Systematic Review

Stellate Ganglion Block Therapy for Complex Regional Pain Syndrome: A Systematic Review and Meta-Analysis

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Background: Sympathetic ganglion block (SGB) technique is becoming increasingly prevalent in the treatment of complex regional pain syndromes (CRPS). Given the varied reported effectiveness of these techniques and the heterogeneity of treatment regimens, there is an urgent need for consistent and high-quality evidence on the efficacy and safety of such procedures.

Objectives: This study aimed to compare the efficacy of SGB therapy for CRPS-related pain.

Study Design: A meta-analysis of randomized controlled trials (RCTs).

Methods: PubMed, EMBASE, Web of Science, CINAHL, US National Institutes of Health Clinical Trials Registry, Google Scholar, and Cochrane Library Databases were systematically searched between January 1967 and April 2023. A meta-analysis of the included RCTs on SGB was conducted to evaluate the effectiveness and risk of bias (ROBs) of SGB.

Results: After screening 8523 records, 12 RCTs were included in this meta-analysis. Compared with controls, the visual analog pain score decreased by a weighted mean difference (WMD) of -6.24 mm (95% CI, -11.45, -1.03; $P = 0.019$) in the random-effects model, and the numerical scale score was reduced by a WMD of -1.17 mm (95% CI, -2.42, 0.08; $P = 0.067$) in the fixed-effects model, indicating a pain relief. The methodological quality of the included RCTs was high, with an average PEDro score of 7.0 (range: 5-9).

Limitations: The number of included trials was limited.

Conclusions: SGB therapy can reduce pain intensity in patients with CRPS with few adverse events. However, owing to the relatively high heterogeneity of the included RCTs, a larger sample of high-quality RCTs is needed to further confirm this conclusion.

Key words: Complex regional pain syndrome, stellate ganglion block, lumbar sympathetic nerve block, pain management, efficacy

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Complex regional pain syndrome (CRPS) is a chronic pain condition that can affect any part of the body, especially the extremities (1,2). The term "CRPS" was first proposed in 1993, and since then the current diagnostic criteria for CRPS have been established, refined, validated, and then adopted by the International Association for the Study of Pain (IASP) (3,4). Since its publication, the Budapest criteria have been well validated and are considered the gold standard for diagnosing CRPS in clinical practice and research. The Budapest criteria provide standardized and widely accepted diagnostic guidelines for CRPS, requiring clinical symptoms and signs in at least 3 of 4 categories: sensory (hyperalgesia and/or allodynia), vasomotor (temperature asymmetry, skin color changes), sudomotor/edema (edema, sweating changes), and motor/trophic (decreased range of motion, motor dysfunction) (3,4). CRPS currently has a prevalence of 5.4-26.2 per 100,000 persons (5), and it is most commonly reported in the adult population (6). Commonly, CRPS affects females more frequently than males and has an increased incidence in older adults compared to younger adults, which could be because geriatric fractures become more common with increasing age (7,8). CRPS can be classified into types I and II. Type I CRPS, formerly known as reflex sympathetic dystrophy (RSD), arises following limb trauma and is characterized by dysfunction of the affected body segment (9) that is not related to direct nerve injury. In contrast, type II CRPS, also known as causalgia, is associated with direct injury to a specific nerve, usually due to surgical intervention or trauma (10). Based on current epidemiological data, CRPS type I is more common than type II (5.46 per 100,000 person-years vs. 0.82 per 100,000 person-years) (11). The upper limbs, especially the hands and wrists, are affected more often than the lower limbs.

The pathophysiology of CRPS remains unclear. It may involve erroneous coupling between peripheral efferent sympathetic and afferent sensory neurons, causing sympathetic overflow (12). Based on this, CRPS is treated in a multifaceted manner, and the conservative approach of drug treatment, including typical pain medications such as nonsteroidal antiinflammatory drugs, opioids, and gabapentin, which were prevalent in the early years, is ineffective in many cases (13). Consequently, interventional treatments have become popular, and stellate ganglion block (SGB) has the potential to reduce pain in patients with CRPS (14-19). The stellate ganglion refers to the cervical sympathetic ganglion formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion. It is located at the C7 level, anterior to the neck of the first rib, and contains sympathetic neuronal cell bodies that innervate the head, neck, and upper extremities. Localization of the stellate ganglion depends on 2 distinct body landmarks. One is the Chassaignac tubercle, a bony projection on the anterior surface of the 6th cervical vertebra (C6) formed by the anterior tubercle of the transverse process of C6. The second is the longus cervicis, a flexor in the anterior cervical column that spans the cervical spine of C2-T3 and lies in front of the cervical body deep into the prevertebral fascia. These provide important surface landmarks for identifying the location of the stellate ganglion. Anatomical knowledge of these structures is critical for safely and effectively performing ultrasound or fluoroscopy-guided stellate ganglion blocks. However, clinical guidelines remain conservative in recommending SGB and may consider various effectiveness reports (20-23); therefore, consistent and high-quality evidence on the efficacy and safety of these SGB techniques is needed. To obtain reliable data for the clinical decision-making process, we performed a comprehensive systematic review and meta-analysis of the effectiveness of SGB therapy and its adverse effects on CRPS-related pain.

Methods

Data Sources

We searched PubMed, EMBASE, Web of Science, CINAHL, US National Institutes of Health Clinical Trials Registry, Google Scholar, and Cochrane Library databases for original articles on the clinical efficacy of SGB published between January 1967 and April 2023. Two reviewers independently searched for articles, screened the studies, and extracted the data. Any inconsistencies between reviewers were resolved by consensus. The detailed protocol for this meta-analysis is available in PROSPERO (CRD42023391488).

Search Strategy

We used the following search terms to identify articles on complex regional pain syndrome and associated conditions: "CRPS" OR "reflex sympathetic dystrophy" OR "RSD" OR "complex regional pain syndrome" OR "causalgia," and then added the following search terms to identify articles on CRPS treatment: "treatment" OR "therapy" OR "therapeutic" OR "therapies" OR "treatments."

Study Selection Criteria

Articles were included if they fulfilled the following criteria: (1) fully published randomized controlled trials (RCTs) for patients receiving sympathetic blockade using SGB and meeting the Orlando IASP and Budapest criteria (17,24); (2) trials involving patients over 18 years of age of both genders; (3) pain duration of at least 6 months; and (4) trials in which pain was measured using a quantifiable scale or outcome, such as the visual analog scale (VAS), pain intensity, numeric rating scale (NRS), or pain relief.

The exclusion criteria were as follows: (1) studies using animal models, case reports, and case series; (2) trials that could not be separated from patients with other diseases or studies that could not extract sufficient information regarding the methodology, patient demographics, complications, and outcomes; and (3) studies with no access to official publications and non-English articles that could not be translated into English.

Data Extraction and Risk of Bias (ROB) Evaluation

A data extraction sheet was developed for the included studies. Two reviewers (TYS and HY) examined the titles, abstracts, full texts, and supplementary materials of the retrieved literature according to the inclusion criteria. A third author (HTY) was consulted if a disagreement persisted. The extracted data included study hallmarks, patient characteristics, intervention features, outcome indicators, and other findings of concern. The previously extracted data were standardized to evaluate ROB. The ROB of individual studies was first assessed using the Cochrane Review Manager 5.4. The Cochrane Collaboration's ROB assessment tool (25) was used to assess the methodological quality using the Physiotherapy Evidence Database (PEDro) classification scale (26). Discrepancies were resolved by consensus.

Outcomes

For efficacy, the primary outcomes were treatment effects on pain intensity, including VAS and NRS scores. The effects of pain relief were calculated as weighted mean differences (WMDs) compared to the control group. Secondary outcomes, including hemodynamic responses such as blood pressure, heart rate, and skin temperature, were calculated as standardized mean differences (SMDs) compared with the control group.

Statistical Analysis

Stata 17.0 and Cochrane Review Manager 5.4 software were used for data processing, merging, drawing an inverted funnel plot, etc. The effect index of the enumeration data was represented by odds ratios (OR) and 95% CI, whereas the effect index of the measurement data was represented by WMD or SMD and 95% CI.

Heterogeneity was qualitatively assessed by comparing the basic characteristics of included RCTs within Stata 17.0 software by Q test. Heterogeneity was determined by the *P*-value and I^2 value (27). When $I^2 \leq 50\%$ or $P > 0.10$ was presented, it was considered that there was a small homogeneity among all studies, and a meta-analysis was performed using the fixed-effect model. If $I^2 > 50\%$ or $P \leq 0.10$ was presented, it was considered that there was a small homogeneity among all studies; a meta-analysis was performed using the random-effects model.

Publication bias was investigated by visual inspection of a funnel plot and was assessed using Egger's regression asymmetry test if the funnel plot was not symmetrical (28,29). The occurrence of adverse effects in each treatment group is also described. The PEDro score was used to determine the methodological quality of the study (26). A $P < 0.05$ value was considered statistically significant.

Results

Study Selection and Study Characteristics

A database search identified 8523 potentially eligible records. A total of 747 full-text articles were evaluated, and 7 trials were determined to be eligible. In addition, 149 records from 9 systematic review articles were evaluated, and 8 trials were finally determined to be eligible. After eliminating 3 duplicate articles, the final sample consisted of 12 RCTs (9,30-40) (Fig. 1). All trials published between 1967 and 2023 included 422 patients aged 18-85 years. The characteristics of the included studies are shown in Supplementary Table 1.

Primary Outcomes: Effect on Pain Relief

Four trials (9,32,38,40) reported pain intensity using the VAS. The primary evaluation using a fixed-effects model showed heterogeneity ($I^2 = 98.1\%$; $P < 0.001$). Therefore, the random-effects model was subsequently used to analyze VAS transformed to 0-100 mm continuous data, and the results showed that VAS decreased in the SGB therapy group by a WMD of -6.24 mm (95% CI, -11.45, -1.03; $P = 0.019$) compared with the control group. The random-effects model showed

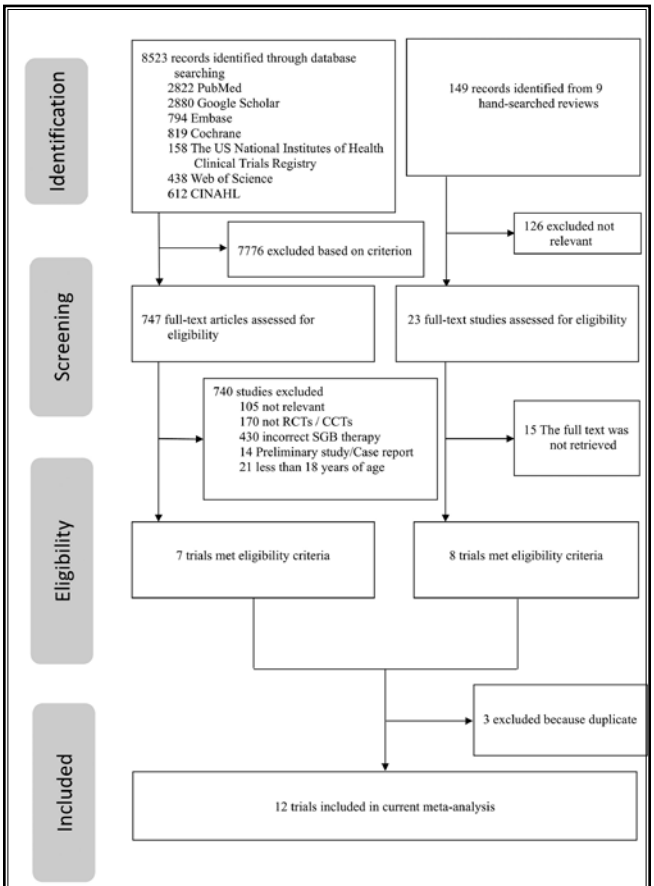

Fig. 1. *Literature retrieval and identification of studies involved in current meta-analysis.*

high heterogeneity (I^2 = 98.1%, P < 0.001; Fig. 2A).

NRS scores for pain evaluation were reported in 3 trials (9,31,32). Heterogeneity was present in the fixed-effects model (I^2 = 88.9%, P < 0.001), thus, a random-effects model was used. Analysis of the transformed NRS data revealed that compared with the control group, pain decreased in the SGB therapy group by a WMD of -1.17 mm (95% CI, -2.42, 0.08; P = 0.067) with significant heterogeneity (I^2 = 88.9%, P < 0.001; Fig. 2B).

To compare the effects of fluoroscopy and ultrasound-guided stellate ganglion blocks, a subgroup analysis was performed in Fig. 2C. In the ultrasound-guided group, the NRS scores decreased by a WMD of -0.61 mm (95% CI, -1.11, -0.11; P < 0.001). In the fluoroscopy group, the NRS score decreased by a WMD of -2.31 mm (95% CI, -3.05, -1.57; P < 0.001). The difference between groups was not significant: the WMD with decreased NRS score was -1.14 mm (95% CI, -1.56, 0.73; P > 0.05).

Secondary Outcome Measures

Immediate hemodynamic responses following SGB were determined in 2 studies (30,33), with one comparing heart rate (33) and the other comparing both heart rate and blood pressure (30). The effect size of heart rate, which is reflected by combined SMD, was -2.56 (95% CI, -3.24, -1.89; P < 0.001), and heterogeneity was present (I^2 = 94.7%; P < 0.001; Fig. 3A) in the random-effects model. In addition, 3 studies reported changes in skin temperature before and after treatment (32,35,38) with a combined SMD effect size of 0.81 (95% CI, 0.12, 1.50; P = 0.021), heterogeneity was present (P < 0.001; I^2 = 98.1%; Fig. 3B) in the random-effects model.

ROB in the Included Studies

The risk of bias in each study was determined using the Cochrane RoB tool. As shown in Fig. 4, 7 studies were evaluated as having a high risk of selection bias for allocation concealment (31,34-38,40). Eight studies (30-32,34-35,38-40) had a high risk of performance and detection bias owing to the lack of blinding. Regarding attrition bias, 2 studies (9,39) were considered high-risk. No study was found to have a high risk of reporting bias. Other biases were high in one study (37) and unclear in 7 (30,32-35,39-40). Fig. 4 shows the summary bias of the 12 studies, and Fig. 5 shows the percentages of the 6 risks of bias in the included studies. Two assessors calculated the PEDro scores for the 12 included studies (9,30-40). Four studies had diverging scores; therefore, a third evaluator was asked to obtain the final PEDro score for the 4 trials (31,34-35,40). As shown in Table 1, one of the 12 studies was defined as excellent, 10 as good, and one as fair. The average PEDro score of all the included studies was 7.0 (range, 5-9), indicating a generally high methodological quality.

Adverse Events

Adverse events were reported in 3 (9,30,39) out of 12 studies, accounting for approximately 25.00%. Eleven adverse reactions were reported, with dizziness and headache being the most frequent (Supplementary Table 2).

Publication Bias

As only 7 trials (9,30-33,38,40) were included in the group comparisons for pain reduction; the detection of publication bias from the funnel plot was limited. When the funnel plot was used to test publication bias,

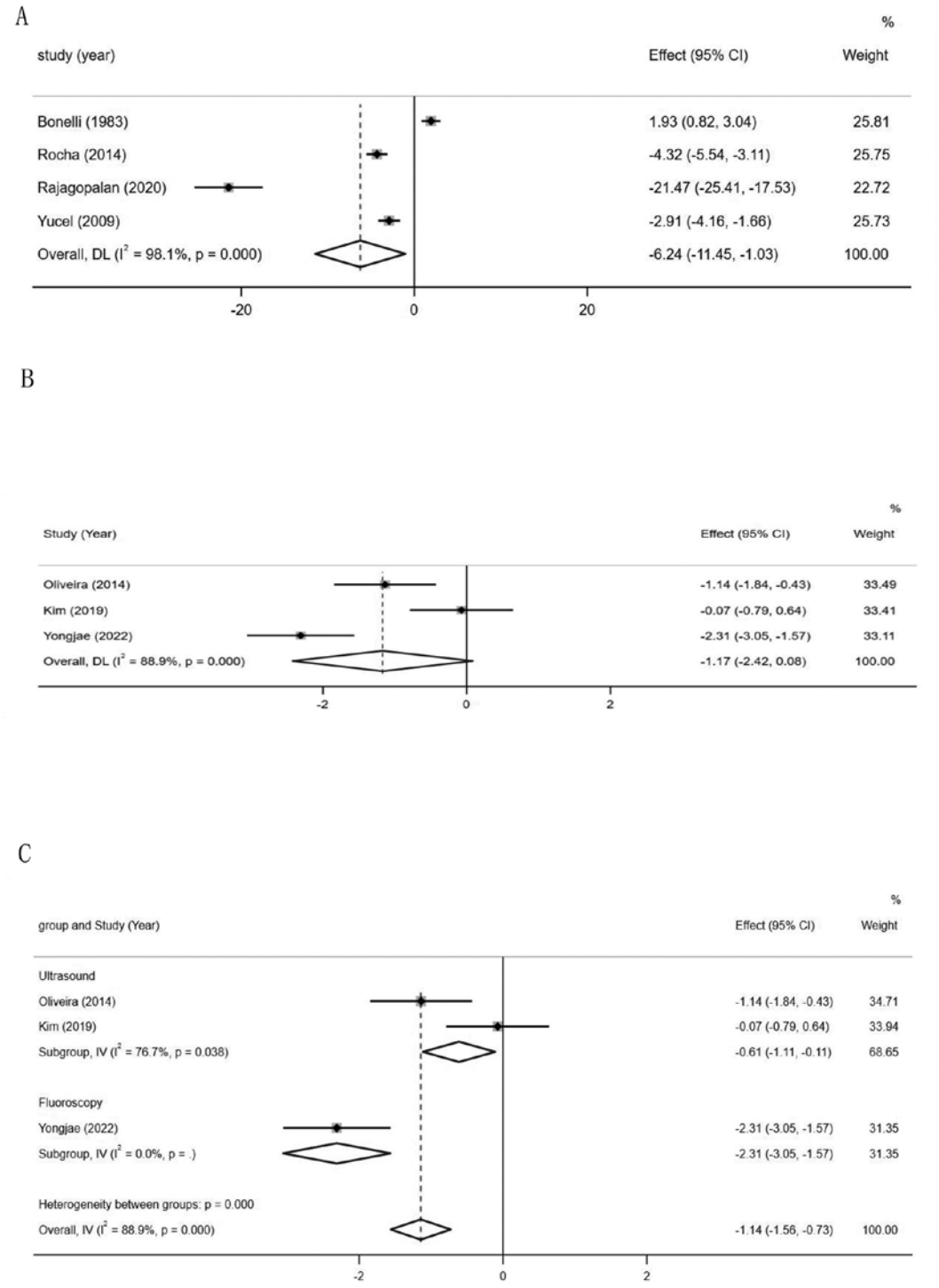

Fig. 2. *Forest plots of the meta-analysis using VAS and NRS to evaluate efficacy of the pain relief. (A) The overall WWD showed a decrease of VAS by -6.24 mm in 4 trials. (B) The overall WWD showed a decrease of NRS by -1.17 mm in 3 trials. (C) A comparison of the pain alleviation provided by fluoroscopy- and ultrasound-guided stellate ganglion blocks.*

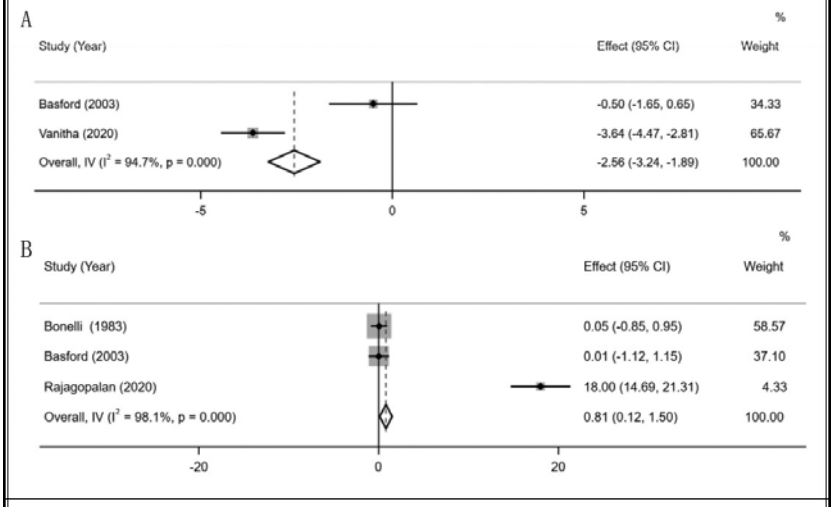

Fig. 3. *Analysis of hemodynamic response following SGB therapy. The change in heart rate was reflected by a combined SMD of -2.56 following SGB compared with the placebo groups. (B) Change in skin temperature, reflected by a combined SMD of 0.81 following SGB therapy.*

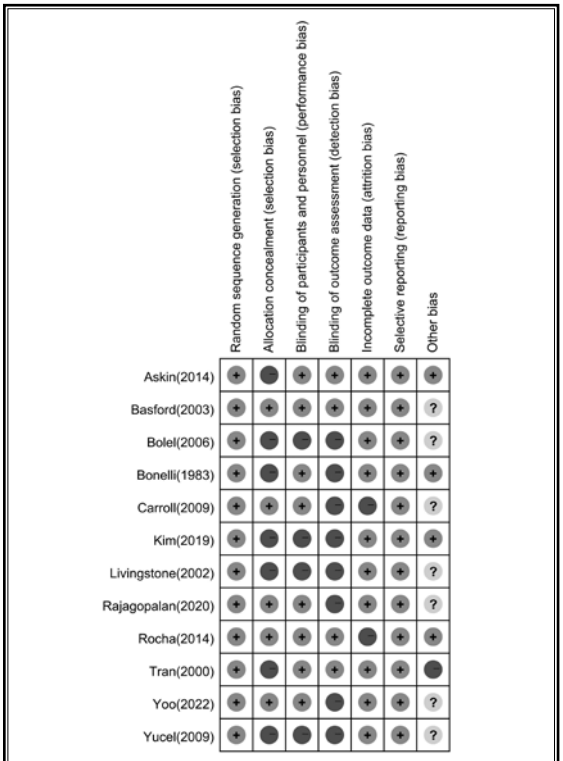

Fig. 4. *Methodological quality of included RCTs. This 'risk of bias' tool incorporates assessment of randomization, blinding, completeness of outcome data, selection of outcomes reported, and other sources of bias. The items are scored a 'yes (+),' 'no (-),' or 'unsure (?).'*

one point deviated significantly from the research center. The other 6 scattered points were symmetrical in distribution, and all studies were within the 95% confidence level. This suggested that there was no significant publication bias (Fig. 6).

Discussion

The current systematic review and meta-analysis report the efficacy of SGB treatment for CRPS-related pain. Compared to the control group, both VAS and NRS scores in the SGB therapy group decreased during treatment, and the skin temperature of patients increased (30,33,38), indicating an ameliorative benefit of such an SGB therapy strategy. Meticulous SGB is vital for effective and prolonged sympatholysis. Blocking the stellate ganglion can regulate nervous system responses, improve local blood circulation and metabolism, and reduce inflammation and pain. SGB is considered a relatively high-risk procedure because of potential complications such as lidocaine toxicity/seizures, carotid dissection/quadriplegia, laryngeal nerve paralysis, and persistent ptosis (41). However, for patients suffering from CRPS pain, SGB, especially SGB under ultrasound or fluoroscopic guidance, is worth trying. In the current analysis, only 4 of 12 patients with invasive SGB reported side effects (9,30,40), which is consistent with the results of earlier studies (42,44). Experienced clinicians can perform blinding of SGB in selected cases. However, these outcomes were less reliable. An appropriate technique is crucial for any approach to maximize efficacy and safety. Thus, fluoroscopy- or ultrasound-guided SGB is generally superior to the blind technique, with a tradeoff between radiation

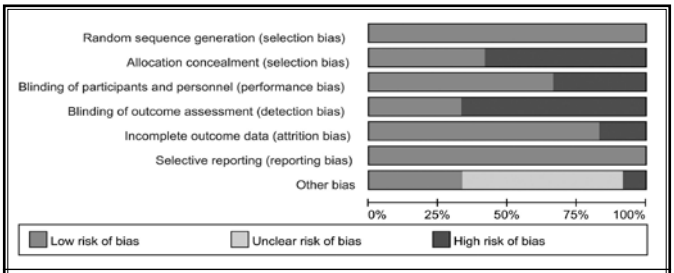

Fig. 5. *Risk of bias graph: authors' judgments about each risk of bias item presented as percentages across all included studies.*

exposure and fluoroscopy guidance. Ultrasound-guided blocks have emerged as reasonable alternatives to fluoroscopy owing to their improved safety and accuracy. Consistent with the results of Chun-De Liao's research (24), the PEDro scores of the 12 studies indicated that the methodological quality of all studies was generally high; thus, the current study had strong clinical guiding significance from a statistical point of view. In contrast, in existing studies, there was no significant difference in the patients' heart rate and blood pressure before and after SGB treatment, suggesting that this treatment strategy has little effect on hemodynamics (30,33).

Many aspects should be considered when using SGB to treat CRPS. The first is the classification of CRPS. Among the SGB therapy studies included in this review, 8 trials were related to CRPS-I, one trial was related to CRPS-II, 2 included both CRPS I/II, and one trial was not clearly classified. SGB therapy is reported to be more prevalent in CRPS type I (30,42), which is in line with our analysis of the included articles. Second, owing to differences in the lesion sites of CRPS, appropriate SGB therapy will vary. For example, SGB and LSB effectively treat upper-extremity and lower-extremity CRPS, respectively. SGB treatment offers better pain relief in patients with upper limb injuries than in patients with both upper and lower limb injuries. Furthermore, local anesthetic blockade of the stellate ganglion is a common practice, however, there is still a difference in medicines used for injection (43). For example, a crossover injection of botulinum toxin is efficient in prolonging the duration of pain relief and enhancing the efficiency of the block compared with bupivacaine (32).

The success rate of treatment can be enhanced when combined with other guidance techniques, such as CT-guided and ultrasound-guided SGB, which can improve postoperative recovery in patients with CRPS with excellent effects

Table 1. *Summary of the methodological quality based on the PEDro classification scale*

Study	Overall[a]	Eligibility criteria[#]	Random allocation	concealed allocation	Baseline comparable	Subject Blinding	Therapist Blinding	Assessor Blinding	Adequate follow-up	Intention to treat	Between -group comparison	Point estimates & variability
Bonelli (1983)	7	1	1		1	1	1		1		1	1
Carroll (2009)	8	1	1	1	1	1	1			1	1	1
Rocha (2014)	9	1	1	1	1	1	1	1	1		1	1
Askin (2014)	7	1	1		1	1	1	1	1			1
Basford (2003)	8	1	1	1	1	1	1	1		1		1
Bolel (2006)	6[@]	1	1		1					1	1	1
Kim (2009)	6[@]	1	1		1	1					1	1
Rajagopalan (2020)	7	1	1	1	1	1	1				1	1
Yoo (2022)	8	1	1	1	1	1	1		1		1	1
Livingstone (2002)	5[@]	1	1		1						1	1
Tran (2000)	7	1	1		1	1	1	1			1	1
Yucel (2009)	6[@]	1	1		1				1		1	1
Summary*		12	12	5	12	9	8	4	5	3	10	12

[a]Points of methodological quality were "1" when a criterion was fulfilled. Methodological quality: 9–10, excellent; 6–8, good; 4–5, fair;<4, poor. *This was calculated as the number of studies satisfied.
[@]This item was not used to calculate the total score.
[#]The score was determined by a third assessor.

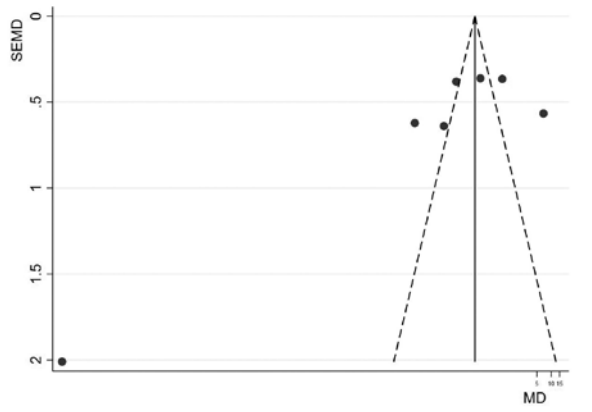

Fig. 6. *Publication bias from the funnel plot.*

and few side effects (44,45). Additionally, early adoption of SGB treatment can improve the effectiveness of blockade since shortening the time from symptom onset to SGB treatment contributes to the reduction of VAS scores (40), therefore early identification of CRPS is clinically important. However, the current clinical diagnosis of CRPS is not accurate and is typically judged by vague signs and symptoms; therefore, accurate diagnosis of SGB needs to be explored in the future. On the other hand, we also compared the therapeutic benefits of fluoroscopy-guided SGB against ultrasound guidance. Fig. 2C shows that fluoroscopy-guided SGB has a greater impact on pain alleviation. However, further research evidence is needed due to the limited number of available research.

Although this study confirmed the efficacy of SGB in the treatment of CRPS-related pain, there are some limitations to the current study. The first is the high heterogeneity of the data. The results from the fixed-effects/random-effects models were the same for the VAS and NRS data analyses, indicating that heterogeneity was not due to the model. However, the different types of CRPS, treatment of different affected limbs, and various narcotic drugs in the studies may explain the high heterogeneity. On the other hand, while describing the random assignment design of related studies, there was one study with a random assignment ratio of 1:1:1 (36) and 4 studies with a random assignment ratio of 1:1 (30-32,35). Additionally, only 6 studies out of 12 studies clearly described allocation concealment. These changes may have contributed to methodological heterogeneity. In addition, the funnel plot results showed no significant publication bias, and the methodological quality of all the included studies was high. Therefore, publication bias was not a source of the methodological heterogeneity.

In the current investigation, only RCTs were selected to ensure a higher quality of the included studies. However, owing to the limited number of RCTs and the small number of patients, the conclusions of the study did not seem particularly compelling. Larger sample sizes and higher-quality multicenter RCTs are required in the future to produce more persuasive evidence for clinical treatment.

Conclusions

Studies have shown that SGB therapy is effective and safe for patients with CRPS. The average PEDro score for methodology quality was 7.0 (range: 5-9), indicating that the overall methodology quality was good. The funnel plot results showed no significant publication bias. However, there was large heterogeneity and small sample sizes of the studies included in this review. Therefore, more high-quality studies should be included in future studies.

Supplemental material available at www.painphysicianjournal.com

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Supplemental Table 1. *Characteristics in RCTs of Included Studies.*

Study	Year	Fluoroscopy/ Ultrasound	treatment method	Multi/ Single centre	Age (y/r) mean ± SD	Sex F/M	No. per group	Trial design	Condition treated	Side treated	limb	Groups
Bonelli	1983	*	SGB	Multi	52.33 ± 5.04	NA	10	RCT	RSD	R/L	upper	Tr1: SGB
					42.77 ± 4.65	NA	9					Tr2: regional intravenous guanethidine blocks
Carroll	2009	Fluoroscopy	SGB	Multi	NA	NA	9	double-blind; controlled; crossover; RCT	CRPS (type I)	*	lower	Tr1: LSB
												Tr2: LSB+BTA
Rocha	2014	Fluoroscopy	SGB	Single	42.00 ± 13.50	8/9	17	double-blind; RCT	CRPS (type I)	R/L	upper	Gr1: TSB
					44.40 ± 8.90	11/8	19					Gr2: Control
Askin	2014	Ultrasound	SGB	Multi	45.17 ± 13.44	7/6	13	Double blind	CRPS (type I)	R/L	upper	Gr1: SG-US (0.5wt/cm²)
						7/6	13	parallel; RCT				Gr2: SG-US (3wt/cm²)
					45.80 ± 13.50	5/9	14					Gr3: Placebo
Bolel	2005	*	SGB	Multi	44.60 ± 16.40	6/9	15	RCT	RSD	R/L	upper	Gr1: SG-TENS
					41.10 ± 20.80	6/9	15					Gr2: Control*
Basford	2003	Fluoroscopy	SGB	Single	45.50 ± 12.30	5/1	6	Double blind	CRPS (type I)	R	*	Tr1: SGL
					*	5/1	6	crossover; placebo-controlled				Tr2: Placebo
Kim	2019	Ultrasound	SGB	Single	49.33 ± 9.28	2/13	15	Prospective; Randomized; Crossover Trial	CRPS	R/L	upper	Gr1: SGB
						2/13	15					Gr2: T2 PVB
Vanitha	2020	*	SGB	*	28.00 ± 8.00	0/30	30	RCT; Double-blind; Placebo-controlled Trial	CRPS (type II)	*	upper	Gr1: groups bupivacaine
					31.00 ± 9.00	1/29	30					Gr2: saline
Yoo	2022	Fluoroscopy	SGB	Single	44.80 ± 12.20	11/12	23	parallel; RCT; double-blind	CRPS (type I/II)	R/L	lower	Gr1: botulinum toxin group
					43.70 ± 12.30	12/12	26					Gr2: control group
Yucel	2009	*	SGB	*	50.70 ± 15.00	13/9	14	RCT	CRPS (type I)	*	upper	Gr1: 1
							8					Gr2: 2

Supplemental Table 1 cont. *Characteristics in RCTs of Included Studies*.

Study	Year	Fluoroscopy/ Ultrasound	treatment method	Multi/ Single centre	Age (y/r) mean ± SD	Sex F/M	No. per group	Trial design	Condition treated	Side treated	limb	Groups
Livingstone	2002	*	SGB	*	61.70 ± 2.10	26/1	27	Randomized; RCT	CRPS (type I)	*	upper	Gr1: Guanethidine
					61.60 ± 2.50	28/2	30					Gr2: Control
Tran	2000	Fluoroscopy	SGB	*	46.00 ± 6.30	11/4	15	randomized; double-blinded	CRPS (type I/II)	R/L	upper/ lower	Gr1: Iohexol
				*	46.00 ± 6.30	7/6	13					Gr2: Normal saline

Supplemental Table 1 cont. *Characteristics in RCTs of Included Studies*.

Study	Year	Outcome measures	Pain duration (months)	Skin temperature (°C)	Skin temperature (°C)	Numeric rating scale		SSR(sympathetic skin response)			
								amplitude values		latency values	
				Baseline	after	Baseline	after	before	after	before	after
Bonelli	1983	skin temperatures; VAS.	6.55 ± 3.94	*	32.34 ± 3.13	*	*	*	*	*	*
			17.55 ± 14.90		32.21 ± 2.34						
Carroll	2009	VAS	*	*	*	*	*	*	*	*	*
Rocha	2014	BPI	22.70 ± 26.30	*	*	5.35 ± 2.10	3.47 ± 3.50	*	*	*	*
			21.00 ± 21.60			6.37 ± 1.90	5.86 ± 2.90				
Askin	2014	VAS	57.00 (38.00 - 156.00)	*	*	*	*	700.0 (333.2 - 1840.7)	555.2 (203.1 - 1451.3)	1447.2 (527.3 - 2030.0)	1350.0 (1071.8 - 1900.0)
		DASH	62.00 (25.00 - 161.00)	*	*	*	*	729.5 (311.1 - 2134.2)	694.4 (410.9 - 2075.4)	1420.3 (1100.0 - 1626.5)	1515.6 (1251.4 - 1704.6)
		SSR	70.50 (15.00 - 162.00)	*	*	*	*	685.6 (230.1 - 1512.4)	693.5 (133.7 - 1961.6)	1424.2 (786.4 - 1925.7)	1445.5 (1025.9 - 1862.3)
Bolel	2005	SSR	9.70 ± 4.30	*	*	*	*	757.20 + 580.74	686.20 + 552.58	1319.00 + 163.21	1381.00 + 156.00
			10.00 ± 4.00	*	*	*	*	724.60 + 444.62	366.73 + 293.88	1236.00 + 181.62	1485.86 + 149.99
Basford	2003	VAS	25.00 (9.00 – 103.00)	28.92 ± 2.83	28.58 ± 3.83	*	*	*	*	*	*
		Skin temperature	NA	30.10 ± 2.48	29.75 ± 2.53	*	*	*	*	*	*
Kim	2019	Numeric rating scale	*	*	*	8.00 ± 0.38	9.26 ± 2.21	*	*	*	*
			*			7.87 ± 0.51	37.20 ± 12.14				
Vanitha	2020	Visual analog scale (VAS) score; Heart rate (bpm); Mean blood Pressure (mm Hg)	9.50 ± 3.70	31.30 ± 1.30	34.00 ± 1.30	*	*	*	*	*	*
			9.90 ± 4.40	32.20 ± 1.90	32.20 ± 2.00	*	*	*	*	*	*

Supplemental Table 1 cont. *Characteristics in RCTs of Included Studies*.

Study	Year	Outcome measures	Pain duration (months)	Skin temperature (°C)	Skin temperature (°C)	Numeric rating scale		SSR(sympathetic skin response)			
								amplitude values		latency values	
				Baseline	after	Baseline	after	before	after	before	after
Yoo	2022	NRS; VAS	26.70 ± 10.30	*	*	7.60 ± 1.40	5.60 ± 2.10	*	*	*	*
			25.20 ± 10.70	*	*	7.20 ± 1.50	6.60 ± 2.00	*	*	*	*
Yucel	2009	Pain intensity; VAS	17.00 ± 6.30								
			49.80 ± 17.60								
Livingstone	2002	*	*	*	*	*	*	*	*	*	*
			*	*	*	*	*	*	*	*	*
Tran	2000	VAS	*	*	*	*	*	*	*	*	*
			*								

Supplemental Table 1 cont. *Characteristics in RCTs of Included Studies*.

Study	Year	Visual analogue scale		Conflict of interest	Age range (year)	Funds	Diagnose criteria	No. of total study arm (right/left)	No. of randomised
		baseline	after						
Bonelli	1983	70.5 ± 27.36	61.1 ± 22.47	*	≥18	*	IASP criteria	*	*
		65.0 ± 25.46	43.2 ± 33.28						
Carroll	2009	*	*	NA	21 - 80	NA	IASP criteria	*	*
Rocha	2014	3.50 ± 3.20	3.47 ± 3.50	NA	18 – 70	Yes	IASP (Budapest criteria)	9 /10	*
		4.80 ± 2.70	5.86 ± 2.90					16 /1	
Askin	2014	4.00 (2.00 - 8.00)	0.00 (0.00 - 6.00)	NA	*	*	IASP criteria	6/7	1/1/1
		3.00 (2.00 - 7.00)	0.00 (0.00 - 1.00)					5/8	
		4.00 (2.00 - 6.00)	0.00 (0.00 - 1.00)					2/12	
Bolel	2005	*	*	*	*	*	IASP criteria	8/7	1/1
		*	*					9/6	
Basford	2003	*	*	*	18 – 72	Yes	IASP criteria	*	*
		*	*						
Kim	2019	*	*	*	≥19	*	IASP criteria	9/6	1/1
Vanitha	2020	6.90 ± 1.20	1.20 ± 1.30	NA	18 - 65	Yes	American Society of Anesthe-siologists (ASA)	*	1/1
		6.00 ± 1.10	5.10 ± 1.40						
Yoo	2022	2.20 ± 1.00	2.00 ± 1.00	NA	18 - 85	Yes	IASP (Budapest criteria)	13/10	1/1
		1.00 ± 1.60	0.60 ± 1.60					11/13	
Yucel	2009	7.70 ± 1.10	0.90 ± 0.70	NA	18 - 85	*	IASP criteria	12/10	*
		7.90 ± 1.10	2.10 ± 1.30						
Livingstone	2002	*	*	NA	23 - 86	Yes	IASP criteria	*	*
		*	*						
Tran	2000	57.00 ± 11.00	22.00 ± 6.00	*	*	*	IASP criteria	7/8	*
		*	*					4/9	

NA: RCT=randomized control trial; NA=not available; R=right; L=left; Gr=group; Tr=treatment; SG-US=ultrasound therapy to the stellate ganglion; SGB=stellate ganglion blockade; BTA=botuli toxin A; SGL=Light irradiation to the stellate ganglion; LSB=lumbar sympathetic block; TSB=thoracic sympathetic block; *:No reported data

Supplemental Table 2. *Adverse Events of CRPS Treatment in RCTs of Included Studies*.

ID	treat-ment method	Study	Year	Adverse effect 1	No. of adverse effect 1 (%)	Adverse effect 2	No. of adverse effect 2 (%)	Adverse effect 3	No. of adverse effect 3 (%)	Adverse effect 4	No. of adverse effect 4(%)	Adverse effect 5	No. of adverse effect 5(%)	Adverse effect 6	No. of adverse effect 6(%)	Adverse effect 7	No. of adverse effect 7(%)
1	SGB	Bonelli	1983	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2	SGB	Carroll	2009	nausea and emesis	1/9	*	*	*	*	*	*	*	*	*	*	*	*
3	SGB	Rocha	2014	Claude Bernard-Horner's	7 (41.2%)	puncture pain	65%	dyspnoea	35%	*	*	*	*	*	*	*	*
4	SGB	Askin	2014	*	*	*	*	*	*	*	*	*	*	*	*	*	*
5	SGB	Bolel	2006	*	*	*	*	*	*	*	*	*	*	*	*	*	*
6	SGB	Basford	2003	*	*	*	*	*	*	*	*	*	*	*	*	*	*
7	SGB	Kim	2019	*	*	*	*	*	*	*	*	*	*	*	*	*	*
8	SGB	Rajagopalan	2020	few episodes of nausea	*	shivering	*	*	*	*	*	*	*	*	*	*	*
9	SGB	Yoo	2022	*	*	*	*	*	*	*	*	*	*	*	*	*	*
10	SGB	Yucel	2009	*	*	*	*	*	*	*	*	*	*	*	*	*	*
11	LSB/GSB	Livingston	2002	*	*	*	*	*	*	*	*	*	*	*	*	*	*
12	SGB	Tran	2000	*	*	*	*	*	*	*	*	*	*	*	*	*	*

NA: a: reported adverse events but did not specify the number of people reported; *:No reported adverse events