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PUBLISHED BY
ELSEVIER

The Journal of Pain, Vol 24, No 7 (July), 2023: pp 1298−1306
Available online at www.jpain.org and www.sciencedirect.com

Spinal Cord Stimulation for Failed Back Surgery Syndrome: to Trial or Not to Trial?

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Abstract: **Spinal cord stimulation (SCS) is a recommended therapy to treat failed back surgery syndrome (FBSS). A trial period is practiced to enhance patient selection. However, its fundamental evidence is limited, especially concerning long-term benefit and therapy safety. We compared the long-term (5.3 ± 4.0 years) clinical outcome and therapy safety of a trialed and nontrialed implantation strategy, including multidimensional variables and pain intensity fluctuations over time. A multicenter cohort analysis was performed in 2 comparable groups of FBSS patients. Regarding eligibility, patients had to be treated with SCS for at least 3 months. While the Trial group comprised patients who underwent an SCS implantation after a successful trial, the No-Trial group encompassed patients who underwent complete implantation within 1 session. The primary outcome measures were pain intensity scores and complications. The Trial and No-Trial groups consisted of 194 and 376 patients (N = 570), respectively. A statistically but not clinically significant difference in pain intensity (*P* = .003; effect = 0.506 (.172−.839)) was found in favor of the Trial group. No interaction between a time dependency effect and pain intensity was noted. Whereas trialed SCS patients were more likely to cease opioid usage (*P* = .003; OR = .509 (.326−.792)), patients in the No-Trial group endured fewer infections (*P* = .006; proportion difference = .43 (.007−.083)). Although the clinical relevance of our findings should be proven in future studies, this long-term real-world data study indicates that patient-centered assessments on whether an SCS trial should be performed have to be investigated. According to the current ambiguous evidence, SCS trials should be considered on a case-by-case basis.**

Perspective: ***The currently available comparative evidence, together with our results, remains ambiguous on which SCS implantation strategy might be deemed superior. An SCS trial should be considered on a case-by-case basis, for which further investigation of its clinical utility in certain patient populations or character traits is warranted.***

Received September 13, 2022; Revised February 16, 2023; Accepted February 27, 2023.
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No funding was received for conducting this research.
The authors declare that they have had no conflict of interest during the conduct of this study.
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1526-5900/$36.00

https://doi.org/10.1016/j.jpain.2023.02.032

Key Words: *Failed back surgery syndrome, Spinal cord stimulation, Screening trial, Trial period, Pain Intensity, Medication intake, Multidimensional outcomes, Long-term follow-up, Therapy safety, Complications.*

Failed Back Surgery Syndrome (FBSS), for which "chronic pain after spinal surgery"[35] and "persistent spinal pain syndrome"[8] have been recently proposed as novel terminologies, is a refractory chronic pain syndrome which emerges after spinal surgery,[40] in about 30% of the cases.[18] Combined with conservative treatment strategies (eg, physical therapy, psychological rehabilitative care, and cognitive behavioral therapy), FBSS patients tend to use various types of medication, including opioids and antineuropathics.[2,11] Besides, spinal cord stimulation (SCS) is recommended as a symptomatic treatment.[20,21]

The SCS device system consists of an electrode implanted into the epidural space and an implantable pulse generator (IPG). Commonly, as recommended by national and international clinical guidelines, as well as health insurers' reimbursement criteria, patients must undergo an SCS trial period with an external IPG.[10,28] Regarding the electrode being used, the physician could either utilize a temporary or permanent electrode, of which the manner will be replaced by another electrode if the trial is deemed successful. Both strategies hold their pros and cons.[19] Although the duration of the trial usually varies between 5 days and several weeks,[5] the optimal duration has not been determined since trial periods range from minutes[4] to even 65 days.[26] When the patient's pain relief is adequate (ie, ≥50% on the visual analogue scale [VAS]), and if the patient is willing to proceed to permanent implantation, the SCS trial is considered successful, after which the SCS system will be fully internalized during a second session. In contrast with this biphasic procedure, in some situations (eg, high perioperative risk due to comorbidity), the electrode and IPG are completely internalized within one session (ie, the nontrialed implantation strategy).

Trialing affords the opportunity to assess the possible therapeutic effect and concomitant side-effects (eg, unpleasant paresthesia) before committing to permanent implantation.[10] In other words, SCS trials are considered to enhance patient selection. However, disadvantages of a trialed SCS implantation have also been reported. The study of Oakley et al.[31] demonstrated that SCS trials could be a false-negative predictor. As part of a larger study, 12 patients who failed their SCS trial (ie, defined as < 50% pain relief) were still implanted with a permanent SCS system, after approval by the patients and the ethics committee. At various follow-up moments, up to 18 months, some patients experienced ≥ 50% pain relief. Furthermore, the trial duration has been found to be positively correlated to the infection risk[30] and patients are exposed twice to risks associated with hospital admission and surgery.[13] It should also be noted that patients are mostly trialed with only 1 SCS waveform due to the limited time span of an SCS trial, despite the increasing availability of different SCS stimulation paradigms with their individual efficacy and implantation indications. Therefore, trialing patients with multiple waveforms might become highly relevant.[3] Although SCS relieves pain in a cost-effective way,[29] SCS trials may raise healthcare costs in some cases or could even exceed cost-effectiveness[14] due to a higher infection rate, repeated surgery, and potential second trials if patients are reconsidered to undergo SCS therapy.[12,34]

The overall evidence for the use of SCS trials is incomplete. Recently, the first randomized controlled study reported that SCS trials might exhibit some diagnostic utility despite no patient outcome benefit.[14] Although these findings are an important step forward, the observed complications were solely reported through descriptive statistics, and the studied cohort comprised heterogenous neuropathic pain conditions. The latter was considered a strength of the study as it reflected the current clinical practice. However, similar evidence in the type of patients most often considered for SCS (ie, FBSS patients) is lacking. Likewise, long-term outcomes concerning a trialed versus a nontrialed SCS implantation have not been reported. Therefore, by assessing both SCS implantation strategies in a large homogeneous cohort of FBSS patients, we aimed to compare their long-term clinical outcome and therapy safety multidimensionally, including any fluctuations in pain intensity.

Methods

Study Population

All medical records of adult patients (≥ 18 years) who received SCS therapy to treat FBSS in 2 collaborating hospitals (ie, Radboud University Medical Center and the Sint Maartenskliniek) were reviewed manually by 2 researchers independently (R.W. and E. K.), after retrieval of written informed consent. Ethical approval for conducting this study was waived by the medical research ethics committee (CMO RadboudUMC; file number: 2020-6194). Regarding inclusion, the minimal treatment duration with a percutaneous cylindrical SCS electrode was 3 months in order to have sufficient data available for each patient and to diminish the effect of dynamic changes to the stimulation parameters during the early postoperative period, especially since the nontrialed patients also required time to become used to the SCS system. Patients were excluded if they suffered from psychiatric health conditions (eg, depression) or coexisting chronic pain syndromes as those were believed to interfere with the patient's pain sensation and hence, their reported pain intensity scores regarding SCS outcomes. Another exclusion criterium was the absence of a baseline pain intensity score. Two groups were identified. Whereas the Trial group comprised patients who underwent an SCS implantation during a second session after a successful trial period of 2 weeks,

the No-Trial group consisted of patients who had their SCS system completely implanted within one session.

SCS Implantation Strategies as Practiced in Both Hospitals

Trialed Implantation

Patients included in the Trial group received a permanent trial electrode during the first session if the approximate on-table paresthesia coverage was at least 80% during tonic stimulation (ie, as experienced by the patient), together with no concomitant undesirable side-paresthesias. All electrodes were placed percutaneously and connected to an external IPG. Subsequently, patients underwent a trial period that lasted for 2 weeks. An SCS trial was considered to be successful if the patient was willing to proceed to permanent implantation and if the patient's pain relief was $\geq$ 50% based on the mean VAS, measured through a digital pain diary which was required to be filled in 3 times a day during the last 4 days. During a second session, the external IPG was replaced by the definitive IPG, which was implanted subcutaneously in the inferior abdominal or gluteal region.

Nontrialed Implantation

In the No-Trial group, all patients received a complete percutaneously implanted SCS system within one session if the approximate on-table paresthesia coverage with tonic stimulation was at least 80% and no uncomfortable concomitant side-paresthesias were noted.

Almost all nontrialed implantation patients were treated at the same of both contributing hospitals. Within the corresponding hospital, the standard care practice provided the nontrialed implantation strategy. Barely any patient-specific indications to practice the nontrialed strategy were present. For example, a few patients received this type of implantation as they developed an infection during a successful SCS trial earlier, which led to the removal of the entire SCS system.

Data Retrieval

Data were collected between June 2020 and February 2021. Patient characteristics were collected from before SCS implantation. The retrospectively gathered VAS scores were disclosed through a digital pain diary that had to be filled in 3 times a day on 4 consecutive days prior to each follow-up visit. In order to determine a multidimensional outcome of the SCS implantation strategies, multiple questionnaires were used, including the 36-Item Short Form Health Survey (SF-36),[1] the Pain Catastrophizing Scale (PCS),[38] the Hospital Anxiety and Depression Scale (HADS)[37] and the McGill Pain Questionnaire Dutch Language Version (MPQ-DLV questionnaire).[42,43] The measurements regarding pain intensity and questionnaires were collected during intake (ie, baseline) and follow-up (ie, 1, 3, 6, 12 months and each consecutive year). Opioid usage was determined as a binary variable prior to SCS implantation and during the last follow-up moment. All data except the complications were extracted from a previous prospectively registered database, after which the data was verified during the manual medical record reviewing process. The already existing database was previously filled automatically through online patient reported outcome measure files, meaning no interpretation bias could have been present. Concerning the complications, a predefined classification was established through multidisciplinary sessions of both hospitals. A nurse practitioner and physician verified all retrospectively retrieved complications.

Statistical Assessment

The primary outcome measures were the influence and clinical relevance of the type of implantation strategy on the pain intensity scores and number of complications. Secondary outcome measures comprised the statistical correlations between each implantation strategy and quality of life, the questionnaire data and the probability of ceasing opioids. To allow for the analyses of repeated pain intensity scores in a patient within 1 comprehensive analysis, we applied a longitudinal multilevel linear regression analysis. The regression model included the time of measurement (categorical <1 year; 1−3 years; >3 years), implantation strategy, gender, age, height, and body mass index (BMI). Whether a patient used opioids before implantation and their number of previous back surgeries were comprised as independent variables. The model was extended with an interaction term between the time variables and the implantation strategy. Hence, within a singular model, the effect of the implantation strategy on multiple moments in time and their potentially reciprocal interactions could be estimated. Complications were delineated and both the differences in proportions as statistical significance between both groups were determined using the Agresti-Caffo method. The influence of the type of implantation strategy on the probability of ceasing opioid usage, together with the independent variables gender, age, height, and BMI, was determined through a logistic regression analysis.

In terms of the questionnaire data, a Quality of Life Index (QLI) was determined using the MPQ-DLV questionnaire.[43] Using data from 1-year and 3-years follow-up separately, multiple linear regressions adhering to the last observation carried forward method were performed to test for significant influence of the same explanatory variables as within the pain intensity score analysis, except for the time of measurement. All statistical tests were 2-sided and significance was assumed when $P < .05$. The statistical assessments were performed through SPSS (*IBM Corp (2017). IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.*), and R (*R Core Team (2019). R: A language and environment for statistical computing, Version 3.6.2. Austria, Vienna: R Foundation for Statistical Computing*). Literature was managed by means of EndNote (*Clarivate Analytics. Released 2019. EndNote X9.2 for Windows.*).

Results

A total of 570 patients were included. The Trial and No-Trial groups consisted of 194 and 376 patients, respectively. The corresponding patient demographics are depicted in Table 1. The vast majority of the patients received tonic stimulation, but burst and high-density SCS were also practiced. Implantations were performed from 1998 until 2020. Some data concerning the number of previous back surgeries were missing (Trial: 34/194; No-Trial: 72/376). Therefore, all analyses were performed twice (ie, both with inclusion and exclusion of the variable "number of previous back surgeries"). Since the output in terms of significance did not differ, only the models without the number of previous back surgeries are presented.

In the analysis of the pain intensity scores over time, the interaction between implantation strategy and time did not significantly improve the model. Therefore, any differences in pain intensity between the groups may solely be accredited to the type of implantation strategy used, and only the results from the model without interaction are presented. The Trial group was found to be superior to the No-Trial group, as a lower pain intensity was reported (P = .003; effect = .506 (.172−.839)) (Table 2). Hence, a significantly higher post-implantation pain intensity score in the No-Trial group of .506 on the VAS was found. However, this difference was deemed not clinically meaningful as the minimal clinically important difference of the VAS in low back pain patients has been reported to be 1.5 points[32] or even 1.9 points in chronic low back pain patients.[15] Compared to the initial therapeutic effect, pain intensity scores increased over time in both groups. Whereas the increase on the VAS was .749 regarding mid-term follow-up (P < .001), the pain intensified by 1.137 VAS points at long-term follow-up (P < .001), both as compared to pain intensity scores measured in the first year after the SCS implantation (ie, short-term follow-up). No statistically significant contributions caused by the patient's age, height, BMI and gender were found.

The numbers of complications are shown in Table 3. A significant difference favoring the No-Trial group was found regarding the number of infections (P = .006; proportion difference = .43 (.007−.083)). All infections were confirmed by a positive microbiological culture test. No significant differences were demonstrated concerning electrode migration, electrode failure (ie, defect contacts, electrode breakage or disconnection), pain resulting from implanted material (eg, IPG suppressing adjacent costae during movement), hematomas, dural punctures, and number of explantations. No neurological complications were observed.

In terms of analgesics, trialed SCS implantations were shown to enhance the statistical probability of a particular patient to cease opioid usage (Table 4). This probability was significant in the overall cohort of patients who used opioids preimplantation (n = 360; (P = .003; OR = .509 (.326−.792)) as when the number of previous back surgeries was encompassed (n = 310; P = .038). It must be noted that patients were not required to discontinue opioid use before SCS implantation in both hospitals, however, they were encouraged to do so. From 3 months follow-up onwards, each patient was further stimulated to fully taper opioid usage. Furthermore, a patient's height was also positively related to the probability of weaning off their opioids (P = .033 and P = .030, respectively). No explanatory relationship could be hypothesized.

Since the questionnaires were incorporated into our follow-up trajectory 4 years ago, long-term data were unavailable. In line with this, the included patients per analysis varied from approximately 30 to 90 patients. Whether the Trial group or the No-Trial group was significantly superior for each questionnaire outcome has been summarized in Table 5. Although barely any differences were observed between the 2 groups, the Trial group showed to be superior across the general health subscale and all pain rating indices of the MPQ-DLV questionnaire at one-year follow-up. These differences disappeared at 3-year follow-up. Regarding the same explanatory variables as used within the other analyses, patients who used opioids before implantation

Table 1. Patient Demographics at Implantation

	Trial	*No-Trial*
Male : Female (N = 280 : 290)	104 : 90 (53.6% male)	176 : 200 (46.8% male)
Age (years)	54.0 ± 10.4	53.9 ± 10.6
Height (cm)	173.6 ± 9.5	173.8 ± 9.6
BMI (kg/m2)	27.3 ± 4.6	27.3 ± 4.3
Follow-up duration (years)	5.2 ± 4.2	5.3 ± 3.9
Number of previous back surgeries*	2.0 ± 1.1†	2.2 ± 1.6†
Number of opioid users (N = 360; 63.2%)	138 (71.1%)	222 (59.0%)

Abbreviation: BMI, body mass index. the Trial and No-Trial group included 194 and 376 patients, respectively.
*Only back surgeries preceding SCS implantation were included.
†Thirty-four and 72 patients were missing regarding the Trial and No-Trial group, respectively.

Table 2. Longitudinal Multilevel Linear Regression for Relation Between Explanatory Variables and Pain Intensity Scores, as Measured Over Time (N = 570; Number of Measurements = 4048)

	Effect (95%-CI)	P-*value*
No-Trial (reference is "Trial")	.506 (.172 to .839)	**.003**
Time: 1-3 years (reference is "<1 year")	.749 (.596 to .901)	**<.001**
Time: >3 years (reference is "<1 year")	1.137 (.989 to 1.281)	**<.001**
Gender (reference is "Female")	.078 (-.361 to .518)	.727
Age (years)	.004 (-.012 to .019)	.664
Height (cm)	-.009 (-.033 to .014)	.423
BMI (kg/m^2)	-.029 (-.064 to .007)	.119
Opioid usage at baseline	.270 (-.060 to .599)	.109

The bold values are the significant values (significance was assumed when P <0.005).
Abbreviation: BMI, body mass index.

Table 3. Number of Complications

	Trial	*No-Trial*	*Difference in Proportions (95%-CI)*	P-*value*
Infection (N = 19)	12	7	.43 (0.007−.083)	**.006**
Electrode migration (N = 53)	15 (n = 12/194)	38 (n = 37/376)	-.037 (-.080 to .012)	.140
Electrode failure (N = 67)	29 (n = 25/194)	38 (n = 32/376)	.044 (-0.010 to .101)	.099
Pain due to implants (N = 84)	23 (n = 20/194)	61 (n = 45/376)	-.017 (-.069 to .040)	.555
Hematoma (N = 5)	1	4	-.005 (-.021 to .015)	.506
Dural puncture (N = 7)	3	4	.005 (-.016 to .030)	.620
Explantation (N = 22)	7	15	-.004 (-.036 to .033)	.823

The bold values are the significant values (significance was assumed when $P < 0.005$).
Legend: The Trial and No-Trial group included 194 and 376 patients, respectively. Some patients endured the same complication more than once. Hence, the number of patients is depicted next to amount of complications occurred if this was the case. The difference in proportions and p-values are based on the number of patients instead of number of complications.

reported inferior physical role functioning scores and QLIs but were more positive regarding their overall subjective pain index at 1-year follow-up. Lastly, patients with a greater BMI were more likely to rate their pain indices more negatively at 3-year follow-up.

Discussion

In terms of pain relief, our findings show that the trialed SCS implantation strategy is statistically superior, though not clinically meaningful. This finding was not significantly influenced by a potential time dependency effect. Furthermore, patients who underwent a screening trial prior to SCS implantation showed a higher rate of discontinuation of opioids after permanent implantation. Regarding therapy safety, the number of infections was significantly lower in the No-Trial group.

The first randomized controlled study comparing a trialed and a nontrialed implantation strategy reported that an SCS trial affords no patient outcome benefit, and neither does it enhance cost-effectiveness.[14] No statistical differences were found at their longest follow-up (ie, 6 months), independent of whether imputation or exploratory interaction analyses were incorporated.[14] Even though the current study showed statistical superiority concerning the trialed implantation strategy in terms of pain relief, the reported change of 0.506 VAS points was deemed not clinically meaningful. Hence, this finding complements the statement by Eldabe et al that an SCS trial might not hold patient outcome benefit, at least in terms of pain relief, particularly as this study comprised a large cohort of homogeneous patients and encompassed long-term outcomes. Another contributing factor within the study of Eldabe et al that indirectly strengthens their statement is that their patients who did not undergo an SCS trial endured pain significantly longer, which is a negative outcome predictor according to a univariate meta-regression analysis.[39] Additionally, as we were unable to incorporate any failed SCS trial patients, such a preselection might have benefited the results of the Trial group slightly. Besides, the current study elaborated on medication intake and showed that trialed SCS implantation patients are more likely to cease opioid usage. To the authors' knowledge, no other study addressed this subject by comparing the 2 implantation strategies. Within the study of Eldabe et al, only 4 patients managed to cease their analgesic intake, but no intergroup difference was determined. Currently, we are not aware of a clarification for the positive correlation between trialed implantations and discontinuation of medication intake. However, this might be a clinically relevant difference as decreased medication usage leads to fewer concomitant side effects. Furthermore, subsequent reported pain intensity scores are the result of merely the SCS treatment and will not be influenced by the antinociceptive effects of drugs.

Another unexplored uncertainty within the literature should also be noted. Since the optimal SCS trial duration has not been determined, we might not be looking at 'the best case scenario results'. Despite that all our patients underwent the same trial period duration (ie, 2 weeks), results might alter when other trialing durations or strategies are adhered to. Within the randomized controlled trial, the median trial duration was 7 days (range: 5−22; mean: 9.3) and possibly varied across the 3 contributing clinics. No motivation was given concerning the inter-patient trial duration differences. It may be hypothesized that when patients proceed to definitive implantation exclusively based on whether they meet the requirements in terms of treatment outcome, independent of time, such as a predefined minimum trial duration, the decision on this definitive implantation might be arranged during an overly optimistic point of view, possibly at the cost of long-term sustainability (eg, in a stage where the early results are overshadowed by placebo-like factors and unrealistic expectations). At least up to 6 days after a

Table 4. Logistic Regression Analysis for Relation Between Explanatory Variables and Ceasing Opioids (n = 360; Trial: 138, No-Trial: 222)

	OR (95%-CI)	P-*value*
No-Trial (reference is "Trial")	.509 (.326−.792)	**.003**
Gender (reference is "Female")	1.119 (.604−2.072)	.720
Age (years)	1.006 (.984−1.028)	.614
Height (cm)	1.037 (1.003−1.072)	**.033**
BMI (kg/m^2)	1.036 (.985−1.091)	.171

The bold values are the significant values (significance was assumed when $P < 0.005$).
Abbreviation: BMI, body mass index.

Table 5. Multiple Linear Regressions for Relation Between Questionnaire Data and Whether a Trialed or a Nontrialed Implantation Strategy was Adhered

Outcome Measure	At 1-Year Follow-up			At 3-Year Follow-up		
	N (LOCF)*	Effect (95%-CI) (reference is "Trial")†	P-value	N (LOCF)*	Effect (95%-CI) (reference is "Trial")†	P-value
QLI	43 (18)	-.482 (-3.864 to 2.899)	.774	29 (8)	7.256 (-1.906 to 16.418)	.114
HADS: total	88 (24)	.322 (-2.133 to 2.777)	.795	59 (15)	.116 (-4.225 to 4.457)	.958
HADS: anxiety	88 (24)	.527 (-.680 to 1.734)	.388	59 (15)	.000 (-1.814 to 1.813)	1.000
HADS: depression	88 (24)	-.209 (-1.763 to 1.344)	.789	59 (15)	.272 (-2.590 to 3.135)	.849
PCS: total	88 (23)	2.553 (-1.580 to 6.685)	.223	58 (15)	-.340 (-6.496 to 5.817)	.912
PCS: helplessness	88 (23)	.861 (-1.403 to 3.125)	.451	58 (15)	-.056 (-3.529 to 3.416)	.974
PCS: magnification	88 (23)	.240 (-.501 to .981)	.521	58 (15)	.140 (-1.061 to 1.342)	.815
PCS: rumination	88 (23)	1.544 (-.043 to 3.130)	.056	58 (15)	.540 (-1.457 to 2.537)	.589
SF-36: physical functioning	90 (23)	5.696 (-3.648 - 15.040)	.229	26 (13)	-1.990 (-18.786 to 14.806)	.806
SF-36: physical role functioning	94 (27)	1.906 (-13.484 - 17.297)	.806	30 (12)	-3.027 (-41.972 to 35.917)	.873
SF-36: mental health	92 (24)	-3.261 (-9.370 - 2.847)	.291	29 (11)	0.023 (-18.864 to 18.911)	.998
SF-36: emotional role functioning	94 (26)	-11.649 (-29.795 - 6.497)	.205	30 (12)	-35.521 (-88.898 to 17.855)	.181
SF-36: vitality	92 (25)	1.095 (-7.412 to 9.603)	.799	29 (12)	-0.338 (-13.445 to 12.769)	.958
SF-36: social functioning	93 (25)	-1.562 (-11.648 to 8.524)	.759	30 (13)	-10.400 (-42.014 to 21.213)	.502
SF-36: pain	94 (25)	1.803 (-7.841 to 11.447)	.711	30 (11)	1.008 (-14.895 to 16.911)	.897
SF-36: general health	89 (24)	-8.564 (-15.907 to -1.221)	**.023**‡	26 (10)	-17.691 (-37.829 to 2.448)	.082
MPQ-DLV: sensory PRI	42 (17)	20.620 (8.156 - 33.084)	**.002**‡	29 (8)	4.099 (-19.853 to 28.051)	.726
MPQ-DLV: affective PRI	42 (17)	12.137 (5.856 - 18.418)	**.000**‡	29 (8)	8.693 (-4.662 to 22.047)	.190
MPQ-DLV: evaluative PRI	42 (17)	4.508 (0.179 - 8.837)	**.042**‡	29 (8)	5.476 (-3.666 to 14.618)	.227
MPQ-DLV: total PRI	39 (16)	37.330 (16.070 - 58.590)	**.001**‡	28 (8)	15.780 (-25.028 to 56.587)	.429

The bold values are the significant values (significance was assumed when $P < 0.005$).
Abbreviations: HADS, Hospital Anxiety and Depression Scale; MPQ-DLV, McGill Pain Questionnaire Dutch Language Version; PCS, Pain Catastrophizing Scale; PRI, Pain Rating Index; QLI, Quality of Life Index; SF-36, 36-Item Short Form Health Survey. Within each analysis, the variables gender, age, height, BMI, baseline score and whether a patient used opioids before implantation were also included. Except the SF-36, a lower score indicated improvement.
*Missing data was handled through the last observation carried forward method, of which the corresponding number of patients is depicted between parenthesis.
†The effect in case of a "No-Trial" is presented, as a reference to the "Trial" condition.
‡The Trial group was found to be superior.

trialed SCS implantation, the patient's reports on the SCS treatment effect might be inaccurate.[7] Vice versa situations have also been described, as an SCS trial could be a false-negative predictor for long-term outcomes in some patients.[31]

Though, the shorter the trial period, the lower risk for infections or other complications.[30] The only observed statistically significant difference in the current study was the number of infections, favoring the No-Trial group (P = .006). We hypothesize that the reported difference can mainly be accredited to the doubled number of procedures required during a trialed implantation strategy since significance would have disappeared if the number of infections had been corrected for the number of procedures performed. Though, both contributing hospitals implanted permanent trial leads, which hold a higher risk of developing an infection or impeding wound healing.[36] Any inter-site variations could also have contributed to the presented complications, as both hospitals adhered to a slightly different antibiotic regimen. One hospital administered cefazolin both preoperatively and postoperatively, whereas the other clinic (which performed most of the nontrialed implantations) administered cefazolin only preoperatively. Unfortunately, we were unable to correct for these intersite dissimilarities. Currently, no other comparative evidence is available. Therefore, the nontrialed implantation strategy may be preferred in terms of complications and perhaps also due to the indirectly linked raised healthcare costs related to complications such as infections. The contribution of complications to any cost-benefit analysis has not been determined. Though, 2 studies stated that the outcome benefit resulting from an SCS trial becomes irrelevant concerning the significantly high associated costs, comparing a trialed and a nontrialed implantation strategy.[12,14] Their findings are not easily generalizable, however, as trial to implant ratios vary greatly between the United States[16,17,27] and Europe,[41] as well as across different medical indications for implantation.[12,16] Also, long-term outcomes were not incorporated.

Although the current evidence points out some possible advantages regarding a nontrialed implantation strategy, an SCS trial might still also hold potential. First, as the treatment relationship between the patient and healthcare providers lengthens, more contacts will be held, resulting in enhanced patient education and more shared decision-making processes.[33] This could lead to more adequate choices based on realistic expectations and the patient's preferences and values more often, which have been suggested as positive outcome predictors.[9] Also, if chronic pain patients have the feeling of being more involved and thus experience autonomy regarding their treatment trajectory, preferably at their own pace, their related outcomes will be positively enhanced.[22,24] It is known that patients tend toward

improved treatment outcome, satisfaction and psychological and sensory aspects after they have had the opportunity to choose whether or not to undergo a certain treatment.[23] One could argue that such a decision benefits from a trialed implantation strategy as patients have more input and time to contemplate. This may have been why our Trial group patients reported superior pain rating indices at 1-year follow-up. Although the above findings advocate potential benefits of a trialed SCS implantation strategy, particularly as the trial duration lengthens, we should then also consider the accompanying risks such as infections.[30] Moreover, a qualitative study concluded that patients disfavored the trialed SCS implantation strategy due to the related burdens of the external IPG and cable wires, 2 recovery periods being required and the increased time and cost consuming aspects.[6] The current study missed such nuances in the patients' perspectives. Therefore, their findings are complementary to ours, and while they more firmly advocate for a nontrialed implantation strategy, they also opt for the development of a patient-centered decision-making framework based on complete and reliable information provision, expectation management and optimization of coping strategies. While it still seems reasonable that an SCS trial would positively contribute to such core values as part of an overall SCS therapy plan, we reckon that other opportunities as a possible substitute should also be investigated, such as adjuvant psychological treatment.[25] Perhaps we will be able to fully address these important principles without the need for an invasive SCS trial while still improving SCS treatment outcomes.

Strengths and Limitations

To the best of the authors' knowledge, this multicenter study currently holds the largest assessment on whether a trialed or a nontrialed SCS implantation strategy should be performed. Our 2 homogeneous FBSS groups, as patient demographics were found to be similar, studied outcomes at a much longer follow-up than investigated before. The contributing hospitals mainly adhered to only one of both implantation strategies, mitigating any negative outcome factors related to relatively less experienced procedures or learning curve effects of the staff. Although data was insufficient to study the role of different stimulation modalities, the inclusion of various stimulation paradigms and multivendor data might enhance the generalizability of the current findings. Similarly, data regarding opioid dosages and preimplantation duration of pain were only available for an insufficient number of patients. Inherently to the retrospective design of this study, we could not correct for any inter-site differences and contextual factors, such as the exact antibiotic regimen that was administered or to which extent patients were educated preoperatively. However, all contributory healthcare providers collaborated intensively and frequently. One example was recurring multicenter multidisciplinary sessions on patient cases, SCS indications and implantation strategies. Therefore, the authors deem these limitations of limited value in the context of the research aim of this study. Lastly, patients could not choose between both implantation strategies in the past, which impeded the shared decision-making process and perhaps also negatively influenced the corresponding outcomes.

Conclusion

Although the current study showed statistically superior, but not clinically meaningful results concerning nontrialed SCS patients, none of the SCS implantation strategies can be deemed superior. Together with the other currently available ambiguous literature, it could be argued SCS trials should be considered on a case-by-case basis. We should dive deeper into its clinical utility in certain patient populations or character traits first, as well as to investigate any possible alternatives. An SCS trial could still be beneficial as part of a multidimensional assessment to determine sustainability regarding permanent implantation and clinical outcome, especially in patients with significantly high opioid usage, a doubtful implantation indication or a combination of multiple positive and negative outcome predictors.

References

1. Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R, Sprangers MA, te Velde A, Verrips E: Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. J Clin Epidemiol 51:1055-1068, 1998

2. Amirdelfan K, Webster L, Poree L, Sukul V, McRoberts P: Treatment options for failed back surgery syndrome patients with refractory chronic pain: An evidence based approach. Spine (Phila Pa 1976) 42(Suppl 14):S41-S52, 2017

3. Buchanan P, Kiker D, Katouzian A, Kia F, Pope JE: Multisystem spinal cord stimulation trialing: A single center, retrospective, observational study. Pain Pract 21:778-784, 2021

4. Burchiel KJ, Anderson VC, Brown FD, Fessler RG, Friedman WA, Pelofsky S, Weiner RL, Oakley J, Shatin D: Prospective, multicenter study of spinal cord stimulation for relief of chronic back and extremity pain. Spine (Phila Pa 1976) 21:2786-2794, 1996

5. Camberlin C, Miguel LS, Smit Y, Post P, Gerkens S, Laet CD: Neuromodulation for the management of chronic pain: Implanted spinal cord stimulators and intrathecal analgesic delivery pumps. Brussels, Health Technology Assessment (HTA). KCE Report 189C, Belgian Health Care Knowledge Centre (KCE), KCE Report 189C, D/2012/10.273/76, 2012

6. Chadwick R, McNaughton R, Eldabe S, Baranidharan G, Bell J, Brookes M, Duarte RV, Earle J, Gulve A, Houten R, Jowett S, Kansal A, Rhodes S, Robinson J, Griffiths S, Taylor RS, Thomson S, Sandhu H: To trial or not to trial before spinal cord stimulation for chronic neuropathic pain: The patients' view from the TRIAL-STIM randomized controlled trial. Neuromodulation 24:459-470, 2021

7. Chincholkar M, Eldabe S, Strachan R, Brookes M, Garner F, Chadwick R, Gulve A, Ness J: Prospective analysis of the trial period for spinal cord stimulation treatment for chronic pain. Neuromodulation 14:523-528, 2011

8. Christelis N, Simpson B, Russo M, Stanton-Hicks M, Barolat G, Thomson S, Schug S, Baron R, Buchser E, Carr DB, Deer TR, Dones I, Eldabe S, Gallagher R, Huygen F, Kloth D, Levy R, North R, Perruchoud C, Petersen E, Rigoard P, Slavin K, Turk D, Wetzel T, Loeser J: Persistent spinal pain syndrome: A proposal for failed back surgery syndrome and ICD-11. Pain Med 22:807-818, 2021

9. Cormier S, Lavigne GL, Choiniere M, Rainville P: Expectations predict chronic pain treatment outcomes. Pain 157:329-338, 2016

10. Deer TR, Mekhail N, Provenzano D, Pope J, Krames E, Leong M, Levy RM, Abejon D, Buchser E, Burton A, Buvanendran A, Candido K, Caraway D, Cousins M, DeJongste M, Diwan S, Eldabe S, Gatzinsky K, Foreman RD, Hayek S, Kim P, Kinfe T, Kloth D, Kumar K, Rizvi S, Lad SP, Liem L, Linderoth B, Mackey S, McDowell G, McRoberts P, Poree L, Prager J, Raso L, Rauck R, Russo M, Simpson B, Slavin K, Staats P, Stanton-Hicks M, Verrills P, Wellington J, Williams K, North R, Neuromodulation Appropriateness Consensus C: The appropriate use of neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: The Neuromodulation Appropriateness Consensus Committee. Neuromodulation 17:515-550, 2014

11. Desai MJ, Nava A, Rigoard P, Shah B, Taylor RS: Optimal medical, rehabilitation and behavioral management in the setting of failed back surgery syndrome. Neurochirurgie 61 (Suppl 1):S66-S76, 2015

12. Duarte RV, Thomson S: Trial versus no trial of spinal cord stimulation for chronic neuropathic pain: Cost analysis in United Kingdom National Health Service. Neuromodulation 22:208-214, 2019

13. Eldabe S, Buchser E, Duarte RV: Complications of spinal cord stimulation and peripheral nerve stimulation techniques: A review of the literature. Pain Med 17:325-336, 2016

14. Eldabe S, Duarte RV, Gulve A, Thomson S, Baranidharan G, Houten R, Jowett S, Sandhu H, Chadwick R, Brookes M, Kansal A, Earle J, Bell J, Robinson J, Walker S, Rhodes S, Taylor RS: Does a screening trial for spinal cord stimulation in patients with chronic pain of neuropathic origin have clinical utility and cost-effectiveness (TRIAL-STIM)? A randomised controlled trial. Pain 161:2820-2829, 2020

15. Hagg O, Fritzell P, Nordwall A, Swedish Lumbar Spine Study G: The clinical importance of changes in outcome scores after treatment for chronic low back pain. Eur Spine J 12:12-20, 2003

16. Hayek SM, Veizi E, Hanes M: Treatment-limiting complications of percutaneous spinal cord stimulator implants: A review of eight years of experience from an academic center database. Neuromodulation 18:603-608, 2015

17. Huang KT, Martin J, Marky A, Chagoya G, Hatef J, Hazzard MA, Thomas SM, Lokhnygina Y, Lad SP: A national survey of spinal cord stimulation trial-to-permanent conversion rates. Neuromodulation 18:133-139, 2015

18. Kapural L, Peterson E, Provenzano DA, Staats P: Clinical evidence for spinal cord stimulation for Failed Back Surgery Syndrome (FBSS): Systematic review. Spine (Phila Pa 1976) 42(Suppl 14):S61-S66, 2017

19. Kumar K, Buchser E, Linderoth B, Meglio M, Van Buyten JP: Avoiding complications from spinal cord stimulation: Practical recommendations from an international panel of experts. Neuromodulation 10:24-33, 2007

20. Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB: Spinal cord stimulation versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain 132:179-188, 2007

21. Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB: The effects of spinal cord stimulation in neuropathic pain are sustained: A 24-month follow-up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. Neurosurgery 63:762-770, 2008

22. Lee YY, Lin JL: Trust but verify: The interactive effects of trust and autonomy preferences on health outcomes. Health Care Anal 17:244-260, 2009

23. Lindhiem O, Bennett CB, Trentacosta CJ, McLear C: Client preferences affect treatment satisfaction, completion, and clinical outcome: A meta-analysis. Clin Psychol Rev 34:506-517, 2014

24. Matos M, Bernardes SF, Goubert L: The relationship between perceived promotion of autonomy/dependence and pain-related disability in older adults with chronic pain: The mediating role of self-reported physical functioning. J Behav Med 39:704-715, 2016

25. McCarron TL, MacKean G, Dowsett LE, Saini M, Clement F: Patients' experience with and perspectives on neuromodulation for pain: A systematic review of the qualitative research literature. Pain 161:1708-1715, 2020

26. Meglio M, Cioni B, Visocchi M, Tancredi A, Pentimalli L: Spinal cord stimulation in low back and leg pain. Stereotact Funct Neurosurg 62:263-266, 1994

27. Murphy KR, Han JL, Hussaini SM, Yang S, Parente B, Xie J, Lad SP: The volume-outcome effect: Impact on trial-to-permanent conversion rates in spinal cord stimulation. Neuromodulation 20:256-262, 2017

28. NICE. National Institute for Health and Care Excellence. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: Technology appraisal guidance [TA159]. 2008

29. Niyomsri S, Duarte RV, Eldabe S, Fiore G, Kopell BH, McNicol E, Taylor RS: A systematic review of economic evaluations reporting the cost-effectiveness of spinal cord stimulation. Value Health 23:656-665, 2020

30. North R, Desai MJ, Vangeneugden J, Raftopoulos C, Van Havenbergh T, Deruytter M, Remacle JM, Shipley J, Tan Y, Johnson MJ, Van den Abeele C, Rigoard P, Group PS: Postoperative Infections Associated With Prolonged Spinal Cord Stimulation Trial Duration (PROMISE RCT). Neuromodulation 23:620-625, 2020

31. Oakley JC, Krames ES, Stamatos J, Foster AM: Successful long-term outcomes of spinal cord stimulation despite limited pain relief during temporary trialing. Neuromodulation 11:66-73, 2008

32. Ostelo RW, Deyo RA, Stratford P, Waddell G, Croft P, Von Korff M, Bouter LM, de Vet HC: Interpreting change scores for pain and functional status in low back pain: Towards international consensus regarding minimal important change. *Spine (Phila Pa* 1976*)* 33:90-94, 2008

33. Pieterse AH, Stiggelbout AM, Montori VM: Shared decision making and the importance of time. JAMA 322:25-26, 2019

34. Provenzano DA, Falowski SM, Xia Y, Doth AH: Spinal cord stimulation infection rate and incremental annual expenditures: Results from a United States payer database. Neuromodulation 22:302-310, 2019

35. Schug SA, Lavand'homme P, Barke A, Korwisi B, Rief W, Treede RD, Pain ITftCoC: The IASP classification of chronic pain for ICD-11: Chronic postsurgical or posttraumatic pain. Pain 160:45-52, 2019

36. Simopoulos T, Sharma S, Aner M, Gill JS: A Temporary vs. permanent anchored percutaneous lead trial of spinal cord stimulation: A comparison of patient outcomes and adverse events. Neuromodulation 21:508-512, 2018

37. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM: A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol Med 27:363-370, 1997

38. Sullivan MJL, Bishop SR, Pivik J: The pain catastrophizing scale: Development and validation. Psychol Assessment 7:524-532, 1995

39. Taylor RS, Desai MJ, Rigoard P, Taylor RJ: Predictors of pain relief following spinal cord stimulation in chronic back and leg pain and failed back surgery syndrome: A systematic review and meta-regression analysis. Pain Pract 14:489-505, 2014

40. Thomson S: Failed back surgery syndrome - Definition, epidemiology and demographics. Br J Pain 7:56-59, 2013

41. Thomson SJ, Kruglov D, Duarte RV: A spinal cord stimulation service review from a single centre using a single manufacturer over a 7.5 year follow-up period. Neuromodulation 20:589-599, 2017

42. Vanderiet K, Adriaensen H, Carton H, Vertommen H: The McGill Pain Questionnaire constructed for the Dutch language (MPQ-DV). Preliminary data concerning reliability and validity. Pain 30:395-408, 1987

43. Verkes RJ, Vanderiet K, Vertommen H, Kloot WAvd: Meij Jvd: De MPQ-DLV: Een standaard Nederlandstalige versie van de McGill Pain Questionnaire voor België en Nederland. Swets Zeitlinger 57-78, 1989