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Meta analysis of ultrasound-guided posterior and paravertebral block for postoperative analgesia and adverse reactions in thoracic surgery

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Abstract: *This article used meta-analysis and systematic evaluation methods to compare the analgesic effect and incidence of adverse reactions of ultrasound-guided posterior block (RLB) and paravertebral block (PVB) in patients undergoing thoracic surgery. Pub Med, Cochrane Library, EMBase, CNKI, Wanfang Database, Vip Database, and China Biomedical Full-text Database were searched from the establishment of the library to 2022-12-01, and randomized controlled trials (RCTs) on the analgesic effect of ultrasound-guided RLB and PVB in thoracic surgery were collected and compared. Among them, the patients in the control group used ultrasound-guided RLB composite general anesthesia, and the patients in the experimental group used ultrasound-guided PVB combined general anesthesia. The primary outcomes were 2h, 6h, 12h, 24h, and 48h postoperative resting state and motor state NRS scores; Secondary outcomes were the number of analgesia and the incidence of adverse effects such as nausea, vomiting, and dizziness after surgery. Data were meta-analysed using Rev Man 5.3 software. A total of 220 patients in 4 RCT studies were included, including 110 cases in the RLB block group and 110 cases in the PVB group. The results of meta-analysis showed that compared with the PVB group (control group), the NRS score in the RLB group (experimental group) at rest at 6(MD=0.45,95%CI 0.16~-0.75,P=0.003) hand 24 h (MD=0.26, 95%CI 0.05~0.47, P=0.01) and NRS at 24h (MD=0.25, 95%CI 0.02~-0.48, P=0.03) exercise were significantly increased. There were no significant differences in NRS scores of resting state at 2h (MD=0.32,95%CI -0.22~0.66,P=0.06), 12h (MD=0.17,95%CI -0.03~0.36,P=0.09) and 48h (MD=0.07,95%CI -0.09~0.24,P=0.37) after surgery, NRS scores of exercise status at 2h (MD=0.26,95%CI -0.68~0.17,P=0.24), 6h (MD=0.09,95%CI -0.22~0.40,P=0.57), 12h (MD=0.04,95%CI -0.25~0.32,P=0.80) and 48h (MD=0.04,95%CI 0.22~0.30,P=0.74) after surgery, the number of postoperative remedial analgesia (RR=1.12,95%CI 0.45~2.79,P=0.82), postoperative vomiting nausea (RR=0.64,95%CI 0.34~1.19,P=0.16), dizziness (RR=0.61,95%CI 0.22~1.64,P=0.32) and other adverse reactions. The available clinical evidence shows that ultrasound-guided PVB is better than RLB in the early postoperative (24h) analgesia of thoracic surgery, and there is no significant difference between the two in the long-term (48h) analgesia after surgery, and the incidence of adverse reactions such as nausea, vomiting and dizziness does not increase compared with RLB.*

Keywords: *Ultrasound; Postlaminar block; Paravertebral block; Thoracic surgery; Meta-analysis*

1. Introduction

Intercostal nerve injury, muscle injury, rib compression fractures, and pleural injury caused by thoracotomy and thoracoscopy surgery can all result in severe postoperative pain in patients [1]. This type of pain can increase respiratory system complications, hospitalization time, and reduce patient satisfaction [2]. Therefore, safe and effective pain management will improve a patient's lung recovery ability and improve their prognosis. Currently, commonly used pain management methods include the use of intravenous analgesics and regional analgesia. Traditional intravenous analgesic drugs can cause respiratory depression, incomplete pain relief, increased time to recovery after surgery, nausea, vomiting, dizziness and other adverse reactions, which limits the application of intravenous analgesia to some extent [3]. Regional nerve block involves the injection of local anesthetics around the spinal nerves and their branches, which block the transmission of pain signals, resulting in analgesic effects. This method significantly reduces the use of intravenous analgesics such as opioids during the perioperative period and reduces the incidence of postoperative lung infections and lung collapse [4]. Currently, ultrasound-guided paravertebral block (PVB) and thoracic epidural block techniques have been used for the perioperative analgesia of thoracic surgery patients [5-8]. PVB [9] is a classic nerve block technique that has been proven to effectively reduce post-thoracic surgery pain and opioid consumption. However, its small anatomical space reduces anatomical structure recognition and is more difficult for beginners, requiring a longer learning curve. In addition, it is also prone to pleural and spinal nerve root damage. In recent years [5], ultrasound-guided RLB has also been found to be effective in relieving postoperative pain in thoracic surgery patients. Compared to PVB, it is a relatively safe and simple nerve block technique due to its injection site being further away from the pleura and spinal nerve roots and its superficial anatomical location. However, it is currently unclear which of these two techniques has better analgesic effects and is more suitable for postoperative analgesia in thoracic surgery. Therefore, this study aims to conduct a Meta-analysis of completed randomized controlled clinical studies both domestically and internationally, to screen relevant literature that meets the criteria, and to systematically evaluate and compare the analgesic effects and adverse reactions of ultrasound-guided RLB and PVB on thoracic surgery patients, providing reference for clinical doctors in selecting appropriate regional nerve block methods for performing thoracic surgery.

2. Materials and Methods

2.1 Document Retrieval

A computerized search will be conducted in the PubMed, Cochrane Library, EMBASE, China National Knowledge Infrastructure (CNKI), Wanfang Database, VIP Database, and China Biology Medicine Database from the establishment of the databases to December 1st, 2022, to identify randomized controlled trials regarding the use of ultrasound-guided RLB and PVB in thoracic surgery. The Chinese search terms will include ultrasound, ultrasound-guided, B-mode ultrasonography, retrolaminar block, thoracic paravertebral block, paraspinal thoracic nerve block, thoracic paravertebral nerve block, thoracotomy, and thoracoscopy. The English search terms will include ultrasound-guided, ultrasound, type-B ultrasonic, retrolaminal block, paravertebral nerve block, paraspinal thoracic nerve block, thoracotomy, and thoracoscopy. The literature search will follow the requirements of the Cochrane Collaboration.

2.2 Literature inclusion and exclusion criteria

Literature inclusion and exclusion criteria:

① randomized controlled trials;

② patients undergoing open thoracic surgery or thoracoscopic surgery;

③ comparison of ultrasound-guided RLB and PVB for nerve block;

④ primary outcome measures include NRS scores at rest and during movement 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours after surgery;

⑤ secondary outcome measures include rescue analgesic requirements and incidence of adverse reactions such as nausea, vomiting and dizziness. Exclusion Criteria: studies that are duplicated, case reports, literature reviews, animal experimental studies, and non-vital studies and so on.

2.3 Literature Screening and Data Extraction

Two researchers independently used Note Express 3.2 reference management software to screen the literature, delete duplicated literature, exclude literature that did not meet the inclusion criteria by reading titles and abstracts, and then evaluate the full text of the literature in detail. The literature that meets the PICOS principle is included. If there is disagreement during the screening process, it will be resolved by two researchers or a third researcher. Two researchers independently extracted the data, and then checked against each other. If there were, they were verified by a third party.

2.4 Quality Assessment of Studies

Two researchers used the Cochrane Handbook 5.1.0 risk of bias assessment tool to independently

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evaluate the quality of the literature that met the inclusion criteria. The contents of the evaluation include: random methods, allocation concealment, blinding of researchers and subjects, blinded assessment of research results, integrity of result data, selective reporting of results, and other biases. If there is disagreement, they will be evaluated by discussion or a third researcher.

2.5 Statistical Analysis

RevMan5.3 software was used for statistical analysis of the data. Continuous data were represented by standardized mean differences (standard mean difference, SMD) and their 95% confidence intervals (confidence interval,CI), and binary data were represented by odds ratios (odds ratio,OR) and their 95% CI. I2 and Q were used for heterogeneity testing. When $P \geq 0.1$ and $I2 \leq 50\%$, it indicates that there is no significant heterogeneity among the studies and a fixed-effect model is used for analysis; when $P<0.1$ and $I2>50\%$, it indicates significant heterogeneity, and a random effects model is used for analysis. A funnel used to evaluate publication bias for indicators with many included studies. For continuous data represented by median and interquartile range, if contacting the original authors is unsuccessful, an online calculator (http://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html) [10-11] is used to convert them to mean and standard deviation. For research data presented only in images, if contacting the original authors is unsuccessful, Web Plot Digitizer is used to extract data[12].

3. Result

3.1 Literature Screening Results

A total of 24 studies were retrieved according to the search method in the article. After a layered screening based on the inclusion and exclusion criteria, four RCTs were finally included. See Figure 1.

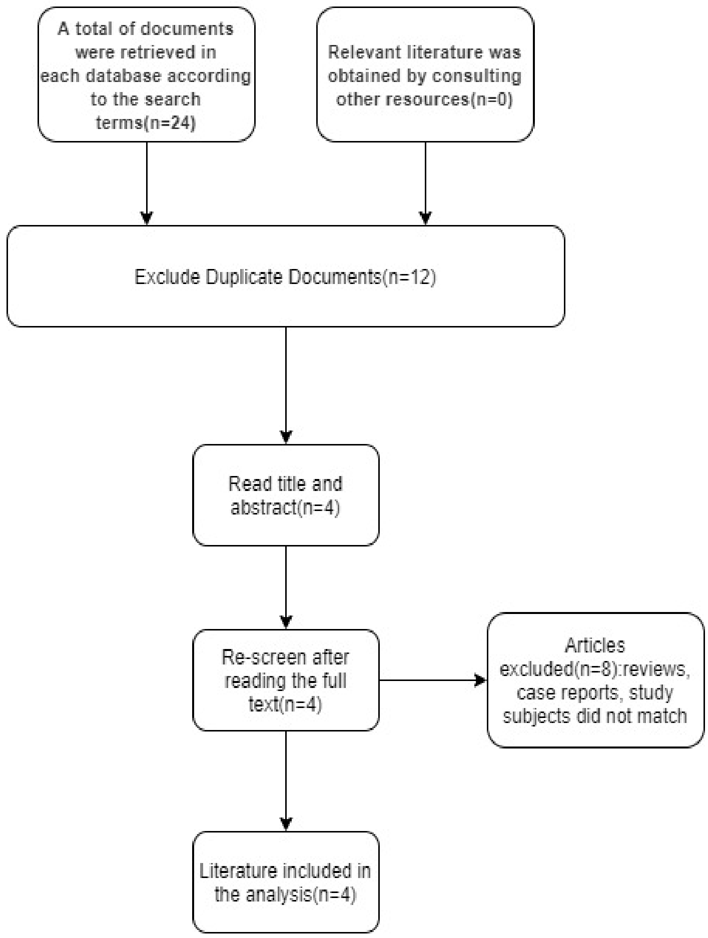

Figure 1: Document screening flow chart

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3.2 Basic Characteristics of the Included Literature and Bias Risk Assessment

The basic characteristics of the included literature are shown in Table 1, and the bias risk assessment of the literature is shown in Figure 2.

Note: 1, 2, 3, 4, and 5 represent the NRS scores at rest at 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours, respectively, after the operation; 6, 7, 8, 9, and 10 represent the NRS scores during movement at 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours, respectively, after the operation; 11 refers to the number of rescue analgesia times; 12 refers to nausea and vomiting; 13 refers to dizziness.

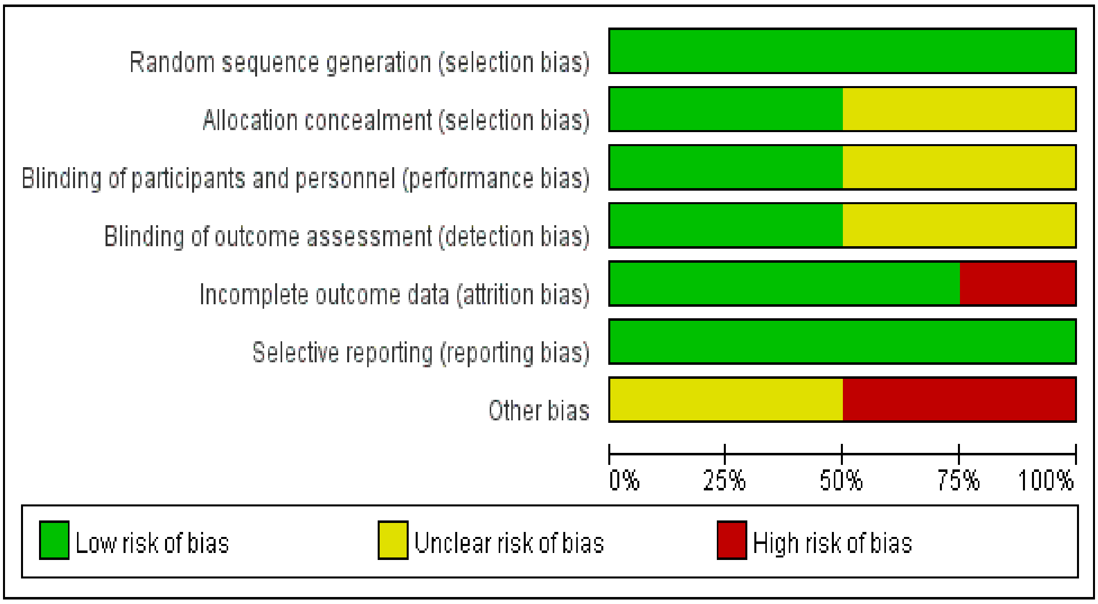

Figure 2: Risk of bias assessment chart

3.3 Results of Meta-analysis

3.3.1 NRS Scores at Different Time Points at Rest between the Two Groups of Patients

Three studies [5-6,8] compared the NRS scores at rest at 2 hours after the operation, with no significant heterogeneity (I2=50%, P=0.12). The fixed-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores at rest between the two groups of patients at 2 hours after the operation (MD=0.32, 95%CI -0.22 to 0.66, P=0.06) (Figure 3-A). Two studies [6-7] compared the NRS scores at rest at 6 hours after the operation, with significant heterogeneity (I2=89%, P=0.002).

The random-effect model was adopted, and the meta-analysis results showed that the NRS scores at rest in the PVB group were significantly lower than those in the RLB group at 6 hours after the operation (MD=0.45, 95%CI 0.16 to 0.75, P=0.003) (Figure 3-B). Three studies [5-7] compared the NRS scores at rest at 12 hours after the operation, with significant heterogeneity (I2=59%, P=0.09). The random-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores at rest between the two groups of patients at 12 hours after the operation (MD=0.17, 95%CI -0.03 to 0.36, P=0.09) (Figure 3-C). Four studies [5-8] compared the NRS scores at rest at 24 hours after the operation, with no significant heterogeneity (I2=35%, P=0.20). The fixed-effect model was adopted, and the meta-analysis results showed that the NRS scores at rest in the PVB group were significantly lower than those in the RLB group at 24 hours after the operation (MD=0.26, 95%CI 0.05 to 0.47, P=0.01) (Figure 3-D). Four studies[5-8] compared the NRS scores at rest at 48 hours after the operation, with significant heterogeneity (I2=64%, P=0.04). The random-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores at rest between the two groups of patients at 48 hours after the operation (MD=0.07, 95%CI -0.09 to 0.24, P=0.37) (Figure 3-E).

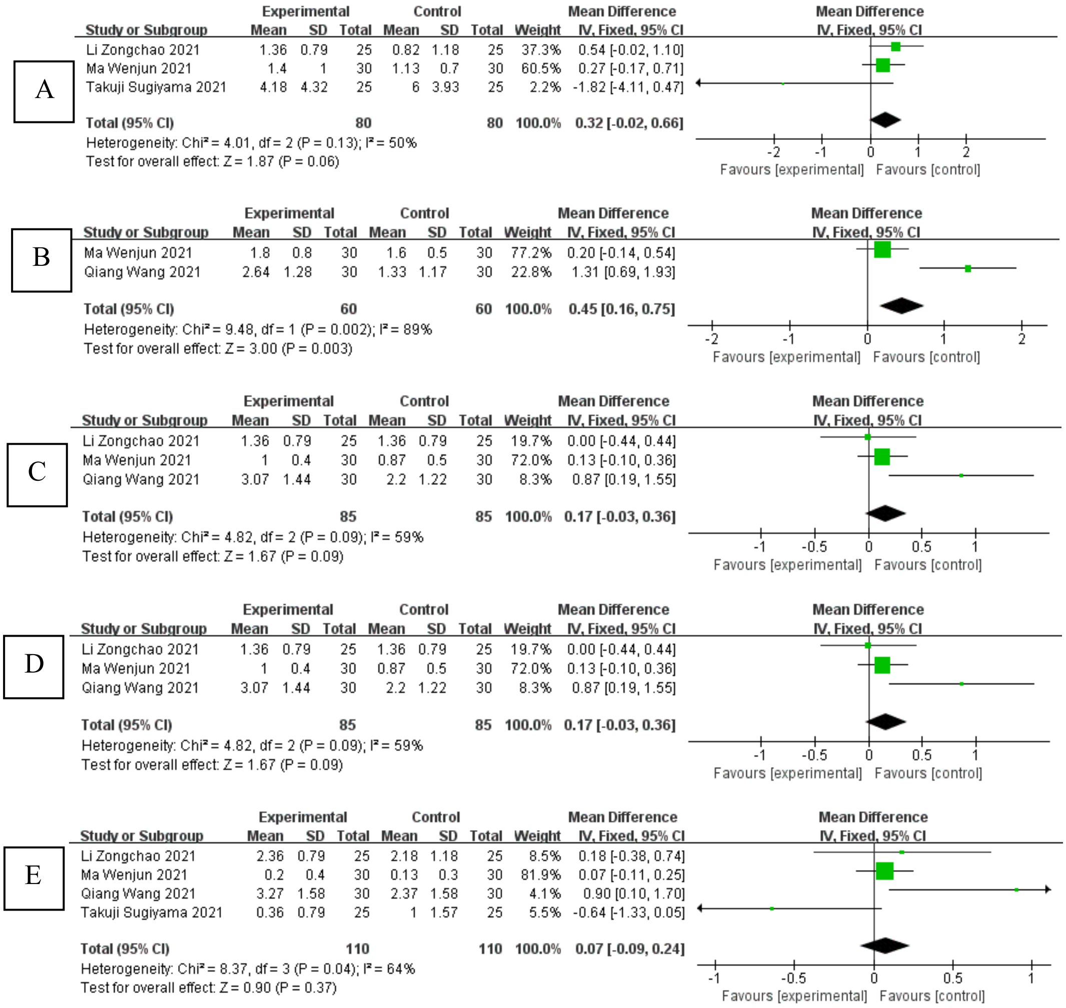

Figure 3: NRS scores of resting states at different tim points after surgery

3.3.2 NRS Scores in Different Time Points during Movement between the Two Groups of Patients

Two studies[6, 8] compared the NRS scores during movement at 2 hours after the operation, with no significant heterogeneity (I2=46%, P=0.17). The fixed-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores during movement between the two groups of patients at 2 hours after the operation (MD=0.26, 95%CI -0.68 to 0.17, P=0.24) (Figure 4-A). Two studies[6-7] compared the NRS scores during movement at 6 hours after the operation, with significant heterogeneity (I2=90%, P=0.002). The random-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores during movement between the two groups of patients at 6 hours after the operation (MD=0.09, 95%CI -0.22 to 0.40, P=0.57) (Figure 4-B). Two studies[6-7] compared the NRS scores during movement at 12 hours after the operation, with significant heterogeneity (I2=78%, P=0.03). The random-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores during movement between the two groups of patients at 12 hours after the operation (MD=0.04, 95%CI -0.25 to 0.32, P=0.80) (Figure 4-C). Three studies[6-8] compared the NRS scores during movement at 24 hours after the operation, with no significant heterogeneity (I2=40%, P=0.19). The fixed-effect model was adopted, and the meta-analysis results showed that the NRS scores during movement in the PVB group were significantly lower than those in the RLB group at 24 hours after the operation (MD=0.25, 95%CI 0.02 to -0.48, P=0.03) (Figure 4-D). Three studies[6-8] compared the NRS scores during movement at 48 hours after the operation, with no significant heterogeneity (I2=0%, P=0.67). The fixed-effect model was adopted, and the meta-analysis results showed no significant difference in NRS scores during movement between the two groups of patients at 48 hours after the operation (MD=0.04, 95%CI 0.22 to 0.30, P=0.74) (Figure 4-E).

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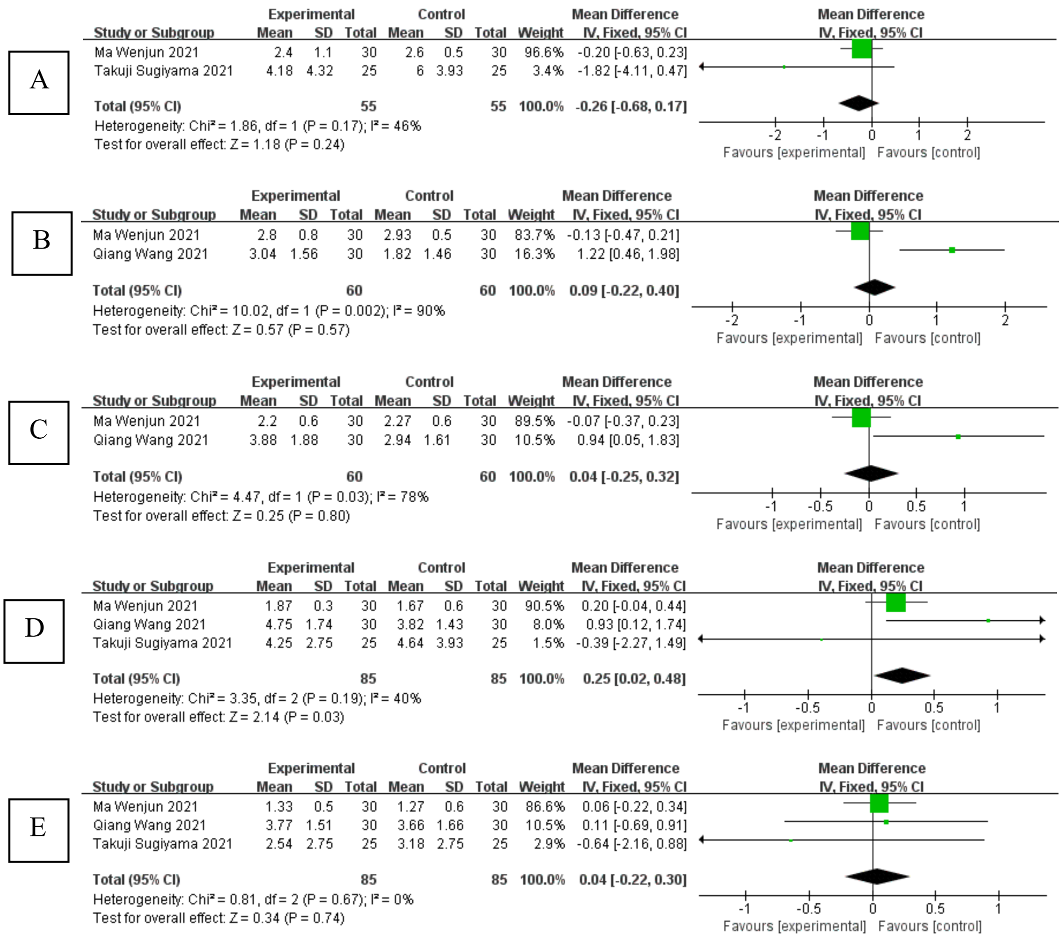

Figure 4: NRS scores of motor status at different time points after surgery

3.3.3 Number of Rescue Analgesia in the Two Groups of Patients

Three studies[5-6, 8] compared the number of rescue analgesia after the operation, with no significant heterogeneity (I2=0%, P=0.51). The fixed-effect model was adopted, and the meta-analysis results showed no significant difference in the number of rescue analgesia between the two groups of patients after the operation (RR=1.12, 95%CI 0.45 to 2.79, P=0.82) (Figure 5).

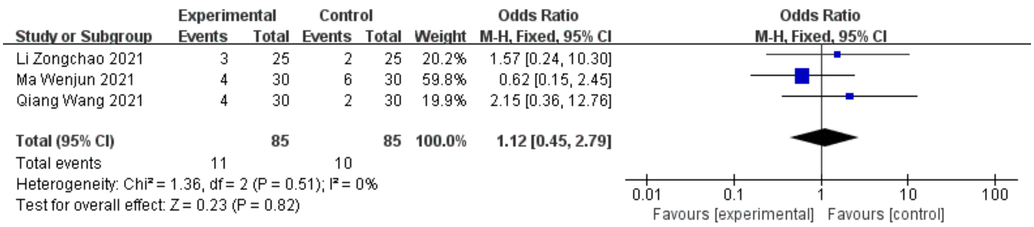

Figure 5: Number of postoperative salvage analgesia

3.3.4 Incidence of Adverse Reactions after the Operation

Four studies[5-8] mentioned the occurrence of postoperative nausea and vomiting, with significant heterogeneity (I2=69%, P=0.02). The random-effect model was adopted, and the meta-analysis results showed no significant difference in the incidence of postoperative nausea and vomiting between the two groups of patients (RR=0.64, 95%CI 0.34 to 1.19, P=0.16) (Figure 6-A). Two studies[6-7] mentioned the occurrence of postoperative dizziness, with no significant heterogeneity (I2=0%, P=0.72). The fixed-effect model was adopted, and the meta-analysis results showed no significant difference in the incidence of postoperative dizziness between the two groups of patients (RR=0.61, 95%CI 0.22 to 1.64, P=0.32) (Figure 6-B).

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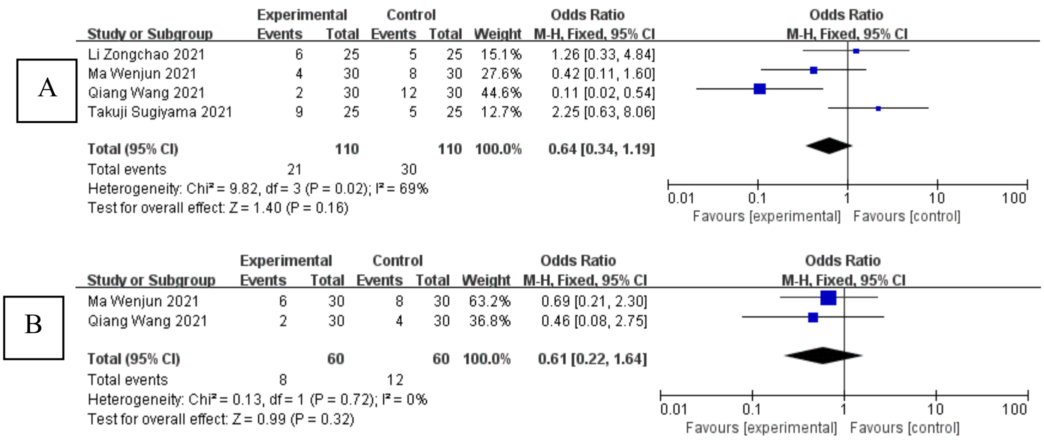

Figure 6: Incidence of postoperative adverse reactions

3.3.5 Publication Bias

A funnel plot was drawn based on the postoperative 24-hour resting NRS scores of the two groups of patients, and the funnel plot showed a symmetrical distribution, suggesting a relatively small publication bias (Figure 7)

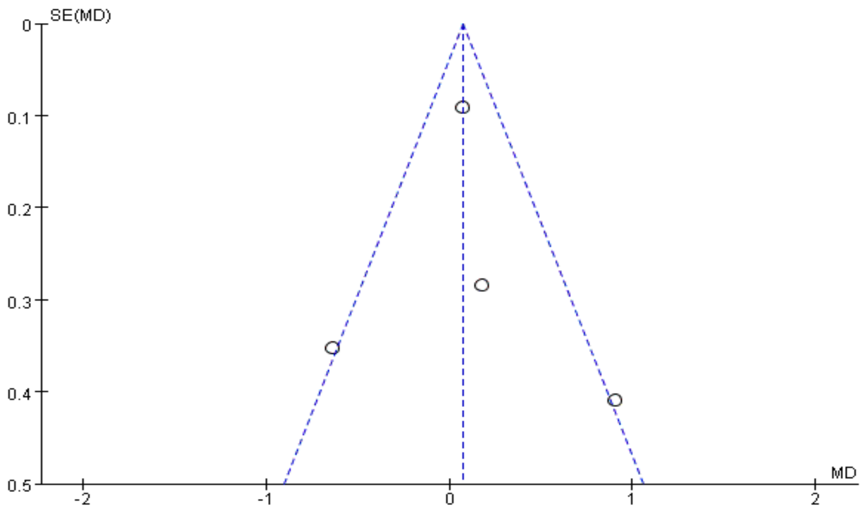

Figure 7: Publication bias funnel plot of NRS score at resting state 24 hours after surgery

4. Discuss

This study included 4 RCTs and a total of 220 patients. The aim was to directly evaluate the postoperative analgesic effects and adverse reactions of ultrasound-guided RLB and PVB for thoracic surgery. Currently, PVB in the chest area is a mature technique for perioperative analgesic management in thoracic surgery[13]. In 1905, Hugo Sellheim[14] first described this technique and it has since been improved. However, the potential risks of adverse reactions such as pneumothorax, block site infection, nerve and vascular injuries are still a concern. In addition, the long operating time and high difficulty have led some inexperienced anesthesiologists to choose to abandon PVB or use other nerve block techniques instead[15]. In 2006, an improved paravertebral technique - RLB - was proposed as an alternative to classic PVB[16]. In this technique, the puncture needle does not directly enter the paravertebral interspace and the injection site is located at the posterior part of the vertebral plate. RLB theoretically has the advantage of reducing the risk of pleural injury because the puncture position is at a more medial puncture site, avoiding the needle being pushed forward and approaching the pleura[17]. This method is considered not only safe but also a simple, fast, and effective alternative to paravertebral analgesia. Compared with PVB, the exact analgesic mechanism of RLB is not yet fully understood. In a cadaver study, the possible mechanism of RLB is the diffusion of the local anesthetic through the rib transverse ligament into the paravertebral interspace, and the anterior and posterior branches of the thoracic spinal nerves are mainly blocked by the indirect effect of RLB, thereby producing an analgesic effect[18]. In contrast, PVB produces an analgesic effect by depositing the local anesthetic directly into the paravertebral interspace to block the anterior and posterior branches of the thoracic spinal nerve roots[19]. Compared to the indirect mechanism of RLB, the direct mechanism of PVB may lead to superior analgesic effects. The meta-analysis results of this study suggest that ultrasound-guided PVB is superior to RLB for early postoperative (24 hours) analgesia for thoracic surgery, possibly related to the direct mechanism of PVB.

Some limitations of this systematic review include: (1) The concentration and dose of local anesthetics in the included studies were not completely the same, which may increase clinical heterogeneity; (2) There were fewer high-quality studies included. In conclusion, due to the limitations of the quantity and quality of existing original studies, this study's conclusions need to be verified by large-scale, multicenter, and high-quality RCTs.

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Table 1: Basic Characteristics of the Included Studies

Literature	Sample size		Age(Years)		Gender(m/f)		BMI(kg/cm2)		ASA Classification (Class I/II)		Duration of surgery(min)		Amount of local anesthetic		Outcome measures	
	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group	RLB Group	PVB Group
Li Zongchao 2021[5]	25	25	58.5±5.7 1	56.4±6.2	11/14	12/13	24.1±3.0	23.3±3.1	17/8	16/9	128.2±24.6	143.7±30.8	0.5% Ropicacaine 20 ml	0.5% Ropicacaine 20 ml	1,3,4,5,11,12	1,3,4,5,11,12
Ma Wenjun 2021[6]	30	30	39.0±11.0	35.2±13.0	11/19	16/14			18/12	20/10	63. 3 ± 15. 2	66.7 ± 14.3	0.5% Ropicacaine 20ml + dexamethasone 5mg Mixture	0.5% Ropicacaine 20ml + dexamethasone 5mg Mixture	1,2,3,4,5,6,7,8,9,10,11,12,13	1,2,3,4,5,6,7,8,9,10,11,12,13
Qiang Wang 2021[7]	30	30	55.3 ± 11.8	53.7 ± 14.0	25/5	22/8	23.2 ± 3.5	24.3 ± 3.0	6/24	4/26	116.2 ±49.9	112.8 ±35.5	0.5% Ropicacaine 15 ml	0.5% Ropicacaine 15 ml	2,3,4,5,7,8,9,10,11,12,13	2,3,4,5,7,8,9,10,11,12,13
Takuji Sugiyama 2021[8]	25	25	56.0 ± 33.0	58.4 ± 26.7	14/11	20/5	21.4± 2.4	22.4 ± 2.4	7/18	5/20	101.2 ±26.7	108.4 ±43.2	0. 25% Ropicacaine 40 ml	0. 25% Ropicacaine 40 ml	1,4,5,6,9,10,12	1,4,5,6,9,10,12