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CLINICAL ARTICLE - FUNCTIONAL

Younger age predicts greater effectiveness of spinal cord stimulation for chronic pain

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Abstract
Background Spinal cord stimulation (SCS) is an accepted surgical treatment for neuropathic pain in failed back syndrome or complex regional pain syndrome. However, even in the best selected surgical cases the predictors of adequate pain control are not well defined. The aim of this study was to identify predictors of outcome in patients who underwent SCS in our center.
Methods We performed a retrospective analysis of our neurosurgical database for patients who underwent SCS over the last 8 years in an attempt to identify factors predictive of outcome.
Results Forty-one patients underwent implantation of epidural electrodes, 34 patients had a successful stimulation trial and received permanent devices. Nine patients experienced a late failure at a median time of 7.8 months (range, 4.5–19 months) after implantation. Age was significantly associated with outcome. Younger patients had a significantly lower rate of treatment failure, and none of the patients above 65 years had a successful long-term outcome.
Conclusions Our results suggest that younger age is associated with greater long-term effectiveness of spinal cord stimulation and therefore age may influence the success of SCS therapy with older patients having a greater tendency to failure. Earlier intervention may be beneficial in these chronic pain patients.

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Keywords Neuropathic pain · Spinal cord stimulation · SCS

Introduction

Spinal cord stimulation (SCS) has been shown in several randomized prospective trials to be an effective surgical treatment for neuropathic pain in failed back surgery syndrome (FBSS) or complex regional pain syndrome (CRPS) [2, 10, 14]. SCS may modulate pain perception by electrical stimulation of the dorsal columns in the spinal cord, causing paresthesia and inhibiting pain signals transduction to the brain [12, 13, 16, 20]. Although it is widely accepted that careful patient selection is an important determinant of outcome after SCS, predictive factors are not well defined. In general, patients undergo interdisciplinary assessment to exclude underlying psychiatric and/or social factors complicating chronic pain presentation. Current literature suggests that psychological factors such as somatization, depression, anxiety, and poor coping, are important predictors of poor outcome [4]. Furthermore, the outcome of SCS in workers' compensation settings may not offer an advantage over the best medical treatment [18]. In many centers, a trial stimulation is conducted before permanent implantation to assess adequate coverage of the painful area while avoiding unpleasant paresthesia. However, percutaneous trials are unreliable predictors and only about 50–60 % of the patients implanted with a permanent system achieve long-term satisfactory pain relief [3, 5, 8, 10, 11, 17]. Further studies to understand predictors of outcome after SCS are desirable in order to help physicians define the population that stands to benefit most from the procedure and counsel patients regarding the long-term chances of success. The purpose of this study was to retrospectively analyze patients who underwent SCS at our center in order to identify clinically relevant predictors of outcome.

Methods

We searched our neurosurgical database for consecutive patients who underwent SCS implantation between 2006 and 2012. We reviewed medical records of these patients to collect data on demographics, etiology of pain, previous spinal surgery profiles, psychiatric assessments, and pre- and post-operative VAS (visual analog scale) outcomes. We also collected information on the reported outcomes of intra- and post-operative stimulation (qualitative coverage and percentage if charted).

It is our usual policy to implant surgical leads under local anesthesia, and use extension wires for the trial period. All but two patients underwent a laminotomy for implantation of the epidural electrodes (models 39565 or 3587A electrodes, Medtronic, Inc., Minneapolis, MN). In two patients a percutaneous approach was used (Octad electrodes, Model 3777, Medtronic, Inc., Minneapolis, MN). We performed a 2–7 days of trial stimulation in-house in all cases before proceeding with permanent implantation. Patients with adequate coverage of painful area and >50 % reduction in pain severity underwent permanent lead implantation. Failures were categorized as early if the patient failed the stimulation trial and was not implanted with an IPG. As primary outcome of success, we considered whether or not the patient was using the SCS at last follow-up. Patients who stopped using the device after IPG implantation were defined as late failures. This was considered a more accurate indicator of efficacy imparted by SCS, since drug regimens were not controlled during the study.

Continuous variables were reported either by means and standard deviations or by the median and the interquartile range, depending on their normal or non-normal distribution, respectively. Categorical variables were reported by their relative frequencies. Univariate analysis was used to characterize the examined variables by result of treatment (success vs. failure). The Pearson Chi-square test or Fisher's exact was used to compare the outcome groups with respect to categorical variables. Two-sample *t* test was used to compare age between groups. Two-sample Wilcoxon test was used to compare the groups with respect to duration of symptoms. Statistical analysis was performed by SAS for Windows, version 9.4. The study was conducted with approval from our institutional ethics board.

Results

Forty-one patients who underwent 43 procedures for implantation of SCS were identified (Table 1). The mean age was 49.2 ± 12.5 years (range, 22–73) and 46 % were females ($n = 19$). The most common preoperative diagnosis was FBSS in 53.6 % of the patients (22 patients), 22 % of patients (nine patients) had a diagnosis of CRPS and the remaining patients had peripheral neuropathies (eight patients, 19.5 %) or neuropathic pain

Table 1 Patients' characteristics and outcome

Patient Number*	Sex	Age	Etiology	Pain duration (years)	Outcome
1	F	43	FBSS	8	Success
2	F	32	CRPS	1	Early failure
3	M	22	CRPS	13	Success
3	M	25	CRPS	1	Early failure
3	M	27	CRPS	3	Success
4	M	51	FBSS	15	Success
5	M	40	FBSS	5	Late failure
5	M	42	FBSS	7	Late failure
6	M	51	PN	2	Success
7	F	47	FBSS	2	Success
8	M	53	CRPS	4	Early failure
9	M	50	PN	20	Early failure
10	M	56	FBSS	9	Success
11	F	71	FBSS	3	Late failure
12	F	65	FBSS	21	Late failure
13	M	54	PHN	1	Success
14	F	69	FBSS	3	Early failure
15	M	46	Other	9	Success
16	M	56	FBSS	12	Success
17	M	60	CRPS	16	Success
18	F	52	FBSS	7	Early failure
19	F	25	FBSS	5	Success
20	M	44	FBSS	8	Early failure
21	F	56	FBSS	9	Success
22	Male	45	PN	2	Success
23	Female	47	PN	8	Late failure
24	Male	42	FBSS	1	Late failure
25	Male	56	CRPS	12	Success
26	Male	50	FBSS	15	Success
27	Female	49	FBSS	7	Success
28	Male	60	FBSS	5	Late failure
29	Male	47	FBSS	5	Success
30	Female	39	CRPS	5	Success
31	Female	37	CRPS	1	Late failure
32	Male	47	PN	7	Early failure
33	Female	37	CRPS	16	Success
34	Male	32	PN	14	Success
35	Female	40	CRPS	10	Success
36	Female	69	FBSS	7	Late failure
37	Female	73	PN	10	Early failure
38	Male	56	FBSS	5	Late failure
39	Female	68	FBSS	9	Late failure
40	Male	54	PN	6	Success
41	Female	60	FBSS	5	Late failure

FBSS failed back surgery syndrome, *CRPS* complex regional pain syndrome, *PN* peripheral neuropathy, *PHN* post-herpetic neuralgia

* Where repeated, indicates procedures performed for same patient

Table 2 Univariate analysis of predictors of outcome in the whole cohort of patients who underwent trial of SCS

Variable	Failure ($n = 20$)	Success ($n = 23$)	p value
Age, mean (SD)	53.9 (12.5)	45.3 (10.9)	0.021
Duration of pain (years), median (Q1, Q3)	6.0 (3.5, 8.0)	9.0 (5.0, 14.0)	0.08
Gender, *n* (%)			0.18
Female	11 (55 %)	8 (35 %)	
Male	9 (45 %)	15 (65 %)	
Etiology, *n* (%)			0.36
CRPS	3 (15 %)	7 (30 %)	
FBSS	13 (65 %)	10 (43 %)	
Other	4 (20 %)	6 (26 %)	

secondary to a disease process (two patients, one post-herpetic neuralgia, and one spinocerebellar atrophy).

Seven patients (17 %) had an early failure and had the epidural electrodes removed at the end of the trial stimulation period. This was due to failure in achieving satisfactory coverage of the painful area or due to bothersome paresthesia. Two patients had multiple procedures performed. One patient (#5 in Table 1) who lost benefit from stimulation with a Resume© electrode (i.e., late failure) had it replaced with a Medtronic 565© electrode to allow more stimulation options, but also eventually failed. A second patient (#3 in Table 1), who had a successful outcome for unilateral leg pain, developed pain on the other side after a car accident. He underwent two further attempts for implantation of SCS at a higher spinal level, with a successful outcome after the second surgery and currently has two systems implanted.

Thirty-five stimulation trials (79.5 %) were successful and resulted in implantation of permanent stimulation system; we did not use rechargeable systems. Median follow-up was 26.6 months (range, 6.5–59 months). Twelve of the implanted patients (34 %) experienced a late failure defined as loss of benefit from stimulation and stopped using the SCS at the last follow up. Median time to failure after implantation was 8.8 months (range, 4.5–20.5 months). Reasons for failure were bothersome paresthesia and/or no benefit from stimulation. In five cases, the system was explanted on request by the patients. Overall, 22 patients (53.6 %) were considered to have successful outcomes at the last follow-up defined as at least 50 % pain relief without bothersome side effects.

In an attempt to identify factors related to successful outcome following SCS therapy, we tested the relationship between age, gender, etiology, and duration of pain before surgery with outcome in the whole cohort (i.e., all patients who underwent trial) and also only in chronically implanted patients (Tables 2 and 3). In both groups, only age was found to be significantly associated with outcome with older patients having a higher rate of failures ($p < 0.05$). Mean age of patients having a successful outcome was 45.3 ± 11 years compared to 53.9 ± 12.5 years in patients who failed ($p = 0.02$). Figure 1 demonstrates the proportion of successful vs. failed outcomes in the three age groups (22–39 years, 40–59 years and 60 and older). None of the six patients over the age of 65 in our cohort had a successful outcome; four of them were implanted with a permanent system but experienced a late failure.

Discussion

The outcome after SCS is clearly influenced by multiple interrelated variables. Based on our study, age appears to be a variable of important consideration. In our cohort, SCS benefit was in the younger population, while none of the patients over 65 years of age in our study were satisfied with their treatment results. In previous studies, age has not been shown to be associated with

Table 3 Univariate analysis of predictors of outcome in chronically implanted patients.

Variable	Late failure ($n = 12$)	Success ($n = 23$)	p value
Age	54.8 (12.5)	45.3 (10.9)	0.026
Duration of pain (years), median (Q1, Q3)	5.0 (4.0, 7.5)	9.0 (5.0, 14.0)	0.08
Gender, *n* (%)			0.18
Female	7 (58 %)	8 (35 %)	
Male	5 (42 %)	15 (65 %)	
Etiology, *n* (%)			0.12
CRPS	1 (8 %)	7 (30 %)	
FBSS	10 (83 %)	10 (43 %)	
Other	1 (8 %)	6 (26 %)	

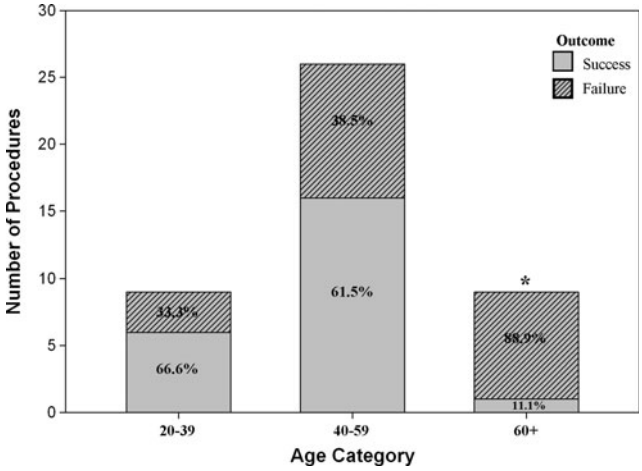

Fig. 1 Outcomes of spinal cord stimulation therapy by age categories. Presented are histograms of successful outcomes vs. failures, patients were grouped into three age groups: 22–39 years, 40–59 years, and 60 and older. Patients in age group 60 and older had a significantly higher proportion of failed outcomes as compared to younger age groups (Chi-squared, $p = 0.04$)

the outcome after SCS. In a relatively young cohort (median age, 51 years), Kumar et al. (1998) reported no effect of age on outcome after SCS. They compared the outcomes in patients above and below 51 years of age to study this association [11]. Similarly, Van Eijs et al., using the mean age (40 years) as a cutoff for comparison, found no significant effect of age on outcome, however none of the subjects in their cohort was above 65 [19]. It is not surprising therefore that these studies did not show the effect of age on outcome after SCS since the cutoff ages used were skewed towards younger patients and therefore not appropriate to detect the effect of older age (>65) on outcome.

There may be several reasons for the greater tendency to failure of SCS in older patients. The effect of aging on pain perception and pain report is well recognized in the literature. Older age was identified as a significant predictor of both the onset of and non-recovery from a persistent pain condition [9]. Furthermore, evidence from basic research of pain modulatory mechanism points to a reduced pain-modulatory capacity in the elderly [6, 7, 21]. This impact of aging on the plasticity of pain responses is of particular importance for neuromodulatory therapies like SCS. We also hypothesize based on our clinical experience that older patients have more difficulties adjusting and optimizing the technology-intensive stimulator and therefore do not enjoy the full benefits.

Although no statistical effect was found, it is possible that the pathophysiology of neuropathic pain influenced outcomes as well, since CRPS patients in our cohort were younger and had a longer duration of pain prior to surgery. Given our study population, we cannot study these subgroups further. Future studies would benefit from categorization based on age and pathophysiology of pain.

Recently, Taylor et al. conducted a comprehensive literature review on the predictors of pain relief following SCS. The average pain relief across studies was 58 % and no patient- or technology-related factors were found to be predictive of outcome on multivariate meta-regression analysis [17]. However, success of SCS depends on normal neural conductivity in the dorsal column-lemniscal system, as was shown by Sindou et al. [16]. These authors suggested that preoperative somatosensory evoked potentials (SSEPs) provide an objective prediction of patient outcome after SCS and therefore patients with abnormal SSEPs should not undergo SCS. Although we used primarily surgical leads, we do not think our findings are related to the technology. Both cylindrical percutaneous leads and surgical paddle leads were shown to be effective treatment options [14, 15]. Surgical leads were found to be associated with slightly higher initial complication rate, however with significantly lower long-term complication rates [1]. We performed all trials in-house, and, as such, extensive trialing was performed on a daily basis and we were able to reach a conclusion regarding the efficacy of treatment and proceed to permanent implantation within a few days.

The significant findings of this study could be of value for future patient selection in clinical settings. We propose that balancing expectations of pain relief and educating older patients about the nuances of technology-intensive SCS therapy may optimize outcomes.

A major limitation of this study is a small sample size and the inherently limitation of a retrospective data analysis. Future prospective studies should investigate the relation of age, among other potential predictive factors, with tendency to failure after SCS.

Conclusions

Age of patients undergoing SCS may influence the success of the procedure with older patients having a greater tendency to failure.

Compliance with ethical standards

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Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

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