

## Review Article

# Meta-Analysis of Open-Heart Surgery Pain Relief Using Transversus Thoracic Plane Blocks

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Received 15 August 2023; Accepted 25 January 2024; Published 7 February 2024

Academic Editor: Frederico Benetti

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**Background.** Severe postoperative pain is commonly reported following open-heart surgery, necessitating the implementation of effective pain management strategies to facilitate patient recovery. The benefits of the transverse thoracic muscle plane (TTMP) block for open-heart surgery remain unclear. Therefore, a meta-analysis was conducted to systematically evaluate the effect of TTMP on postoperative analgesia and recovery in patients undergoing open-heart surgery. **Methods.** A computer search was performed in PubMed, Cochrane, Embase, CNKI, and Wangfang databases. The primary outcome was 24-hour postoperative opioid consumption, and the secondary outcomes were 12- and 24-hour postoperative resting and motor pain scores, time of first analgesia demand, extubation time, length of stay in the intensive care unit (ICU), time of first feces, incidence of nausea and vomiting, and length of hospitalization. **Results.** Thirteen randomized controlled trials (RCTs) involving a total of 766 patients were included in this meta-analysis. Compared with the control group, the TTMP group showed a significant reduction in opioid consumption within 24 h postoperatively (mean difference = -41.88 mg; 95% confidence interval: -51.99, -31.77;  $p < 0.001$ ; and  $I^2 = 98\%$ ). However, the 12- and 24-hour postoperative resting and moment VAS pain scores were significantly lower in the TTMP group. In addition, the TTMP group had a longer time of first analgesic demand; shorter endotracheal intubation time, ICU stay duration, time of first feces, and length of hospital stay; and a lower incidence of nausea and vomiting. **Conclusions.** Perioperative TTMP block can reduce the use of opioids in patients undergoing open-heart surgery for 24 h postoperatively, decrease the early postoperative pain scores, prolong the time of first analgesic demand, shorten the time of extubation and the length of ICU stay and hospitalization, and reduce the incidence of nausea and vomiting, which are all conducive to the recovery of patients. **Registration.** This trial is registered with PROSPERO database (CRD42022312435).

## 1. Introduction

Patients undergoing open-heart surgery with midsternotomy incision often experience severe pain after surgery. Early postoperative pain exacerbates stress response; increases the incidence of pulmonary atelectasis, pneumonia, and cardiovascular adverse events; prolongs hospitalization; and increases mortality [1]. Poor control of acute pain in the early postoperative period may develop into chronic pain, significantly affecting patients' quality of life in the long term [2]. Therefore, pain management in patients after cardiac surgery is of paramount importance. High-dose opioid is the primary

perioperative analgesic for open-heart surgery. However, opioids have been associated with ventilator-associated pneumonia, prolonged time on tubes, and prolonged intensive care unit (ICU) stays and hospitalizations [3]. At present, with the promotion of ultrasound technology in the field of anesthesia, multimodal analgesia based on the regional nerve block has been widely used and achieved promising results [4].

The sources of pain in open-heart surgery are complex; they include pain from superficial, deep somatic sources and postoperative visceral components. Midsternotomy incision is considered the primary source of pain, with the most

severe pain occurring within the first 24 h. The sternal region is mainly sensed by the intercostal nerves [5]. Sensation in this region was mainly innervated by the anterior cutaneous branch of the intercostal nerve, which migrated from the intercostal nerve in the paraspinal region [6]. Transverse thoracic muscle plane (TTMP) block is a blocking technique developed in recent years. It involves injecting local anesthetic between the intercostal muscles and the transverse pectoral muscles, effectively blocking the anterior cutaneous branch of the intercostal nerve [7]. Several studies reported the use of TTMP in different types of surgeries, including mastectomy, sternal fractures, open pectus carinatum, pericardiocentesis, and cardiac implantable electronic device insertions involving the anterior chest wall [8–12]. In 2019, a pilot feasibility study explored the efficacy and safety of TTMP for analgesia in open-heart surgery [13]. Subsequently, several studies reported the application of TTMP in cardiac surgery, but the sample size of individual studies is small and their clinical effects are still controversial. The advantages of TTMP after open-cardiac surgery have not yet been fully and effectively demonstrated.

Therefore, this study aimed to evaluate the analgesic effect of TTMP on recovery after midsternotomy cardiac surgery by meta-analysis to provide reference for postoperative analgesia and accelerated recovery of cardiac surgery patients.

## 2. Materials and Methods

**2.1. Literature Review and Search Strategy.** This study followed the Preferred Reporting Items for Systematic Evaluation and Meta-Analysis, and it was registered on the PROSPERO website. Computerized searches, without language restriction, were performed by two independent investigators on PubMed, Cochrane, Embase, CNKI, and Wanfang databases. The time period was from database construction to March 2023. The search terms were “transverse thoracic muscle plane block, cardiac surgery, postoperative.” Trial registries were searched in accordance with prepublished protocols to identify ongoing trials. Manual searches were performed through the reference lists of relevant primary and review articles to ensure completeness. The supplementary files provide records of specific searches (Supplementary Table 1).

**2.2. Inclusion and Exclusion Criteria.** The inclusion criteria for this meta-analysis were as follows: (1) study design: randomized controlled trials (RCTs); (2) study population: adult patients undergoing midsternotomy cardiac surgery; (3) intervention: receiving TTMP guided by ultrasound for the experimental group and a blank control or placebo for the control group; and (4) outcome measures: at least one outcome parameter, including postoperative opioid consumption, early postoperative pain scores, duration of endotracheal intubation, length of ICU stay, and incidence of nausea and vomiting. The exclusion criteria were as follows: (1) reviews or case reports and retrospective studies, (2) pediatric patients, (3) conference abstracts, (4) duplicate publications, and (5) incomplete data in literature.

**2.3. Data Retraction.** EndNote 20 was used to select trials from duplicates that matched the study. Two researchers (RPZ and XLY) examined the titles and abstracts for eligibility and carefully assessed the full texts to ensure they met the inclusion criteria. They independently performed documentation and data extraction and resolved any disagreements by mutual discussion or consultation with a third party (YZ). Attempts were made to contact corresponding authors with incomplete data or studies in progress for further information. The general data extracted were as follows: name of the first author, time of publication, sample size, intervention, analgesic regimen, and so on. The primary outcome extracted was 24-hour postoperative opioid consumption. The secondary outcomes included pain scores at rest and during exercise at 12 h and 24 h postoperatively, time of first analgesia demand, extubation time, length of stays in ICU, time of first feces, incidence of nausea and vomiting, and length of hospitalization. Postoperative opioid consumption was converted to oral morphine equivalents (morphine iv 10 mg = morphine oral 30 mg = hydromorphone iv 1.7 mg = tramadol oral 150 mg = pethidine iv 75 mg = sufentanil iv 15  $\mu$ g = fentanyl iv 150  $\mu$ g) [14]. All postoperative pain scores were converted to equivalent scores on a 0–10 cm visual analog scale (VAS).

**2.4. Quality Assessment.** For the included RCTs, the recommended criteria of Cochrane Systematic Evaluation Manual 5.1.0 were strictly followed, and a third evaluator was asked to judge any inconsistent results [15]. The following criteria were mentioned in the evaluation of the quality of literature: (1) generation of randomized sequences; (2) whether the allocation was hidden; (3) blinding of investigators and subjects; (4) blinding of study results; (5) completeness of the outcome data; (6) selective reporting of study results; and (7) other biases. Each included literature was evaluated in accordance with the abovementioned criteria and judged as “high risk of bias,” “low risk of bias,” or “unclear risk of bias.”

**2.5. Statistical Analysis.** Statistical analysis was performed using RevMan 5.3 software. Continuous data were expressed as the mean difference (MD), and its 95% confidence interval (CI) and statistical transformations were used to estimate the mean and SD when the mean and 95% CI were reported or if the median (IQR) and median (min and max) were reported [16]. If data could not be transformed and contacting the authors was unsuccessful, the data were not included in the analysis. The heterogeneity of the literature was assessed by calculating the  $I^2$  coefficients.  $I^2 > 50\%$  was considered significant heterogeneity and a random-effects model was applied, whereas  $I^2 < 50\%$  was considered small heterogeneity and a fixed-effects model was applied. Subgroup and sensitivity analyses were performed to explore the sources of heterogeneity for the main surgical outcomes, focusing on the surgical type, use of cardiopulmonary bypass, and timing of blockade. A  $p$  value  $< 0.05$  was considered statistically significant. The funnel plot of the main outcome indicators was used to assess the publication bias of the included studies.

### 3. Results

**3.1. Search Results.** A total of 653 studies (PubMed, 35; Embase, 102; Cochrane 477; CNKI, 20; and Wangfang, 19) were searched. Among them, 215 studies were obtained after eliminating duplicates. Then, 37 studies were included after reading the titles and abstracts and excluding articles that did not meet the inclusion criteria. Finally, 13 studies were included after reading the full text, including seven studies in English [13, 17–22] and six non-English [23–28] studies. Zhao et al. [26] performed TTMP with different local anesthetic concentrations for comparison, and we selected the higher concentration group for inclusion in the analysis. The total number of patients was 805, of which 404 were categorized into the TTMP group and 401 into the control group. The studies were published between 2019 and 2023, which indirectly indicates that TTMP is a new technique. The flowchart of literature screening is shown in Figure 1.

The basic characteristics of the included studies are shown in Table 1. The patients included in the study were above 18 years of age, and they underwent different types of surgeries, such as coronary artery bypass grafting, aortic valve replacement, mitral valve replacement, or multiple valve replacement. TTMP was performed before induction of anesthesia in four studies, after induction of anesthesia in seven studies, and at the end of surgery in two studies. Seven studies involved placebo injections of saline, and six studies had blank control. Patient-controlled intravenous analgesia was chosen as the postoperative analgesic modality in 10 studies.

**3.2. Quality Assessment.** In accordance with the Cochrane risk-of-bias tool, most of the included articles were assessed to have low risk of bias. All included studies showed a low risk of randomization. Eight of the 13 studies did not describe allocation concealment in detail, and five of these were from non-English literature. The specific risk assessments are shown in Figure 2.

The evidence was formally graded using GRADEpro software to provide an overall level of evidence for the effectiveness of ultrasound-guided TTMP for analgesia in open-heart surgery. The quality levels for each secondary outcome ranged from low to high, as shown in Table 2. Detailed information was provided in the supplementary material (Supplementary Table 2).

#### 3.3. Primary Outcomes

**3.3.1. Postoperative Opioid Consumption during the First 24 H.** Among the included literature, 11 compared the 24-hour postoperative opioid consumption [13, 17–22, 24–27]. The results of the heterogeneity test showed significant heterogeneity ( $I^2 = 98\%$ ). Thus, the studies were analyzed using a random-effects model, and the results showed that the 24-hour postoperative opioid consumption in the TTMP group (MD =  $-41.88$  mg; 95% CI  $-51.99, -31.77$ ;  $p < 0.001$ ; and  $I^2 = 98\%$ ) was significantly less than that in the control (Figure 3). According to the GRADE system, the quality of evidence for our primary outcome was moderate.

To explore the high heterogeneity observed in the study, we first performed sensitivity analyses for each exclusion of results, and the heterogeneity did not change significantly. Subsequently, we performed subgroup analyses in accordance with the type of surgery, timing of block, and postoperative analgesia modality. Similarly, no source of heterogeneity was identified (Supplementary Figure 1).

#### 3.4. Secondary Outcomes

**3.4.1. Postoperative VAS Score.** Among the included studies, nine compared postoperative 12-hour resting pain scores [13, 17–20, 23, 26, 27] and eleven compared postoperative 24-hour resting pain scores [13, 17–23, 26–28]. Furthermore, eight studies [13, 17, 19, 20, 22, 23, 26, 27] compared the 12- and 24-hour postoperative moment pain scores. The 12 h postoperative resting (MD =  $-1.36$ ; 95% CI  $-1.60, -1.12$ ;  $p < 0.001$ ; and  $I^2 = 5\%$ ) and moment (MD =  $-2.32$ ; 95% CI  $-3.31, -1.33$ ;  $p < 0.001$ ; and  $I^2 = 91\%$ ) VAS pain scores were significantly lower in the TTMP group than those in the control group. The 24-hour resting (MD =  $-1.04$ ; 95% CI  $-1.53, -0.55$ ;  $p < 0.001$ ; and  $I^2 = 84\%$ ) and moment (MD =  $-1.44$ ; 95% CI  $-2.69, -0.19$ ;  $p = 0.02$ ; and  $I^2 = 96\%$ ) VAS pain scores were also significantly lower in the TTMP group (Figure 4).

**3.4.2. Time of First Analgesic Demand.** Of the studies included, four studies [13, 17, 18, 20] reported the time of first analgesic demand. The TTMP group showed a statistically significant prolongation of the time of first analgesic demand compared with the control group. The quality of evidence was downgraded to low due to heterogeneity and imprecision (Table 2).

**3.4.3. Extubation Time.** Among the studies included, 12 studies [13, 17–24, 26–28] compared the postoperative time of extubation, and it was significantly shorter in the TTMP group than in the control group. The level of evidence was rated as moderate due to significant heterogeneity (Table 2).

**3.4.4. Length of ICU Stay.** Among the included studies, 11 studies [17–21, 23–28] compared the length of stays in the ICU. The TTMP group had a significantly shorter ICU stay than the control group. Due to the significant heterogeneity, the level of evidence was rated as moderate (Table 2).

**3.4.5. Time of First Feces.** Three studies [19, 21, 25] compared the time of first feces. The TTMP group had a significantly shorter time of first feces than the control group. The quality of evidence was downgraded to low due to heterogeneity and imprecision (Table 2).

**3.4.6. Incidence of PONV.** Of the included studies, seven studies [13, 17, 21, 22, 24–26] reported the incidence of nausea and vomiting in patients, and it was lower in the

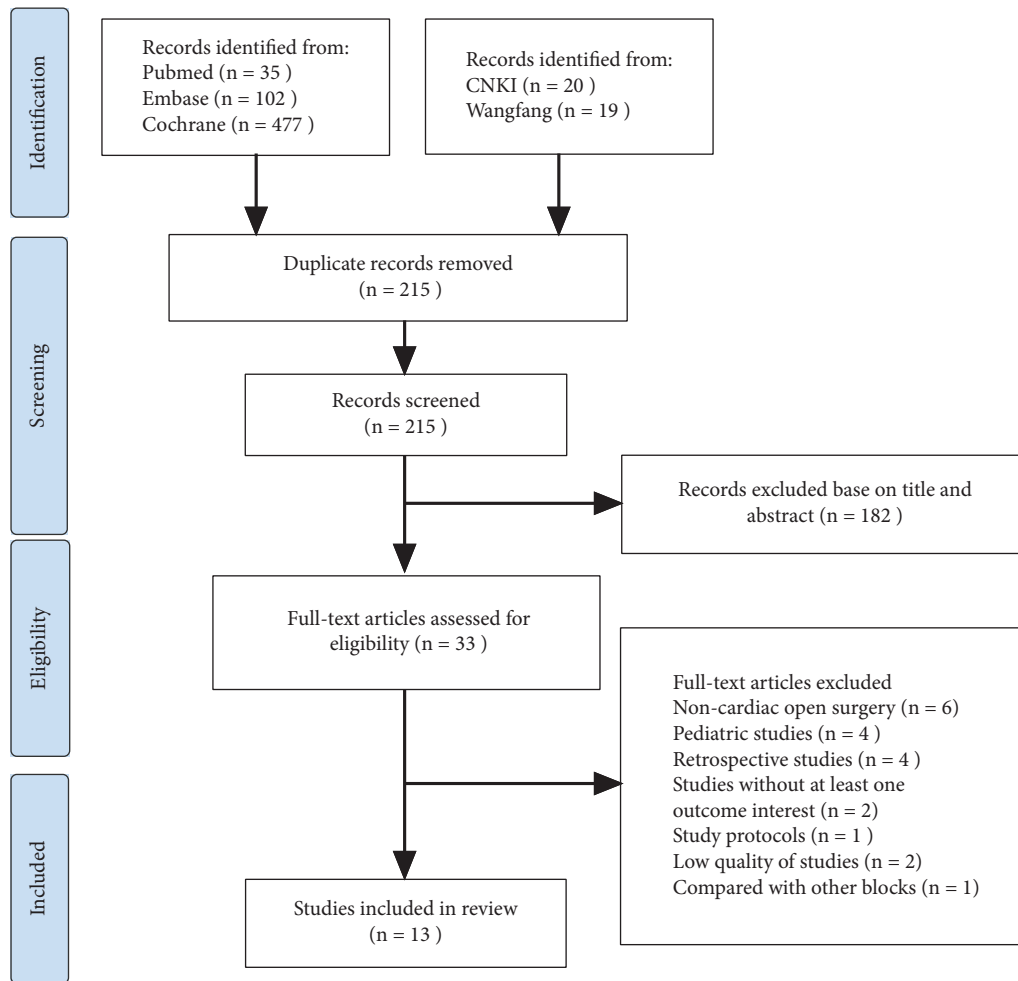


FIGURE 1: Flowchart of the search strategy to identify the eligible randomized controlled trials.

TTMP group than in the control group. The quality of evidence was downgraded to low due to heterogeneity and imprecision (Table 2).

**3.4.7. Length of Hospital Stay.** Among the studies included, five studies [19–21, 24, 25] reported the length of hospitalization of the patients, and it was shorter in the TTMP group than in the control group. The quality of evidence was downgraded to low due to heterogeneity and imprecision (Table 2). Forest plots for secondary endpoints are shown in the Supplementary file (Supplementary Figure 2).

**3.5. Publication Bias.** A funnel plot based on comparisons of postoperative opioid use for the primary outcome showed that the included studies were generally symmetrical, suggesting no significant publication bias (Figure 5).

## 4. Discussion

The results of this study showed that the perioperative ultrasound-guided TTMP block was effective in reducing opioid consumption during the first 24 h and lowering the pain scores postoperatively in patients undergoing open-

heart surgery compared with those in the blank or placebo groups. Moreover, it showed advantages in prolonging the time of first analgesia demand, shortening the time of extubation, shortening ICU stay and hospitalization, and decreasing nausea and vomiting in the postoperative period.

Pain management after sternotomy cardiac surgery has always been a concern for anesthesiologists. A large number of opioids are used in the perioperative period of cardiac surgery to suppress surgical stress [29]. The use of large doses of opioids may cause postoperative respiratory depression, prolong the duration of mechanical ventilation, and increase the incidence of nausea and vomiting [3, 30]. In addition, the use of perioperative opioids is being reexamined due to societal concerns about opioid abuse [31]. Multimodal analgesic regimens combining regional nerve blocks with nonopioid medications have been extensively studied to promote rapid recovery of patients who underwent cardiac surgery [4]. Previous studies showed that epidural anesthesia and paravertebral nerve blocks provide excellent analgesia after cardiac surgery, reduce myocardial oxygen consumption, and decrease cardiac surgery mortality. However, perioperative heparinization and anticoagulation for cardiac surgery may increase the risk of intrathecal hematoma [32–35]. The anterior serratus plane block and pectoralis plane (PECS) block

TABLE 1: Characteristics of the included studies.

Study	Country	Language	Type of operation	Age (years)	Participants (n)		Timing of the nerve block	Level	Intervention		Postoperative analgesia	Outcomes
					TTMP group	Control group			TTMP group Type and dose	Control group Type and dose		
Fujii 2019	Japan	English	CABG AVR MVR	18-90	9	8	End of the surgery	T4-T5	0.3% or 0.5% ropivacaine 20 ml	No block	Hydromorphone, acetaminophen (iv, rescue)	①②③④⑦
Aydin 2020	Turkey	English	CABG AVR MVR	18-65	24	24	After anesthesia induction	T4-T5	0.25% bupivacaine 20 ml	Sham block normal saline	Paracetamol (1 g/6 h), fentanyl (PCIA)	①②③④⑤⑦
Shokri 2021	Egypt	English	CABG AVR MVR	55-74	30	30	After anesthesia induction	T4-T5	0.25% bupivacaine 15 ml	Sham block normal saline	Acetaminophen (1 g/6 h), morphine (iv)	①②③④⑤
Zhang 2021	China	English	Median open-heart surgery	18-70	30	30	After anesthesia induction	T4-T5	0.4% ropivacaine 20 ml	Sham block normal saline	Flurbiprofen axetil (50 mg/6 h), sufentanil (PCIA)	①④⑤⑥⑦
Ye 2020	China	Chinese	OPCABG	45-77	30	30	Before anesthesia induction	T3-T4	0.3% ropivacaine 15 ml	No block	Sufentanil (PCIA)	②④⑤
Zhang 2020	China	Chinese	AVR MVR	18-60	30	30	Before anesthesia induction	T4-T5	0.25% ropivacaine 20 ml	No block	Flurbiprofen axetil (50 mg/8 h), sufentanil (PCIA)	①④⑤⑦⑧
Wang 2020	China	Chinese	OPCABG	50-63	30	30	Before anesthesia induction	T3-T4	0.375% ropivacaine +0.5% lidocaine 20 ml	Sham block normal saline	Oxycodone (iv, rescue), sufentanil (PCIA)	①⑤⑥⑦⑧
Zhao 2021	China	Chinese	CABG	50-75	20	20	After anesthesia induction	T4-T5	0.375% ropivacaine 20 ml	No block	Dezocine (iv, rescue), sufentanil (PCIA)	①②④⑤⑦
Tao 2021	China	Chinese	AVR MVR	35-65	20	20	Before anesthesia induction	T4-T5	0.25% ropivacaine 20 ml	No block	Flurbiprofen + sufentanil (PCIA)	①②④⑤
Zhang 2023	China	Chinese	AVR MVR AVR + MVR	Over 65 years old	29	29	Before anesthesia induction	T4-T5	0.25% ropivacaine 20 ml	No block	Hydromorphone + tramethamine (PCIA)	②④⑤⑧
Hamed 2022	Egypt	English	AVR MVR	Over 18 years old	35	35	End of the surgery	T4-T5	0.25% bupivacaine 20 ml	Sham block normal saline	Paracetamol (1 g/6 h) fentanyl (PCIA)	①②③④⑤⑦

TABLE 1: Continued.

Study	Country	Language	Type of operation	Age (years)	Participants (n)		Timing of the nerve block	Level	Intervention		Postoperative analgesia	Outcomes
					TTMP group	Control group			TTMP group Type and dose	Control group Type and dose		
Chen 2023	China	English	AVR MVR AVR + MVR	Over 65 years old	52	51	After anesthesia induction	T4-T5	0.30% ropivacaine 20 mL	Sham block normal saline	Flurbiprofen axetil (50 mg/6 h), sufentanil (PCIA)	①②④⑤⑥⑦⑧
Vilvanathan 2020	India	English	CABG	50-70	45	45	After anesthesia induction	T2-T6	0.5% bupivacaine 1.5 ml/point	No block	Tramadol (iv, rescue)	②④⑤⑦

Notes: ①, opioid consumption in the first 24 hours; ②, postoperative 12-hour and 24-hour VAS score; ③, time of first analgesic demand; ④, time of extubation; ⑤, length of ICU stay; ⑥, time of first faeces; ⑦, incidence of PONV; and ⑧, length of hospital stay. CABG, coronary artery bypass grafting; OPCABG, off-pump coronary artery bypass grafting; AVR, aortic valve replacement; MVR, mitral valve replacement; TTMP, transversus thoracic muscle plane; iv, intravenous injection; and PCIA, patient-controlled intravenous analgesia.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aydin 2020	+	?	?	?	+	+	+
Chen 2023	+	+	+	+	+	+	+
Fujii 2019	+	+	+	+	+	+	+
Hamed 2022	+	+	+	+	+	+	+
Shokri 2021	+	+	+	+	+	+	+
Tao 2021	+	?	?	?	+	+	+
Vilvanathan 2020	+	?	?	?	+	+	+
Wang 2020	+	?	+	+	+	+	+
Ye 2020	+	?	?	?	+	+	+
Zhang 2020	+	+	?	?	+	+	+
Zhang 2021	+	+	+	+	+	+	+
Zhang 2023	+	?	?	?	+	+	+
Zhao 2021	+	?	?	?	+	+	+

FIGURE 2: A summary of bias for each included study.

are commonly used blocks for chest wall nerve blocking [36]. Jack et al. analyzed 51 clinical studies and showed that the anterior serratus plane block and PECS II reduced pain scores and opioid consumption after open-heart surgery [37]. However, Fusco et al. showed that the anterior serratus plane block was effective on the long thoracic nerve, thoracic dorsal nerve, and lateral cutaneous branch of the intercostal nerve but less effective on the anterior cutaneous branch of the intercostal nerve [38]. Song et al. applied PECS combined with paraspinal nerve block to breast cancer resection, and the postoperative pain in the combined paraspinal nerve block group was reduced compared with that in the PECS-alone

group [39]. This finding suggested that the anterior serratus plane block or PECS for median open-heart surgery may have the risk of incomplete analgesia [40].

Ultrasound-guided TTMP is a method of targeting the anterior cutaneous branch of the intercostal nerve. Local anesthetic injected between the transversus pectoralis and intercostal muscles blocks the anterior cutaneous branches of the intercostal nerves 2–6, thus producing analgesia in the medial mammary region and the anterior sternal region [7]. Cadaveric studies showed that the injection of local anesthetic into the T4-5 intercostal space is more preferable than injection into the T3-4 intercostal space because it has a wider diffusion range [41]. The results of the present study showed that patients who underwent TTMP during the perioperative period of median sternotomy for cardiac surgery showed a decrease in opioid use at 24 h postoperatively and a decrease in pain scores at 12 h and 24 h postoperatively. These findings were related to the fact that TTMP blocked the anterior cutaneous branch of the intercostal nerve and produced analgesia in the anterior region of the sternum. The good analgesic effect of TTMP may also be reflected in the recovery benefits for patients, including prolonging the time of first postoperative analgesia demand; shortening postoperative endotracheal tube exposure, ICU stay, and hospitalization; and decreasing the incidence of postoperative nausea and vomiting. In two studies of TTMP in pediatric cardiac surgery, TTMP was shown to be effective in providing analgesia and accelerating recovery [42, 43]. In addition, a study comparing the analgesic effects of TTMP with the pectointercostal fascial block in open-heart surgery showed that TTMP and pectointercostal fascial block had similar effects on morphine consumption and pain scores in cardiac surgery patients at 24 h after surgery [44]. This finding is not difficult to understand because although the pectointercostal fascial block is injecting local anesthetic between pectoralis major and intercostal muscles, the nerves acted on are the anterior cutaneous branch of intercostal nerves. Even some scholars suggested that it is a different name for the same type of nerve block [45].

Similar to other chest wall nerve blocks, TTMP is a simple and safe procedure and no block-related adverse events were described in the included studies. Sepolvere et al. noted that the TTMP injection site is adjacent to the internal mammary artery, which may have an effect on the need to access the internal mammary artery for coronary artery bypass grafting. In patients with a history of sternotomy, the tissue scarring may interfere with the diffusion of the drug, thus affecting the block's effectiveness [46]. Some studies attempted continuous TTMP block using catheter placement [47], but similar to continuous parasternal block, the risk of infection must be considered [48].

A recent meta-analysis study evaluated the analgesic effect of TTMP for thoracic surgery [49]. However, the studies included cardiac surgery, cardiac implantable electronic device surgery, and mastectomy; moreover, the intervention was combined with other fascial blocks in some of the included studies, which showed greater heterogeneity. The results showed a large degree of heterogeneity. In comparison, the present study has the following advantages: (1) it only included open-heart surgeries, which are known

TABLE 2: Secondary endpoint results.

Outcomes	Studies included	Mean difference or RR (95% CI)	<i>p</i> value for statistical significance	<i>p</i> value for heterogeneity	<i>I</i> <sup>2</sup> test for heterogeneity (%)	Quality of evidence (GRADE)
Postoperative opioid consumption during the first 24 hours	11	-41.88 (-51.99, -31.77)	<0.001	<0.001	98	⊕⊕⊕⊖ moderate
Postoperative 12-hour VAS score at rest (cm)	9	-1.36 (-1.6, -1.12)	<0.001	0.4	5	⊕⊕⊕⊕ high
Postoperative 12-hour VAS score at moment (cm)	8	-2.32 (-3.31, -1.33)	<0.001	<0.001	91	⊕⊕⊕⊖ moderate
Postoperative 24-hour VAS score at rest (cm)	11	-1.04 (-1.53, -0.55)	<0.001	<0.001	84	⊕⊕⊕⊖ moderate
Postoperative 24-hour VAS score at moment (cm)	8	-1.44 (-2.69, -0.19)	0.02	<0.001	95	⊕⊕⊕⊖ moderate
Time of first analgesic demand	4	6.12 (1.27, 10.97)	0.01	<0.001	95	⊕⊕⊕⊖ low
Time extubation	12	3.04 (4.37, 1.71)	<0.001	<0.001	98	⊕⊕⊕⊖ moderate
Length of ICU stay	11	-12.17 (-17.26, -7.09)	<0.001	<0.001	94	⊕⊕⊕⊖ moderate
Time of first faeces	3	-5.74 (-9.13, -2.35)	<0.001	0.15	48	⊕⊕⊕⊖ low
Incidence of PONV	7	RR 0.33 (0.18, 0.6)	<0.001	0.08	48	⊕⊕⊕⊖ low
Length of hospital stay	5	-1.87 (-3.16, -0.57)	0.005	<0.001	95	⊕⊕⊕⊖ low

VAS, visual analog scale; ICU, intensive care unit; GRADE, grades of recommendation, assessment, development, and evaluation; PONV, postoperative nausea and vomiting.

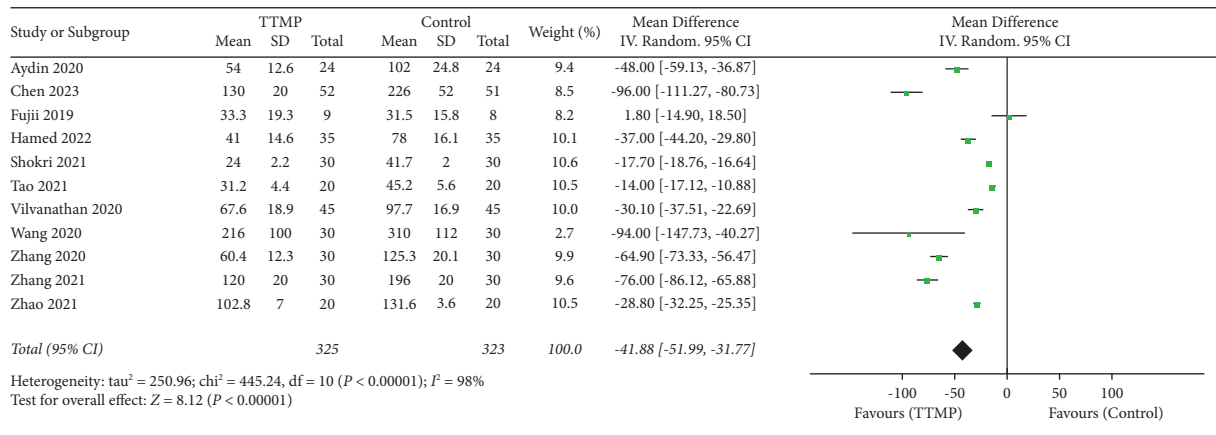


FIGURE 3: Postoperative opioid consumption during the first 24-hours forest plot.

to cause severe postoperative pain [50] and may provide a more accurate evaluation of the clinical effects of TTMP. (2) Necessary sensitivity analyses and separate subgroup analyses were performed on the basis of type of surgery, timing of block, and postoperative analgesia to obtain the sources of high heterogeneity. Although the issue of high heterogeneity could not be resolved, it may be related to the fact that open-heart surgery involves complex sources of pain due to the involvement of body surface tissues, sternum, thoracic cavity, and intracardiac manipulation. Most of the studies did not mention drain placement, and the location of the drain may be a place that could not be covered

by TTMP, thereby suggesting the need for more analgesic modalities to alleviate pain after cardiac surgery. In addition, each institution has its own unique pain management strategies, which were converted statistically in this study, and such difference may also be a source of heterogeneity. (3) This study found that TTMP reduced patients' pain scores 24 hours after surgery. However, this result is consistent with previous studies. Local anesthetics are generally not effective for more than 24 h. We speculate that it may be related to the timing of the block. (4) Recently added studies and non-English published studies were included, which increased the sample size of the study.



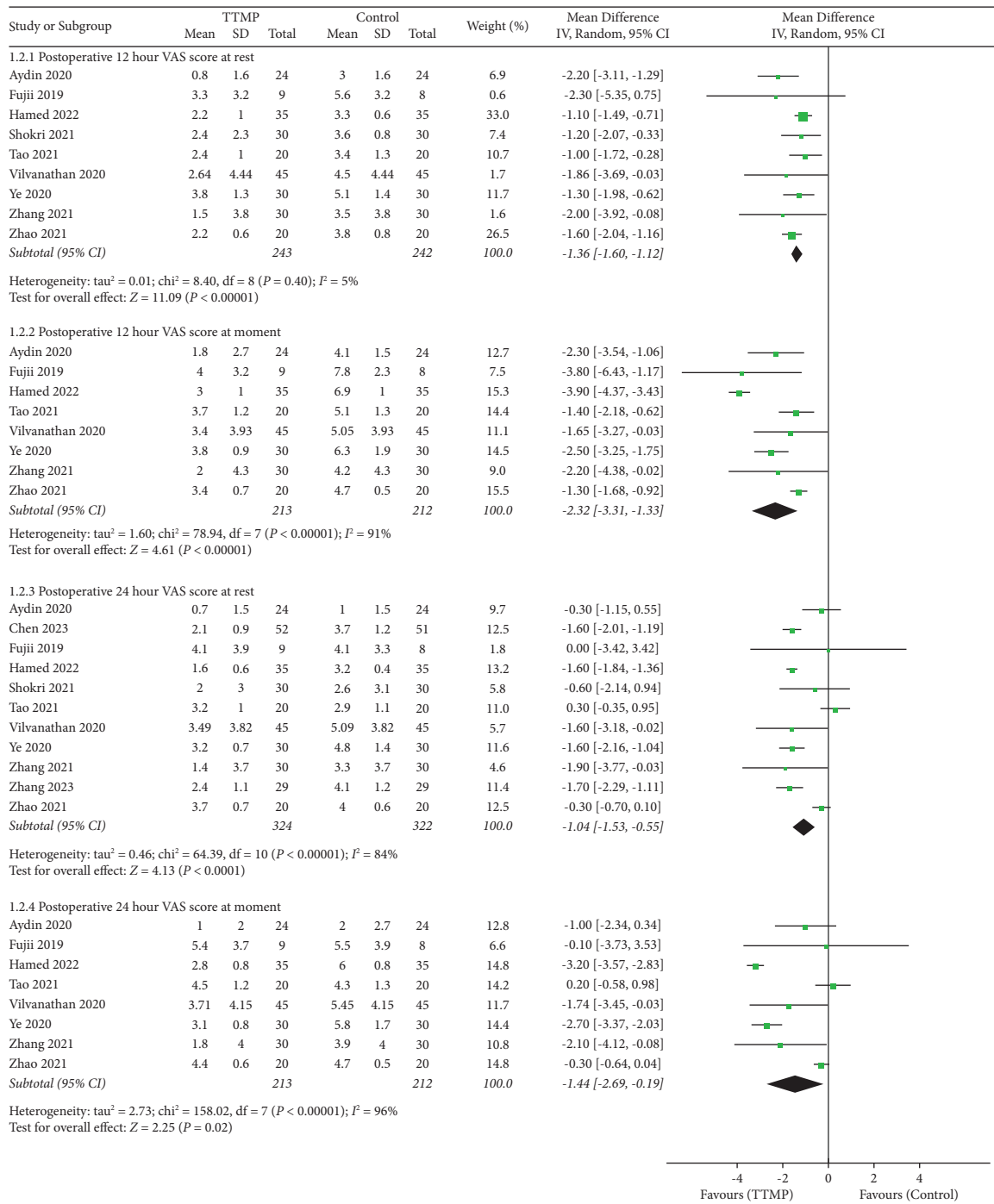


FIGURE 4: Postoperative VAS score forest plot.

**4.1. Study Limitations.** (1) The sample sizes of the included studies were small and further confirmation from large sample RCTs is needed. (2) Intraoperative opioid use was not extracted in this study, and the high use of intraoperative opioids may have an effect on patient outcome indicators. (3) The control groups of the included studies

were possibly a blank control or a placebo group for medical ethical reasons, and the effect of local anesthetic for the fascial block may be derived from blood absorption although this is still controversial [51]. (4) The study did not investigate the occurrence of mid-to-long-term postoperative pain.

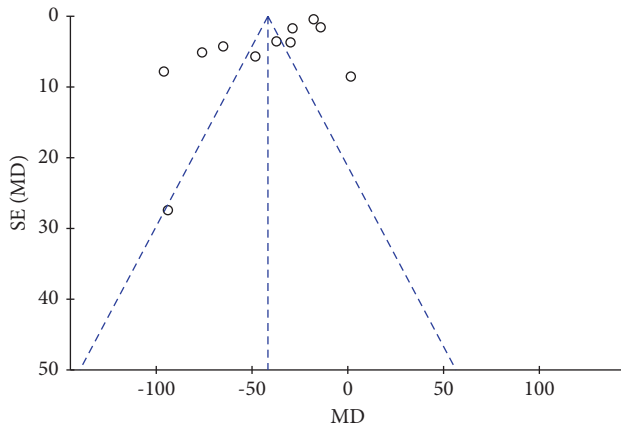


FIGURE 5: Funnel plot to detect publication bias.

## 5. Conclusions

This meta-analysis of moderate evidence confirmed that ultrasound-guided TTMP reduces opioid consumption after open-heart surgery, lowers patients' early postoperative pain scores, prolongs the time of first analgesic demand, shortens extubation time and ICU stay, reduces the incidence of nausea and vomiting, and accelerates patients' recovery for discharge. However, a notable detail is that the complexity of cardiac surgery requires a large-scale randomized controlled trial or a multicenter study to confirm the findings of this study.

## Abbreviations

CABG:	Coronary artery bypass grafting
OPCABG:	Off-pump coronary artery bypass grafting
AVR:	Aortic valve replacement
MVR:	Mitral valve replacement
TTMP:	Transversus thoracic muscle plane
iv:	Intravenous injection
PCIA:	Patient-controlled intravenous analgesia
VAS:	Visual analog scale
ICU:	Intensive care unit
GRADE:	Grades of recommendation, assessment, development, and evaluation
PONV:	Postoperative nausea and vomiting.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

RPZ and XLY conceived the study and designed the protocol; XLY and YZ integrated the data and drafted the manuscript; ZRP, YZ, XLY, WDL, GMH, and YJC were responsible for the study selection, data extraction,

assessment of study quality, and analysis and interpretation of data; and RPZ and XLY revised the manuscript critically. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All the authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Acknowledgments

The authors thank Ms. Mingzhu Zou for providing language help and writing assistance. This research was funded by Jiangxi Provincial Health Commission Science and Technology Program Project (no. 202212471).

## Supplementary Materials

Supplemental document provides the following: Supplementary Table 1: literature search summary. Supplementary Table 2: GRADEpro-TTMP for cardiac surgery patients. Supplementary Figure 1: pairwise heterogeneity analysis. Supplementary Figure 2: secondary outcomes forest plot. (*Supplementary Materials*)

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