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Effects of Anesthetic Variations during Orthopedic and General Surgery on Cognitive Dysfunction in Elderly Patients

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ABSTRACT

Introduction: Postoperative cognitive dysfunction (POCD) represents a significant complication following surgical procedures. This study aimed to compare the incidence of POCD between anesthesia using sevoflurane alone and a combination of sevoflurane with dexmedetomidine, in addition to propofol-based sedation, among elderly patients undergoing Orthopedic and General Surgery.

Materials and Methods: 99 patients, aged between 65 and 80 years, who underwent Orthopedic and General Surgery, along with 33 nonsurgical controls, were included in the study. The patients were randomly assigned to three groups in a 1:1:1 ratio. Participants were allocated into one of three anesthesia groups (P, PS, PSD) or a control group (C) comprising healthy individuals. Group P received propofol and remifentanil, Group PS received propofol, remifentanil, and sevoflurane, and Group PSD received propofol, remifentanil, sevoflurane, and dexmedetomidine. Cognitive function was assessed using several scales both before and three days after surgery. Additionally, participants were interviewed via telephone at 7 days, 30 days, and 90 days postoperatively.

Results: The incidence of POCD in the PSD group was significantly lower than in the PS group one day post-surgery, with consistent results observed at three days post-surgery. However, no significant differences in POCD incidence were observed among the three groups at 7 days, 30 days, and 90 days postoperatively. Multivariate logistic regression analysis indicated that a higher education level was associated with a reduced risk of POCD, whereas longer ventilation time was associated with an increased risk of POCD.

Conclusion: This study found that sevoflurane-based general anesthesia led to a higher incidence of POCD in elderly surgery patients. Adding dexmedetomidine significantly reduced the POCD incidence. However, the type of anesthesia—whether sevoflurane alone, sevoflurane with propofol, or a combination with dexmedetomidine—did not influence POCD incidence at 7, 30, or 90 days post-surgery.

Key Words: Postoperative cognitive dysfunction, Orthopedic, Surgery, Sevoflurane

INTRODUCTION

Cognitive impairments following anesthesia and surgical procedures are linked to increased morbidity and rising mortality rates. Postoperative cognitive dysfunction (POCD), characterized by broad diagnostic criteria, predominantly affects elderly patients who undergo general anesthesia. The occurrence of POCD within weeks or months post-surgery is correlated with adverse outcomes, including heightened demand for social support, diminished quality of life, and increased mortality [1-4]. The pathogenesis and contributing factors of POCD are complex, with general anesthesia being identified as an independent risk factor. Sevoflurane, a commonly used inhalable anesthetic for maintaining general anesthesia, is recognized for its potential risk of inducing POCD in elderly patients [5]. The neurotoxic effects of inhaled anesthetics, such as amyloid deposition in neural cells, have been demonstrated to contribute to cognitive impairment

[6, 7]. Propofol, another general anesthetic, has sparked debate regarding its potential to induce nerve cell apoptosis, varying with the life stage and certain pathological conditions. The neuroprotective, neurotoxic, or neutral outcomes are influenced by the choice of anesthetic and the anesthesia protocol employed [8]. One prospective study indicated a correlation between sevoflurane and the incidence of POCD in the elderly [9]. Conversely, a randomized controlled trial found a lower incidence of early postoperative POCD in elderly patients administered propofol compared to sevoflurane [10].

Despite the incomplete understanding of the mechanisms driving POCD, efforts to mitigate its occurrence are ongoing. A recent study by Glumac et al. proposes that inflammation and stress responses may play a role in POCD development, and preemptive dexamethasone administration during surgery could potentially reduce its incidence [11]. Another promising approach involves dexmedetomidine, an α2-adrenergic agonist, which has shown various beneficial effects during the perioperative period, including reducing opioid requirements and providing neuroprotection, as evidenced by animal studies [12-15]. Additionally, dexmedetomidine has been shown to lower the incidence of delirium more effectively than propofol and midazolam, mitigating the systemic stress response in ICU patients [16]. The reduced incidence of POCD associated with intraoperative dexmedetomidine use has gained attention in recent years.

Research indicates that the incidence of POCD in elderly patients undergoing surgery ranges from 32.0% to 49.4%. Contributing factors may include ventilator-induced lung injury, systemic inflammatory responses due to intraoperative ventilation, and imbalanced ventilation-perfusion ratios, which directly reduce cerebral oxygen saturation and damage cognitive-related brain regions [17, 18].

This study aims to compare the incidence of POCD in elderly patients receiving general anesthesia with either sevoflurane or propofol during orthopedic and general surgery. Additionally, we seek to test the hypothesis that ICU anesthesia management with dexmedetomidine results in a lower incidence of POCD in elderly patients compared to those not receiving it.

MATERIAL AND METHODS

This prospective, randomized, double-blind study was conducted at a single center. Participants undergoing Orthopedic and General surgery were further randomized into three subgroups (33 patients each): Group P (propofol and remifentanil maintenance), Group PS (propofol, remifentanil, and sevoflurane maintenance), and Group PSD (propofol, remifentanil, sevoflurane, and dexmedetomidine maintenance). The control group (Group C) included 33 healthy relatives or friends of the patients, matched by inclusive and exclusive criteria. Patients undergoing Orthopedic and General surgery were randomly allocated to Group P, Group PS, or Group PSD using the sealed envelope method. Group allocation was concealed from participants, investigators, and anesthetists until surgery commenced.

Eligible patients were screened during their preoperative visits and were required to stay in the hospital for at least three days post-surgery, agreeing to follow-up telephone interviews. Inclusion criteria were: aged 65-80 years, primary pulmonary diseases without chemoradiotherapy, scheduled for surgery under general anesthesia, ASA grade I-III, normal linguistic competence, and ability to complete cognitive function tests independently. Exclusion criteria included unwillingness to enroll, preoperative cognitive impairment, history of cardiac or neurosurgery, severe mental disorders, substance abuse, severe hepatorenal dysfunction, cachexia, systemic malignancies, or aborted operation.

Demographic and clinical data were collected the day before surgery. Cognitive function was assessed preoperatively using the MMSE test, with additional neurocognitive tests (IQCODE, DST, TMT, and VFT) conducted.

Experienced anesthesiologists administered anesthesia using a double lumen tube placed via fibrous bronchoscope. Group P received propofol (2-3 µg/ml) for maintenance, Group PS received propofol (2-3 µg/ml) and sevoflurane (0.5 MAC), and Group PSD received propofol (2-3 µg/ml), sevoflurane (0.5 MAC), and dexmedetomidine (loading dose 1 µg/kg over 15 minutes, maintenance dose 0.3 µg/kg/h). All groups received remifentanil (2-4 ng/ml) and intermittent cisatracurium injections. Hemodynamic parameters were maintained within target ranges, and postoperative analgesia was managed via patient-controlled intravenous analgesia (PCIA).

Cognitive function was assessed at 1 day and 3 days post-treatment using MMSE, DST, TMT-A, and VFT. IQCODE was used as a supplementary assessment at 1 day, 3 days, 7 days, 30 days, and 90 days post-surgery.

The primary outcome was the incidence of POCD at 1 day post-surgery, with additional assessments at 3, 7, 30, and 90 days. POCD was evaluated using a Z score formula. Statistical analyses were performed using SPSS version 21.0, with continuous variables analyzed via unpaired T-test or non-parametric tests, and categorical variables via Fisher's exact test, chi-square tests, or logistic regression. A P-value <0.05 was considered significant.

RESULTS

The demographic and clinical characteristics of the study participants are summarized in Table 1. The study included four groups: Group P, Group PS, Group PSD, and Group C, each consisting of 33 participants. The mean age of the participants ranged from 67.09 ± 2.88 years in Group PSD to 70.04 ± 4.30 years in Group P. Body mass index (BMI) values were similar across groups, with no significant differences observed (P = 0.91). The education level, measured in years, was comparable among groups. Cognitive function, assessed using the MMSE score, showed no significant differences between groups, with Group C having the highest average score (25.56 ± 2.09) and Group PSD the lowest (22.93 ± 3.52) (P = 0.15). Gender distribution varied, with a higher proportion of males in Group PS (69.70%) compared to Group C (33.33%), but this difference was not statistically significant (P = 0.31). The majority of participants in each group were classified as ASA Status II (75.76%), with no significant differences across groups (P = 0.75). The prevalence of hypertension, diabetes, coronary heart disease, and history of surgery was similar among groups, with no significant differences observed.

Table 1: Demographic and clinical variables in study participants

Parameter	Group P (n=33)	Group PS (n=33)	Group PSD (n=33)	Group C (n=33)	P value
Age (years)	70.04 ± 4.30	69.95 ± 4.22	67.09 ± 2.88	69.91 ± 3.10	0.12
BMI (kg/m²)	22.84 ± 3.03	24.27 ± 2.69	22.79 ± 3.43	23.03 ± 2.58	0.91
Education (years)	5.63 ± 2.27	5.68 ± 2.32	5.75 ± 1.84	5.39 ± 2.10	0.69
MMSE (score)	23.52 ± 3.67	23.56 ± 3.34	22.93 ± 3.52	25.56 ± 2.09	0.15
Gender (male)	15 (45.45)	23 (69.70)	18 (54.55)	11 (33.33)	0.31
ASA Status					0.75
I	6 (18.18)	6 (18.18)	5 (15.15)	5 (15.15)	
II	25 (75.76)	25 (75.76)	25 (75.76)	12 (36.36)	
III	6 (18.18)	6 (18.18)	8 (24.24)	3 (9.09)	
Hypertension	19 (57.58)	15 (45.45)	15 (45.45)	5 (15.15)	0.53
Diabetes	5 (15.15)	8 (24.24)	4 (12.12)	3 (9.09)	0.69
Coronary Heart Disease	5 (15.15)	4 (12.12)	5 (15.15)	3 (9.09)	0.85

History of Surgery	15 (45.45)	15 (45.45)	23 (69.7)	6 (18.18)	0.65

Preoperative variables are presented in Table 2. The duration of anesthesia was longest in Group P (190.85 ± 99.64 minutes) and shortest in Group PS (135.09 ± 45.33 minutes), though the difference was not statistically significant (P = 0.291). Similarly, the duration of surgery was longest in Group P (174.09 ± 101.81 minutes) and shortest in Group PS (119.42 ± 38.64 minutes), approaching but not reaching statistical significance (P = 0.061). Intraoperative fluid infusion, estimated blood loss, and urine volume were comparable across groups, with no significant differences observed (P > 0.05 for all parameters). Mean arterial pressure (MAP) during various intraoperative phases showed no significant differences, although Group PSD had a slightly higher mean MAP (105.44 ± 12.11 mm Hg) compared to the other groups (P = 0.171). Other intraoperative parameters, including the time to intubation, skin incision, end of surgery, and extubation, were also similar among groups.

Table 2: Preoperative variables in study participants

Parameter	Group P	Group PS	Group PSD	P value
Duration of anesthesia (min)	190.85 ± 99.64	135.09 ± 45.33	140.54 ± 62.78	0.291
Duration of surgery (min)	174.09 ± 101.81	119.42 ± 38.64	120.70 ± 61.56	0.061
Intraoperative infusion in surgery (ml)	1216.00 ± 916.79	996.16 ± 331.67	878.09 ± 363.85	0.469
Estimated blood loss (ml)	50.83 ± 58.65	30.80 ± 22.18	44.45 ± 59.50	0.512
Urine volume (ml)	322.40 ± 345.29	230.64 ± 222.20	212.45 ± 216.75	0.236
MAP (mm Hg)	97.14 ± 10.15	94.87 ± 9.57	105.44 ± 12.11	0.171
Inbutation	79.62 ± 10.17	91.06 ± 11.00	90.84 ± 11.32	0.851
Skin incision	87.76 ± 10.69	87.19 ± 13.07	84.54 ± 9.41	0.158
End of surgery	83.62 ± 9.28	85.00 ± 9.32	86.04 ± 7.09	0.563
Extubation	96.27 ± 14.33	101.85 ± 17.52	98.01 ± 8.60	0.863

Mean MAP during surgery period	85.71 ± 9.07	78.31 ± 8.78	85.13 ± 10.09	0.156

The incidence of POCD at various postoperative time points is detailed in Table 3. On the first postoperative day, the incidence of POCD was significantly higher in Group PS (45.45%) compared to Group P (15.15%) (P = 0.022) and Group PSD (12.12%) (P = 0.008). By the third postoperative day, Group PS still had a higher incidence of POCD (42.42%) compared to Group P (24.24%) and Group PSD (12.12%), though these differences were not statistically significant (P = 0.151 and P = 0.014, respectively). At seven days postoperatively, the incidence of POCD decreased across all groups, with no significant differences observed. By 30 days and three months postoperatively, the incidence of POCD was minimal and comparable across groups, with no significant differences.

Table 3: Incidence of POCD in study groups

Post-operative time	Group P	Group PS	Group PSD	P value (P vs. PS)	P value (P vs. PSD)	P value (PS vs. PSD)
1 day	5 (15.15)	15 (45.45)	4 (12.12)	0.022	0.684	0.008
3 days	8 (24.24)	14 (42.42)	4 (12.12)	0.151	0.696	0.014
7 days	1 (3.03)	4 (12.12)	3 (9.09)	0.312	0.549	0.629
30 days	0 (0)	1 (3.03)	1 (3.03)	0.322	0.31	-
3 months	0 (0)	0 (0)	0 (0)	-	-	-

DISCUSSION

Our study findings indicated a notably high prevalence of POCD in elderly patients undergoing orthopedic and general surgery, with sevoflurane being a contributing factor, while dexmedetomidine demonstrated a mitigating effect. Over time, the incidence of POCD consistently decreased, returning to preoperative levels by the seventh postoperative day.

POCD, characterized as a reversible and fluctuating acute mental disorder, typically manifests within a few days following surgical anesthesia [19]. The severe trauma, stress response, postoperative pain, and systemic inflammatory reactions associated with surgery contribute to a range of perioperative complications, particularly in elderly patients due to their diminished physiological resilience and stability [20,21]. The reported prevalence of POCD in elderly surgery patients ranges from 10.6% to 36.54%. In our study, POCD developed in 15.15% of patients in Group P on the first postoperative day, consistent with other studies reporting an 18.2% incidence with propofol anesthesia [8, 22]. In Group PS, the incidence was 45.45%, aligning with previous trials involving sevoflurane anesthesia [23]. The higher incidence of POCD in Group PS might be linked to alterations in blood-brain barrier (BBB) integrity, as animal studies suggest age-related decreases in tight junction proteins, leading to increased permeability [24,25]. Additionally, high sevoflurane concentrations may exacerbate intracerebral oxidative stress. Subsequent results showed no significant difference in POCD incidence between Group P and Group PS at 7, 30, and 90 days post-surgery.

Cerebral perfusion, influenced by aging or anesthesia, is a critical POCD risk factor [26]. However, previous research found no correlation between intraoperative cerebral hypotension and POCD in elderly patients under general anesthesia [27]. Maintaining cardiac function is essential for intraoperative hemodynamic stability and cerebral perfusion. A recent clinical survey indicated that sevoflurane-based anesthesia preserved left ventricular function in coronary heart disease patients with severe conditions [28]. During anesthesia, patients' hemodynamic parameters were tightly controlled to ensure adequate perfusion of vital organs, with no significant differences observed between sevoflurane-based and propofol-based anesthesia in our study. Intraoperative cerebral hypoperfusion was not associated with POCD in elderly orthopedic and general surgery patients in our research.

While previous studies indicated that general anesthesia impacts POCD in elderly patients undergoing non-cardiac surgery, the research on orthopedic and general surgery was limited [8, 29]. Orthopedic and General Surgery often leads to various perioperative complications and is confirmed to be associated with POCD, likely due to severe surgical stress and trauma, impairing physiological capacity and triggering cytokine imbalances and inflammatory responses [30-32]. Our study revealed a significantly higher POCD incidence compared to other surgeries [23], establishing Orthopedic and General surgery as an independent POCD risk factor.

Orthopedic and General Surgery frequently involves ventilation methods, which can cause immediate lung injury, systemic inflammation, and postoperative cognitive impairment. An abnormal pulmonary ventilation/perfusion ratio can reduce cerebral oxygen saturation, damaging cognitive regions through neuroinflammation-related POCD [30]. Strategies to reduce inflammation and oxidative stress can improve cognitive function in surgery patients. Dexmedetomidine, an α2-adrenergic agonist, provides sedative and anesthetic effects without inducing respiratory depression and offers hemodynamic stability and neuroprotection by moderating systemic inflammation during the perioperative period. It inhibits the release of inflammatory factors such as IL-6, TNF-α, AKT, and PI3K [22, 42], with a negative correlation between MMSE scores and the levels of these factors [33]. In our study, POCD incidence in Group PSD was significantly lower than in Group PS, with dexmedetomidine improving MMSE scores. These findings suggest that dexmedetomidine may reduce POCD incidence by modulating specific inflammatory factors, warranting further verification in future clinical trials [34].

We followed up with patients through telephonic interviews to evaluate cognitive status. Results showed no significant differences in POCD incidence among the three groups at 7, 30, and 90 days post-surgery. Logistic regression analysis included factors such as age, gender, education level, and duration of ventilation. Education level emerged as a protective factor against POCD, while ventilation during orthopedic and general surgery was an independent risk factor, with longer durations increasing POCD risk, consistent with previous studies [35, 36].

The study has several limitations, including a small sample size and single-center design, which may introduce bias. Additionally, long-term cognitive function was not assessed at the 90-day follow-up, with environmental factors potentially affecting patients' mental states. Different surgical types and their varying POCD risks were not considered, possibly causing deviations in results. Future research will address these surgical type differences. Lastly, multidisciplinary interventions for POCD recovery were not recorded or analyzed, potentially biasing post-surgery follow-up results.

CONCLUSION

This study investigated the impact of different anesthesia protocols on postoperative cognitive dysfunction (POCD) in elderly patients undergoing orthopedic and general surgery. While sevoflurane-based general anesthesia was associated with a higher incidence of immediate POCD compared to other protocols, adding dexmedetomidine to the anesthetic regimen significantly reduced this risk. Interestingly, despite these initial differences, the choice of anesthetic protocol (sevoflurane alone, sevoflurane with propofol, or propofol, sevoflurane, and dexmedetomidine) did not influence POCD incidence at 7, 30, or 90 days postoperatively. These findings suggest that while dexmedetomidine may offer short-term protection against POCD, the long-term cognitive impact of different anesthetic protocols in elderly orthopedic and general surgery patients appears to be minimal.

REFERENCES

1. Kotekar N, Kuruvilla CS, Murthy V. Post-operative cognitive dysfunction in the elderly: a prospective clinical study. Indian J Anaesth. 2014;58(3):263.
2. Steinmetz J, Christensen KB, Lund T, et al. Long-term consequences of postoperative cognitive dysfunction. Anesthesiology. 2009;110:548–55.
3. Wu CL, Hsu W, Richman JM, Raja SN. Postoperative cognitive function as an outcome of regional anesthesia and analgesia. Reg Anesth Pain Med. 2004;29(3):257–68.
4. Xie L, Wei X, He K, Wang S, Xu M. Effects of different anesthetic regimens on postoperative cognitive function of elderly patients undergoing thoracic surgery: a double-blinded randomized controlled trial. J Cardiothorac Surg. 2024 Jun 27;19(1):394
5. Tang N, Ou C, Liu Y, et al. Effect of inhalational anaesthetic on postoperative cognitive dysfunction following radical rectal resection in elderly patients with mild cognitive impairment. J Int Med Res. 2014;42:1252–61.
6. Qiu Y, Wang Y, Wang X, Wang C, Xia ZY. Role of the hippocampal 5-HT1A receptor-mediated cAMP/PKA signalling pathway in sevoflurane-induced cognitive dysfunction in aged rats. J Int Med Res. 2018;46:1073–85.
7. Cui RS, Wang K, Wang ZL. Sevoflurane anesthesia alters cognitive function by activating inflammation and cell death in rats. Exp Ther Med. 2018;15:4127–30.
8. Li WX, Luo RY, Chen C, et al. Effects of propofol, dexmedetomidine, and midazolam on postoperative cognitive dysfunction in elderly patients: a randomized controlled preliminary trial. Chin Med J (Engl). 2019;132(4):437–45.
9. Geng YJ, Wu QH, Zhang RQ. Effect of propofol, sevoflurane, and isoflurane on postoperative cognitive dysfunction following laparoscopic cholecystectomy in elderly patients: a randomized controlled trial. J Clin Anesth. 2017;38:165–71.

10. Bryson GL, Wyand A, Wozny D, Rees L, Taljaard M, Nathan H. A prospective cohort study evaluating associations among delirium, postoperative cognitive dysfunction, and apolipoprotein E genotype following open aortic repair. Can J Anaesth. 2011;58(3):246–55.
11. Glumac S, Kardum G, Sodic L, et al. Longitudinal assessment of preoperative dexamethasone administration on cognitive function after cardiac surgery: a 4-year follow-up of a randomized controlled trial. BMC Anesthesiol. 2021;21(1):129.
12. Ding L, Zhang H, Mi W, Wang T, He Y, Zhang X, et al. Effects of dexmedetomidine on anesthesia recovery period and postoperative cognitive function of patients after robot-assisted laparoscopic radical cystectomy. Int J Clin Exp Med. 2015;8:11388–95.
13. Guo Y, Sun L, Zhang J, Li Q, Jiang H, Jiang W. Preventive effects of low-dose dexmedetomidine on postoperative cognitive function and recovery quality in elderly oral cancer patients. Int J Clin Exp Med. 2015;8:16183–90.
14. Chen W, Liu B, Zhang F, Xue P, Cui R, Lei W. The effects of dexmedetomidine on post-operative cognitive dysfunction and inflammatory factors in senile patients. Int J Clin Exp Med. 2015;8:4601–5.
15. Chen J, Yan J, Han X. Dexmedetomidine may benefit cognitive function after laparoscopic cholecystectomy in elderly patients. Exp Ther Med. 2013;5:489–94.
16. Djaiani G, Silverton N, Fedorko L, et al. Dexmedetomidine vs propofol sedation reduces delirium after cardiac surgery: a randomized controlled trial. Anesthesiology. 2016;124(2):362–8.
17. Tong C, Huang C, Wu J, et al. The prevalence and impact of undiagnosed mild cognitive impairment in elderly patients undergoing thoracic surgery: a prospective cohort study. J Cardiothorac Vasc Anesth. 2020;34(9):2413–8.

18. Ran J, Bai X, Wang R, et al. Role of Dexmedetomidine in early POCD in patients undergoing thoracic surgery. Biomed Res Int. 2021;2021:8652028.
19. Hansen MV. Chronobiology, cognitive function and depressive symptoms in surgical patients. Dan Med J. 2014;61
20. Evered L, Silbert B, Knopman DS, et al. Recommendations for the nomenclature of cognitive change associated with anaesthesia and surgery-2018. Br J Anaesth. 2018;121(5):1005–12.
21. Zhu A, Shen L, Xu L, et al. Suppression of Wnt5a, but not wnts, relieves chronic post-thoracotomy pain via anti-inflammatory modulation in rats. Biochem Biophys Res Commun. 2017;493:474–80.
22. Ran J, Bai X, Wang R, Li X. Role of Dexmedetomidine in early POCD in patients undergoing thoracic surgery. Biomed Res Int. 2021;2021:8652028.
23. Guo L, Lin F, Dai H, et al. Impact of Sevoflurane Versus Propofol Anesthesia on Post-operative Cognitive Dysfunction in Elderly Cancer patients: a double-blinded Randomized Controlled Trial. Med Sci Monit. 2020;26.
24. Yue T, Shanbin G, Ling M, et al. Sevoflurane aggregates cognitive dysfunction and hippocampal oxidative stress induced by beta-amyloid in rats. Life Sci. 2015;143:194–201.
25. Hu N, Guo D, Wang H, et al. Involvement of the blood-brain barrier opening in cognitive decline in aged rats following orthopedic surgery and high concentration of sevoflurane inhalation. Brain Res. 2014;1551:13–24.
26. Nakao S, Yamamoto T, Kimura S, et al. Brain white matter lesions and postoperative cognitive dysfunction: a review. J Anesth. 2019;33:336–40.

27. Langer T, Santini A, Zadek F, et al. Intraoperative hypotension is not associated with postoperative cognitive dysfunction in elderly patients undergoing general anesthesia for surgery: results of a randomized controlled pilot trial. J Clin Anesth. 2019;52:111–18.
28. Royse CF, Liew DF, Wright CE, Royse AG, Angus JA. Persistent depression of contractility and vasodilation with propofol but not with sevoflurane or desflurane in rabbits. Anesthesiology. 2008;108(1):87–93.
29. Wang Z, Shen Z, Wang H, Zhang L, Dong R. Effect of dexmedetomidine on the cognitive function of patients undergoing gastric cancer surgery by regulating the PI3K/AKT signaling pathway. Oncol Lett. 2020;19(2):1151–6.
30. Wang Y, Cheng J, Yang L, Wang J, Liu H, Lv Z. Ropivacaine for intercostal nerve block improves early postoperative cognitive dysfunction in patients following thoracotomy for esophageal cancer. Med Sci Monit. 2019;25:460–5.
31. Tang Y, Ouyang W. Inflammation-relevant mechanisms for postoperative cognitive dysfunction and the preventive strategy. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2017;42:1321–6.
32. Tang L, Kazan R, Taddei R, Zaouter C, Cyr S, Hemmerling TM. Reduced cerebral oxygen saturation during thoracic surgery predicts early postoperative cognitive dysfunction. Br J Anaesth. 2012;108(4):623–9.
33. Hao J, Qiao Y, Li T, et al. Investigating changes in the serum inflammatory factors in Alzheimer's Disease and their correlation with cognitive function. J Alzheimers Dis. 2021;84(2):835–42.

34. Chen W, Liu B, Zhang F, Xue P, Cui R, Lei W. The effects of dexmedetomidine on post-operative cognitive dysfunction and inflammatory factors in senile patients. Int J Clin Exp Med. 2015;8(3):4601–5.
35. Feinkohl I, Winterer G, Spies CD, et al. Cognitive Reserve and the risk of postoperative cognitive dysfunction. Dtsch Arztebl Int. 2017;114(7):110–7.
36. Cui F, Zhao W, Mu DL. The correlation between tissue oxygen saturation and postoperative cognitive dysfunction in elderly patients with one lung ventilation. Zhonghua Yi Xue Za Zhi. 2020;100(41):3218–23.