

## Original Article

# Influence of nerve block combined with general anesthesia on cognitive function and postoperative pain in patients undergoing knee joint replacement

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Received April 13, 2022; Accepted May 19, 2022; Epub June 15, 2022; Published June 30, 2022

**Abstract:** Objective: To investigate the influence of nerve block combined with general anesthesia on the cognitive function and postoperative pain of patients undergoing knee joint replacement and analyze the risk factors of postoperative cognitive dysfunction. Methods: A retrospective analysis was conducted on 104 elderly patients undergoing knee joint replacement in our hospital between January 2018 and January 2021. The control group (n=50) received laryngeal mask anesthesia, while the observation group (n=54) received ultrasound-guided nerve block combined with laryngeal mask anesthesia. The visual analogue scale (VAS) was adopted for scoring the pain intensity of both groups, and the Mini-Mental State Examination (MMSE) was used for evaluating changes in cognitive function before and after operation. The self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were adopted for scoring patients before and after operation. Additionally, the time to spontaneous breathing recovery, time to wake up, time to open eyes when ordered, and extubation time of the two groups were recorded. The changes in serum IL-6, cortisol (Cor), and IL-10 before and after operation were compared. The two groups were compared in the dosage of used analgesic drugs, the first getting out-of-bed time, treatment expense, and hospitalization time. The correlation between VAS score and IL-6, Cor and IL-10 before and after treatment was analyzed. The adverse reactions of the two groups were also compared. Logistic regression was used to analyze risk factors for cognitive dysfunction. Results: After operation, the observation group experienced shorter spontaneous breathing recovery time, time to wake up, time to open eyes when ordered, and extubation time, than the control group ( $P<0.05$ ). The observation group also consumed less sufentanil than the control group ( $P<0.05$ ). Additionally, the observation group had lower VAS and MMSE scores than the control group at 6 and 12 h after operation ( $P>0.05$ ) and lower SAS and SDS scores than the control group ( $P<0.05$ ). Moreover, at 6 h after operation, the control group showed higher levels of IL-6, Cor and IL-10 than the observation group ( $P<0.05$ ), and the control group experienced later first getting out-of-bed time and a longer hospitalization time than the observation group ( $P<0.05$ ). There was a positive correlation between VAS score and IL-6 as well as Cor before and after treatment ( $P<0.05$ ). The two groups were similar in treatment expense ( $P>0.05$ ) and the incidence of adverse reactions ( $P>0.05$ ). Age and anesthesia scheme were risk factors for postoperative cognitive dysfunction. Conclusion: Nerve block combined with general anesthesia can effectively improve the cognitive function and analgesic effect of elderly patients undergoing knee joint replacement, and accelerate recovery time, without increasing adverse reactions, and can also accelerate recovery of their cognitive function.

**Keywords:** General anesthesia, nerve block, knee replacement, elderly, postoperative cognitive function, analgesic effect

## Introduction

With the aging of the population, people over 65 years old in China have exceeded 11.9% of the total population [1]. Knee arthritis is a frequent disease of the elderly, which brings about a great impact on patients' daily life and compromises their quality of life (QoL) [2]. Knee osteoarthritis is a manifestation of degenerative change of knee joints, with primary fea-

tures of hardening of articular cartilage or hyperosteoegeny, which gives rise to narrowing of the knee joint space and is the main reason for limited activity and physical disability in the elderly [3, 4]. Therefore, the goal of knee osteoarthritis treatment includes relieving pain and improving QoL.

Total knee arthroplasty (TKA), as a crucial operation for repairing knee joint injury, has been

extensively adopted in clinical practice over the past few years. It can not only solve serious knee joint diseases, but also correct knee joint deformities triggered by various reasons and restore the function of the knee joint [5, 6]. However, patients treated with TKA will experience severe postoperative pain [7]. This will prolong the patient's hospitalization time and is also likely to give rise to postoperative infection and deep venous thrombosis of lower limbs. Additionally, persistent severe pain can also give rise to a severe stress reaction in patients, affecting their normal physiologic function by bringing about anxiety, insomnia, loss of appetite, and deterioration of early postoperative QoL, thus increasing the use of related drugs. If it is not treated in time, it will inevitably prolong postoperative hospitalization time, hinder postoperative recovery, and increase medical expense [8, 9]. Therefore, how to improve perioperative analgesia triggered by TKA is key to the postoperative rehabilitation.

Currently, the traditional clinical analgesia methods include oral drug analgesia, intravenous analgesia, epidural analgesia, and analgesia with local nerve block [10]. Different analgesic methods have advantages and disadvantages. General anesthesia is a method for knee prosthesis, but patients receiving it will suffer many complications in the anesthesia process. In addition, this method of anesthesia can greatly damage the patient's body and affect their cognitive function after surgery [11]. Postoperative cognitive dysfunction is a disorder affecting orientation, attention, perception, consciousness and judgement that occurs after surgery [12]. In clinical practice, it is mainly characterized by inattention, and reduced learning and memory. Patients with postoperative cognitive dysfunction often get a decline in social adaptation and understanding of language, loss of the ability to live alone, and impairment of logical abstract thinking and orientation, and in severe cases, mental confusion, personality changes, and anxiety. Ultrasound-guided nerve block is a new method of TKA analgesia during recent years. With the help of ultrasound imaging technology, the nerve to be blocked can be accurately located, with advantages of quick and long-term effect. Combined nerve block can reduce the consumption of anesthetic drugs, improve analgesia effect, and reduce the patient's postoperative cognitive impairment [13].

This study investigated the effect of nerve block combined with general anesthesia on analgesia effect and cognitive function in elderly patients who underwent knee arthroplasty, and, for the first time, analyzed the risk factors for cognitive dysfunction by a regression model.

### Materials and methods

#### *Clinical data*

A retrospective analysis was conducted on 104 elderly patients undergoing knee joint replacement in our hospital between January 2018 and January 2021. The control group (n=50) received laryngeal mask anesthesia, while the observation group (n=54) received ultrasound-guided nerve block combined with laryngeal mask anesthesia. This study was performed with permission from the Medical Ethics Committee of Ningbo No. 6 Hospital (2018009).

#### *Inclusion and exclusion criteria*

*Inclusion criteria:* Patients with indications for knee arthroplasty; patients who were given unilateral replacement; patients diagnosed with primary knee osteoarthritis by X-ray examination and guidelines for diagnosis and treatment of osteoarthritis (2018 version) [14]; patients whose knee osteoarthritis had reached end stage, with moderate or severe persistent pain, with failed conservative treatment; patients  $\geq 60$  years old; and patients who signed informed consent after being apprised of the study.

*Exclusion criteria:* Patients with hepatic and renal insufficiency before operation; patients who had taken anticoagulant drugs before operation and with a history of coagulation disorders; patients with a history of addiction to narcotic drugs or analgesics or drug allergy.

#### *Sources of anesthesia drugs*

Sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., State Food and Drug Administration (SFDA) approval no.: H20054172), midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., SFDA no.: H20031037), etomidate fat emulsion injection (Jiangsu Nhwa Pharmaceutical Co., Ltd., SFDA no.: H20020511), propofol (Sichuan Guorui Pharmaceutical Co., Ltd., SFDA no.: H20163045), rocuronium bromide (North China Pharmaceutical Co., Ltd., SFDA no.: H2010-

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3235), sevoflurane (Jiangsu Shengdi Pharmaceutical Co., Ltd., SFDA no.: H20050672), benzenesulfonate cisatracurium (Zhejiang Xianju Pharmaceutical Co., Ltd., SFDA no.: H2009-0202), and ropivacaine (Anhui Welman Pharmaceutical Co., Ltd., SFDA no.: H20050672).

### *Anesthesia scheme*

All patients were treated by knee arthroplasty, and it was unilateral in all cases. Specifically, all patients were fasted for 12 h and deprived from water for 6 h before operation. Venous access was established, followed by determination of hemodynamic indexes.

Patients in the control group were given combined intravenous and inhalation anesthesia with a laryngeal mask. To induce anesthesia, 0.1 mg/kg midazolam and 0.3 mg/kg etomidate fat emulsion were used. After the patient fell asleep, 0.3 µg/kg sufentanil and 0.5 mg/kg rocuronium were given to complete laryngeal mask placement. During the operation, anesthesia was maintained with 4 mg/kg propofol and 2% sevoflurane. Butorphanol (China, Jiangsu, Hengrui Pharmaceutical Co., Ltd., H20020454) were added as needed.

Patients in the observation group were treated with ultrasound-guided nerve block combined with general anesthesia. Under the guidance of portable ultrasound, the sciatic nerve was found and femoral nerve block was conducted. Each patient was placed in a supine position, with hips and lower knee both bent, and calf rotated by 45°. The probe was placed vertically away from the groin skin fold (8 cm) and moved to the posterior medial side of the lesser trochanter of femur. After obtaining a clear cross-sectional hyperechoic image of the sciatic nerve, the local skin was routinely disinfected, and a short oblique nerve block needle was used to connect the nerve stimulator. The puncture needle was used to puncture from the inside of the thigh to the outside, parallel to the probe, during which the sciatic nerve was kept in the center of the screen. Under the guidance of ultrasound images, the injection needle was slowly pushed in until it reached the sciatic nerve. The parameters of neurostimulator were adjusted to as follows: stimulation frequency: 2 Hz; pulse width: 0.1 ms, and current: 0.5-0.2 mA. During inducing dorsiflexion or toe flexion, 15 mL ropivacaine (0.5%) was injected step by

step, and the puncture needle was adjusted to make the drug spread around the nerve. The probe was replaced with a high-frequency ultrasound probe, and the femoral artery fluctuation point was found and marked, followed by routine disinfection. The short axis segment of femoral nerve at the marked point was scanned to find the femoral nerve. The probe was moved to the echo image of femoral nerve, causing it to be located in the center of the screen, and the middle of the probe was selected as the entry point. The needle was used to slowly enter and reach the femoral nerve under the guidance of the ultrasound image, followed by injection of 15 mL ropivacaine (0.5%). The needle was adjusted to make the drug spread around the femoral nerve. After nerve block for 15 min, laryngeal mask airway was placed under intravenous inhalation combined with general anesthesia by the same method as the control group.

### *Serum detection*

Serum interleukin-6 (IL-6, ml058097), interleukin-10 (IL-10, ml064299) and plasma cortisol (Cor, ml711149) levels were detected by ELISA with kits, all from Shanghai Milbio.

### *Outcome measures*

Primary outcome measures: The visual analogue scale (VAS) was adopted for scoring the analgesic effect of patients before and after operation [15]. The scale ranges from 0-10 points, with a higher score indicating more severe pain. The Mini-Mental State Examination (MMSE) was adopted for evaluating the changes of cognitive function of patients before and after operation, which covers orientation, memory and language ability, with a total score of 30 points [16]. A higher score indicates better cognitive function. The cognitive dysfunction of patients at 12 h after operation was evaluated, and patients with a MMSE score below 27 at 12 h after operation were deemed to be with cognitive dysfunction. The self-rating anxiety scale (SAS) and self-rating depression scale (SDS) with a total score for each of 100 points were adopted for scoring the anxiety and depression of patients before and after operation [17, 18], and a higher score indicated more severe anxiety and depression. The dosages of consumed analgesic drugs in the two groups were compared.

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**Table 1.** Baseline data

Item	Observation group (n=54)	Control group (n=50)	t/ $\chi^2$ value	P value
Gender			0.899	0.343
Male	22	25		
Female	32	25		
Average age (years)	70.2±5.35	69.4±5.73	0.712	0.478
BMI (kg/m <sup>2</sup> )	22.53±2.35	23.03±1.51	1.328	0.187
ASA classification			0.210	0.647
Class I	24	20		
Class II	30	30		
Smoking history			1.353	0.245
Yes	23	27		
No	31	23		
Drinking history			0.115	0.734
Yes	10	8		
No	44	42		
Surgical side			2.517	0.113
The left side	24	30		
The right side	30	20		

Secondary outcome measures: The differences in clinical data between the two groups were compared. Additionally, the spontaneous breathing recovery time, time to wake up, time to open eyes when ordered, and extubation time of the two groups were recorded. The changes in serum IL-6, cortisol (Cor), as well as IL-10 before and after operation were compared. The time to first out-of-bed activity, treatment expense, and hospitalization time were recorded. Logistic regression was conducted for analyzing the risk factors for postoperative cognitive dysfunction. The correlation between VAS score and IL-6, Cor. and IL-10 before and after treatment was analyzed.

### Statistical analyses

GraphPad 8 software package was adopted for data analysis and figure rendering. The measured data (Mean  $\pm$  SD) were compared using the independent-samples T test between groups, and the one-way ANOVA followed with post-hoc LSD-t test among groups. The comparison of data at different temporal points was conducted using the repeated measures analysis of variance with post-hoc Bonferroni test. Counted data (%) were analyzed using the chi-square test. Pearson test was used to analyze the correlation between VAS score and IL-6, Cor, and IL-10. Logistic regression was conducted to analyze the risk factors for post-

operative cognitive dysfunction.  $P < 0.05$  indicated a significant difference.

## Results

### Comparison of clinical data

According to comparison of clinical data between groups, the two groups were similar in age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, smoking history, and alcoholism history ( $P > 0.05$ , **Table 1**).

### Comparison of postoperative recovery

According to comparison of postoperative recovery between the two groups, after operation, the observation group experienced shorter time to spontaneous breathing re-

covery, time to wake up, time to open eyes when ordered, and extubation time than the control group ( $P < 0.05$ , **Figure 1**).

### Comparison of the dosage of used analgesic drug

According to comparison of consumed sufentanil dosage after operation between the two groups, the control group consumed a larger dosage of sufentanil than the observation group ( $P < 0.05$ , **Figure 2**).

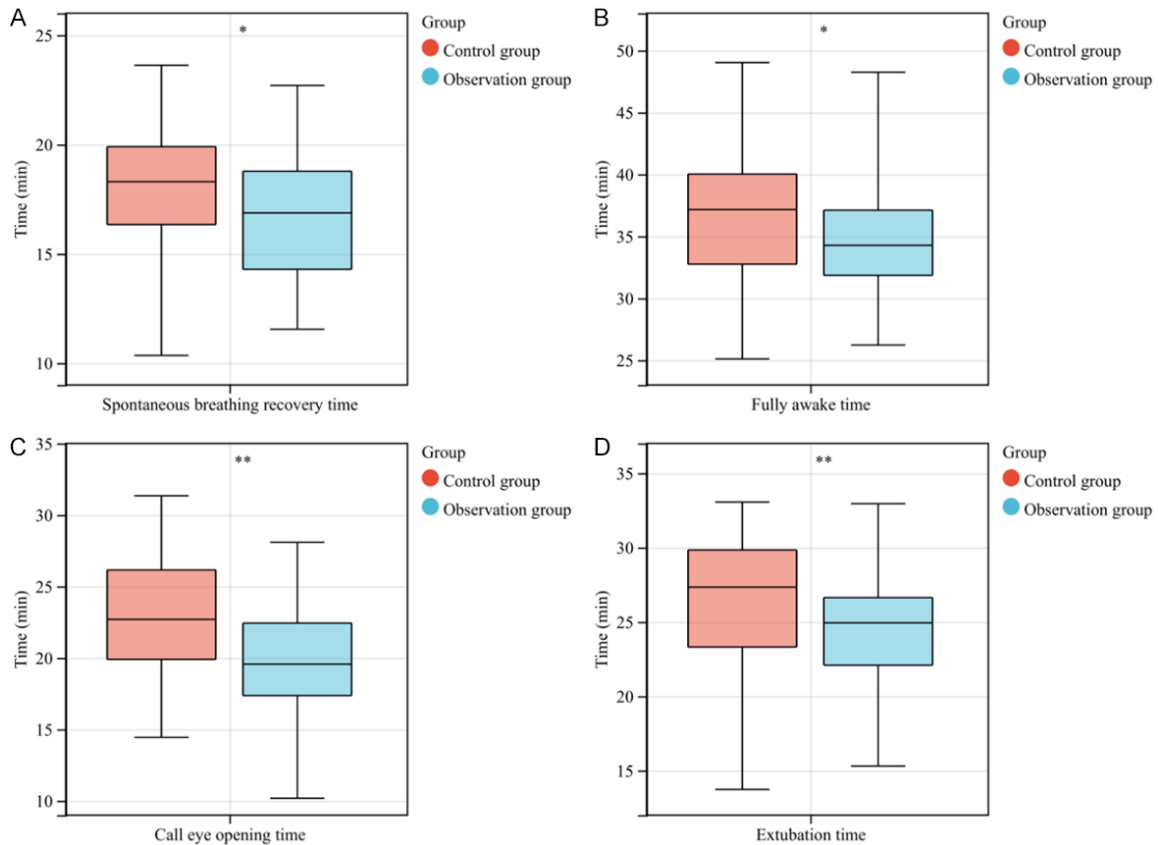
### Comparison of pain before and after operation

The VAS scores of the two groups before operation and at 6 and 12 h after operation were compared, and the results showed that VAS scores of the two groups decreased at 6 and 12 h after operation in contrast to those before operation, with lower VAS scores at 12 h after operation than at 6 h after operation ( $P < 0.05$ ). Additionally, before operation, the VAS scores of the two groups were similar ( $P > 0.05$ ), but at 6 and 12 h after operation, the observation group got lower VAS scores than the control group ( $P > 0.05$ , **Table 2**).

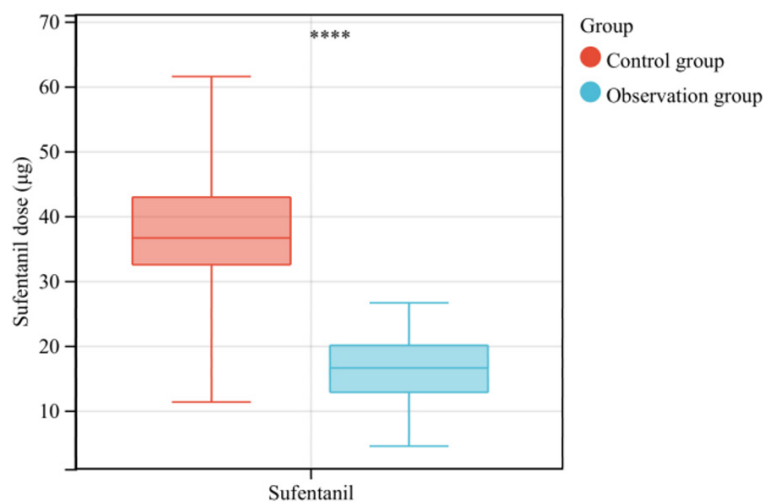
### Changes of cognitive function of patients before and after operation

The MMSE scores of the two groups before operation and at 6 and 12 h after operation

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**Figure 1.** Comparison of postoperative recovery between groups. A. Comparison of spontaneous breathing recovery time (min) between groups. B. Comparison of the time to get full waking (min) between groups. C. Comparison of the time to open eyes when ordered (min) between groups. D. Comparison of extubation time (min) between groups. \* $P < 0.05$ , \*\* $P < 0.01$ .



**Figure 2.** Comparison of sufentanil dosage between the two groups. \*\*\*\* $P < 0.0001$ .

were compared, and the results showed that MMSE scores of the two groups decreased at 6 and 12 h after operation in contrast to tho-

se before operation ( $P < 0.05$ ). Additionally, before operation, the MMSE scores of the two groups were similar ( $P > 0.05$ ), but at 6 and 12 h after operation, the observation group got higher MMSE scores than the control group ( $P > 0.05$ , **Table 3**).

### *Changes in patients' negative emotions before and after operation*

The SAS and SDS scores of the two groups before operation and after 72 hours of treatment were also compared, and the results revealed that no difference was observed between the two groups in SAS and SDS scores before therapy, ( $P > 0.05$ ), but SAS and SDS scores of the two groups decreased after

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**Table 2.** Comparison of VAS scores

Group	Before operation	At 6 h after operation	At 12 h after operation	F value	P value
Control group	4.28±1.08	3.42±1.10 <sup>a</sup>	2.46±0.78 <sup>a,b</sup>	40.978	<0.001
Observation group	4.03±0.97	2.70±0.66 <sup>a</sup>	2.03±0.77 <sup>a,b</sup>	84.710	<0.001
T value	1.203	4.035	2.757		
P value	0.232	0.001	0.007		

Notes: a, indicates P<0.05 vs. Before operation; b, indicates P<0.05 vs. at 6 h after operation.

**Table 3.** Comparison of MMSE scores

Group	Before operation	At 6 h after operation	At 12 h after operation	F value	P value
Control group	27.42±1.35	22.74±1.95 <sup>a</sup>	26.42±1.12 <sup>a,b</sup>	131.316	<0.001
Observation group	27.24±1.81	24.81±1.95 <sup>a</sup>	27.39±0.99 <sup>a,b</sup>	41.820	<0.001
T value	0.567	5.408	4.649		
P value	0.572	<0.001	<0.001		

Notes: a, indicates P<0.05 vs. Before operation; b, indicates P<0.05 vs. at 6 h after operation.

**Table 4.** Comparison of SAS and SDS scores

Group	SAS score		SDS score	
	Before treatment	After 72 hours of treatment	Before treatment	After 72 hours of treatment
The control group	57.94±4.62	43.74±5.05 <sup>a</sup>	55.04±4.81	42.94±4.61 <sup>a</sup>
Observation group	57.11±5.35	40.51±4.55 <sup>a</sup>	56.53±5.30	37.85±4.42 <sup>a</sup>
T value	0.841	3.416	1.504	5.697
P value	0.402	0.001	0.135	<0.001

Note: a, indicates P<0.05 vs. Before treatment.

therapy (P<0.05), with lower SAS and SDS scores in the observation group than in the control group (P<0.05, **Table 4**).

### *Changes of serum IL-6, Cor, and IL-10 before and after operation*

The changes of IL-6, cortisol (Cor), and IL-10 in the two groups before operation, and at 6 and 12 h after operation were analyzed. According to the results, the levels of IL-6, Cor, and IL-10 in the two groups increased at 6 and 12 h after operation as compared with those before operation (P<0.05), with lower levels in the two groups at 12 h after operation than at 6 h after operation (P<0.05). Additionally, before surgery, no difference was observed between the two groups both before operation and at 12 h after operation (P>0.05), but at 6 h after operation, the control group showed higher levels of IL-6, COR and IL-10 than the observation group (P<0.05, **Figure 3**).

### *Relationship between VAS score and IL-6, Cor, and IL-10*

The correlation between VAS scores and IL-6, Cor, and IL-10 was analyzed by Pearson's test,

which revealed a positive correlation between VAS score and IL-6 as well as between VAS score and Cor before and 12 hours after treatment (**Figure 4**, P<0.05), but not with IL-10 (**Figure 4**, P>0.05).

### *Comparison of the first getting out-of-bed time, treatment expense, and hospitalization time*

According to comparison of the first getting out-of-bed time, treatment expense, and hospitalization time between the two groups, the control group experienced later first getting out-of-bed time and a longer hospitalization time than the observation group (P<0.05), and the treatment expense of the two groups were similar (P>0.05, **Figure 5A, 5B**).

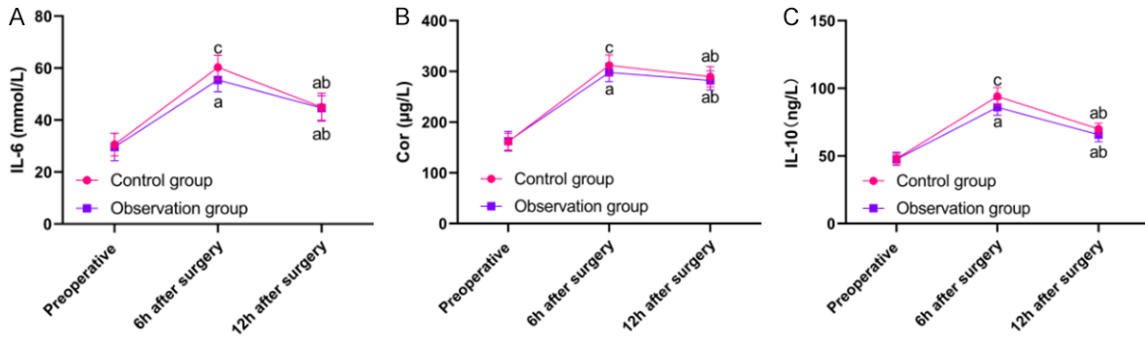
### *Comparison of adverse reactions*

According to comparison of adverse reactions in the two groups, the incidence of adverse reactions between them was not different (P>0.05, **Table 5**).

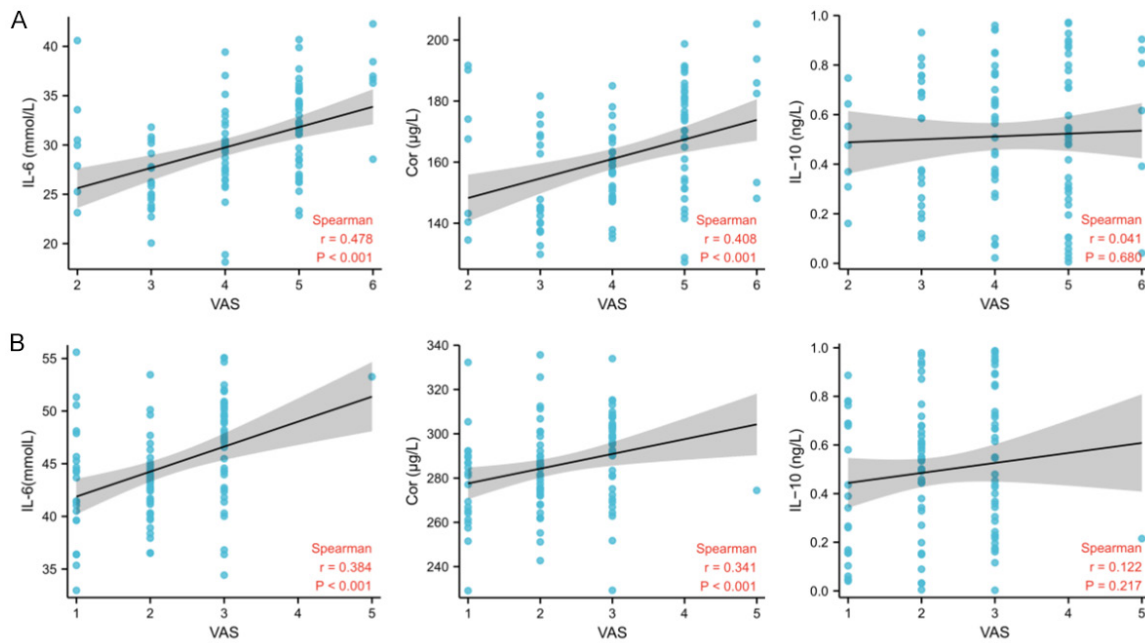
### *Risk factors of cognitive dysfunction*

We analyzed the occurrence of postoperative cognitive dysfunction in patients and found 19

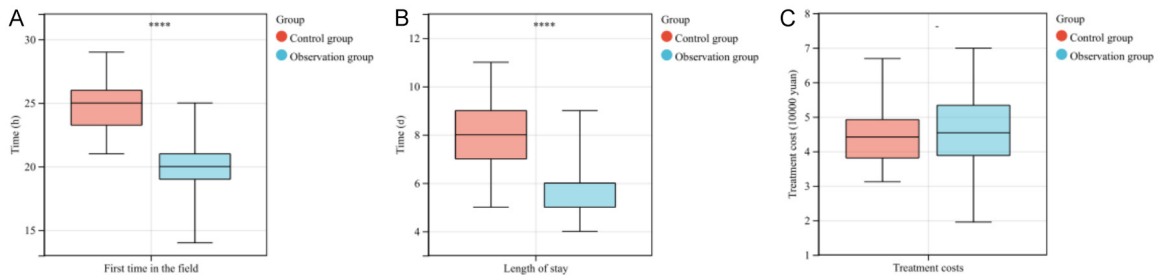
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**Figure 3.** Changes of IL-6, Cortisol (Cor), and IL-10 levels in patients before and after operation. A. Changes of IL-6 level before operation and at 6 and 12 h after operation. B. Changes of Cor level before operation and at 6 and 12 h after operation. C. Changes of IL-10 level before operation and at 6 and 12 h after operation. a, indicates  $P < 0.05$  vs. Before operation; b, indicates  $P < 0.05$  vs. at 6 h after operation; c, indicates  $P < 0.05$  vs. the observation group.



**Figure 4.** Correlation between VAS score and IL-6, cor, and IL-10 levels before and after treatment. A. Correlation between VAS score and IL-6, cor, and IL-10 levels before treatment. B. Correlation between VAS score and IL-6, cor, and IL-10 levels after treatment.



**Figure 5.** Comparison of the first getting out-of-bed time, hospitalization time and treatment expense of patients after operation. A. Comparison of the first getting out-of-bed time after operation between the two groups. B. Comparison of hospitalization time after operation between the two groups. C. Comparison of treatment expense after operation between the two groups. \*\*\*\* $P < 0.0001$ .

**Table 5.** Comparison of adverse reactions

Group	Deep venous thrombosis of lower limbs	Nausea and vomiting	Dizziness	Respiratory depression	Total adverse reaction rate
The control group	2	6	3	2	26.00%
Observation group	1	5	2	1	16.67%
$\chi^2$	0.427	0.206	0.299	0.427	1.356
<i>P</i> value	0.513	0.649	0.584	0.513	0.244

**Table 6.** Multivariate analysis

Item	Occurrence group (n=19)	No-occurrence group (n=85)	t/ $\chi^2$ value	<i>P</i> value
Age			6.801	0.009
≥70 years old (n=54)	15	39		
<70 years old (n=50)	4	46		
Gender			0.089	0.764
Male (n=47)	8	39		
Female (n=57)	11	46		
BMI (kg/m <sup>2</sup> )			0.230	0.632
≥25 (n=91)	16	75		
<25 (n=13)	3	10		
Hypertension			0.244	0.621
Yes (n=44)	9	35		
No (n=60)	10	50		
Diabetes mellitus			0.549	0.458
Existence (n=31)	7	24		
No (n=73)	12	61		
Anesthesia scheme			5.084	0.024
Combined anesthesia (n=54)	5	49		
General anesthesia (n=50)	13	37		
ASA classification			0.244	0.621
Class I (n=44)	9	35		
Grade II (n=60)	10	50		
Smoking history			0.193	0.660
Yes (n=50)	10	40		
No (n=54)	9	45		
Drinking history			0.227	0.633
Yes (n=18)	4	14		
No (n=86)	15	71		

**Discussion**

The trend of global aging is unstoppable. With the acceleration of population aging in China, the incidence of knee osteoarthritis is increasing annually, which seriously compromises the QoL of patients [19]. At the final stage of knee joint disease, knee joint replacement is often needed. Reasonable anesthesia can ensure the smooth implementation of the operation, and a good postoperative analgesic effect facilitates postoperative rehabilitation [20]. However, prior research has revealed that the slow recovery of patients with knee joint replacement after operation and unsatisfactory effect of early functional exercise are mostly related to severe pain after operation [21]. Severe postoperative pain compromises the mental and psychological health of most patients, which results in their rejection to functional

cases of cognitive dysfunction in the two groups. The patients were assigned to the occurrence group or the non-occurrence group in the light of occurrence of cognitive dysfunction. Multivariate analysis showed that age (OR: 5.542, 95% CI: 1.610-19.079) and anesthesia scheme (OR: 0.208, 95% CI: 0.065-0.667) were risk factors for postoperative cognitive dysfunction (Tables 6 and 7).

exercise and slow postoperative recovery. Additionally, it increases the incidence of pulmonary infection, pressure sore and deep vein thrombosis. Therefore, it is of crucial importance to choose appropriate analgesia methods for postoperative recovery [22].

General anesthesia is one crucial anesthesia method for knee arthroplasty, but the patients



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**Table 7.** Multivariate analysis

Factor	$\beta$	SE	Wals	P value	OR value	95% CI	
						Upper limit	Lower limit
Age	1.712	0.631	7.371	0.007	5.542	1.610	19.079
Anesthesia scheme	-1.572	0.595	6.972	0.008	0.208	0.065	0.667

will suffer many complications in the anesthesia process. In addition, this anesthesia method will greatly harm the patients' body, which will affect their nervous system, circulatory system, and respiratory system [23, 24]. At the current stage, general anesthesia alone and combined nerve block anesthesia are both suitable for total knee arthroplasty. Many scholars at home and abroad have done research on the advantages and disadvantages of anesthesia methods and the effects on postoperative analgesia and cognitive function, but the comparative reports on the effects on analgesia and cognitive function are few and not uniform. In our study, the observation group experienced shorter time to spontaneous breathing recovery, time to wake up, time to open eyes when ordered, and extubation time than the control group, and the MMSE scores of the two groups showed an upward trend with the prolongation of postoperative time, with higher MMSE scores in the observation group than in the control group. In addition, the observation group consumed less analgesic dosage than the control group. The results suggest that multi-mode combined anesthesia can achieve stable anesthetic effect while reducing the dosage of opioid anesthetics and speeding up the recovery of patients' spontaneous breathing and the recovery of patients, thus accelerating the recovery of postoperative cognitive function.

Anesthesia and surgical operation can plunge patients into negative emotions such as anxiety and fear and enhance the stress response of the body [25]. In our study, the observation group had lower SAS and SDS scores than the control group, suggesting that nerve block combined with general anesthesia can alleviate the postoperative anxiety and depression of patients. The choice of anesthesia and analgesia is strongly bound up with postoperative infection and inflammatory factors [26]. According to research, persistent severe pain can also give rise to severe stress reaction in patients, affecting their normal physiologic func-

tions. If it is not treated in time, it will inevitably prolong postoperative hospitalization time, hinder postoperative recovery, and increase medical expenses [27, 28]. The changes in IL-6, a pro-inflammatory factor, can directly reflect the degree of inflammation in patients [29]. IL-10 is a multifunctional cytokine, which regulates the growth and differentiation of cells, and participates in inflammatory and immune responses [30]. Cortisol (Cor), synthesized in large quantities in various stress states, is a sensitive stress indicator. Long-term or excessive stress reaction can lead to Cor dysfunction, causing inflammatory reaction and persistent pain [31]. In our study, the observation group showed lower levels of IL-6, Cor, and IL-10 than the control group at 6 hours after operation, and also got lower VAS scores than the control group at 6 h after operation, but the two groups were not greatly different in these indexes and VAS scores at 12 h after operation. The results suggest that nerve block combined with general anesthesia can reduce inflammatory stress, improve immune metabolism, and deliver a more significant analgesic effect on patients. Moreover, correlation analysis found that VAS score was positively correlated with IL-6 and Cor before and after treatment. It is suggested that pain is closely related to inflammatory reaction. In addition, we also analyzed the first getting out-of-bed time, hospitalization time, treatment expense, and adverse reactions of the two groups after operation. The control group experienced later postoperative getting out-of-bed time and longer hospitalization time than the observation group, but the treatment expense and incidence of adverse reactions were not greatly different between the two groups. The results imply that nerve block combined with general anesthesia can reduce the hospitalization time of patients and will not increase the economic burden and adverse reactions of patients. The main reason is that getting out of bed as early as possible can promote the recovery of patients' body function, thus shortening the hospitalization time.

At the end of the study, we analyzed the risk factors for postoperative cognitive dysfunction and found that old age was the risk factor of postoperative cognitive dysfunction, while nerve block combined with general anesthesia was the protective factor of postoperative cognitive dysfunction. The structure and function of the brain will change with age. The decrease of blood flow, the number of neurons in cerebral cortex and the affinity of neurotransmitters and receptors may lead to cognitive dysfunction in patients [32]. According to research [33], opioids can cause cognitive dysfunction or abnormal brain memory in patients. Nerve block combined with general anesthesia can reduce the use of opioids and thus reduce cognitive dysfunction and delirium.

In this study, through experimental analysis, we found that nerve block combined with general anesthesia can effectively improve the cognitive function and analgesic effect on elderly patients after knee replacement, without increasing the postoperative adverse reactions. However, this study still has some limitations. First, this study is a retrospective study, so we are unable to follow up the patients. Second, the sample size in this study is small. Finally, there are few indicators that we can collect in this study. Therefore, we hope to carry out randomized controlled trials in the future and collect a large number of clinical samples and more indicators of inflammatory, immune and stress functions to improve our research conclusions.

To sum up, nerve block combined with general anesthesia can effectively improve the cognitive function of and analgesic effect in elderly patients undergoing knee joint replacement, and accelerate their recovery, without increasing the adverse reactions, so it is worthy of clinical application.

### Disclosure of conflict of interest

None.

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