

# Combined acupuncture-medicine anesthesia used in thyroid surgery

# A systematic review and meta-analysis

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# Abstract

**Background:** Combined acupuncture-medicine anesthesia (CAMA) is extensively used in thyroid surgery in China. We conducted a systematic review and meta-analysis to assess the efficacy and safety of CAMA.

**Methods:** We searched the China National Knowledge Infrastructure (CNKI), VIP database, WanFang database, PubMed, EMBASE, and the Cochrane Library for relevant literature. The term of literature was published before April 18, 2020, and there were no restrictions on publication language, region, or publication year. The inclusion criteria included a randomized controlled trial (RCT) of acupuncture combined with cervical plexus anesthesia. We used RevMan5.3 software for data analysis. If the chi-square test showed no significant heterogeneity (P > .10,  $l^2 < 50\%$ ), we used the fixed-effect model to calculate risk ratio (RR) and mean difference. Otherwise, the random-effects model was used.

**Results:** Overall, 18 RCTs involving 1211 patients were included in the study. The anesthesia significant rate (ASR) in the transcutaneous electrical acupoint stimulation (TEAS) plus cervical plexus block anesthesia (CPBA) and electroacupuncture (EA) plus CPBA groups was significantly higher compared with the CPBA group (TEAS + CPBA: P < .001; EA + CPBA: P < .001). The pooled effect values of the intraoperative heart rate (HR) and mean arterial pressure (MAP) were significantly lower in both the TEAS + CPBA and EA + CPBA groups relative to the control group (HR: P = .05, P < .001; the MAP: P = .002, P < .001; respectively). Moreover, the postoperative adverse reaction was markedly lower in the experimental group than in the control group (RR = 0.30, P < .001), and there was no heterogeneity between the two groups (P = .71,  $I^2 = 0$ %).

**Conclusion:** Combined acupuncture-medicine anesthesia significantly increases the anesthesia significance rate, reduces the intraoperative heart rate, and blood pressure, and reduces the incidence of postoperative adverse reactions. However, more high-quality future studies should be conducted to validate the efficacy and safety of acupuncture combined anesthesia further.

**Abbreviations:** AA = acupuncture anesthesia, CAMA = combined acupuncture-medicine anesthesia, CI = confidence interval, CPBA = cervical plexus block anesthesia, EA = electroacupuncture,  $l^2 = l$ -square, MD = mean difference, RCT = randomized controlled trial, RR = risk ratio, TEAS = transcutaneous electrical acupoint stimulation.

Keywords: acupuncture anesthesia, cervical plexus block anesthesia, combined acupuncture-medicine anesthesia, thyroid surgery

# 1. Introduction

In recent years, the incidence of thyroid cancer globally has rapidly increased.<sup>[1]</sup> Among all malignant tumors in women, thyroid cancer grows at the rate of 20% per year in China.<sup>[2]</sup>

For its treatment, thyroidectomy is one of the important methods and has a good prognosis.<sup>[3]</sup> Therefore, the rate of thyroid surgery is continually increasing. Presently, the anesthesia used during thyroid surgery includes local infiltration anesthesia, cervical plexus block anesthesia, epidural anesthesia, general anesthesia, combined anesthesia, and acupuncture anesthesia unique to China.<sup>[4–6]</sup>

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Local infiltration anesthesia is easy to implement, low cost, often short in duration, and patients may not easily stressed. However, the effect of local infiltration anesthesia may be incomplete, and sometimes leads to adverse reactions, such as convulsions, cardiac suppression, and hypoxemia.<sup>[7–9]</sup> The management of epidural block is complicated and can cause complications, including total spinal cord anesthesia and spinal nerve root injury. In severe cases, the needle enters the blood vessel or penetrates the dura, etc.<sup>[10]</sup> Research evidence shows that the incidence of central nervous system toxicity caused by epidural anesthesia in the European and American countries is 3/10,000.<sup>[11,12]</sup> After cervical

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plexus block anesthesia (CPBA), the carotid sinus and vagus nerves are partially or entirely blocked, and sympathetic nerve activity is relatively enhanced, which frequently raises blood pressure and accelerates the heart rate, and increases the surgical risk for patients with hypertension and cardiac insufficiency.<sup>[13]</sup> In addition, although the incidence is about one in ten thousand, the deep cervical plexus block can injure the recurrent laryngeal and septal nerve, resulting in hoarseness and dyspnea.<sup>[13]</sup> In contrast, general anesthesia has improved outcomes; however, the operation is complicated, and it is costly.<sup>[14]</sup> The establishment of artificial airways leads to postoperative throat pain.<sup>[15]</sup> Besides, the fasting and water requirements before and after anesthesia and the administration of multiple drugs significantly interfere with the physiological state of the patient.[16] Nonetheless, acupuncture anesthesia (AA) has been shown to improve the pain threshold and causes insignificant physiological disturbance to the patient.<sup>[6]</sup> This is despite its analgesic effect being not optimal, with incomplete muscle relaxation, and cannot completely alleviate the thyroid reflex.<sup>[17]</sup>

CPBA is simple for thyroid surgery, with an optimal analgesic effect, but usually increases the central rate and blood pressure during the operation, accompanied by various adverse drug reactions.<sup>[13]</sup> However, AA, which is developed from the traditional Chinese acupuncture analgesia, has an optimal analgesic effect by affecting the production and release of neurotransmitters, significantly controlling the increase in blood pressure and heart rate during surgery and reduces the cardiovascular response after cervical plexus block.<sup>[6,18]</sup> A combination of the two referred to as combined acupuncture-medicine anesthesia (CAMA) effectively makes up for the deficiencies of the single anesthesias, with less physiological interference on the patients and faster postoperative recovery.<sup>[19]</sup> However, based on the small sample size and different measurement indexes in each study, evaluating the efficacy and safety of acupuncture combined with cervical plexus anesthesia and simple cervical plexus anesthesia in thyroid surgery is a challenge. Therefore, this necessitates a meta-analysis for more powerful conclusions on the safety and efficacy of CAMA.

#### 2. Materials and Methods

#### 2.1. Literature search

We searched for the eligible studies in PubMed, EMBASE, Cochrane Library, China National Knowledge Infrastructure, WanFang databases, and VIP databases. There were no restrictions in the language of publication, region, and publication year. We used the following combined text and MeSH terms: "Acupuncture" and "Analgesia" and "Thyroid Gland." The complete search used for PubMed was: ((((Acupuncture [Mesh]) OR Pharmacopuncture [Text Word])) AND ((Analgesia [Mesh]) OR Analgesias [Text Word])) AND (((((((("Thyroid Gland" [Mesh]) OR Glands, Thyroid [Text Word]) OR Gland, Thyroid [Text Word]) OR Thyroid Glands [Text Word]) OR Thyroid [Text Word]) OR Thyroids [Text Word])) OR thyroid surgery [Text Word]) OR thyroid operative [Text Word]) OR thyroidectomy [Text Word]) OR Thyroidectomies [Text Word]). The Chinese search strategy included (Zhen ci OR Zhen jiu OR Dian zhen OR Xue wei) AND Jia zhuang xian shou shu AND Ma zui. We considered all potentially eligible studies for the review, irrespective of the primary outcome or language. All studies searched were retained for screening.

#### 2.2. Inclusion criteria

The inclusion criteria for eligible studies included: the study must be a randomized controlled trial (RCT) focused on acupuncture combined with cervical plexus anesthesia used in thyroid surgery; the experimental group was CAMA and CPBA as the control group. Acupuncture was limited to manual acupuncture, electroacupuncture (EA), and transcutaneous electrical acupoint stimulation (TEAS); the patients were diagnosed with thyroid lump and must have undergone traditional thyroid surgery; and the studies had clear cases diagnosis/inclusion criteria and efficacy criteria.

#### 2.3. Exclusion criteria

Study exclusion criteria constituted Non-RCT, reviews, animal experiments, case reports, and studies without clear criteria of diagnosis and efficacy; studies comparing different types of acupuncture; studies with incomplete reporting of results; therefore, could not be quantitatively computed; the patients were underwent endoscopic thyroid surgery or thyroid nodule ablation; and the initial research process was not standard and had evident mistakes.

#### 2.4. Trial selection and quality assessment

After finalizing the literature searches, the duplicate studies were discarded, followed by independent reviewing of the retained articles by two authors. The potentially eligible studies were selected by screening the titles or abstracts. If the title or the abstract was inadequate to guarantee a final decision, we screened the full text. If multiple publications from the same trial met the inclusion criteria, we selected the latest version. Disparities were resolved through a discussion or based on the opinion of a third researcher.

We used the Cochrane risk of bias tool to evaluate the methodological quality of RCTs.<sup>[20]</sup> The assessment tool consisted of seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. The risk of bias for each domain was rated as low, high, or unclear.

#### 2.5. Data extraction and statistical analysis

Two reviewers extracted data independently using a predefined data extraction form. Disagreements were resolved through a discussion or consensus with a third reviewer. The data extracted consisted of the first author, year of publication, sample size, age of patients, acupoint, interventions, and outcome measures.

Dichotomous data were analyzed using the risk ratio (RR) computed using the Mantel Haenszel method (fixed or random models). Continuous outcomes measured on the same scale were expressed as a mean value and standard deviation and were analyzed using mean differences (MD). We performed the *I*-square ( $I^2$ ) test to assess the impact of study heterogeneity on the meta-analysis results. Based on the Cochrane review guide-lines, in the presence of severe heterogeneity at  $I^2 > 50\%$ , the random effect models were chosen; otherwise, the fixed-effect models were used.<sup>[21]</sup> Moreover, we performed sensitivity analyses by omitting each study at a time to evaluate the quality and consistency of the results. Furthermore, we constructed a funnel plot to assess publication bias.<sup>[20]</sup>

The analysis was performed as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>[22]</sup> Ethical approval was not deemed necessary because this is a literature-based study.

# 3. Results

# 3.1. Study characteristics

Based on the search strategy, we initially identified 608 relevant articles. Of these, 244 and 298 articles were excluded as duplicates, and after the title and abstract screening, respectively. After a thorough and careful review, 18 studies<sup>[17–34]</sup> met the eligibility criteria for the systematic review and meta-analysis (The flow chart of the article selection process is shown in Fig. 1).

The characteristics of the included studies are shown in Table 1. All the 18 articles were RCTs and were published in the Chinese language. The overall sample size was 1211 cases consisting of 651 patients in the experimental group and 560 patients in the control group. Moreover, all the cases met the indications of thyroid surgery. Among them, the experimental treatment in 5 studies<sup>[26,28,30,35,36]</sup> constituted a combination of transcutaneous electrical acupoint stimulation and cervical plexus anesthesia, while the other 13 studies<sup>[23-25,27,29,31-34,37-40]</sup> involved electroacupuncture combined with cervical plexus anesthesia. In the control group in all the included studies, simple cervical plexus block anesthesia treatment was used.

#### 3.2. Quality assessment

The quality assessment results for the included articles are shown in Figure 2. Randomization was performed in all the studies, and 7<sup>[23,26–28,31,36,40]</sup> of them detailed the randomization methods. Moreover, blinding of participants and personnel was mentioned in only two articles.<sup>[26,27]</sup> Notably, one study<sup>[31]</sup> explicitly mentioned that blinding was not applied in outcome assessment; therefore, we considered high-risk detection bias. Overall, the risk of bias was low for incomplete outcome data, selective reporting, and other forms of bias.

#### 3.3. Subgroup analysis

We used a subgroup analysis to study the effect of different acupuncture methods on CAMA. The combined analysis of all outcome indicators was divided into two groups, namely TEAS + CPBA and EA + CPBA.

# 3.4. Sensitivity analysis

We adopted the method of excluding one article at a time for sensitivity analysis to evaluate the stability of the results. The combined RR value of the incidence of adverse reactions was stable and did not evidently fluctuate. In the anesthetic significance rate, the operation heart rate, and blood pressure, Huang et al,<sup>[28]</sup> Liu et al,<sup>[31]</sup> and Jia<sup>[29]</sup> led to the generation of heterogeneity, respectively. After removing these three articles, the *I*<sup>2</sup> of the anesthetic significance rate decreased from 84 to 0, the central rate decreased from 67 to 32, and the intraoperative blood pressure reduced to 15 from 67, respectively.

#### 3.5. Anesthetic significance rate

Overall,  $10^{[23-28,30,33,38,40]}$  studies used 3 levels of significant anesthesia, incomplete anesthesia, and ineffective anesthesia. The anesthesia significance rate constituted the number of significant anesthesia divided by the total number of cases in the group. TEAS + CPBA vs CPBA; three studies<sup>[26,28,30]</sup> in this group, and the heterogeneity test result was chi<sup>2</sup> = 12.42, P = .002,  $I^2 = 84\%$ . After Huang et al<sup>[28]</sup> was excluded, the heterogeneity test results was chi<sup>2</sup> = 0.25, P = .62,  $I^2 = 0\%$ .



Figure 1. Flowchart of search results for meta-analysis. RCT = randomized controlled trial.

Table 1		
Characteristics	of the included	studies.

Author	Year	Sample size (T/C)	Gender (M/F)	Age, years (SD)	Acupoint	Intervention	Outcome
Bai	2019	37	9/28	46.82 (6.20)	LI 4, PC 6	EA + CPBA	SBP, DBP, HR, SpO <sub>2</sub> , AR
		37	7/30	46.78 (6.17)		CPBA	
Fu	2017	37	21/16	38.89 (2.09)	LI 4, PC 6	EA + CPBA	ASR, AR
		37	20/17	39.26 (2.28)		CPBA	
Gao	1999	22	-	18-72	LI 4, PC 6	EA + CPBA	ASR
		22				CPBA	
Gao	2008	60	10/50	18–59	LI 4, PC 6	TAES + CPBA	ASR, MAP, SPO2, HR, AR
		20	3/17	22–57		CPBA	
Huang	2011	30	16/14	43.67 (13.28)	LI 4, PC 6	EA + CPBA	ASR, MAP, HR, SpO <sub>2</sub>
		30	15/15	44.50 (12.88)		CPBA	-
Huang	2020	34	15/19	49.59 (12.42)	LI 4, PC 6	TAES + CPBA	ASR, MAP, SPO2, AR
		34	11/23	49.50 (12.08)		CPBA	
Jia	2018	30	8/22	35.67 (4.58)	LI 4, PC 6	EA + CPBA	SBP, DBP, HR, AR
		30	9/21	35.82 (4.72)		CPBA	
Li	2008	40	5/35	42 (7)	LI 4, PC 6	TAES + CPBA	ASR, SBP, DBP, HR, SpO <sub>2</sub> , RR
		20	3/17	39 (9)		CPBA	
Liu	2006	30	35/25	18–55	LI 4, PC 6	EA + CPBA	MAP, HR, AR
		30				CPBA	
Liu	2010	30	23/37	35–66	LI 4, PC 6	EA + CPBA	SBP, DBP, HR, SpO <sub>2</sub>
		30				CPBA	
Liu	2019	38	14/24	47.2 (11.9)	LI 4, PC 6	EA + CPBA	ASR, BP, HR
		38	16/22	48.3 (12.4)		CPBA	
Luo	2018	47	21/26	48.2 (4.5)	LI 4, PC 6	EA + CPBA	AR
		47	19/28	47.8 (4.7)		CPBA	
Shu	2001	10	1/9	41.4 (10.9)	LI 4, PC 6	EA + CPBA	SBP, DBP, HR, SP02
		10	1/9	42.1 (11.2)		CPBA	
Wang	2013	60	11/49	47.0 (11.8)	LI 4, PC 6	EA + CPBA	ASR, SBP, DBP, HR, AR
		30	5/25	48.6 (12.9)		CPBA	
Wang	2016	40	-	-	LI 4, PC 6	IAES + CPBA	AR
		40	19/21	22–61		CPBA	
Xie	2007	32	2/30	20-65	LI 4, PC 6	EA + CPBA	SBP, DBP, HR, SpO <sub>2</sub> , AR
		31	2/29	20–47		CPBA	
Xiong 2009	49	10/39	38.5 (15.5)	LI 4, PC 6	TAES + CPBA	MAP, HR, AR	
		49	9/40	37.5 (15.6)	11 4 50 5	CPBA	
Zhang	2018	25	3/22	41.87 (3.29)	LI 4, PC 6	EA + CPBA	ASR, CRP, AR
		25	4/21	43.28 (2.68)		CPBA	

AR = adverse reactions, ASR = anesthetic significance rate, BP = blood pressure, C = control group, CPBA = cervical plexus block anesthesia, CRP = C-reactive protein, DBP = diastolic blood pressure, EA = electroacupuncture, F = female, HR = heart rate, LI4 = hegu, M = male, MAP = mean arterial pressure, PC 6 = neiguan, RR = respiratory rate, SBP = systolic blood pressure, SD = standard deviation,  $SpO_2 =$  blood oxygen saturation, T = treatment group, TEAS = transcutanclus electrical acupoint stimulation.

The pooled data indicated that the TEAS + CPBA group was significantly better compared with CPBA (RR = 5.18, 95% confidence interval [CI], 2.01–13.30; P = .0006; Fig. 3). Seven studies<sup>[23–25,27,33,38,40]</sup> reported EA + CPBA vs CPBA. The heterogeneity test result was chi<sup>2</sup> = 8.14, P = .23,  $I^2 = 26\%$ . The pooled results indicated that EA + CPBA was superior to CPBA (RR = 1.29, 95% CI, 1.15–1.45; P < .001; Fig. 3). There was heterogeneity between the two groups (chi<sup>2</sup> = 8.20, P = .004,  $I^2 = 87.8\%$ ; Fig. 3). Collectively, these data imply that CAMA improves the anesthetic effect.

# 3.6. Heart rate

Thyroid surgery can cause traction reflex or traction pain when pulling the thyroid; hence, we selected the heart rate when the thyroid is pulled to represent the intraoperative heart rate. Overall, 9 studies<sup>[23,26,29–32,37–39]</sup> had heart rate outcomes. TEAS + CPBA vs CPBA; two homogenous<sup>[26,30]</sup> studies were included in this subgroup, and the results combined with the random effect model indicated that the difference in heart rate between the two groups was statistically significant (Fig. 4).

EA + CPBA vs CPBA; overall, seven articles<sup>[23,29,31,32,37-39]</sup> were included, and the results showed that the heart rate of EA + CPBA was markedly lower (MD = -13.35, 95% CI [-15.81, -10.89]). The test result of heterogeneity was P = .006,

 $I^2 = 67\%$ . Liu et al<sup>[25]</sup> did not specify the drugs used for cervical plexus anesthesia in the experiment, and considering the significant heterogeneity, we excluded this study. The sensitivity analysis results after exclusion still supported that the heart rate of the EA + CPBA group was lower compared with the control group (MD = -16.40, 95% CI [-19.46, -13.34]; Fig. 4).

# 3.7. Blood pressure

As with the intraoperative heart rate, we opted for the mean arterial pressure when pulling the thyroid to represent the intraoperative blood pressure. The pooled data indicated that the blood pressure values in the TEAS + CPBA and EA + CPBA groups were distinctly lower relative to the CPBA group (P = .002, P < .001, respectively; Fig. 5). After excluding the Jia et al<sup>[29]</sup> study, the *P* value still supported lower intraoperative blood pressure in the EA + CPBA group (P < .001; Fig. 5). The sensitivity analysis revealed that the combined results were stable.

## 3.8. Adverse reactions

Twelve studies<sup>[23,24,26,28,29,31,34–36,38–40]</sup> conducted analyses on the postoperative adverse reactions. Our heterogeneity analysis revealed that multiple studies were homogeneous, and there was no significant difference between the two groups



Figure 2. Risk of bias summary. Judgments about each risk of bias item for each included study.

(chi<sup>2</sup> = 0.14, P = .71,  $I^2 = 0\%$ ; Fig. 6). The funnel plot indicated a lower risk of publication bias (Fig. 7). The pooled analysis results was (RR = 0.30, 95% CI [0.21, 0.43], P < .001; Fig. 6). This indicated that the adverse reactions of CAMA were remarkably less compared with the control group. This implies that CAMA reduces the occurrence of adverse reactions after thyroid surgery.

# 4. Discussion

Adequate anesthesia is a prerequisite for any operation to proceed smoothly. Reasonable anesthesia implementation promotes postoperative recovery and improves patient satisfaction with treatment.<sup>[41]</sup> In this study, we included 18 studies by formulating detailed search strategies and strict screening criteria. Consequently, our meta-analysis revealed that CAMA significantly improves the efficiency of anesthesia. Acupuncture anesthesia is developed from the traditional Chinese acupuncture analgesia.<sup>[6,17]</sup> Modern medical research considers that the role of acupuncture analgesia is closely related to neurotransmitters, such as opioid peptides and serotonin.<sup>[18,42,43]</sup> Acupuncture causes the brain to release opioid peptides and other substances that interact with specific opioid peptide receptors to produce analgesic effects via mediating non-neuronal pathways.[42-45] However, simple acupuncture anesthesia has an insufficient analgesic effect and causes evident traction reaction and muscle tension.<sup>[17]</sup> Cervical plexus anesthesia is simple for thyroid surgery, with an optimal analgesic effect, but frequently increases the intraoperative heart rate, blood pressure, and causes various adverse drug reactions.<sup>[13]</sup> Combining these two makes up for their deficiencies effectively.<sup>[19]</sup> For a long time, CAMA has been widely used globally, but there is still insufficient evidence. Our study provides evidence of its use. However, due to the limited number of articles included, more high-quality research should be conducted to validate our findings.

In addition to improving the effect of anesthesia, in this meta-analysis, we established that compared with simple cervical plexus block anesthesia, CAMA effectively reduces the intraoperative heart rate, blood pressure, and the incidence of postoperative adverse reactions. CPBA frequently and significantly increases the heart rate, and existing studies show that acupuncture anesthesia excites the vagus nerve, dilates blood vessels, reduces peripheral circulation resistance.[6,18] At the same time, AA regulates the renal sympathetic activity, reduces the expression of epinephrine, norepinephrine, and  $\beta$ 1-AR, to prevent the excessive increase of the heart rate and blood pressure.<sup>[46]</sup> Furthermore, studies indicate that acupuncture has good myocardial protection, improves myocardial anti-ischemic hypoxia ability, anti-oxidative damage, inhibits myocardial cell apoptosis, promotes recovery of myocardial cells, and improves cardiac function.<sup>[47,48]</sup> According to the theory of passing the meridians, attending the centers in traditional Chinese medicine, acupuncture at Hegu can treat symptoms, like fever, headaches, and sore throat. Moreover, acupuncture neiguan improves sleep, relieves fatigue, improves chest pain, and palpitations, relieves abdominal distension, plays a role in calming, and anti-vomiting. Current studies additionally reveal that acupuncture has an analgesic role at the time of surgery, and post-surgery.<sup>[49]</sup> These include reducing postoperative incision pain, nausea and vomiting, skin itching and respiratory complications, protecting the heart and the brain and other important organ functions, and stabilizing the physiological state of the patient during surgery and strengthen immune function, and promote postoperative recovery.[49-51]

Although the findings of the present study show that CAMA is more advantageous than simple cervical plexus anesthesia, there are still some limitations. Not all studies included in this meta-analysis mentioned the safety of acupuncture. Previous studies reported that acupuncture could cause adverse events,

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.1.1 TEAS+CPBA VS	СРВА						
Gao 2008	24	60	2	20	2.2%	4.00 [1.04, 15.44]	
Huang 2020	29	34	21	34	0.0%	1.38 [1.02, 1.86]	
Li 2008	26	40	2	20	1.9%	6.50 [1.71, 24.68]	$\longrightarrow$
Subtotal (95% CI)		100		40	4.1%	5.18 [2.01, 13.30]	
Total events	50		4				
Heterogeneity: Chi <sup>2</sup> = 0	).25, df = 1	(P = 0.6	62); I² = 0	%			
Test for overall effect: 2	Z = 3.42 (P	= 0.000	06)				
1.1.2 EA+CPBA VS C	РВА						
Bai 2019	29	37	23	37	16.7%	1.26 [0.93, 1.71]	
Fu 2017	36	37	30	37	21.8%	1.20 [1.02, 1.41]	
Gao1999	20	22	17	22	12.3%	1.18 [0.91, 1.53]	<b>+-</b>
Huang 2011	13	30	7	30	5.1%	1.86 [0.86, 4.00]	
Liu 2019	31	33	23	35	16.2%	1.43 [1.11, 1.84]	
Wang 2013	26	60	8	30	7.7%	1.63 [0.84, 3.14]	
Zhang 2018	23	25	22	25	16.0%	1.05 [0.87, 1.26]	<u>+</u> .
Subtotal (95% CI)		244		216	95.9%	1.29 [1.15, 1.45]	•
Total events	178		130				
Heterogeneity: Chi <sup>2</sup> = 8	8.14, df = 6	(P = 0.2	23); l² = 2	6%			
Test for overall effect: 2	Z = 4.24 (P	< 0.000	01)				
		244		256	100.0%	4 45 14 27 4 651	
Total (95% CI)	000	344	404	200	100.0%	1.45 [1.27, 1.05]	•
I otal events	228	o (5 o	134	= 404			
Heterogeneity: $Chi^2 = 2$	27.84, df =	8 (P = 0	0.0005); l <sup>2</sup>	= /1%			0.1 0.2 0.5 1 2 5 10
Test for overall effect:	Z = 5.63 (P	< 0.000		Favours [experimental] Favours [control]			
Test for subgroup diffe	rences: Ch	i² = 8.20	), df = 1 (	P = 0.0	04), l² = 8	7.8%	· · · · · · · · · · · · · · · · · · ·

Figure 3. Meta-analysis of the RCTs comparing anesthesia significance rate between acupuncture group and control group. CI = confidence interval, CPBA = cervical plexus block anesthesia, EA = electroacupuncture,  $l^2 = I$ -square, RCT = randomized controlled trial, TEAS = transcutaneous electrical acupoint stimulation.

	Exp	eriment	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed, 95% Cl	IV, Fixed, 95% CI
1.2.1 TEAS+CPBA V	S CPBA								
Gao 2008	93.3	18.1	60	98	12	20	13.9%	-4.70 [-11.67, 2.27]	
Li 2008	92	15	40	97	12	20	13.7%	-5.00 [-12.02, 2.02]	
Subtotal (95% CI)			100			40	27.7%	-4.85 [-9.80, 0.10]	$\bullet$
Heterogeneity: Chi <sup>2</sup> =	0.00, df =	= 1 (P =	0.95);	l² = 0%					
Test for overall effect:	Z = 1.92	(P = 0.	05)						
1.2.2 EA+CPBA VS (	CPBA								
Bai 2019	92.57	13.13	37	106.32	14.68	37	16.8%	-13.75 [-20.10, -7.40]	
Jia 2018	92	13	30	109	15	30	13.4%	-17.00 [-24.10, -9.90]	
Liu 2006	85.4	7.7	30	93.2	8.6	30	0.0%	-0.94 [-1.48, -0.41]	
Liu 2010	88.7	10.3	30	109.84	13.71	30	18.0%	-21.14 [-27.28, -15.00]	
Shu 2001	83.6	9.3	10	97.9	18.2	10	4.2%	-14.30 [-26.97, -1.63]	
Wang 2013	91	18.03	60	98	23	30	7.6%	-7.00 [-16.41, 2.41]	
Xie 2007	91	14	32	110	16	31	12.3%	-19.00 [-26.4311.57]	
Subtotal (95% CI)			199			168	72.3%	-16.40 [-19.46, -13.34]	◆
Heterogeneity: Chi <sup>2</sup> =	7.40. df :	= 5 (P =	0.19):	l² = 32%					
Test for overall effect:	Z = 10.5	0 (P < 0	).00001	)					
		-		-					•
Total (95% CI)			299			208	100.0%	-13.20 [-15.81, -10.60]	$\bullet$
Heterogeneity: Chi <sup>2</sup> =	22.55, di	f = 7 (P	= 0.002	2); I <sup>2</sup> = 69	%				
Test for overall effect:	Z = 9.94	(P < 0.	00001)						-20 -10 0 10 20
Test for subaroup diff	erences:	$Chi^2 = 1$	5.14. d	f = 1 (P •	< 0.000	1),   <sup>2</sup> =	93.4%		Favours [experimental] Favours [control]

Figure 4. Meta-analysis of the RCTs comparing heart rate between acupuncture group and control group. CI = confidence interval, CPBA = cervical plexus block anesthesia, EA = electroacupuncture, I<sup>2</sup> = I-square, RCT = randomized controlled trial, TEAS = transcutaneous electrical acupoint stimulation.

such as vascular injuries and local pain.<sup>[52–55]</sup> Therefore, more research should be conducted to verify the safety and efficacy of acupuncture anesthesia. Moreover, in the present study, the intraoperative respiration and blood oxygen concentration did not differ between groups. Therefore, they were not included in the analysis. Besides, we used a subgroup analysis for the potential heterogeneity of different acupuncture methods. In addition to the incidence of adverse reactions, the combined results of

the other three outcomes revealed the presence of heterogeneity among the groups. However, due to the small number of studies in the percutaneous electrical stimulation group and lack of direct comparison between the two acupuncture and moxibustion methods, it was not convenient for us to analyze the difference in the amount of the combined effects between the two groups. In the included studies, the drugs used for cervical plexus anesthesia in the different studies were different, which

	Experimental Control							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.3.1 EA+CPBA VS (	СРВА						-		
Gao 2008	99.3	15.5	40	105	16	20	5.0%	-5.70 [-14.20, 2.80]	
Huang 2020	93.35	6.2	34	97.18	5.64	34	45.3%	-3.83 [-6.65, -1.01]	
Li 2008	100.3	11.7	40	105	17.6	20	5.0%	-4.70 [-13.22, 3.82]	
Subtotal (95% CI)			114			74	55.3%	-4.08 [-6.63, -1.52]	$\bullet$
Heterogeneity: Chi <sup>2</sup> =	0.19, df	= 2 (P =	0.91);	$ ^2 = 0\%$					
Test for overall effect:	: Z = 3.13	8 (P = 0.	002)						
1.3.2 TEAS+CPBA V	S CPBA								
Bai 2019	98.5	14.97	37	111	16.7	37	6.9%	-12.50 [-19.73, -5.27]	
Jia 2018	108.7	15.5	30	107.3	15.9	30	0.0%	1.40 [-6.55, 9.35]	
Liu 2006	86	8.2	30	98.3	7.4	30	23.0%	-12.30 [-16.25, -8.35]	
Liu 2010	93.2	12.52	30	110	14.01	30	8.0%	-16.80 [-23.52, -10.08]	
Wang 2013	103.5	17.08	40	109	14.76	20	5.2%	-5.50 [-13.86, 2.86]	
Xie 2007	100.3	14.68	10	117.7	18.56	10	1.7%	-17.40 [-32.07, -2.73]	
Subtotal (95% CI)			147			127	44.7%	-12.54 [-15.38, -9.70]	◆
Heterogeneity: Chi <sup>2</sup> =	4.70, df	= 4 (P =	0.32);	l² = 15%	6				
Test for overall effect:	: Z = 8.66	6 (P < 0.	00001)	)					
Total (95% CI)			261			201	100.0%	-7.86 [-9.76, -5.96]	•
Heterogeneity: Chi <sup>2</sup> =	23.79, d	f = 7 (P	= 0.00	1); l² = 7	'1%				
Test for overall effect:	: Z = 8.12	(P < 0.	00001)						-20 -10 0 10 20
Test for subaroup diff	erences:	Chi <sup>2</sup> = 1	, 18.90. d	df = 1 (P	< 0.000	01), l² =	94.7%		Favours [experimental] Favours [control]

Figure 5. Meta-analysis of the RCTs comparing blood pressure between acupuncture group and control group. CI = confidence interval, CPBA = cervical plexus block anesthesia, EA = electroacupuncture,  $l^2$  = I-square, RCT = randomized controlled trial, TEAS = transcutaneous electrical acupoint stimulation.

	Experimental		Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% Cl
1.4.1 TEAS+CPBA VS	S CPBA						
Gao 2008	6	60	5	20	6.6%	0.40 [0.14, 1.17]	
Huang 2020	3	34	10	34	8.9%	0.30 [0.09, 1.00]	
Wang 2016	5	40	16	40	14.2%	0.31 [0.13, 0.77]	
Xiong 2009	2	49	13	49	11.5%	0.15 [0.04, 0.65]	
Subtotal (95% CI)		183		143	41.2%	0.28 [0.16, 0.49]	<b>•</b>
Total events	16		44				
Heterogeneity: Chi <sup>2</sup> =	1.16, df = 3	(P = 0.	76); l² = 0	%			
Test for overall effect:	Z = 4.48 (P	< 0.00	001)				
1.4.2 EA+CPBA VS C	PBA						
Bai 2019	1	37	8	37	7.1%	0.13 [0.02, 0.95]	
Fu 2017	3	37	10	37	8.9%	0.30 [0.09, 1.00]	
Jia 2018	1	30	4	30	3.5%	0.25 [0.03, 2.11]	
Liu 2006	7	30	16	30	14.2%	0.44 [0.21, 0.91]	<b>_</b> _
Luo 2018	4	47	7	47	6.2%	0.57 [0.18, 1.82]	
Wang 2013	2	60	1	30	1.2%	1.00 [0.09, 10.59]	
Xie 2007	2	32	6	31	5.4%	0.32 [0.07, 1.48]	
Zhang 2018	2	25	14	25	12.4%	0.14 [0.04, 0.56]	
Subtotal (95% CI)		298		267	58.8%	0.32 [0.21, 0.50]	◆
Total events	22		66				
Heterogeneity: Chi <sup>2</sup> =	4.76, df = 7	(P = 0.	69); l² = 0	%			
Test for overall effect:	Z = 4.99 (P	< 0.00	001)				
Total (95% CI)		481		410	100.0%	0.30 [0.21, 0.43]	◆
Total events	38		110				
Heterogeneity: Chi <sup>2</sup> =	6.13, df = 1	1 (P = 0	.86); l² =	0%			
Test for overall effect:	Z = 6.70 (P	< 0.00	001)				0.01 0.1 1 10 10
Test for subgroup diffe	erences: Ch	i <sup>2</sup> = 0.14	4, df = 1 (	P = 0.7	1), $l^2 = 0\%$	, D	Favours [experimental] Favours [control]

Figure 6. Meta-analysis of the RCTs comparing adverse reactions between acupuncture group and control group. CI = confidence interval, CPBA = cervical plexus block anesthesia, EA = electroacupuncture,  $l^2 = I$ -square, RCT = randomized controlled trial, TEAS = transcutaneous electrical acupoint stimulation.

affected the experimental results to a certain extent. Particularly, Huang et al,<sup>[28]</sup> Liu et al,<sup>[31]</sup> and Jia<sup>[29]</sup> generated heterogeneity because of the anesthetic drugs. In acupuncture anesthesia, there are some differences in the frequency selection of electroacupuncture. Some studies indicate that the effects of different frequencies of electroacupuncture on anesthesia are not similar.<sup>[56]</sup> Because of the small number of studies, meta-analyses have not been conducted. However, research evidence shows that the electroacupuncture frequency of 100 hertz has a better anesthetic effect.<sup>[28,29,31,56,57]</sup> Besides, the choice of acupuncture points has a significant influence on the effect of anesthesia,<sup>[58]</sup> which is an additional issue that requires research.

In this study, we searched the CNKI, VIP, WanFang database, PubMed, EMBASE, and the Cochrane Library databases using strict criteria and strategy for literature inclusion that we established. All eligible randomized controlled trials were included





**Figure 7.** Funnel plot of included studies in the analysis for adverse reactions. CPBA = cervical plexus block anesthesia, EA = electroacupuncture, RR = risk ratio, TEAS = transcutaneous electrical acupoint stimulation.

in the meta-analysis to evaluate the effectiveness of combined anesthesia with acupuncture and medicine. However, the study has some limitations, i.e., the quality of the included studies is low, and the strength of the evidence is not high, which considerably weakens the validity of our analysis. Furthermore, since most of the included studies did not use the blinding method in the initial research process and evaluation stage, performance and detection bias inevitably occurred. There, future research should be conducted to address these limitations.

## 5. Conclusion

Herein, we established that acupuncture combined with anesthesia for thyroid surgery has distinct advantages. However, because of the lack of high-quality research and uniform implementation standards, our findings are limited. In the future, while emphasizing high quality, large-scale randomized controlled studies implementing uniform standards should be carried out to validate our findings. Additionally, future studies should explore different acupuncture methods, different frequencies, and intensity of acupuncture and acupuncture points, improve the effect of acupuncture combined with cervical plexus anesthesia. Notably, unlike electroacupuncture, transcutaneous electrical acupoint stimulation should not implement the piercing of the needle into the body, which reduces pain, bleeding, needle breakage, and other adverse reactions. Moreover, the operation is more straightforward and safer, hence necessitates further research.

# **Author contributions**

WZ and MZ provided full financial support for the research process and final publication. YXH, YHL, and CPS designed the study. WZ and YXH performed the literature search, screening, selecting of studies, and data extraction. MZ and YCL carried out the trial selection and study supervision. WZ and YXH performed data analyses, manuscript drafting, and editing. CPS, YHL, and YCL edited the manuscript. All authors endorsed the final manuscript.

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