the impact on cognitive function in the postoperative period.

Inflammation plays a key function in the pathophysiology of POCD and cognitive deficits. Previous studies have reported activation of the immune system through general anesthesia and surgical stress [7] and trigger infiltration of immune cells such as macrophages and neutrophils by disrupting the integrity of the CNS blood-brain barrier, and resulting inflammation can lead to POCD episodes in postoperative anesthesia [25]. At the same time, general anesthesia and surgical stress also stimulate the peripheral immune system to release inflammatory factors such as TNF-α, leading to POCD [26]. In our study, we found no significant difference in the inflammatory indicators CRP, IL-1β, and TNF-α between the two groups of patients before surgery. However, they were all significantly elevated postoperatively, which is consistent with the reported results. More importantly, they were more significantly elevated in the control group than in the NT depth monitoring patients, suggesting that POCD was more likely to occur in the control group.

Serum brain-specific biomarkers help to predict the prognosis of various brain injects, such as NSE from neurons, and MBP from axons help to find its detection and quantify the severity of brain injury, and response to therapeutic interventions [27]. MBP is a highly sensitive indicator of damage to the central nervous system. It is released when the CNS is damaged, and elevated MBP levels in the blood can significantly reflect the extent of POCD in patients [28]. NSE is an enzyme involved in glycolysis secreted by neurons and neuroendocrine cells, and when neurons are damaged, NSE is rapidly released outside the cells and enters the blood circulation system [29]. Therefore, elevated serum NSE concentrations imply neuronal damage and correlate with the development of POCD [30]. In this study, it was found that MBP, as well as NSE, were significantly lower in both groups compared to preoperative, but the reduction was more significant in the NT monitoring group. The results suggest that intraoperative NT monitoring of anesthesia depth in patients helps to reduce brain damage, improve the repair of neuronal cells, and reduce the likelihood of POCD.

Conclusions

In conclusion, the data from this study suggest that intraoperative NT depth of anesthesia monitoring significantly reduces the occurrence of POCD in patients and may be related to its timely regulation of patients' cerebral oxygen metabolism levels and reduction of patients' immune inflammatory response and brain injury.

Abbreviations

DOA	Depths of anesthesia
EEG	Electroencephalogram
HR	Heart rate
GA	General anesthesia
MAP	Mean arterial pressure
MMSE	Mini-mental state examination
NT	Narctreend
POCD	Postoperative cognitive dysfunction

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02762-9.

Supplementary Material 1

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Not Applicable.

Author contributions

X.Z. M and H.F. N designed the research study. X.L. Z, R.N. G and Z.X. H performed the research. X.Z. M, J.H. L and H.F. N analyzed the data. X.Z. M and H.F. N wrote the manuscript. X.Z. M and H.F. N contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Data availability
Corresponding authors may provide data and materials.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Human ethics and consent to participate
All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Research Ethics Committee of The First Hospital of Xingtai. Furthermore, the study was successfully registered at the Chinese Clinical Trial Center (clinical trial number: ChiCTR2400087688, date of the registration: 2024-08-05).

Conflict of interest
There is no conflict of interest in this study.

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