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Meta analysis of the effect of ultrasound-guided rhomboid intercostal and sub–serratus on perioperative analgesia in patients undergoing thoracic surgery

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Abstract: *The purpose of this article is to systematically evaluate the impact of ultrasound-guided rhomboid intercostal and subcostal serratus (RISS) plane block on perioperative analgesia and safety in patients undergoing thoracic surgery. Retrieve Cochrane, Pubmed, Embase, Wanfang, VIP, and CNKI to collect randomized controlled trials on the perioperative analgesic effect and safety of ultrasound guided RISS in patients undergoing thoracic surgery. The search was conducted from the establishment of the database until February 2024. According to the Cochrane guidance manual, literature was independently screened, data was extracted, and the risk of bias was evaluated for inclusion in the study, using RevMan 5 Perform meta-analysis using 3 software. A total of 4 RCTs were included, with a total of 230 patients, 115 in the RISS group and 115 in the control group (Control group). Compared with the Control group, the RISS group showed a significant decrease in resting state pain scores at 2 hours postoperatively (MD=-1.55, 95% CI -1.64-1.46, P<0.0001), 6 hours postoperatively (MD=-1.35, 95% CI -1.46-1.24, P<0.0001), 12 hours postoperatively (MD=-1.20, 95% CI -1.33-1.08, P<0.0001), 24 hours postoperatively (MD=-1.09, 95% CI -1.21-0.96, P<0.0001), and 48 hours postoperatively (MD=-0.32, 95% CI -0.44-0.21, P<0.0001). Compared with the Control group, the RISS group showed a significant decrease in motor pain scores at 2 hours post surgery (MD=-1.70, 95% CI -1.86-1.54, P<0.0001), 6 hours post surgery (MD=-1.38, 95% CI -1.61-1.16, P<0.0001), 12 hours post surgery (MD=-1.79, 95% CI -1.99-1.59, P<0.0001), and 24 hours post surgery (MD=-1.11, 95% CI -1.29-0.93, P<0.0001). Compared with the Control group, the RISS group showed a significant decrease in the effective number of postoperative analgesia pump presses (MD=-6.46, 95% CI -6.90-6.01, P<0.0001), the number of postoperative salvage analgesia cases (RR=0.11, 95% CI 0.05-0.23, P<0.0001), and the incidence of postoperative nausea and vomiting (RR=0.27, 95% CI 0.12-0.64, P=0.003).Current clinical evidence suggests that ultrasound-guided arcuate flexible RISS combined with general anesthesia is more effective in postoperative analgesia of thoracic surgery than simple general anesthesia, while reducing the incidence of adverse reactions such as nausea and vomiting.*

Keywords: *Ultrasound; rhomboid intercostal and subcostal serratus; thoracic surgery; analgesia; Meta analysis*

1. Introduction

Thoracic surgery has significant trauma, and due to intraoperative tissue damage, nerve traction, and postoperative drainage tube stimulation, patients undergoing related surgery often experience severe pain after surgery[1], which is not conducive to patient recovery. Multiple Enhanced Recovery After Surgery (ERAS) guidelines [2,3,4] point out that low opioid/de opioid multimodal pain management can reduce perioperative adverse reactions and help patients achieve rapid recovery, with the combined use of nerve block being an important pain management method. In 2018, Elsharkawy et al. [5] proposed a new nerve block method combining rhomboid intercostal and sub serratus (RISS) block. This method is easy to operate, with a block range of up to T4-T10, and has a clear analgesic effect on breast, chest wall, and upper abdominal surgery [6]. However, due to the short clinical application time of RISS and limited research on the analgesic effect of this method combined with general anesthesia in thoracic surgery, there are few reports on its adverse reactions, and there is no consensus on which is better or worse

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compared to simple general anesthesia. Therefore, this study intends to conduct a meta-analysis of randomized controlled trials (RCTs) that have been completed both domestically and internationally, screen literature that meets quality standards, and systematically evaluate and compare the analgesic effects and adverse reactions of general anesthesia combined with RISS combined with postoperative PCIA and simple general anesthesia combined with postoperative PCIA in patients undergoing thoracic surgery, in order to provide reference for clinical practice.

2. Materials and Methods

2.1 Literature search

Computer searches include Cochrane, Pubmed, Em base, Wanfang, VIP, and CNKI. The search period is from database establishment to March 2023. The Chinese search terms include ultrasound, ultrasound guided, B-ultrasound, rhomboid muscle intercostal muscle low anterior serratus muscle, and lung. The English search terms include ultrasonic guided, ultrasonic, type-b ultrasonic, rhomboid intercostal and sub-serratus and lung. Adjust the search method according to the search rules of different databases and implement literature search, while also consulting the references included in the literature. When the literature data is incomplete, try to contact the original author to obtain relevant data information. When the screening results of two independent researchers are inconsistent, a third researcher will evaluate and analyze the literature.

2.2 Inclusion and Exclusion Criteria

Literature inclusion criteria: ① Research type: randomized controlled trial; ② Research subjects: Patients undergoing lung surgery; ③ Intervention measures: Comparison between ultrasound-guided RISS combined general anesthesia and simple general anesthesia; ④ Main outcome measures: resting state pain score at 2, 6, 12, 24, and 48 hours postoperatively, and motor state pain score at 2, 6, 12, and 24 hours postoperatively; ⑤ Secondary outcome measures: number of effective compressions with postoperative pain pump, number of postoperative rescue analgesia, and incidence of postoperative nausea and vomiting.Exclusion criteria for literature: ① Research with incomplete data or inability to obtain full text, resulting in low literature quality; ② The outcome indicators do not match; ③ Repeated studies, case reports, literature reviews, animal experiments, and non in vivo studies.

2.3 Literature screening and quality evaluation

This study evaluated the literature quality of the included literature according to the recommended criteria in the Cochrane Handbook for evaluators. If there were any inconsistent results, a third researcher was asked to make an evaluation. The evaluation criteria for literature quality mention the following seven items: (1) random sequence generation; (2) Whether to hide the allocation of random schemes; (3) Blinding of researchers and subjects; (4) Blind evaluation of research results; (5) Integrity of result data; (6) Whether to selectively report research results; (7) Other biases. The researchers evaluated the included literature based on the seven criteria mentioned above and made judgments of "high risk bias," "low risk bias," and "unclear risk bias." If all 7 out of 7 fields have a bias risk of "low risk bias", the study is classified as "low risk bias". If one or more fields are classified as "high bias" or "unclear bias," the study is classified as "high-risk bias."

2.4 Data extraction

The included research data extraction includes basic literature information (author, publication year), included research features (sample size, age, gender, BMI, ASA grading, surgical time, type and dosage of local anesthesia). The main outcome measure is the resting state pain score at 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours after surgery, as well as the exercise state pain score at 2 hours, 6 hours, 12 hours, and 24 hours after surgery. The secondary outcome measure is the number of effective compressions of the postoperative analgesic pump. The frequency of postoperative relief analgesia and the incidence of postoperative nausea and vomiting.

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2.5 Statistical analysis

RevMan 5.3 software was used to analyze the included studies. Perform heterogeneity testing on the data, and if there is no significant heterogeneity (I^2<50%, P>0) 1) Using a fixed effects model; If there is significant heterogeneity ($I^2 \geq 50\%$, $P \leq 0$.) 1) Then, a random effects model is used. The mean difference (MD) or standard mean difference (SMD) and their 95% confidence interval (CI) used to represent continuous variables; The binary variables are represented by odds ratio (OR) and its 95% CI. P<0.05 indicates a statistically significant difference.

3. Results

3.1 Literature screening results

According to the retrieval method in the article, a total of 22 articles were retrieved, and after layer by layer screening based on inclusion and exclusion criteria, 4 RCTs [7-10] were ultimately obtained. See Figure 1.

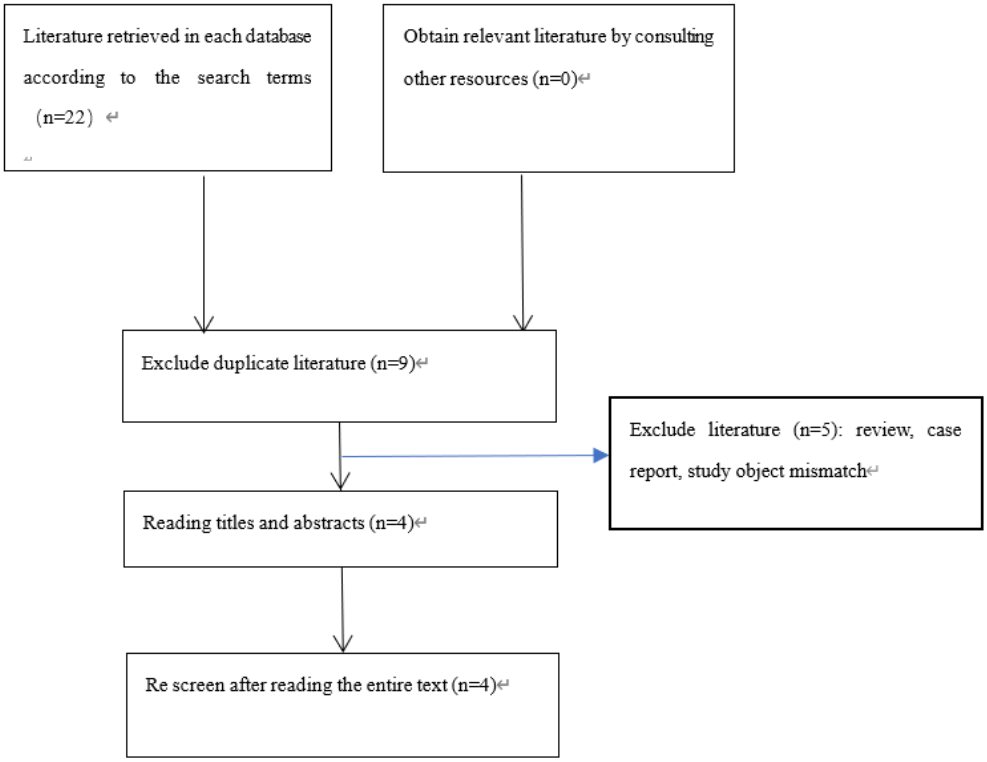

Figure 1: Literature Screening Process

3.2 Basic information and bias risk assessment of included 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	Control group	RISS group	Control group	RISS group	Control group	RISS group	Control group	RISS group	Control group	RISS group	Control group	RISS group	Control group	RISS group	Control group
Zhang LS 2021 [7]	35	35	34.51±3.51	33.48±3.62	31/4	29/6	22.12±1.32	22.43±1.41	28/7	30/5	61.23±5.24	60.84±5.32	0.4% ropivacaine 15ml		1、2、3、4、5、6、7、8、9、10、11、12	
Yi QL 2021 [8]	30	30	42. 64±6. 21	43. 12±5. 01	17/13	14/16	22. 75±0. 99	22. 37±1. 28			204. 53±48. 27	216. 32±36. 49	0. 2%ropivacaine 30 ml		1、2、3、4、6、7、8、9、10、11、12	
Liu FF 2022 [9]	30	30	43.8±11.5	46.5±16.8	20/10	18/12	23.5±2.8	22.4±3.0	7/23	5/25	130.0±3.6	130.0±6.6	0.5%ropivacaine15ml		1、3、4、11、12	
Wang M 2022 [10]	20	20	65.2±4.9	67.7±5.5	10/10	12/8	23.3±1.7	22.1±2.2	4/11/5	3/13/4	135.6±14.9	150.4±18.7	0.3%ropivacaine 30ml		2、4、5、10、11	

1, 2, 3, 4, and 5 are the resting state pain scores at 2 hours, 6 hours, 12 hours, 24 hours, and 48 hours postoperatively, respectively; 6. 7, 8, and 9 are pain scores for motor status at 2, 6, 12, and 24 hours postoperatively, respectively; 10 is the effective number of compressions of the postoperative analgesic pump; 11 is the number of times postoperative salvage analgesia is performed; 12 is the occurrence of postoperative nausea and vomiting.

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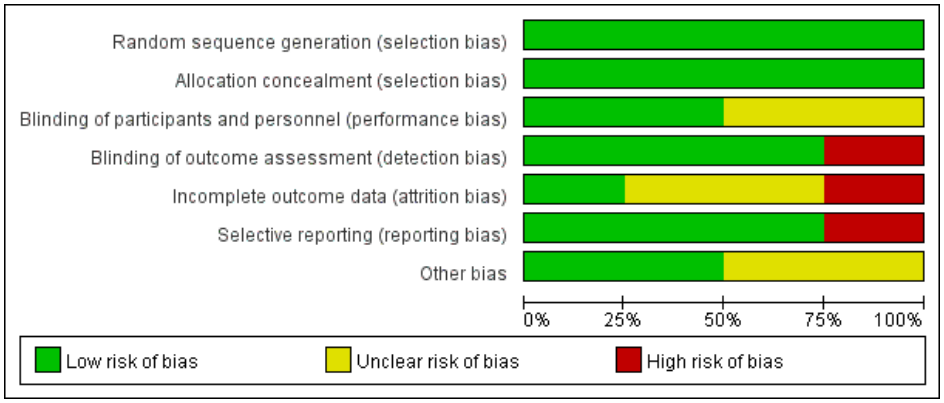
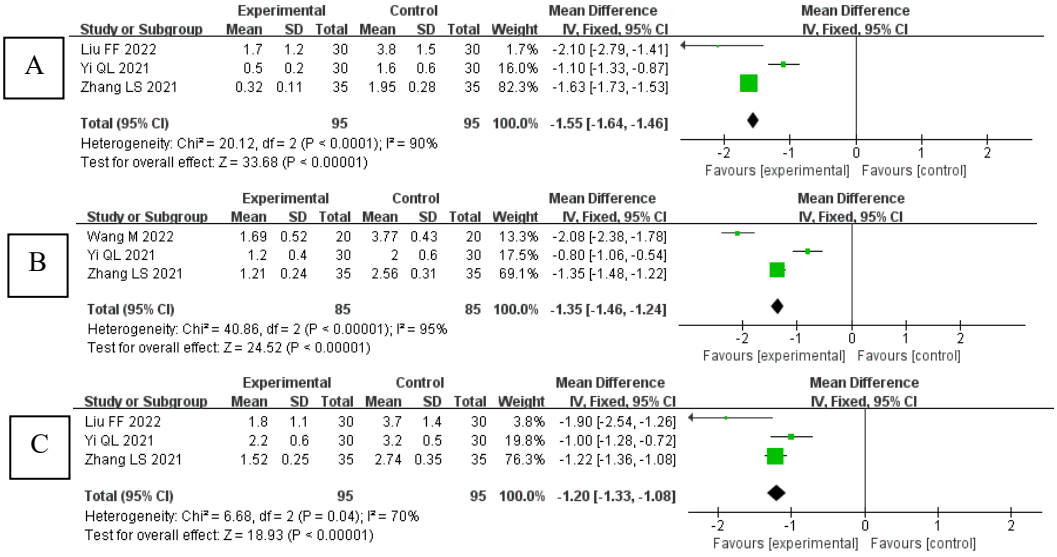


Figure 2: Bias Risk Assessment Chart

3.2.1 Resting state pain scores at different time points after surgery for two groups of patients

Three articles [7-9] compared the resting state pain scores at 2 hours post surgery, showing significant heterogeneity (I^2=90%, P<0.0001). Using a random effects model, meta-analysis results showed that the resting state pain scores at 2 hours post surgery in the experimental group were significantly lower than those in the control group (MD=-1.55, 95% CI -1.64-1.46, P<0.0001) (Figure 3-A). Three articles [7-8,10] compared the resting state pain scores at 6 hours post surgery, showing significant heterogeneity (I^2=95%, P<0.0001). Using a random effects model, meta-analysis results showed that the resting state pain scores in the experimental group were significantly lower than those in the control group at 6 hours post surgery (MD=-1.35, 95% CI -1.46-1.24, P<0.0001) (Figure 3-B). Three articles [7-9] compared the resting state pain scores at 12 hours post surgery, showing significant heterogeneity (I^2=70%, P=0.04). Using a random effects model, meta-analysis results showed that the resting state pain scores in the experimental group were significantly lower than those in the control group at 12 hours post surgery (MD=-1.20, 95% CI -1.33-1.08, P<0.0001) (Figure 3-C). Four articles [7-10] compared the resting state pain scores at 24 hours after surgery, showing significant heterogeneity (I^2=88%, P<0.0001). Using a random effects model, meta-analysis results showed that the resting state pain scores in the experimental group were significantly lower than those in the control group (MD=-1.09, 95% CI -1.21-0.96, P<0.0001) (Figure 3-D). Two studies [7,10] compared the resting state pain scores at 48 hours post surgery, showing significant heterogeneity (I^2=91%, P=0.001). Using a random effects model, meta-analysis results showed that the resting state pain scores in the experimental group were significantly lower than those in the control group at 48 hours post surgery (MD=-0.32, 95% CI -0.44-0.21, P<0.0001) (Figure 3-E).



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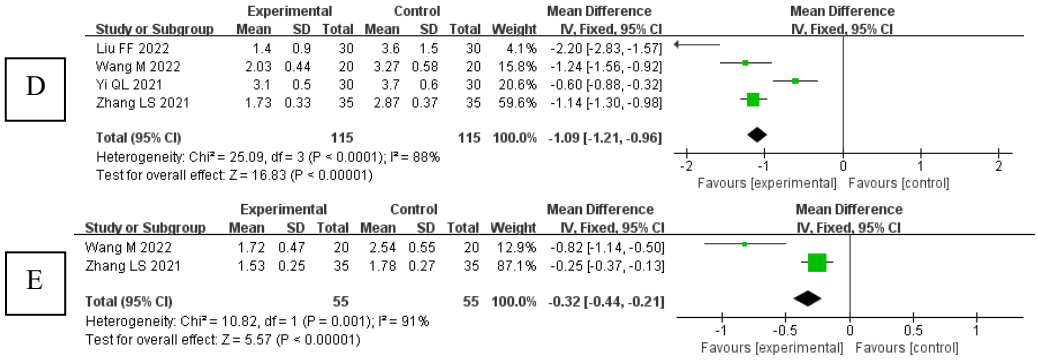

Figure 3: Resting state pain scores at different time points after surgery

3.2.2 Postoperative pain scores of two groups of patients at different time points

Two articles [7-8] compared the postoperative 2-hour motor state pain scores, showing significant heterogeneity (I^2=80%, *P*=0.03). Using a random effects model, meta-analysis results showed that the experimental group had significantly lower motor state pain scores than the control group (MD=-1.70, 95% CI -1.86-1.54, *P*<0.0001) (Figure 4-A). Two articles [7-8] compared the postoperative 6-hour motor state pain scores without significant heterogeneity (I^2=0%, *P*=0.90). Using a fixed effects model, meta-analysis results showed that the experimental group had significantly lower motor state pain scores than the control group at 6 hours post surgery (MD=-1.38, 95% CI -1.61-1.16, *P*<0.0001) (Figure 4-B). Two articles[7-8]compared the postoperative 12 hour motor state pain scores without significant heterogeneity (I^2=39%, *P*=0.20). Using a fixed effects model, meta-analysis results showed that the experimental group had significantly lower motor state pain scores than the control group (MD=-1.79, 95% CI -1.99-1.59, *P*<0.0001) (Figure 4-C). Two articles [7-8] compared the postoperative 24-hour motor state pain scores, showing significant heterogeneity (I^2=99%, *P*<0.00001). Using a random effects model, meta-analysis results showed that the experimental group had significantly lower postoperative motor state pain scores than the control group (MD=-1.11, 95% CI -1.29-0.93, *P*<0.00001) (Figure 4-D).

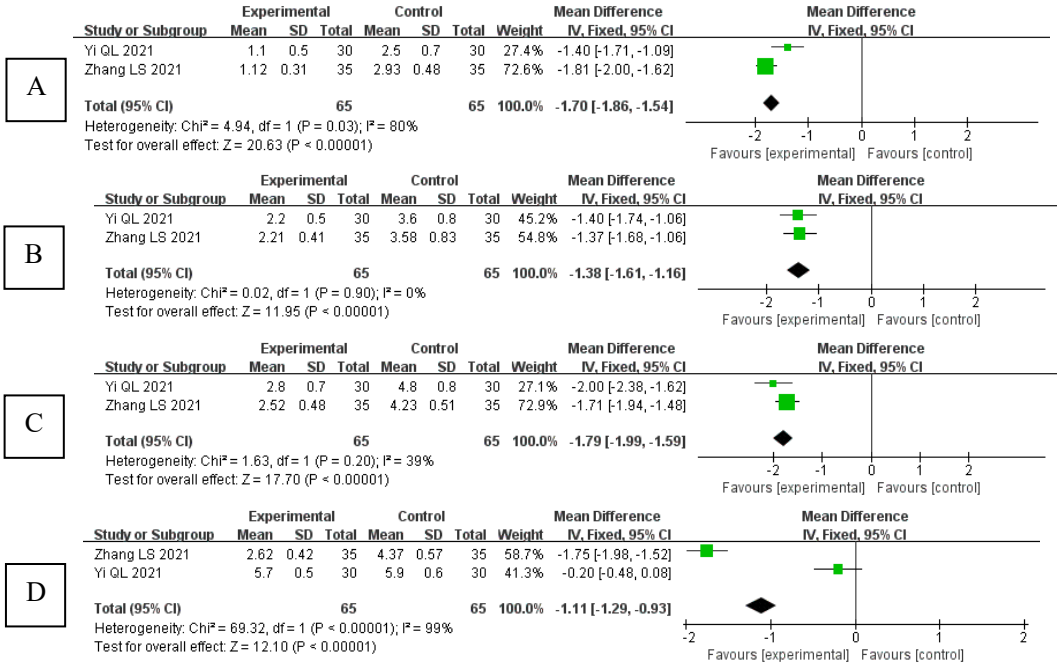

Figure 4: Postoperative pain scores at different time points during exercise

3.2.3 Effective number of postoperative analgesia pump presses for two groups of patients

Three articles [7-8,10] compared the effective press frequency of postoperative analgesic pumps, showing significant heterogeneity (I^2=99%, *P*<0.0001). Using a random effects model, meta-analysis results showed that the effective press frequency of postoperative analgesic pumps in the experimental group was significantly lower than that in the control group (MD=-6.46, 95% CI -6.90-6.01, *P*<0.0001) (Figure 5).

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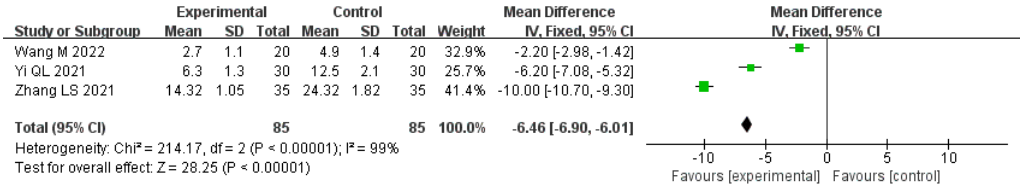

Figure 5: Effective number of compressions of the analgesic pump

3.2.4 Number of cases of postoperative salvage analgesia in two groups of patients

Four articles [7-10] compared the number of postoperative salvage analgesia cases without significant heterogeneity (I^2=46%, *P*=0.14). Using a fixed effects model, meta-analysis results showed that the number of postoperative salvage analgesia cases in the experimental group was significantly lower than that in the control group (RR=0.11, 95% CI 0.05-0.23, *P*<0.0001) (Figure 6).

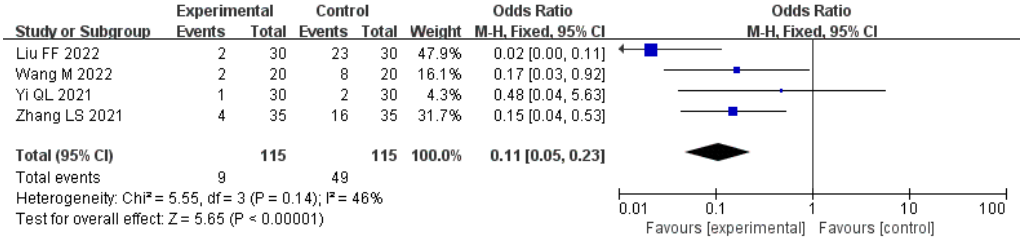

Figure 6: Number of cases of rescue analgesia

3.2.5 Incidence of postoperative nausea and vomiting

Three studies [7-9] mentioned the occurrence of postoperative nausea and vomiting without significant heterogeneity (I^2=0%, *P*=0.64). Using a fixed effects model, meta-analysis results showed that the incidence of postoperative nausea and vomiting in the experimental group was significantly lower than that in the control group (RR=0.27, 95% CI 0.12-0.64, *P*=0.003) (Figure 7).

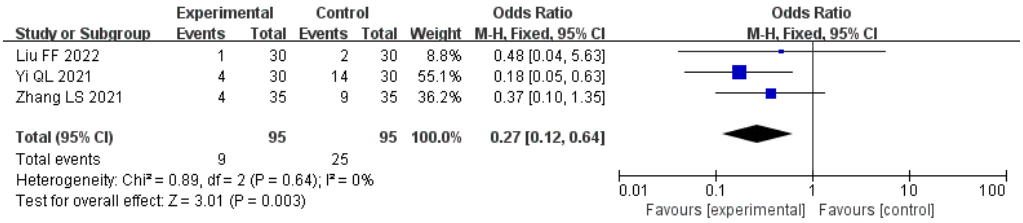

Figure 7: Postoperative nausea and vomiting incidence

3.2.6 Publication bias

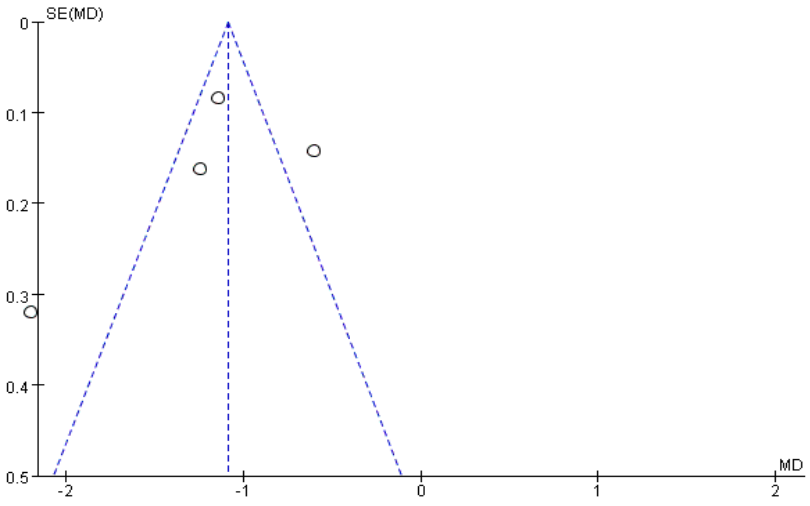

Figure 8: Funnel plot of publication bias in resting state pain scores at 24 hours post surgery

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A funnel plot was drawn based on the resting state pain scores of two groups of patients at 24 hours post surgery. The funnel plot was symmetrically distributed, and the results indicated a relatively small publication bias. (Figure 8)

4. Discussion

This study included 4 RCTs with a total of 230 patients, aiming to directly evaluate the postoperative analgesic effect and adverse reactions of ultrasound-guided RISS combined with general anesthesia in patients undergoing thoracic surgery. The nerve fibers that transmit bodily and visceral pain sensation are abundant in the chest wall and chest cavity. Tissue damage, pleural injury, and the influence of thoracic drainage tubes caused by thoracic surgery can easily lead to the release of a large amount of inflammatory mediators, causing severe postoperative pain in patients [7]. Postoperative pain stimuli from physical and visceral pain not only easily cause respiratory complications, such as hypoxia, atelectasis, and pneumonia; There is also a risk of evolving into chronic pain, which seriously affects the quality of rehabilitation for patients [8]. The postoperative analgesia methods for thoracic surgery [9,10] include patient-controlled intravenous analgesia (PCIA), epidural analgesia (EB), and thoracic paravertebral nerve block (TPVB). PCIA often adds opioid drugs, which may cause adverse reactions such as nausea, vomiting, and constipation after intravenous injection; The care and maintenance of EB analgesic catheters are inconvenient, and there is a risk of epidural hematoma; The analgesic effect of TPVB is comparable to that of epidural catheterization, but there is a risk of hemopneumothorax in patients during the operation [10,11]. RISS [5,12], as an emerging technique for thoracic nerve block, performs biplane block at the rhomboid intercostal plane and the low anterior serratus plane in the back, blocking the lateral cutaneous branches of the T4-T10 intercostal nerve, reducing the transmission of somatic pain sensation, and producing a sufficient analgesic effect covering the surgical range of the chest.

This meta-analysis showed that compared to the simple general anesthesia group, patients under RISS combined general anesthesia had a significant decrease in postoperative pain scores in both resting and moving states, and had fewer times of postoperative relief analgesia. The number of effective compressions of the analgesic pump was also reduced, proving that RISS combined general anesthesia can have a more comprehensive analgesic effect on thoracic surgery, reduce postoperative pain in lung surgery patients, and improve postoperative comfort. Analysis of reasons: Simple general anesthesia [13,14] only exerts its effects by inhibiting the hypothalamus, cerebral cortex, and other parts, without directly blocking the transmission of harmful stimuli caused by trauma to the central nervous system; Therefore, a large amount of inflammatory mediators are secreted during surgery, causing circulatory fluctuations and postoperative pain hypersensitivity; As mentioned earlier, RISS [5,15] can not only block the transmission of somatic pain to the central nervous system, but also block the effects of local anesthetics spreading to the thoracic vertebrae on the thoracic nerve roots and sympathetic nerves, achieving a blockade of visceral pain transmission and producing a more comprehensive analgesic effect. This is the reason for the significant decrease in postoperative pain scores in the RISS combined general anesthesia group. However, there was no statistically significant difference in pain scores between the two groups of patients during exercise 48 hours after surgery, possibly due to the limited duration of single RISS analgesia. This result is similar to the study by Elsharkawy et al. [5], which found that the duration of a single RISS was 12-24 hours. The above effects may also be the reason why the analgesic effect of RISS group was strengthened, which led to the decrease of the amount of opioids used in perioperative period, and thus the reduction of related side effects (nausea, vomiting, urinary retention).

5. Result

In summary, the application of general anesthesia combined with ultrasound guided RISS in thoracic surgery patients is significantly better than simple general anesthesia. The former can significantly reduce the use of opioids, reduce the incidence of adverse reactions, lower postoperative pain scores, significantly improve perioperative comfort, and promote rapid recovery of patients.

There are several shortcomings in the current evaluation of this system: (1) Some studies included in the literature have different ultrasound scanning methods, surgical methods, types, concentrations, and doses of local anesthesia drugs, which may increase clinical heterogeneity; (2) There are relatively few high-quality literature included in the literature; (3) The assessment of pain severity varies among different studies, which may lead to measurement bias. Taking into account the aforementioned shortcomings and limited by the current number of original studies, the conclusions of this study still

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need to be validated through multi center, large sample, and high-quality RCTs.

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