



Systematic review and meta-analysis of the efficacy of general anesthesia combined with a thoracic nerve block in modified breast cancer surgery

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Background: Breast cancer is a malignant tumor disease that poses a significant threat to women's health. In recent years, the incidence of breast cancer in China has been increasing. This report aims to explore the effects of general anesthesia combined with a thoracic nerve block in modified breast cancer surgery.

Methods: A computer-based search of PubMed, Web of Science, Embase, and the Cochrane Library was performed to identify randomized controlled studies on breast cancer, general anesthesia combined with a thoracic nerve block, modified breast cancer surgery, and other breast cancer treatments. Further search criteria included postoperative pain score, postoperative morphine equivalents given 24 hours after surgery, and operation duration. After an initial selection process, the studies were evaluated using the Jadad scale and the Cochrane Handbook for Systematic Reviews of Interventions to assess their suitability for inclusion in the subsequent meta-analysis of the experimental data, which was carried out using RevMan 5.3.

Results: A total of 8 studies comprising a total of 624 patients were selected for inclusion in this report. According to the meta-analysis, the analytical structure of the thoracic nerve group and the control group had a mean difference (MD) of -1.27 [95% confidence interval (CI): -1.68 to -0.86], the structure of the statistical test was $Z=6.08$ ($P<0.00001$), the MD of the total analysis structure of morphine equivalents was -2.71 (95% CI: -4.98 to -0.44), and the statistical test structure was $Z=2.34$ ($P=0.02$).

Discussion: General anesthesia combined with a thoracic nerve block in breast cancer surgery may effectively improve postoperative pain in patients and reduce the need for analgesic drugs. However, the outcome indicators included in this study are not sufficient. It is necessary to increase both the sample size and the number of outcome indicators to provide further theoretical evidence for the subsequent application of thoracic nerve block in modified breast cancer surgery.

Keywords: General anesthesia; complex thoracic nerve block; postmastectomy pain syndrome (PMPS); modified breast cancer surgery

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Introduction

Breast cancer is an exceedingly common form of malignant tumor disease and is considered to be one of the greatest threats to women's safety and health. According to relevant data, breast cancer ranks first among all malignant tumors in women (1-3). The incidence of breast cancer in China is increasing year by year and becoming more prominent in areas with underdeveloped medical services. Early detection and treatment of breast cancer can greatly improve the survival rate of patients, and the primary treatment for early breast cancer patients is surgical resection. Postmastectomy pain syndrome (PMPS) is a chronic neuropathic pain syndrome that can occur after a mastectomy (4-6). In current cases, the syndrome produces pain that lasts for at least 3 months although it has been known to last up to 9 years. The etiology and mechanism of PMPS are still unclear. The current mainstream view is that intercostal nerve damage is caused after mastectomy, which in turn causes intercostal neuralgia. The type of surgery, radiotherapy, chemotherapy, age, perioperative treatment, and tumor size are all risk factors for PMPS (7). Some patients go on to develop PMPS, partly because they are not well-informed about the condition. Most patients do not come forward for formal diagnosis and treatment at the onset of pain, choosing instead to self-manage intense postoperative pain (8). Thus, research and awareness of postoperative complications need to be expanded in China.

Related studies have found that the occurrence of PMPS is predictable and can be effectively prevented with the timely detection and management of risk factors in clinical practice. The development of PMPS after surgery is generally influenced by several factors, and data show that PMPS is inextricably linked to the severity of acute postoperative pain (9-11). If acute postoperative pain is not treated, it is highly likely to develop into PMPS. Currently, opioid analgesics are the most frequently prescribed for the clinical treatment of PMPS. Both the analgesic effect and adverse reactions to these drugs are proportional to the dosage. If a favorable analgesic effect is to be achieved, the dosage should be increased; however, the incidence of adverse reactions, such as vomiting and respiratory depression, will also increase accordingly (12). Studies indicate that a perioperative nerve block combined with opioids can effectively lower the required dosage of the latter, reducing adverse reactions while maintaining a strong analgesic effect (13). Intercostal nerve block has the advantages of less trauma, low cost and obvious effect. The completion of puncture and drug delivery with

the assistance of ultrasound can significantly improve the success rate and safety of nerve block, and effectively reduce the occurrence of complications (14). Researchers have found that an intercostal nerve block in breast cancer surgery can have a powerful analgesic effect, effectively reducing the use of postoperative analgesic drugs and adverse reactions (15).

As medical technology has developed in recent years, thoracic nerve blocks have become more widely used for breast cancer surgery, providing the advantages of a simpler, shorter, and lower-risk operation. The thoracic type-1 nerve block was first proposed as early as 2011 (16,17) and can completely anesthetize the medial and lateral thoracic nerves, providing a good anesthetic effect on the medial side of the chest wall. In addition, a thoracic type-2 nerve block can provide axillary anesthesia, mainly with long thoracic nerve and intercostal nerve blocks. The combination of the two types of nerve block can provide good perioperative anesthesia and postoperative analgesia for patients (18,19) and constitutes an excellent treatment for acute pain in breast cancer patients.

At present, there are few systematic reviews about the effects of general anesthesia and nerve block anesthesia on postoperative analgesia and prognosis of breast cancer patients. In order to provide more research evidence. This report analyzes and explores the efficacy of general anesthesia combined with a thoracic nerve block in modified breast cancer surgery and provides a reference for the future clinical treatment and prognosis of breast cancer. We present the following article in accordance with the PRISMA reporting checklist (available at <https://dx.doi.org/10.21037/gs-21-719>).

Methods

Study identification and selection

A computer-based search of English-language databases including PubMed, Web of Science, Embase, and the Cochrane Library was carried out. The date parameter for the search was set from January 2000 to September 2020. Search terms included "general anesthesia", "compound pectoral nerve block", "postmastectomy pain syndrome", and "modified operation for breast cancer", among others.

Inclusion and exclusion criteria

For inclusion in this meta-analysis, studies were required

to have the following characteristics: (I) a focus on general anesthesia combined with a thoracic nerve block in modified breast cancer; (II) a direct or indirect evaluation of patient experience after breast cancer surgery; and (III) a sample size of at least 15 patients.

Studies were excluded in the following cases: (I) if they repeated publication of a set of data from another study; (II) if they were a review, a conference report, an experience lecture, a case report; (III) if the research was unrelated to the topic of this report; (IV) if the study did not set a control group, or if the data between the groups are not comparable; or (V) if the outcome indicators were not reported clearly and the results data were incomplete.

Quality assessment

After the initial selection, two researchers independently read the full texts of the studies and extracted any relevant information. Disagreements or disputes were resolved through discussion or with the assistance of a third investigator. The Jadad scale was used to evaluate the methodological quality of the selected studies and assessed the following parameters: (I) whether the study was a randomized trial; (II) whether the randomization method used was appropriate; (III) whether the study used double blinding; (IV) whether the double-blind method was appropriate; and (V) whether there was a description of patient withdrawals or dropouts. A yes answer received 1 point, and a no received 0 point for a total score out of 5. A score of less than 2 indicated low-quality research, while a score of greater than 2 indicated high-quality research.

Subsequently, the Cochrane Handbook for Systematic Reviews of Interventions (version 4.2.5) was used to evaluate the risk of bias in each study and assessed the following: (I) whether it was a randomized trial; (II) whether there was allocation concealment; (III) whether blind testing was used; (IV) whether the reported results were complete; (V) whether there was selective reporting of results; and (VI) whether there was any other bias.

Data extraction

The following data were extracted from the studies: (I) the name of the first author, year of publication, and evaluation results; (II) the number of study participants, experimental design, specific measures, study time, and outcome indicators; (III) the baseline data of patients; and (IV) the

indicators of feedback and research quality.

Statistical analysis

RevMan 5.3, (Cochrane Collaboration), was used for statistical data analysis. First, Peto's method was used to analyze the heterogeneity of the studies with a cutoff point of $\alpha=0.05$: when $I^2<50\%$, no heterogeneity in the literature, and the fixed effects model is used for analysis; when I^2 is greater than 50%, heterogeneity is considered to be present in literature, and the random effects model is used for analysis. The weighted mean difference (WMD) is used to represent the results of measurement data using the same unit of measurement; otherwise, the standardized mean difference (SMD) is used to represent the results. The results of counting data are expressed by relative risk (RR). All results are expressed here with 95% confidence interval (CI). A funnel plot was drawn, and the publication bias was evaluated by the symmetry of the funnel plot and concentration of literature to the midline. Sensitivity analysis was used to assess the reliability and stability of the results.

Results

Literature search results and profile analysis

A total of 1,662 records were initially retrieved from the database, and 1,207 abstracts were subsequently obtained after duplicates were eliminated. Once the two researchers had read the titles and abstracts, 385 studies that met the inclusion criteria were preselected. After a review of the full text of the studies, those that were found to be not random, repeat publications, or unavailable in full-text were excluded, and 8 studies that met the inclusion criteria were chosen for this review (20-27). A diagram of the literature retrieval process is shown in *Figure 1*, and the basic characteristics of the studies selected for this report are shown in *Table 1*.

Bias risk assessment of included literature

The bias risk assessment tool recommended by the Cochrane Handbook for Systematic Reviews of Interventions was used to evaluate the quality of the included literature, and the results are shown in *Figures 2,3*. None of the studies were found to have random sequence generation (selection bias), incomplete outcome data (selection bias), or selective

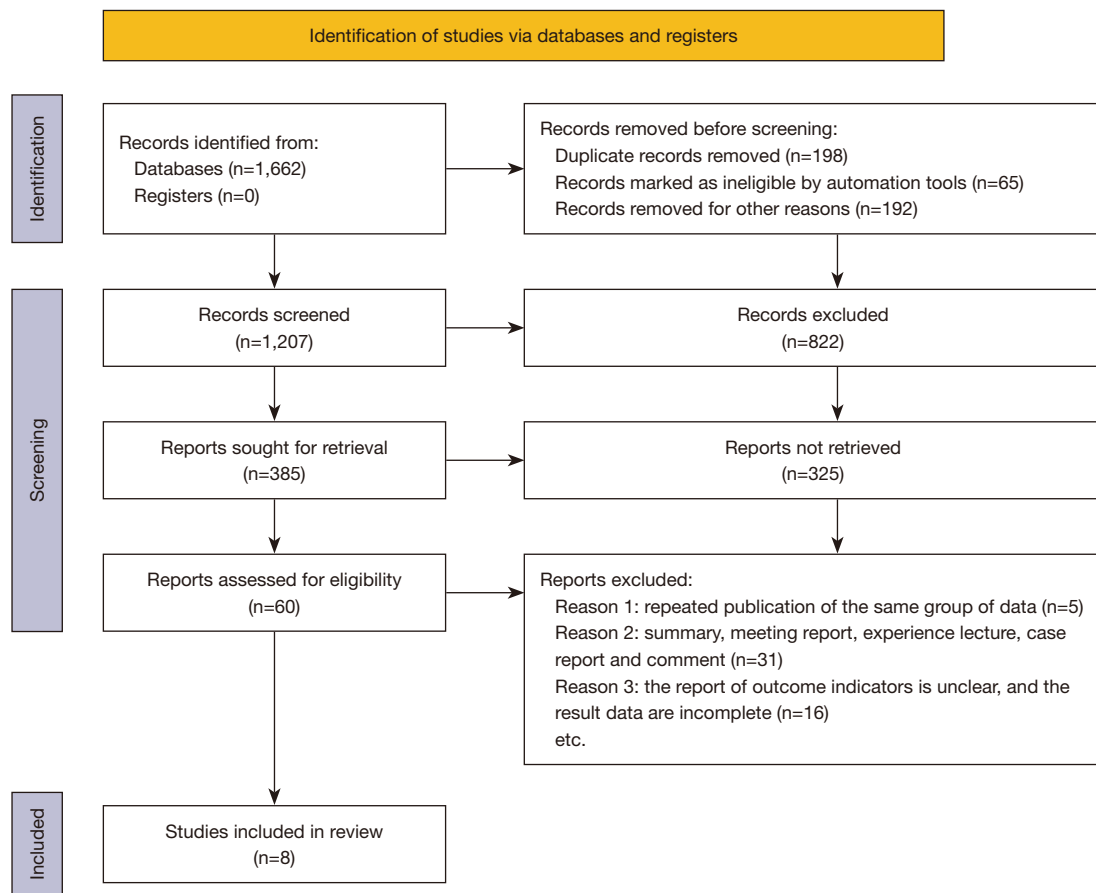


Figure 1 Schematic diagram of the literature screening process.

Table 1 Basic characteristics of the included studies

First author	Year of publication	Outcome indicators	PECS	Osteoporotic
Matsumoto M	2018	Pain, morphine equivalents	25	24
Bashandy GM	2015	Pain, morphine equivalents, operation duration	60	60
Cros J	2018	Pain	62	66
Kamiya Y	2018	Pain, morphine equivalents, operation duration	29	30
Lanier ST	2018	Pain, morphine equivalents	23	22
Kim DH	2018	Pain, morphine equivalents, operation duration	40	38
Neethu M	2018	Pain, morphine equivalents	30	30
Versyck B	2017	Pain, operation duration	45	40

PECS, pectoral nerve.

reporting (reporting bias), and the overall risk of the studies included in this report was low.

The Jadad scale was used to assess the quality of each

study, with the results shown in *Table 2*. The 8 studies included in this report all had a low risk of bias and met the requirements for subsequent analysis.

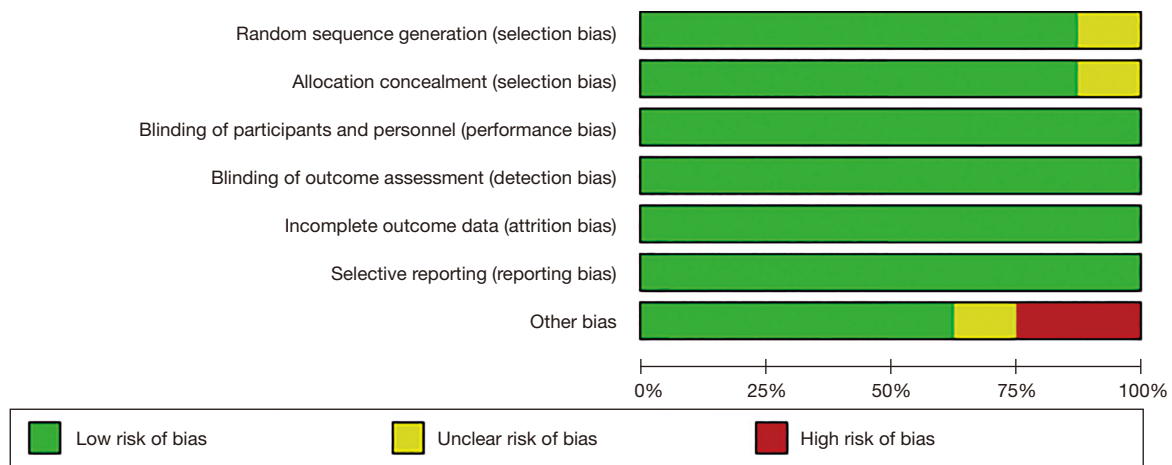


Figure 2 Bar chart of the bias risk assessment of the included literature.

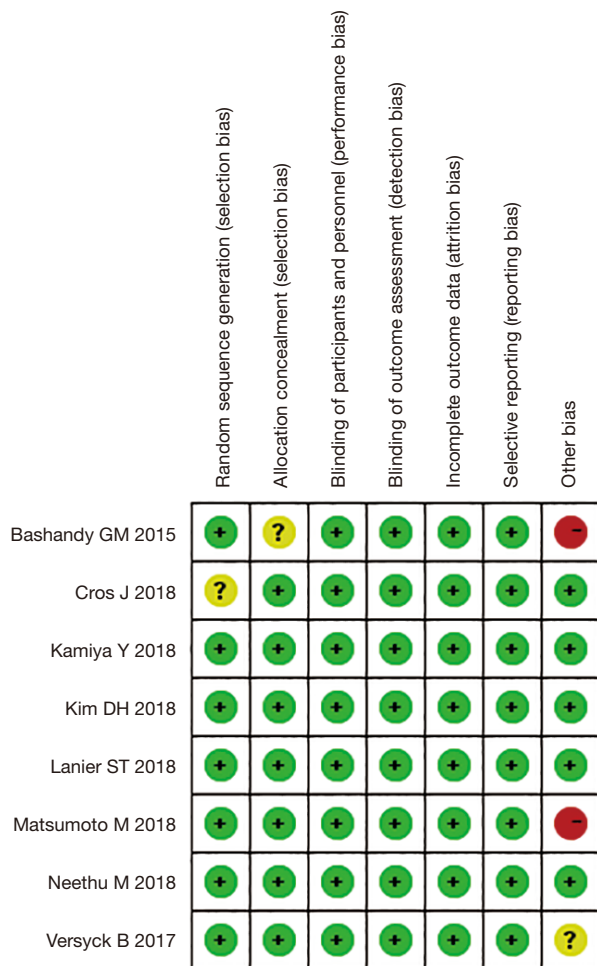


Figure 3 Summary chart of bias risk assessment for the selected studies.

Meta-analysis of pain score

All 8 studies compared the pain scores of patients in two trial groups: a thoracic nerve group, who received both a general anesthetic and a thoracic nerve block for modified breast surgery; and a control group, who underwent modified breast surgery with only a general anesthetic. The results are shown in Figure 4. The pain scores of the thoracic nerve group and the control group were heterogeneous ($I^2=71\%$; $P=0.0009$). Therefore, the random effects model was used for statistical analysis. The MD of the total pain score of the thoracic nerve group and the control group was -1.27 (95% CI: -1.68 to -0.86). The statistical test structure was $Z=6.08$ ($P<0.00001$). These results indicated that the pain scores of the two groups of patients differed significantly.

Meta-analysis of the total amount of morphine equivalents given to patients after surgery

Of the selected studies, 6 evaluated in detail the total amount of morphine equivalents given to patients after surgery. These were compared, with results shown in Figure 5. Heterogeneity between the thoracic nerve group and the control group was detected ($I^2=98\%$; $P<0.00001$). Therefore, the random effects model was used for statistical analysis. The MD of morphine equivalents used in the thoracic nerve group and the control group was -2.71 (95% CI: -4.98 to -0.44). The statistical test structure was $Z=2.34$ ($P=0.02$). These results indicated that the total amount of morphine equivalents used after surgery in the two groups

Table 2 Jadad scale assessment of the quality of the included studies

First author	Randomization	Blinding	Allocation concealment	Withdrawals and dropouts	Reason of dropouts and withdrawals	Jadad
Matsumoto M	Yes	No	NMT	MT	No	3
Bashandy GM	Yes	No	NMT	MT	Yes	3
Cros J	Yes	No	NMT	MT	Yes	3
Kamiya Y	Yes	No	NMT	MT	Yes	3
Lanier ST	Yes	No	NMT	MT	No	3
Kim DH	Yes	No	NMT	MT	No	3
Neethu M	Yes	No	NMT	MT	No	3
Versyck B	Yes	No	NMT	MT	No	3

MT, mentioned; NMT, not mentioned.

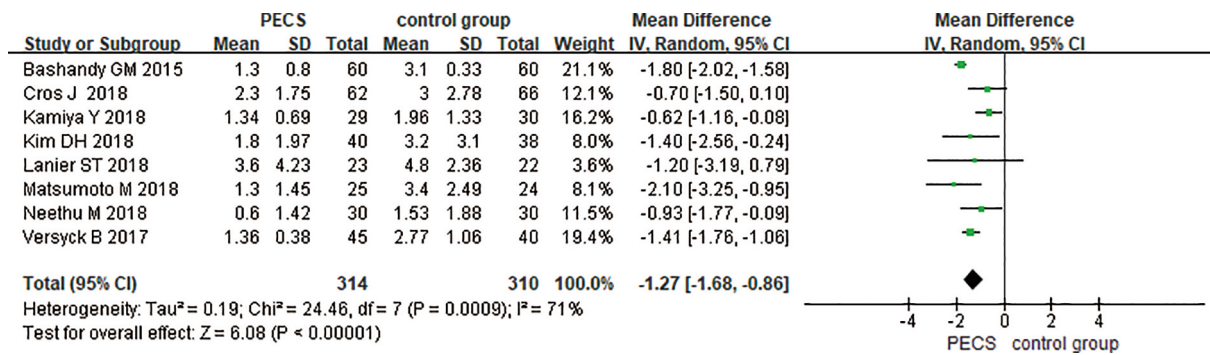


Figure 4 Forest plot of patients pain score after modified breast cancer surgery with general anesthesia combined with a PECS block. PECS, pectoral nerve.

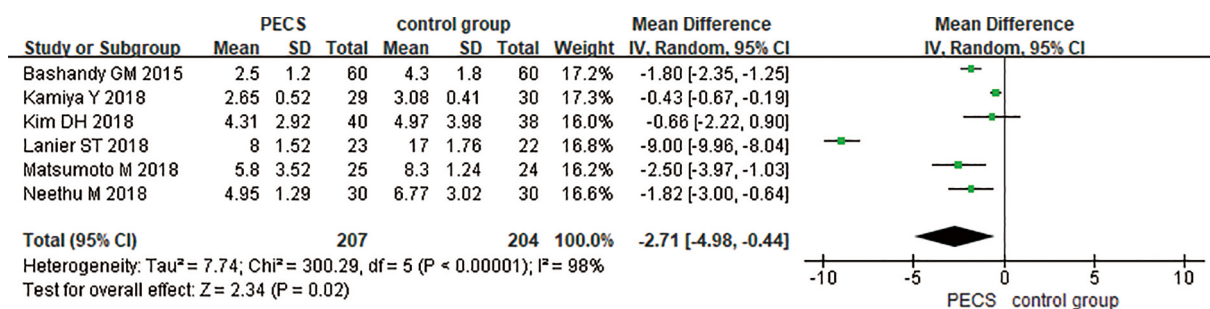


Figure 5 Forest plot of the total amount of morphine equivalents given to patients after surgery. PECS, pectoral nerve.

differed significantly.

Meta-analysis of operation duration

Of the studies included in this review, 4 provide a detailed assessment of the duration of the operation. These were

compared, with results shown in *Figure 6*. No heterogeneity was detected between the thoracic nerve group and the control group (I²=0%; P=0.71). Therefore, a fixed effects model was used for statistical analysis. The MD of operation duration of the thoracic nerve group and the control group was 2.11 (95% CI: -2.35 to 6.58). The statistical test

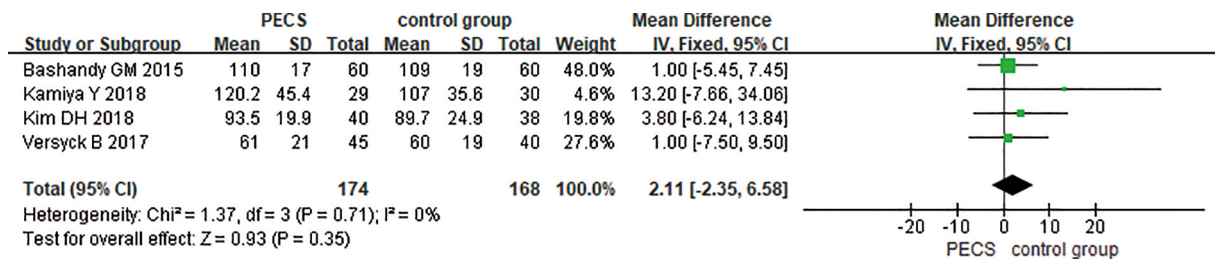


Figure 6 Forest plot of operation duration. PECS, pectoral nerve.

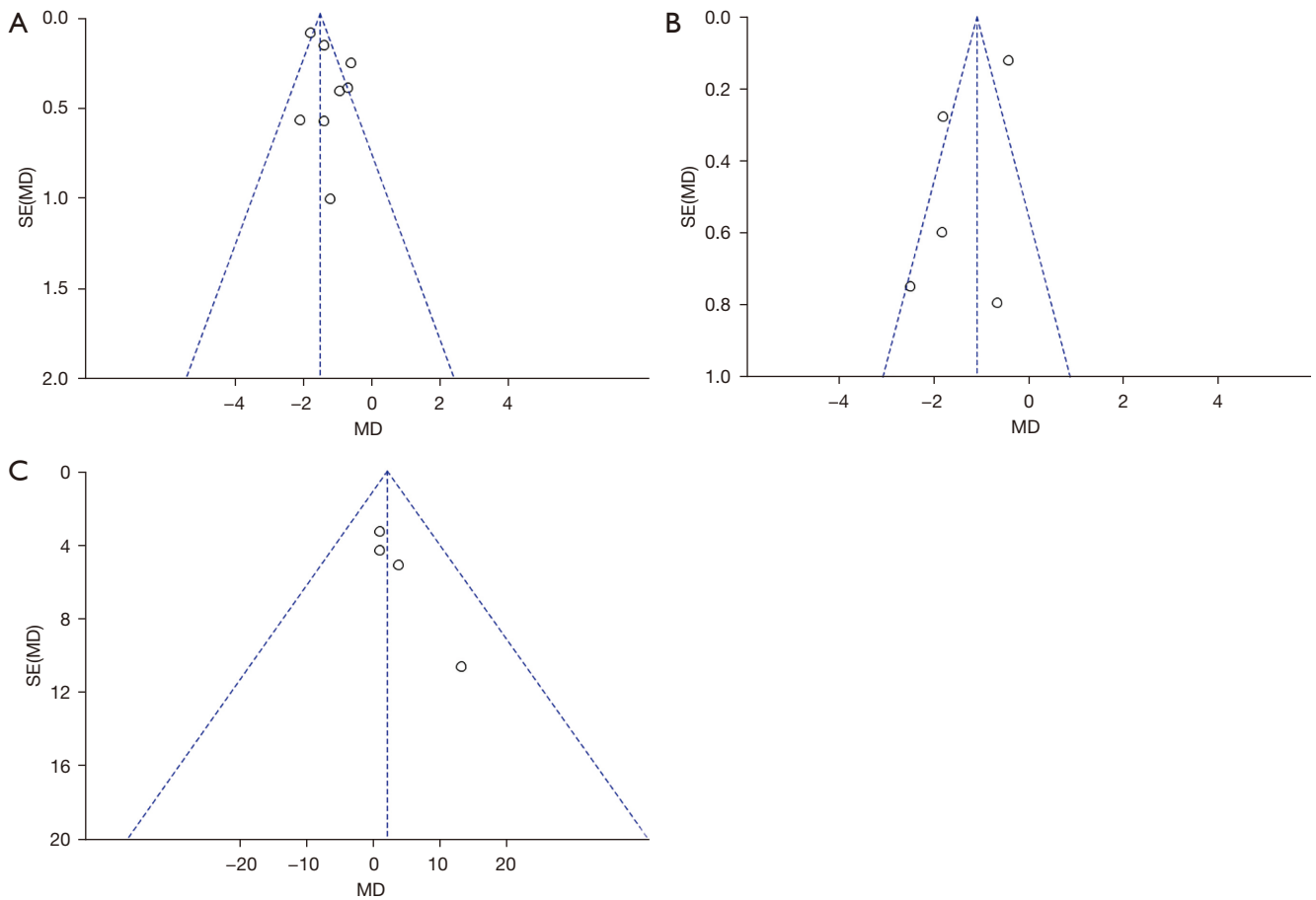


Figure 7 Funnel plots for evaluation indicators (A) for total pain score; (B) for morphine equivalents given in the 24 hours after surgery; (C) for operation duration.

structure was $Z=0.93$ ($P=0.35$). These results indicated that the operation duration scores of the two groups of patients did not differ significantly.

Publication bias analysis

Publication bias regarding the three evaluation indicators

[postoperative pain score (pain), morphine equivalents given in the 24 hours after surgery, and operation duration] of the thoracic nerve group and the control group was also analyzed, with results shown in Figure 7. As can be seen, the funnel plots for the postoperative pain score, the 24-hour dosage of morphine equivalent, and the length of operation are all approximately symmetrical, and the data are also relatively

concentrated. As seen in *Figure 7B*, only a few samples do not fall within the funnel on the chart. This indicates that there is no significant publication bias regarding the three functional indicators included in studies under review.

Discussion

In current radical mastectomy surgery, there are still many patients who suffer PMPS, a chronic neuropathic pain syndrome that may occur after mastectomy. The diagnosis of this condition requires the elimination of other causes including long-term pain from preoperative diseases or pain from other external causes, such as malignant tumors and infection. This type of chronic neuropathic pain usually has certain unique characteristics, such as tenderness, loss of sensation, and increasing pain if exacerbated by external factors. This places a serious burden on the physical and psychological well-being of patients who have undergone breast cancer surgery and can significantly affect their postoperative recovery.

The occurrence of PMPS is generally affected by a variety of factors. Because modified radical mastectomy for breast cancer is characterized by excessive cutting and pulling and a large trauma area (28,29), it can cause damage to the thoracic dorsal and intercostal arm nerves. In addition, nerve compression caused by adhesion after surgery may lead to PMPS. External factors such as the patient's age and psychological condition, tissue damage caused by the tumor, and the degeneration of sensory neurons may affect the incidence of PMPS. Currently, there is no clear clinical explanation for the pathogenesis of PMPS. However, relevant data suggest that it is inextricably related to the degree of acute postoperative pain, which, if not correctly managed, is likely to develop into PMPS.

As research into anesthesiologic methods develops, the importance of anesthesia has become apparent not only for the perioperative phase but also for postoperative recovery and patient comfort. With an increasing amount of research being carried out on local nerve blocks in anesthesiology, an abundance of relevant data now shows that a thoracic nerve block can have a good analgesic effect on patients in modified breast cancer surgery. While some related meta-analyses (30,31) have found that a thoracic paravertebral nerve block (TPVB) can significantly reduce the incidence of PMPS, the procedure is relatively complex and can lead to vascular puncture, nerve damage, or other adverse reactions and complications during an operation. Compared with other nerve block methods, thoracic nerve blocks provide the

advantages of a simpler, lower-risk, and shorter operation.

In addition to PMPS, postoperative complications such as nausea and vomiting can seriously affect a patient's postoperative comfort and recovery progress. The incidence of postoperative nausea and vomiting is generally correlated to the degree of pain a patient suffers (32,33). Opioid analgesics can effectively relieve postoperative pain but will increase the incidence of postoperative nausea and vomiting. In addition, postoperative vomiting often brings greater pain to patients, and violent vomiting may lead to the surgical wound opening and can affect the patient's ability to take food and medication, which will, in turn, have a serious impact on their postoperative recovery. However, the bone markers need to be clarified before the nerve block puncture, and the dose of local anesthetics needs to be strictly controlled. It is necessary to control the depth of the puncture needle during operation to prevent pneumothorax from puncturing the pleura. At the same time, it is necessary to repeatedly suck back before injecting the drug to avoid local anesthetic drug poisoning.

In summary, this study analyzed and compared the efficacy of a thoracic nerve block in modified radical mastectomy for breast cancer. The results show that a thoracic nerve block can effectively reduce both the amount of morphine used during surgery and the postoperative pain of patients. However, due to the limited number of evaluation indicators in this study, further research with a larger number of indicators is recommended.

Conclusions

In all, 8 suitable references comprising 624 patients were selected to explore the effect of general anesthesia combined with a thoracic nerve block in modified breast cancer surgery. Outcome indicators were the postoperative pain score, postoperative morphine equivalents given in the 24 hours after surgery, and operation duration. The Jadad tool and the Cochrane Handbook for Systematic Reviews of Interventions were used to evaluate the quality of the selected studies, and RevMan 5.3 was used to conduct a meta-analysis of the experimental data. According to the results of the meta-analysis, the total amount of morphine equivalents in the thoracic nerve group and the control group was heterogeneous ($I^2=98\%$; $P=0.02$). The MD of the total pain score was -1.27 (95% CI: -1.68 to -0.86), and the statistical test result was $Z=6.08$ ($P<0.00001$). The MD for operation duration was 2.11 (95% CI: -2.35 to 6.58), and the statistical test result was $Z=0.93$ ($P=0.35$). In

summary, the results show that general anesthesia combined with a thoracic nerve block can effectively improve the postoperative pain of patients with breast cancer surgery and effectively reduce the use of analgesics. However, the outcome indicators included in this study are insufficient, and it is necessary to increase the sample size and number of outcome indicators to provide further theoretical evidence for the subsequent application of thoracic nerve blocks in modified breast cancer surgery.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/gs-21-719>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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