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Pain Reduction in Chronic Lumbar Patients Using Spinal Cord Stimulation

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Abstract

Background: Spinal cord stimulation (SCS) is commonly used to treat chronic neuropathic pain. A common indication for the SCS is failed back surgery syndrome (FBSS). There are many interventional approaches to treating lumbar pain; however, the SCS may provide the greatest benefit in terms of health care utilization and overall pain relief to the patient.

Objective: The goal of this paper is to assess the effectiveness of SCS compared to conventional therapies such as physical therapy, oral medications, radiofrequency ablations (RFA), epidural steroid injections (ESI), and intrathecal pain pumps (IT pain pump) in patients with chronic lumbar pain due to FBSS.

Methods: A comprehensive literature review was conducted to determine the effectiveness of the SCS. Interventions to treat FBSS were identified from least invasive to most invasive. PubMed and Google Scholar were primarily used to search for relevant literature. The following terms were used for this review: "spinal cord stimulation," "chronic low back pain," "conservative treatments," "costs and cost analysis," and "failed back surgery syndrome."

Discussion: Treatment for chronic lumbar pain begins with minimally invasive treatments such as physical therapy and medication management, and then may progress to more invasive treatments such as ESI, RFA, or IT pain pumps. When compared to these therapies, the SCS was associated with favorable outcomes and found to be more cost effective.

Conclusion: For the treatment of chronic lumbar pain, the majority of studies suggest SCS as potentially more cost effective and efficient than conventional therapies; however, a multidisciplinary approach may provide the greatest benefit. SCS therapy may yet play a role in mitigating the financial burden associated with chronic lumbar pain.

Introduction

Spinal cord stimulation (SCS) has been around since the late 1960s and was initially used to treat neuropathic pain in cancer patients. Today, the most common indication for SCS is failed back surgery syndrome (FBSS) followed by Chronic Regional Pain Syndrome (CRPS) in attempts to treat chronic intractable pain, with a majority of SCS implants going to FBSS patients.[7] Indications for back surgery include degenerative disc disease, spinal stenosis, spondylolisthesis, fractures, and tumors. FBSS is a frequently encountered disease following lumbar surgery. The diagnosis is made when chronic lumbar or leg pain is present after a successfully performed lumbar surgery and there is no specific etiology of the pain. More than 50,000 SCS devices are implanted each year.[1]

Estimates of the percentage of adults over the age of 18 who experience chronic lumbar pain during their lifetime ranges from 60-80%.[7] The incidence increases with increasing age and female gender. Approximately 10% of individuals suffering from lumbar pain have symptoms lasting longer than 3 months. As a consequence, the incidence of lumbar surgery increases. The term FBSS refers to a condition of continuing pain and is not meant to imply there was necessarily a problem during surgery. The incidence of FBSS is between 20-40%, with an increased likelihood with repeated surgery. Increased complexity of back surgery also increases the rate of FBSS.

The goal of the SCS is to alleviate patient suffering and improve the quality of life of patients while attempting to reduce the use of chronic opioid therapy. Routine visits with a pain management provider may be needed to reprogram the SCS device to provide greater therapeutic benefit. The SCS is an effective therapeutic alternative for the treatment of chronic intractable pain compared to physical therapy, oral medications, injections, and other surgical interventions

such as radiofrequency ablation and intrathecal pain pump (IT pain pump) implantation. This raises the question of the effectiveness of the SCS device at reducing pain compared to conventional therapies in chronic lumbar pain patients. The purpose of this paper is to determine the effectiveness of the SCS device in regards to health care utilization, costs, and overall pain relief to the patient. First a background of the different interventions for lumbar pain will be discussed, then the literature surrounding different SCS and the different waveforms of the SCS will be reviewed, and finally we will discuss final recommendations and further directions that the SCS may have in future medical practice.

Background

Non-Invasive Modalities. Starting with the least invasive interventions, physical therapy and medication management have been the cornerstone in attempts to reduce pain. Qaseem et al conducted a systematic review for noninvasive treatments for chronic low back pain, including nonpharmacologic treatments, such as exercise and physical therapy. This study proposed guidelines to present evidence and provide clinical recommendations for noninvasive treatments for low back pain. See Table 1 in Appendices. Patients were identified based on chronicity of lumbar pain, being placed in acute, subacute, or chronic subgroups. Nonpharmacologic interventions included exercise/physical therapy, motor control exercise (MCE), Pilates, Tai Chi, yoga, psychological therapies, multidisciplinary rehabilitation, acupuncture, massage, spinal manipulation, use of ultrasound, TENS, and lumbar support.

Moderate quality evidence showed that exercise/physical therapy resulted in small improvements of pain relief and quality of life compared to no exercise/physical therapy. Moderate quality evidence showed no clear differences between different exercises/physical therapy regimens in more than twenty head-to-head random control trials in patients with chronic

lumbar pain. MCE focuses on restoring coordination, control, and strength of muscle groups that control and support the spine.[5] Low quality evidence demonstrated that MCE moderately decreased pain scores and slightly improved function in short- to long-term follow up compared with minimal intervention. Low quality evidence showed little to no differences in pain with a combination of MCE and exercise/physical therapy versus exercise/physical therapy alone. Pilates demonstrated low quality evidence which resulted in little to no clear effects on pain and quality of life compared with usual care plus physical activity. Low quality evidence showed that yoga resulted in moderately lowered pain scores and improved quality of life. Low quality evidence demonstrated that yoga resulted in a small decrease in pain intensity when compared to exercise/physical therapy. Low quality evidence showed that progressive relaxation therapies moderately improved pain intensity and quality of life compared with wait list controls. Low quality evidence showed moderately improved pain relief with cognitive behavioral therapy combined with psychological therapies when compared to wait list controls.

More invasive treatment options were reviewed and the results are as follows: moderate quality evidence showed that multidisciplinary rehabilitation slightly reduced long term pain intensity and disability compared with usual care. Acupuncture demonstrated low quality evidence and was associated with moderate improvements in pain immediately after treatment and up to twelve weeks later. Low quality evidence for acupuncture showed small improvements in pain relief when compared to NSAIDS, muscle relaxants, and analgesics. Although continuous development of new drugs appears on the market for neuropathic pain, these medications provide limited relief for patients long-term.[5] Low quality evidence showed little to now difference in pain between food reflexology and usual care for patients with chronic lumbar pain. Low quality evidence demonstrated little to now difference in pain with spinal

manipulation compared to sham manipulation. Low quality evidence showed little to no difference between ultrasound and sham ultrasound for pain at the end of treatment. Utilization of a TENS unit demonstrated low quality evidence and showed no difference between TENS and sham TENS for pain intensity or quality of life. Low quality evidence showed no difference between TENS and acupuncture in long term pain. Evidence was insufficient to compare lumbar support versus no lumbar support.

According to Dr. Qaseem et al, if nonpharmacologic therapy was inadequate, clinicians should consider pharmacologic treatments such as nonsteroidal anti-inflammatory drugs (NSAIDs) as first line therapy followed by Tramadol, Duloxetine, or antiepileptics as second line therapy in chronic pain patients. Specific antiepileptics, such as Gabapentin and Pregabalin have been shown to reduce neuropathic pain after lumbar surgery. Opioids should be considered if the aforementioned treatments have failed and only if the potential benefits outweigh the risks. A potential weakness in Dr. Qaseem's review is that the use of opioids for chronic pain requires further research to compare benefits and risks of therapy. Information regarding patient outcomes such as disability or return to work were also largely unavailable in this study. Baber and Erdek also argue that noninvasive treatments such as physical therapy and oral medications should be used first line for the management of FBSS. This supports the study conducted by Dr. Qaseem, et al in their approach of initially managing patients with FBSS. Physical therapy can help optimize gait and posture and can improve muscle strength and function.[6] However, studies show that the SCS can demonstrate tremendous potential in the management of FBSS when compared to other interventions alone. A neuromodulation reference study, the Prospective Randomized Controlled Multicenter Trial of the Effectiveness of Spinal Cord Stimulation demonstrated improved outcomes with the SCS compared with conventional therapies alone in

the treatment of neuropathic pain from FBSS.[6] The use of non-invasive therapy is considered first line management of FBSS, however, the SCS may provide greater benefit in the long-term.

Researchers have studied treatments to evaluate the outcomes of regimens in patients with FBSS. Treatments reviewed involved medication management, SCS, epidural steroid injections, exercise therapy, and psychotherapy. The quality of the assessment and the level of evidence were analyzed using a checklist designed by Scottish Intercollegiate Guideline Network. See Table 2 in Appendices. Twenty-three articles were reviewed. Studies reported that Gabapentin showed more pain reduction than Naproxen in a six-month random control trial. This finding was also supported by James Danielle, professor at the University of Adelaide in Australia, et al. According to Dr. Qaseem et al, moderate quality evidence showed that NSAIDs were associated with a small to moderate improvement in pain intensity. Oral corticosteroids may provide a burst of pain relief however long-term use of steroids is not recommended for FBSS.[3] Both Dr. Baber et al and Dr. Qaseem et al argue that opioid use provides short term improvements in pain; however chronic opioid use for noncancer pain is associated with an increased morbidity and mortality and does not reliably improve long term pain and function scores.[6]

Invasive Modalities. After noninvasive treatment options have been exhausted, epidural steroid injections, radiofrequency ablations, and intrathecal pain pumps may be considered as an alternative treatment approach to FBSS. This section will first discuss current research on invasive modalities used to treat FBSS and then compare those approaches to the SCS.

Epidural Steroid Injections. Epidural steroid injections (ESIs) are one of the most commonly performed procedure in pain clinics around the world.[6] ESI can be administered by three approaches: interlaminar, transforaminal, or caudally. This literature review will focus on

transforaminal ESI as it is one of the most common routes of admission. Indications for ESI include radiculopathy which is common in FBSS patients. ESIs can be a useful tool for both treating the symptoms of lumbar pain after surgery and preventing or delaying the need for surgical intervention.[9] Most patients would consider pursuing an ESI injection as it may prolong the need to pursue lumbar surgery. A randomized, controlled, double blind, active control trial was conducted by Dr. Laxmaiah Manchikanti et al to assess the effectiveness of transforaminal ESI of local anesthetic with or without steroids in managing chronic lumbar pain in patients with disc herniation and radiculitis. 120 patients were randomly assigned to 2 groups. One group received a mixture of lidocaine and sodium chloride in their injection, and the other group received a mixture of lidocaine, sodium chloride, and betamethasone. Primary outcomes were measured with a numerical pain score indicator and the Oswestry Disability Index. The Oswestry Disability Index is described as a tool to measure a patient's permanent functional disability[8]. A high score on the Oswestry indicates increased disability. At 2 years, there was significant improvement in all participants in 65% who received local anesthetic alone and 57% who received local anesthetic and steroid. When separated into non-responsive and responsive categories based on initial relief of at least 3 weeks with 2 procedures, significant improvement was seen in 80% in the local anesthetic group and 73% in the local anesthetic with steroid. Limitations of this study included a lack of a placebo group. Conclusions of this study found that transforaminal ESIs of local anesthetic with or without steroids might be an effective therapy for patients with lumbar pain. The evidence illustrates a lack of superiority of steroids compared with local anesthetic at 2-year follow up.

Dr. Kasra Amirdelfan et al conducted a study for FBSS treatments. Treatment for FBSS may be generally categorized as physical therapy, oral medications, interventional procedures,

SCS, and reoperation. The study concluded that there is weak evidence for improvements in pain with medications and reoperation but report also strong evidence for physical therapy and interventional procedures, such as ESI injections and the SCS. A weakness noted in the study of this study is varying pain reported by patients during their evaluations by providers. The SCS showed the strongest evidence and promising results for the long-term treatment of patients with FBSS. Optimizing analgesia via pharmacologic interventions in conjunction with ESIs can be aimed at treating neuropathic pain.[9] These findings align similarly with the results found in the studies by Dr. Baber et al, Dr. Cho et al, and Dr. Qaseem et al and suggests that a multidisciplinary approach may provide the greatest benefit.

Ismail Yuce et al conducted a retrospective study for the diagnosis and treatment of transforaminal ESIs in lumbar spinal stenosis. In this study, 37 patients were included and treated with transforaminal ESI for low back pain related to lumbar stenosis. Regular assessments were conducted at 2 weeks, 3 months, 6 months, and 12 months after treatment was administered. Visual analogue scale (VAS) and Oswestry Disability Index scales were used to evaluate effectiveness of treatment. The average VAS score was 5.1±0.3 before the ESI procedure and improved to 2.7±0.1 at the 2-week interval. At 3 months the mean VAS score was 2.8±0.2, and at 6 months the score was 3.1±0.1. The average Oswestry Disability Index score was 29.6±0.4 before the ESI procedure. At the 2-week mark the Oswestry Disability Index was 14.1±0.3. At the 3-month interval, the mean score was 15.3±0.5, and at 6 months the mean score was 24.4±0.2. A strength noted in this study was the use of the VAS and Oswestry Disability Index, which are widely and commonly used to evaluate the neurological status and pain complaints of patients. This study concluded that transforaminal ESIs are a safe procedure for the nonsurgical treatment of lumbar pain. This finding aligns with the results of Dr. Manchikanti et al in that

transforaminal ESI may be an effective therapy. This method suggests that 2 ESIs per year may be all that is needed to have adequate pain relief and prolong the need for lumbar surgery; however, the results from Dr. Manchikanti et al suggests that routine injections of local anesthetic and normal saline may be sufficient in reducing pain. This may be feasible for some but may be difficult to achieve for others, especially with the elderly. This procedure may be preferred support to the indication of surgical treatment.[10] This finding aligns similarly with the results found in the study by Dr. Amirdelfan et al in that ESIs may prolong the need for lumbar surgery.

A meta-analysis of randomized controlled trials by Dr. Seoyon Yang et al was conducted to compare clinical effectiveness of ESI versus conservative treatments for patients with radicular lumbosacral pain. Outcomes were measured using VAS, pain scores, Oswestry disability index, or successful events. A pain score is defined as a numerical scale, usually 0-10, that the patient may use to indicate the level of pain they are experiencing. A lower pain score correlates to little or no pain while a higher pain score correlates in severe pain. Successful events were defined as the reduction of pain. Conservative treatments were defined by this study as bed rest, pharmacologic therapy, exercise, and physiotherapy.

Six randomized controlled trials that included 249 patients with ESI and 241 patients with conservative treatments for lumbosacral pain were identified in this meta-analysis. The outcome of the pooled analysis demonstrated that ESI was beneficial for short-term and intermediate-term follow up when compared to conservative treatment; however, benefit from ESI in the long-term was not maintained. This contradicts the findings in the study Dr. Manchikanti et al, who suggests long term benefit from ESIs can be achieved. Successful event rates were significantly higher in patients who received an ESI than in patients that received

conservative treatments. This also goes against the study conducted by Dr. Qaseem et al who suggests that noninvasive treatments alone should provide adequate pain relief. Limitations of this meta-analysis resulted from the variation in types of interventions. Another weakness noted in this study was the small sample size. A strength noted was the use of the same outcome tools, VAS and Oswestry disability index, were used in the study conducted by Ismail Yuce et al. In the conclusion of this study, the use of ESI was more effective for alleviating radiating lumbosacral pain than conservative treatments in the short-term and intermediate term; however, limited benefit was noted in the long term. Patients also reported more successful outcomes after receiving an ESI when compared to conservative treatments. In other words, patients who had received an ESI could expect to receive about 6 months of pain relief before the need to pursue another injection or another intervention.

Masoud Hashemi et al conducted an observational study to evaluate the effectiveness of transforaminal lumbar ESI in patients with unilateral radiculopathy due to lumbar intervertebral disc protrusion regarding pain intensity, functional disability, current opioid intake, and patient satisfaction. This study was conducted in at a pain management center in Tehran, Iran in 2018. Inclusion criteria involved patients greater than age 18 and has had radiculopathy for more than 6 months due to imagine-proved lumbar intervertebral disc protrusion and no response to conservative treatments. Exclusion criteria were spinal canal stenosis, lumbar surgery, and inability to communicate in Persian language. Outcomes were measured using VAS, functional ability, satisfaction according to the patient satisfaction score, and report current opioid use and additional infection and/or surgery. 43 patients were used for this study with a mean age of 59.14 yeas. 16 patients were male and the rest were female. Patients were monitored for two years after initial ESI. Mean VAS prior to intervention was 6.91. After administration of ESI, the mean

VAS was 4.67. Mean functional disability before intervention was 47.23 and after intervention was 37. Mean patient satisfaction score was 3.07 while 18 cases reported a patient satisfaction score level less than or equal to 4. Ten cases reported using opioid analgesia, 23 cases reported receiving additional transforaminal ESI, and 11 reported having undergone lumbar surgery. A weakness noted in this study was the small sample size and inclusion criteria needed to participate in this study. A strength noted was the variety of measured outcomes used, including VAS score which was referenced in the studies by Ismail Yuce et al and Dr. Yang et al. Conclusions of this study yielded that lumbar ESI injection is an effective nonsurgical treatment option with regard to pain relief and improvement in functional ability; however, it is noted that about 25% of patients in this study pursued a repeat injection and even fewer proceeded to surgical intervention. Other interventions may be used if ESIs cannot be pursued.

Radiofrequency Ablation. Radiofrequency ablation (RFA), or radiofrequency rhizotomy, is a minimally invasive surgery used to treat facet mediated lumbar pain. Lumbar facet pain is difficult to identify as it cannot be accurately found by clinical assessment or by imaging modalities.[14] Successful targeting of the intended nerve is achieved by the use of medial branch block (MBB) injections. RFA is a commonly used intervention that selectively cauterizes lesions to sensory nerves supplying painful joints identified by MBBs. Results and length of treatment may vary as the nerves can regenerate over time. A clinical trial by Y Pevsner et al was conducted to assess the role of radiofrequency in the treatment of mechanical pain of spinal origin. 122 patients with minimal follow up of 1 year were examined after having undergone a radiofrequency heat lesion of the medical branch for spine pain. They were followed up at 1, 3, 6, and 12 months after treatment. 22 of them were additionally followed up at 18 months. Patient outcomes were measured by VAS and by selecting options from a list of options as follows: Pain

Free, Good Pain Relief, Moderate Pain relief, or No Effect. At 1 month, 75% of patients had significant reduction in pain. At 3 months 71% reported some improvements: 9 patients were pain free, 51 patients reported good relief, 27 patients reported moderate relief and 35 patients showed no effect. At 6 months, 7 patients remained pain free, 41 patients had good pain relief, 32 patients had moderate pain relief, and 42 patients showed no effect. At 1 year, 7 patients were pain free, 36 patients had good pain relief, 34 patients had moderate pain relief, and 45 patients had no effect. The 22 patients that were followed up at 18 months noted significant pain relief. A weakness noted in this study was a lack of a placebo group and a high complication rate. This study concluded that the RFA procedure has a role in treating patients with lumbar pain; however, it should be performed as a second line treatment after conservative treatments have failed.

Dr. Jordan Starr, a physician at the University of Washington, et al conducted a retrospective cohort study to describe the trends in utilization and cost of the lumbar RFA and joint injections. The patient sample was derived from IBM/MarketScan Commercial Claims and Encounters Databases from 2007-2016. Two primary cohorts were identified from patients who received lumbar RFA or lumbar facet injections. Results indicated lumbar RFA performed per one hundred thousand patients per year increased from 49 to 113, a 130.6% overall increase. Lumbar facet injection use increased from 201 to 251 sessions per one hundred thousand patients, a 24.9% overall increase. Conclusions found in this study showed consistent growth in both the frequency and procedure cost of the lumbar RFA procedure. Similar results were found in the study conducted by Dr. Baber et al; however, this contradicts the findings in the study by Y Pevsner et al in that the RFA procedure should be used as a second line therapy option.

A study conducted by Yuntao Xue et al aimed to investigate the effects of RFA for lumbar pain; however, Yuntao Xue et al advocate for the use of endoscopic guidance (ERFA). This prospective study enrolled 60 patients that were split into two groups: 30 patients in the control group that underwent traditional RFA, and 30 patients that underwent ERFA. VAS was used to evaluate the outcomes just as in the studies by Ismail Yuce et al and Dr. Seoyon Yang et al. Frequent assessments postoperatively were made at 1 day, 1 month, 3 months, 6 months, and 12 months. There was no difference in VAS scores in both groups prior to the procedure. VAS scores in all other postoperative times were significantly lower than preoperative values in both groups. No significant differences were noted between the two groups in VAS at day 1, 1 month, and 3 months postoperatively; however, the ERFA demonstrated significant benefit at 3-month and 6-month intervals. The VAS scores of the 1 year follow up in the ERFA group was higher than that of the control group. Complications in the ERFA group were also noted to be lower than the control group. Controlled MBB was the only diagnostic method to identify patients. A potential weakness in this study was the rate of false positives of uncontrolled MBB. Yuntao Xue et al concluded that ERFA has advantages of accurate positioning, more thorough denervation, fewer complications, lower risks, and better long-term efficacy. While Yuntao Xue et al focused primarily on EFRA, in general, the RFA procedure may provide long term benefit. This conclusion is similar to the results found in the studies by Dr. Jordan Starr et al and Y Pevsner et al.

Intrathecal Pain Pumps. When minimally invasive interventional pain management techniques have failed, continuous intrathecal analgesic administration may be considered. Intrathecal pain pumps (IT pain pumps) are implantable devices with a reservoir that store pain medication, such as Morphine, Hydromorphone, Ziconotide, Fentanyl, or Bupivacaine, and release it at a

continuous rate.[17] A trial is often recommended which involves placement of a temporary lead and a bolus dose of the desired medication. Patients may choose to continue for implantation of the IT pain pump pending a successful trial. The pump is implanted subcutaneously, usually in the lower abdomen, and the medication is fed through a lead which releases it into the cerebrospinal fluid (CSF).[18] As a result, the IT pain pump can offer quick and effective pain relief. If appropriate, patients may also have the option to administer a bolus dose of medication a few times per day. Depending on how much medication is needed, patients should follow up with their pain specialists for refill of their reservoirs every 1-2 months. Ultrasound guidance allows for accurate delivery of medication during a refill. Complications of the IT pain pump may arise in the form of a catheter tip granuloma, which occurs over a long period of time and may obstruct passage of medication.[17]

Dr. Nikolai Rainov et al conducted a clinical trial to assess the long-term intrathecal infusion of drug combinations for chronic back and leg pain. This study represents a long-term evaluation of the treatment regimen consisting of Morphine, mixed with Bupivacaine, Clonidine, or Midazolam in patients with chronic nonmalignant back and leg pain. 26 patients have been followed up for 3.5 years. Combination of Morphine with a second drug was used in 10 cases, Morphine with 2 additional drugs in 12 cases, and Morphine with 3 additional drugs in 4 cases. Patient outcomes were measured using VAS. 19 patients reported excellent or good treatment results, 6 patients had sufficient results, and only 1 patient mentioned poor therapeutic effects. A weakness noted in this study was a small number of participants. A strength noted was the use of standardized pain scales. Mean Morphine doses had to be increased from 1.2mg at baseline to 5.1mg at 2 years due to tolerance development and disease progression. This study suggests that IT polyanalgesia employing Morphine combined with an additional non-opioid drug can have a

favorable outcome in patients with complex chronic pain of spinal origin. In other words, combination therapy using different classes of medications may provide adequate pain relief.

A comprehensive literature review conducted by Dr. Timothy Deer et al to evaluate the evidence for Morphine and Ziconotide as first line IT pain pump analgesics for patients with chronic pain. The literature reviewed included noncontrolled, prospective, retrospective, and observational studies. Methods used for this study involved a Medline search for "Ziconotide" or "Morphine" and "intrathecal" and "chronic pain." The literature supports the use of Morphine and Ziconotide as first line treatments for IT therapy. This aligns with the 2016 Polyanalgesic Consensus Conference (PACC) guidelines which recommend either Morphine or Ziconotide as first line IT monotherapy for chronic pain; however, one consensus point emphasized Ziconotide use in patients with chronic, non-cancer related pain. PACC guidelines recommend conservative initial dosing strategies. Due to its narrow therapeutic window and contraindication in patients with psychosis, Ziconotide requires careful dosing. IT Morphine administration may be associated with serious side effects, such as respiratory depression.[17] Data is needed to further understand the benefits and risks associated with initial IT pain medication in diverse chronic pain patients. A strength noted in this study was patient contribution to help identify which medication would work best for them. This study concluded that both Morphine and Ziconotide are recommended as first line IT monotherapy for cancer related and non-cancer related pain. The choice should take into consideration patient characteristics and the risks versus benefits of each medication. Combination therapy may be considered only after the failure of IT Morphine or Ziconotide monotherapy, which is a result shared by findings of Dr. Rainov et al.

Dr. Denise Wilkes, physician at the University of Texas, et al had conducted a retrospective study to assess the success of microdosing Morphine method in a community pain

clinic stetting by monitoring follow up frequency, dose escalation, and monotherapy/polytherapy ratio. The microdose method involves a pretrial reduction of systemic opioids followed by a period of abstinence.[18] IT Morphine is then started at doses less than 0.2mg per day. Systemic opioid abstinence is then continued after the IT pain pump has been implanted and IT Morphine monotherapy has started. 60 patients were selected who had completed a microdose regimen and had an IT pain pump implanted. Dose changes, pain scores, side effects, max doses, and duration of therapy was recorded. Out of 60 patients, 35 were successfully managed on Morphine microdose monotherapy. No additional oral medication was needed to control pain. Significant reductions in pain scores were noted, going from 7.4±0.32 before microdose to 4.8±0.3 after microdose therapy. Any weakness in the study was related to the retrospective nature. Selection of patients who were able to wean and willing to commit to a microdose plan can affect the outcome. Another weakness noted was that the study primarily focused on Morphine microdosing and did not evaluate the success of other regimens such as Hydromorphone or Ziconotide, as in the studies conducted by Dr. Deer et al and Dr. Rainov et al. A strength noted in this study was the multiple disciplinary approach, such as physical therapy and follow up visits with pain specialists, established after microdose therapy has been initiated. Physical therapy was highly encouraged as a conservative treatment by both Dr. Qaseem et al and Dr. Amirdelfan et al.

Spinal Cord Stimulation. All interventions discussed thus far have been aimed to reduce neuropathic pain in chronic lumbar pain patients. Chronic neuropathic pain is still not extensively understood which makes it challenging to treat. The present alternative treatment considered as the gold standard for many types of chronic neuropathic pain is the spinal cord stimulator (SCS). There are also many waveforms that the SCS can administer to reach

therapeutic effect. As previously mentioned, the SCS appeared into clinical practice in the 1960s with the concept of gate control theory (GCT), which was first conceptualized by Patrick Wall and Ronald. Melzack.[19] Today, the technology of the SCS is more refined. Wall and Melzack theorized that the nociceptive signal would be inhibited by antidromic activation of collateral myelinated alpha-beta fibers in the dorsal columns.[19] The first reported clinical application of the dorsal column stimulation came two years later. At the time, the SCS was thought to act merely at the spinal segment level. However, GCT theory did not take into account two evident contradictions. The first is that SCS should be more effective in controlling acute nociceptive pain, which is not the case. Secondly, Wall and Melzack's theory is not able to explain the pain free interval that is often noticed after discontinuation of stimulation. For these reasons, GCT theory is more and more inconsistent to explain the mechanism of action of the SCS. The SCS is deemed to neutralize the overexcitability of wide dynamic range neurons in the dorsal horn by increasing GABA.[19] Wide dynamic range neuron wind-up caused by excessive nociceptive inputs is believed to trigger the lateral pain pathway, giving the start to the abnormal transmission of pain sensation to the brain. To this point, it remains unclear whether the SCS rebalancing effect of the system occurs solely as a result of presynaptic inhibition of wide dynamic range neurons through antidromic activation or if it is due to most complex combined pre/postsynaptic phenomena.[19]

The SCS consists of a small battery that emits electrical impulses through 2-4 leads with metal contacts. The battery is placed subcutaneously and the leads are placed in the epidural space via fluoroscopy. Electrical signals convey the sense of paresthesia to the patient effectively blocking pain signals to the brain with success rates ranging from 50-75%.[4] However, before the SCS is implanted, patients must complete a one-week trial in order to determine if it will provide

benefit. The most common complications to the SCS treatment include lead migration, infection, and pain over the implant site.[2] The most common indication for the SCS is FBSS, CRPS, radicular and nerve root pain, postherpetic neuralgia, pain due to peripheral nerve injury, intercostal neuralgia, and phantom pain.[21] SCS main contraindications include infection, coagulopathy, spinal stenosis, psychiatric disorders, and substance abuse. After a diagnosis has been established and a patient wishes to pursue the SCS, they must first complete a trial phase. The trial phase consists of temporary leads implanted via fluoroscopy. The leads are attached to an external battery which mimics the effects of the SCS. The battery and surgical incisions are secured by a dressing. If the patient passes the trial, then they are able to schedule their implant date. Patients may also have the choice between a rechargeable and a non-rechargeable SCS device, depending on the brand.

Dr. Zucco et al conducted an observational, multicenter, longitudinal, ambispective randomized controlled trial to assess the cost effectiveness and cost utility of SCS in patients with FBSS refractory to conventional therapies. 80 patients were recruited and received the SCS and conventional therapy treatments. Patients were monitored for 24 months after implantation of the SCS. Outcomes such as pain intensity, Oswestry Disability Index, quality of life scales, and direct costs before and after the SCS were measured. After implantation, quality of life had significantly improved. Societal costs increased by nearly 50% per patient per year. Accordingly, this study suggests that if patients are willing to pay for the procedure, then the implantation would be cost effective in the long term. A weakness noted in this study was the small population size. This study concluded that the SCS combined with conventional therapies may provide good value for money.

A recent study conducted by Ontario Health (Quality) was done to assess the 10-kHz high frequency SCS in adults with chronic noncancer pain that was refractory to medical management. This included an evaluation of effectiveness, the budget impact of publicly funding 10-kHz high frequency SCS, and patient preferences and values. This study involved a systematic literature search and a systematic economic literature review. Seven publications were included in this study. The risk of bias was assessed of each study using the Cochrane Risk of Bias and ROBINS-I tools, and the quality of the body of evidence according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. Analysis of the 5-year budget impact of publicly funding 10-kHz high-frequency SCS in Ontario for adults with chronic noncancer pain was performed. Results indicated a GRADE score of "moderate" that 10-kHz high frequency SCS likely provides reductions in pain intensity and functional disability, and improvements in quality of life in people with chronic noncancer pain. With a GRADE score of "low," patients may reduce their opioid consumption with 10-kHz high-frequency SCS. The two included economic evaluations found that 10-kHz high frequency SCS was cost-saving compared with the conventional SCS. Limited evidence was found about the effectiveness of 10-kHz high-frequency SCS in people who have first tried and failed conventional SCS at lower frequencies as a cost-effective analysis was not conducted. The comparisons in the randomized controlled trials all involved conventional low-frequency SCS as the active comparator. There were no trials of 10-kHz high-frequency SCS compared with a sham arm to evaluate placebo response. For adults with chronic noncancer pain that was refractory to medical management, 10-kHz high frequency SCS was effective in relieving pain, reducing disability, and improving quality of life.

A study by Dr. Terje Kirketeig of Uppsala University Hospital in Sweden was conducted to review outcomes using burst SCS stimulation in the treatment of chronic, intractable pain. The concept of burst SCS was first introduced in 2010 by Dirk DeRidder and colleges, targets the dorsal columns in stimulus bursts comprised of five 1-ms pulses with an intraburst frequency of 500Hz, delivered with a frequency of 40Hz in a passive recharging paradigm to maintain charge balance across the electrical contacts.[22] When the burst SCS pattern was electrically applied to the dorsal columns at adequate settings, it was effective at producing analgesia without the need for paresthesia. A narrative clinical literature review was conducted utilizing search terms including key words for burst spinal cord stimulation. Synthesis and reporting of data from publications including an overview of comparative SCS outcomes was conducted. Medline and Embase databases were used. Results of this study found that burst SCS provided greater pain relief over conventional stimulation. This was demonstrated in multiple studies which included blinded, sham-controlled, and randomized trials. Additionally, burst stimulation impacts multiple dimensions of pain, including somatic pain as well as emotion and psychological elements. Patient preference is also geared toward burst SCS over conventional SCS due to increased pain relief, a lack of paresthesia, and impression of change in condition. Burst SCS has been shown to be both statistically and clinically superior to conventional SCS and may provide additional benefits through different mechanisms of action. Conventional SCS was also found to be inferior in the study conducted by Ontario Health; however, Ontario Health was comparing results with high frequency SCS. There is a high level of clinical evidence for the efficacy of burst SCS on pain intensity after one year of therapy in patients suffering from a variety of chronic pain conditions. Moreover, there are many blinded, sham-controlled randomized controlled trials indicating clinical superiority over both placebo and conventional SCS. The overall level of

evidence in trials reviewed for this study was variable, ranging from high-quality prospective trials with long follow up periods to a number of low- to medium-quality trials. Although there is data on a variety of neuropathic pain conditions, future studies should also better focus on individual pain conditions, such as FBSS, CRPS, peripheral neuropathies, postsurgical chronic pain, ischemic pain conditions, visceral pain, and post stroke pain.

Another study, conducted by Dr. Jay Karri et al, aimed to provide evidence for various SCS waveforms- including burst, high frequency, and conventional relative to each other for treating chronic lumbar pain. To conduct this study, Dr. Karri et al performed a systematic review based on conventional methodology described by Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISM). PubMed, Medline, Cochrane Library, priory systematic reviews, and reference lists were screened for all randomized trials and prospective cohort studies comparing different SCS waveforms for treatment of chronic lumbar pain. In terms of analgesic efficacy, five studies reported pain scores and standard deviations for patients who received burst or conventional waveforms. These studies were pooled for meta-analysis. 11 studies were identified that included waveform comparisons for treating lumbar pain. Of the 11, 6 studies compared burst versus conventional, 2 studies compared burst versus high frequency, and 3 studies compared conventional versus high frequency. A meta-analysis of 5 studies comparing burst versus conventional SCS was conducted. Meta-analysis of these five trials revealed a significant reduction in pain scores favoring burst over tonic waveforms. These results support the findings by Dr. Kirketeig et al. In regards to conventional versus high frequency SCS, 3 studies showed both meaningful pain reduction with high frequency waveforms relative to baseline and noninferiority of high frequency waveforms relative to conventional SCS. This finding agrees with the finding from the study conducted by Ontario Health (Quality) et al. There

is a dearth of evidence comparing burst and high frequency waveforms for the treatment of chronic lumbar pain. Two studies were found to compare burst versus high frequency stimulation; however, there was no meaningful superiority of either waveform in treating back pain but found that burst was superior to high frequency stimulation in reducing leg pain at 3- and 12- month intervals. Of note, a few studies that reported benefit with the use of burst waveform were not included due to lack of obtaining standard deviations for the reported mean pain scores. A sensitivity analysis was performed on the 5 studies included for the burst versus conventional meta-analysis. The analysis was performed by sequentially removing each individual trial and evaluating how it affected the pooled estimate of the primary outcome. This process failed to find a significant difference. A limitation noted in this study was that both randomized controlled trials and prospective cohort studies were included in this meta-analysis. Several studies included a high risk of bias in at least one domain.

Dr. Charles Odonkor et al performed a retrospective cohort study to appraise literature evidence supporting the health care resource utilization and cost effectiveness of the SCS compared with conventional therapies for chronic lumbar and leg pain. Databases from PubMed, Medline, Embase, CINAHL, and Rehabilitation and Sport Medicine were used using the terms "spinal cord stimulation," "chronic pain," "back pain," "patient readmission," "economics," and "costs and cost analysis." After initial screening of 204 studies, 11 studies meeting inclusion criteria were analyzed, representing 31,439 SCS patients and 299,182 conventional therapy patients. Conventional therapies were defined as medication management, physical therapy, ESIs, trigger point injections, nerve blocks, chiropractic treatments, massage therapy, acupuncture, and surgery. Primary outcome measures were cost and health care resource utilization. The most commonly reported measures of health care resource utilization were

annual imaging rates, opioid usage, and hospitalizations. The mean age was 53 years for the SCS and 55.6 years for conventional therapies. In six of 11 studies evaluating SCS versus conventional therapies in relation to cost implications/quality outcomes, SCS was associated with favorable outcomes and found to be more cost effective than conventional treatment approaches for chronic lumbar pain. For the remaining studies, two studies were retrospective reviews of claims data, one study compared costs of rechargeable versus non-rechargeable SCS systems, another compared costs of imaging amount patients with SCS implants versus patients projected to require SCS imaging in one year, and the other study used values from the published literature to create cost analysis models from the SCS cost estimates were derived. The most common indication for the SCS is FBSS, which was evaluated in six of the 11 studies. Other indications included CRPS, peripheral artery disease (PAD), refractory angina pectoris (RAP), chronic back and leg pain, chronic axial lumbar pain, degenerative disc disease, radiculitis, neuropathic leg and back pain, and chronic benign pain syndrome. Several drivers of high resource utilization in SCS therapy were identified, which included cost of imaging, costs related to management of complications, and delay in time to delivery of SCS therapy. In regards to pain relief, three of 11 studies included pain relief outcomes. There was a large discrepancy in reported pain relief outcomes depending on the type of study and population evaluated; however, SCS treatment was shown to decrease the numerical rating scale score at 24 months from 7.56 to 5.11, and this pain reduction was both statistically and clinically significant. In six of 11 studies analyzing costs associated with SCS therapy, SCS was associated with favorable outcomes in terms of cost-effectiveness and health resource utilization compared to conventional therapies in the long term; however, in the short term the SCS was found to be less cost effective to patients. Adverse events with SCS were reported in three of 11 studies. When compared to lumbar

surgery, the SCS resulted in a lower complication rate of 8.6% versus 16.52% for lumbar surgery. Other types of complications included renal, cardiac, neurological, pulmonary, deep vein thrombosis/pulmonary embolism, systemic infection, and battery site wound infection. The overall costs between the SCS and lumbar surgery were similar but the SCS is associated with fewer complications and improved outcomes. A strength noted in this study was the inclusion of comparative health utilization of the SCS versus conventional therapies. The use of clinical registries also allowed for real time tracking for SCS patients to collect data. A limitation noted was the upfront costs of the SCS procedure which could guide care of patients for their chronic pain. The systematic review of health care resource utilization in the treatment of chronic limb and back pain underscores low to fair evidence favoring SCS over conventional therapies as a more cost-effective modality with less resource utilization.[24] For the treatment of chronic lumbar and leg pain, the majority of studies are of fair quality, with level 3 to 4 evidence in support of SCS as potentially more cost-effective than conventional therapies, with less resource expenditure but higher complications rates. This result shares similarities with the studies conducted by Dr. Zucco et al, Dr. Kirketeig et al, Dr. Karri et al, and Ontario Health (Quality).

Methods

PubMed and Google Scholar databases were used for this study. Studies that were mostly published from 2018 to 2021 were reviewed using the following terms, “spinal cord stimulation,” “chronic low back pain,” “conservative treatments,” “costs and cost analysis,” and “failed back surgery syndrome.” The database search was time limited to the last 3 years to make sure the literature review was current and up to date. Older articles were used to provide background information. The basic search strategy was modified for each database to optimize results for each database. Additional sources include direct contact with an expert pain specialist

for their input. Studies that met the following criteria were included: patient population suffering from chronic lumbar pain, patients treated with SCS implant and/or conventional therapies and medical management, studies evaluating the economics and/or cost effectiveness of SCS compared with conventional therapies, and studies evaluating hospitalization and health resource utilization. Exclusion criteria involved any studies with children, pregnant women, patients with significant psychological disorders, and patients who are not able to sign informed consent. The Population, Intervention, Comparison, and Outcome (PICO) framework informed study screening. See Table 3 in Appendices. Primary outcome measures were health care utilization and costs.

Discussion

This literature review of the treatment of chronic lumbar pain underscores fair evidence favoring the SCS over conventional therapies in regards to health care utilization and over all pain relief. Both Dr. Qaseem et al and Dr. Baber et al agree that noninvasive treatment options should be used first line; however, Dr. Baber et al suggest that the SCS providers greater pain relief and reduced overall cost to the patient than non-pharmacologic noninvasive treatments. According to Dr. Qaseem et al, if non-pharmacologic intervention fails, medications such as NSAIDS, Tramadol, Duloxetine, Gabapentin, and Pregabalin may be used. This statement contradicts the claims of Dr. Amrdelfan et al who found low quality evidence in managing pain with oral medication alone. Both Dr. Qaseem et al and Dr. Baber et al argue that opioid use may provide short term pain relief but should not be used as a long-term treatment option.

Dr. Amirdelfan et al suggests that physical therapy and other interventions, such as ESI, should be started as first line therapies for chronic lumbar pain. This is in agreement with Ismail Yuce et al who also suggest that ESIs are a safe alternative for nonsurgical treatment for lumbar

pain. A similar result was also found by Masoud Hashemi et al; however, in that study, there was a significant percentage of participants that pursued a repeat injection and even some that required repeat surgery. In line with the hypothesis of ESI for lumbar pain, Dr. Yang et al concluded that ESI injections provide adequate pain relief in the short- and intermediate- term, but minimal evidence exists for long term benefit. This contradicts the findings in the study Dr. Manchikanti et al where long-term benefit was found with ESIs. A strength noted in the studies of Ismail Yuce et al, Masoud Hashemi et al, and Dr. Yang et al was the use of the VAS score as a standard to measure the outcome of patient relief and satisfaction.

In regards to the RFA procedure, Dr. Starr et al believes that the RFA procedure produces greater relief and fewer complications than facet injections. While Dr. Baber et al notes there is benefit with the RFA procedure, he argues that the SCS device would provide greater benefit. Yuntao Xue et al also argues that RFA can provide adequate pain relief; however, ERFA was thoroughly examined. On average ERFA provides significant benefits at 3- and 6-month intervals. Yuntao Xue et al also utilized the VAS score to measure patient outcome. This finding contradicts the results by Y Pevsner in that the RFA procedure should be used as a second line therapy after conventional therapies have been trialed.

The studies conducted by Dr. Deer et al and Dr. Wilkes et al argue that IT pain pumps with Morphine may be more effective at treating chronic lumbar pain; however, Dr. Rainov et al suggests that intrathecal Morphine combined with another non-opioid medication may provide adequate benefit. According to Dr. Deer et al, Ziconotide may be used in place of Morphine but the procedure itself is more invasive than the SCS. Another limiting factor of the IT pain pump is that the patient can still potentially be on long term opioid use. This goes against the

recommendations set by Dr. Qaseem et al and Dr. Baber et al. The SCS does not administer medication and therefore the potential for abuse is limited.

In regards to the SCS, there are many waveforms to choose from for the patient. The study conducted by Ontario Health (Quality) et al found significant evidence that 10-kHz high frequency SCS may reduce pain and functional disability when compared to conventional SCS. It was also found that high frequency SCS may also reduce opioid consumption in the long term which aligns with the results found by Dr. Baber et al. When compared to conventional SCS, Dr. Kirketeig et al found that the burst waveform of the SCS provided greater pain relief in patients with chronic lumbar pain. This result was also found in the study conducted by Dr. Karri et al who also found that the burst waveform provided greater benefit than conventional SCS. Dr. Karri et al had also found significant improvements when comparing high frequency SCS to conventional SCS, a result shared with Ontario Health (Quality) et al. Dr. Karri et al has also compared the effectiveness of high frequency SCS and burst waveform SCS and had found that there are minimal differences between them. Regardless of waveform, the SCS has found to be a promising alternative to conventional pharmacologic and surgical interventions for chronic lumbar pain. The study conducted by Dr. Odonkor et al and Dr. Zucco suggests that the SCS may provide higher incremental monetary value by decreasing long term chronic pain burden.

Any recommendation for the SCS as a cost effective first line therapy for chronic low back pain is limited by the need for more robust evidence regarding related resource utilization and therapeutic benefits over conventional treatment modalities. Chronic pain occurs over time, and it would be beneficial to know at which point in the pain timeline process that the SCS would yield the highest return per unit cost of therapy per patient. Variations in reported pain relief from SCS versus conventional therapies could be due to several reasons, including

differences in study populations and settings, unmeasured latent factors and confounders, and study designs. Further research studies are needed to get a better understanding of the SCS can be better utilized. Further studies are also needed that may focus on relative cost effectiveness of different SCS waveforms versus conventional therapies.

Conclusion

The goal of this paper was to compare the effectiveness of the SCS versus conventional therapies for patients with chronic lumbar pain. Thus far, different interventions have been discussed for the treatment of chronic lumbar pain. Each intervention has been discussed in detail and while each modality may provide benefit alone, a multidisciplinary approach may provide the greatest benefit. The outcomes all suggest that noninvasive treatments should be trialed first before moving on to more invasive interventions for lumbar pain. Noninvasive treatments include pharmacologic intervention, physical therapy, and routine exercise, which have been proven to reduce pain slightly. Further studies for specific medication management are needed to find the best combination for pain relief.

The results all suggest that ESIs provide adequate pain relief in the short- and intermediate term but does not provide much benefit in the long term. Patients with chronic lumbar pain may receive benefit from ESIs but repeat injections are often needed. ESIs may also post pone the need for surgery. A strength noted in these studies included the use of the VAS scale to standardize patients' pain levels. The studies concluded that the RFA procedure may have significant reductions in pain, and even greater improvement with ERFA. Pain relief was greatest at 3 and 6 months; however, there is limited evidence for significant pain relief lasting longer than 6 months; however, some believe the RFA procedure should be used after other therapies have failed. The outcome for the studies suggests that an IT pain pump filled with

Morphine may provide significant pain relief; however, this intervention is the most invasive and would still require the need for monthly refills to provide benefit. IT pain pumps filled with Morphine and another non-opioid medication provide adequate pain relief. Finally, the studies conducted on SCS thus far all suggest that the SCS is more cost effective, provides significant pain relief, and reduces overall health care utilization than conventional therapies.

The topic of chronic pain may be difficult for patients to grasp and a caring approach is often needed. Fortunately, there exists a wide variety of treatments for chronic lumbar pain and a multimodality treatment plan is recommended. Treatment plans should start with the least invasive and moving on to more invasive treatment plans. Patient risks and benefits should always be discussed with the patient. The SCS can provide adequate pain relief but even more so when paired with other interventions, such as physical therapy, medication management, and ESIs. Further studies are needed to assess multiple interventions effectiveness with concurrent use of the SCS. Not every case of lumbar pain is an indication for the SCS but when it is, the long-term benefit from the SCS may outweigh the risks. It is important to understand that the SCS does not change the physiology of a patient's spine but rather helps mask pain. Patients may elect for a repeat lumbar surgery if the SCS is not indicated or cannot be pursued. Routine follow up with a pain specialist is recommended and will allow patients to view their treatment options while in a controlled and safe environment. The SCS may result in better health related quality of life and quality adjusted life years for patients suffering with chronic lumbar pain when combined with conventional therapies.

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Appendices:

Table 1. American College of Physicians Guideline Grading System

Table.1 The American College of Physicians Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	**Benefits Finely Balanced With Risks and Burden**
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup.

Table 2. Criteria for Judgement of Quality Assessment and Degree of Evidence.

++	All or most of all standards are met. It is certain that the results of the study will not be changed by the unmet standards.
+	Some of the standards are met. It is thought that the results of the study will not be changed by the unmet standards.
-	All or most of all standards are not met. It is thought that the results of the study may be changed by the unmet standards.

1++	- High quality meta-analysis and systematic review conducted by randomized clinical trials - Randomized controlled trials with a very low risk of bias
1+	- Well-designed meta-analysis and systematic review conducted by randomized or non-randomized clinical trials - Randomized or non-randomized clinical trials with a low risk of bias
1-	- Meta analysis and systematic review conducted by randomized or non-randomized clinical trials - Randomized or non-randomized clinical trials with a high risk of bias
2++	- High-quality systematic review conducted by a patient control study, cohort study, or diagnosis analytic study - High-quality patient control study, cohort study, or diagnosis analytic study of very low risk of confounding, bias or contingency,, or a high possibility of cause and effect relationship
2+	- High-quality patient control study, cohort study, or diagnosis analytic study of the low risk of a confounding, bias or contingency, or the normal possibility of a cause and effect relationship
2-	- Patient control study, cohort study, or diagnosis analytic study of the high risk of a confounding bias or contingency, or the low possibility of a cause and effect relationship
3	- Non-analytic studies, e.g., before-and-after study, case series, case report
4	- Expert opinion

Table 3. PICO Framework for Screening Studies

CRITERIA	INCLUSION
Population	The population was composed of adults (age greater than 18 years) of both genders diagnosed with chronic lumbar pain
Intervention	Spinal cord stimulation therapy
Comparison	Conventional therapies (medication, physical therapy, ESI, radiofrequency ablation, IT pain pump)
Outcome	Improvement in total medical expenditure related to chronic pain, average duration of pain relief, percent reduction of opioids, improved quality of life, reduction of adverse events, and improved utility score with the SCS

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