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The use of peripheral nerve block decrease incidence of postoperative cognitive dysfunction following orthopedic surgery: A systematic review and meta-analysis

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Abstract

Background Postoperative neurocognitive disorders (PNDs) frequently occur following orthopedic surgery and are closely associated with adverse prognosis. PNDs are an emerging concept that includes both postoperative cognitive dysfunction (POCD) and postoperative delirium (POD). The prevention of combined use of peripheral nerve block (PNB) and general anesthesia (GA) on POCD and/or POD incidence following orthopedic surgery remains unknown. We aimed to investigate the effect of this combined anesthesia method on POCD/POD incidence after orthopedic surgery, compared with GA.

Methods The databases of PubMed, Web of Science, Embase via Ovid, and the Cochrane Central Register of Controlled Trials were searched for all available randomized controlled trials (RCTs). The incidence of POD/POCD was the primary outcome. Continuous and dichotomous outcomes are represented as standardized mean differences [SMD, 95% confidence interval (CI)] and risk ratios [RR, 95%CI], respectively.

Results Meta-analysis of twelve RCTs with a total of 1488 patients revealed that compared with GA, PNB plus GA decreased the incidence of POCD (RR: 0.58, 95%CI: 0.35 to 0.95, $P = 0.03$, $I^2 = 0\%$), while the incidence of POD had no significant difference (RR: 0.87, 95%CI: 0.54 to 1.40, $P = 0.57$, $I^2 = 67\%$). Compared with GA alone, a significant decrease of intraoperative and postoperative opioid consumption (SMD: -1.54, 95%CI: -2.26 to -0.82, $P < 0.0001$, $I^2 = 89\%$; SMD: -7.00, 95%CI: -9.89 to -4.11, $P < 0.00001$, $I^2 = 99\%$) and postoperative nausea and vomiting incidence (RR: 0.16, 95%CI: 0.06 to 0.44, $P = 0.0004$, $I^2 = 0\%$) was found with PNB plus GA.

Conclusions The combined use of PNB and GA decreases the incidence of POCD but not POD following orthopedic surgery.

Trial registration The protocol of this study was registered with PROSPERO (Registration Number: CRD42022366454).

Keywords Peripheral nerve block, Combined anesthesia, Postoperative neurocognitive disorders, Orthopedic surgery

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Background

Postoperative neurocognitive disorders (PNDs) are the most common postoperative complications in elderly surgical patients [1]. PNDs is a comprehensive term that includes postoperative cognitive dysfunction (POCD) and postoperative delirium (POD) [2–4]. POD is an acute change of mental status typically reported during 2–5 days after surgery, while POCD manifests a chronic cognitive impairment usually detected from several days to years postoperatively [5]. Since the PNDs is inclusive of POCD and POD, and POD and/or POCD were closely studied in the trials reported previously, the terminology of POD and POCD will be used in this meta-analysis. Both of these neurological complications following surgery are closely associated with the increasing risk of long-term cognitive dysfunction and dementia, increased mortality and morbidity, and increased impendence, which impose a huge economic and social burden on society [6, 7].

A cohort study suggested that the presence of POCD/POD would result in an average increase in payments of $17,275 within 1 year after surgery [1]. Therefore, it is important to figure out a better anesthetic strategy to reduce their incidence. Increasing age, poor education, frailty, pre-existing cognitive dysfunction, specific types of surgery, preoperative cognitive function, and perioperative opioid use are the common risk factors of POCD/POD [8, 9].

Orthopedic surgery is one of the most common surgeries, and an increasing number of old-aged patients are undergoing various kinds of orthopedic surgeries. Globally, healthcare is facing a substantial increase in orthopedic surgery patients, with approximately 22.3 million surgeries in 2017 and an annual growth rate of 4.9%. There are many complications after orthopedic surgery, and POCD/POD is one of the most common. The reported incidence of POD in patients with orthopedic surgery ranges from 4.5 to 41.2% [10–12]. The incidence of POCD varies according to the patient population, surgery duration, operation type, and anesthetic management, which was approximately 30% in orthopedic surgery in some reports [3, 13–16].

The risk of POCD or POD was found to be associated with perioperative opioid consumption and not effective pain relief [17–20]. Thus, it is essential to reduce the use of opioids and provide effective pain management. As an essential part of multimodal analgesia, peripheral nerve block (PNB) has been popularly used due to its effective pain management and at the same time lowering opioid consumption compared with general anesthesia (GA) [21–23]. Recent studies indicated that the application of PNB reduced the incidence of POCD/POD and improved postoperative cognitive function [24–26]. Nevertheless, inconsistent results were also reported [27].

Therefore, this meta-analysis was designed to identify studies with patients over 18 years old who underwent orthopedic surgery with PNB plus GA, and to explore the effect of this combined anesthesia on POCD/POD incidence. We aimed to provide guidance for the decision-making for better preventive strategies tackling POCD and POD occurrence.

Methods

This meta-analysis was performed based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline [28]. This study protocol was registered in the PROSPERO database (Registration Number: CRD42022366454).

Search strategy

The database, including PubMed, Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL), and Embase via Ovid, were searched with keywords of peripheral nerve block, postoperative neurocognitive outcomes, and orthopedics by two researchers independently to gain full access to relevant studies from inception to December 2022, updated to November 2023. The detailed search strategies are presented in Supplementary File 1. There were no language restrictions.

Selection criteria and study design

The randomized controlled trials were searched, which investigated the effect of PNB plus GA on postoperative cognitive function undergoing orthopedic surgery following the PICOS (Participants, Interventions, Comparisons, Outcomes, and Study design) principle. The key selective principle included (P) adults undergoing orthopedic surgery (aged $\geq$ 18 years); (I) Anesthesia management strategy: PNB + GA; (C) Anesthesia management strategy: GA; (O) the incidence of POCD/POD; (S) randomized controlled trials (RCTs).

The primary outcome of this meta-analysis was the comparative incidence of POD/POCD. Secondary outcomes were as follows: severity of POD or POCD (based on cognitive score), intraoperative and postoperative opioid consumptions, postoperative pain score, incidence of postoperative nausea or vomiting, and length of hospital stay.

Data extraction and assessment for risk of bias

Data extraction and quality evaluation were performed independently by two authors, who double-checked for data consistency and completeness. Any disagreements and quality assessment matters were handled by discussion or reviewed by a third author. After removing the duplicates, the preliminary quality of studies according to the title and abstract was assessed. The final assessment was then done through reading the full text. The data and information was extracted including as follows: first author, year of publication, sample size, patient characteristics, American Society of Anesthesiologists (ASA) classification, type of surgery, duration of surgery, duration of anesthesia, type of nerve block, type of PNDs, incidence of POCD/POD, timing and method of cognitive assessment, severity of cognitive dysfunction, intraoperative and postoperative opioid consumptions, postoperative pain score, time to first postoperative analgesic, postoperative occurrence of nausea or vomiting, and length of hospital stay.

Two researchers independently used the Cochrane risk of bias tool (RoB 2.0) to evaluate the risk of bias for the included studies. Each study was assessed from seven fields: bias sourced from the randomization process, bias due to deviation from the intended intervention, bias due to missing outcome data, bias in outcome measures, and bias in the selection of reported outcomes [29]. Each section was categorized into 'Low,' 'High' risk of bias, or "Some concerns." If necessary, the third investigator would join the discussions to resolve the disagreement. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria was applied to evaluate the quality of evidence [30].

Data synthesis and statistical analysis

Data synthesis and meta-analysis were performed with Review Manager 5.4 software (The Cochrane Library, Oxford, England). Continuous and dichotomous outcomes are represented by standardized mean differences [SMD, 95% confidence interval (CI)] and risk ratios [RR, 95%CI], respectively. In the original protocol, dichotomous outcomes were intended to be represented by the odds ratios [OR, 95%CI]. However, based on the opinions of statisticians and previous literature, it was found that RR was more suitable for the purpose of this article. Therefore, we adopted RR to present dichotomous outcomesduring the data processing. Heterogeneity was tested using the I^2 index ($I^2 > 50\%$ indicates significant heterogeneity) [31]. If there is significant heterogeneity of the data, a random effects model was applied, otherwise, a fixed effects model was used.

If a significant heterogeneity existed, subgroup analysis was performed based on the type of surgery and PNB. We performed subgroup analysis when there were at least two studies in each subgroup. Sensitivity analysis was performed by taking away one study at one time repetitively. The meta-analysis was considered to be reliable and stable if there was no change in the final pooled results after removing one study.

Results

Literature search

A total of 3528 studies were found according to the search strategies. 804 articles were excluded due to duplicate, and 2619 studies were excluded according to the inclusion criteria after reading the titles and abstracts. The remaining 105 articles were downloaded, and we read the full text for further screening. Finally, twelve RCTs with a total of 1488 cases were included in this meta-analysis [12, 24, 27, 32–40] (Fig. 1).

Study characteristics and quality assessment

The baseline characteristics of these eligible studies are presented in Table 1. POD was assessed in five studies using the Nursing Delirium Screening Scale (Nu-Desc) [27, 32] or the Confusion Assessment Method (CAM) [24, 35]. POCD was assessed in nine studies using the Mini-mental State Examination (MMSE) [27, 33–37, 39, 40], Montreal Cognitive Assessment (MoCA) [39], Postoperative Quality Recovery Scale (PQRS) [36] or Short Portable Mental State Questionnaire (SPMSQ) [12]. POD/POCD were assessed on the 1^{st} -7^{th} day postoperatively. The types of surgery included hip fracture surgery, knee arthroplasty, and hip arthroplasty. PNB applicated intraoperatively included femoral nerve block, sciatic nerve block, fascia iliac compartment block, lumbosacral plexus block and lumbar plexus nerve block. The evaluation of methodological quality was performed based on RoB 2.0, and each domain was determined as low bias risk, high bias risk, or unclear bias risk (Fig. 2).

Outcomes of the incidence of POCD/POD

Combined use of PNB and GA did not reduce the incidence of PNDs compared with the control group (RR: 0.84, 95%CI: 0.62 to 1.15, $P=0.28$, $I^2=59\%$) [12, 24, 27, 32–35, 37, 38, 40] (Fig. 3). There was no significant publication bias regarding the effect of combined anesthesia on PNDs by visual inspection of funnel plots (Supplementary file 2). The combined results remained reliable by removing one study at one time from the included studies for sensitivity analysis (Supplementary file 3). The quality was moderate according to the GRADE criterion (Supplementary file 4). However, the incidence of POCD as a sole outcome indicator was reduced in the intervention group, compared with control group (RR: 0.58, 95%CI: 0.35 to 0.95, $P=0.03$, $I^2=0\%$) [33, 34, 38](Fig. 4A). The quality of evidence was moderate (Supplementary file 4). The incidence of POD as a sole outcome indicator was not reduced by PNB plus GA (RR: 0.87, 95%CI: 0.54 to 1.40, $P=0.57$, $I^2=67\%$) [24, 27, 32, 35, 37, 40] (Fig. 4B). The quality of evidence was low (Supplementary file 4).

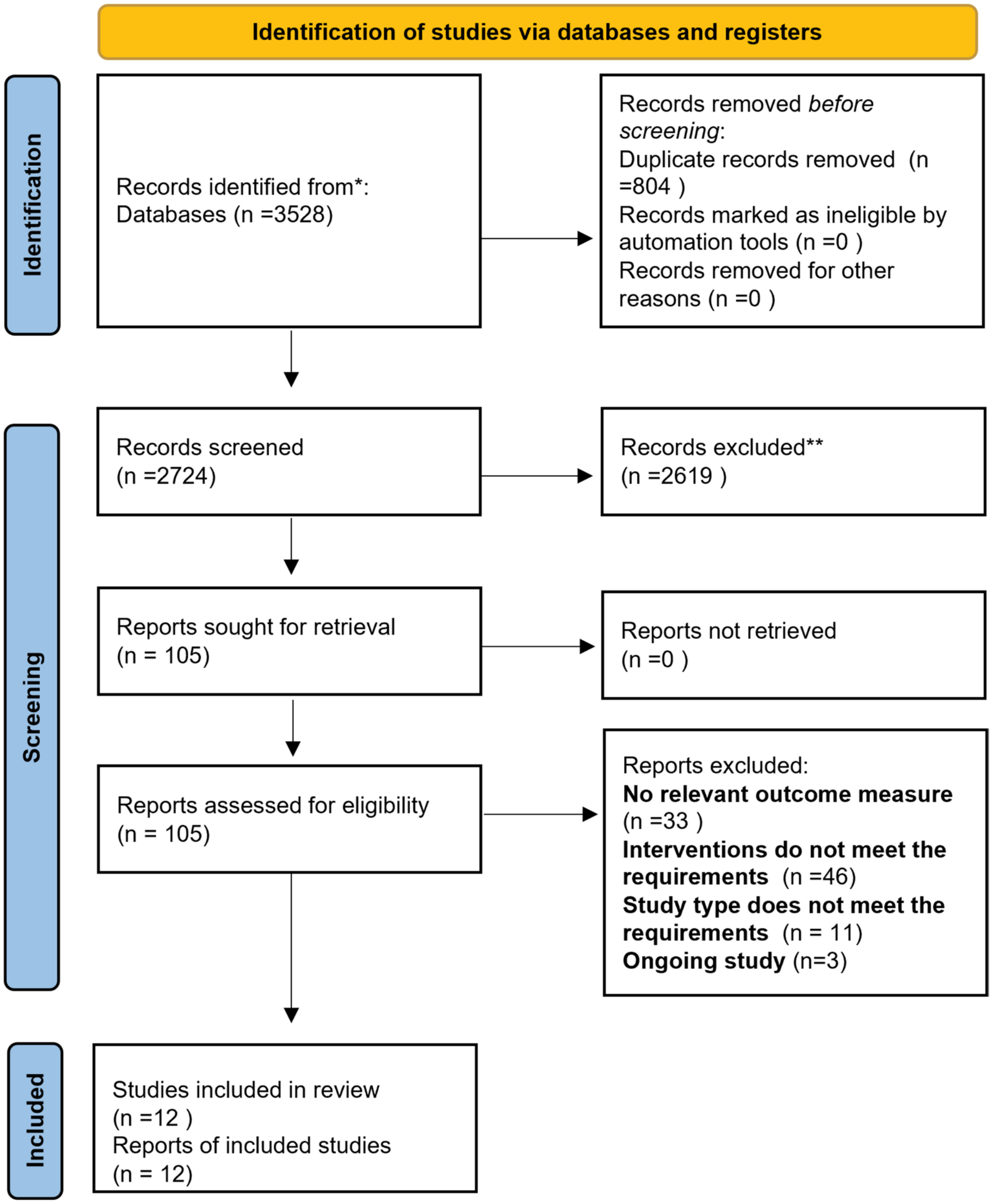

Fig. 1 Flow diagram of the study selection process

In the subgroup analysis based on surgery type, combined anesthesia could reduce the incidence of PNDs of knee arthroplasty compared with the control group (RR: 0.28, 95%CI: 0.10 to 0.82, $P=0.02$, $I^2=0\%$) [32, 33] (Supplementary file 5).

Secondary outcomes between the combined anesthesia group and general anesthesia group

MMSE scores

Postoperative MMSE scores were higher in patients using PNB plus GA ($P=0.001$) [27, 33, 35, 37–40] (Table 2; Supplementary file 6). The quality of evidence was low (Supplementary File 4).

Table 1 Characteristics of included trials

First author	Year	Age (EG vs. CG)	Sample size (EG /CG)	Cognitive score pre-surgery (EG/CG)	Surgery type	Anesthesia method in EG	Anesthesia method in CG	PNDs type	Assessment time	Assessment methods
Anna Unneby	2021	83.7 ± 7.1 vs. 84.4 ± 6.4	236(116/120)	/	HFS	FNB plus GA	GA	Delirium, POCD	Day 3–5 after surgery	Nu-DESC, MMSE
Yuxia Jiao	2019	73.44 ± 4.53 vs. 75.29 ± 5.28	60(30/30)	MoCA: 27.44 ± 1.09/27.57 ± 1.13	KA	FNB plus GA	GA	Delirium	PACU	Nu-DESC
Rui Fan	2017	72.3 ± 4.3 vs. 72.9 ± 4.5	65(35/30)	MMSE: 28.6 ± 1.4/28.1 ± 1.7	KA	FNB + SNB plus GA	GA	POCD	Day 0–3 after surgery	MMSE
Hongling Nie	2015	73.6 ± 2.1 vs. 68.2 ± 2.1	106(53/53)	/	HFS	FICB plus GA	GA	Delirium	Day 0–2 after surgery	CAM
Pär Wennberg	2019	84.6 ± 6.7 vs. 84.9 ± 7.7	127(66/61)	/	HFS	FICB plus GA	GA	Cognitive impairment	Day 1 after surgery	SPMSQ
V. Perrier	2010	82 ± 10 vs. 83 ± 6	65(31/34)	/	HS	FICB plus GA	GA	POCD	Day 1–2 after surgery	MMSE
Bin Mei	2017	75 ± 6 vs. 74 ± 7	136(68/68)	MMSE: 25.4 ± 1.6/25.3 ± 1.1	HA	LSNB plus GA	GA	Delirium, POCD	Day 3,7 after surgery	CAM, MMSE
Chen Chen	2017	70 (65 to 73) vs. 71 (64 to 75)	92(46/46)	MMSE: 26 (25 to 27)/26 (24 to 28)	KA/HA	KA: FNB + SNB plus GA, HA: LPNB + SNB plus GA	GA	Delirium, POCD	Day 7 after surgery	MMSE
Jing Li	2018	71.6 ± 7.2 vs. 68.3 ± 8.5	60(30/30)	MMSE: 27.4 ± 1.9/27.2 ± 1.7	HA	LPNB plus GA	GA	POCD	Day 1,3,7 after surgery	MMSE
Yan-hong Guo	2017	65.86 ± 7.79 vs. 66.31 ± 7.46	70(35/35)	MMSE: 27.44 ± 3.15/27.62 ± 3.09	HA	LPNB + SNB plus GA	GA	POCD	Day 1,3 after surgery	MMSE, MoCA
JunLe Liu	2014	65–75year: 61.9% vs. 63.0%; 76–85year: 29.5% vs. 29.6%; 86–89year:8.6% vs. 7.4%	213(105/108)	/	KA	LPNB + SNB plus GA	GA	Cognitive impairment	Day 1,3,7 after surgery	PQRS
Yao Xiao	2023	70.23 ± 6.6 vs. 68.80 ± 6.24	191(97/94)	MMSE:23.60 ± 3.06/23.23 ± 2.82	HS	LPNB plus GA	GA	Delirium	Day 1,2,3 after surgery	MMSE

EG Experiment group, *CG* Control group, *HFS* Hip fracture surgery, *KA* Knee arthroplasty, *HA* Hip arthroplasty, *HS* Hip surgery, *FNB* Femoral nerve block, *SNB* Sciatic nerve block, *FICB* Fascia iliaca compartment block, *LSNB* Lumbosacral plexus block, *LPNB* Lumbar plexus nerve block, *GA* General anesthesia, *POCD* Postoperative cognitive dysfunction, *MMSE* Mini-mental State Examination, *Nu-DESC* Nursing Delirium Screening Scale, *CAM* Confusion Assessment Method, *SPMSQ* Short Portable Mental State Questionnaire, *PQRS* Post-operative quality recovery scale, *MoCA* Montreal Cognitive Assessment. The data was expressed as follows: mean ± SD, median(interquartile range)

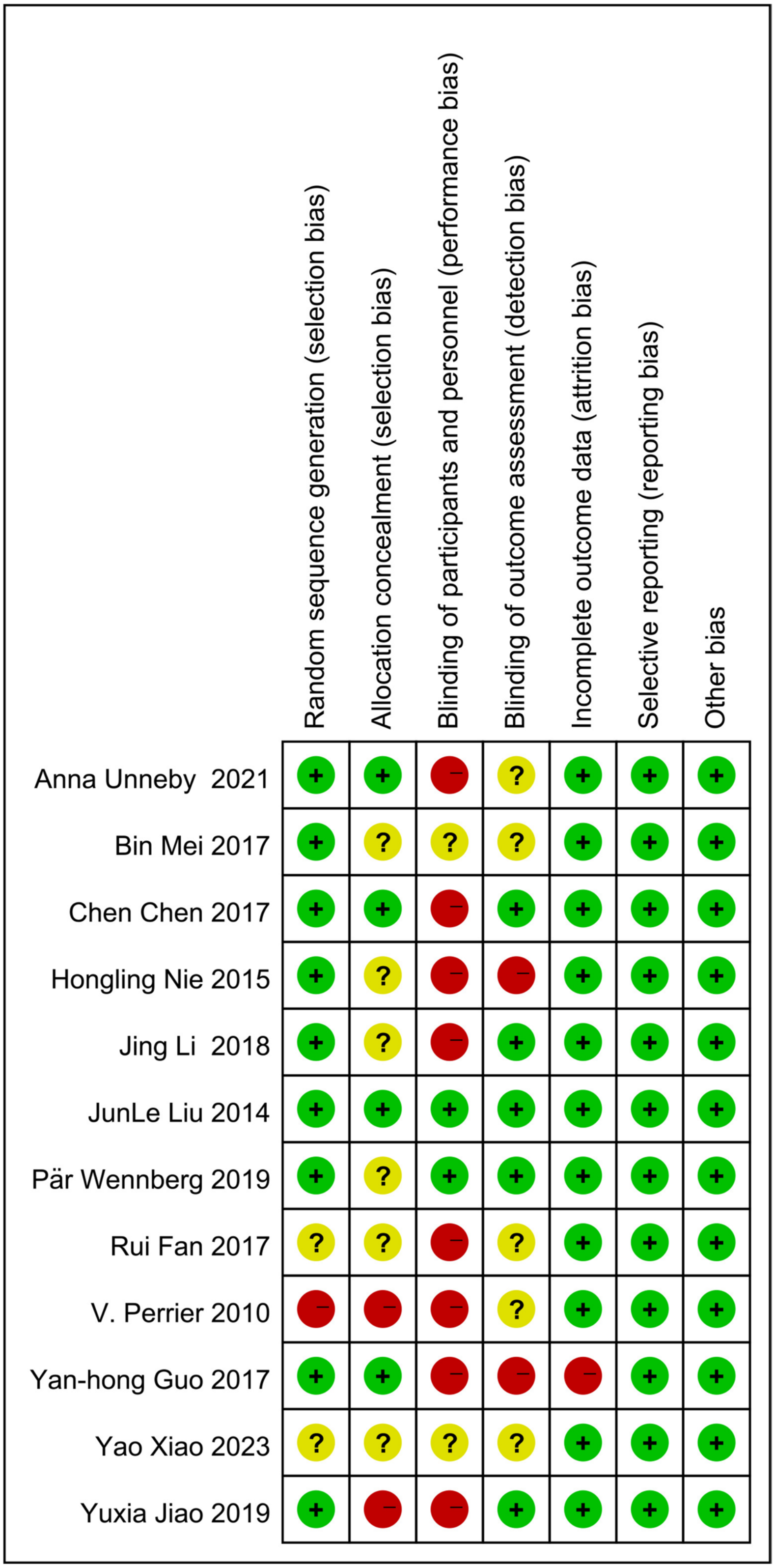

Fig. 2 Risk of bias of the included randomized controlled trials (+: low risk, –: high risk, ?: unclear risk)

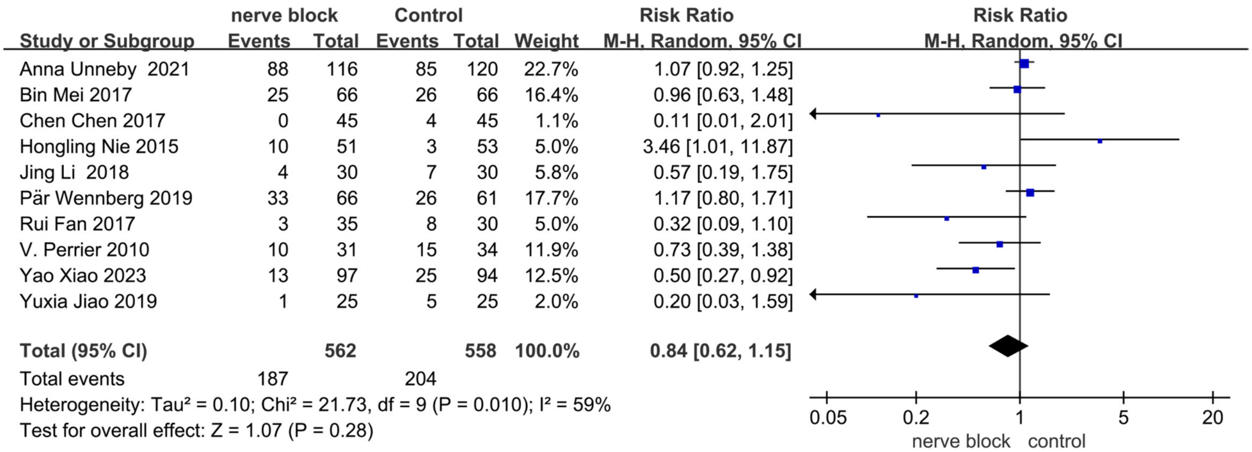

Fig. 3 Forest plot for the incidence of POCD/POD

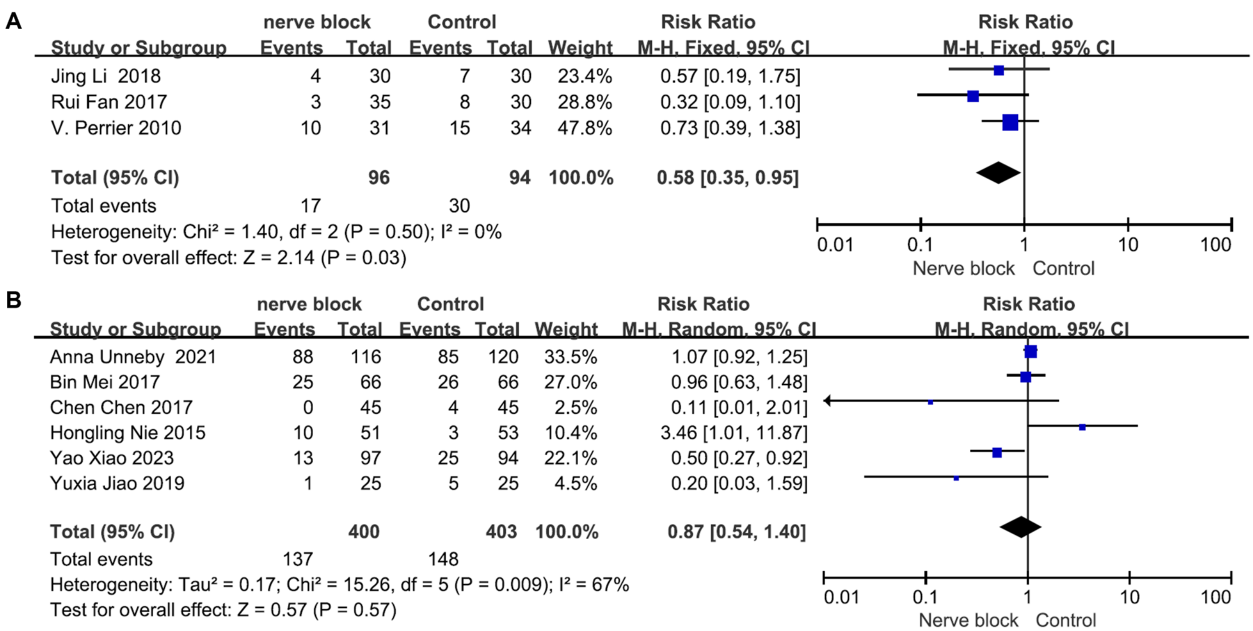

Fig. 4 Forest plot for the incidence of POCD (A) and POD (B)

Table 2 The meta-analysis of secondary outcomes

Outcomes	Studies included	I^2	SMD or OR (95%CI)	*P*
1. MMSE scores	7	75%	0.47 (0.18 to 0.75)	0.001
2. Intraoperative opioid consumption	3	89%	-1.54 (-2.26 to -0.82)	< 0.0001
3. postoperative opioid consumption	4	99%	-7.00 (-9.89 to -4.11)	< 0.00001
4. postoperative pain scores	6	98%	-0.98 (-2.24 to 0.29)	0.13
5. Postoperative nausea or vomiting	4	0%	0.16 (0.06 to 0.44)	0.0004
6. Length of hospital stay	3	94%	0.31 (-0.49 to 1.11)	0.45

SMD Standardized mean difference, *OR* Odds Ration, *MMSE* Mini-mental State Examination

Opioid consumption

Among the twelve studies included in this meta-analysis, three studies compared the intraoperative opioid consumption, and showed that the intraoperative opioid consumptions were less in the combined anesthesia group than in the control group, with a statistically significant difference (SMD: -1.54, 95%CI: -2.26 to -0.82, $P<0.0001$, $I^2=89\%$) [34–36] (Table 2; Supplementary file 7). Four studies compared postoperative opioid consumption between the two groups and showed a statistically significant difference with less postoperative opioid consumption in the PNB plus GA group than in the control group (SMD: -7.00, 95%CI: -9.89 to -4.11, $P<0.00001$, $I^2=99\%$) (Table 2; Supplementary file 8). however, the heterogeneity was high. And the quality of evidence was moderate [24, 34–36] (Supplementary file 4).

Postoperative pain scores

Five studies assessed the patients' pain scores postoperatively and showed that there was no significant difference between the two groups (SMD: -0.98, 95%CI: -2.24 to 0.29, $P=0.13$, $I^2=98\%$) [27, 33–35, 38, 40] (Table 2; Supplementary file 9). The quality of evidence was low (Supplementary File 4).

Postoperative nausea or vomiting

Four studies compared the incidence of postoperative nausea or vomiting between the two groups and showed a statistically significant difference with a lower incidence of postoperative nausea or vomiting in the combined anesthesia group compared to the control group (RR: 0.16, 95%CI: 0.06 to 0.44, $P=0.0004$, $I^2=0\%$) [24, 33, 38, 39](Table 2; Supplementary file 10). The quality of evidence was moderate (Supplementary File 4).

Length of hospital stay

Three studies focused on the length of hospital stay and found no significant difference between the two groups (SMD: 0.31, 95%CI: -0.49 to 1.11, $P=0.45$, $I^2=94\%$) [24, 27, 35] (Table 2; Supplementary file 11). The quality of evidence was low (Supplementary File 4).

Discussion

In this meta-analysis of the effect of combined anesthesia (PNB plus GA) on POCD/POD incidence, our data indicated that when comparing with the GA group, PNB plus GA reduced the incidence of POCD in patients undergoing orthopedic surgery, while the incidence of POD was not significantly different. Besides, combined anesthesia was associated with low intraoperative and postoperative opioid consumption and a lower incidence of postoperative nausea or vomiting, while the scores of postoperative pains and the length of hospital stay did not differ significantly between groups.

Potential causes and the underlying mechanisms of POCD/POD after orthopedic surgery currently remain unclear. Previous studies demonstrated the possible link with postoperative pains [41–43]. For example, Wang Y. et al. reported that those with higher postoperative pain scores were more prone to develop POCD/POD than those with no pain [41]. Patients undergoing orthopedic surgery often experience severe pain after surgery. Therefore, effective pain relief has been recommended for preventing the occurrence of POCD/POD. However, both intraoperative and postoperative opioid consumption are recognized as risk factors for POCD/POD [44–46]. Many observational studies found a positive association between opioid consumption and the risk of POCD/POD [45, 46]. Although PNB is known to reduce intraoperative and postoperative opioid use and is also a reliable measure of pain control, its effectiveness for prophylaxis against POCD/POD remains controversial [12, 47, 48]. Given the reported merit of reducing opioid consumption and postoperative pain scores, accumulative evidence from clinical trials demonstrated that GA combined with PNB may be associated with a low risk of POCD/POD compared to GA alone [47, 48]. A previous study reported PNB as an independent protective factor against cognitive dysfunction after orthopedic surgery [48]. However, a recent RCT demonstrated that PNB did not decrease the incidence of postoperative cognitive impairment among patients undergoing orthopedic surgery [12]. Therefore, there is still a lack of sufficient evidence to support the specific role of PNB in the occurrence and development of POCD/POD when combined use with GA.

In this meta-analysis, we found that PNB plus GA reduced the incidence of POCD but not POD compared with GA alone controls. This difference may be likely due to sedation level during surgery, which is a significant risk factor for POD in patients undergoing regional anesthesia. A study conducted by Sieber et al. demonstrated that the prevalence of POD decreased with mild sedation in elderly patients undergoing hip fracture repair under spinal anesthesia compared with deep sedation [49]. However, owing to the scarcity of data, it is difficult to evaluate the effect of sedation level on the incidence of POD in patients undergoing PNB plus GA. The heterogeneity of the tools for POD assessment may influence the data quality. Interestingly, in the subgroup analyses of surgery type, PNB plus GA reduced the incidence of POCD/POD for knee arthroplasty, which warrants further study.

The reduced risk of POCD might be attributed to low intraoperative and postoperative opioid consumption in patients with combined anesthesia than that in those receiving GA alone. Moreover, PNB plus GA significantly reduced the incidence of postoperative nausea or vomiting. However, there were only three to four studies examining these outcomes with high heterogeneity. Considering the high heterogeneity and limited number of studies in our meta-analysis, further high-quality research is needed to make the outcomes more solid.

As far as we know, this is the first systematic review and meta-analysis to comprehensively assess the effect of combined use of peripheral nerve block and general anesthesia on postoperative cognitive function in patients undergoing orthopedic surgery. A meta-analysis by Memtsoudis et al. [50] examined the effect of PNB on postoperative complications in adults after hip and knee arthroplasty, which did not consider other types of orthopedic surgery. Another systematic review and meta-analysis conducted by Kim et al. [51] discussed the effect of regional nerve block on POD after hip fracture surgery. Similarly, other forms of PNDs and other types of orthopedic surgery were not included. In our meta-analysis, we comprehensively consider the PNDs types and surgery types to make conclusions as rigorous as possible.

There are several limitations in this meta-analysis. First, the type and dosage of general anesthetics in orthopedic surgery varied with patients among the included trials, which may contribute to the inconsistent results. Second, POD can be further divided into hypoactivity, hyperactivity, and mixed forms and we could not further investigate the impact of the PNB in these subtypes with limited studies available [52, 53]. Third, due to the high degree of heterogeneity and the exclusion of some patients who were randomized but did not receive the assigned intervention in the original studies included, the interpretation of some results should be approached with caution.

Conclusion

The current meta-analysis showed that PNB plus GA decreased the incidence of POCD but not POD and lowered opioid consumption while undergoing orthopedic surgery compared with GA alone. Due to the limited number of studies on POCD in this meta-analysis, future research with larger sample sizes and more rigorous study are needed to focus more on this outcome indicator to explore the impact of PNB combined with GA on the risk of POCD.

Abbreviations

PNDs	Postoperative neurocognitive disorders
POCD	Postoperative cognitive dysfunction
POD	Postoperative delirium
PNB	Peripheral nerve block
GA	General anesthesia
Nu-Desc	Nursing delirium screening scale
CAM	Confusion assessment method
MoCA	Montreal cognitive assessment
PQRS	Post-operative quality recovery scale
SPMSQ	Short portable mental state questionnaire

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02743-y.

Supplementary Material 1.
Supplementary Material 2.
Supplementary Material 3.
Supplementary Material 4.
Supplementary Material 5.
Supplementary Material 6.
Supplementary Material 7.
Supplementary Material 8.
Supplementary Material 9.
Supplementary Material 10.
Supplementary Material 11.
Supplementary Material 12.

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Authors' contributions
Liyun Deng: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. Bo Jiao: Methodology, Software, Formal analysis, Data curation, Writing - original draft. Jingjing Cai: Methodology, Software, Writing - original draft. Xiaolin Xu: Methodology, Writing - review & editing. Mingyuan Chen: Data curation, Writing - review & editing. Caiyi Yan: Writing - original draft, Writing - review & editing. Tao Zhu: Visualization, Supervision, Writing - review & editing. Jin Liu: Investigation, Resources, Writing - review & editing. Daqing Ma: Methodology, Writing - review & editing. Chan Chen: Conceptualization, Methodology, Writing - review & editing. All authors read and approved the final version of the manuscript.

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The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
The authors declare no competing interests.

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