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The impact of spinal cord stimulation on opioid utilization in failed back surgery syndrome and spinal surgery naïve patients

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ABSTRACT

Background: Spinal cord stimulation (SCS) has been utilized for failed back surgery syndrome (FBSS) with well-documented improvements in pain and function. However, limited studies have investigated the relationship between spinal surgery, SCS and opioid use outcomes.

Methods: A narrative review utilizing the scale for the quality assessment of narrative review articles (SANRA) methodology looking at trials involving SCS and opiates.

Results: Twenty-six studies met inclusion criteria. Surgery-naïve subjects had the greatest mean opioid dose reduction of 50.39% morphine milliequivalents, and the greatest number of patients who discontinued opioids at 53.72%. No statistical analysis was performed due to heterogeneous data.

Conclusion: SCS has a positive impact on opioid reduction, regardless of prior spinal surgical history. However, due to a lack of homogenous data, a formal conclusion comparing outcomes between spinal surgical histories cannot be drawn. There is an inherent difficulty in evaluating this topic given its complexity and multifactorial origin. Studies would require collaboration between pain physicians, societies and industry. Even then, patient biases such as psychological and expectation would be difficult to account for. This topic remains an ongoing challenge for interventional pain physicians.

1. Introduction

Chronic pain is one of the leading causes of disability worldwide. One-hundred million people in the United States live with chronic pain and healthcare costs approach $90 billion in services annually [1]. There are multiple etiologies of chronic low back (CLBP) and limb pain, most commonly spondylosis, spinal stenosis, radiculopathy, tumors, infections, and others [2]. Conservative treatment options such as physical therapy, medications, and interventional procedures are a common means for management, but the efficacy of these treatments varies due to diverse etiologies and heterogeneity in study designs. Limited conservative management outcomes increase the likelihood of surgical intervention [3]. An important cause of CLBP, failed back surgery syndrome (FBSS) is estimated to affect 10–40% of patients who undergo spinal surgery and unfortunately the etiology and pathophysiology is unclear in most cases [4]. Beginning in the late 1900s patients who failed conservative treatments usually ended up on chronic opioid therapy, a model initially developed to treat exclusively cancer related pain [5]. Long-term opioids have been associated to increase the risk of both addiction and overdose. Despite recent changes and heightened awareness, opioid over prescription, misuse, and harm remain a significant public health concern.

In 2015 roughly 240 million opioid prescriptions were filled in the United States. This has led to an increase in both the overall addiction as well as death rates from opioid abuse [6]. In 2015 a review found that 21–29% of prescription opioid users misused and 8–12% were addicted [7]. Unfortunately, in 2019 roughly 71,000 Americans died from opioid overdose [8]. Astoundingly, this number increased by more than 30% in some states during the COVID pandemic [9]. In addition to the aforementioned, opioid misuse has been shown to have a significant socioeconomic impact affecting both patients, hospitals, and health systems [10]. A systematic review and meta-analysis conducted by Busse et al., in

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2018 showed that for chronic non-cancer pain there was a decrease of only 0.79 on the 0–10 VAS scale for those who utilized opiates [11].

With the worsening opioid crisis, the Center for Disease Control (CDC) placed new guidelines in 2016 and adjusted the algorithm to reflect a more reasonable route allowing physicians to decide opioid versus intervention. This implementation started the shift away from prescription opiates and towards alternatives to reduce opioid use [12]. Presently, the CDC guidelines are being revised and updated again.

Spinal cord stimulation (SCS) has a documented history of treating CLBP, and recent technological advances in waveforms, programming, frequencies, and surgical techniques have improved the efficacy beyond early results, including overall healthcare cost reduction and utilization in chronic axial low back pain, in addition to neuropathic pain [13]. Despite this robust evidence, limited studies evaluate the impact of SCS on opioid use, particularly in FBSS subjects compared to spinal survey-naive subjects. Therefore, this review discusses the available evidence on the impact of SCS on opioid utilization in FBSS compared to spinal surgery naïve patients.

2. Methods

A comprehensive literature review was executed utilizing PubMed, Cochrane and CINAHL from 1/1/00 to 3/22/22. Search terms included "spinal cord stimulation" and "opioid" and "failed back surgery syndrome" and "low back pain". Manuscript eligibility included clinical studies with human subjects written in the English language, involving adult (age >18 years old) subjects who underwent SCS to treat CLBP, neuropathic lower limb pain from a spinal etiology (lumbar radiculopathy) and FBSS. All search results were screened for eligibility. Initial title review followed by abstract and full text review. Records not meeting inclusion criteria were excluded and all duplicates were removed. Exclusion criteria included conditions other than the aforementioned (such as neuropathic lower limb pain not of lumbar origin, diabetic peripheral neuropathy, CRPS, vascular and visceral pain, etc), case reports, case series, and studies not documenting outcomes associated to opioid use. Records meeting inclusion criteria were retained for final synthesis. To minimize missed studies, after the initial review the snowball strategy was employed, reviewing all references and citations. This review utilized the scale for the quality assessment of narrative review articles (SANRA) methodology to reduce selection bias and standardized

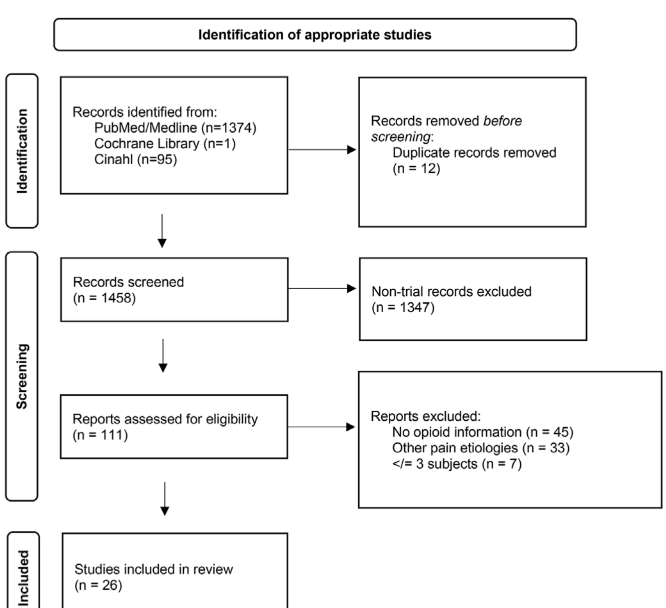

Fig. 1. Flow chart methodology for the identification, screening, eligibility and inclusion and exclusion process.

inclusion and exclusion criteria, which is outlined in Fig. 1. Due to a high level of heterogeneity among the studies reviewed, statistical analysis was restricted and secondary to the lack of standardization between outcome measurements and treatment groups, a meta-analysis was not performed. However, a narrative analysis was performed by breaking down studies into etiology, spinal surgical history and later analyzing opioid use among study participants. A total of 1470 studies were screened of which 12 were duplicates. After removal of duplicates, and inclusion and exclusion screening criteria, 26 studies were included. Data points associated to study design, number of subjects, follow-up interval, SCS indication, and opioid use outcomes were collected, and results were tabulated in Tables 1–4.

3. Results

3.1. Failed back surgery syndrome (FBSS)

We found 10 studies reporting opioid outcomes after SCS implantation associated to a history of FBSS, compromising a total of 564 subjects over a 6-to-36-month period with an average of 12 months follow-up. Of these, four were randomized controlled trials (RCTs) evaluating percutaneous versus paddle SCS placement, reoperation, and conservative management. Table 1 summarizes the studies key findings.

North *et al (2005)* completed the first randomized control trial involving 24 patients comparing paddle to percutaneous electrode SCS. At 36 months they reported an opioid dose reduction in 29% of subjects implanted with both percutaneous and paddle leads [14]. A follow-up study also conducted by North *et al (2005)* found that 87% of subjects in the SCS group reduced their opiates, in contrast to 58% in the reoperation group, including laminectomy, foraminotomy and/or discectomy with or without fusion or instrumentation. Of note, there was a small cohort who increased their opioid use, yet this was statistically significantly lower than those who underwent reoperation [15]. Similarly, Nissen *et al (2021)* and Rigoard *et al (2019)* found a slight increase dose of opioids among their small cohort of subjects, yet again these were found to be statistically significantly lower, when compared to the conservative management cohort [16,17].

Two other RCTs were completed by Kumar *et al* (*2007*) and Rigoard *et al* (*2019*) both comparing spinal cord stimulation to conservative medial management which included anything from mindfulness and therapies to injections. In both studies' exclusion criteria included surgery, other stimulators devices and intrathecal pumps. Both studies found clinically and statistically significant reduction in daily morphine milliequivalent (MME) dosing compared to conservative management at 6-month follow-up [17,21]. Additionally, Kumar *et al* (*2007*) found roughly one third of subjects stopped using opioids all together. This elimination rate was seen consistently throughout all studies reported (Table 1) [16,20,23].

The remaining smaller cohort studies reproduced the other RCT findings including MME dose reduction and opioid use reduction [18–20, 22]. Nissen *et al* (*2021*) compared opioid use in those with a successful SCS implant (>2 years without explanation) to those without a successful implant (explanted due to inadequate pain relief) and found a greater proportion of patient with a successful trial discontinued opioids.

The averaged combined opioid use reduction was 30.7% and elimination was 22.7%. There was also a 9.44% average reduction in daily MME, compared to conservative management or reoperation. (Table 2).

3.2. Non-specific surgical history

We found 11 studies with 825 subjects that underwent SCS placement for CLBP and/or neuropathic leg pain of spinal origin, however these studies did not account for a pre-existing lumbar surgical history; therefore, these were determined as studies with a non-specific surgical history. Of these, two were RCTs. Key summary findings were reported in Table 3.

Kapural *et al (2015)* completed the first RCT in this group comparing

Table 1
Studies evaluating spinal cord stimulation in failed back surgery patients and its relationship to opioid dosing and consumption.

Reference/year/ waveform	Design	(n)	Follow up	Baseline MME	Follow up MME	MME change p =	% patients who reduced (R)/ eliminated (E)
Nissen, 2021 (trad) [16]	P-SC	160 (SCS 131, Unsuccessful SCS 29)	24mo	SCS 30.2 Unsuccessful SCS 56.5	SCS 36 Unsuccessful SCS 82	0.001 (between)	SCS 23% E Unsuccessful SCS 0% E
Kallewaard, 2021 (HF) [23]	P-SC	60	12mo	NR	NR	NR	20% R 24% E
Dougherty, 2019 (NR) [19]	Review	85	12mo	NR	NR	NR	45.9% R
Simopoulos, 2019 (trad) [20]	Ret-SC	98	12mo	NR	NR	NR	20/98 (20%) E 11/98 (11%) R
Rigoard, 2019 (trad) [17]	P-MC-RCT (SCS vs CMM)	195 (SCS 78, CMM 117)	6mo	SCS 59.5 CMM 57.5	SCS 58.5 CMM 64.8	0.031 (between)	NR
Sanders, 2016 (trad) [22]	Ret-SC	81	12mo	62.73	34.75	0.01	NR
Rapcan 2015 (HF) [18]	P-SC	21	12mo	NR	NR	NR	65% R/E
Kumar, 2007 (trad) [21]	P-MC-RCT (SCS vs CMM)	59 (SCS 28, CMM 31)	6mo	SCS 139 CMM 214	SCS 68.3 CMM 96.9	0.21 (between)	SCS 8/28 (29%) E CMM 1/31 (3%) E
North, 2005 (trad) [15]	P–SC–RCT SCS vs re-operation	49 (SCS 23, re-op 26)	6mo	NR	NR	NR	SCS 87% R 13% increased Re-op 58% R 42% increased
North, 2005 (trad) [14]	P–SC–RCT (Paddle vs electrode)	24 (12 each)	36mo	NR	NR	NR	7/24 (29%) R

Legend: Trad - Traditional SCS HF - High frequency SCS P - prospective.
Ret – Retrospective SC - Single center MC - Multicenter.
CMM - Conservative medical management NR - Not reported R - Reduced E – Eliminated.

Table 2
Averaged results of the included studies.

Pain Syndrome	# Studies	n =	MME reduction (%)	#n patient Reduced (%)	#n patients Eliminated (%)
FBSS	10	564	9.44	30.68	22.7
Non-specific surgical hx	11	825	33.3	47.15	29.33
Surgery Naive	5	76	50.39	36.49	53.72
All low back	26	1437	27.5	40.35	28.81

traditional to high-frequency SCS. At 12 months they found one third of all subjects had reduced their opioids. In addition, there was a statistically significant reduction in daily MME in the high-frequency group compared to the traditional SCS arm [24]. Mekhail *et al (2020)* completed a second RCT comparing open to closed-loop SCS and found that nearly half of all subjects reduced or eliminated their opioid use at the 12-month follow-up [25].

D'Souza *et al* (*2021*) performed a Post Hoc analysis of the SUNBURST (success using neuromodulation with BURST SCS) trial [27]. The SUNBURST trial involved 100 subjects who underwent either burst or tonic SCS then crossed over at 12 weeks. After the crossover period (24 weeks) subjects could choose their preferred method and continue this for 1 year [44]. The studies focus was on safety and efficacy but did have data on opioid use on 69 total patients. At 1 year follow up D'Souza found a significant reduction in MME for all patients in both groups. In addition, nearly half of all patients reduced their opiates and 16% discontinued them all together. Further breakdown of these rates based on stimulation pattern was not completed. Like previously mentioned studies a small subset had increased their opioid use as well [27]. Di-Benedetto *et al* (*2018*) was the only other study to perform statistical analysis on the change in MME and they found a statistically significant reduction from baseline [32].

There was variability amongst the remaining studies in terms of cohort size, follow up and outcome measures however some trends did appear. This included a large proportion of patients throughout the trials having reduced or eliminated their opiates [32,34]. For the studies that reported on opioid discontinuation rates there was a trimodal finding that roughly one fifth, one third or one half of patients stopped using opiates [26,28–31,33] (Table 3).

Among all studies reviewed, the averaged data for percentage of patients that reduced opioid use was 47.15% and eliminated 29.33%. There was also an average 33% significant reduction in daily MME opioid dose in the combined studies (Table 2). It should be noted that Rapcan, Kapural, Mekhail, Russo and Di Benedetto did not delineate between those that had reduced and those that had eliminated opiates and instead combined the two percentages. Thus, these were not included in final synthesis when obtaining the averages documented in Table 2.

3.3. Surgery naive

We found four studies involving SCS reporting opioid outcomes in subjects without a history of lumbar spine surgery, denominated as surgery naïve, totaling 76 patients over 12 months. Key findings are summarized on Table 4.

Vallejo *et al (2012)* conducted the only comparative study evaluating SCS compared to medical management including pharmacotherapy and physical therapy. They found a statistically significant reduction in opioid dosing at 12-months in the SCS cohort, and a statistically significant increase in opioids for those not in the SCS cohort [35]. Of the other reported cohorts 2 performed statistical analysis on the change in opioid dosing. They both found statistically significant reductions in opioid doses for those who underwent SCS [36,37]. This was consistent with what Vallejo reported. There was again appreciable variability throughout the remaining studies in terms of reductions and eliminations. However three of the four studies did report a >50% discontinuation rate for opioids in their trials [36,38,39] (Table 4). When combining data from the above-cited studies, there was an averaged

Table 3
Studies evaluating spinal cord stimulation in patients with an unspecified spinal surgery history and its relationship to opioid dosing and consumption.

Reference/year/waveform	Design	(n)	Follow up	Baseline MME	Follow up MME	MME change p =	% Patients who reduced (R)/eliminated (E)
Feng, 2021 (HF) [31]	Ret-SC	37	0–48mo	83.7	35.5	NR	48% E
Falowski, 2021 (burst) [30]	P-MC	159	12mo	49.7	37	NR	19% E 57% R
D'Souza, 2021 (burst, trad) [27]	Post Hoc (SUNBURST)	69 (45 burst, 24 tonic	12mo	All 79.19 Tonic 131.28 Burst 68.83	All 53.94 Tonic 76.3 Burst 55.23	All 0.008 Tonic >0.05 Burst >0.05	15.9% E 50.7% R 17.4% increased
Lucia, 2021 (burst, trad) [29]	P-SC	10	3mo	NR	NR	NR	20% E
Russo, 2020 (evoke) [34]	P-MC (Avalon)	50	12mo	62.9	32.3	NR	68.8% R/E
Mekhail, 2020 (evoke) [25]	MC-RCT-DB (closed vs. open)	118	12mo	Closed 80.1 Open 66.4	Closed 45 Open 44.5	0.72 (between)	Closed 55% R/E Open 40% R/E
Gee, 2019 (Trad) [33]	P-SC	53	12mo	NR	NR	NR	26/53 (49%) E 2/53 (4%) R
Di-Benedetto, 2018 (HF) [32]	Ret-SC	21	12mo	92.2	66	0.001	71.4% R/E
Kapural, 2015 (HF) [24]	P-MC-RCT	171 (HF 90, trad 81)	12mo	HF 112.7 Trad 125.3	HF 87.9 Trad 118	0.014 (between)	HF 35.5% R/E Trad 26.4% R/E
Al-Kaisy, 2014 (HF) [26]	P-MC	65	24mo	84	27	0.001	38% R 34% E
Van Buyten, 2013 (HF) [28]	P-MC	72	6mo	NR	NR	NR	62% R 38% E

Legend: Trad - Traditional SCS HF - High frequency SCS P - prospective.
Ret – Retrospective SC - Single center MC - Multicenter.
CMM - Conservative medical management NR - Not reported R - Reduced E – Eliminated.

Table 4
Studies evaluating spinal cord stimulation in surgery naive patients and its relationship to opioid dosing and consumption.

Reference/year/waveform	Design	(n)	Follow up	Baseline MME	Follow up MME	MME change p =	% patients who reduced (R)/eliminated (E)
Mehta, 2021 (HF) [37]	P-SC	16	12mo	10.68	7.75	0.07	3/16 (19%) E 7/16 (44%) R
Baranidharan, 2020 (HF) [36]	P-MC	14	12mo	50.71	31.79	0.018	6/14 (43%) E 1/14 (7%) R
Al-Kaisy, 2018 (HF) [39]	P-SC	17	36mo	112	40	NR	89% E
Al-Kaisy, 2017 (HF) [38]	P-SC	20	12mo	112	40	NR	59% E
Vallejo, 2012 (trad) [35]	P-SC (SCS vs CMM)	SCS 9 CMM 4	12mo	SCS 46.1 CMM 30	SCS 18.1 CMM 46.3	SCS 0.036 CMM 0.001	SCS 69% R CMM 54% increased

Legend: Trad - Traditional SCS HF - High frequency SCS P - prospective.
Ret – Retrospective SC - Single center MC - Multicenter.
CMM - Conservative medical management NR - Not reported R - Reduced E – Eliminated.

opioid use reduction of 36.49%, 53.72% elimination and 50.39% daily MME decrease in surgery-naive subjects who underwent SCS (Table 2).

4. Discussion

Our review suggests reductions in opioid use regardless of surgical history. However, it also points to the inherent challenges and difficulties within this topic itself.

Though statistical analysis was not performed, and the data was heterogeneous our averaged reduction and elimination rates for FBSS did coincide closely with other larger scale studies. Adil *et al* (*2020*) conducted a review of 8500 subjects who underwent SCS, of whom 46.4% had a diagnosis of FBSS. Similarly, they found opioid use reductions in 34.2% and eliminations in 17% of subjects at one year [40]. In addition to the above, Eckermann *et al* (*2021*) conducted a systematic review focusing on the impact of SCS in surgery naive patients and found similar elimination rates ours. They found 41.7% of patients eliminated their opioids at 12 months [42]. Lastly, Fraifeld *et al* (*2021*) conducted a large epidemiological study involving 5878 patients evaluating SCS impact and opioid use in conjunction with overall healthcare cost. Their primary finding was a healthcare cost breakeven point of 3.1 years. Their secondary endpoint showed of the 5878 patients 20% had large reductions (>50%) in opioid use (22%) stopped use all together [46]. However, even though our data and above studies do coincide. since this review is limited no formal correlations can be made.

Additionally, important opioid use data can be seen in the following studies conducted by Smith, Nissen, Sharan and Vu. Smith *et al (2022)* reported a positive impact of SCS on curbing opioid use at 12 months, again regardless the surgical history. Interestingly the study found a direct correlation between patients who have a preimplantation average opioid dose of 20–42.5 MME and post-implantation opioid elimination, as compared to other preimplantation opioid doses [41]. This was also seen in Nissen's *et al* (*2021*) study in which through analysis they determined the ideal cutoff for improvement was 35MME [16]. This is an important correlation because as seen by Sharan's *et al* (*2018*) review investigating the impact of pre-implant opioid use and the rate of explanation; escalating opioid dosages or higher pre-implant doses are correlated with an increased risk of explanation [45]. Lastly Vu *et al (2022)* conducted a large analysis study which involved more than 500, 000 subjects with a diagnosis of FBSS who underwent SCS compared to medical management. They reported that subjects in the SCS cohort were associated with an increased likelihood of not being on opioids, both in the opioid-naive ($p = 0.001$) and the chronic opioid use cohort ($p = 0.02$), findings that were statistically significant at 12 months [43].

The above studies in conjunction with our reported data help tie together the possible impact of surgical history, opioid use, and spinal cord stimulation. Though there is robust data to support SCS and its positive impact on opioid use, many of the reviews are low quality and obtain data from prior studies or historical logs. The question this review aims to address is multi-faceted and very complex. More formal and standardized studies need to be complete in order to fully evaluate this topic.

5. Limitations

Our study has both inherent and technical limitations. This topic is particularly difficult to evaluate given then lack of sham control studies and overall complexity of the problem it aims to address. For example, once implanted clinicians may require patients to reduce opioids more so than those that have not had an intervention. Patients may also have a bias that because they had an intervention their pain should be better and therefore; they should reduce their opioids. On the other hand, patients may have psychological dependence on opioids and opt to remain on their current opioid dose despite actual pain improvement or they may even refrain from enrolling in a study in the first place further introducing bias. Lastly, studies funded by industry usually have inherent bias towards their product. Technical limitations included heterogenous data amongst the studies requiring averaging of the data but the inability to perform metanalysis. Furthermore, it is prudent to comment on the limitations of generalizability in the setting of our narrative review. Although we followed the SANRA methodology, due to the high level of heterogenicity, further statistical analysis and a systematic review was limited given the lack of standardization between reported outcomes among the studies included. The high level of heterogenicity among studies also raise potential cofounders and variables, such as changes to opiates before or after the SCS implant, duration of chronic opiate use, dosing during that time, past medical history, and variables associated with prior lumbar surgical history that could affect opioid-related outcomes.

6. Conclusion

Spinal cord stimulation has a positive impact on opioid use, regardless of prior spinal surgical history. However, given the lack of high-quality evidence, statistical analysis and homogeneity between the studies, drawing a more definitive conclusion is not appropriate. Most importantly this review points to the lack of sham-control and level one studies evaluating this specific problem. This is likely due to the complexity, inherent challenges and multifaceted origin of the topic itself. Evaluating the association between prior spinal surgical history, SCS and opioid use would require very specific protocols and controls. This would likely involve a collaborative effort from physicians, societies and industry. This topic remains an ongoing challenge for pain physicians.

7. Practice points

- SCS has a positive impact on opioid use, regardless of prior spinal surgical history.
- These findings may suggest a benefit from earlier implementation of spinal cord stimulation in the pain management algorithm.
- There is a lack of sham-control and level one studies evaluating the true association between spinal surgery history, SCS and opioid utilization. This is a multifaceted and very complex problem in pain medicine that requires a collaborative effort from physicians, pain societies and industry; therefore, further studies are needed to firmly address this gap in the current literature.

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