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REVIEW

Effect of electrical stimulation on the fusion rate after spinal surgery: a systematic review and meta-analysis

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Abstract
Electrical stimulation is an important adjuvant therapy for spinal surgery, but whether receiving electrical stimulation can improve the fusion rate after spinal surgery is still controversial. The purpose of this study was to analyse and evaluate the effect of electrical stimulation on the fusion rate after spinal surgery. We systematically searched for related articles published in the PubMed, Embase and Cochrane Library databases on or before September 30, 2023. The odds ratio (OR) with 95% confidence interval (CI) and the fusion rates of the experimental group and the control group were calculated by a random-effects meta-analysis model. The analysis showed that receiving electrical stimulation significantly increased the probability of successful spinal fusion (OR 2.66 [95% CI 1.79–3.97]), and the average fusion rate of the electrical stimulation group (86.8%) was significantly greater than that of the control group (73.7%). The fusion rate in the direct current (DC) stimulation group was 2.33 times greater than that in the control group (OR 2.33 [95% CI 1.37–3.96]), and that in the pulsed electromagnetic field (PEMF) group was 2.60 times greater than that in the control group (OR 2.60 [95% CI 1.29–5.27]). Similarly, the fusion rate in the capacitive coupling (CC) electrical stimulation group was 3.44 times greater than that in the control group (OR 3.44 [95% CI 1.75–6.75]), indicating that regardless of the type of electrical stimulation, the fusion rate after spinal surgery improved to a certain extent. Electrical stimulation as an adjuvant therapy seems to improve the fusion rate after spinal surgery to a certain extent, but the specific effectiveness of this therapy needs to be further studied.

Keywords Electrical stimulation · Fusion rate · Spinal surgery · Systematic review and meta-analysis

Introduction

Spinal disease is a musculoskeletal disease [1] that includes degenerative diseases, fractures, etc. [2, 3] and often causes neck, back and waist pain. Moreover, excessive strain on the lower limb joints can result in morphological changes in the spine and joint pain, affecting the normal life and labour of patients. By 2016, 32% of European adults had spinal disease [1]. With the increasing prevalence of spinal disease in the population, how to treat spinal diseases and improve patients' quality of life has become the focus.

At present, Spinal surgery is one of the ways to treat spinal disorders. Although spinal surgery can significantly improve quality of life, complications such as nonunion and pseudarthrosis are generally not conducive to improving patient prognosis, and patients may experience persistent or recurrent pain at the surgical site [4]. The incidence of nonunion is approximately 25–81%, and the incidence of pseudarthrosis is as high as 81% [5]. The success of spinal

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fusion often determines whether such complications will occur. Spinal fusion is one of the important criteria for of successful spinal surgery [6]. Therefore, researchers have proposed a number of adjuvant therapies, such as biological agents or electrical stimulation therapy (EST), to promote spinal fusion [7, 8]. To date, there are three kinds of electrical stimulation therapy: direct current (DC), pulsed electromagnetic field (PEMF) and capacitive coupling (CC) stimulation. DC stimulation involves the application of a continuous electrical current to promote cellular biological responses. The primary mechanism is through the creation of a stable electric field, which influences the cell membrane potential, thereby regulating cell proliferation, differentiation, and migration. This form of stimulation is widely applied in tissue repair and regeneration. PEMF utilizes short, rapidly changing electromagnetic fields to induce currents, leading to physiological changes both inside and outside cells. PEMF has been demonstrated to have beneficial effects in the repair of bone and soft tissues, primarily by influencing cellular signaling pathways and gene expression. CC stimulation refers to the application of a fixed current intensity to cells or tissues. The goal of CC stimulation is to ensure uniformity and reproducibility of the stimulus by maintaining a consistent current intensity. This method is employed in the recovery of neural and muscular function. PEMF and CC stimulation are noninvasive techniques that do not cause wounds, as only closeness to the skin is needed. DC stimulation requires that an implant be placed in the fusion site and soft tissue to provide continuous stimulation at the fusion site. All three kinds of electrical stimulation fusion therapies have their own advantages [9, 10].

At present, it is controversial whether electrical stimulation can improve the rate of spinal fusion. Massari, L. et al. [10] explored the effect of DC electrical stimulation on the fusion rate after spinal surgery. The results showed that the postoperative fusion rate of patients in the DC electrical stimulation group was significantly greater than that of patients in the nonelectrostimulation group. However, in a study of 60 patients [11], electrical stimulation did not lead to spinal fusion, so there is no unified conclusion on this issue.

The causes of these disputes may be related to the type of electrical stimulation and the differences in patient characteristics. However, the effect of electrical stimulation as an adjuvant therapy on the fusion rate after spinal surgery is unclear. We reviewed the previous literature on electrical stimulation and spinal fusion surgery and conducted a more comprehensive meta-analysis to evaluate the effect of electrical stimulation on the spinal fusion rate.

Methods

Standard protocol approvals and registrations

The study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and the Cochrane Handbook. The protocol of the review is registered with PROSPERO and can be accessed on the official website.

Search strategy

From inception to September 30, 2023, two independent investigators systematically searched the PubMed, Embase and Cochrane Library electronic databases without limiting the language or publication date. We used Medical Subject Headings (MeSH) terms to search PubMed and the Cochrane Library; Embase subject headings (Emtree) to search the EMBASE database; and combined free text words (including synonyms and closely related words) related to spinal surgery, electrical stimulation and the postoperative spinal fusion rate. The search terms used included "spinal fusion", "spinal dysraphism", "electric stimulation", "electromagnetic field", "electric stimulation therapy", and "fusion rate". The search strategy used for the databases is presented in eTable 1.

To ensure that no relevant articles were omitted, the researchers also hand searched for recent systematic reviews, meta-analyses, and any articles included in our review for other relevant articles. When articles described the same cohort, we retained only the latest publication or the article with the largest sample size.

Selection criteria

The study was performed in accordance with the PICOS guidelines, and two reviewers independently screened the studies according to the selection criteria. Only studies that met the following criteria were included:

(1) Participants: Patients who had undergone spinal fusion surgery.
(2) Intervention: Patients received any of the three types of electrical stimulation—DC, PEMF or CC stimulation—during the course of treatment.
(3) Control: There must be a control group in the study; that is, a group of patients who were given a placebo.
(4) Results: The main outcome was the fusion rate.
(5) Study type: Randomized controlled trial (RCT) or cohort study.

Reviews, letters, case reports, studies of animal models, studies not reporting fusion rates, studies lacking data for the control group and studies whose adjuvant therapy was not electrical stimulation were excluded (Fig. 1).

Data extraction

The two reviewers independently extracted relevant data with the predesigned data extraction table. consulting third party. The following data were extracted: first author, year of publication, geographical area, observation period, sample size, percentage of women, average age, type of electrical stimulation, treatment time, site of spinal surgery, segment and type of spinal fusion, methods for determining the fusion rate, difference in the fusion rate between the experimental group and control group, follow-up date and so on (Table 1).

Quality assessment

Two reviewers used the Risk of Bias 2 tool (ROB 2) and Newcastle−Ottawa Scale (NOS) to strictly evaluate the quality of the RCTs and cohort studies. The ROB 2 assessment involved five domains: study selection bias, diagnostic bias, reporting bias, integration of bias factors and overall bias risk. Each domain was considered to have a low risk of bias (Fig. 2). The NOS consisted of three parameters of quality, selection, comparability, and outcome, with a total possible score of 9 for each study. A score ≥ 8 indicated high quality (low bias risk) (Table 2).

Statistical analysis

Analyses were performed using STATA software (version 16.0; STATA, University Station, Texas, USA). A random-effects meta-analysis was employed because of anticipated between-study heterogeneity, and the average fusion rate of the electrical stimulation group and the control group was determined. In general, fully-adjusted effect estimates (ORs) for the association between electrical stimulation and spinal surgical fusion rates were used to derive pooled risk estimates, depicted graphically with forest plots. Heterogeneity between studies was evaluated using the Cochrane Q test and I2 test, and heterogeneity was judged to be statistically

Fig. 1 Flowchart of the study selection

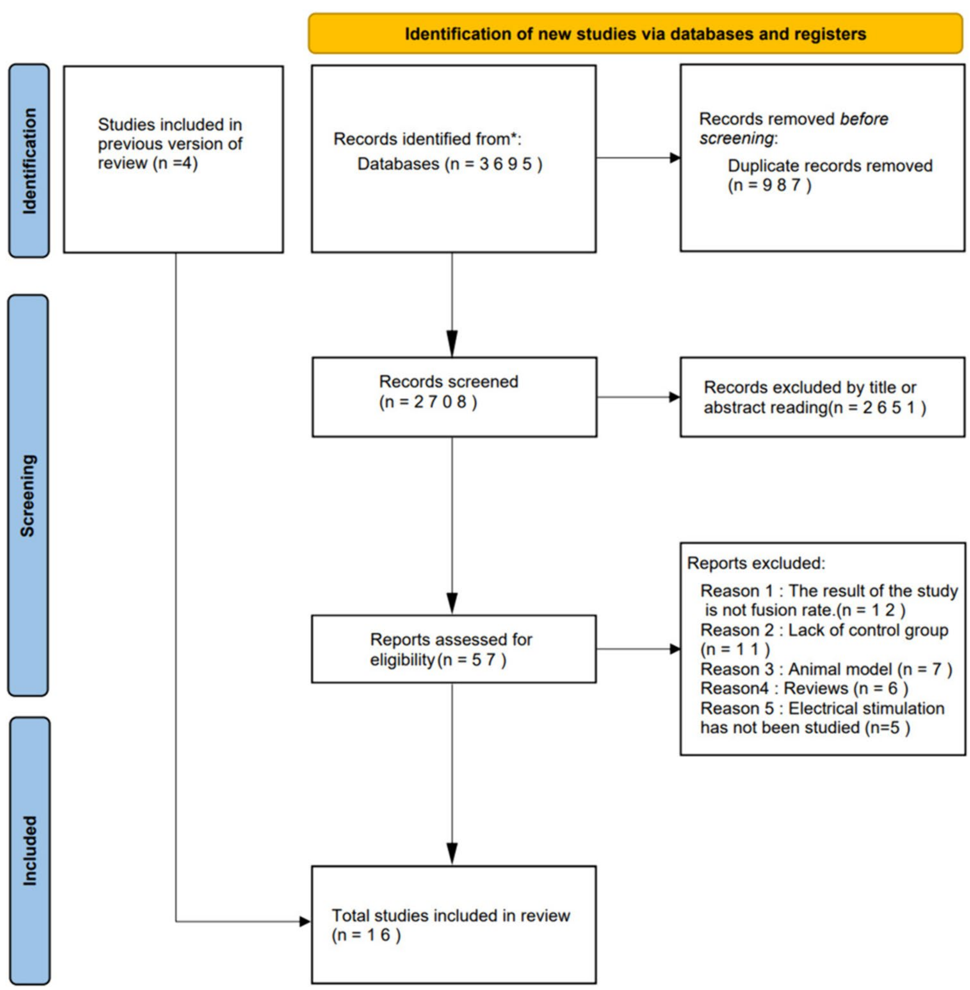

Table 1 Characteristics of the studies included in the meta-analysis

Trail	First author	Year	Region	Observation Period	Sample size (EST/Control)	Average age (years)	Female (%)	Type of stimulation
RCTs								
1	Kane, W. J	1988	USA	NR	31/28	39.51	NR	DC
2	Goodwin, C. B	1999	USA	1992–1997	85/94	42.37	45.81	CC
3	Mooney, V	1999	USA	NR	98/97	NR	NR	PEMF
4	Linovitz, R. J	2002	USA	1993–1998	125/118	57.00	49.38	PEMF
5	Foley, K. T	2008	USA	NR	163/160	NR	45.82	DC
6	Andersen, T	2009	Denmark	NR	53/42	70.25	65.26	DC
7	Andersen, T	2010	Denmark	2001–2005	43/32	71.79	63.75	DC
8	Massari, L	2020	Italy	NR	16/15	56.40	52.38	CC
9	Jenis, L. G	2000	USA	1995–1997	39/22	50.31	47.54	DC/PEMF
Cohort studies								
1	Mooney, V	1990	USA	NR	64/53	NR	NR	PEMF
2	Meril, A. J	1994	USA	1986–1988	122/103	NR	48.32	DC
3	Rogozinski, A. & Rogozinski, C	1996	USA	1990–1992	53/41	39.69	38.30	DC
4	Kucharzyk, D. W	1999	USA	1993–1994	65/65	55.15	52.31	DC
5	Marks, R. A	2000	USA	1987–1994	42/19	40.60	49.10	PEMF
6	Cheaney, B	2020	USA	2015–2017	40/20	57.52	36.66	PEMF
7	Coric, D	2018	USA	2007–2014	217/92	51.88	52.76	PEMF

First author	Fusion column	Type of fusion	Method of fusion assessment	Treatment Duration	Treatment Fusion Rate (%)	Control Fusion Rate (%)	Follow-up	Fusion level
RCTs								
Kane, W. J	Spine	Anterior and Posterior Lumbar Interbody Fusions	XR	18 months	80.66	53.57	18 months	Mixed
Goodwin, C. B	Lumber	Anterior and Posterior Lumbar Interbody Fusions	XR	NR	84.71	64.89	3.8 years	Mixed
Mooney, V	Lumbar	NR	XR	NR	91.84	68.04	49.3 months	Mixed
Linovitz, R. J	Lumbar	IF	XR	9 months	83.20	82.20	9 months	Mixed
Foley, K. T	Cervical	IF	CT	3 months	92.64	86.88	12 months	Mixed
Andersen, T	Lumbar	PF	CT	24 months	32.08	28.57	24 months	Mixed
Andersen, T	Lumbar	PF	CT	6 months	34.88	34.38	12 months	Mixed
Massari, L	Lumbar	Anterior and Posterior Lumbar Interbody Fusions	VAS/ODI/SF-36	3 months	87.50	46.67	10 years	NR
Jenis, L. G	Lumbar	PF	XR	1 month	97.44	95.45	1 year	Mixed
Cohort studies								

Table 1 (continued)

Trail	First author	Year	Region	Observation Period	Sample size (EST/Control)	Average age (years)	Female (%)	Type of stimulation
Mooney, V	Lumbar	Anterior and Posterior Lumbar Interbody Fusions	XR	NR	92.19	67.92	NR	Mixed
Meril, A. J	Lumbar	Anterior and Posterior Lumbar Interbody Fusions	XR/CT	6 months	92.62	74.76	42 months	Mixed
Rogozinski, A. & Rogozinski, C	Spine	PF	MRI	1 month	96.23	85.37	20.5 months	Multi-level
Kucharzyk,D.W	Lumbar	NR	XR/CT	NR	95.38	86.15	NR	NR
Marks, R. A	Spine	NR	XR	4–6 months	97.62	52.63	15.6 months	Mixed
Cheaney, B	Thoracic /lumbar	PF	XR	NR	80.00	100	28 months	NR
Coric, D	Cervical	AF	XR	3–6 months	92.63	82.61	12 months	Multi-level

EST electrical stimulation therapy, RCT Randomized Controlled Trials, *NR* not reported, *DC* direct current stimulation, *CC* capacitive coupling, PEMF pulsed eletromagnetic field, *PF* posterior/posterolateral fusion, *IF* interbody fusion, XR X-ray, *CT* computed tomography, *MRI* magnetic resonance imaging, Mixed = mixture of single and multi-level procedures

significant at I2 ≥ 50% or $P < 0.05$. Publication bias was assessed by visually assessing the symmetry of funnel plots. Sensitivity analysis was performed through the sequential omission of individual studies to evaluate the stability of the results.

In addition, we also carried out a subgroup analysis according to smoking status, the number of fused segments, and whether internal fixation was performed.

Results

Literature search

We initially identified a total of 3695 citations through a keyword search, and 2708 citations remained after identifying and deleting duplicate literature. According to the citation titles and abstracts, 57 articles were included for full-text review. After reviewing the full texts, 9 RCTs [9, 10, 12–18] involving 1261 patients and 7 cohort studies [11, 19–24] involving 996 patients were included in the meta-analysis, and 41 additional articles were excluded (Fig. 1). Among the 41 excluded articles, the exclusion criteria were studies focused on pain, studies analysing the function rate rather than fusion rate ($n = 12$), studies lacking a control group ($n = 11$), animal model studies ($n = 7$), review articles ($n = 6$), and studies not using electrical stimulation ($n = 5$).

Baseline characteristics

All the included studies were published between 1988 and 2020, and the baseline characteristics of the included studies are shown in Table 1. Among the 9 RCTs included, 4 [9, 12, 17, 18] used DC electrical stimulation, 4 [9, 14–16] used PEMF electrical stimulation, and 2 10, 13 used CC electrical stimulation. Among the 7 cohort studies included, 3 [20–22] used DC electrical stimulation, and 4 [11, 19, 23, 24] used PEMF electrical stimulation. Among all the studies, thirteen were conducted in the United States, two were conducted in Denmark and one was conducted in Italy. Eleven studies used X-ray imaging to evaluate the success of fusion, five studies used CT, two used both X-ray and CT, one used MRI, and one used VAS, ODI and SF-36 scores.

Effect of EST on spinal fusion

In all the studies, electrical stimulation increased the probability of successful spinal fusion by 2.66 times (OR 2.66 [95% CI 1.79–3.97]) (Fig. 3). There was a significant difference in the fusion rate between the two groups. The average fusion rate of the group treated with electrical stimulation (86.8%) was greater than that of the control group (73.7%) (Table 3). The same results were obtained regardless of

Fig. 2 Methodological quality score of the included studies based on Version 2 of the Cochrane tool for assessing risk of bias in randomized trials (RoB2)

which kind of electrical stimulation was used (DC, PEMF or CC). The fusion rate after DC electric stimulation treatment increased 2.33 times (OR 2.33 [95% CI 1.37–3.96]), the fusion rate after PEMF stimulation increased 2.60 times (OR 2.60 [95% CI 1.29–5.27]), and the fusion rate after CC stimulation increased 3.44 times (OR 3.44 [95% CI 1.75–6.75]) (eFigure 1).

In the RCT, the fusion rate of the electrical stimulation group was also significantly higher (OR 2.10 [95% CI 1.35–3.27]) (eFigure 2) than that of the control group (81.2% and 68.2%, respectively) (Table 3), while in the cohort study, the electrical stimulation group also showed a higher fusion rate (OR 3.80 [95% CI 1.93–7.49]) (eFigure 3) than the control group (93.2% and 80.7%, respectively) (Table 3). Sensitivity analysis revealed that after excluding a single study, the combined OR did not significantly change (lowest OR = 2.47, 1.70 to 3.59; highest OR = 2.92, 1.97 to 4.33) (eTable 2). A visual examination of the funnel plot showed that the data were basically symmetrical, indicating that there was no publication bias (eFigure 4).

Table 2 Methodological quality score of the included studies based on the Newcastle–Ottawa Scale (NOS) tool

Author	year	Study Design	Selection				Comparability	Exposure/Outcome			Total Score	Risk of Bias
			Representa-tiveness of cohort *	Selection of control cohort *	Ascertainment of exposure *	Outcome not present at start *	Comparability of cohorts **	Assessment of outcome *	Length of follow-up *	Adequacy of follow-up *	Total score 9*	
Mooney, V et al	1990	Prospective study	*	*	*	*	**	*	*	*	9	Low
Meril, A. J et al	1994	Prospective &Retrospective study	*	*	*	*	**	*	*	*	9	Low
Rogozinski, A & Rogozinski, C et al	1996	Prospective study	*	*	*	*	**	*	*	*	9	Low
Kucharzyk, D. W et al	1999	Prospective study	*	*	*	*	**	*	*	*	9	Low
Marks, R. A et al	2000	Retrospective study	*	*	*	*	**	*	*	*	9	Low
Cheaney, B et al	2020	Retrospective study	*	*	*	*	**	*	*	*	9	Low
Coric, D et al	2018	Retrospective study	/	*	*	*	**	*	*	*	8	Low

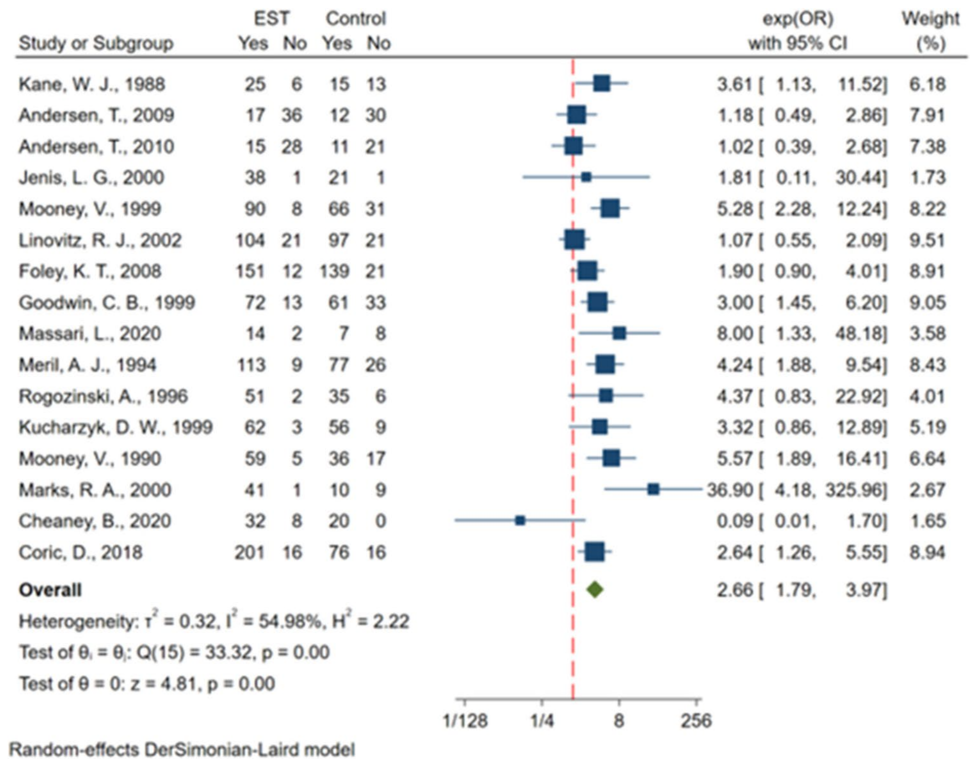

Fig. 3 Pooled fusion success rate (OR) after electrical stimulation compared to no stimulation

Effect of DC stimulation on spinal fusion

RCT data

A total of 4 RCTs [9, 12, 17, 18] reported the relationship between DC and the postoperative fusion rate after spinal surgery. Posterolateral fusion was used in all the operations studied by an RCT with DC electrical stimulation. The fusion rate of the treatment group was 65.7% (30%-93.8%), while that of the control group was 54.5% (24.0%-83.4%) (Table 3). However, there was no significant difference in the effect of DC electrical stimulation or nonelectrical stimulation (OR 1.50 [95% CI 0.84–2.69]) (Fig. 4) on the fusion rate according to the meta-analysis. Sensitivity analysis revealed that after excluding a single study, the combined odds ratio (OR) did not significantly change (the lowest OR = 1.14, 0.60 to 2.16; the highest OR = 1.86, 0.86 to 4.05) (eTable 2). A visual examination of the funnel plot showed that the data were basically symmetrical, indicating no publication bias (eFigure 5).

Cohort study

Three cohort studies [20–22] examined the effect of DC on spinal fusion; only one study [21] used only posterolateral fusion, and the other two studies [20, 22] used both anterior and posterior lumbar interbody fusion. The fusion rate in the treatment group was 94.3% (90.9%-97.0%), while that in the control group was 81.5% (73.3%-86.0%) (Table 3). According to our meta-analysis, the average fusion rate of patients receiving DC stimulation was almost 4 times greater than that of patients not receiving electrical stimulation (OR 4.03 [95% CI 2.12–7.66]) (Fig. 4). Sensitivity analysis revealed that after excluding a single study, the combined OR did not significantly change (the lowest OR = 3.71, 1.30 to 10.59; the highest OR = 4.26, 2.06 to 8.84) (eTable 2). A visual examination of the funnel plot showed that the data were basically symmetrical, indicating no publication bias (eFigure 6).

Effect of PEMF therapy on spinal fusion

RCT data

Four RCTs [9, 14–16] reported the effect of PEMF electrical stimulation as an adjuvant therapy on the fusion rate after spinal surgery. All operations were performed with interbody fusion. The fusion rate was 90.5% (85.1%-94.9%) in the treatment group and 83.0% (72.6%-91.4%) in the control group (Table 3). According to the results of the meta-analysis, there was no obvious difference in the average fusion rate between the treatment group and the control group (OR 2.03 [95% CI 0.91–4.54]) (Fig. 4). Sensitivity analysis revealed that after excluding a single study, the combined OR did not significantly change (lowest OR = 1.37, 0.84 to 2.23; highest OR = 2.82, 1.20 to 6.66) (eTable 2). A visual examination

Table 3 Mean fusion rates and odds ratios for the RCTs and cohort studies determined by random effects meta-analysis

Type of study	Type of EST	Authors & Year	Fusion Rate (no. fused/total)		I^2	OR (95% CI) & p Value
			Stimulation Group	Control Group		
RCTs	DC	Kane, W. J. 1988	25/31	15/28	5.66%	1.50 (0.84—2.69) p = 0.36
		Andersen, T. 2009	17/53	12/42		
		Andersen, T. 2010	15/43	11/32		
		Jenis, L. G. 2000	17/17	21/22		
		Overall (95% CI)	65.7% (30.0%—93.8%)	54.5% (24.0%—83.4%)		
	PEMF	Mooney, V. 1999	90/98	66/97	65.66%	2.03 (0.91—4.54) p = 0.03
		Linovitz, R. J. 2002	104/125	97/118		
		Foley, K. T. 2008	151/163	139/160		
		Jenis, L. G. 2000	21/22	21/22		
		Overall (95% CI)	90.5% (85.1%—94.9%)	83.0% (72.6%—91.4%)		
	CC	Goodwin, C. B. 1999	72/85	61/94	0.00%	3.44 (1.75—6.75) p = 0.32
		Massari, L. 2020	14/16	7/15		
		Overall (95% CI)	85.7% (77.8%—92.3%)	62.7% (53.2%—71.9%)		
	All	Overall (95% CI)	81.2% (67.1%—92.2%)	68.2% (53.9%—81.0%)	45.42%	2.10 (1.35—3.27) p = 0.06
No RCTs	DC	Meril, A. J. 1994	113/122	77/103	0.00%	4.03 (2.12—7.66) p = 0.95
		Rogozinski,A. & RogozinskiC. 1996	51/53	35/41		
		Kucharzyk, D. W. 1999	62/65	56/65		
		Overall (95% CI)	94.3% (90.9%—97.0%)	81.5% (73.3%—86.0%)		
	PEMF	Mooney, V. 1990	59/64	36/53	74.42%	3.46 (0.84—14.31) p = 0.01
		Marks, R. A. 2000	41/42	10/19		
		Cheaney, B. 2020	32/40	20/20		
		Coric, D. 2018	201/217	76/92		
		Overall (95% CI)	91.8% (85.8%—96.4%)	79.6% (59.8%—94.3%)		
	All	Overall (95% CI)	93.2% (90.2%—95.7%)	80.7% (71.3%—88.7%)	49.83%	3.80 (1.93—7.49) p = 0.06
All		Overall (95% CI)	86.8% (79.4%—92.8%)	73.7% (64.8%—81.8%)	54.98%	2.66 (1.79—3.97) p = 0.00

RCT Randomized Controlled Trials, *EST* electrical stimulation therapy, *DC* direct current, *CC* capacitive coupling, *PEMF* pulsed eletromagnetic field

of the funnel plot showed that the data were basically symmetrical, indicating no publication bias (eFigure 7).

Cohort study data

A total of 4 cohort studies [11, 19, 23, 24] examined the effect of PEMF stimulation on spinal fusion. The fusion rate was 91.8% (85.8%-96.4%) in the treatment group and 79.6% (59.8%-94.3%) in the control group (Table 3). According to the results of the meta-analysis, there was no significant difference in the effect of PEMF stimulation on the spinal fusion rate between the PEMF stimulation group and the nonstimulation group (OR 3.46 [95% CI 0.84–14.31]) (Fig. 4). Sensitivity analysis revealed that after excluding a single study, the combined OR did not significantly change (lowest OR = 2.11, 0.54 to 8.28; highest OR = 5.67, 1.79 to 17.90) (eTable 2). A visual examination of the funnel plot showed that the data were basically symmetrical, indicating no publication bias (eFigure 8).

Effect of CC stimulation on spinal fusion

Only 2 RCTs [10, 13] described the application of CC electrical stimulation in spinal fusion patients, and both of these studies involved anterior and posterior lumbar interbody fusion. The fusion rate of the treatment group was

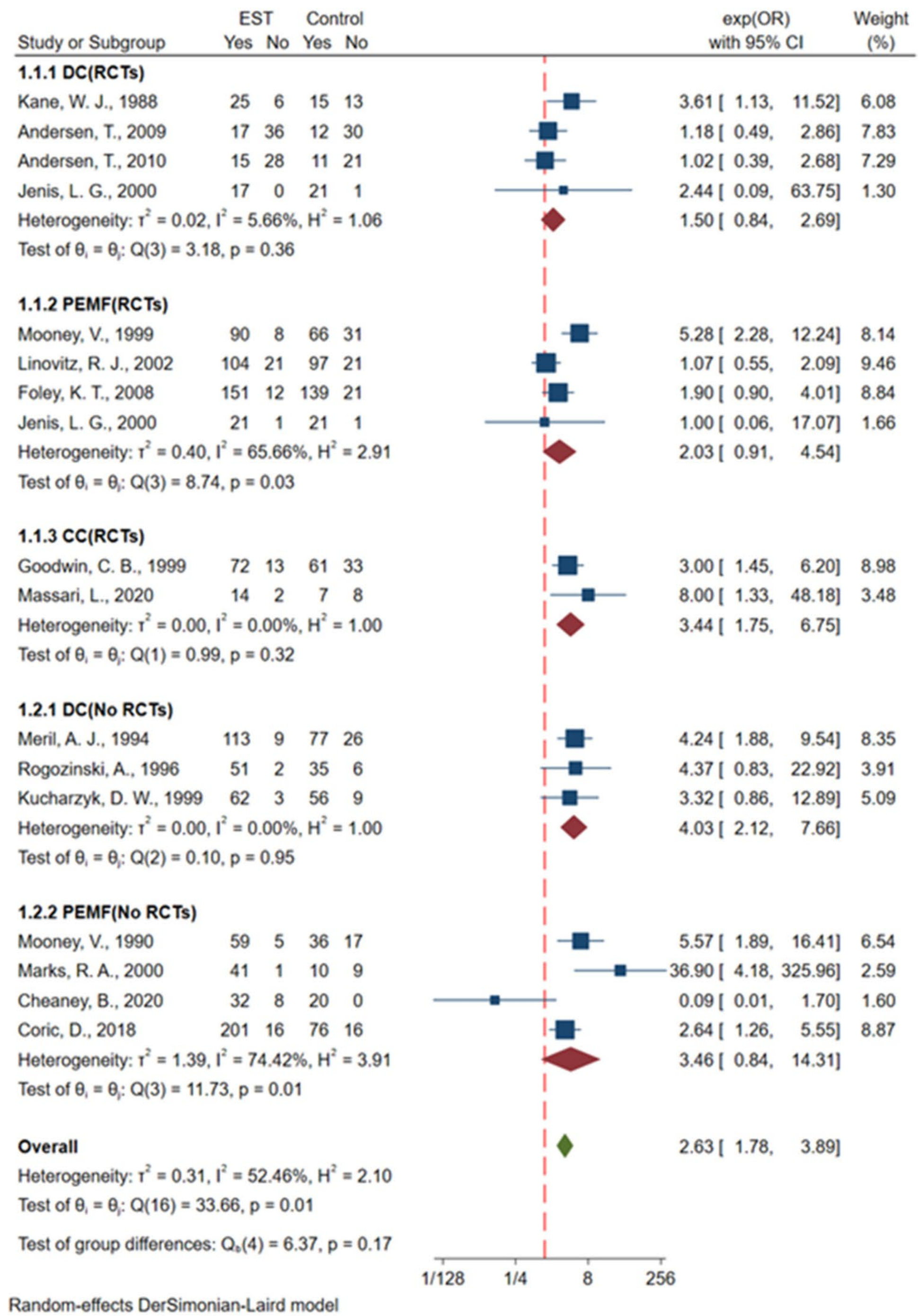

Fig. 4 Pooled fusion success rate (OR) after electrical stimulation according to the type of stimulation compared to no stimulation in different studies

85.7% (77.8%-92.3%), which was significantly greater than that of the control group (62.7%) (53.2%-71.9%) (Table 3). According to our meta-analysis, the average fusion rate among patients who received CC stimulation was significantly greater than that of patients who did not receive electrical stimulation (OR 3.44 [95% CI 1.75–6.75]) (Fig. 4). A visual examination of the funnel plot showed that the data were basically symmetrical, indicating no publication bias (eFigure 9).

Subanalysis

Meta-analysis revealed that the success rate of fusion in the group of patients receiving some form of electrical stimulation was almost 118% greater than that in the control group. Considering that smoking status and the degree of fusion may affect the fusion rate among patients, for example, patients who smoke have a high incidence of postoperative complications after spinal surgery, we were interested in determining whether there were differences in treatment among these subgroups. Table 4 summarizes the subgroup meta-analysis of randomized controlled trials and cohort studies (eFigure 10, eFigure 11; eFigure 12, eFigure 13). The variables included smoking history, nonsmoking status, single- and multi-segment fusion status, and whether the patients underwent internal fixation.

Notably, in the RCTs, the fusion rate among patients who received electrical stimulation was greater than that of patients who did not receive electrical stimulation, and the fusion rate of patients who received electrical stimulation without internal fixation was slightly lower than that of patients who did not receive electrical stimulation, which may be due to the decrease in the intensity of electrical stimulation received by patients without internal fixation. Only patients who underwent multi-segment fusion and internal fixation were included in this subgroup, and the difference in the fusion rate between the two groups was significant. In contrast, there was no obvious difference in the fusion rate between patients in the electrical stimulation group and those in the control group in the following subgroups: smokers, nonsmokers, single-segment fusion patients, and patients without internal fixation.

In the cohort studies, the fusion rate of patients who received electrical stimulation was obviously greater than that of patients who did not receive electrical stimulation. In addition, in all the subgroups we investigated, a meta-analysis showed that there was a marked difference in the fusion rate between patients in the electrical stimulation group and patients in the control group.

Discussion

Principal findings

Spinal fusion is one of the most important operations for the treatment of spinal disease, and successful spinal fusion is still a challenge. We performed this meta-analysis to comprehensively evaluate the effect of electrical stimulation on the fusion rate after spinal fusion surgery. The meta-analysis gathered data from 16 studies, 9 RCTs [9, 10, 12–18] and 7 cohort studies [11, 19–24] and revealed that spinal fusion patients who received some kind of electrical stimulation had better surgical fusion rates than did those who did not receive electrical stimulation.

Comparison with other studies

We found that the effect of electrical stimulation on the fusion rate after spinal surgery was similar to that of most previously published RCTs or cohort studies, most of which showed that electrical stimulation could increase the fusion rate after spinal surgery. However, the study of Cheaney, B. et al. [11] involved 72 participants but did not conclude that electrical stimulation was associated with a better fusion rate. This may be because the retrospective study did not consistently obtain patient bone mineral density information or data on patient compliance with electrical stimulation. In a subgroup analysis of smoking and nonsmoking individuals, Jenis, L. G et al. [9] did not find that the postoperative fusion rate in the electrical stimulation group was better than that in the nonelectrical stimulation group. This may be related to the duration and mode of the electrical stimulation intervention and the lack of research participants. This study, the most comprehensive to date, involved 2151 participants and meta-analysed the relationship between different types of electrical stimulation and spinal fusion rates.

Potential mechanisms

The mechanism through which electrical stimulation increases the rate of spinal fusion is complex and multifaceted and involves a variety of biological and physiological mechanisms. Although a large number of studies have been carried out, there is no definite evidence that electrical stimulation directly increases the rate of spinal fusion. However, some studies have suggested possible mechanisms that can explain how electrical stimulation contributes to fracture healing and spinal fusion.

Studies have shown that electrical stimulation can promote the proliferation and differentiation of bone cells (such as osteoblasts and chondrocytes), thus contributing to the formation of new bone tissue [25]. This can be achieved by regulating cellular signalling pathways and gene expression. For example, electrical stimulation can promote the proliferation and differentiation of osteocytes by activating the Wnt/β-catenin signalling pathway, thereby promoting bone formation [26, 27]. Moreover, electrical stimulation can improve blood perfusion in surrounding tissue by increasing capillary volume [28]. Improving blood flow can help eliminate metabolites and provide the necessary growth factors, which are essential for the supply of oxygen and nutrients to support the growth of new bone tissue [29]. Moreover, electrical stimulation can promote collagen deposition by regulating the osteogenesis of MC3T3-E1 cells, which helps to maintain the stability of the fracture or fusion area [30]. Several scholars have also shown that inflammation may have a negative impact on bone fusion. Electrical stimulation can promote bone fusion by reducing the inflammatory response and reducing the interference of inflammation with the healing process [31].

It should be noted that although some studies support the positive effect of electrical stimulation on spinal fusion, there is no clear evidence that electrical stimulation directly increases the rate of spinal fusion. Therefore, more studies

Table 4 Random-effects subgroup meta-analysis of the RCTs and cohort studies

Variable	Type of study	Type of EST	Authors & Year	Fusion Rate (no. fused/total)		I^2	OR (95% CI) & p Value
				Stimulation Group	Control Group		
Smoker	RCTs	DC	Jenis, L. G. 2000	5/10	8/13	/	0.63 (0.12—3.32) /
			Overall (95% CI)	50.0% (23.7%—76.3%)	61.5% (35.5%—82.3%)		
		PEMF	Mooney, V. 1999	13/20	7/11	17.12%	1.82 (0.87—3.78) p = 0.31
			Linovitz, R. J. 2002	8/16	3/12		
			Foley, K. T. 2008	53/61	45/65		
			Jenis, L. G. 2000	6/12	8/13		
			Overall (95% CI)	66.2% (42.9%—86.3%)	57.1% (37.4%—75.8%)		
		CC	Goodwin, C. B. 1999	17/25	13/26	/	2.13 (0.68—6.64) /
			Overall (95% CI)	68.0% (48.4%—82.8%)	50.0% (32.1%—67.9%)		
		All	Overall (95% CI)	65.1% (48.4%—80.2%)	57.2% (44.2%—69.7%)	5.01%	1.72 (0.99—2.98) p = 0.38
	No RCTs	DC	Meril, A. J. 1994	85/92	42/59	0.00%	4.55 (1.95—10.59) p = 0.73
			Rogozinski,A. & RogozinskiC. 1996	24/26	14/18		
			Overall (95% CI)	92.7% (87.0%—97.0%)	73.0% (62.2%—82.6%)		
		PEMF	Mooney, V. 1990	24/27	12/20	53.69%	13.89 (1.04—185.44) p = 0.14
			Marks, R. A. 2000	18/19	0/3		
			Overall (95% CI)	91.5% (81.0%—98.5%)	50.7% (27.8%—73.4%)		
		All	Overall (95% CI)	92.5% (87.6%—96.4%)	63.5% (42.2%—82.6%)	0.00%	5.38 (2.62—11.06) p = 0.42
	All		Overall (95% CI)	78.5% (66.9%—88.3%)	60.2% (49.5%—70.6%)	36.55%	2.49 (1.42—4.39) p = 0.12
Nonsmoker	RCTs	DC	Jenis, L. G. 2000	6/7	8/9	/	0.75 (0.04—14.58) /
			Overall (95% CI)	85.7% (48.7%—97.4%)	88.9% (56.5%—98.0%)		
		PEMF	Mooney, V. 1999	26/31	17/19	31.48%	1.07 (0.37—3.08) p = 0.23
			Foley, K. T. 2008	49/61	36/53		
			Jenis, L. G. 2000	7/10	8/9		
			Overall (95% CI)	81.1% (72.5%—88.6%)	80.2% (63.1%—93.3%)		
		CC	Goodwin, C. B. 1999	51/60	47/68	/	2.53 (1.05—6.08) /
			Overall (95% CI)	85.0% (73.9%—91.9%)	69.1% (57.4%—78.8%)		
		All	Overall (95% CI)	83.4% (76.9%—89.1%)	76.5% (66.6%—85.3%)	9.52%	1.62 (0.88—2.98) p = 0.35
	No RCTs	DC	Meril, A. J. 1994	26/28	14/20	0.00%	5.76 (1.28—26.00) p = 0.94
			Rogozinski,A. & RogozinskiC. 1996	27/27	21/23		
			Overall (95% CI)	97.6% (91.0%—100.0%)	82.5% (69.2%—93.0%)		

Table 4 (continued)

Variable	Type of study	Type of EST	Authors & Year	Fusion Rate (no. fused/total)		I²	OR (95% CI) & p Value
				Stimulation Group	Control Group		
		PEMF	Mooney, V. 1990	35/37	24/33	0.00%	9.23 (2.23—38.21) p = 0.39
			Marks, R. A. 2000	23/23	10/16		
			Overall (95% CI)	97.6% (91.2%—100.0%)	69.6% (55.6%—82.1%)		
		All	Overall (95% CI)	97.7% (92.9%—100.0%)	75.7% (62.2%—87.1%)	0.00%	7.39 (2.63—20.79) p = 0.81
	All		Overall (95% CI)	91.1% (83.8%—96.7%)	76.5% (68.8%—82.9%)	30.24%	2.39 (1.24—4.63) p = 0.18
Single level fusion	RCTs	DC	Kane, W. J. 1988	14/16	10/16	/	4.20 (0.70—25.26) /
			Overall (95% CI)	87.5% (64.0%—96.5%)	62.5% (38.6%—81.5%)		
		PEMF	Mooney, V. 1999	26/36	21/24	66.44%	1.38 (0.39—4.86) p = 0.05
			Foley, K. T. 2008	24/26	21/25		
			Linovitz, R. J. 2002	46/67	30/66		
			Overall (95% CI)	77.6% (62.3%—90.0%)	72.9% (41.5%—95.6%)		
		CC	Goodwin, C. B. 1999	41/48	34/51	/	2.93 (1.09—7.89) /
			Overall (95% CI)	85.4% (72.8%—92.8%)	66.7% (53.0%—78.0%)		
		All	Overall (95% CI)	80.7% (70.7%—89.2%)	69.4% (52.0%—84.5%)	44.09%	2.01 (0.97—4.18) p = 0.13
	No RCTs	DC	Meril, A. J. 1994	85/93	49/73	0.00%	5.15 (2.22—11.93) p = 0.93
			Rogozinski,A. & RogozinskiC. 1996	16/16	18/20		
			Overall (95% CI)	93.9% (88.1%—98.1%)	72.8% (63.1%—81.7%)		
		PEMF	Mooney, V. 1990	43/46	29/40	22.68%	8.69 (1.73—43.70) p = 0.26
			Marks, R. A. 2000	18/18	6/12		
			Overall (95% CI)	96.4% (89.5%—100.0%)	67.9% (54.1%—80.4%)		
		All	Overall (95% CI)	95.3% (90.5%—98.8%)	71.9% (58.6%—83.6%)	0.00%	5.80 (2.89—11.64) p = 0.67
	All		Overall (95% CI)	89.1% (81.1%—95.3%)	70.2% (59.5%—80.0%)	41.84%	3.03 (1.68—5.45) p = 0.09
Multilevel (≥ 2) fusion	RCTs	DC	Kane, W. J. 1988	11/15	5/12	/	3.85 (0.76—19.47) /
			Overall (95% CI)	73.3% (48.0%—89.1%)	41.7% (19.3%—68.0%)		
		PEMF	Mooney, V. 1999	13/15	3/6	0.00%	2.43 (1.43—4.14) p = 0.64
			Linovitz, R. J. 2002	21/37	12/31		
			Foley, K. T. 2008	78/96	60/93		
			Overall (95% CI)	75.1% (56.3%—90.2%)	52.8% (32.3%—72.9%)		
		CC	Goodwin, C. B. 1999	31/37	27/43	/	3.06 (1.05—8.93) /
			Overall (95% CI)	83.8% (68.9%—92.3%)	62.8% (47.9%—75.6%)		
		All	Overall (95% CI)	76.9% (65.8%—86.6%)	54.9% (42.6%—66.9%)	0.00%	2.63 (1.66—4.15) p = 0.87

Table 4 (continued)

Variable	Type of study	Type of EST	Authors & Year	Fusion Rate (no. fused/total)		I^2	OR (95% CI) & p Value
				Stimulation Group	Control Group		
	No RCTs	DC	Meril, A. J. 1994	28/29	28/30	0.00%	3.20 (0.75—13.64) p = 0.64
			Rogozinski,A. & RogozinskiC. 1996	35/37	17/21		
			Overall (95% CI)	95.5% (88.6%—99.6%)	88.9% (78.3%—96.6%)		
		PEMF	Mooney, V. 1990	16/18	7/13	0.00%	4.60 (2.27—9.33) p = 0.47
			Marks, R. A. 2000	23/24	4/7		
			Coric, D. 2018	186/200	50/64		
			Overall (95% CI)	93.9% (90.2%—96.9%)	68.4% (48.5%—85.7%)		
		All	Overall (95% CI)	94.3% (91.1%—96.9%)	77.9% (63.5%—89.8%)	0.00%	4.30 (2.28—8.10) p = 0.75
	All		Overall (95% CI)	86.9% (79.1%—93.2%)	65.6% (53.4%—76.9%)	0.00%	3.11 (2.14—4.51) p = 0.86
Fixation	RCTs	PEMF	Mooney, V. 1999	11/12	6/8	/	3.67 (0.27—49.29) /
			Overall (95% CI)	91.7% (64.6%—98.5%)	75.0% (40.9%—92.9%)		
		CC	Goodwin, C. B. 1999	53/65	47/77	/	2.82 (1.30—6.13) /
			Overall (95% CI)	81.5% (70.4%—89.1%)	61.0% (49.9%—71.2%)		
		All	Overall (95% CI)	83.9% (74.3%—91.8%)	62.9% (51.7%—73.4%)	0.00%	2.88 (1.37—6.06) p = 0.85
	No RCTs	DC	Meril, A. J. 1994	24/24	51/63	/	11.89 (0.68—209 20) /
			Overall (95% CI)	100.0% (86.2%—100.0%)	81.0% (69.6%—88.8%)		
		PEMF	Mooney, V. 1990	44/48	28/39	0.00%	4.01 (1.24—12.95) p = 0.71
			Marks, R. A. 2000	9/10	1/1		
			Overall (95% CI)	92.4% (83.1%—98.6%)	80.6% (60.3%—96.0%)		
		All	Overall (95% CI)	96.0% (86.4%—100.0%)	84.9% (74.2%—93.7%)	0.00%	4.69 (1.58—13.87) p = 0.74
	All		Overall (95% CI)	92.1% (82.9%—98.3%)	75.8% (63.7%—86.5%)	0.00%	3.37 (1.82—6.21) p = 0.88
Non-Fixation	RCTs	PEMF	Mooney, V. 1999	28/39	18/22	/	0.57 (0.16—2.05) /
			Overall (95% CI)	71.8% (56.2%—83.5%)	81.8% (61.5%—92.7%)		
		CC	Goodwin, C. B. 1999	19/20	14/17	/	4.07 (0.38—43.38) /
			Overall (95% CI)	95.0% (76.4%—99.1%)	82.4% (59.0%—93.8%)		
		All	Overall (95% CI)	81.1% (69.7%—90.5%)	82.1% (67.9%—93.1%)	51.50%	1.17 (0.18—7.56) p = 0.15
	No RCTs	DC	Meril, A. J. 1994	89/98	26/40	/	5.32 (2.07—13.69) /
			Overall (95% CI)	90.8% (83.5%—95.1%)	65.0% (49.5%—77.9%)		
		PEMF	Mooney, V. 1990	15/16	8/14	0.00%	19.26 (3.17—117.03) p = 0.45
			Marks, R. A. 2000	23/23	9/18		
			Overall (95% CI)	98.7% (90.9%—100.0%)	53.1% (35.2%—70.7%)		

Table 4 (continued)

Variable	Type of study	Type of EST	Authors & Year	Fusion Rate (no. fused/total)		I^2	OR (95% CI) & p Value
				Stimulation Group	Control Group		
		All	Overall (95% CI)	95.2% (87.3%—99.7%)	59.9% (48.0%—71.3%)	4.64%	7.29 (2.95—18.02) p = 0.35
	All		Overall (95% CI)	91.6% (81.1%—98.5%)	68.3% (55.7%—79.7%)	67.86%	4.37 (1.10—17.34) p = 0.01

RCT Randomized Controlled Trials, *EST* electrical stimulation therapy, *DC* direct current, *CC* capacitive coupling, *PEMF* pulsed eletromagnetic field

are needed to further verify the effectiveness and safety of electrical stimulation as a method for promoting spinal fusion.

Implications

Our study has several implications for the clinical practice of spinal fusion surgery. We evaluated the success rate of spinal fusion in patients who did and did not receive electrical stimulation. In the early stage before surgery, different treatment methods can be chosen according to the different conditions of patients, which has important clinical significance for improving the success rate of fusion after spinal surgery. At present, there is still some controversy about whether spinal surgery should be assisted by electrical stimulation and which kind of electrical stimulation should be used, and improving the spinal fusion rate is still a difficult problem. This study may provide new reference value for clinicians when dealing with these patients, which is helpful for improving the fusion rate after spinal surgery.

Strengths and limitations

The main strengths of our meta-analysis are as follows. First, the relevant articles included in this study were determined to be the most comprehensive in the meta-analysis of this topic. Other articles included original articles without comparison, while the original articles included in this meta-analysis included control groups, which provided the latest evidence that electrical stimulation increases the fusion rate after spinal surgery. Second, our meta-analysis included a wider range of RCTs and cohort studies. Third, subject words and free words were used to comprehensively search the literature in the PubMed, Embase and Cochrane Library databases, and a retrieval strategy with no language or date restriction was used. In this way, more original articles that met the inclusion criteria could be found, thus avoiding the influence of publication bias on the final results.

There are still some limitations in the existing research. First, we included two articles that showed that electrical stimulation did not increase the fusion rate after spinal surgery, which had a certain impact on our results. Second, we found that regarding single-segment fusion and multi-segment fusion, most of the electrical stimulation methods were meaningless and had high heterogeneity, which may be due to the small sample size. In view of these limitations, additional studies including additional subjects are needed in the future. Thirdly, our results were not confirmed to the same degree in the cohort studies as in the RCTs. This discrepancy may be attributed to differences in study design, patient populations, and methods used to assess fusion outcomes. Cohort studies may be more susceptible to selection bias, potentially inflating the perceived effects of electrical stimulation, while RCTs, with their randomized design, provide a more rigorous evaluation but may include factors that diminish the observed effect size. Finally, Conducting a subgroup analysis based on underlying condition (traumatic fracture, pathologic fracture, degenerative disease, or spinal dysraphism as mentioned above) or presence of osteoporosis is indeed important. Unfortunately, in our current dataset, the information required to consistently categorize patients according to these specific underlying conditions or osteoporosis status was not uniformly reported across all studies.

Conclusions

The present meta-analysis of the effect of electrical stimulation on the fusion rate after spinal surgery showed that electrical stimulation, as an adjuvant therapy, can improve the fusion rate after spinal surgery to some extent. However, the effectiveness of electrical stimulation in improving the fusion rate after spinal surgery needs to be further evaluated in large studies.

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Authors' contributions ML and XZ contributed to the study conception and design. Data collection and analysis were performed by XZ, LJ and HW. The first draft of the manuscript was written by ML and XZ, and all authors commented on previous versions of the manuscript. Final version of the article reviewed by ST and ZX.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate Ethical assessment and informed consent were not required since primary data collection was not undertaken.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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