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Original Article

Effects of anesthetic depth on postoperative cognitive dysfunction (POCD) in non-cardiac surgical patients: a meta-analysis

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Abstract: Objective: The current study aimed to summarize related published articles concerning the depth of anesthesia and postoperative cognitive dysfunction (POCD) in non-cardiac surgical patients. Moreover, this study aimed to investigate the effects of the depth of anesthesia on short- or long-term POCD. Methods: Medline, Embase, Ovid, Cochrane Library, Google Scholar, CNKI, and Wan-fang databases were searched. Researchers focused on the effects of the depth of anesthesia on POCD and on postoperative S100-β protein levels. Results: A total of 2,625 patients from 20 randomized controlled trials (RCTs) were enrolled. The current meta-analysis shows that deep anesthesia significantly decreased incidence of POCD, compared with light anesthesia, on day 1 [OR, 0.31; 95% CI (0.24, 0.40), P < 0.00001, from 3 to 5 days [OR, 0.35; 95% CI (0.24, 0.52), P < 0.00001], day 7 [OR, 0.45; 95% CI (0.27, 0.74), P=0.002], and from 1 to 3 months [OR, 0.66; 95% CI (0.45,0.99), P=0.04] after surgery. Serum S100-β protein levels in patients that received deep anesthesia were much lower than those in patients receiving light anesthesia [MD, -270.29; 95% CI (-295.81, -244.77), P < 0.00001] on postoperative day 1. Conclusion: Deep anesthesia can significantly reduce incidence rates of short- or long-term POCD. Serum S100-β protein levels on postoperative day 1 could be reduced with deep anesthesia.

Keywords: Anesthetic depth, POCD, S100-β protein, non-cardiac surgery, meta-analysis

Introduction

Postoperative cognitive dysfunction (POCD) is a common complication in non-cardiac surgical patients [1-3]. POCD can remarkably increase the cost of care and hospitalization expenses, while decreasing patient quality of life [4, 5]. The relationship between anesthetic depth and POCD has attracted much attention. Extensive research in this area has been conducted. However, controversies remain concerning the results of these studies. Some studies have shown that deep anesthesia could reduce incidence of POCD [6, 7], while others have found that anesthetic depth had no effects on POCD [8, 9]. Devices and techniques for monitoring anesthetic depth have developed rapidly in recent years. Monitoring parameters mainly include the bi-spectral index (BIS), auditory evoked potential (AEP), auditory evoked potential index (AAI), Narcotrend index (NTI), Narcotrend scale (NTS), and cerebral state index (CSI). Therefore, the current meta-analysis concerning the depth of anesthesia and POCD in non-cardiac surgical patients was conducted, aiming to determine the effects of anesthetic depth on POCD and levels of serum S100-β protein, an early and sensitive marker of brain insult [10, 11].

Materials and methods

Study identification

The current meta-analysis aimed to identify all clinical randomized controlled trials (RCTs) concerning the effects of the depth of anesthesia on short- or long-term POCD, as well as postoperative S100-β protein levels, in non-cardiac surgical patients.

Data sources and search strategy

This meta-analysis was conducted in accordance with methods recommended by the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) and the

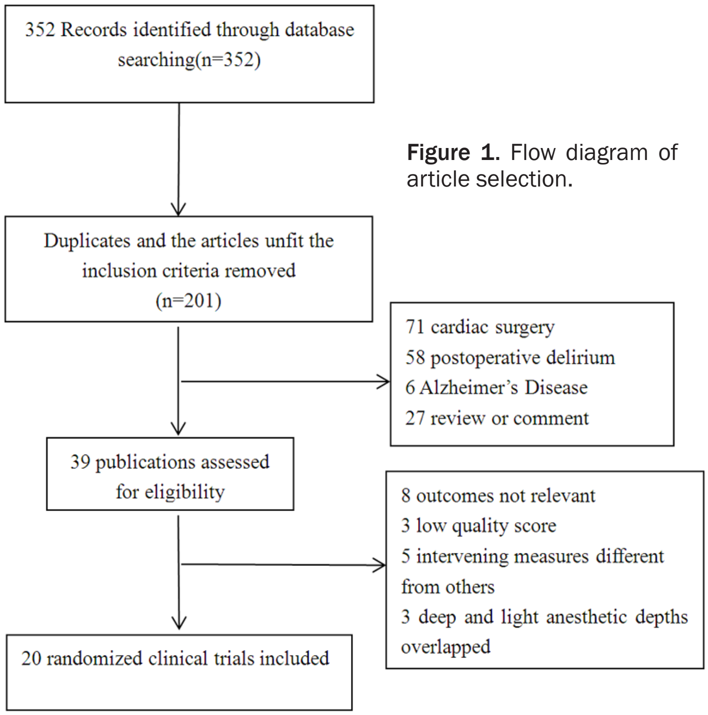

Figure 1. Flow diagram of article selection.

Cochrane Handbook for systematic reviews of interventions [12]. Based on keywords or MeSH terms, including "depth of anesthesia", "anesthetic depth", "consciousness monitors", "bispectral index", "BIS", "auditory evoked potential", "AEP", "auditory evoked potential index", "AAI", "cerebral state index", "CSI", "Narcotrend", "NTI", "NTS", "postoperative cognitive dysfunction", "POCD", "S100-β", "S100b", and "S100beta", an electronic search for relevant articles was conducted in Medline (-present), Embase (-present), Ovid (-present), the Cochrane Library (-present), Google Scholar (-present), China National Knowledge Infrastructure (CNKI, -present), and Wan-fang (-present) databases without language restrictions.

Literature screening

After a thorough literature search, two investigators (Ran An and Qianyun Pang), independently, reviewed the titles and abstracts of all identified studies. They excluded those that were obviously irrelevant or duplicates. Full articles of the remaining studies were then reviewed using a structured form, determining their eligibility and extracting data. Disagreements were resolved by discussion with all authors, if necessary. The authors were contacted for clarification and further information when necessary.

Inclusion and exclusion criteria

Inclusion criteria: (i) Trials with a clear boundary of anesthetic depth; (ii) Trials involving elective non-cardiac surgery under general anesthesia; (iii) Trials with patients older than 18 years old; (iv) Randomized controlled trials (RCTs); and (iv) Trials that mentioned incidence of POCD or serum S100-β protein levels. Exclusion criteria: (i) Patients with serious diseases (severe heart disease, kidney failure, respiratory failure, severe systemic infections); (ii) Patients with neurological or mental disorders/or those that took psychiatric drugs preoperatively; (iii) Patients with Alzheimer's disease or severe cognitive dysfunction; (iv) Patients that were unable to communicate or had preoperative MMSE scores < 17; (v) Patients with history of brain surgery or cerebral trauma; and (vi) Patients with a history of alcohol abuse or drug addiction.

Quality assessment

Risk of bias was checked by appraising various parameters, including "adequate sequence generation" "allocation concealment", "blinding", "incomplete outcome data addressed", "free of selective reporting", and "free of other bias". As recommended by the Cochrane Collaboration Publication, bias was evaluated using Egger's test with Stata 12.0 software (College station, TX, USA). $P>0.05$ indicates no statistically significant publication bias.

Data extraction

Data regarding the number of patients, patient age, basic information of the study, research title, first author, and publication times, research design types, key elements of evaluation, methods of POCD assessment, types of surgery, incidence of POCD, and S100-β protein levels were extracted from included articles.

Statistical analysis

The current meta-analysis was performed using Review Manager Version 5.3 for Windows (the Cochrane Collaboration, Oxford, UK).

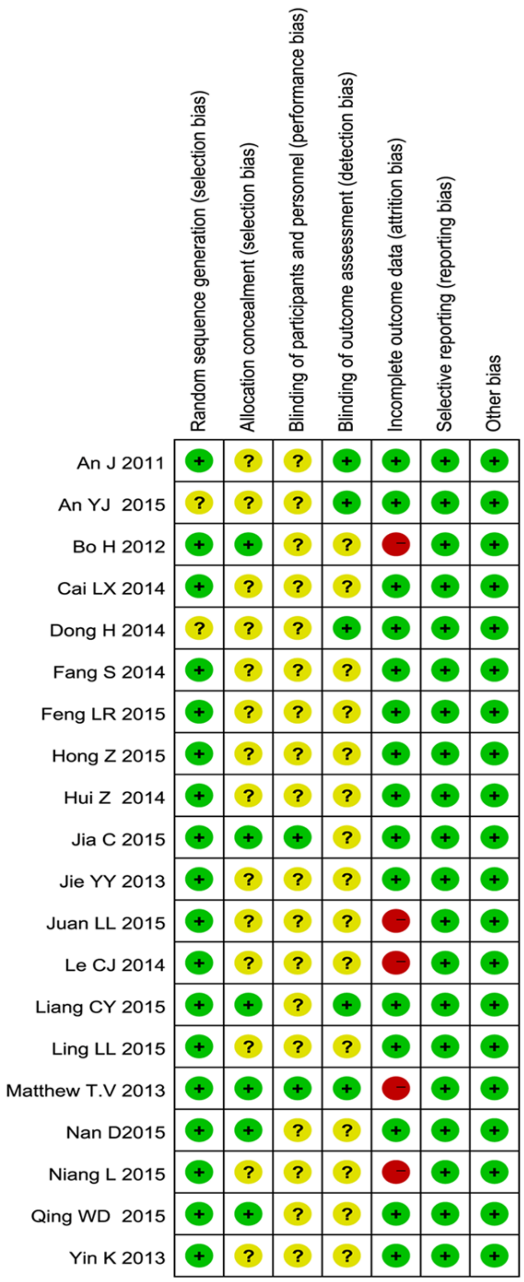

Figure 2. Risk of bias summary. Green indicates low risk of bias, red indicates high risk of bias, and yellow indicates unclear risk of bias.

Calculations of effect size for con-tinuous data are expressed as the mean difference (MD). Dichotomous data are expressed as odds ratios (OR) with 95% confidence intervals (CIs). Statistical heterogeneity was assessed using I^2 statistics. Heterogeneity was significant when $I^2 \geq 50\%$ or $P < 0.01$. Thus, a random-effects model was used. Planned subgroup analyses were conducted, identifying potential sources of heterogeneity. If necessary, a fix-effects model was used when $I^2 \leq 50\%$ or $P \geq 0.01$.

Results

Literature search findings

A total of 352 relevant articles were identified through keywords and MeSH terms. After screening and conducting a detailed selection process, 20 RCTs remained with 2,625 patients [13-32]. Details of the screening process are presented in **Figure 1**. Risk of bias is summarized in **Figure 2**. For anesthetic depth monitoring in these 20 RCTs, BIS was used in 11 trials, NTI was used in 7 trials, AAI was used in 1 trial, and CSI was used in 1 trial. To diagnose POCD, the Mini-mental State Examination (MMSE) was used in 11 RCTs, the value Z was used in 3 RCTs, and standard deviation (SD) was used in 4 RCTs. There were no descriptions of the methods for POCD diagnosis in the remaining 2 RCTs (**Table 1**).

Results of the meta-analysis

Effects of anesthetic depth on short-term POCD: A total of 13 RCTs with 1,287 patients [15-27] analyzed the impact of anesthetic depth on POCD on day 1 after surgery. I^2=0 and a fixed-effects model was used. There were 7 RCTs (n=703) that reported the effects of anesthetic depth on POCD from 3 to 5 days after surgery [13, 17, 19-21, 24, 27]. I^2=0 and a fixed-effects model was used. A total of 9 RCTs (n=1617) reported the effects of anesthetic depth on POCD on day 7 after surgery [15-17, 19, 20, 28-31]. I^2=53% and a random-effects model was used. Results showed much lower incidence rates of POCD in the deep anesthesia group, compared to the light anesthesia group, on day 1 [OR, 0.31; 95% CI (0.24-0.40), P < 0.00001], from 3 to 5 days [OR, 0.35; 95% CI (0.24-0.52), P < 0.00001], and on day 7 [OR, 0.27; 95% CI (0.27-0.74), P=0.002] after surgery (**Figure 3**). There was no significant publication bias, according to Egger's testing (*P*=0.357, P=0.284, P=0.264).

Subgroups were created to analyze the effects of anesthetic depth on POCD on day 7 after surgery. BIS values were used in 5 RCTs (n=1279) [14, 17, 19, 20, 30]. I^2=74% and a random-effects model was used. Results showed much lower incidence rates of POCD in the deep anesthesia group (BIS 30-50), compared to

Table 1. Characteristics of studies included in the meta-analysis

Author	No. of cases A/B▲	Age(yr) A/B	Surgery	Anesthetic monitoring	Diagnostic method	Outcomes
Jian X [13]	40/40	45±7.93	Microvascular decompression surgery	BIS (30-40/54-65)	Value Z	B
Matthew T.V [14]	412/423	A: 61.8±8.2 B: 67.6±8.3	Elective surgery	BIS (31-49/48-57)	Value Z	D
Jin LC [15]	50/50	A: 67.6±2.4 B: 68.7±2.8	Abdominal operation	NTI (20-36/46-64)	MMSE	A, E
Bo H [16]	42/38	A: 70.2± 8.3 B: 69.15±9.0	Noncardiac surgery	CSI (41-50/51-60)	MMSE	A, C
Juan JJ [17]	116/137	A: 59±11.9 B: 68.3±9.2	General surgery operation	BIS (30-39/50-59)	MMSE	A, B, C
Ling LL [18]	100/100	A: 68.4±2.6 B: 68.4±2.6	Abdominal operation	NTI (20-36/46-64)	MMSE	A
Hui Z [19]	32/32	A: 51.9±8.7 B: 68.4±5.2	Gastrointestinal surgery	BIS (30-39/50-59)	MMSE	A, B
Hong Z [20]	60/60	A: 67.2±7.3 B: 65.8±6.2	Elective laparoscopic surgery	BIS (30-45/50-60)	SD	A, B, C
Cai LX [21]	20/20	A:>40 B:>40	Stomach cancer surgery	BIS (30-40/55-65)	SD	A, B
Feng LR [22]	20/20	A: 67±16.85 B: 66±16.74	TURP	NTI (20-36/46-64)	MMSE	A, E
An YJ [23]	51/51	A: 68.2±2.5 B: 67.5±2.6	Abdominal surgery	BIS (30-45/≥ 45)	MMSE	A, E
Dong H [24]	30/30	A: 68±5 B: 67±5	Abdominal cancer surgery	BIS (30-39/50-59)	MMSE	A, B
Jie YY [25]	40/40	A: 68.6±2.1 B: 68.0±2.3	Abdominal surgery	NTI (20-36/46-64)	MMSE	A, E
Qing WD [26]	18/16	A: 69.6±2.41 B: 68.3±1.73	Abdominal surgical	NTI (20-36/46-64)	MMSE	A, E
Fang S [27]	43/43	A: 73±8 B: 71±9	Gastrointestinal surgery	BIS (30-40/40-65)	MMSE	A, B
Yin K [28]	49/96	A: 70.5±3.67 B: 71.9±5.18	Elective laparoscopic surgery for colorectal	NTI (20-36/46-64)	Value Z	C
Niang L [29]	16/32	A: 60±7.0 B: 59.8±6.7	Elective laparoscopic surgery for colorectal	NTS (E1/D0-D2)	SD	C
Jia C [30]	53/54	A: 68.6±2.1 B: 68.0±2.3	Abdominal surgical	BIS (30-45/45-60)	Unclear	C, D
Nan D [31]	36/35	60-80	Abdominal surgical	AAI (20-30/30-40)	SD	C, D, E
Liang CY [32]	60/60	A: 69.69±7.1 B: 69.71±7.0	Elective laparoscopic surgery	BIS (30-45/45-60)	Unclear	E

▲: Deep anesthesia group/Light anesthesia group; A: Incidence of POCD on postoperative day 1; B: Incidence of POCD from 3 to 5 days after surgery; C: Incidence of POCD on postoperative day 7; D: Incidence of POCD from 1 to 3 months after surgery; E: Serum S100-β protein levels on postoperative day 1; SD: standard deviation; MMSE: mini-mental state examination.

the light anesthesia group (BIS 50-65), on day 7 after surgery [OR, 0.36; 95% CI (0.15-0.86), P=0.02]. There was no significant publication bias, according to Egger's testing (P=0.93).

NTI values were used in 2 RCTs (n=193) [28, 29]. I^2=0 and a fixed-effects model was used. Results showed no differences in incidence of POCD between deep anesthesia (NTI 20-36) and light anesthesia (NTI 46-64) [OR, 0.69; 95% CI (0.34-1.37), P=0.28] (**Figure 4**).

Effects of anesthetic depth on long-term POCD: Three RCTs (n=961) reported the effects of anesthetic depth on long-term POCD [14, 30, 31]. BIS values were used in all three RCTs. I^2=0 and a fixed-effects model was used, showing that deep anesthesia could reduce incidence of POCD more than light anesthesia from 1 to 3 months after surgery [OR, 0. 66; 95% CI (0.45-0.99), P=0.04] (**Figure 5**). There was no significant publication bias, according to Egger's testing (P=0.43).

	deep anesthesia		light anesthesia			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
1.1.1 The incidence of POCD on postoperative day 1						
Feng LR 2015	4	20	12	20	2.1%	0.17 [0.04, 0.69]
Qing WD 2015	6	31	18	31	3.0%	0.17 [0.06, 0.54]
An YJ 2015	7	51	24	51	3.7%	0.18 [0.07, 0.47]
Ling LL 2015	13	100	41	100	5.2%	0.22 [0.11, 0.44]
Le CJ 2014	7	50	21	50	3.6%	0.22 [0.08, 0.60]
Hui Z 2014	10	32	20	32	3.4%	0.27 [0.10, 0.77]
Juan LL 2015	37	116	83	137	6.7%	0.30 [0.18, 0.51]
Jie YY 2013	6	40	14	40	3.2%	0.33 [0.11, 0.97]
Dong H 2014	11	30	19	30	3.3%	0.34 [0.12, 0.96]
Bo H 2012	8	42	14	38	3.5%	0.40 [0.15, 1.11]
Fang S 2014	16	43	23	43	4.2%	0.52 [0.22, 1.22]
Cai LX 2014	14	20	16	20	2.1%	0.58 [0.14, 2.50]
Hong Z 2015	17	60	22	60	4.8%	0.68 [0.32, 1.47]
Subtotal (95% CI)		**635**		**652**	**48.7%**	**0.31 [0.24, 0.40]**
Total events	156		327			
Heterogeneity: Tau² = 0.00; Chi² = 10.89, df = 12 (P = 0.54); I² = 0%						
Test for overall effect: Z = 9.21 (P < 0.00001)						
1.1.2 The incidence of POCD from 3 to 5 days after surgery						
Hui Z 2014	5	32	14	32	2.8%	0.24 [0.07, 0.78]
Fang S 2014	5	43	15	43	3.0%	0.25 [0.08, 0.76]
Dong H 2014	5	30	13	30	2.7%	0.26 [0.08, 0.87]
An J 2011	4	40	11	40	2.6%	0.29 [0.08, 1.02]
Juan LL 2015	19	116	46	137	6.0%	0.39 [0.21, 0.71]
Hong Z 2015	7	60	13	60	3.5%	0.48 [0.18, 1.30]
Cai LX 2014	3	20	3	20	1.5%	1.00 [0.18, 5.67]
Subtotal (95% CI)		**341**		**362**	**22.2%**	**0.35 [0.24, 0.52]**
Total events	48		115			
Heterogeneity: Tau² = 0.00; Chi² = 2.98, df = 6 (P = 0.81); I² = 0%						
Test for overall effect: Z = 5.36 (P < 0.00001)						
1.1.3 The incidence of POCD on postoperative day 7						
Juan LL 2015	6	116	28	137	3.9%	0.21 [0.08, 0.53]
Hui Z 2014	5	32	14	32	2.8%	0.24 [0.07, 0.78]
Jia C 2015	9	29	19	30	3.2%	0.26 [0.09, 0.77]
Hong Z 2015	0	60	1	60	0.5%	0.33 [0.01, 8.21]
Bo H 2012	2	42	5	38	1.6%	0.33 [0.06, 1.81]
Nan D2015	3	36	6	29	2.0%	0.35 [0.08, 1.54]
Yin K 2013	11	49	30	96	4.6%	0.64 [0.29, 1.41]
Niang L 2015	4	16	9	32	2.3%	0.85 [0.22, 3.35]
Matthew T.V 2013	83	382	93	401	8.2%	0.92 [0.66, 1.29]
Subtotal (95% CI)		**762**		**855**	**29.1%**	**0.45 [0.27, 0.74]**
Total events	123		205			
Heterogeneity: Tau² = 0.26; Chi² = 16.94, df = 8 (P = 0.03); I² = 53%						
Test for overall effect: Z = 3.13 (P = 0.002)						
Total (95% CI)		**1738**		**1869**	**100.0%**	**0.36 [0.28, 0.45]**
Total events	327		647			
Heterogeneity: Tau² = 0.14; Chi² = 47.07, df = 28 (P = 0.01); I² = 41%						
Test for overall effect: Z = 8.58 (P < 0.00001)						
Test for subgroup differences: Chi² = 1.60. df = 2 (P = 0.45). I² = 0%						

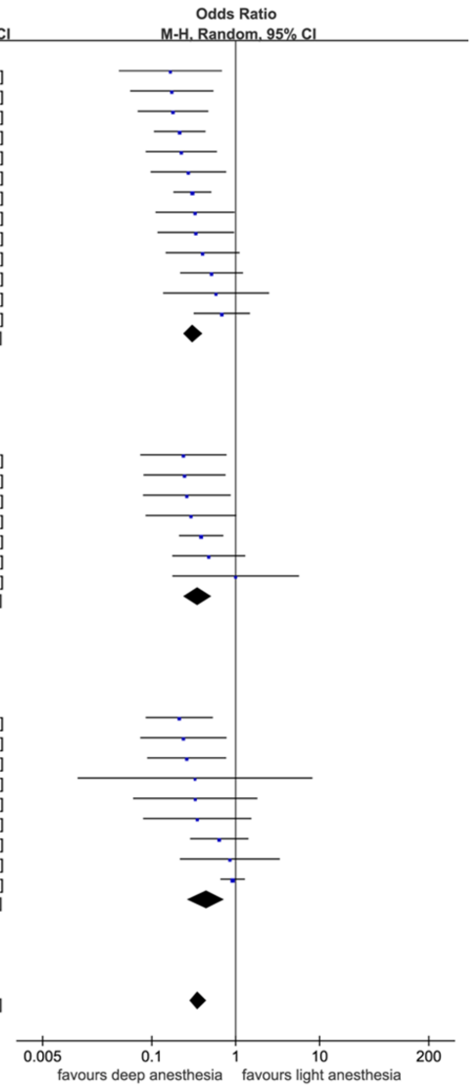

Figure 3. Forest plot of effects of anesthetic depth on short-term POCD.

Effects of anesthetic depth on serum S-100β protein levels: Seven RCTs (n=686) studied the effects of anesthetic depth on serum S100-β levels on day 1 after surgery [15, 18, 22, 23, 25, 26, 32], with I^2=0. Results of fixed effects-model analysis showed that serum S100-β protein levels in the deep anesthesia group were much lower than those in the light anesthesia group [MD, -270.29; 95% CI (-295.81, -244.77), P < 0.00001] (**Figure 6**). There was no obvious publication bias, according to the funnel plot (**Figure 7**).

Discussion

POCD is a common complication after surgery and anesthesia. Previous studies have shown that incidence rates of POCD are approximately 25% in the first week after surgery and approximately 10% after 3 months [33, 34]. Many factors, including patient age, sex, education levels, alcoholism, preoperative comorbidity, types of surgery, anesthesia, and postoperative infections, can induce or facilitate the development of POCD [4]. The current study analyzed the effects of anesthetic depth on POCD development. Results showed that deep anesthesia could reduce incidence of short or long-term POCD. The mechanisms may be that deep anesthesia can decrease cerebral oxygen metabolism, reduce perioperative stress, and inhibit the release of inflammatory cytokines, compared to light anesthesia. The boundary between deep and light anesthesia was based on the criteria in included trials. BIS 30-50, NTI 20-36, and AAI 20-30 were regarded as deep

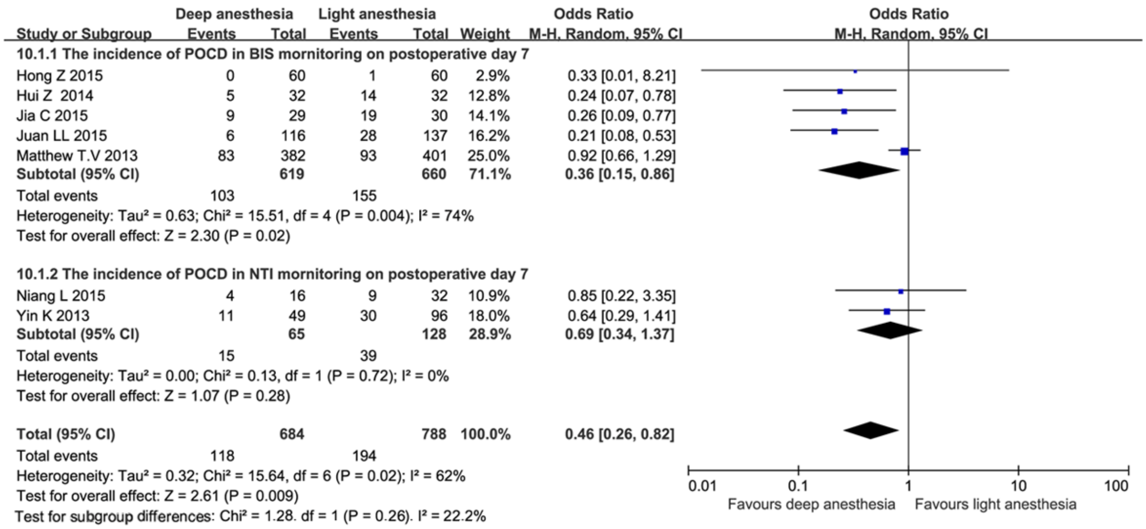

Figure 4. Forest plot of effects of anesthetic depth with BIS and NTI monitoring on short-term POCD.

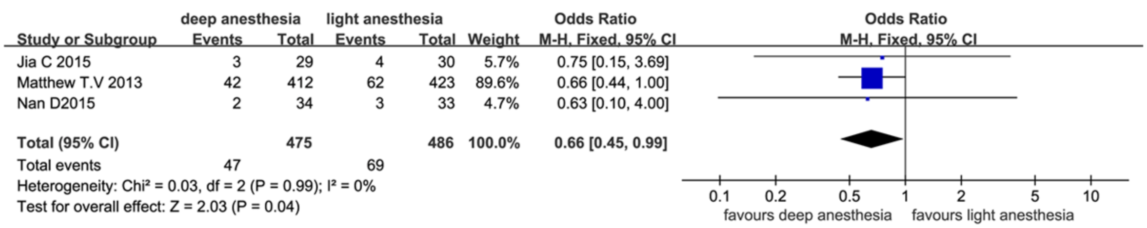

Figure 5. Forest plot of effects of anesthetic depth on long-term POCD.

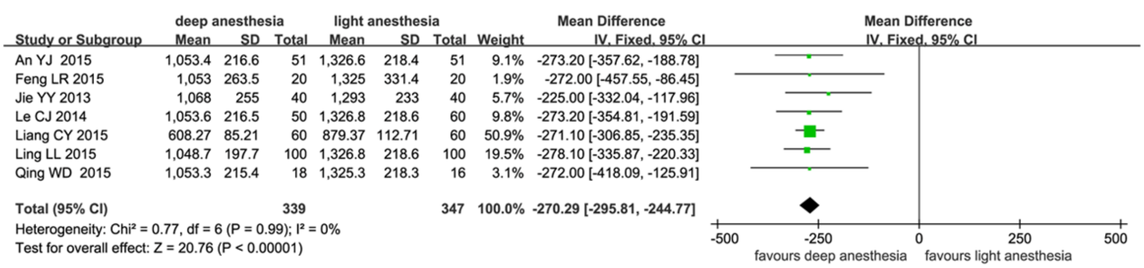

Figure 6. Forest plot of effects of anesthetic depth on serum S100-β protein levels on postoperative 1 day.

anesthesia. BIS 50-65, NTI 46-64, and AAI 30-40 were regarded as light anesthesia. Results of this meta-analysis showed that, when the BIS value was used, deep anesthesia (BIS 30-50) could reduce incidence of POCD on day 7 after surgery, compared with light anesthesia (BIS 50-65). However, when the NTI value was used, there were no differences between deep and light anesthesia. NTI values were only from 2 RCTs. The sample size was small. Furthermore, the methods used to diagnose POCD were different between these two trials. Burrow B [35] found that depth with a BIS value of 40-50 could facilitate patient rehabilitation. However, other studies showed that the time that the BIS value was less than 45 was positively related to postoperative mortality [36, 37]. Therefore, choosing an appropriate anesthetic depth that can reduce POCD incidence and facilitate postoperative rehabilitation needs to be examined.

Current results suggest that deep anesthesia can reduce incidence of POCD from 1 to 3 months after surgery. A cohort study from Ehab et al. showed that deep anesthesia could facilitate recovery of POCD from 4 to 6 weeks after surgery, especially with the ability to process

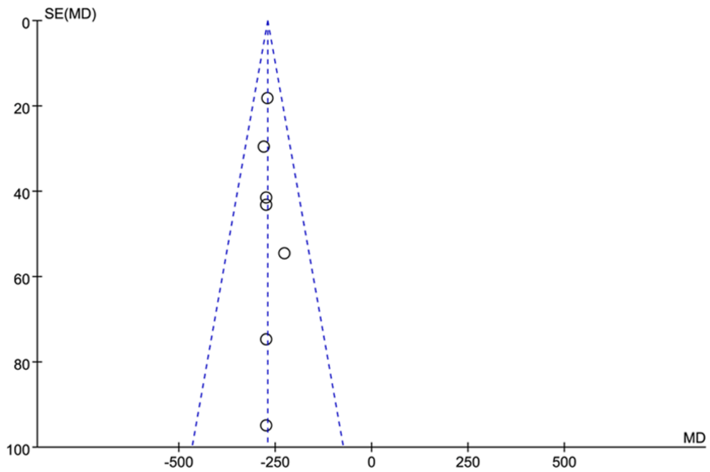

Figure 7. Funnel plot of effects of anesthetic depth on serum S100-β protein levels on postoperative 1 day.

information [7]. Aging is an independent risk factor for long-term POCD [33], but the effects of the depth of anesthesia on long-term POCD require further study.

S100-β protein is secreted from glial cells in the central nervous system. This protein has a wide range of biological functions, including protecting neurons and promoting glial proliferation and differentiation, as well as playing an important role in learning and memory. Excessive expression of serum S100-β protein can lead to inflammatory response and dysfunction of neural cells [38]. Increasing serum concentrations of S100-β protein can reflect brain injuries [11]. Current meta-analysis results showed that deep anesthesia could attenuate the postoperative elevation of serum S100-β protein levels, which may be closely related to development of POCD.

The current study had some limitations. The methods for POCD diagnosis were not uniform in these included trials. Devices monitoring the depth of anesthesia, ages of the patients, surgical procedures, and anesthetic agents were also different, to some degree, in these trials. This may have affected short- or long-term POCD results. In addition, the sample size was not large enough. Prospective randomized trials with large sample sizes should be conducted in the future.

Conclusion

Deep anesthesia can significantly reduce incidence rates of short- or long-term POCD after surgery. It may also reduce serum S100-β protein levels on postoperative day 1. These levels may be closely related to development of short- or long-term POCD.

Acknowledgements

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Disclosure of conflict of interest

None.

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References

[1] Rohan D, Buggy DJ, Crowley S, Ling FK, Gallagher H, Regan C and Moriarty DC. Increased incidence of postoperative cognitive dysfunction 24 hr after minor surgery in the elderly. Can J Anaesth 2005; 52: 137-142.

[2] Murray AM, Levkoff SE, Wetle TT, Beckett L, Cleary PD, Schor JD, Lipsitz LA, Rowe JW and Evans DA. Acute delirium and functional decline in the hospitalized elderly patient. J Gerontol 1993; 48: M181-186.

[3] O'Keeffe ST and Ni Chonchubhair A. Postoperative delirium in the elderly. Br J Anaesth 1994; 73: 673-687.

[4] Moller JT, Cluitmans P, Rasmussen LS, Houx P, Rasmussen H, Canet J, Rabbitt P, Jolles J, Larsen K, Hanning CD, Langeron O, Johnson T, Lauven PM, Kristensen PA, Biedler A, van Beem H, Fraidakis O, Silverstein JH, Beneken JE, Gravenstein JS. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. international study of post-operative cognitive dysfunction. Lancet 1998; 351: 857-861.

[5] Hartholt KA, van der Cammen TJ and Klimek M. Postoperative cognitive dysfunction in geriatric patients. Z Gerontol Geriatr 2012; 45: 411-416.

[6] Jildenstal PK, Hallen JL, Rawal N, Gupta A and Berggren L. Effect of auditory evoked potential-guided anaesthesia on consumption of anaesthetics and early postoperative cognitive dys-

function: a randomised controlled trial. Eur J Anaesthesiol 2011; 28: 213-219.

[7] Farag E, Chelune GJ, Schubert A and Mascha EJ. Is depth of anesthesia, as assessed by the Bispectral Index, related to postoperative cognitive dysfunction and recovery? Anesth Analg 2006; 103: 633040.

[8] Radtke FM, Franck M, Lendner J, Kruger S, Wernecke KD and Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth 2013; 110 Suppl 1: i98-105.

[9] Steinmetz J, Funder KS, Dahl BT and Rasmussen LS. Depth of anaesthesia and post-operative cognitive dysfunction. Acta Anaesthesiol Scand 2010; 54: 162-168.

[10] Kim JS, Yoon SS, Kim YH, Ryu JS. Serial measurement of interldukin-6, trans forming growth factor-beta, and S-100 protein in patients with acute stroke. Stroke 1996; 27: 1553-1557.

[11] Peng L, Xu L and Ouyang W. Role of peripheral inflammatory markers in postoperative cognitive dysfunction (POCD): a meta-analysis. PLoS One 2013; 8: e79624.

[12] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009; 339: 1-34.

[13] An J, Fang Q, Huang C, Qian X, Fan T, Lin Y and Guo Q. Deeper total intravenous anesthesia reduced the incidence of early postoperative cognitive dysfunction after microvascular decompression for facial spasm. J Neurosurg Anesthesiol 2011; 23: 12-17.

[14] Chan MT, Cheng BC, Lee TM, Gin T and Group CT. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol 2013; 25: 33-42.

[15] Jin LC. The effects of different anesthesia management modes on the S100-β protein level and the cognitive function of the elderly patients after operation. Chin J Lab Diagn 2014; 18: 912-915.

[16] Bo H. Effect of depth of anesthesia on early postoperative cognitive function of the elderly patients. J Clin Res 2012; 29: 157-159.

[17] Juan LL. Impact of different anesthesia depth on cognitive function of elderly patients after general anesthesia. Journal of Clinical Medical Literature 2015; 2: 1470-1471.

[18] Ling LL, Ying LX, Tao C, Juan G, Yi L and Qiang Z. The influence of different depth of anesthesia on cognitive function and serum S100-βprotein level of elderly patients after operation. Med J West China 2015; 2: 1352-1358.

[19] Hui Z, Jiang FS, Qun S and Jun WS. Effects of different depth of anesthesia in elderly patients with postoperative cognitive dysfunction occur. China Medicine and Pharmacy 2014; 4: 86-88.

[20] Hong Z, Xin W, Liang CY, Xue LA, Bin LW, Jing H and Qun ZZ. Effect of different depth of sevoflurane inhalation anesthesia on postoperative cognitive function in senile patients after laparoscopic surgery. China Medical Herald 2015; 12: 105-108.

[21] Cai LX, Bin XK, Gang C, Gang WT, Fu C, Jie ZX, Ping LY, Hong ZX, Yan QJ, Xin Z and Qiang HQ. Related study of depth of anesthesia and postoperative cognitive function. Mu Dan Jiang Medical University 2014; 35: 94-96.

[22] Feng LR, Ying ZS and Liang ZZ. Observation and analysis effect of different anesthesia and anesthesia depth on postoperative cognitive function and S100-β protein level for elderly patients after TURP. Heilongjiang Medicine Journal 2015; 25: 357-359.

[23] An YJ. Effect of different depths of anesthesia on postoperative cognitive functionand serum S100-β level in the elderly. Chin J Mult Organ Dis Elderly 2015; 14: 775-778.

[24] Dong H and Jin YZ. Effects of different depth of anesthesia in elderly patients with postoperative cognitive dysfunction occurs. Chin J Anesthesiol 2014; 34: 251-252.

[25] Jie YY. Effects of different depth of anesthesia on the postoperative cognitive function and S-100 B protein levels in elderly patients. He Bei Medical University 2013; 7-22.

[26] Qing WD, Pei XJ, Qin D, Yue W and Lan XC. Effects of deferent depth of postoperative cognitive function in elderly patients after abdomen surgery. Chinese and Foreign Medical Research 2015; 32: 40-41.

[27] Fang S. Effect of different depth of general anesthesia on postoperative cognitive function in elderly patients. Chinese Baby 2014; 17: 1-3.

[28] Yin K, Jiao DL, Dong ZG, Hong L, Feng LH and Yun TK. Effects of different depths of anesthesia on early postoperative cognitive days function in elderly patients undergoing elective laparoscopic surgery for colorectal cancer. J Clin Anesthesiol 2013; 29: 734-737.

[29] Niang L. Effect of different depths of anesthesia on early postoperative cognitive dysfunction in elderly patients undergoing elective laparoscopic surgery for colorectal cance. Contemporary Medicine 2015; 21: 82-83.

[30] Jia C, Xuan QC, Xiu TG, Tong W, Chang L, Ming DK, Bin DJ, Bin DJ, Lian GQ and Wen OY. Effects of depth of anesthesia on postoperative cognitive function and HMG B1 in peripheral blood in middle-aged and elderly patients. J Clin Anesthesiol 2015; 31: 38-42.

[31] Nan D, Yong P, Jin JJ and Xia ZY. Effects of postoperative cognitive function in the different anesthesia depth for laparoscopic gastrointestinal operation elderly. J Clin Pathol Res 2015; 35: 1932-1936.
[32] Liang CY, Xue LA, Xue LA, Bin LW, Hong Z and Jing H. Influence of sevoflurane of different concentrations for anesthesia on elderly patients' cognitive function after laparoscopic surgery. Hannan Med 2015; 26: 1604-1606.
[33] Johnson T, Monk T, Rasmussen LS, Abildstrom H, Houx P, Korttila K, Kuipers HM, Hanning CD, Siersma VD, Kristensen D, Canet J, Ibañaz MT, Moller JT; ISPOCD2 Investigators. Postoperative cognitive dysfunction in middle-aged patients. Anesthesiology 2002; 96: 1351-1357.
[34] Newman MF, Kirchner JL, Phillips-Bute B, Gaver V, Grocott H, Jones RH, Mark DB, Reves JG, Blumenthal JA; Neurological Outcome Research Group and the Cardiothoracic Anesthesiology Research Endeavors Investigators. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001; 344: 395-402.
[35] Burrow B, McKenzie B and Case C. Do anaesthetized patients recover better after Bispectral Index Monitoring? Anaesth Intensive Care 2001; 29: 239-245.
[36] Monk TG, Saini V, Weldon BC, Sigl JC. Anesthetic management and one-year mortality after noncardiac surgery. Anesth Analg 2005; 100: 4-10.
[37] Kertai MD, Pal N, Palanca BJ, Lin N, Searleman SA, Zhang L, Burnside BA, Finkel KJ, Avidan MS; B-Unaware Study Group. Association of perioperative risk factors and cumulative duration of low bispectral index with intermediate-term mortality after cardiac surgery in the B-Unaware Trial. Anesthesiology 2010; 112: 1-11-6-1127.
[38] Kleindienst A, Hesse F, Bullock MR and Buchfelder M. The neurotrophic protein S100B: value as a marker of brain damage and possible therapeutic implications. Prog Brain Res 2007; 161: 317-325.