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Research Article

The Use of Spinal Cord Stimulators for the Treatment of Abdominal Pain: A Comprehensive Review

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Abstract

Introduction: Abdominal pain is a challenging condition to treat due to its broad etiology, often refractory response to medical management, and often negative workup. Spinal cord stimulators (SCS) are a known gold standard for refractory chronic pain conditions, but their published use in the treatment of abdominal pain is relatively rare. Therefore, a literature search was undertaken from January 2000 through December 2022 and twenty-seven relevant articles were included in this review. Our goal was to provide a comprehensive review and source of information for interventional pain physicians on available literature regarding abdominal pain and the use of SCS for its treatment.

Objectives: The purpose of this article is to review the current use of spinal cord stimulators in the setting of abdominal pain and support its continued use.

Study design: This is a narrative review article with the goal of reviewing pertinent case reports, case series, prospective and retrospective studies, from January 2000 to December 2022 on the use of spinal cord stimulators in the treatment of abdominal pain.

Conclusion: Overall, the use of SCS resulted in decreased abdominal pain scores, relief of gastrointestinal symptoms, decreased morphine milligram equivalent requirements, and improved quality of life. These results support the initiation of randomized controlled trials in order to establish strong evidence for their use in the treatment of abdominal pain.

Keywords: Abdominal pain; spinal cord stimulator; neuromodulation; pain management; chronic pain

Key Points

a) Over two decades of articles were included in this review on the use of spinal cord stimulators for the treatment of abdominal pain.

b) The use of spinal cord stimulator was found to decrease abdominal pain scores in the patient population reviewed.

c) The use of spinal cord stimulator was found to decrease morphine milligram equivalent requirements in the patient population reviewed.

d) The use of spinal cord stimulator was also found to decrease gastrointestinal symptoms, such as nausea, vomiting, diarrhea, and constipation in the patient population reviewed.

e) The use of spinal cord stimulator was found to improve quality of life and daily functional ability in the patient population reviewed.

f) Given the lack of randomized control trials on the use of spinal cord stimulators for abdominal pain, the evidence for its use is considered insufficient, although can result in improvement.

Background

Abdominal pain is a challenging condition for primary care providers, gastrointestinal specialists, and chronic pain providers to treat due to the broad-ranging differentials of its etiology and often refractory response to medical management in combination with often negative workup. Additionally, patients often have debilitating gastrointestinal symptoms that in combination

with their refractory pain, have profound negative effects on psychological well-being and quality of life. The etiologies of abdominal pain vary and can be divided into the four subtypes, which are functional gastrointestinal disorders, abdominal pain of a visceral origin, abdominal wall pain conditions, and abdominal pain syndromes that result from generalized diseases. Additionally, abdominal pain can also be viewed from a viewpoint of being either neuropathic or nociceptive in origin. In neuropathic pain, according to the International Association for the Study of Pain (IASP), there is a lesion or disease of the somatosensory nervous system that results in pain.

Nociceptive pain, in contrast, arises from actual or threatened damage to non-neural tissues and is due to the activation of nociceptors. The pathophysiology of abdominal pain is incredibly complex and includes many overlapping components such as the "Brain-gut axis", the dorsal column, unmyelinated C fibers, and alpha-delta pain fibers. The "Brain-gut axis" describes the bidirectional neural circuit which integrates peripheral input (sensory, motor, and autonomic) and central nervous system input to end organs in addition to its role in gastrointestinal physiology [1]. It had previously been believed that abdominal pain was nociceptive in origin however, recent evidence points to a neuropathic nature. Additionally, the dorsal column plays a key role in both the transmission and modulation of visceral pain and can be subject to changes in signal transduction from conditions that result in chronic stimulation or inflammation of peripheral nerves. A more detailed discussion on this topic can be found in the above-mentioned textbook by Dr. Kapural [2].

Current treatments for chronic abdominal pain are wide-ranging and include lifestyle changes, pain-targeted psychotherapy, cognitive behavioral therapy, non-opioid analgesics, neuropathic medications, non-steroidal anti-inflammatory drugs, muscle relaxants, opioid medications, epidural steroid injection, nerve blocks, medial branch blocks, radiofrequency ablations, peripheral stimulation, and even surgery. Spinal cord stimulators have long been commonly used as the gold standard to treat a variety of refractory chronic pain conditions, however their use in the treatment of abdominal pain is still currently relatively rare and even less studied or published. Herein, we present the most comprehensive review, including case reports, case series, retrospective studies, prospective studies, national surveys, randomized crossover studies, and trials published in English from January 2000 to December 2022 on the use and effectiveness of spinal cord stimulators for the treatment of abdominal pain and presented our findings.

Materials and Methods

Criteria For Considering Studies for This Review

a) Types of studies: Case reports, case series, retrospective studies, prospective studies, national surveys, and randomized crossover studies, published in English from January 2000 to December 2022 were included, to evaluate the most current literature.

b) Types of participants: The patients included in this review varied in age, gender, ethnicity, etiology of abdominal pain, and characterization of abdominal pain.

c) Types of interventions: This review exclusively focused on the use of spinal cord stimulators as the intervention.

d) Types of outcomes: Given the non-standardization of outcome measures across the articles included in this review, specific outcome measures were not an inclusion criteria. This review mainly focused on abdominal pain scores, morphine milligram equivalent (MME) requirements, gastrointestinal symptom relief, and quality of life as primary outcome parameters.

Methods

We performed a comprehensive search using systematic review search methods adhering to the PRISMA-S for Searching checklist [3]. We searched Ovid MEDLINE, Ovid EMBASE, Cochrane Central, and Web of Science. Databases were searched from inception to December 29, 2022. Search structures, subject headings, and keywords were tailored to each database by a medical research librarian (KJK) specializing in systematic reviews in consultation with co-authors. Searches were restricted to English language articles but were not restricted by any other type of limit. We included grey literature resources such as conferences, dissertations, reports, and other unpublished studies for additional relevant citations. Deduplication was performed manually in Endnote. The full search strings for all databases can be found in supplementary (Table 1).

Selection Process

After the initial search, Rayyan software (Rayyan Systems Inc, Cambridge, Massachusetts) was used to screen the citations. Two of the principal investigators (OA, SJ) independently screened the titles and abstracts of the articles to identify potentially relevant studies. Disagreements were resolved by consensus. Studies that passed the title/abstract review were retrieved for full-text review. The two investigators (OA, SJ) then independently screened the remaining full-text articles. Disagreements were resolved by consensus.

Eligibility Criteria

We included case reports, case series. retrospective studies, prospective studies, and national surveys reporting on adult patients (age 18 and above) with any form of non-acute abdominal pain of any origin that underwent treatment with SCS. Primary outcomes were focused on pain scores and gastrointestinal symptom relief. Secondary outcomes included impacts on quality of life, disability, activities of daily living, and pain interference. Review articles, meta-analyses studies, and conference abstracts were not included. We also excluded animal studies, studies performed before 2000, studies that were not in English, studies reporting on pelvic pain, and studies that involved dorsal root ganglion stimulators as the intervention utilized. We identified and linked multiple reports of the same study, and we excluded them if they were duplicated or not relevant. We combined reports that described different findings from the same study and excluded papers that reported results that had already been published.

Data Collection

We extracted data on the following: type of study, year published, language published, number of patients in each study, abdominal pain type and origin, stimulator lead type and lead tip position, type of waveform utilized, and primary and secondary outcomes after SCS placement. Two review authors (OA, SJ) independently extracted data using a data extraction form created with Excel. We resolved any disagreements by discussion. We considered studies to have sufficient data if at least one data point was discussed in the data categories mentioned above. Studies were presented in a table by year with information on the aforementioned data presented in an organized fashion. In our discussion, we grouped studies by types of abdominal pain: mesenteric ischemia, irritable bowel syndrome, chronic pancreatitis, etc.

Results

We retrieved 450 unique articles for review. Of these, 27 studies met all the criteria for inclusion in this systematic review. These included 14 case reports, 5 case series, 5 retrospective studies, 1 national survey, 1 randomized crossover pilot study, and 1 prospective study. The PRISMA flow diagram (Figure 1) shows the entire selection process from the original search results to the final selection of studies (Table1).

Table 1: Search Strings.

OVID EMBASE

1. exp spinal cord stimulator/
2. exp spinal cord stimulation/
3. ("spinal cord stimulat*" or "spinal cord epidural stimulat*").ti,ab.
4. OR/1-3
5. exp Abdominal Pain/
6. exp Epigastric pain/
7. Exp Inflammatory bowel disease/
8. Crohn Disease/
9. Ulcerative colitis/
10. ((pain* ADJ3 abdom*) or "Abdominal Pain*" or "Abdominal visceral pain*" or "Abdominal wall pain*" or "Abdominal neuropathic pain*" or "chrohn* disease" or "epigastric pain*" or "epigastric discomfort" or "Gastrointestinal disorder*" or "Gastrointestinal Pain*" or "inflammatory bowel disease" or "Irritable bowel syndrome" or "Mesenteric ischaemia" or Pancreatitis or "pancreatic pain" or "pancreatic cancer pain*" or "Sphincter ODDI" or "ODDI sphincter" or "ulcerative colitis" or "Visceral abdominal pain*").ti,ab.
11. OR/5-10
12. AND/4,11
13. Limit 12 to english language

OVID MEDLINE

1. exp spinal cord stimulation/
2. ("spinal cord stimulat*" or "spinal cord epidural stimulat*").ti,ab.
3. OR/1-2
4. Abdominal Pain/
5. Exp Inflammatory bowel diseases/
6. Crohn Disease/
7. Colitis,Ulcerative/
8. ((pain* ADJ3 abdom*) or "Abdominal Pain*" or "Abdominal visceral pain*" or "Abdominal wall pain*" or "Abdominal neuropathic pain*" or "chrohn* disease" or "epigastric pain*" or "epigastric discomfort" or "Gastrointestinal disorder*" or "Gastrointestinal Pain*" or "inflammatory bowel disease" or "Irritable bowel syndrome" or "Mesenteric ischaemia" or Pancreatitis or "pancreatic pain" or "pancreatic cancer pain*" or "Sphincter ODDI" or "ODDI sphincter" or "ulcerative colitis" or "Visceral abdominal pain*").ti,ab.
9. OR/4-8
10. AND/3,9
11. Limit 10 to english language

COCHRANE

Abdominal Pain or Abdominal visceral pain or Abdominal wall pain or Abdominal neuropathic pain or chrohn disease or epigastric pain or epigastric discomfort or Gastrointestinal disorder or Gastrointestinal Pain or inflammatory bowel disease or Irritable bowel syndrome or Mesenteric ischaemia or Pancreatitis or pancreatic pain or pancreatic cancer pain or Sphincter ODDI or ODDI sphincter or ulcerative colitis or Visceral abdominal pain in Title Abstract Keyword AND spinal cord stimulation in Title Abstract Keyword - (Word variations have been searched)

Web of Science

("Abdominal Pain*" or "Abdominal visceral pain*" or "Abdominal wall pain*" or "Abdominal neuropathic pain*" or "chrohn* disease" or "epigastric pain*" or "epigastric discomfort" or "Gastrointestinal disorder*" or "Gastrointestinal Pain*" or "inflammatory bowel disease" or "Irritable bowel syndrome" or "Mesenteric ischaemia" or Pancreatitis or "pancreatic pain" or "pancreatic cancer pain*" or "Sphincter ODDI" or "ODDI sphincter" or "ulcerative colitis" or "Visceral abdominal pain*") (All Fields) and **«spinal cord stimulat*»** (All Fields)

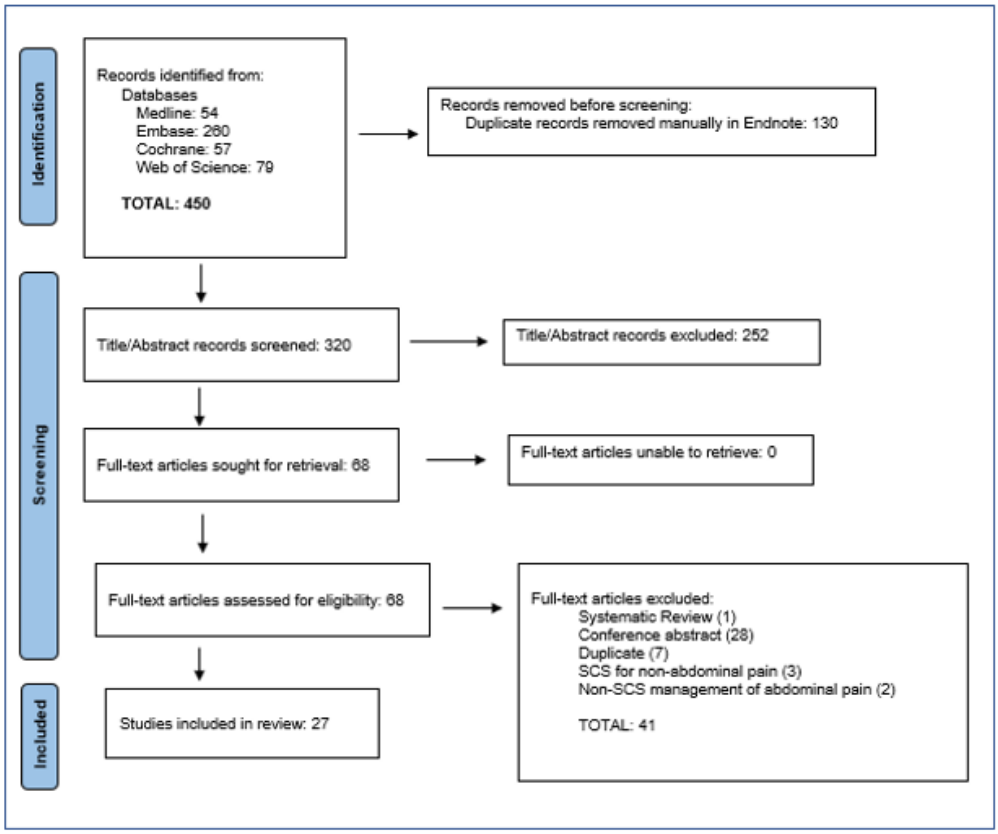


Figure 1: PRISMA Flow Diagram.

Results

Search Results

A total of 450 relevant articles were identified in the literature search (Figure 1). Of these articles, 27 were found to meet the inclusion criteria of the focus of this review and were included. Articles that were excluded were those that did not include abdominal pain as the primary patient presentation, those that did not include the use of a spinal cord stimulator in the treatment of abdominal pain, studies on non-human subjects, review papers, and those that were published in any language other than English. The included studies are the following: 14 case reports, 5 case series, 5 retrospective studies, 1 national survey, 1 randomized crossover pilot study, and 1 prospective study (Table 2).

Table 2: Summary of Articles on the Use of Spinal Cord Stimulators for the Treatment of Abdominal Pain.

Author/Year	Study Design	Number of Patients	Abdominal Pain Type/ Etiology	Lead Type/Lead Tip Position/ Waveform Type	Outcome After Spinal Cord Stimulator Placement
Ceballos et al 2000 (4)	Case Report	1 patient	Chronic colicky post-prandial visceral abdominal pain from mesenteric ischemia	Medtronic tetrapolar system/T8/ Tonic	The patient had complete analgesia at 12 month follow-up and cessation of all analgesic medications.
Krames et al 2004 (5)	Case Report	1 patient	Visceral (cramping, sharp, stabbing, electrical-like shooting upper) abdominal pain from irritable bowel syndrome	Medtronic quadropolar system/ T8/Tonic	The patient had 90% pain relief during the 2 week trial period so a permanent SCS was implanted. At 10 month follow-up, the patient had decreased pain scores and MME requirements, was diarrhea free, and improved quality of life.
Khan et al 2005 (6)	Case Series	9 patients	Visceral abdominal pain (Patients 1-5 had deep, sharp, achy, and shooting epigastric pain from chronic nonalcoholic pancreatitis, patient 6, 7, and 8 had generalized abdominal pain and sharp pain localized to incisional neuromas, and patient 9 had generalized abdominal pain after post-traumatic splenectomy)	Patients 1, 2, and 3: Medtronic or Advanced Neuromodulation System (ANS) octapolar system/T5–T6/ Tonic Patient 4: Medtronic or ANS octapolar system /T5-T6/Tonic Patient 5: Medtronic or ANS octapolar system /One lead was placed at T5–T6 and the another at T6–T8/ Tonic Patients 6 and 7: ANS octapolar system/T6–T7/Tonic Patient 8: ANS octapolar system /T5–T7/Tonic Patient 9: ANS octapolar system /T6–T7/Tonic	There was an overall mean reduction of 4.9 points in the VAS score for pain intensity and a > 50% decrease in narcotic use. All the patients were followed for more than one year with "excellent outcomes and minimal complications".
Kapur et al 2006 (7)	Case Series	2 patients	Both patients experienced paroxysmal abdominal pain secondary to Familial Mediterranean fever Case 1: Intense. Burning, and stabbing lower abdominal pain in the T10–T12 dermatomes Case 2: Diffuse and poorly localized abdominal pain in the T8–T11 dermatomes	Case 1: Advanced Neuromodulation octorpolar system/T8–T9/Tonic Case 2: Precision octapolar system/ T6–T7/Tonic	Case 1: The patient was weaned off all systemic opioids and was able to return to her full-time job by 6 months. Three-year follow -up showed that the degree of analgesia was maintained. Case 2: At 3-month follow-up after implantation of SCS, the patient's VAS decreased from 10/10 to 1/10.
Tiede et al 2006 (8)	Case Series	2 patients	Both patients had refractory visceral abdominal pain Case 1: Postprandial abdominal pain and debilitating nausea, diarrhea, and vomiting. PMH of laparoscopic cholecystectomy with many complications and revision fundoplications and splenectomy Case 2: Debilitating postprandial pain secondary to extensive GI history and surgical complications after Roux-en-Y surgery,	Case 1: Advanced Neuromodulation octapolar system /T2/Genesis IPG neuropulse system Case 2: Advanced Neuromodulation octapolar system /T2/ Genesis IPG neuropulse system	Case 1: The patient had decreased pain scores, discontinuation of opioids, and was able to return to work but had long term response failure secondary to lead migration. Case 2: The patient's post-prandial pain decreased to 2-3 out of 10 from 10/10, she discontinued her PRN hydromorphone, and decreased morphine dose by 33%. At 3-month follow-up, the patient continued to have significant pain relief.

Kapural et al 2008 (9)	Case Report	1 patient	Chronic visceral abdominal pain from chronic pancreatitis	Advanced Neuromodulation octapolar system/ Right lead tip at T7 and left lead tip at T6/ION Pulse Generator	The patient's VAS pain score decreased from 8 to 1 during the two-week trial and remained at three months follow-up after SCS implant. The patient had complete cessation of opioids and the pain disability index decreased from 62 to 15.
Kim et al 2009 (10)	Case Report	1 patient	Intractable visceral abdominal pain from nonalcoholic pancreatitis	Advanced Neuromodulation octapolar system/ Right lead tip at T6 and left lead tip at T8/Tonic	The patient was followed up for more than 14 months and had decreased pain scores, from 10/10 to 5/10 in VAS, from 44/75 to 36/75 in pain rating index, and from 45/70 to 42/70 in functional disability, and decreased MME requirements.
Yakolev et al 2009 (11)	Case Report	1 patient	Intractable stabbing periumbilical visceral abdominal pain Bannayan-Riley- Ruvalcaba syndrome	Medtronic Octapolar System/Right lead tip at T6 and left lead tip at T7/RestoreUltra Generator	The patient was followed for six months and reported 100% pain relief, was able to discontinue all pain medications, had an improvement in her ability to perform activities of daily living, and resolution of constipation.
Kapural et al 2010 (12)	Retrospective Study	35 patients	Chronic visceral abdominal pain 26 with chronic pancreatitis, 6 with post-surgical adhesions, 1 with mesenteric ischemia and gastroparesis, 1 with adhesions and mesenteric ischemia, and 1 with post-gastric surgery syndrome	In most patients: St. Jude Medical or Boston Scientific quadriopolar and/or octapolar systems/ T5 or T6/Tonic For patients with lower abdominal quadrant pains: one octapolar or dual octapolar systems or transverse tripol using one octapolar and two quadripolar systems/ T11 or T12/Tonic	Thirty patients (86%) reported at least 50% pain relief upon completion of the trial. Five patients failed the trial. Among the 28 patients who received permanent implant, 19 followed at least a year. One patient, despite the successful trial felt no improvements at 6 months after the implant and requested an explant of the SCS device. Their VAS pain scores remained low (3.8 +/- 1.9 cm; $P < 0.001$) at 1 year, as did opioid use (38 +/- 48 mg morphine equivalents; $P = 0.089$).
Kapural et al 2010 (13)	National Survey	70 patients	Chronic visceral abdominal pain 23 patients with chronic pancreatitis, 20 with post-surgical intra-abdominal adhesions, 9 with gastroparesis, 9 with post-surgical pain, and 9 with undetermined cause. Pain was most commonly described as "burning" or "aching".	Mostly octapolar systems/ Mostly at T5-T6/Tonic	The patients were followed for an average of 84 weeks and pain relief exceeded 50% in 66 of 70 patients (four patients failed the SCS trial) reported in addition to decreased MME requirements. VAS pain scores before an implant were 8 +/- 1.9 cm, while after the implant 2.49 +/- 1.9 cm. The opioid used before an implant was 158 +/- 160 mg and at the last office visit after the implant 36 +/- 49 mg.

Yakovlev et al 2010 (14)	Case Series	15 patients	Intractable lower abdominal pain that was post-herniorrhaphy	Medtronic octapolar system/Lead tip position was T7-T9/Tonic	The patients were followed for 12 months, and all reported significant pain relief (>75% reduction in visual analog scale) and all patients were able to decrease or discontinue use of pain medications. Patients also reported other positive outcomes including the ability to return to family, social, and educational activities.
Caruso et al 2011 (15)	Case Report	1 patient	Severe visceral abdominal pain from mesenteric ischemia	Medtronic octapolar system//T4/Tonic	The patient experienced a reduction in pain scores and opioid consumption after SCS placement. Fifteen days after the permanent implantation, the pain relief was still 75% and only one episode of postprandial pain occurred with an NRS-11 value of 2.
Kapural et al 2011 (16)	Retrospective Chart Review	30 patients	Chronic visceral abdominal pain from chronic pancreatitis	Octapolar system/T5 (ten patients), T6 (ten patients), T4 (four patients)/Tonic	Twenty-four patients (80%) reported at least 50% pain relief on completion of the trial. 20 patients were followed for the whole year after implant and VAS pain scores remained low (3.6 ± 2 cm; $p < 0.001$) at one year, as did opioid use (48.6 ± 58 mg morphine equivalents).
Al-Mahrouqi et al 2012 (17)	Case Report	1 patient	Debilitating upper abdominal visceral pain from chronic pancreatitis secondary to pancreatic divisum	Octapolar system/T8-9/Tonic	The patient was followed for 9 months and described no attacks and minimal pain. Additionally, the patient was reported to have a vastly improved quality of life and ability to work.
Rana et al 2012 (18)	Case Report	1 patient	Visceral abdominal ("crampy and sharp") pain from irritable bowel syndrome	St. Jude Medical tripolar configuration of midline octapolar and two quadripolar leads/T8/Tonic	The patient was followed for one year and had a 60-70% improvement in pain scores, relief of his abdominal and thoracic pain, better management of his gastrointestinal symptoms, and improved quality of life.
Baranidharan et al 2014 (19)	Retrospective Series	26 patients	Visceral neuropathic abdominal pain (dermatomal hyperalgesia or sympathetically mediated neuropathic abdominal pain)	Octapolar system/Electrodes were placed ventrally at T9/10 for upper abdominal pain and at T10/11–T11/12 for lower abdomen pain. 16 patients had ventral column electrodes and 10 had dorsal placement/Tonic	Four patients failed the trial and five patients explanted total, so the remaining 21 patients were followed for 26 months and reported decreased VAS pain scores from 9 to 4 ($p \leq 0.05$), a reduction in MME from 160mg to 26mg ($p < 0.001$). In addition, the authors report that the quality of life, activities of daily living, and patient global impression of change improved for the patients.

Vergani et al 2014 (20)	Case Series	2 patients	Intractable visceral abdominal pain related to chronic pancreatitis (one that was alcoholic in origin and the other non-alcoholic)	Medtronic quadripolar system/T8/ Tonic	The two patients were followed for a mean of 7 years and had a 80% (non-alcoholic pancreatitis) and 90% (alcoholic pancreatitis) decrease in VAS pain scores, respectively. Both patients were able to discontinue pain medications completely.
Lee et al 2015 (21)	Case Report	1 patient	Chronic right upper quadrant visceral abdominal pain from sphincter of Oddi dysfunction	Advanced Neuromodulation System octapolar system/T5/tonic	The patient was followed-up with for more than six months, had >50% pain relief (based on VAS scores) without complications, decreased MME requirements, and was able to complete her daily activities.
Lind et al 2015 (22)	Randomized crossover pilot study	10 patients	Visceral abdominal pain from irritable bowel syndrome	Medtronic quadripolar system/ lead tip position varied from T5 to T7/ Tonic	The patients were followed for 18-78 months. Nine patients completed the entire trial. During stimulation periods, the median pain scores were significantly reduced from (VAS) 7 (4–8) to 3 (2.5–7) and to 4 (2–6) during early and late stimulation periods, respectively ($P < 0.03–0.04$). Pain attacks were numerically reduced. A few patients reported reduced number of diarrheas. After study termination, six patients chose to retain their SCS system.
Delange Segura et al 2019 (23)	Case Report	1 patient	Chronic visceral abdominal pain from chronic pancreatitis	St. Jude Medical octapolar system/ T5 level/Burst stimulation utilized as rescue therapy after tonic stimulation	The patient was followed for 6 months and had >50% reduction in VAS pain scores, decreased MMEs from 300 mg to 125 mg per day, and had a high degree of satisfaction.
Kapural et al 2020 (25)	Prospective, Single-arm, Multicenter Study	24 patients	Intractable chronic visceral abdominal pain 15 patients with gastroparesis, 8 with post-surgical/post-traumatic abdominal pain, 5 with chronic pancreatitis, 3 with generalized abdominal wall pain, 1 with irritable bowel syndrome, and 1 with neuropathy	Senza octapolar system/T4–T8/10-kHz high-frequency stimulation	After 12 months of treatment, 78.3% of subjects were responders (pain relief of ≥50%) and 14 of 22 subjects (63.6%) were remitters (sustained ≤3.0-cm visual analog scale scores). Secondary outcomes, including assessments of disability, mental and physical well-being, sleep quality, perception of improvement, and satisfaction, showed that SCS greatly improved the quality of life of patients with CAP. Observationally, most subjects also reported concurrent reduction or resolution of nausea and/or vomiting.

Berger et al 2020 (26)	Case Report	1 patient	Severe visceral chronic lower abdominal pain of unknown origin and post-laminectomy syndrome	Octapolar system/One lead tip at T8 to address the chronic back pain and radiculopathy and one at T6 to provide lower abdominal coverage/10-kHz high-frequency stimulation	The patient reported 70% improvement in back pain and radiculopathy along with 100% relief of his abdominal pain after SCS placement and continued to endorse good pain relief on follow-up appointments (follow up time not specified).
Richter et al 2020 (27)	Retrospective review	3 patients	Chronic abdominal pain (visceral and mixed) from post-herniorrhaphy pain syndrome, Crohn's disease, abdominal neuropathy	Abbott 5-column paddle system/ T6 (1 patient), T7 (1 patient), T8 (1 patient)/BurstDR	All 3 patients were followed for >24 months. Two patients reported 100% pain relief and one patient reported 60% decrease in severity of monthly pain exacerbations. All patients had decreased MME requirements and reported improved quality of life.
Cox et al 2021(28)	Case Report	1 patient	Visceral epigastric pain from chronic pancreatitis	Octapolar/T7/High-frequency stimulation	The patient was followed for 9 months and endorsed 60-70% relief of axial low back pain, near-total relief of epigastric pain, >50% reduction in MME requirements, and a significant increase in function.
Kapural et al 2021 (29)	Retrospective Chart Review	26 patients	Primary diagnosis of refractory abdominal pain, nausea, and vomiting (20 with gastroparesis or gastroparesis-like diagnosis, 2 with unspecified chronic abdominal pain, and 1 with recurrent small bowel obstruction).	Octapolar system (companies varied)/ One lead tip at T4 and one at T5/Tonic (11 patients) and 10kHz (12 patients)	23 patients were then followed for an average of 41 months (3 failed the trial). 17 out of the 23 patients, at their most recent follow-up, had a >50% reduction in VAS pain scores, >50% reduction in MME requirements, >50% reduction in days of nausea per month, and 50% reduction in vomiting episodes. Additionally, 20 of the 23 patients indicated that they would recommend spinal cord stimulation to others with the same diagnosis.
Shearin et al 2021 (30)	Case Report	1	Chronic visceral periumbilical and right-sided abdominal pain due to uncertain etiology	Boston Scientific octapolar Artisan Paddle system/T6/Tonic in 2008	The patient reported an 80% decrease in pain scores during the 12 years since SCS implantation when compared to before SCS placement. She had no nausea, vomiting, diarrhea, or severe abdominal pain. She stated that her appetite was no longer limited by her symptoms, that she was able to go on daily walks without pain, and that her concentration and overall outlook on life have improved.
Mamaril-Davis et al 2022 (31)	Case Report	1 patient	Refractory right upper quadrant visceral abdominal pain from Sphincter of Oddi dysfunction and chronic pancreatitis	Boston Scientific octapolar system/ T6 to T7 level/Tonic	The patient was followed for 18-months and reported 90% relief of pain and was able to complete daily activities without issue.

Discussion

Our literature search was focused on the effect of spinal cord stimulators in the treatment of any type of abdominal pain and resulted in 27 unique articles over the past two decades. The causes of abdominal pain were diverse, the characterization of the pain varied but was mostly visceral, and the location of pain varied as it was poorly localized. The most common lead type used was an octopolar lead system and the most common lead tip position was the T6 to T8 region. Figure 2 below shows the abdominal dermatomes in relation to the abdominal organs and Figures 3 and 4 below show a graphic of general abdominal dermatome coverage in relation to SCS lead tip placement and location based on the studies included in this article. All patients included received a SCS trial and were only given a permanent SCS if they had a significant reduction in abdominal pain scores during the trial. The follow-up time after permanent SCS implantation varied from one month to seven years but was approximately 12 months in most articles. For the majority of articles, VAS scores were used in pain assessment and the results varied from >50% relief to complete analgesia.

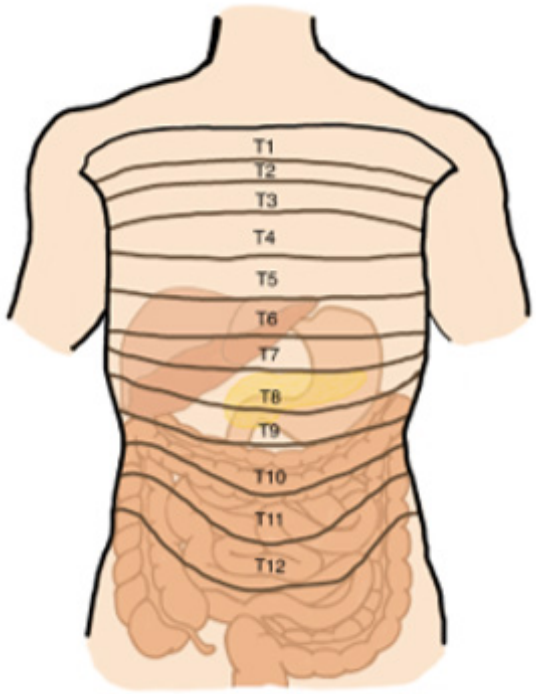
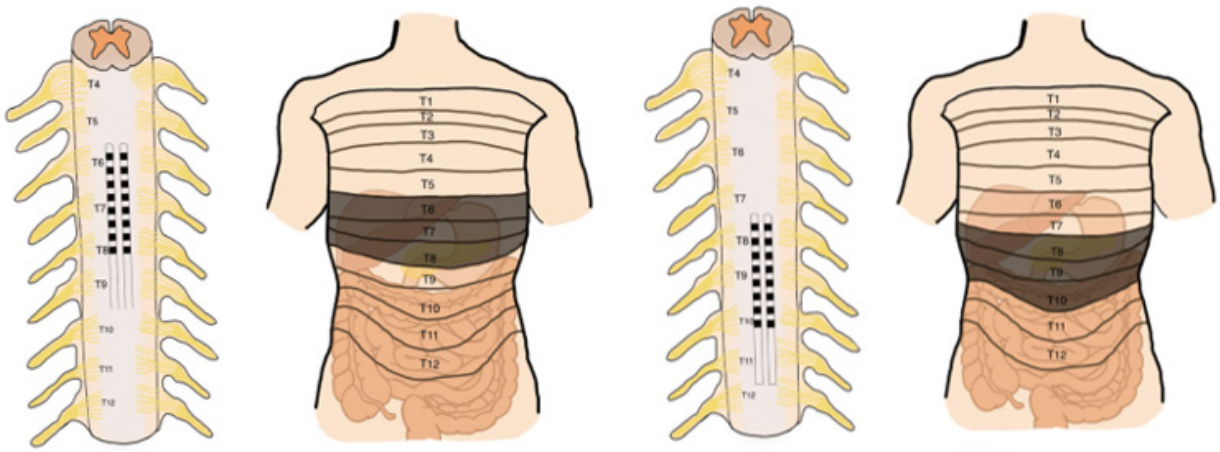


Figure 2: Dermatomes of the abdomen in relation to the abdominal organs.



Figures 3&4: Spinal cord stimulator placement and lead tip position in relation to stimulator coverage in the abdomen generally observed.

In every article review, there is mention of decreased morphine milligram equivalent (MME) requirements. Additionally, many of the articles mention gastrointestinal symptom relief, improvement in quality of life, and ability to return to daily activities (Figures 2-4). The below discussion has the 27 included literature findings grouped by specific etiology of abdominal pain to provide a useful perspective in assessing the efficacy of SCS in treating abdominal pain. This includes mesenteric ischemia, postprandial abdominal pain, irritable bowel syndrome, chronic pancreatitis, more rare etiologies such a familial Mediterranean fever, Bannayan-Riley-Ruvalcaba Syndrome, and sphincter of Oddi dysfunction, and larger studies that focused on visceral abdominal pain of various etiologies. Pain due to mesenteric ischemia can be debilitating in nature and challenging to manage. Ceballos et al and Caruso et al both published case reports of patients with severe abdominal pain due to mesenteric ischemia that was refractory to other medical management who underwent SCS and found complete analgesia and cessation of all other analgesics [4-15].

The discussed mechanisms were thought to be due to inhibition of nociceptive input, decreased secondary sympathetic activity, release of prostaglandins and endorphins that play a role in modulation of nociceptive transmission, and induction of peripheral perfusion in occlusive and vasospastic peripheral arteriopathies. In 2006, Tiede et al presented a patient with refractory postprandial abdominal pain although not from mesenteric ischemia in origin, that reported >50% reduction in pain scores and decreased MME requirements (discontinuation of breakthrough hydromorphone and 33% decrease in morphine dose) at three-month follow-up [16]. Irritable bowel syndrome is an equally challenging condition to manage. In 2004, Krames et al presented a 50-year-old female with a 30-year history of abdominal pain and diarrhea secondary to IBS that experienced decreased pain scores, decreased MME requirements, cessation of diarrhea, and improved quality of life during a ten-month follow-up after SCS placement [17].

The authors discussed the visceral hypersensitivity to luminal distention that occurs in IBS, the role of spinothalamic tracts in the context of chronic pain that is of visceral origin, the role that postsynaptic dorsal column pathways may play in pain signal amplification, and the role of SCS to increase blood flow via antidromic activation of sensory afferents and resulting neuromodulators substance release. Similarly, in 2012, Rana et al presented a case report on a 36-year-old male with an eight-year history of "crampy and sharp" abdominal pain secondary to constipation predominant IBS which had failed conservative therapy including opioids and psychologic treatment [18]. The patient received a SCS with the lead tip at T8 and was followed for one year during which he reported greater than 60-70% improvement in pain scores, improvement in IBS symptoms, improved quality of life, and ability to function at work. Moreover, in a randomized crossover pilot study of ten patients with chronic abdominal pain secondary to IBS who received a SCS with lead tip at T5-T8 and were followed over 28 weeks, nine completed the trial and reported decreased VAS pain scores (from 7 to 3 and to 4 during early and late stimulation periods, respectively, P <0.03-0.04), decreased pain attacks, and reduced episodes in diarrhea in some patients [19-22].

Chronic pancreatitis is another debilitating diagnosis and can be extremely difficult to manage the pain. In 2005, Khan et al present nine patients with varying etiologies of abdominal pain including chronic pancreatitis, generalized abdominal pain, abdominal wall neuroma, and post-traumatic splenectomy. All the patients received a SCS and were followed for more than one year in which all with an overall mean reduction of 4.9 points in the VAS score for pain and >50% in MME requirements. The authors discuss the importance of dermatomal paresthesia, in the context of abdominal visceral pain modulation, in order to ensure concordance with the viscerotomal nervous distribution of the various abdominal pain conditions in their patients. This was reflected by pancreatic pain covered via SCS placement at T5-T6 and post-splenectomy pain coverage via SCS placement at T6-T7. Moreover, Kapural et al. published a retrospective chart review of 30 patients (20 females and 10 men) with chronic pancreatitis (for an average of 7.8 years +/- 5 years) that was epigastric in location for most and sharp, stabbing, and aching in nature.

24 patients reported at least 50% pain relief with the trial (6 failed the trial) and, of them, 20 patients received an implant (one patient was lost to follow-up and three were removed due to infection). The 20 patients were followed for a year and continued to report both greater than 50% reduction in pain scores in addition to decreased MME requirements [23]. More recently, In 2020, Kapural et al presented the first prospective (12- month, single-arm) study on the safety and efficacy of SCS in 24 patients with intractable chronic abdominal pain [24]. The diagnosis of the patients varied (see Table 1 above), average age of 47.7, gender majority female (19 out of 24), and average diagnosis duration was 7.8 years. With the SCS trial (leads placed from T4-T8), 23 out of the 24 patients reported at least 70% pain relief and these 23 patients received an SCS implant. After a 12-month follow-up, 78.3% of the patients reported 50% or more pain relief as well as improvements in many patients in secondary outcomes of functional capacity, quality of life, sleep, and gastrointestinal symptom relief [25]. In addition to the widely accepted gate control theory of pain as a mechanism through which SCS provides benefit in this setting, other mechanisms presented include neural conduction blockade, activation of putative supraspinal pain centers, supraspinal or intraspinal sympathetic blockade, and release of neuromodulators.

Of note, Ranayake et al published a thorough systematic review in 2019 focused on the utilization of SCS in treating abdominal pain specifically from chronic pancreatitis. The seven articles from that systematic review are included in this article. SCS has shown beneficial for rare causes of abdominal pain as well. In 2006, Kapur et al presented two patients with paroxysmal abdominal pain, fever, nausea, and vomiting secondary to familial Mediterranean fever. Both patients received a SCS, and both reported decreased VAS pain scores and decreased MME requirements. In 2009, Yakovlev et al presented an eighteen-year-old female with intractable chronic periumbilical abdominal pain secondary to Bannayan-Riley-Ruvalcaba Syndrome that had failed conservative therapy, extensive workup, and medical management. The patient received a SCS at T6-T7 and reported >50% decrease in pain scores, discontinued

all pain medications, had an improvement in her ability to perform daily activities, and resolution of constipation.

The following year, Yakovlev et al presented a case series of 15 patients with intractable abdominal pain that was post-herniorrhaphy. The patients received a SCS at T7-T9 and were followed for 12 months after which they all reported significant pain relief (>75% reduction in visual analog scale) and all patients were able to either decrease or discontinue use of pain medications. In 2015, Lee et al presented a case report of a 58-year-old female with chronic right upper quadrant abdominal pain due to sphincter of Oddi dysfunction that received a SCS at T5-7. She was followed for more than six months and reported >50% reduction in VAS pain scores and decreased MME requirements. Mamaril-Davis et al presented a case report, most recently, in 2022 on a patient in their thirties with chronic abdominal pain secondary to medically refractory sphincter of Oddi dysfunction and chronic pancreatitis.

The had as successful seven-day SCS trial and underwent permanent SCS placement with dual octopolar electrodes at T6-7 and reported, at 18-month follow-up, 90% pain relief and ability to return to normal daily activities. In 2020, Berger et al presented a case report on a 56-year-old male with chronic severe lower abdominal pain and chronic back pain that had failed medical management, psychotherapy, cognitive behavior therapy, lumbar and epidural steroid injections, and nerve blocks [26]. The patient received two 8-contact leads placed (one at T8 to address the chronic back pain and one at T6 for lower abdominal pain coverage). The patient reported 100% relief of abdominal pain and 70% relief of back pain during follow-up appointments. That same year, Richter et al presented a clinical series of 3 patients with chronic abdominal pain of different origins (post-herniorrhaphy pain syndrome, Crohn's disease, and intercostal neuralgia) that received a 5-column paddle SCS (one patient at T6, one patient at T7, and one patient at T8 for lead tip position) [27].

The patients were followed for at least two years and two patients reported being entirely pain free. The third patient reported a 60% decrease in pain severity, a 33% in frequency of the monthly pain exacerbations, and was able to completely discontinue all opioids. All three patients reported an improvement in quality of life. In 2021, Shearin et al presented a case report on a 57 year-old female with over 20 years of visceral abdominal pain of uncertain etiology that was refractory to medical management and multiple interventional pain procedures [28]. The patient received a paddle SCS at T6/T7 and during 12 years of follow-up, reported a 80% decrease in pain scores since SCS implantation when compared to before SCS placement and improved quality of life. The authors thus propose that SCS, in the context of the aforementioned mechanisms it is believed to decrease visceral pain, as an alternative treatment in patients with chronic abdominal pain that is refractory to non-surgical interventions.

In 2021, Kapural et al presented a retrospective chart review of 26 patients that underwent a SCS trial for a primary diagnosis of refractory abdominal pain, nausea, and vomiting. 23 of the 26 patients reported >50% reduction in pain after the trial and were followed for an average of 41 months after permanent SCS implantation (either low or high frequency devices used) [29]. At last follow-up, there was a >50% reduction in pain scores and MME requirements. Additionally, the days of nausea per month decreased from 26.3 days to 11.7 days per month. 20 out of the 23 patients reported being satisfied with their therapy and would recommend it to others with the same diagnosis. The authors note that the improvement in nausea and vomiting seen in their patients may be related to decreased opioid requirements, the anti-emetic effects from gastric physiology modulation, and possibly improvement in gastric emptying among the majority of patients that had gastroparesis.

There were, however, select cases where the use of SCS did not provide relief of abdominal pain. In 2006, Tiede et al presented a patient with chronic abdominal pain that ultimately had response failure to SCS due to lead migration from a fall. Kapural et al reported five patients in 2010 that failed SCS trial that were later trialed on alternative therapies. In a 2011 retrospective chart review, Kapural et al reported six patients that failed SCS trial, with mention of those patients having a higher rate of depression, alcoholism, and poor response to sympathetic nerve block. In 2014, Baranidharan et al reported four patients that failed SCS trial with mention that initial failure of neuromodulation was seen in patients that had a lack of response to sympathetic blocks and exhibited opioid-seeking behaviors [30,31]. This review, although is the most comprehensive of its kind to date, does have some limitations.

This selected timeframe was purposely chosen in order to review the early use of SCS for abdominal pain and track its progression in the context of patient outcomes to present date. This review article included literature published only in English. For the relevant articles that were included in this narrative review, the sample size was relatively small due to the still relatively rare use of spinal cord stimulators for the treatment of abdominal pain. The characterization and location of abdominal pain varied amongst the review patient population and it is recognized that, in discussing outcomes, pain is subjective. Additionally, the articles presented may not be fully representative of the experience with SCS in the treatment of abdominal pain due to negative publication bias. Lastly, the time to follow-up between patients varied and is included in Table 1 above.

Conclusion

In our review we present the most comprehensive review of SCS on abdominal pain to date. Although the patients were heterogenous in age along with gender and the etiologies of abdominal pain in the patients reviewed varied, along with the location and type of pain experienced, the majority of patients in this review experienced a benefit from SCS placement. This was supported by decreased pain scores, decreased morphine milligram equivalent requirements, reported relief of gastrointestinal symptoms, improvement in quality of life, and improvements in daily functional ability. As the use of SCS for the treatment of chronic abdominal pain is currently considered "off-label" by The United States Food and Drug Association, this review supports the commencement of randomized controlled trials to further explore SCS as a treatment option for chronic abdominal pain.

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Conflict of Interest

No conflict of Interest.

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