

Spinal cord stimulation: indications and outcomes

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✓ Spinal cord stimulation (SCS) is the most commonly used implantable neurostimulation modality for management of pain syndromes. In this paper the authors describe the current indications for SCS and its efficacy in the treatment of those diseases. Specifically, the literature on patient selection and outcomes after SCS for failed-back surgery syndrome (FBSS), refractory angina pectoris, peripheral vascular disease, and complex regional pain syndrome (CRPS) Type I was reviewed. Effective pain relief was obtained in 60 to 80% of patients with FBSS and CRPS Type I. Furthermore, these patients had significant improvements in quality of life (QOL) and a significantly greater chance of returning to work than patients who did not undergo SCS. The use of SCS in patients with inoperable angina (that is, refractory angina pectoris) resulted in significant decreases in chest pain and hospital admissions as well as increased exercise duration, with less morbidity than with open procedures that were performed for pain control only. Patients with inoperable PVD also demonstrated significant improvements in pain relief, QOL, and limb mobility. Reported complications were mostly related to hardware and were relatively minor. Review of randomized controlled studies supports the use of SCS as an effective treatment modality for pain associated with FBSS, refractory angina pectoris, peripheral vascular disease, and CRPS Type I.

KEY WORDS • pain • failed-back surgery syndrome • complex regional pain syndrome
• angina pectoris • spinal cord stimulation • neuromodulation

SPINAL cord stimulation is a pain treatment modality predicated on reducing the intensity, duration, and frequency with which pain is felt. Although it was developed on the basis of the gate control theory of pain proposed by Melzack and Wall,³⁷ its mechanism of action involves more than inhibition of pain pathways in the dorsal horn nucleus.³⁹ Experimental studies involving neurotransmitters (for example, γ -aminobutyric acid and adenosine^{34,40}) have been used to explain other pathways by which SCS works. Furthermore, modulation of the autonomic nervous system may explain the efficacy of SCS for pain syndromes such as refractory angina pectoris and CRPS.^{2,7,13,20} Although its exact mechanisms of action are not fully understood, SCS has been shown to be beneficial in the treatment of several pain syndromes, with fairly consistent results.^{9,28,32,46} A number of randomized controlled trials and numerous case series with long-term follow-up reports on SCS have been performed.^{9,12,21,24,25,27,28,31,42–44,59,60} In this paper we discuss general patient selection criteria for SCS and summarize indications and outcomes that have been reported for SCS in the treatment of FBSS, refractory angina pectoris, peripheral vascular disease causing critical leg ischemia, and CRPS Type I.

Abbreviations used in this paper: CRPS = complex regional pain syndrome; FBSS = failed-back surgery syndrome; QOL = quality of life; SCS = spinal cord stimulation; VAS = Visual Analog Scale.

Protocol for SCS

Patient Selection

In a recently published case series of 410 patients treated over a 22-year period (mean follow-up duration 97.6 months), investigators described the selection criteria they used when considering a patient for SCS.²⁸ These included the following: 1) pain not associated with malignancy; 2) poor response to conservative treatment for at least 6 months; 3) remedial surgery inadvisable; 4) no major psychiatric disorder, including somatization complaints; 5) willingness to stop inappropriate drug use before implantation; 6) no secondary gain or litigation involved; and 7) ability to give informed consent for the procedure.

Psychological Testing

Once they are deemed suitable candidates, patients at most centers undergo psychological testing to evaluate and treat their comorbid psychiatric conditions and to assess their overall mechanisms and support systems for dealing with their pain. The prognostic value of this testing has not been well defined, and further studies are warranted. One study revealed that the predictive value of psychological testing correlated significantly with short-term follow-up findings only.⁴⁵ Kumar et al.²⁸ described functional evaluation in which the Oswestry Disability Index, the McGill Pain Questionnaire (short form), the Roland Morris Questionnaire, and the Beck Depression Inventory were used.

Trial Period of Stimulation

After they are selected for SCS, patients then undergo a trial period of stimulation for 4 to 7 days to assess their response to the treatment. During this trial phase, pain relief can be evaluated using a modified VAS. Patients are often asked to record their VAS in a diary multiple times daily.^{10,20,28} Only individuals who achieve 50% or greater pain relief are candidates for internalization of the SCS devices. Even with their strict criteria, Kumar et al. found a 20% failure rate after trial stimulation. In this series, the long-term success rate with SCS was 74.1% at a mean of 97 months of follow up, comparable with other series in the literature.

Follow-Up Evaluations

Generally, postoperative clinical evaluations are performed at 6-month intervals for the first 3 years, and annually thereafter. Monitoring of a patient's pain should be assessed using a standardized method. Most commonly, VAS findings and a patient's medication use are monitored. Although postoperative evaluation of pain relief varies from center to center, generally responses are categorized as follows: excellent (> 75% pain relief), good (\geq 50% pain relief), and poor (< 50% pain relief).²⁸

Indications for SCS

Failed-Back Surgery Syndrome

The definition of FBSS is as follows: persistent or recurrent pain, mainly involving the lower back and/or legs, even after previous anatomically successful spinal surgery.³³ Because FBSS is considered a diagnosis of exclusion, neuroimaging examinations must demonstrate that there are no surgically correctable lesions present. Kumar et al.²⁸ used either computed tomography or magnetic resonance imaging studies to confirm the absence of surgical lesions and the possible presence of epidural or perineural fibrosis, or of arachnoiditis, conditions that generally do not respond to surgery, but that may respond to SCS.

A number of controlled studies and case series, some with as much as 10 years of follow up, have been performed to assess the efficacy of SCS in reducing the pain associated with FBSS.^{3,8,31,64} The clinical factors that were found to be reliable indicators for a good response to SCS in FBSS were as follows: 1) early treatment (0–3 years) after first failed back surgery; 2) predominance of neuropathic leg pain; and 3) absence of psychological conditions, such as depression.^{28,63}

A recent review of the literature revealed one randomized controlled study, one cohort study, and 72 case series on treatment of FBSS.⁶⁰ In the randomized controlled study, researchers compared SCS to repeated operation in patients with FBSS.⁴⁴ Fifty patients enrolled and their outcomes were followed for a mean of 3 years. Significantly more patients receiving SCS (47%) achieved 50% or more pain relief compared with those who underwent repeated operation (12%; $p < 0.01$). Patients treated with SCS required substantially fewer opioid analgesic drugs than the patients who underwent repeated operation ($p = 0.025$). Twenty-one percent of patients treated with SCS opted for crossover to repeated operation, whereas 54% of

patients who underwent repeated operation opted for crossover to SCS ($p = 0.02$). See Table 1 for a summary of randomized controlled trials of SCS.

A metaanalysis of the 72 case studies of patients in whom SCS was used to treat refractory neuropathic back and leg pain or FBSS showed that 62% of patients with SCS achieved 50% or more pain relief and that 53% of patients no longer required analgesic drugs.⁵⁹ Specifically, one study showed that after 12 months of treatment with SCS, the majority of patients reported fair to excellent pain relief in both the low back (68.8% of patients) and legs (88.2%).⁸ Significant improvement was noted in QOL and functional capacity.^{3,4,29,64} A 10-year follow-up study showed a significant increase in the level of independence.⁶⁴ Up to 70% of patients who underwent SCS were satisfied with their treatment,⁶⁰ and 75% of patients said they would have the procedure again if they had known their outcome before implantation.⁴⁹ It has been reported in follow-up studies that 30 to 40% of patients returned to work.^{60,64} Overall, there was a significant increase in the proportion of patients working after SCS than before receiving this treatment.⁶³

Refractory Angina Pectoris

Refractory angina pectoris is defined as “a chronic condition characterized by the presence of angina, caused by coronary insufficiency in the presence of coronary artery disease, which cannot be adequately controlled by a combination of medical therapy, angioplasty, and coronary artery surgery.”³⁵ Spinal cord stimulation is one of the most promising treatment options for this disease, and has been shown to modulate the function of the sympathetic nervous system and the increase of norepinephrine release seen in refractory angina pectoris.⁴¹ Its efficacy and cost-effectiveness has proven comparable to both medical and interventional approaches for treating coronary ischemia.^{7,12,38} Reluctance to use this option on the part of clinicians is likely due to treatment paradigms emphasizing revascularization.⁷

Prospective randomized controlled studies of SCS showed benefits both in QOL and cardiac indices.^{12,21,22} Specifically, exercise duration and time to angina significantly increased in the SCS group compared with the controls.²¹ Nitrate consumption, ischemic episodes at rest and with exercise, and pain significantly decreased.²¹ In another prospective study of 104 patients, it was demonstrated that a significant improvement of angina symptoms occurred in 73% of patients. The Canadian Cardiovascular Society angina category improved by one or more classes in 80% and by two or more classes in 42% of patients. Furthermore, the rate of hospital admissions and days spent in the hospital because of angina were significantly reduced ($p < 0.0001$ for both).¹⁴

A retrospective study of 24 patients with angina who underwent SCS confirmed these results. The patients in this study showed a significant decrease in frequency of angina episodes, from a median of 14 to 2.3 attacks per week, and nitroglycerin intake, from a median of 27.5 to 1.5 doses per week.⁶⁵ Also of note, these patients' Canadian Cardiovascular Society angina class improved from a median of Class 3 to Class 2 ($p < 0.001$). Whereas these patients had an increasing rate of hospitalization

TABLE 1
Literature review of randomized controlled trials of SCS*

Authors & Year	Diagnosis	Cohort	Findings in SCS vs Control Group	Mean FU
North et al., 2005	FBSS	SCS vs back reop	less pain (p < 0.01), reduced opioid use (p = 0.025), less cross-over to alternative treatment (p = 0.02)	3 yrs
Kemler et al., 2000	CRPS I	SCS + PT vs PT alone	less pain (p < 0.001), improved QOL (p = 0.02)†	2 yrs
McNab et al., 2006	RAP	SCS vs myocardial laser revascularization	no difference in exercise capacity (p = 0.989), angina class (p = 0.263), or QOL	1 yr
de Jongste et al., 1994	RAP	SCS vs medical therapy	reduction in ischemia on ECG (p < 0.05), in pain relief (p < 0.01), & in nitrate use (p < 0.01); increase in exercise capacity (p < 0.03), QOL (p < 0.005)	1–2 mos
Hautvast et al., 1998				
Jessurun et al., 1999				
Suy et al., 1994	CLI	SCS vs medical therapy	improvement in clinical stage (p < 0.05)	1 yr
Jivegård et al., 1995	CLI	SCS vs medical therapy	reduced tissue loss (p < 0.05); no difference in limb survival	18 mos
Clayes & Horsch 1996	CLI	SCS + prostaglandins vs prostaglandins alone	significant improvement in clinical stage (p = 0.0014) & ulcer healing (p < 0.0001); no difference in limb survival	1 yr
Klomp et al., 1999	CLI	SCS vs medical therapy	improvement in clinical stage/mobility (p = 0.0014), less pain/opioid use (p < 0.001); no difference in limb survival (p = 0.47)	2 yrs
Spinemaille et al., 2000				

* CLI = critical limb ischemia; ECG = electrocardiography; FU = follow up; NS = not significant; PT = physical therapy; RAP = refractory angina pectoris.

† The reduction in pain was no longer significant at the 5-year follow-up evaluation.

before SCS, at 1 year of follow up the duration of hospitalization decreased to a median of 0 days/patient/year (p < 0.001).⁶³ Compared with patients undergoing coronary artery bypass grafts performed for improvement of symptoms rather than survival, the mortality and the cerebrovascular morbidity rates were significantly higher in the group that received grafts, but there was no difference in the cardiac morbidity or in the long-term survival.^{16,60}

Peripheral Vascular Disease

Peripheral vascular disease can lead to critical limb ischemia. This term refers to a condition manifested by ischemic pain at rest, ulcers, or gangrene in one or both legs due to a proven arterial occlusive disease.⁴⁷ Spinal cord stimulation is indicated when critical limb ischemia becomes inoperable.⁴⁰ Several parameters can be used to predict the percentage of limb salvage. The best parameters are a baseline transcutaneous PO₂ of 10 to 30 mm Hg obtained with the patient’s leg supine and a transcutaneous PO₂ greater than 15 mm Hg when the leg is in the dependent position.¹⁹ One negative predictor that needs to be evaluated is the presence of severe diabetic neuropathy. One study of 60 patients with critical limb ischemia included 28 individuals with severe diabetic neuropathy.⁴⁹ Only three of these 28 patients attained any benefit with SCS. Spinal cord stimulation has shown a significant effect in alleviating pain,⁵⁸ but several controlled trials have shown limited benefits on limb survival.^{1,11,23,27,54,58}

Recently, a Cochrane systematic review of the aforementioned studies was performed, in which it was suggested that these limited benefits may have been secondary to relatively small sample sizes.⁶¹ To be included in the Cochrane review, patients had to have inoperable critical limb ischemia with ischemic pain at rest or ulcers smaller than 3 cm in diameter, and to have received control treatment, which consisted of optimum conservative therapy, including local wound care and analgesic, anticoagulant, or antibiotic medications as necessary. Metaanalysis of the limb salvage data showed a significant treatment effect in favor of SCS after 12 months. The group extrapolated that nine patients need to be treated to pre-

vent one more major amputation.⁵² Specific findings of the studies are discussed.

In one prospective study of 120 patients with critical limb ischemia, outcomes were compared in 60 patients who underwent medical treatment alone and 60 with medical treatment and SCS. The investigators found that the number of patients undergoing major amputations in the SCS group with intermediate transcutaneous PO₂ values was half of that in the standard group (14 compared with 28 patients; 24% compared with 48%; p = 0.17).⁵⁴ They also showed significantly improved energy and mobility and the use of significantly fewer analgesic drugs in patients treated with SCS.⁵³ Two multicenter prospective controlled studies of patients with critical limb ischemia showed a significant improvement in pain relief (p < 0.005).^{1,23} The transcutaneous PO₂ value (p < 0.001) also improved in patients who received SCS compared with control patients.¹ Tissue loss was less (p = 0.05) in the SCS group.²³ The number of patients whose clinical stage improved from critical leg ischemia to intermittent claudication was significantly higher in the group treated with SCS than in the group treated conservatively (p = 0.0014).²⁷

There have also been some retrospective case series of patients with critical limb ischemia associated with Buerger disease and end-stage renal disease, in which investigators have suggested that SCS may also be useful in these patient subsets. The retrospective study of 29 patients with Buerger disease who underwent SCS showed an improved regional perfusion index, lack of progression of trophic lesions, and a limb survival rate of 93%.¹⁵ In eight patients with peripheral vascular disease who were undergoing hemodialysis, SCS treatment led to a decrease in pain medication intake in all patients, there were no new skin lesions, and the limb survival rate at 1 year was 75%.⁶

Complex Regional Pain Syndrome

The CRPSs can be divided into Types I and II.^{55,56} In CRPS Type I, formerly called reflex sympathetic dystrophy, no known nerve injury is present. In CRPS Type II,

formerly called causalgia, a known nerve injury is present. The goal of the treatment of CRPS Type I is to restore use of the affected limb as much as possible. The use of SCS has been shown to be effective in helping restore normal function in affected limbs, especially if used early in the course of the disease.⁵⁵ Specifically, if patients do not respond to conventional treatment within 12 to 16 weeks, a trial of SCS should be considered.⁵⁵

Kemler et al. emphasized that the success of SCS in CRPS is based on following strict criteria, including these three: 1) clinical diagnosis of CRPS Type I; 2) a limb that had been affected for at least 6 months and did not have a sustained response to less invasive therapies; and 3) a patient who had at least a mean pain intensity of 5 on a VAS assessment. Patients with psychiatric disorders, preexisting neurological conditions, and Reynaud disease were excluded.²⁴ Another predictor of success with SCS in patients with CRPS Type I was the response to sympathetic blockade manifested by an increase in mobility of an affected limb, because this response determines whether the condition is sympathetically maintained or sympathetically independent and thus determines responsiveness to SCS.⁵⁵ Kumar et al.³¹ have shown that all 14 of their patients who initially responded to sympathetic blockade (that is, patients who have sympathetically maintained pain), experienced effective pain relief with SCS.³⁰ Other studies have yielded similar results.²⁰

Generally, SCS has been shown to be highly effective in the treatment of CRPS Type I. In early reports it was suggested that SCS resulted in the relief of pain in the majority of patients with CRPS and that this treatment helped to reduce the edema associated with the condition.^{43,5,50} A recent review of the literature revealed data from one randomized controlled trial, 25 case series, and one economic evaluation for treatment of CRPS with SCS.⁶⁰ Prospective studies confirmed a significant reduction in pain intensity at the 1-year follow-up review^{17,20,24} and a significant improvement in QOL.⁴⁸ Cervical and lumbar devices appear equally effective.¹⁷

In the one prospective, randomized, controlled study of these patients in the literature, SCS plus physical therapy was compared with physical therapy alone in a total of 52 patients.²⁴ Pain intensity was significantly reduced (by 3.6 cm on the VAS) in patients receiving SCS, compared with an increase of 0.2 cm in the patients undergoing physical therapy ($p < 0.001$). Fifty-eight percent of SCS-treated patients described a "much improved" global perceived effect compared with the physical therapy group (6%). The efficacy persisted at 2 years;²⁵ however, in the patient group the effect was no longer significant at the 5-year follow-up interval.²⁶

Case series in the literature report a more sustained effect. At a mean follow-up interval of 3 years, another group reported that median VAS scores were constant at 2.0, the same score as at the 1-year follow up.²⁰ Seventy-five percent of patients with upper-extremity CRPS continued to have improved fist grip strength, whereas 80% of patients with lower-limb disability resumed walking without crutches. Furthermore, a retrospective report on 32 patients with CRPS Type I or II (26 with Type I and six with Type II) after 8 years of follow up demonstrated that 71.8% continued to receive successful long-term pain relief, although no patients had returned to work.²⁸ A total of

25 case series were identified for CRPS; these provide a median follow-up time of 33 months postimplant, and the authors of the metaanalysis found that 67% of patients with CRPS Type I or II who underwent implantation of an SCS device achieved pain relief of 50% or more and that the QOL was significantly improved.⁵⁹

Rate of Complications

The overall complication rate in all patients receiving SCS was 19.5% in 103 patients at 7 years of follow up.⁵⁷ In a retrospective analysis of a 22-year experience in 410 patients, investigators found the following incidence of complications: displaced electrode (21.5%), fractured electrode (5.9%), other hardware malfunction (8.1%), subcutaneous hematomas (4.4%), infection (3.4%), cerebrospinal fluid leak (0.5%), rotation of the pulse generator (0.7%), and discomfort at the pulse generator site (1.2%).²⁸ The complication rates and types were similar regardless of the indication for the procedure. An SCS complication rate of 18% per year was observed in patients with FBSS and/or leg pain, but most of these complications were reversible and mainly due to electrode or lead problems.⁶⁰ More serious complications such as large epidural hematomas have also been reported.¹⁸

Conclusions

Spinal cord stimulation has been used for more than 30 years, and long-term follow-up results of its use for many indications have been published. As with any technique of neuromodulation, outcomes and reported efficacy vary over time as the technique is modified. Differences in our understanding of the pathophysiological aspects of pain syndromes, changes in patient selection, and evolution of the electrodes, surgical technique, measures of efficacy, and programming have affected outcomes. As we refine our patient selection criteria further and continue to optimize the devices, outcomes for current indications will probably improve. Furthermore, multimodality treatments that include SCS are beginning to be reported, and preliminary results are promising. Unique indications for SCS in the treatment of brain and spinal cord injury and tumors are being explored and the role of spinal neuro-modulation will continue to expand as its effects are better understood.

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