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Meta-analysis of the effects of ultrasound-guided rhomboid-intercostal-low anterior serratus plane block and thoracic paravertebral nerve block for postoperative analgesia in adults undergoing thoracoscopic surgery

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Abstract: *The purpose of this article was to evaluate the effectiveness of ultrasound-guided rhomboid-intercostal-low anterior serratus plane block (RISS) with thoracic paravertebral nerve block (TPVB) for postoperative analgesia in adults undergoing thoracoscopic surgery. We searched Embase, PubMed, Cochrane Library, China Knowledge, Wanfang Data, and Wipro for literature up to January 2024, and included RISS and TPVB for postoperative analgesia in adult thoracoscopic surgery. A randomized controlled trial (RCT) of RISS versus TPVB for thoracoscopic lobectomy in adults was included, and RevMan 5.3 software was used to analyze and compare the primary outcome indicators (VAS scores at 1h, 2h, 4h, 8h, 12h, 24h, and 48h postoperatively) and secondary outcome indicators (time to the first postoperative PCIA, intraoperative remifentanil use, and the incidence of nausea and vomiting) between the two groups. vomiting occurrence). Four RCTs with 314 patients were included in the study.Compared with the control group (TVPB group), the resting state pain scores were significantly higher in the test group (RISS group) at 1h (MD=0.70, 95% CI 0.48-0.92, P<0.00001), 2h (MD=0.14, 95% CI -0.06-0.22, P=0.0009), 12h (MD=0.33, 95% CI 0.19-0.47, P< 0.00001) and 24h (MD=0.17, 95% CI 0.03 to 0.31, P=0.01) resting state pain scores were significantly higher. Compared with the control group (TVPB group), the test group (RISS group) had significantly higher postoperative 1 h (MD=0.80, 95% CI 0.60 to 1.01, P<0.00001), 12 h (MD=0.34, 95% CI 0.18 to 0.51, P<0.00001), and 24 h (MD=0.18, 95% CI 0.03 to 0.34, P= 0.02) motor state pain scores were significantly higher. Compared with the control group (TVPB group), the time to the first postoperative PCIA press (MD=-1.34, 95% CI -1.76 to -0.91, P<0.00001) was significantly earlier in the test group (RISS group). Intraoperative remifentanil use (MD=30.43, 95% CI 6.00 to 54.86, P=0.01) was significantly increased in the test group (RISS group) compared with the control group (TVPB group). There was no statistically significant difference in resting state pain scores between the two groups of patients at 4h (MD=0.01, 95% CI -0.11 to 0.13, P=0.86), 8h (MD=0.24, 95% CI -0.05 to 0.53, P=0.10), and 48h (MD=0.08, 95% CI -0.04 to 0.28, P=0.18) postoperatively. The differences in postoperative motor status pain scores between the two groups of patients at 2 h (MD=0.02, 95% CI -0.10 to 0.14, P=0.78), 4 h (MD=0.06, 95% CI -0.10 to 0.22, P=0.48), 8 h (MD=0.11, 95% CI -0.14 to 0.37, P=0.38), 48 h (MD=0.07, 95% CI - 0.03 to 0.18, P=0.17) The difference in motor status pain scores was not statistically significant. There was no statistically significant difference in the incidence of postoperative nausea and vomiting (RR=1.60, 95% CI 0.66 to 3.87, P=0.29) between the two groups. The results of this study suggest that RISS can provide similar postoperative analgesia as TPVB, but its operation is simple and quick. Therefore, RISS can be a new option for postoperative analgesia in adult thoracoscopic surgery.*

Keywords: *Ultrasound; Rhomboid-intercostal-low anterior serratus plane block; Thoracic paraspinal nerve block; Thoracoscopic surgery; Meta-analysis*

1. Introduction

Patients often experience severe pain after thoracoscopic surgery. If the pain is not well controlled, normal respiratory function is affected, and some patients also develop symptoms such as pulmonary atelectasis and lung infection, and chronic pain occurs in about 20% to 40% of patients 3-6 months after

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surgery[1] , leading to a decrease in the quality of life of patients. Currently, most of the perioperative pain management for thoracoscopic surgery adopts a multimodal analgesia program. Multimodal analgesia refers to the combined application of analgesic drugs or analgesic methods that act on different targets and different mechanisms of action in the pain conduction pathway in order to obtain a more complete analgesic effect, to reduce the dose of analgesic drugs, and to reduce adverse effects, in order to achieve the maximum effect/risk ratio[2-3] .Regional nerve blocks are an important component of multimodal analgesia programs. Thoracic paravertebral nerve block (TPVB) is an injection of local anesthetic into the thoracic paravertebral space, which can provide safe and effective postoperative analgesia for thoracic and abdominal surgery[4-6] . However, the operation is difficult and complications such as pneumothorax, respiratory depression and chest tightness may occur. Rhomboid-Intercostal and Subserratus Plane Block (RISS) is a new fascial plane block technique discovered by foreign scholars Elsharkawy et al. in 2018. With the advantages of easy recognition on ultrasound images, facilitating continuous tube placement and flexible puncture range, it can be safely used for thoracic postoperative analgesia [7]. However, there are controversies about the safety and efficacy of these two techniques for postoperative analgesia in thoracoscopic surgery. Therefore, this meta-analysis aims to compare the efficacy and safety of RISS and TPVB for postoperative analgesia in adults undergoing thoracoscopic surgery using the existing national and international randomized controlled trials [8-11], with the aim of providing new options for postoperative analgesia in this surgery.

2. Materials and Methods

2.1 Literature Search

Literature in Cochrane Library, PubMed, Embase, China Knowledge Network, Wanfang Data and Wipo.com was searched and screened by two researchers for RISS versus TPVB for postoperative analgesic effects of RCTs in adults undergoing thoracoscopic surgery, with a timeframe of search from the library's construction to January 2024.The search was conducted in English with the following terms: ultrasound-guided, ultrasound, type-b ultrasonic, rhomboid intercostal and sub-serratus. English search terms: ultrasound-guided, ultrasound, type-b ultrasonic, rhomboid intercostal and sub-serratus , RISS, thoracic paravertebral nerve block, TPVB and thoracoscopic surgery. Chinese search terms: ultrasound, rhomboid **-** intercostal **-** low anterior serratus plane block, thoracic paravertebral nerve block, paravertebral nerve block and thoracoscopic surgery, etc.

2.2 Data extraction

Literature was screened independently by two investigators, and data were extracted according to the following criteria: (1) Basic information about the article (authors and year of publication); (2) Iinclusion of basic characteristics of the study and specific details of the intervention (number of cases in the RISS group versus the TPVB group, age, sex, BMI, ASA classification, length of the procedure, neurological blocking medication, and outcome indicators).

2.3 Inclusion and Exclusion Criteria

Inclusion criteria: (1) The type of study was RCT; (2) The American Society of Anesthesiologists (ASA) classification of the study subjects was I to III; (3) Thoracoscopic lobectomy or radical lung cancer surgery was used; (4) The age ≥ 18 years; (5) Race and gender were not limited. Exclusion criteria: (1) Age < 18 years old; (2) Incomplete data, unable to extract data; (3) Meta-analysis and review, etc.

2.4 Evaluation of article quality

Risk of bias analysis of the included studies was performed in strict accordance with the criteria recommended by the Cochrane Handbook 5.1.0. All the included literature was judged in seven aspects, including random sequence generation, allocation concealment, double-blinding of investigators and study participants, blinding of outcome evaluation, incomplete data results, selective reporting, and other biases.

2.5 Interventions

In this paper, we systematically evaluated the analgesic effects of RISS and TPVB in the

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postoperative period of adult thoracoscopic surgery according to the PRISMA principle[12]. In the test group (RISS group), RISS was used, and in the control group (TPVB group), TPVB was used.

2.6 Indicators of results

2.6.1 Key indicators

VAS scores at 1h, 2h, 4h, 8h, 12h, 24h and 48h postoperatively during resting and exercise states.

2.6.2 Secondary Indicators

(1) The time of the first postoperative PCIA press; (2) The amount of intraoperative remifentanil used; (3) The incidence of postoperative nausea and vomiting.

2.7 Statistical analysis

Meta-analysis was performed using RevMan 5.3. Continuous measures were expressed as mean difference (MD) and its 95% confidence interval (CI). If continuous variables were presented as medians, extremes or quartiles in the literature, they should be converted to means and standard deviations before calculation[13]. Dichotomous variables were expressed as odds ratio (O^R) and their 95% CI.Heterogeneity was examined using the I^2 test and the Q-value statistic. If the heterogeneity between studies was small (P>0.1, I^2 < 50%), a fixed-effects model was used; when there was significant heterogeneity between studies (P≤0.1, I^2≥ 50%), the possible reasons for heterogeneity needed to be further analyzed, and subgroup analyses and sensitivity analyses could be used to explore the factors that generated heterogeneity. If the source of heterogeneity was unclear and there was no clinical heterogeneity, the random-effects model was used to calculate the statistics. p<0.05 was considered a statistically significant difference.

3. Results

3.1 Literature search results

A total of 12 papers were retrieved according to the search method in the text, and 4 RCTs were finally obtained after a layer-by-layer screening based on the inclusion and exclusion criteria. See Figure 1.

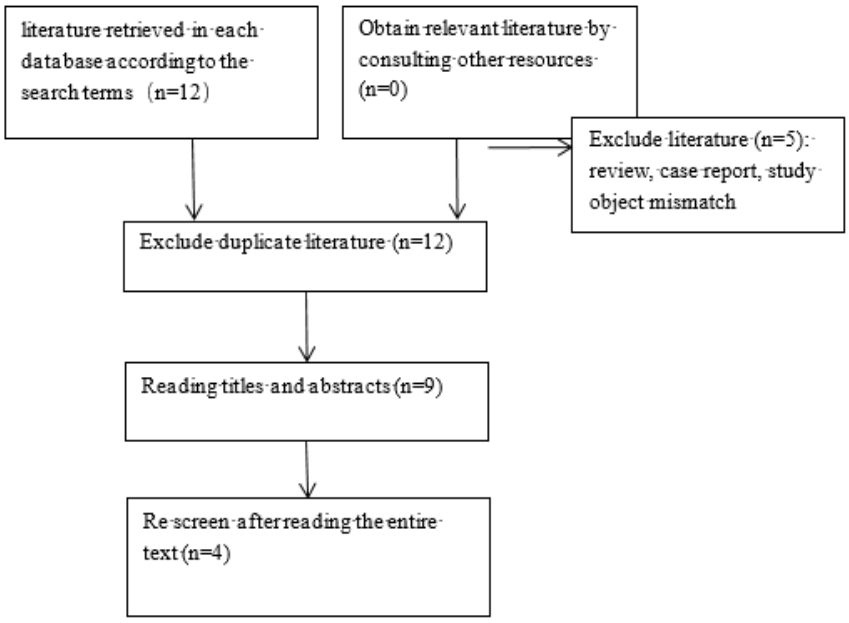

Figure 1: Literature Screening Process

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3.2 Basic information and risk assessment of bias included in the literature.

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

Table 1: Basic characteristics of included studies

literature	sample size		Age (years)		Gender (male/female)		BMI(kg/cm^2)		ASA classification (Level I/II/III)		Surgical time (min)		Local anesthetic dosage		Outcome indicators	
	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group	RISS group	TPVB group
Zhou YK 2021 [8]	73	72	51.9±13.6	50.0±13.6	40/33	42/30	23.88±2.00	23.31±2.07	12/28/33	11/31/30	118.11±35.30	111.99±30.93	0.25% ropivacaine 20ml	0.25% ropivacaine 20ml	1、5-6、8、12-13、15、17	
Zhang LS 2021 [9]	30	30	46.35±4.19	45.21±4.21	20/10	18/12	22. 51±2.46	21.42±2.32	13/17/0	10/20/0	85.15±16.52	84.24±14.61	0. 2%ropivacaine 15 ml	0. 2%ropivacaine 15 ml	2-7、9-17	
Li HT 2022 [10]	32	32	57.82±2.55	58.67±2.38	17/15	16/16	25.74±2.53	26.94±2.31	13/19/0	12/20/0	86.10±14.63	85.63±14.57	0.33%ropivacaine25ml	0.33%ropivacaine25ml	2-3、5-7、9-10、12-14、17	
Zhang F 2023 [11]	23	22	61.91±9.48	62.09±9.69	16/7	14/8	26.13±4.10	26.45±2.82	4/17/2	5/15/2	153.09±9.55	154.27±10.01	0.25%ropivacaine 40ml	0.33%ropivacaine30ml	1-4、6-11、13-14、16、17	

1. 2, 3, 4, 5, 6, and 7 are the resting state pain scores at 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 24 hours, and 48 hours after surgery, respectively; 8. 9, 10, 11, 12, 13, and 14 are pain scores for motor status at 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 24 hours, and 48 hours postoperatively, respectively; 15 is the time for the first postoperative compression of PCIA; 16 is the amount of remifentanil used during surgery; 17 is the occurrence of postoperative nausea and vomiting.

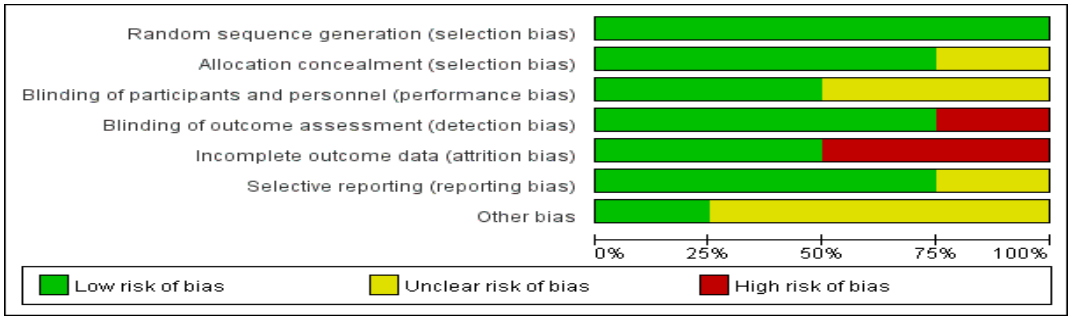
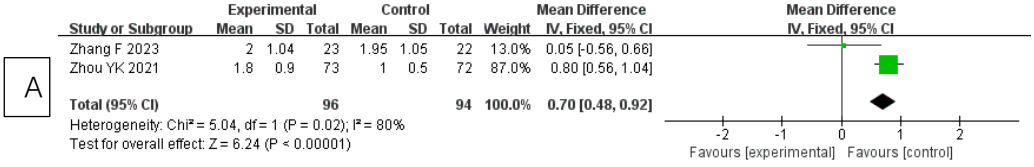


Figure 2: Bias Risk Assessment Chart

3.2.1 Resting state pain scores at different postoperative time points in both groups of patients

Two papers [8, 11] compared postoperative 1-h resting state pain scores with significant heterogeneity (I2=80%, P=0.02), and using a random-effects model, Meta-analysis showed that postoperative 1-h resting state pain scores in the test group were significantly higher than those in the control group (MD=0.70, 95% CI 0.48 to 0.92, P<0.00001) (Figure 3-A) . Three papers [9-11] compared postoperative 2h resting state pain scores with significant heterogeneity (I2=71%, P=0.03), and using a random effects model, Meta-analysis showed that postoperative 2h resting state pain scores in the test group were significantly higher than those in the control group (MD=0.14, 95% CI -0.06 to 0.22, P=0.0009) (Figure 3-B) . Three papers [9-11] compared the postoperative 4-h resting state pain scores without significant heterogeneity (I2=0%, P=0.96), and using a fixed-effects model, Meta-analysis showed that the difference in the postoperative 4-h resting state pain scores between the two groups of patients was not statistically significant (MD=0.01, 95% CI -0.11 to 0.13, P=0.86) (Figure 3-C). Two papers [9, 11] compared postoperative 8 h resting state pain scores without significant heterogeneity (I2=0%, P=0.50), and using a fixed effect model, Meta-analysis showed that the difference in postoperative 8 h resting state pain scores between the two groups of patients was not statistically significant (MD=0.24, 95% CI -0.05 to 0.53, P=0.10) (Figure 3-D).Three papers [8-10] compared the postoperative 12-h resting state pain scores with significant heterogeneity (I2=88%, P=0.0002), and using a random-effects model, Meta-analysis showed that the postoperative 12-h resting state pain scores of the experimental group were significantly higher than those of the control group (MD=0.33, 95% CI 0.19 to 0.47, P<0.00001) (Figure 3-E). Four papers [8-11] compared the postoperative 24-h resting state pain scores without significant heterogeneity (I2=0%, P=0.95), and using a fixed-effects model, Meta-analysis showed that the postoperative 24-h resting state pain scores of the experimental group were significantly higher than those of the control group (MD=0.17, 95% CI 0.03-0.31, P=0.01) (Figure 3-F). Three papers [9-11] compared the postoperative 48h resting state pain scores without significant heterogeneity (I2=0%, P=0.85), and using a fixed effects model, Meta-analysis showed that the difference in postoperative 48h resting state pain scores between the two groups of patients was not statistically significant (MD=0.08, 95% CI -0.04 to 0.28, P=0.18) (Figure 3-G).



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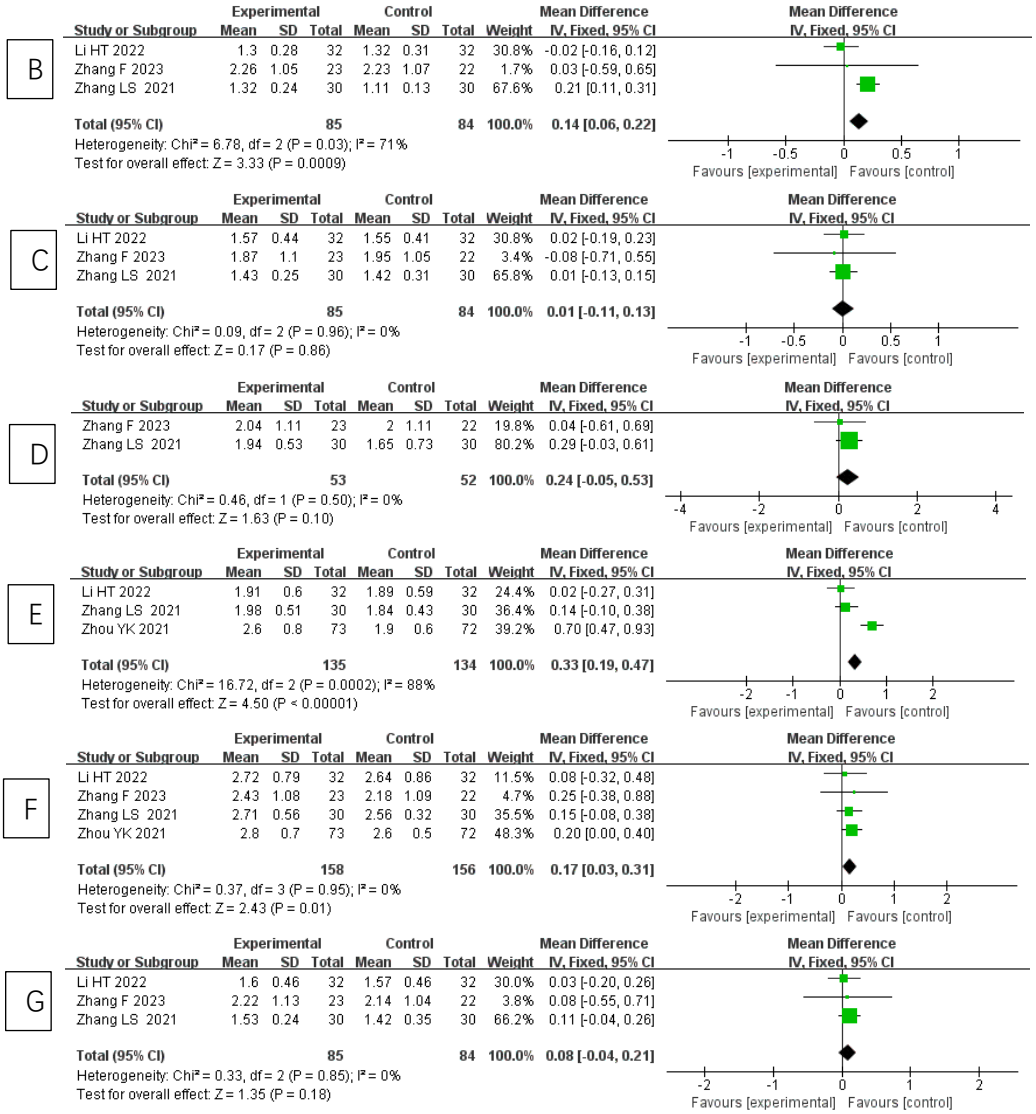

Figure 3: Resting state pain scores at different time points after surgery

3.2.2 Pain scores for motor status at different postoperative time points in both groups of patients

Two papers [8, 11] compared the 1-h postoperative motor status pain scores with significant heterogeneity (I2=86%, P=0.008), and using a random-effects model, Meta-analysis showed that the 1-h postoperative motor status pain scores of the experimental group were significantly higher than those of the control group (MD=0.80, 95% CI 0.60 to 1.01, P<0.00001) (Figure 4-A). Three papers [9-11] compared the postoperative 2-h motion state pain scores without significant heterogeneity (I2=0%, P=0.82), and using a fixed-effects model, Meta-analysis showed that the difference in postoperative 2-h motion state pain scores between the two groups of patients was not statistically significant (MD=0.02, 95% CI -0.10 to 0.14, P=0.78) (Figure 4-B). Three papers [9-11] compared the 4-h postoperative motor status pain scores without significant heterogeneity (I2=0%, P=0.65), and using a fixed-effects model, Meta-analysis showed that the difference in the 4-h postoperative motor status pain scores between the two groups of patients was not statistically significant (MD=0.06, 95% CI -0.10 to 0.22, P=0.48) (Figure 4-C). Two papers [9, 11] compared the 8-h postoperative motor status pain scores without significant heterogeneity (I2=0%, P=0.93), and using a fixed-effect model, Meta-analysis showed that the difference in 8-h postoperative motor status pain scores between the two groups of patients was not statistically significant (MD=0.11, 95% CI -0.14 to 0.37, P=0.38) (Figure 4-D).Three papers [8-10] compared the 12-h postoperative motor status pain scores with significant heterogeneity (I2=88%, P=0.0003), and using a random-effects model, Meta-analysis showed that the 12-h postoperative motor status pain scores of the experimental group were significantly higher than those of the control group (MD=0.34, 95% CI 0.18-0.51, P<0.00001) (Figure 4-E). Four papers [8-11] compared the 24-h postoperative motor status pain scores without significant heterogeneity (I2=0%, P=0.74), and using a fixed-effects model, Meta-analysis

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showed that the test group's 24-h postoperative motor status pain scores were significantly higher than those of the control group (MD=0.18, 95% CI 0.03-0.34, P=0.02) (Figure 4-F). Three papers [9-11] compared the 48-h postoperative motor status pain scores without significant heterogeneity (I2=0%, P=0.46), and using a fixed-effects model, Meta-analysis showed that the difference in the 48-h postoperative motor status pain scores between the two groups of patients was not statistically significant (MD=0.07, 95% CI -0.03 to 0.18, P=0.17) (Figure 4-G).

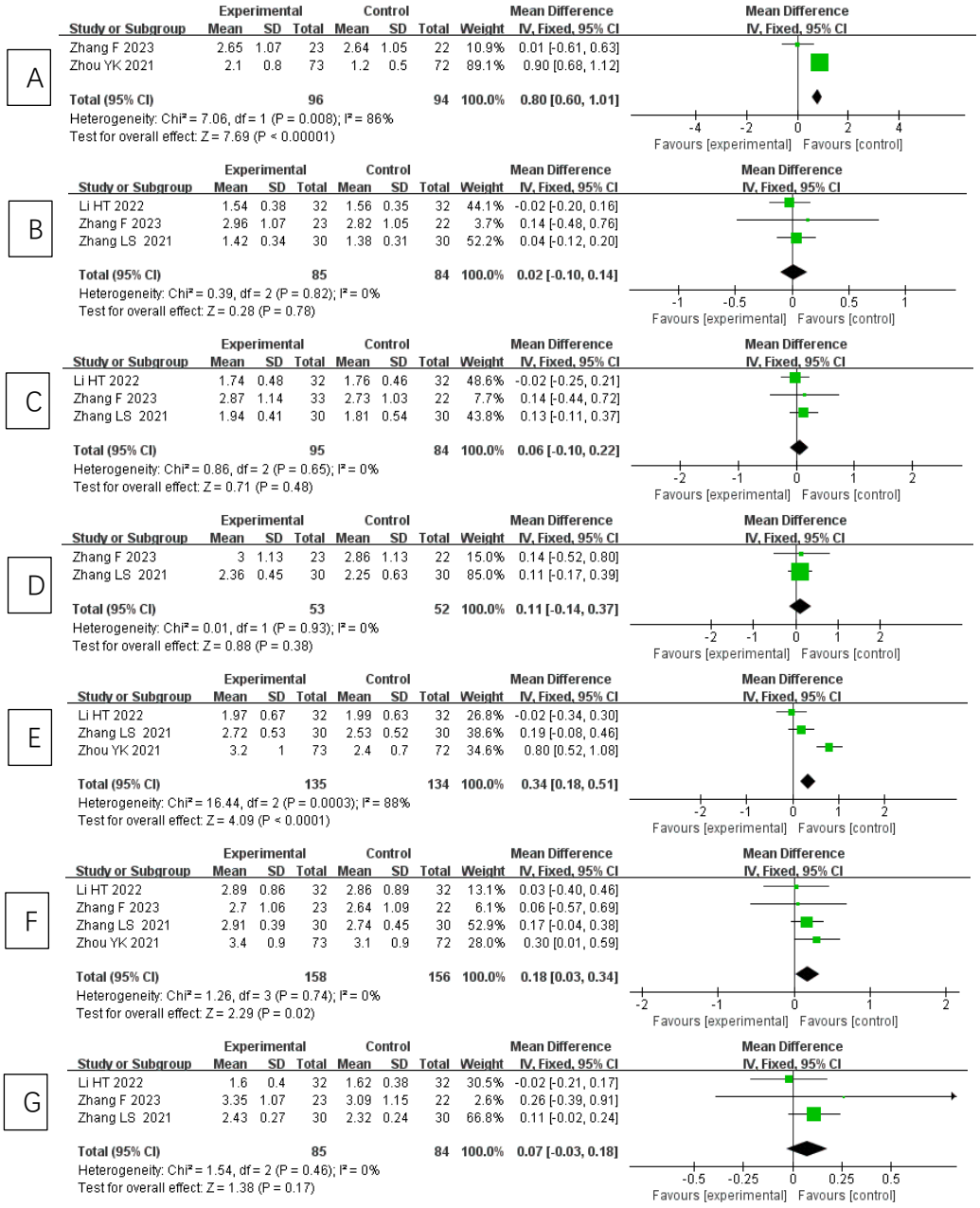

Figure 4: Postoperative pain scores at different time points during exercise

3.2.3 Time to first postoperative PCIA press and intraoperative remifentanil use in both groups

Two papers [8-9] compared the time to first postoperative PCIA with significant heterogeneity (I^2=96%, P<0.00001), and using a random-effects model, Meta-analysis showed that the time to first postoperative PCIA in the experimental group was significantly earlier than that in the control group (MD=-1.34, 95% CI -1.76 to -0.91, P<0.00001) (Figure 5-A). Two papers [9, 11] compared intraoperative remifentanil use without significant heterogeneity (I^2=24%, P=0.25), and using a fixed-effect model, Meta-analysis showed that intraoperative remifentanil use was significantly higher in the experimental group than in the control group (MD=30.43, 95% CI 6.00 to 54.86, P=0.01) (Figure 5-B).

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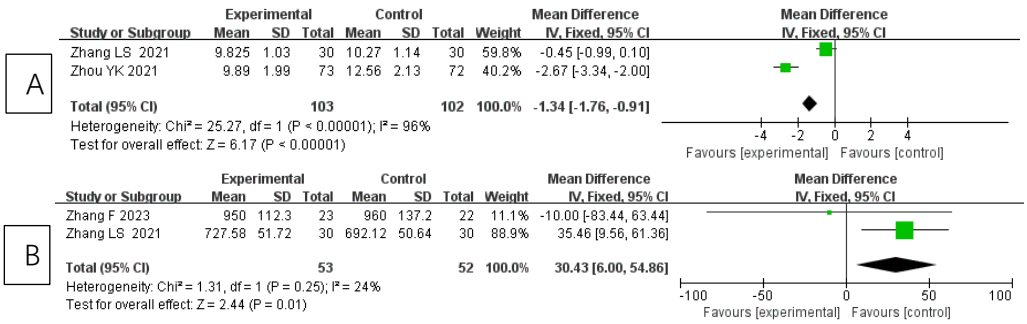

Figure 5: The time of first postoperative pressure on PCIA and the amount of remifentanil used during surgery in two groups of patients

3.2.4 Incidence of postoperative postoperative nausea and vomiting in both groups

Four studies [8-11] mentioned the occurrence of postoperative nausea and vomiting without significant heterogeneity (I2=0%, P=0.65), and using a fixed-effects model, Meta-analysis showed that the difference in the incidence of postoperative nausea and vomiting was not statistically significant between the two groups of patients (RR=1.60, 95% CI 0.66-3.87, P=0.29) (Figure 6).

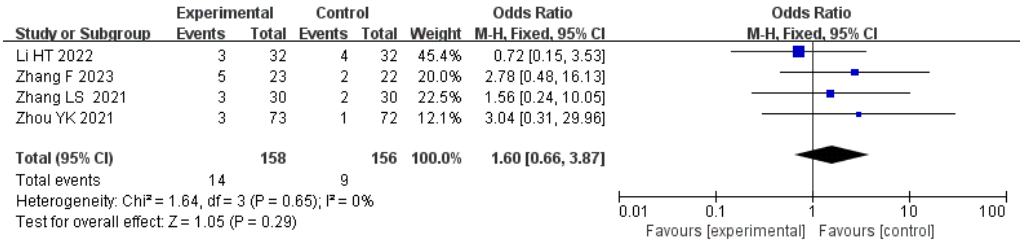

Figure 6: The incidence of postoperative nausea and vomiting in two groups of patients

3.2.5 Publication bias

Funnel plots were drawn based on the 24-h postoperative resting state pain scores of the two groups of patients, which were symmetrically distributed, and the results suggested a relatively small publication bias. (Figure 7)

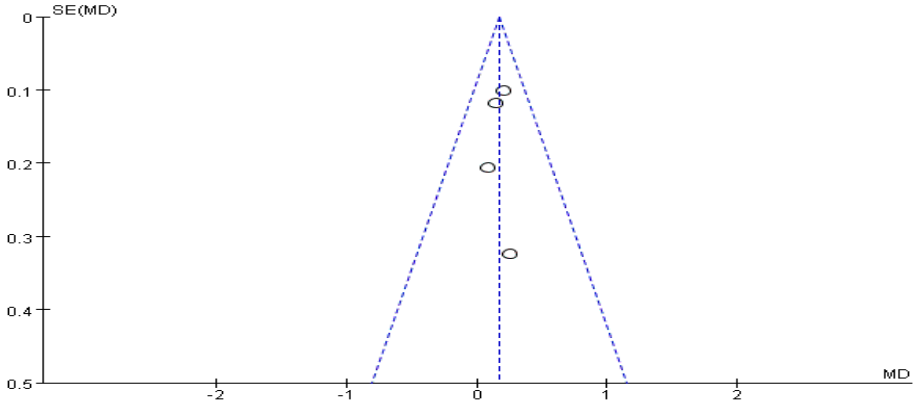

Figure 7: Funnel plot of publication bias in resting state pain scores at 24 hours post surgery

4. Discussion

After thoracoscopic surgery, most patients experience more than moderate pain[14] . Severe pain can severely impede patients' postoperative turning, coughing, and getting out of bed, which in turn may lead to an increased incidence of poor thoracic drainage, limited lung expansion, and infection. Thoracic paravertebral space block is the gold standard for post-thoracoscopic analgesia, and its analgesic effect is comparable to that of epidural block, which can be performed unilaterally with less hemodynamic impact. However, due to the deep location of the thoracic paravertebral space and its proximity to the spinal nerve roots, even with ultrasound guidance, it is sometimes inevitable to cause complications such

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as intravertebral block, nerve root injury, puncture of the pleura, and hemorrhage.Therefore, in recent years, anesthesiologists have carried out a lot of exploratory research in thoracoscopic postoperative analgesia, and some new regional block methods have appeared.Elsharkawy et al.[7] injected methylene blue into the rhomboid muscle-intercostal muscle gap at T5-T 6 by cadaveric bodies respectively, and observed that the diffusion of methylene blue ranged from T 3-T 6; and in the serratus anterior-intercostal muscle at T 7-T 8, and observed that the diffusion range of methylene blue was T 4-T 10. The diffusion range of methylene blue was observed to be T 4 -T 10. Biswas et al [15] used methylene blue 20 ml in the deep surface of the serratus anterior muscle in the 5th intercostal space, and observed that the diffusion range of methylene blue was T 3 -T 7. The diffusion range of the dye was related to the volume of the drug and the injection site, and the dye generally diffused to the cephalic and caudal ends of the segments, each of them being one to two segments. Therefore, theoretically, injection of local anesthetic in the rhomboid-intercostal muscle gap and low anterior serratus muscle gap can block the lateral cutaneous branch of the intercostal nerve in the plane of T 3 -T 9, and complete the cutaneous analgesia of the half side of the chest wall and the epigastric region. Currently, this block is called rhomboid intercostal muscle-low anterior serratus plane block.

Currently, clinical studies on the effectiveness of RISS and TPVB for perioperative analgesia in thoracoscopic surgery have conflicting results, and there is a lack of relevant systematic evaluations to further improve the level of clinical evidence. The results of this Meta-analysis showed that compared with the TPVB group, the RISS group had significantly higher pain scores in the resting state at 1h, 2h, 12h and 24h postoperatively; significantly higher pain scores in the locomotion state at 1h, 12h, and 24h postoperatively; the time of the first postoperative PCIA was significantly earlier; and the amount of intraoperative remifentanil used was significantly higher. There was no statistically significant difference in resting state pain scores at 4h, 8h and 48h postoperatively between the two groups. There was no statistically significant difference in postoperative pain scores at 2h, 4h, 8h and 48h in the motor state between the two groups. There was no statistically significant difference in the incidence of postoperative nausea and vomiting between the two groups. This result suggests that RISS, as a new type of blocking technique, is easy to operate and easy to learn, and its analgesic effect is comparable to that of TPVB, so it can be used as a new choice for postoperative analgesia after thoracoscopic surgery in adults.

This study has the following limitations: (1) the inclusion of the population, the drugs used in general anesthesia and the drugs used in nerve block are not identical, which may be a source of clinical heterogeneity; (2) the types and quantities of postoperative analgesic drugs used in PCA are inconsistent, which may be a source of clinical heterogeneity; (3) Some of the included literature had unclear allocation concealment, poor blinding, incomplete outcome data, and low overall quality of literature. The above defects may affect the results of this Meta-analysis, and further multi-center and large-sample RCTs are needed.

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