JNS SPINE

CLINICAL ARTICLE

Durable responses at 24 months with high-frequency spinal cord stimulation for nonsurgical refractory back pain

Naresh P. Patel, MD,[1] Jessica Jameson, MD,[2] Curtis Johnson, MD,[3] Daniel Kloster, MD,[4] Aaron Calodney, MD,[5] Peter Kosek, MD,[6] Julie Pilitsis, MD, PhD,[7] Markus Bendel, MD,[8] Erika Petersen, MD,[9] Chengyuan Wu, MD, MSBmE,[10] Taissa Cherry, MD,[11] Shivanand Lad, MD, PhD,[12] Cong Yu, MD,[13] Dawood Sayed, MD,[14] Johnathan Goree, MD,[9] Mark K. Lyons, MD,[1] Andrew Sack, MD,[14] Diana Bruce, DMS, PA-C,[11] Manish Bharara, PhD,[15] Rose Province-Azalde, MSBmE,[15] David Caraway, MD, PhD,[15] and Leonardo Kapural, MD, PhD[16]

[1]Department of Neurosurgery, Mayo Clinic, Phoenix, Arizona; [2]Axis Spine Center, Coeur d'Alene, Idaho; [3]Midwest Pain Management Center, Overland Park, Kansas; [4]Crimson Pain Management, Overland Park, Kansas; [5]Texas Spine and Joint Hospital, Tyler, Texas; [6]Oregon Neurosurgery Specialists, Springfield, Oregon; [7]Department of Neurosurgery, Albany Medical Center, Albany, New York; [8]Department of Pain Management, Mayo Clinic, Rochester, Minnesota; [9]Department of Neurosurgery, University of Arkansas for Medical Sciences, Little Rock, Arkansas; [10]Department of Neurosurgery, Thomas Jefferson University Hospitals, Philadelphia, Pennsylvania; [11]Department of Pain Management, Kaiser Permanente, Redwood City, California; [12]Department of Neurosurgery, Duke University Medical Center, Durham, North Carolina; [13]Swedish Health Services, Seattle, Washington; [14]Department of Pain Management, University of Kansas Hospital, Kansas City, Kansas; [15]Clinical Research, Nevro Corp., Redwood City, California; and [16]Carolinas Pain Institute, Winston-Salem, North Carolina

OBJECTIVE The objective of this study was to evaluate the 24-month durability of pain relief, function, quality of life, and safety outcomes for patients with nonsurgical refractory back pain (NSRBP) treated with high-frequency spinal cord stimulation (SCS) within a large, national, multicenter randomized controlled trial (RCT).

METHODS Following the completion of an RCT comparing high-frequency SCS plus CMM with CMM alone for the treatment of NSRBP, patients gave additional consent for a follow-up extension to 24 months. Presented is the cohort analysis of all patients treated with high-frequency SCS following the optional crossover at 6 months. The outcomes assessed to 24 months included responder rate of ≥ 50% pain relief measured according to the visual analog scale [VAS]), disability (Oswestry Disability Index [ODI]), quality of life (EQ-5D 5-level [EQ-5D-5L]), opioid reduction.

RESULTS Of the 125 patients who received a permanent implant, 121 completed the 12-month follow-up, 101 gave additional consent for extended follow-up, and 98 completed the 24-month follow-up. At 24 months after implantation, the mean back pain VAS score was reduced by 73% and the responder rate was 82%. ODI and EQ-5D-5L both improved by at least double the minimal clinically important difference for each measure. No unexpected adverse events were observed, and the rates of serious adverse events (3.4%) and device explantations (4.8%) were low.

CONCLUSIONS The addition of high-frequency SCS to CMM in patients with NSRBP offers profound improvements at 24 months in pain, function, quality of life, and reduced opioid use. This study provides much-needed evidence to inform current clinical practice for managing patients with NSRBP.

Clinical trial registration no.: NCT03680846 (ClinicalTrials.gov)

https://thejns.org/doi/abs/10.3171/2023.9.SPINE23504

KEYWORDS back pain; nonsurgical refractory back pain; chronic low-back pain; pain management; spinal cord stimulation; 10-kHz SCS; high-frequency SCS

ABBREVIATIONS AE = adverse event; CLBP = chronic low-back pain; CMM = conventional medical management; LOCF = last observation carried forward; MCID = minimal clinically important difference; MME = morphine milligram equivalents; NSRP = nonsurgical refractory back pain; ODI = Oswestry Disability Index; PGIC = Patient-Reported Global Impression of Change; PI = permanent implant; RCT = randomized controlled trial; SAE = serious AE; SCS = spinal cord stimulation; VAS = visual analog scale.

SUBMITTED May 8, 2023. **ACCEPTED** September 5, 2023.
INCLUDE WHEN CITING Published online November 17, 2023; DOI: 10.3171/2023.9.SPINE23504.

Chronic low-back pain (CLBP) is a leading cause of disability worldwide and affects an estimated 13% of adults in the United States.[1,2] CLBP is associated with increased patient comorbidities and has detrimental effects on mental health and quality of life and is one of the most common reasons for patients seeking healthcare across a range of medical specialties, including primary and emergency care.[3,4] It also exacts a substantial societal burden stemming from direct costs associated with increased healthcare utilization and indirect costs related to lost productivity.[2]

Treating CLBP presents challenges due to multifactorial etiologies and its frequently refractory nature.[5] Current clinical guidelines recommend a range of conventional medical management (CMM) strategies, often prescribed by primary care providers, that include physical therapies, oral medication trials, and pain management procedures.[6,7] Spine surgery becomes an option when CLBP presents with an identifiable etiology and surgical target; however, many patients present with nonspecific CLBP not amenable to surgical intervention.[8] Nonsurgical refractory back pain (NSRBP) describes chronic back pain refractory to CMM in patients with no history of spine surgery who are not acceptable candidates for spine surgery.[9] These patients often do not achieve therapeutic goals with nonoperative medical management, leaving physicians and patients with few options, which can lead to escalating use of opioids and their associated risks and detriment to quality of life.[10]

Spinal cord stimulation (SCS) is a well-established treatment for chronic pain conditions including refractory CLBP in the setting of failed spine surgery. However, this is yet to be demonstrated in a randomized controlled trial (RCT) specific to the surgery-naive patient population.[5,11,12] A recent systematic review identified 10 primary studies in 357 surgery-naive patients with back pain that consistently demonstrated improved pain, function, and quality of life with SCS treatment.[12] While mostly small, observational, single-arm studies, they supported SCS as a potential option for surgery-naïve patients.[12–15]

To address the small patient numbers studied and the lack of comparative effectiveness data, we designed a national, multicenter RCT to evaluate the efficacy and cost-effectiveness of high-frequency SCS plus CMM compared with CMM alone in a large cohort of patients with NSRBP.[9] The initial efficacy, safety, and cost-effectiveness outcomes have been reported previously.[16,17] Here, we present 24-month follow-up data in all patients who received treatment with high-frequency SCS and discuss the future of SCS in current clinical management paradigms for NSRBP.

Methods

Study Design

The design of this multicenter RCT has been published previously,[9] with the trial protocol registered prior to patient enrollment (identifier no. NCT03680846, ClinicalTrials.gov). Protocol and reporting followed CONSORT guidelines and included outcomes were consistent with IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) guidelines.

Patients diagnosed with chronic, neuropathic, axial, low-back pain refractory to CMM with no previous spine surgery who were deemed unsuitable candidates for spine surgery as assessed by a spine surgeon were eligible for inclusion. The important elements of the inclusion were refractory pain defined based on a published guideline[18] and the requirement of an MRI-based diagnosis and evaluation by a spine surgeon. Data collected during screening included the painDETECT questionnaire that was designed to evaluate the predominance of neuropathic pain and was available to aid the investigator in making that clinical assessment.[19] Patients who met all eligibility criteria (Supplementary Table 1) were randomized 1:1 to CMM alone or high-frequency SCS plus CMM. The contraindications for the surgical implantation of the high-frequency SCS system according to the physician's manual included patients who are poor SCS surgical candidates including those with hemoglobin A1c > 10%, those who do not receive effective pain relief during trial stimulation, and patients who are unable to operate the SCS system.

CMM was the best standard of care as determined by the study investigator for each individual patient, consistent with American College of Physicians and American Pain Society clinical guidelines and American Society of Interventional Pain Physicians management guidelines.

Patients randomized to high-frequency SCS underwent trial stimulation of up to 14 days using percutaneous leads placed in the epidural space at the T8–11 vertebral levels. Paresthesia-free stimulation was delivered at a 10-kHz frequency with pulse width of 30 μsec and current amplitude adjusted to maximize pain relief. Patients with a successful trial (defined as ≥ 50% pain relief) were eligible for permanent SCS implantation (Senza, Nevro Corp.).

Patients were assessed at baseline and follow-up visits for 12 months after permanent implantation. The primary endpoint was responder rate (≥ 50% pain relief) at 3 months. Hierarchical secondary endpoints evaluated improvements in disability, pain intensity, function, quality of life, and opioid medication usage at 6 months. Adverse events (AEs) were assessed at all visits. Optional crossover was available for both arms after 6 months. Patients with a permanent implant (both original group and crossovers) who completed the original 12-month study were eligible for continued follow-up through 24 months after providing additional written informed consent.

Outcomes

Patient outcomes were assessed through 24 months after permanent implantation. Pain relief was measured using a 10-cm visual analog scale (VAS), with response defined as ≥ 50% pain relief, a threshold typically used as the efficacy standard for SCS studies.[14,20,21] Disability was assessed using the Oswestry Disability Index (ODI), with response defined as ≥ 10-point improvement in ODI score, which represents the minimal clinically important difference (MCID).[22] Health-related quality of life was assessed using the EQ-5D 5-level (EQ-5D-5L) instrument score, which evaluates changes across mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[23] EQ-5D-5L MCID varies with disease state and patient population; we used the upper end of the estimated range of 0.037– 0.069

for analysis.[24] Patient satisfaction with treatment was assessed using the Patient-Reported Global Impression of Change (PGIC). Changes in opioid use from baseline were recorded in patients who were taking opioids at baseline.

Analyses

As previously described, the original study sample size calculation was based on an assumption that 60% of the treated group and 36% of the control group would meet the primary endpoint of at least 50% pain relief at 3 months.[9] The primary endpoint was assessed in both the intent-to-treat population and per-protocol population defined as only patients who completed the visit pertaining to the endpoint. The 6- and 12-month endpoints were assessed in the per-protocol population. The analysis population for 24-month follow-up included all patients who received permanent SCS implantation, termed the permanent implant (PI) subgroup. The PI subgroup responder rates were calculated using two imputation methods for missing 24-month VAS back pain scores: multiple imputation using nonmissing scores at other time points and last observation carried forward (LOCF) using the score from the last visit attended. Results from the two analyses, and the tipping point analysis performed, are presented in Supplementary Table 2 and Supplementary Fig. 1. We report results from the LOCF imputation analysis because it produced the most conservative responder rates. Responder rates are also reported using complete case analysis, which includes all reported outcomes at each time point. Responder rates are presented with 95% Wilson score confidence intervals. Changes in pain, disability, quality of life, and PGIC were analyzed in the PI subgroup using LOCF imputation for missing values. The mean change and the 95% CI for the mean change from baseline at each visit were calculated, and the p value from a paired t-test is reported. When analyzing the proportion of minimally disabled patients (ODI ≤ 20) and severely disabled patients (ODI ≥ 41) at baseline and 24 months, Wilson score confidence intervals are used for the proportions at each time point. McNemar's test is used to test for a difference in proportions at the two timepoints. A p value < 0.05 was considered statistically significant.

Results

Patient Disposition

Patient enrollment began September 5, 2018, with 159 patients meeting the eligibility criteria randomized to high-frequency SCS plus CMM (n = 83) or CMM (n = 76). Of patients randomized to high-frequency SCS, 74 of 80 underwent successful trial stimulation, and 69 received a permanent implant. Specific reasons for not undergoing implantation after the trial have been published in detail (Fig. 1).[16] At 6 months, no patients randomized to high-frequency SCS elected to cross over to CMM, while 65 of the 75 patients randomized to CMM elected to cross over to high-frequency SCS. Of those, 61 underwent successful trial stimulation and 56 received a permanent implant. A total of 125 patients received a permanent implant, with 121 completing the 12-month follow-up,[16] 101 consenting to the 24-month follow-up, and 98 completing the 24-month follow-up (Fig. 1). The final visit was completed on November 18, 2022.

Patient Demographics and Baseline Characteristics

At baseline, all patients had CLBP, with a median of 8 years since diagnosis; 61% also had leg pain (details described previously[16] and summarized in Table 1, with the randomized groups similar in terms of all recorded baseline characteristics). Patients presented with multiple pain etiologies, most commonly degenerative disc disease and spondylosis. All patients had previously tried at least one therapy to manage CLBP, with physical therapy and/or injections (e.g., epidural injections, nerve root blocks, and facet injections) tried by > 90% of patients before the study (Supplementary Table 3).

12-Month Outcomes

Outcomes through to 12 months have been reported previously.[16] Briefly, the responder rate at 3 months was significantly higher for high-frequency SCS (80.9%) versus CMM alone (1.3%, p < 0.001; primary outcome), with similar responder rates in both groups at 6 months (80% and 2.7% for the high-frequency SCS and CMM alone groups, respectively). All secondary endpoints were achieved at 6 months. Patient-reported back pain (according to the VAS) was reduced by 72% ± 32% at 6 months in the high-frequency SCS group versus a mean increase of 6% ± 21.7% in the CMM-alone group (p < 0.001). A 10-point ODI improvement was achieved in 79% of patients at 6 months in the high-frequency group versus 4% of the CMM-alone group (p < 0.001). A PGIC improvement of "better" or "a great deal better" was reported by 71% of the high-frequency group compared with 1.3% of the CMM alone group (p < 0.001). Similarly, the EQ-5D-5L utility index increased by 0.201 ± 0.136 in the treatment group, and the mean daily opioid dose was reduced by 17.7 ± 27.0 morphine milligram equivalents (MME) with no change in the CMM alone group (p < 0.001).

24-Month Outcomes

Pain Relief

In the PI subgroup (n = 125), the mean VAS back pain score was significantly decreased from 7.4 at baseline to 2.2 at 3 months after implantation (70% reduction; p < 0.001) and maintained at 6 and 12 months after implantation (p < 0.001 vs baseline). The mean VAS back pain score at 24 months after implantation was 1.9, representing a 5.5-point (74%) reduction from baseline (p < 0.001; Fig. 2A). The mean VAS leg pain score at 24 months was 2.0, representing a 71% reduction from baseline (p < 0.001). The responder rate was 79.2% at 3 months after implantation and was maintained for the duration of the study (Fig. 2A). Overall, 81.6% of all patients who received a PI were classified as pain responders (achieved ≥ 50% pain relief) at 24 months, with 58.4% of all patients classified as profound responders who achieved ≥ 80% pain relief (Fig. 2B). In the complete case analysis (n = 98), the responder rate at 24 months was 87.8%.

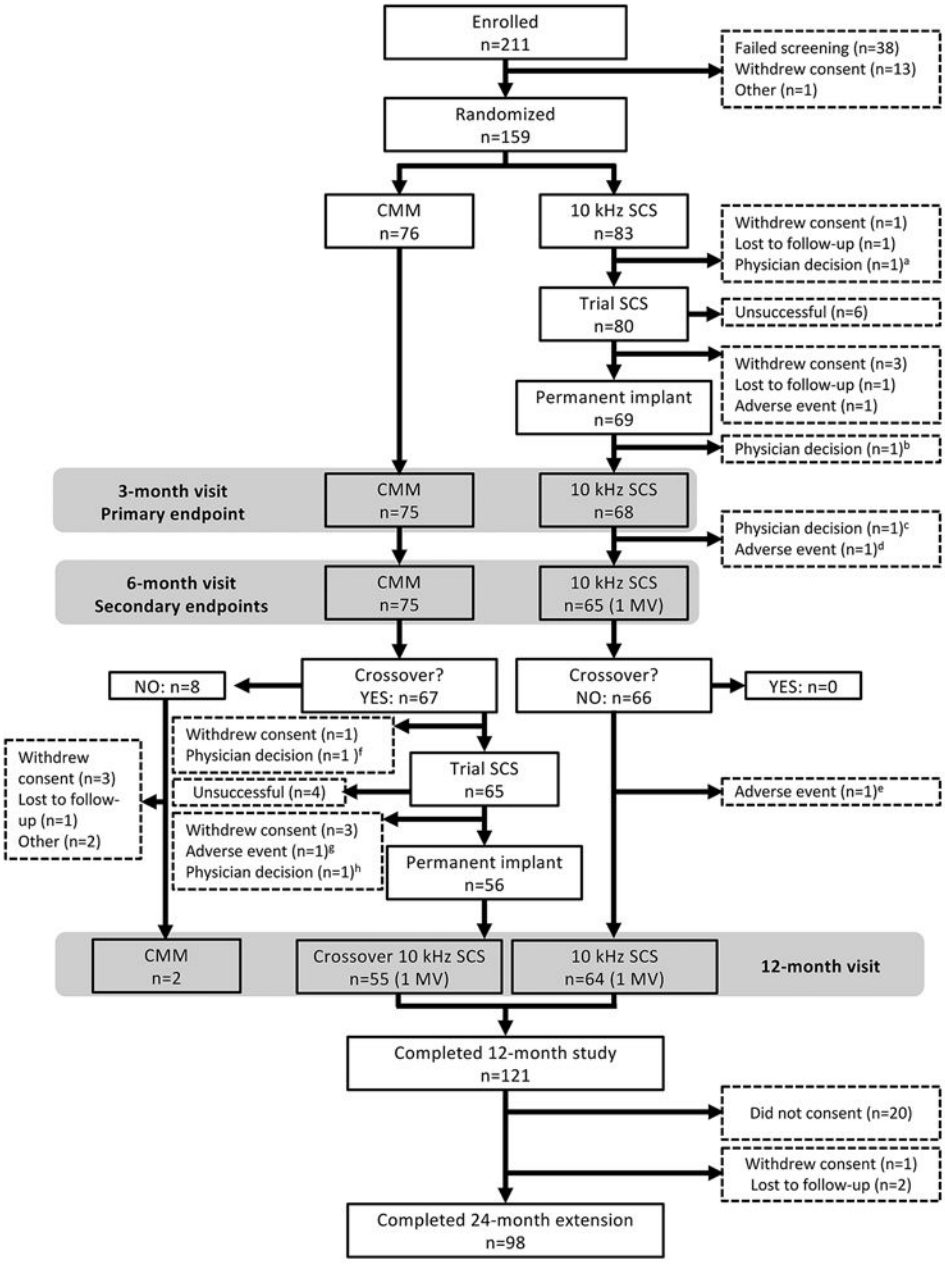

FIG. 1. Disposition of patients participating in the 12-month crossover RCT and the 24-month extension study. MV = missed visit. [a]Concern about COVID-19 risk due to older age and multiple comorbidities. [b]Diagnosis of ruptured discs; study exit to seek surgical interventions. [c]Diagnosis of cervical myelopathy and subsequent cervical spine surgery. [d]Subject experienced increased pain during stimulation. [e]Explant due to infection. [f]Patient required hip surgery. [g]Fall due to increased leg weakness. [h]Perceived risk due to comorbidity.

Disability

In the PI population, the mean ODI score was significantly decreased from 47 at baseline to 26 at 3 months after implantation; this 20-point reduction was maintained through 24 months after implantation ($p < 0.001$ vs baseline for all time points; Fig. 3A). At baseline, 73% of patients reported severe levels of disability (defined as an ODI score 41–60), with only 1% reporting minimal levels of disability (defined as an ODI score 0–20). At 3 months after permanent implantation, the proportion of patients reporting severe disability decreased to 19%, while the proportion reporting minimal levels of disability increased to 46%. These improvements were maintained through 24 months ($p < 0.001$ vs baseline for all time points; Fig. 3B). Overall, 75.2% of patients were classified as ODI responders, achieving ≥ 10-point improvement in ODI score, which represents an MCID (Fig. 3C).

Quality of Life

In the PI subgroup, the mean EQ-5D-5L score was

TABLE 1. Patient demographics and baseline clinical characteristics of the original randomized cohort

	CMM (n = 76)	10-kHz SCS (n = 83)	p Value
Age in yrs, median (range)	58.5 (26.0–77.0)	53.0 (29.0–87.0)	0.364
F/M sex, n	40:36	50:33	0.496
Yrs since diagnosis of CLBP, median (range)	8.00 (1.0–59.0)	8.50 (0.0–52.0)	0.986
Back pain VAS score			0.333
Mean (SD)	7.2 (1.0)	7.4 (1.2)	
Median (range)	7.2 (4.5–9.9)	7.6 (4.0–10.0)	
Baseline leg pain present, n (%)*	45 (59.2)	52 (62.7)	0.745
Pain etiology, n (%)†			
Degenerative disc disease	52 (68.4)	60 (72.3)	0.493
Internal disc disruption/annular tear	6 (7.9)	8 (9.6)	
Spondylosis	49 (64.5)	55 (66.3)	0.975
Lumbar facet-mediated pain	25 (32.9)	24 (28.9)	
Radiculopathy	35 (46.1)	34 (41.0)	0.527
Mild/moderate spinal stenosis	24 (31.6)	23 (27.7)	0.607
Spondylolisthesis	9 (11.8)	7 (8.4)	0.488
Sacroiliac dysfunction	5 (6.6)	3 (3.6)	0.481
Total painDETECT score‡			
Mean (SD)	17.2 (7.4)	17.8 (6.9)	0.577
Median, range	17.5 (0.0–37.0)	18.0 (1.0–33.0)	
Nonsurgical candidate reason, n (%)			0.868
Not a good surgical candidate based on presentation & underlying pathology	61 (80.3)	65 (78.3)	
Candidate for surgery but declined	10 (13.2)	11 (13.3)	
Not recommended due to moderate to high surgical risk related to comorbidities or other clinical conditions (e.g., smoking, obesity, chronic heart failure)	5 (6.6)	6 (7.2)	

CLBP = chronic low back pain; CMM = conventional medical management; SCS = spinal cord stimulation; VAS = visual analog scale.

* Only patients with a left or right lower limb baseline pain score ≥ 5 included.

† Patients may have more than one pain etiology.

‡ The painDETECT is a patient-reported assessment of neuropathic pain; scores range from −1 to 38, with scores ≥ 19 indicating likelihood (> 90% probability) of neuropathic pain.

significantly increased from 0.570 at baseline to 0.766 at 3 months after implantation ($p < 0.001$). This 0.19-point improvement was maintained at 6, 12, 18, and 24 months after implantation ($p < 0.001$ vs baseline at all time points; Fig. 3D). At each time point, the average change in the EQ-5D-5L score was ≥ 2.5 times greater than the MCID of 0.069 points (Fig. 3E).

High levels of patient satisfaction were recorded at 24 months, with 76% of patients reporting that their condition was "better" or "a great deal better" on PGIC (data not shown). Of the 98 patients who completed the 24-month visit, 45 reported using opioids during the study. Opioid use was decrease or stopped in 28 (62%) of these 45 patients, with the mean dose in the PI subgroup decreasing from 35 ± 39 MME at baseline to 15 ± 35 MME at 24 months (data not shown).

Safety

Five study-related serious adverse events (SAEs) were reported during 12-month follow-up, including implant site infection, poor wound healing, postimplant narcotic-induced lethargy, and osteomyelitis (Supplementary Table 4).[16] No further study-related SAEs occurred between 12 and 24 months. Fifty-one study-related AEs were reported during 24-month follow-up, and all but 6 occurred in the first 6 months after permanent implantation. Study-related AEs and their management and outcome are described in Supplementary Table 5.

Over the entirety of the 24-month observation 6 (4.8%) of 125 explantations were performed. Three of the explantations were due to patient dissatisfaction with SCS therapy (2.4%) and 3 because of infection (2 of these patients received a replacement device). Surgical revisions were required in 15 (12%) of 125 patients: 5 for lead dislodgment, 5 because of pain at the implantable pulse generator site, 1 for pain at the lead anchors, and 4 for lead repositioning to address inadequate pain relief.

Discussion

Evidence for high-frequency (10-kHz) SCS in treating refractory CLBP is well established,[20,21,25,26] although generalizability to surgery-naive patients has only recently been addressed.[12–15] We previously reported profound improvements in pain, function, and quality of life in patients with NSRBP treated with high-frequency SCS plus CMM versus CMM alone, representing the first RCT in a large NSRBP population.[16] Here, we present the 24-month outcomes, demonstrating durability of responses across patients treated with high-frequency SCS in addition to CMM.

Most patients maintained a clinically significant re-

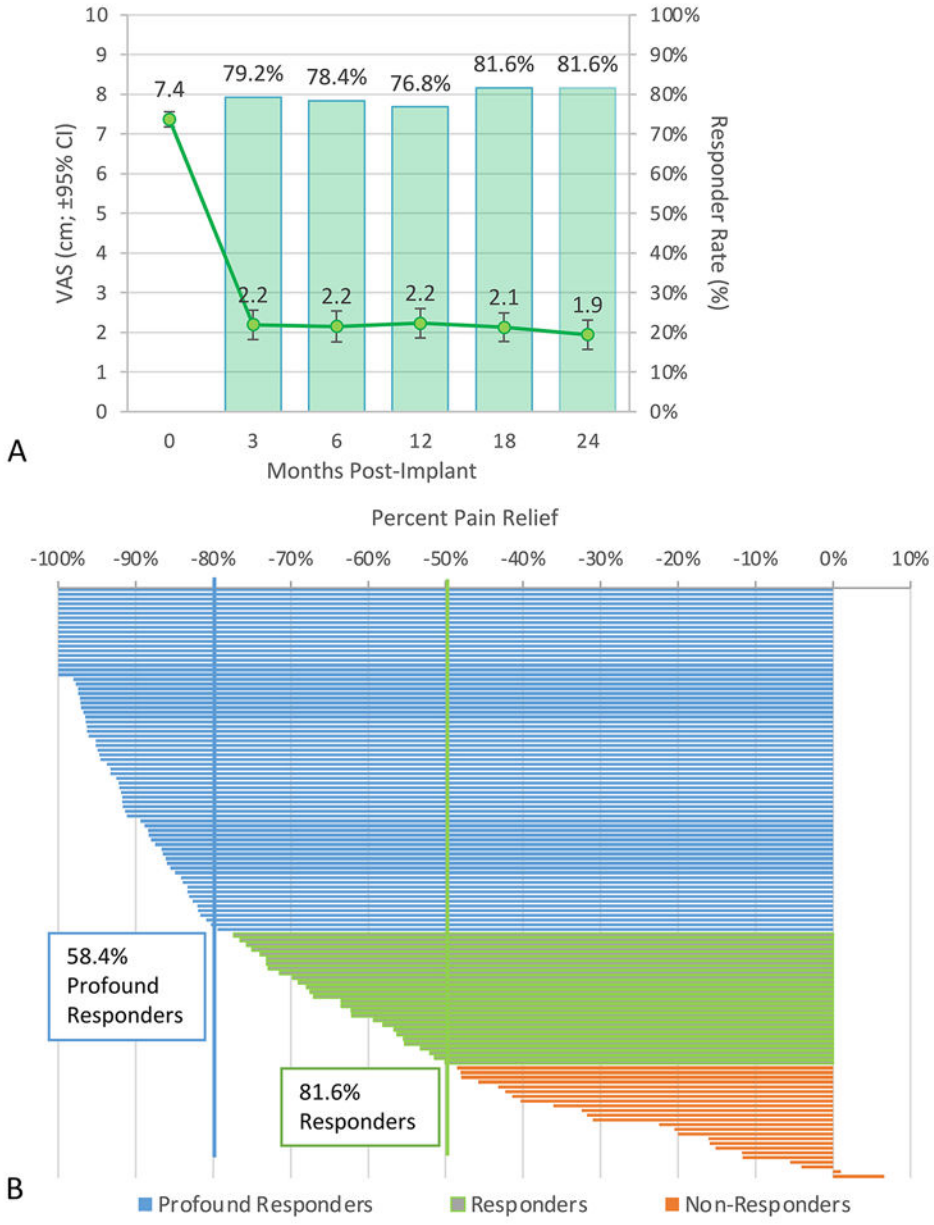

FIG. 2. A: Responder rate (the percentage of patients who achieved ≥ 50% pain relief are shown on the *right axis*) and reduction from baseline in the mean VAS back pain score (*left axis*) at 3, 6, 12, 18, and 24 months after permanent implantation ($p < 0.001$ vs baseline for all time points). **B:** Individual pain relief outcomes at 24 months, measured as the percent change from baseline in the VAS back pain score. Responders achieved ≥ 50% pain relief, profound responders achieved ≥ 80% pain relief. Figure is available in color online only.

sponse out to 24 months, with 82% reporting ≥ 50% pain relief and 58% reporting ≥ 80% pain relief, with an average 73% reduction in VAS back pain score from baseline. High-frequency SCS therapy resulted in clinically significant improvements in disability and quality of life at 24 months, with a 20-point reduction in ODI score representing double the MCID[22] and a 0.19-point reduction in EQ-5D-5L score representing ≥ 2.5 times the MCID.[24] It is uncertain whether conventional low-frequency SCS would produce similar outcomes, as substantially less evidence is available for this modality in the NSRBP population.[12]

The initial 80% response rate at 6 months we previously reported was comparable to the 75% response rate reported in a small feasibility study of high-frequency SCS in 17 surgery-naive patients with CLBP.[14,16] Both studies demonstrated similar durability of response: an 82% response rate at 24 months in this study and 80% response rate at 36 months in the feasibility study.[13] Clinically significant decreases in disability were also observed in both the current study (average 20-point reduction in ODI score at 24 months) and the feasibility study (average 31-point reduction at 36 months), with up to 50% of patients reporting

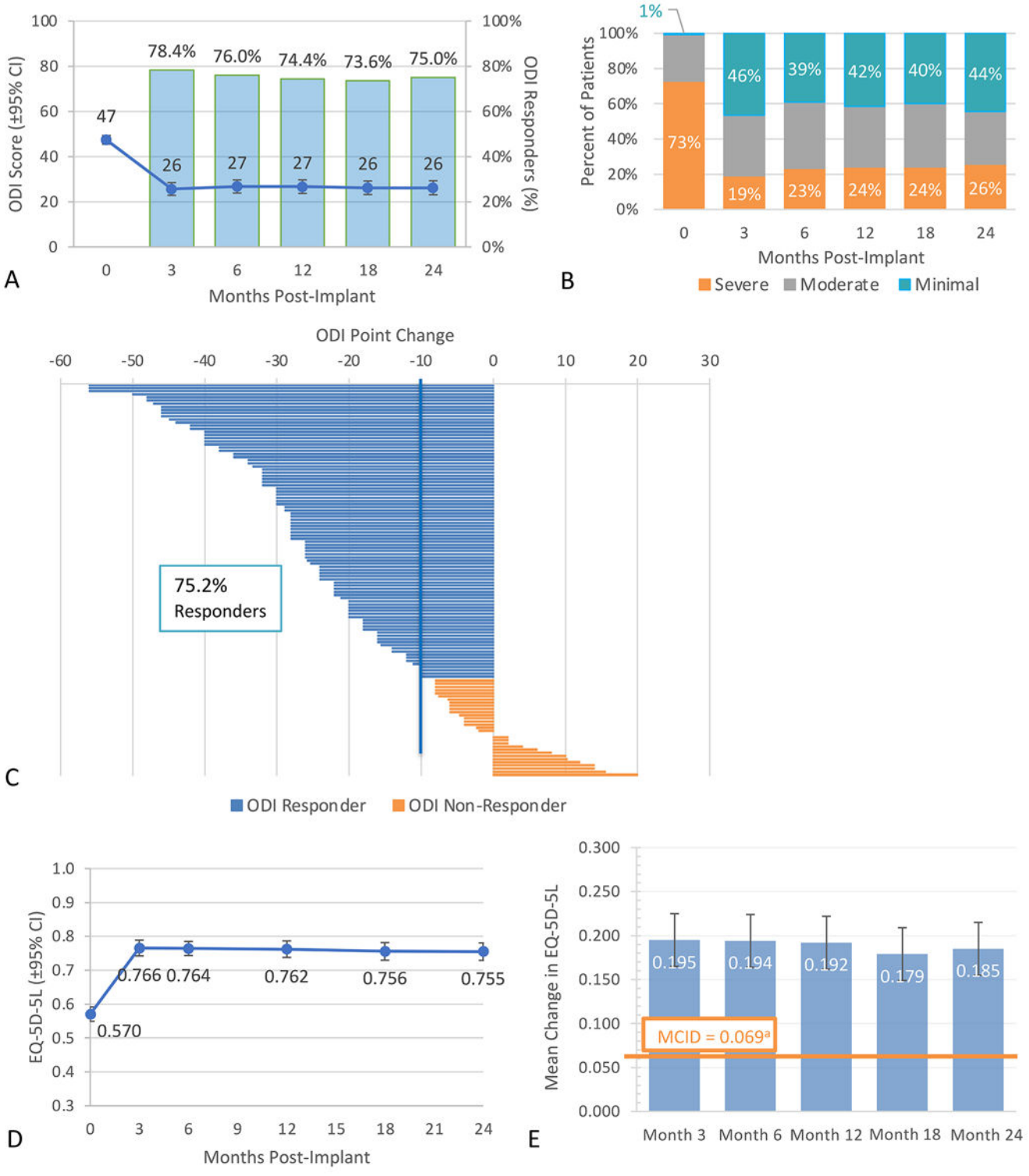

FIG. 3. A: Proportion of ODI responders (the percentage of patients who achieved ≥ 10-point improvement in ODI score are shown on the *right axis*) and reduction from baseline in mean ODI score (*left axis*) at 3, 6, 12, 18, and 24 months after permanent implantation ($p < 0.001$ vs baseline at all time points). **B:** Proportion of patients reporting minimal (ODI score 0–20), moderate (ODI score 21–40), and severe (ODI score 41–60) levels of disability at baseline and at 3, 6, 12, 18, and 24 months after permanent implantation ($p < 0.001$ vs baseline for all time points, McNemar's test for difference in proportions). **C:** Individual ODI scores at 24 months, measured as the point change from the baseline ODI score. Responders achieved ≥ 10-point improvement in the ODI score, which represents an MCID. **D:** Increase from baseline in mean EQ-5D-5L score at 3, 6, 12, 18, and 24 months after permanent implantation ($p < 0.001$ vs baseline for all time points). **E:** The mean change in EQ-5D-5L score at 3, 6, 12, 18, and 24 months after permanent implantation was ≥ 2.5 times greater than the MCID. [a]MCID of 0.069 points (upper end of estimate ranging 0.037–0.069).[24] Figure is available in color online only.

minimal levels of disability after long-term treatment.[13] Given that CLBP represents a leading cause of disability and socioeconomic burden globally,[27] functional improvement is an important measure to evaluate. Treatments that help improve function as well as pain may help address high levels of healthcare utilization currently seen in patients with CLBP.[2]

No new safety signals were identified during the 24-month follow-up, with most study-related AEs occurring in the first 6 months after permanent implantation and no additional SAEs beyond the 6 reported at 12 months.[16] The observed safety profile is consistent with types and rates of real-world AEs reported for high-frequency SCS, as well as safety outcomes generally associated with SCS.[28,29] The explantation rate due to inefficacy was 2.4%, comparable to published explant rates of 5.9% and 7.7% for SCS devices implanted for various chronic pain etiologies.[30,31]

The patients in this study had a median of 8 years since their initial diagnosis of NSRBP. SCS therapy provides an opportunity for patients with chronic pain to reduce opioid use, which we and others have observed.[16,32–34] We suggest that earlier use of SCS may help patients minimize adverse effects and increased healthcare utilization associated with the long-term use of opioids. Long delays in treatment are also problematic because increased pain onset–to–SCS implant time is associated with lower efficacy for pain relief and higher healthcare resource utilization after implantation.[35,36]

A recent retrospective chart review of patients with NSRBP provides real-world evidence that high-frequency SCS significantly reduces pain and healthcare utilization in the 12 months after implantation.[37] When evaluating cost-effectiveness, we found that the addition of high-frequency SCS to CMM was associated with significant improvement in quality of life, reduced frequency of healthcare utilization, and lower costs at 12 months, with high-frequency SCS predicted to be cost-effective for treating NSRBP within 2.1 years.[17] This analysis assumed that patients would experience continued improvement in quality of life out to 2 years,[17] which was confirmed in the current 24-month follow-up. These data support adoption of high-frequency SCS therapy in the management of select patients with NSRBP, given its demonstrated potential to reduce the burden of increased opioid use and healthcare utilization and improve quality of life. The results presented here are congruent with a recent healthcare utilization analysis using a claims database that also supports a 2-year time frame to cost-effectiveness for SCS in NSRBP patients.[38]

Limitations

Limitations associated with study design, and how they were addressed, have been discussed previously.[9,16] A limitation of this 24-month analysis is that it is a single cohort analysis of all patients who were treated with high-frequency SCS in the original RCT. Because of the high crossover rate (67 of 75 in the CMM group elected to cross over) at 6 months to the high-frequency SCS treatment group, there could be no statistical comparison between the original groups following that time point. We analyzed the group who did not cross over to determine if there were characteristics that differentiated this patient group and found that they were similar in all baseline characteristics (Supplementary Table 6). In addition, there was no difference in the reported pain at 6 months, with the crossover group reporting a mean back pain VAS score of 7.8 ± 1.3 versus 7.2 ± 1.3 in the group who did not cross over ($p = 0.21$).

In addition, the original RCT contemplated a 12-month follow-up; therefore, the 2-year follow-up required reconsent. The 12-month attrition for the PI group was only 3% (4/125). For the 24-month extension, 101 patients gave their consent and 98 (78.4%) of 125 patients who received a permanent implant completed the 24-month follow-up. Most of the attrition at 24 months occurred because of nonconsent to study extension ($n = 20$). To mitigate effects of the reduced follow-up rate, the primary analysis presented used LOCF imputation to account for missing data. This produced the most conservative results over a mixed-effects repeated measures model with multiple imputations. Complete accountability records including reasons for withdrawal and nonconsent for the extension study allow evaluation of probability of attrition bias and support accurate long-term effectiveness reporting.

The definition of NSRBP used in this study could be criticized as being not sufficiently specific or standardized, as it does not call out specific etiologies or reasons a patient may be not be a surgical candidate. However, it is based on the recommendation of the spine surgeon because patients may present with spinal conditions for which surgery is typically indicated but the patient might be considered ineligible for surgery due to lack of severity or lack of clearly identifiable structural cause for pain.

CMM modalities were not dictated by protocol but rather based on individualized best practice that included all available nonoperative therapies. The pragmatic inclusion criteria and absence of standardized CMM were deliberate choices to demonstrate whether high-frequency SCS is beneficial for NSRBP in the context of current clinical practice, an outcome highly relevant to real-world patients and their treating physicians.

Future Directions

Efficacy of high-frequency SCS in patients with NSRBP is supported by this study; however, challenges remain to incorporate SCS into clinical management paradigms. Current published guidelines recommend SCS for patients with persistent back pain after spine surgery who do not achieve adequate pain relief and functional restoration with nonsurgical therapies.[7,39–42] For patients with refractory CLBP who have not undergone spine surgery, less clarity exists, although guidelines do support SCS to treat general neuropathic pain.[43]

Our study outcomes afford the following potential management algorithm to guide patient selection for SCS therapy in the absence of expert recommendations for spine surgery in patients with NSRBP (Fig. 4). First, clinical evaluation by a primary care provider to exclude pain etiologies necessitating surgical treatment and documented attempts of all appropriate nonsurgical therapies are recommended. Guidelines state that pharmacotherapy trials should last at least 3 months and that interventional procedures may be started 3 months from the onset of pain if

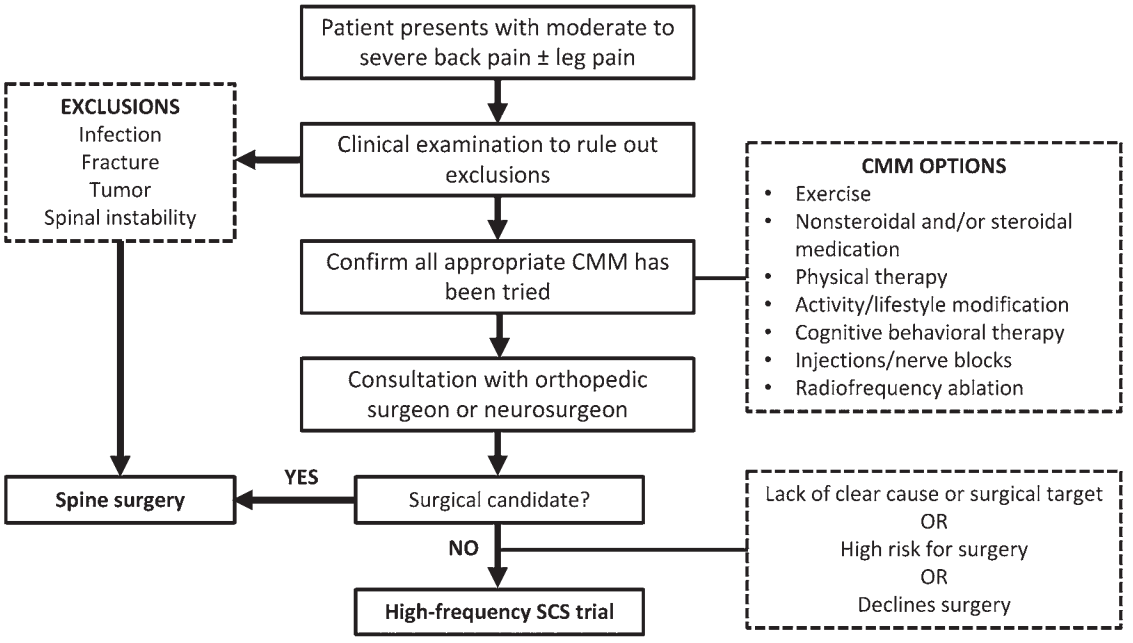

FIG. 4. Proposed diagnostic and treatment algorithm to guide patient selection for SCS therapy in patients with surgery-naive refractory CLBP.

indicated,[44,45] suggesting a minimum CMM trial period of 6 months before referral for SCS.[46,47] If pain remains refractory to CMM, defined as failure to reach treatment goals including pain relief and/or functional improvement, surgical consultation is recommended. Patients deemed unsuitable for spine surgery (i.e., not candidates because of a lack of clear cause or surgical target, or patients considered at high risk due to comorbidities) or declining surgery can be considered for a trial of SCS. Only patients who achieve clear therapeutic benefit from an SCS trial should proceed to permanent implant. In addition, standard of care includes a psychiatric evaluation, which is intended to identify patients who will achieve maximum benefit with SCS therapy. Evaluation of depression, anxiety, somatization, coping skills, and patient's expectations for the therapy are included.[48]

Conclusions

Patients with NSRBP who are not surgical candidates and have not achieved adequate pain relief with best CMM represent a challenging population for treating physicians. The addition of high-frequency SCS to CMM offers profound and durable improvements in pain, function, and quality of life for these patients. This study addresses the unmet need in treating NSRBP and provides evidence to inform current clinical management, highlighting the potential benefits of adding high-frequency SCS therapy to the treatment paradigm.

Acknowledgments

We thank Dr. Karen Murphy, BSc (Hons.), PhD, from Panwar Health for assistance with manuscript preparation, and Colleen Kelly, PhD, PStat, from Kelly Statistical Consulting for performing the statistical analysis.

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Disclosures

This study was funded by Nevro Corp. The sponsor had final approval on study design, which was developed in collaboration with investigators. Nevro designed and owns the data capture system, but data collection and data entry were performed independently by the investigating sites. An independent statistician performed all data analysis. Investigators and Nevro authors contributed to manuscript writing. Dr. Patel reported grants from Mayo Clinic during the conduct of the study. Dr. Jameson reported being a consultant for Nevro, Abbott, and Boston Scientific; and research support from Nevro, Abbott, Boston Scientific, and SPR outside the submitted work. Dr. Calodney reported personal fees from Medtronic, Nevro, Stryker, PainTeq, Saluda, and Boston Scientific outside the submitted work. Dr. Pilitsis reported fellowship grants from Medtronic, Boston Scientific, and Abbott; and grants from NIH (grant nos. 2R01CA166379, R01EB030324, and U44NS115111) and NIH Blueprint (grant no. 3U54EB015408) outside the submitted work; and medical advisor for and stock equity in Aim Medical Robotics. Dr. Petersen reported personal fees from Nevro, Saluda Medical, Presidio Medical, Biotronik, and Medtronic; grants from Nevro and Saluda Medical, and board of directors for and stock options in SynerFuse during the conduct of the study; personal fees from Nalu and grants from Mainstay Medical, Nalu, Neuros Medical, and SPR outside the submitted work; research support from Mainstay, Medtronic, Nalu, Neuros Medical, Nevro Corp, ReNeuron, SPR, and Saluda, personal fees from Abbott Neuromodulation, Biotronik, Medtronic Neuromodulation, Nalu, Neuros Medical, Nevro, Presidio Medical, Saluda, and Vertos; and stock options in neuro42. Dr. Wu reported personal fees from Nevro, Boston Scientific, Abbott, NeuroOne, NeuroPace, and Medtronic outside the submitted work. Dr. Lad reported grants from Nevro during the conduct of the study. Dr. Yu reported grants from Nevro during the conduct of the study and being a consultant for Nevro outside the submitted work. Dr. Sayed reported funded research from Nevro during the conduct of the study; personal fees from Saluda and Abbott; and stock options in Mainstay and PainTeq outside the submitted work. Dr. Goree reported personal fees from Abbott, Saluda, and Stratus outside the submitted work, and research funds to institution from SPR and Mainstay Medical. Dr. Bharara reported being an employee of Nevro Corp. during the conduct of the study. Dr. Azalde reported being an employee of Nevro Corp. during the conduct of the study. Dr. Caraway reported being an employee of Nevro during the conduct of the study. Dr. Kapural reported being on the advisory board for Avanos, Gimer, Neuralace, Neuros, Nevro, Painteq, and Presidio; research support from Avanos and Saluda; and speakers bureau for Avanos, Nevro, Saluda, and Nalu outside the submitted work.

Author Contributions

Conception and design: Calodney, Cherry, Sayed, Lyons, Azalde, Caraway. Acquisition of data: Patel, Jameson, Johnson, Kloster, Calodney, Kosek, Bendel, Petersen, Wu, Cherry, Yu, Sayed, Goree, Lyons, Sack, Bruce, Kapural. Analysis and interpretation of data: Patel, Wu, Sayed, Lyons, Bharara, Azalde, Caraway. Drafting the article: Jameson, Sayed, Lyons, Bharara, Azalde. Critically revising the article: Patel, Jameson, Kosek, Pilitsis, Bendel, Petersen, Lad, Sayed, Goree, Lyons, Sack, Bharara, Azalde, Caraway. Reviewed submitted version of manuscript: Patel, Johnson, Kloster, Calodney, Kosek, Pilitsis, Bendel, Petersen, Wu, Cherry, Lad, Sayed, Lyons, Sack, Bharara, Azalde, Caraway, Kapural. Approved the final version of the manuscript on behalf of all authors: Patel. Statistical analysis: Sayed. Administrative/technical/material support: Bruce, Caraway, Kapural. Study supervision: Johnson, Lad, Bharara, Caraway.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Tables and Figure. https://thejns.org/doi/suppl/10.3171/2023.9.SPINE23504.

Previous Presentations

Portions of this study were presented at the American Association of Neurological Surgeons Annual Scientific Meeting, Los Angeles, California, April 23, 2023.

Correspondence

Naresh P. Patel: Mayo Clinic, Phoenix, AZ. patel.naresh@mayo.edu.