

Spinal Cord Stimulation for Refractory Angina Pectoris

A Systematic Review and Meta-analysis

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Objectives: Paresthesia-free stimulation such as high frequency and burst have been demonstrated as effective therapies for neuropathic pain. The aim of this meta-analysis was to evaluate the efficacy and safety of conventional spinal cord stimulation (SCS) in the treatment of refractory angina pectoris (RAP).

Materials and Methods: Relevant randomized controlled trials that investigated SCS for patients with RAP were comprehensively searched in Medline, Pubmed, Embase, and Cochrane Library. Five meta-analyses were performed examining the changes in Canadian Cardiovascular Society classes, exercise time, Visual Analog Scale (VAS) scores of pain, Seattle Angina Questionnaire, and nitroglycerin use in RAP patients after SCS therapy. We analyzed standardized mean differences (MD) and 95% confidence intervals (CIs) for each outcome by Review Manager 5.0 and STATA 12.0.

Results: A total of 12 randomized controlled trials involving 476 RAP patients were identified. A trend of reduction in the angina frequency (MD = -9.03, 95% CI, -15.70 to -2.36) and nitroglycerin consumption (MD = -0.64, 95% CI, -0.84 to -0.45) could be observed in the SCS group. Compared with the control group, SCS showed benefit on increasing exercise time (MD = 0.49, 95% CI, 0.13-0.85) and treatment satisfaction (MD = 6.87, 95% CI, 2.07-11.66) with decreased VAS scores of pain (MD = -0.50, 95% CI, -0.81 to -0.20) and disease perception (MD = -8.34, 95% CI, -14.45 to -2.23). However, the result did not reach the significance level in terms of physical limitation (95% CI, -8.75 to 3.38; $P = 0.39$) or angina stability (95% CI, -7.55 to 3.67; $P = 0.50$).

Discussion: The current meta-analysis suggested that SCS was a potential alternative in the treatment of PAP patients. Further investigation for finding the appropriate intensity of stimulation is required before this treatment should be widely recommended and applied.

Key Words: spinal cord stimulation, refractory angina pectoris, meta-analysis, randomized controlled trial

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According to the European Society of Cardiology, refractory angina pectoris is a chronic condition characterized by the presence of angina caused by coronary insufficiency in the presence of coronary artery disease that cannot be controlled by a combination of medical therapy, angioplasty, and coronary bypass surgery.¹ There are a considerable number of patients with chronic refractory angina pectoris worldwide. Angina attacks under excessive frequency reduce the life quality of RAP patients, and increase the health and social burdens. To reduce the damage to human health and social resource consumption, numerous therapeutic strategies have been investigated to treat severe chronic angina, and SCS is one of the micro-invasive treatments for RAP.^{2–6}

SCS is a therapy option of stimulating the spinal cord to relieve pain with a low voltage current. Apthorp et al⁷ in 1964 reported that 75% of the patients got significant pain relief after cutting off the sympathetic nervous. Melzack and Wall in 1965⁸ proposed the “pain gate control” theory, which was based on the assumption that impulse was transmitted in the small nociceptive C-fibers of the central nervous system. Decades later, the use of SCS for chronic refractory angina was first described in 1987 according to the theory.⁹ The electric pole connected to the nerve stimulator was inserted into the spinal epidural cavity and then the spinothalamic tract from dorsal horn interneurons was stimulated with a low amplitude current. Consequently, the resulting impulses in the fibers inhibited the conduction of pain signals to the brain and blocked the sensation of pain.

Previous randomized studies^{2–6} have reported the favorable effects of SCS in RAP patients. However, the results were inconsistent, partially due to the relatively limited sample size of the trials. This meta-analysis of all relevant Randomized Controlled Trials (RCTs) was conducted to evaluate the effectiveness and safety of SCS in RAP patients.

MATERIALS AND METHODS

Protocol

The protocol for trial identification, inclusion and data abstraction was specified: the study was carried out in accordance with the Cochrane Handbook of Systematic Reviews and reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.¹⁰ All reviewers were mandated to follow this protocol, and we calculated agreement statistics for the trials included among the reports screened in this systematic review.

Identification of Eligible Studies

A comprehensive electronic search was performed in the databases of Medline, Pubmed, Embase, and Cochrane Library from January 1st, 1930 to June 31st, 2015. To

search and include all potential studies, we applied various combinations of the following key words: spinal cord stimulation, refractory angina pectoris, meta-analysis, randomized controlled trial. No limitation was placed on publication status or language. Two reviewers (X.P. and Y.X.) within the reviewing team independently screened the paper and assessed retrieved articles for eligibility.

Inclusion and Exclusion Criteria

Studies were included for review if they met the following inclusion criteria:

1. Study design is RCT;
2. Patients with RAP must be diagnosed according to the European Society of Cardiology;
3. RAP patients administrated with SCS therapy;
4. Reporting long-term outcome parameters such as exercise time, changes in Canadian Cardiovascular Society (CCS) classes, Visual Analog Scale (VAS) scores of pain, Seattle Angina Questionnaire (SAQ), and nitroglycerin use. The SAQ consists of 5 subgroups: quantifying physical limitation, angina stability, angina frequency, treatment satisfaction, and disease perception.

We excluded the nonhuman studies, letters, case reports, studies including fewer than 10 individuals, and articles not reporting detailed long-term outcomes. In particular, studies were excluded where patients had a myocardial infarction.^{6,11} We also excluded studies that had no relevant event in both the treatment or control groups, for the reason that these trials provided no information on the magnitude of the treatment effects.

Data Extraction

Information from eligible studies was independently extracted by 2 reviewers (X.P. and Y.X.). Discrepancies between the 2 reviewers were resolved by joint discussion with a third reviewer (X.X.) and mutual agreement. Moreover, we contacted corresponding authors if some other information was needed. The following information was abstracted from each study: last name of first author, publication year, number of patients (sample size), interventions of experiment group and control group, and outcomes.

Statistical Analysis

All data in this meta-analysis was calculated and pooled by Review Manager (version 5.0; Cochrane Collaboration, Oxford, UK) and STATA (version 12.0; Stata Corporation, College Station, TX).

A meta-analysis was performed when 2 or more studies measured the same long-term pain outcome parameters. For continuous outcomes, weighted mean difference (MD), and the corresponding 95% confidence intervals (CIs) were applied to evaluate the strength of association between the SCS administration and outcome parameters, whereas for dichotomous outcomes, odds ratio (OR) and 95% CI were used. A Z-test was conducted to assess the statistical significance of the pooled MD and OR. In consequence, a *P*-value < 0.05 was considered statistically significant.¹²

Furthermore, a *Q*-test¹³ was performed to measure significant statistical heterogeneity. For outcome data with evidence of low heterogeneity ($I^2 \leq 30\%$), a fixed-effect model was selected, otherwise, the random-effects model was applied.

To estimate the presence of publication bias, we conducted both Egger's linear regression and Begg's funnel

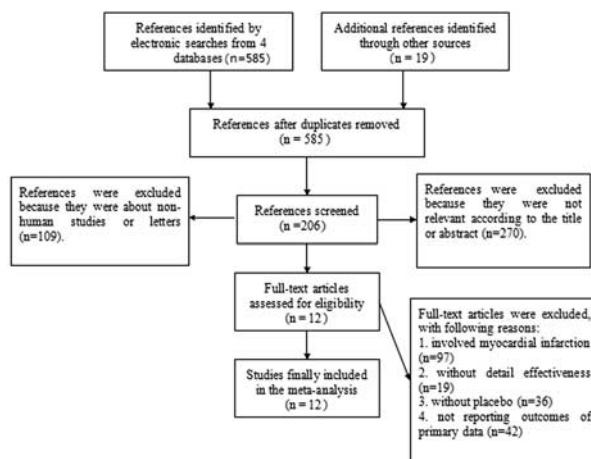


FIGURE 1. Flow diagram. A total of 585 references were retrieved by electronic searches, of which 12 references were finally eligible for inclusion in this review and meta-analysis.

plot, and when the *P*-value < 0.05, it was considered significant.¹⁴

RESULTS

Characteristics of Eligible Studies

A total of 585 references were retrieved by electronic searches using Note Express from 4 databases (Medline,

TABLE 1. Characteristics of Included Trials

References	Group (No. Patients)	Follow-up Time	Outcome Parameters
Bondesson et al ¹¹	SCS (78) Control (43)	6 and 12 mo	Exercise time, changes in CCS
De Jongste et al ¹⁵	SCS (8) Control (9)	12 mo	Exercise time, VAS score, SAQ, nitroglycerin use
Dyer et al ¹⁶	SCS (10) Control (10)	3, 12, and 24 mo	Exercise time, changes in CCS
Eddicks et al ¹⁷	SCS (12) Control (12)	13 mo	Nitroglycerin use, VAS score, SAQ
Greco et al ¹⁸	SCS (23) Control (23)	3 and 24 mo	Exercise time
Hautvast et al ¹⁹	SCS (13) Control (12)	6 wk	Exercise time, nitroglycerin use, VAS score, angina attacks
Jessurun et al ²⁰	SCS (12) Control (12)	2 and 4 wk	Nitroglycerin use, angina attacks
Lanza et al ²¹	SCS (10) Control (15)	3, 6, and 12 mo	Exercise time, VAS score, SAQ, nitroglycerin use
Mannheimer et al ²²	SCS (10) Control (10)	6 mo	Exercise time, time to angina
McNab et al ²³	SCS (34) Control (34)	12 mo	Exercise time, changes in CCS, SAQ
Vulink et al ²⁴	SCS (20) Control (20)	3 and 12 mo	VAS score, nitroglycerin use
Zipes et al ²⁵	SCS (23) Control (23)	6 mo	Exercise time, VAS score, SAQ, nitroglycerin use

CCS indicates Canadian Cardiovascular Society; SAQ, The Seattle Angina Questionnaire; SCS, spinal cord stimulation; VAS score, Visual Analog Scale scores of pain.

TABLE 2. Main Outcomes

Outcomes	No. Patients	No. RCTs	Estimated Benefit (95% CI)	P	I ² test (%)
Exercise time after intervention	286	8	MD = 0.49 (0.13, 0.85)	0.008	36
Changes in CCS classes	229	3	OR = 2.12 (1.19, 3.76)	0.01	0
VAS score	177	6	MD = -0.50 (-0.81, -0.20)	0.001	11
Physical limitation	171	4	MD = -2.69 (-8.75, 3.38)	0.39	0
Angina stability	173	4	MD = -1.94 (-7.55, 3.67)	0.50	41
Angina frequency	174	4	MD = -9.03 (-15.70, -2.36)	0.008	11
Treatment satisfaction	174	4	MD = 6.87 (2.07, 11.66)	0.005	0
Disease perception	174	4	MD = -8.34 (-14.45, -2.23)	0.007	21
Nitroglycerin use	204	7	MD = -0.64 (-0.84, -0.45)	< 0.00001	17

Pain intensity was scored with VAS score.

CI indicates confidence interval; MD, mean difference; OR, odds ratio; VAS, visual analog scale scores of pain.

Pubmed, Embase, and Cochrane Library), of which 12 references were finally eligible for inclusion in the meta-analysis. In total, 573 references were excluded, including 97 studies involved myocardial infarction, 19 references without detail effectiveness, 36 references without placebo, 42 references no reporting outcomes of primary data, 109 references about nonhuman studies or letters, and 270 references which were not relevant according to the title or abstract (Fig. 1).

The basic characteristics of the included RCTs were summarized in Table 1. A total of 476 patients were included in the trials, and the follow-up interval ranged from 2 weeks to 24 months among the 12 RCTs.

Clinical Outcomes

The main outcomes of the included trials are reported in Table 2.

Exercise Time after Intervention

In total, 8 RCTs^{15-19,21,23,25} which reported exercise time (presented as mean ± SD) between baseline and postintervention as primary outcomes were pooled in the meta-analysis (Fig. 2). Two of them were pooled in the subgroup of paresthetic SCS (group PS) versus subliminal SCS (group SS) or “sham” SCS (group NS).^{17,21} In the meta-analysis, it turned out that there were no significant differences between SCS and sham SCS (Fig. 2) trials with 48 patients, exercise time: 0.24, 95% CI, -1.05 to 1.53, I² = 0%). De Jongste et al¹⁵ studied exercise time after SCS intervention in a double-blind placebo controlled trial of 286 patients. In total, 140 patients were allocated to the SCS group and 146 patients were allocated to the control group. Stimulation with so-called conventional stimulation parameters elicits by definition a prickling sensation in the area in which the patient typically experiences angina pectoris. Functional status evaluated by the exercise time was assessed at the end of each 4-week treatment period.

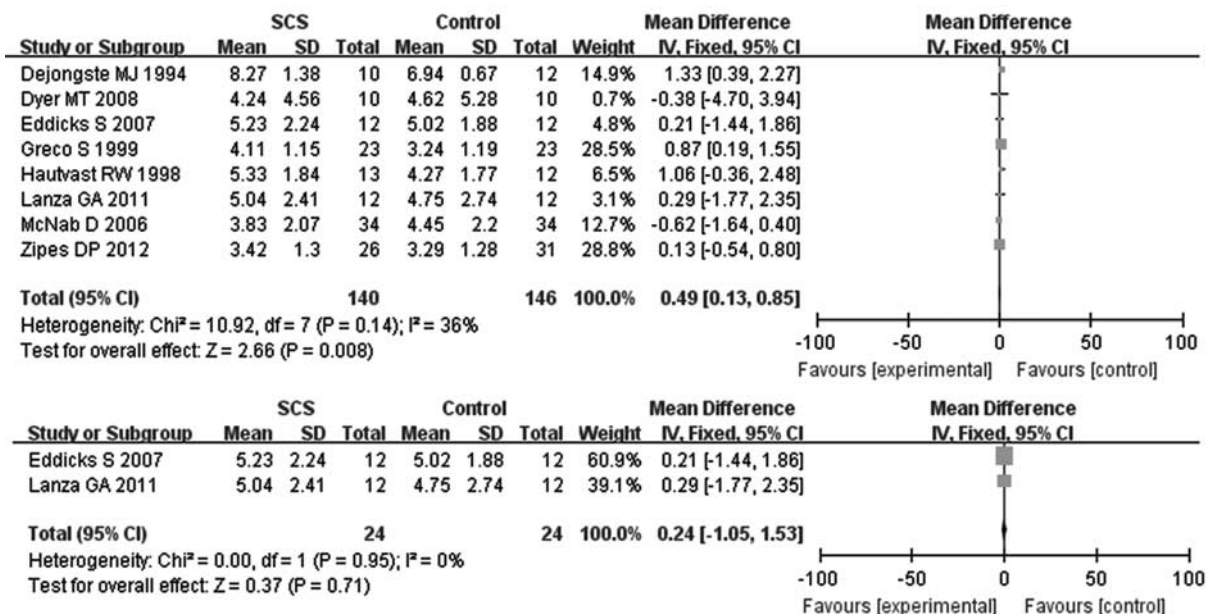


FIGURE 2. Forest plots of exercise time after intervention. Eight trials described exercise time after intervention, and the mean difference was 0.49 (95% CI, 0.13-0.85, P=0.008, I²=36%) compared with the control group. Two trials with 48 patients reported no significant differences in exercise time between spinal cord stimulation (SCS) and sham SCS (0.24, 95% CI, -1.05 to 1.53, P=0.71, I²=0%). CI indicates confidence interval.

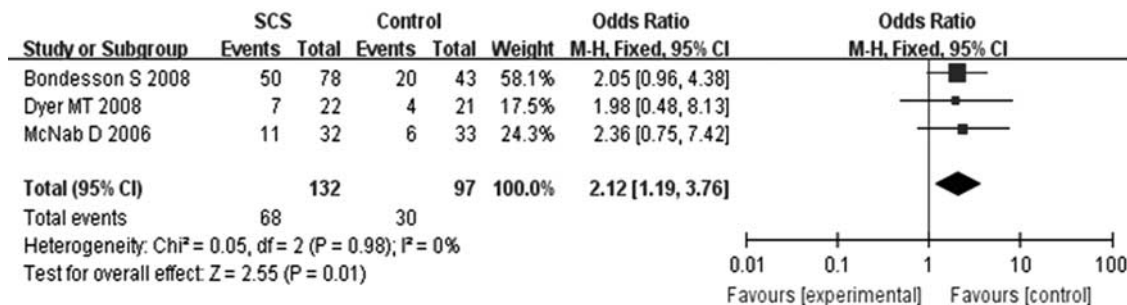


FIGURE 3. Forest plots of changes in Canadian Cardiovascular Society classes. Three trials were observed in this meta-analysis, the logarithm of odds ratio (OR) was 2.12 (95% confidence interval [CI], 1.19-3.76, $P=0.01$, $I^2=0\%$). SCS indicates spinal cord stimulation.

The result was significantly different between the 2 groups during the follow-up visits. The exercise time to onset of angina increased significantly in the SCS group compared with the control group (Fig. 2: 8 trials with 286 patients, mean exercise time: 0.49, 95% CI, 0.13-0.85, $I^2=36\%$).

Changes in CCS Classes

In this analysis, we have excluded the patients who were not available for follow-up at 3 and 12 months. Finally, changes in CCS classes were observed in 3 trials^{11,16,23} across all 12 including studies, and the logarithm of OR was used as effect size to assess differences in the proportion of patients having a decrease of 2 or more CCS classes (considered clinically significant). Efficacy comparison between SCS and control was OR 2.12 (1.19 to 3.76) with no heterogeneity (Fig. 3), which demonstrated that patients treated with SCS therapy had a clinically significant decrease of 2 or more CCS classes.

VAS Score

Refractory angina pain was measured by VAS score, which was described in a pooled meta-analysis of 6 RCT studies including a total of 177 participants.^{15,17,19,21,24,25} Eighty-six RAP patients were allocated to the treatment group, whereas 91 RAP patients were allocated to the control group, and all patients included in the study were followed up for at least 1 month. From following forest plots (Fig. 4), data reporting VAS score at postoperative 1 month was significantly different between the 2 groups. In the SCS group, the score obtained from the VAS was

significantly lower than the control group (MD = -0.50, 95% CI, -0.81 to -0.20, $P=0.001$, $I^2=11\%$). No adverse effects of SCS intervention were reported, however, 1 patient withdrew from the study after 2 weeks for unknown reason.

SAQ

It is well-known that the SAQ consists of 5 following segments: physical limitation, angina stability, angina frequency, treatment satisfaction, and disease perception. Results from the SAQ were significantly different with respect to the 3 parameters of the SAQ: angina frequency, treatment satisfaction, and disease perception. Figure 5 described the main outcomes of the included 4 trials in detail. On one hand, a decrease in angina frequency was reported in the SCS group (MD = -9.03, 95% CI, -15.70 to -2.36, $P=0.008$, $I^2=11\%$) compared with patients in the control group (Fig. 5). In contrast, patients treated with SCS required less disease perception (MD = -8.34, 95% CI, -14.45 to -2.23, $P=0.007$, $I^2=21\%$) and more treatment satisfaction: (MD = 6.87, 95% CI, 2.07-11.66, $P=0.005$, $I^2=0\%$). However, it was worth mentioning that no significant difference was detected in the occurrence of physical limitation or angina stability. Hence, the data of physical limitation or angina stability was not available for the meta-analysis.

Nitroglycerin use

Data reporting nitroglycerin use was described in 7 trials (n = 204).^{15,17,19-21,24,25} The efficacy of SCS for

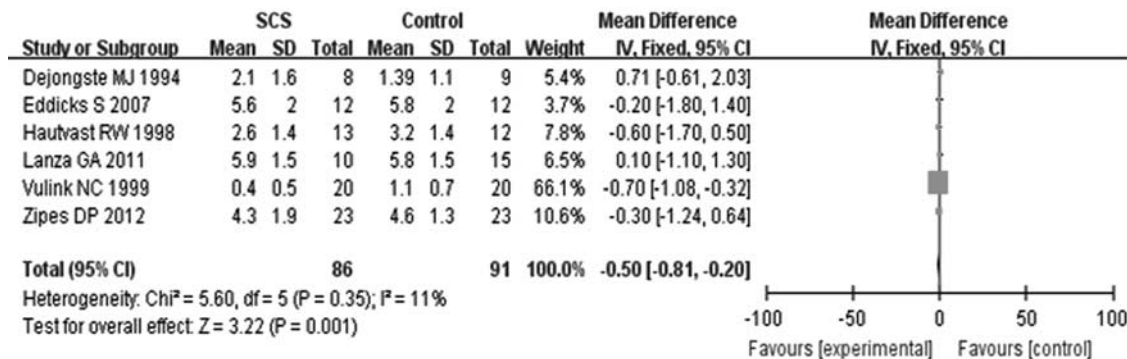


FIGURE 4. Forest plots of the Visual Analog Scale (VAS) score. Six randomized control trial studies including a total of 177 participants described VAS score during postoperative 3 months. (MD = -0.50, 95% CI, -0.81 to -0.20, $P=0.001$, $I^2=11\%$). SCS indicates spinal cord stimulation.

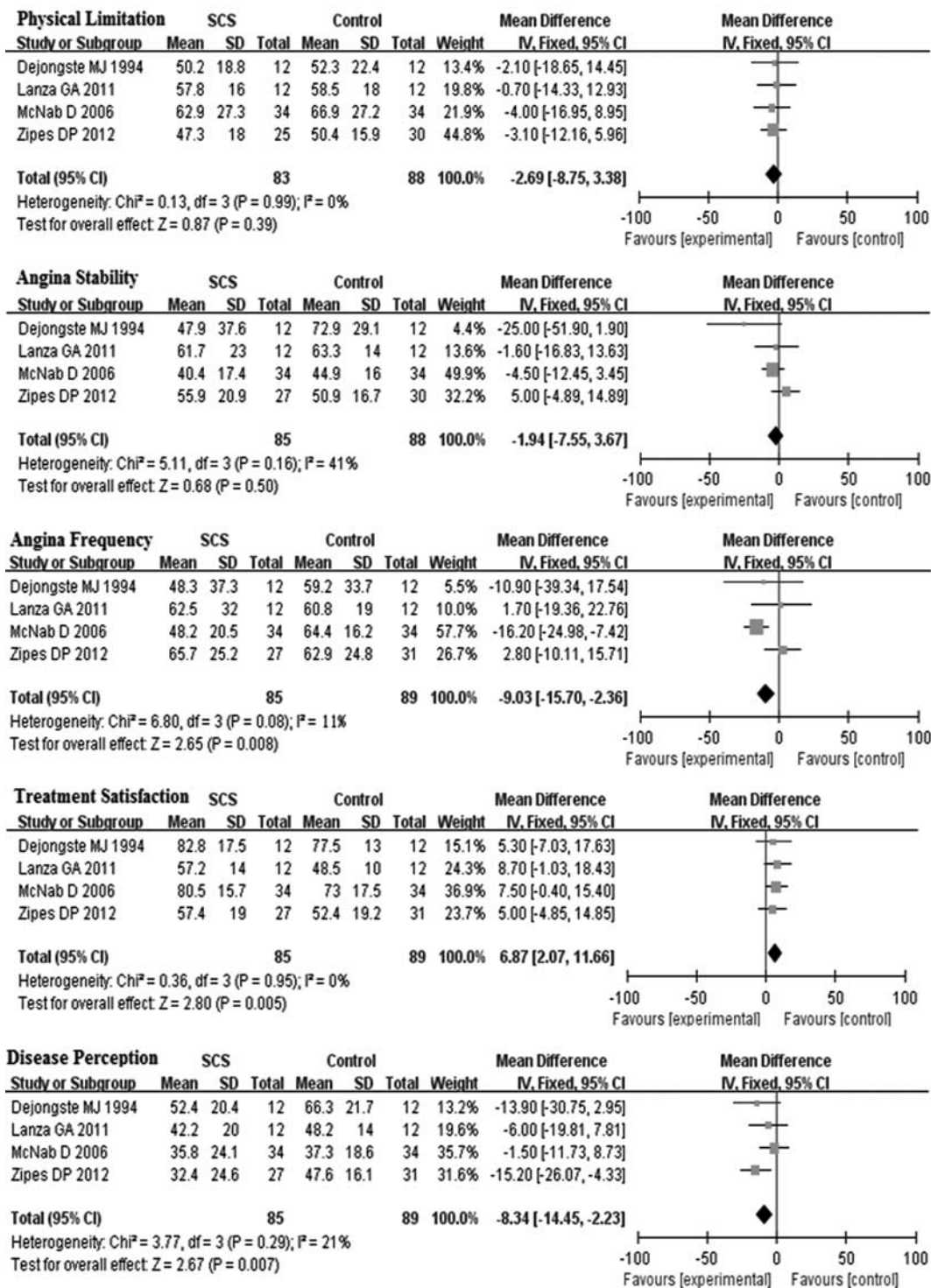


FIGURE 5. Forest plots of the Seattle Angina Questionnaire (SAQ). No significant difference was detected in the occurrence of physical limitation or angina stability. Patients in spinal cord stimulation (SCS) groups showed significant improvements in three parameters of the SAQ (angina frequency, treatment satisfaction, and disease perception) in comparison with control groups (for angina frequency: -9.03 , 95% confidence interval [CI], -15.70 to -2.36 , $I^2 = 11%$, for treatment satisfaction: 6.87 , 95% CI, 2.07 - 11.66 , $I^2 = 0%$, and for disease perception: -8.34 , 95% CI, -14.45 to -2.23 , $I^2 = 21%$).

improving angina status of patients was confirmed by the decreased number of nitroglycerin tablet consumption per day. As derived from the data of the 7 studies, glyceryl

trinitrate consumption was significantly reduced in patients after undergoing SCS for 3 months (MD = -0.64 , 95% CI, -0.84 to -0.45 , $P < 0.00001$, $I^2 = 17%$) compared

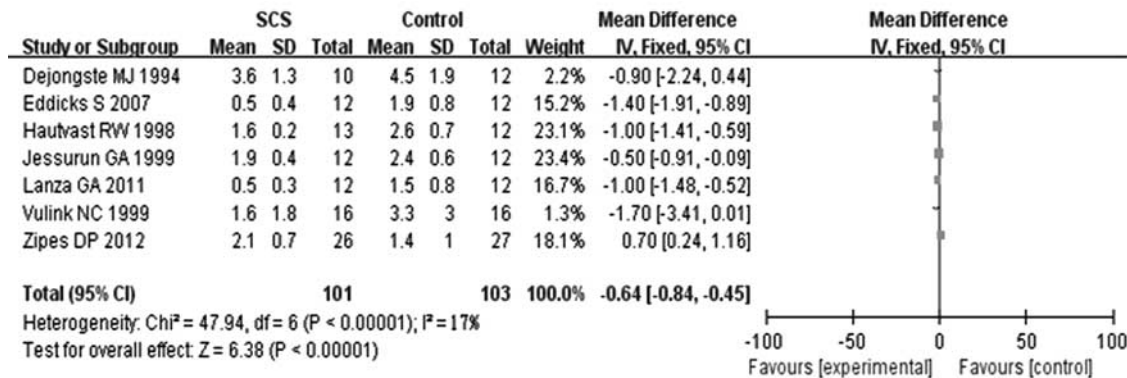


FIGURE 6. Forest plots of nitroglycerin use. Seven trials (n = 204) reported data of nitroglycerin use. Glyceryl trinitrate consumption was significantly reduced in patients after undergoing spinal cord stimulation (SCS) for 3 months (MD = -0.64, 95% confidence interval [CI], -0.84 to -0.45, P < 0.00001, I² = 17%) compared with patients in control group.

with patients in control group. Patients in the control group consumed more nitroglycerin to get angina relief after a month of follow-up, whereas the patients treated with SCS required less nitroglycerin consumption (Fig. 6).

Risk of Bias

Table 3 showed the risk bias in all relevant 12 studies. All studies described random sequence generation, and adequate allocation concealment was absent in only 1 study.¹⁵ Low risk of bias about blinding of outcome assessment existed in most studies except 1 trial.²³ In addition, 9 studies (99 to 103, 104 to 106, 108 to 109) (82%) showed a low risk of incomplete outcome data, and the risk of selective reporting results remained unclear in 3 studies.^{15,19,22}

DISCUSSION

Previous studies have focused on the use of SCS for RAP patients.²⁶⁻²⁹ For example, variable evidence was proposed to support RAP intervention that was then incorporated into a clinical practice guideline for refractory angina management by Taylor et al²⁷ in 2009. Since that analysis, some new literature has been published on this topic. In a series of experimental studies, Simpson et al²⁸ have demonstrated an attenuating effect of electrical

stimulation for chronic pain of neuropathic or ischemic origin. Tsigaridas et al²⁹ have thus stated that a larger, well-designed, multicenter RCT was needed before SCS could be recommended as a routine therapy for refractory angina. There was a need to identify multiple studies and update the review.

In this systematic review and meta-analysis, we successfully evaluated the long-term efficacy and the safety of SCS in patients with refractory angina pectoris. The current systematic review and meta-analysis demonstrated that spinal cord stimulation, applied in RAP, was effective and safe as being reflected in increased exercise time, a decrease of nitroglycerin consumption, significant improvements in the quality of life, and a decrease of disease perception. Meanwhile, the pooled evidence summarized in this meta-analysis has shown that SCS could downgrade the classes of CCS with lower pain scores. Unfortunately, the results did not reach the significance level in terms of physical limitation or angina stability. Furthermore, the clinical safety was explored, and the results confirmed that SCS device could decrease the frequency of angina and disease perception.

The interest in spinal cord stimulation for pain relief was rapidly increasing since it was minimally invasive, safe,

TABLE 3. Risk of Bias

References	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Bondesson et al ¹¹	+	+	+	+	+	+	+
De Jongste et al ¹⁵	+	-	?	+	+	?	+
Dyer et al ¹⁶	+	+	+	+	+	+	+
Eddicks et al ¹⁷	+	+	+	+	+	+	+
Greco et al ¹⁸	+	+	+	+	+	+	+
Hautvast et al ¹⁹	+	+	?	+	+	?	+
Jessurun et al ²⁰	+	+	+	+	+	+	+
Lanza et al ²¹	+	+	?	+	+	+	+
Mannheimer et al ²²	+	+	+	+	+	?	+
McNab et al ²³	+	+	+	?	+	+	+
Vulink et al ²⁴	+	+	+	+	+	+	+
Zipes et al ²⁵	+	+	+	+	+	+	+

+ , low risk; ?, unclear risk; -, high risk.

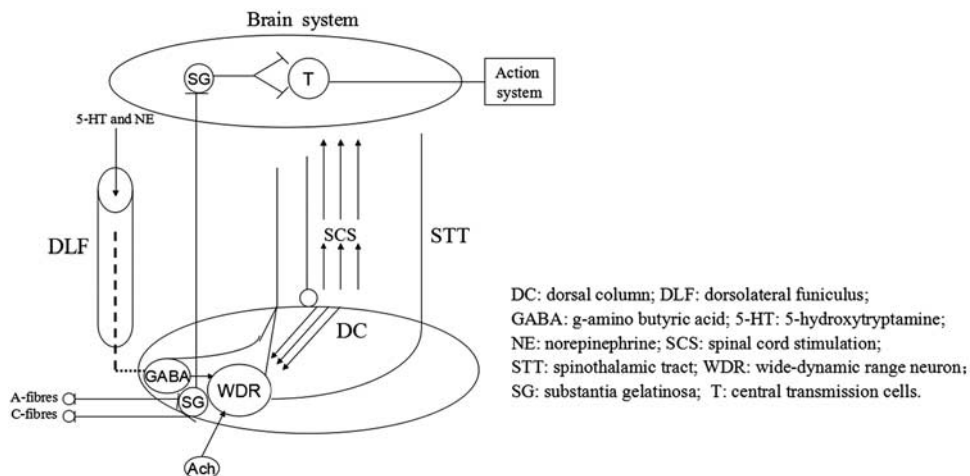


FIGURE 7. A tentative scheme of some essential features of the mode of action of SCS when applied for neuropathic pain.

and reversible with limited side effects. SCS has been shown to decrease sympathetic tone and augment myocardial blood flow to protect the myocardial cells in a large series of experiences in both animals and humans.^{3,30,31} Different hypotheses have been reported in many studies so far. However, there is not yet an ultimate scientific explanation, and a clear understanding of the mechanisms elicited by SCS is still lacking. From a review of the literature, more than a single mechanism seems to be responsible for pain relief with SCS.^{3,32} Previous experimental and clinical data support the idea that the autonomic nervous system might be the major mechanism elicited by SCS, and most experimental studies on SCS have focused on spinal mechanisms involving a segmental gate control, which was antidromically activated by low-threshold afferents in the dorsal

column (DC).³³ Other early studies reported inhibitory effects on dorsal horn neurons through a DC-brain stem-spinal loop.^{34,35} Further evidence for the involvement of supraspinal centers has been provided by a study comparing the inhibitory effects of stimulation of DC nuclei and the raphe magnus nucleus.³⁶

However, Saadé and Linderöth³⁷ in 2015 reported that SCS-induced changes in pain relief were completely attenuated by the dorsolateral funiculi (DLF), suggesting that the mechanisms underlying the effects of SCS involve central influences rather than sympathetic outflow. Activation of the DCs is relayed to supraspinal centers, probably through the descending fibers in the DLF, which is involved in pain modulation and play a significant role in the attenuation of pain-related signs by SCS.³⁷ In particular, the antidromic impulses generated in the DCs activate inhibitory interneurons with an enhanced release of γ aminobutyric acid,³³ which can reduce the activation of the hyperexcitable second-order neurons. As a result, myocardial blood flow was improved at the microvascular level. Meanwhile, another major impulse path is orthodromic to the brain, activating circuitry in the brain stem ultimately giving rise to descending impulses through the DLF amplifying the inhibitory processes at the spinal level.^{37,38} The results provide further support to the notion of important involvement of brain stem pain modulating centers in the effects of SCS. A major component of the inhibitory spinal-supraspinal-spinal loop is mediated by fibers running in the DLF^{37,39} (see Fig. 7 for further details). In conclusion, new perspectives (such as DLF) seem promising as advanced research highlights in the mechanisms involved in SCS effects on RAP patients.

Moreover, it was important to emphasize that some limitations in our meta-analysis should be acknowledged in interpreting the results. First of all, we did not comprehensively evaluate other clinical outcomes, such as the overall cost utility and the average length of stay, which was unable to satisfy the maximum various comprehensive assessment standards. Secondly, the sample size of 4 RCTs^{15-17,22} included in this study was relatively small, which could lighten the significance of statistical

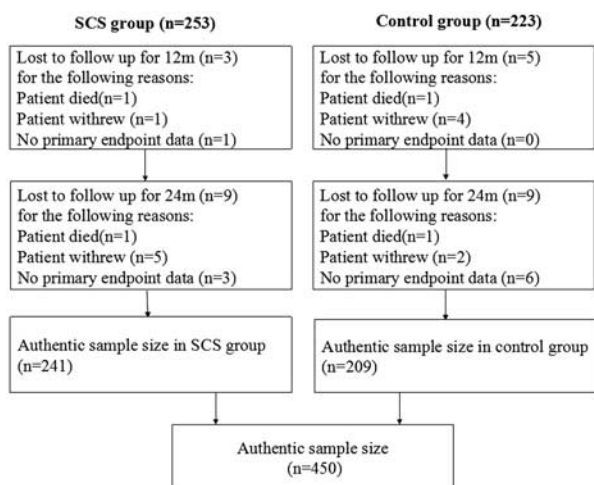


FIGURE 8. Flow diagram of follow-up. Two hundred fifty-three patients were allocated in the spinal cord stimulation (SCS) group, whereas 223 patients in the control group. After the exclusion of 26 patients who were lost to follow-up, complete data were obtained in 450 patients.

difference.³ The lack of statistical significance in physical limitation and angina stability in this study suggested that a possible role for SCS in individual patients deserved to be assessed in larger trials with appropriate statistical power. Thirdly, there was a significant heterogeneity as a result of variable follow-up intervals (ranged from 4 wk to 24 mo) in this review. Clinically, the assessment of efficacy after 4 weeks of treatment or after 12 months might lead to wide differences in treatment outcome. In particular, during the 12-month follow-up period, of the patients allocated to SCS, 1 died, 1 withdrew from the trial, and 1 was unable to do the 12-month exercise test, leaving 24 with exercise test data. Of the patients in control group, 4 died during follow-up, 4 withdrew from the trial, and 8 could not perform an exercise test at 12 months (5 of whom provided quality of life data), leaving 26 patients with exercise test data at 24 months (see Fig. 8 for further details). As a consequence, the ability to provide valid estimates of treatment effect in this systematic review is limited, and more sample sizes are required in future investigations.

SCS has been a recommended treatment for patients with RAP, and several SCS paradigms have been launched, such as bursts of high-frequency pulses (500 Hz) delivered with a lower frequency (40 Hz) and higher frequencies (> 500 Hz; most often 10 kHz). These forms of SCS provide sustained analgesia in a previously difficult patient cohort without paresthesia and have the prime purposes to enable stimulation subthreshold to paresthesia.⁴⁰ Apart from SCS, regional therapeutic approaches, as well as interventions at the level of the peripheral nervous system and particularly the dorsal root ganglion (DRG) are probable new venues for the treatment of RAP patients.^{41,42} Many studies have demonstrated that voltage-gated sodium channels,⁴² which are essential for the generation of action potentials, are potential targets for treating neuropathic pain. Furthermore, the targeted expression of foreign genes to the peripheral nerve system has been applied in the gene therapy of neuropathic pain. Yu et al⁴³ showed the potential of vectors as a viable system for delivering target genes into DRGs to explore basic mechanisms of neuropathic pain, with the potential for future clinical use in the treatment of chronic pain. These findings provide further support for the idea that DRG play a significant and increasing role in the development of new therapies in angina.

CONCLUSIONS

In summary, SCS significantly relieves the symptoms of angina pectoris without increasing the nitroglycerin consumption to some extent. Future larger outcome studies for finding the appropriate intensity of stimulation are worthy of further investigation.

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