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REVIEW

The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain

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Introduction: Painful lumbar spinal disorders represent a leading cause of disability in the US and worldwide. Interventional treatments for lumbar disorders are an effective treatment for the pain and disability from low back pain. Although many established and emerging interventional procedures are currently available, there exists a need for a defined guideline for their appropriateness, effectiveness, and safety.

Objective: The ASPN Back Guideline was developed to provide clinicians the most comprehensive review of interventional treatments for lower back disorders. Clinicians should utilize the ASPN Back Guideline to evaluate the quality of the literature, safety, and efficacy of interventional treatments for lower back disorders.

Methods: The American Society of Pain and Neuroscience (ASPN) identified an educational need for a comprehensive clinical guideline to provide evidence-based recommendations. Experts from the fields of Anesthesiology, Physiatry, Neurology, Neurosurgery, Radiology, and Pain Psychology developed the ASPN Back Guideline. The world literature in English was searched using Medline, EMBASE, Cochrane CENTRAL, BioMed Central, Web of Science, Google Scholar, PubMed, Current Contents Connect, Scopus, and meeting abstracts to identify and compile the evidence (per section) for back-related pain. Search words were selected based upon the

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section represented. Identified peer-reviewed literature was critiqued using United States Preventive Services Task Force (USPSTF) criteria and consensus points are presented.

Results: After a comprehensive review and analysis of the available evidence, the ASPN Back Guideline group was able to rate the literature and provide therapy grades to each of the most commonly available interventional treatments for low back pain.

Conclusion: The ASPN Back Guideline represents the first comprehensive analysis and grading of the existing and emerging interventional treatments available for low back pain. This will be a living document which will be periodically updated to the current standard of care based on the available evidence within peer-reviewed literature.

Keywords: back pain, intervention, clinical guideline, spinal cord stimulation, minimally invasive spine procedure, lumbar disorder, epidural steroid injection, radiofrequency ablation

Introduction

Objectives, Scope, and Goals

The objective of the American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline for Interventional Treatments of low back pain (LBP) is to provide evidence-based recommendations to address the appropriate utilization of interventional treatments for LBP. This guideline is intended to represent a comprehensive review of the spectrum of interventional treatments for LBP. The guideline is based upon the highest quality of clinical evidence available at the time of publication. The goals of the guideline are to assist clinicians in delivering the highest quality evidenced back interventional treatments, as well as understanding the known risks and complications of interventional treatments. The ASPN Back Guideline is intended to be updated periodically to maintain relevance with the current treatment landscape and empirical literature. Although the guideline represents a comprehensive review of the majority of the interventional treatments for LBP, it is important to note that not all interventional techniques were included. Exclusion of any particular technique does not necessarily suggest that the omitted therapies are inappropriate clinical use. The ASPN Back Guideline does not represent a standard of care. Treatment should be based on an individual patient's need and the physician's professional judgement and experience. This guideline is not intended to be used as the sole reason for denial or approval of treatment or services.

ASPN Back Guideline Clinical Committee and Multidisciplinary Collaboration

The ASPN clinical guideline committee is comprised of a diverse group of physicians representing the specialties most commonly involved in the provision of interventional treatments of LBP. This includes physicians from the core specialties of anesthesiology, neurosurgery, physical medicine and rehabilitation, and radiology, as well as a pain psychologist/medical ethicist with many years of experience in consulting with interventional physicians. Committee members were selected based on clinical experience, research, and previous publication history.

Disclosures of Potential Conflicts of Interests

All participants involved in the guideline development have been required to disclose all potential conflicts of interest. All evidence grading was reviewed and validated by committee members with no potential conflict of interest for any particular therapy. Authors with conflicts of interest on subjects with grading criteria were recused from those particular items.

Methods for Literature Search, Evidence Ranking and Consensus Development

The world literature in English from 2000-present was searched using Medline, EMBASE, Cochrane CENTRAL, BioMed Central, Web of Science, Google Scholar, PubMed, Current Contents Connect, Meeting Abstracts, and Scopus to identify and compile the evidence for lower back interventional therapies for the treatment of pain. Search words were created specific to the topics for each major section pertaining to injection therapy, minimally invasive spine procedures and ablative procedures. Identified peer-reviewed literature was critiqued using the United States Preventive Services Task Force (USPSTF) criteria for quality of evidence,[1] with modifications for interventional pain studies (Table 1). The hierarchy of evidence for the project considered RCT as the preeminent classification, followed by prospective observational studies, case series and finally expert opinion. Per the methodology, the process identified RCT and prospective observational studies of STROBE criteria quality in the creation of guidelines. Interventions with more

Table 1 Quality of Evidence Ranking Using United States Preventative Services Task Force Criteria Modified for Interventional Spine Procedures

Grade	Definition	Suggestions for practice
A	The ASPN Back Group recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The ASPN Back Group recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The ASPN Back Group recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The ASPN Back Group recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The ASPN Back Group concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Abbreviation: ASPN, American Society of Pain and Neuroscience.

than one RCT were considered to have sufficient evidence to create conclusions, and observational studies were not considered. Interventions with no RCTs or only one RCT then also utilized prospective observational studies in the creation of guideline recommendations. Should an intervention be found to have no RCTs or observational studies, case series were used. These are clearly denoted by the taxonomy of the recommendation that the predominant quality of evidence is of a classification less than RCT. For interventions where RCT and prospective observational studies are of requisite quality (STROBE) are not available, case series and/or expert opinion may be used in the creation of guidelines to fill in the current literature gap to assist the clinician in selecting care pathways. These designations follow a modified USPSTF process used previously by ASPN and NANS in the creation of guidelines. The details are listed in Table 1. After USPSTF letter grading was assigned, the working subgroup then assigned the "level of certainty regarding benefit" as described in Table 2.

For each major section or topic, the ASPN Back Group formulated consensus points. Consensus points should not be confused with recommendations based on consensus alone, which were rendered as clinical guidance due to the lack of evidence-based literature (such as randomized controlled trials [RCTs], prospective observational studies, retrospective cohort/case series).

Injection Therapy

Epidural Steroid Injections

LBP has consistently been one of the most common causes of functional limitation and absence from work, as it impacts over 80% of the general population around the world.[2,3] A common diagnosis of LBP is lumbar radiculopathy, with a prevalence between 9.9% and 25%.[4] Lumbar radiculopathy is generally defined as LBP that radiates down below the knees to the foot and toes and can be associated with neurological findings such as paresthesia and weakness. Radiculopathy is not only secondary to mechanical compression but may also be due to the release of inflammatory mediators at the site of pathology.[5] When comparing to LBP without radicular symptoms, lumbar radiculopathy is associated with more disability and pain, and thus causes decreased quality of life and increased utilization of health resources.[6] Per current guidelines around the world, treatment for lumbar radiculopathy includes spinal injections, specifically lumbar epidural steroid injections.

Table 2 Levels of Certainty Regarding Net Benefit

Level of certainty	Description
High	The available evidence includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies. **Evidence Level: I-A** - At least one controlled and randomized clinical trial, properly designed
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: • The number, size, or quality of individual studies. • Inconsistency of findings across individual studies. • Limited generalizability of findings to routine primary care practice. • Lack of coherence in the chain of evidence. • As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion. **Evidence Level I-B** - Well-designed, controlled, non-randomized clinical trials (Prospective Observational studies conforming to STROBE criteria) or **Evidence Level I-C** - Retrospective cohort or large case studies (>20 subjects)
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies. • Important flaws in study design or methods. • Inconsistency of findings across individual studies. • Gaps in the chain of evidence. • Findings not generalizable to routine primary care practice. • Lack of information on important health outcome **Evidence Level II** - Expert opinion based of risk-to-benefit or based upon case reports

Abbreviation: STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

Epidural steroid injections are generally performed with three different approaches: interlaminar (midline or parasagittal), transforaminal or caudal. The interlaminar approach is widely used, but limitations can include lack of target specificity and the injectate being distributed to the dorsal epidural space, as opposed to the ventrolateral space.[7] The transforaminal approach, however, is considered to be more specific as this injection localizes the injectate into the ventrolateral epidural space, which is anatomically located in close proximity to the nerve root.[7] The caudal approach can be specifically utilized and may be advantageous in patients with previous spine surgeries, such as a lumbar fusion or laminectomy, in which cases it may be unsafe or anatomically impossible to utilize the interlaminar or transforaminal approach.

Corticosteroid injectable agents are divided into two groups: non-particulate and particulate. Non-particulate corticosteroids are faster in onset but have much shorter acting anti-inflammatory properties. On the other hand, particulate corticosteroids have a slower onset with a longer anti-inflammatory effect. Particulate corticosteroids include triamcinolone, methylprednisolone and betamethasone acetate and are insoluble in saline, local anesthetic and iodinated contrast agents,[8] whereas non-particulate corticosteroids such as betamethasone sodium phosphate and dexamethasone are soluble in all agents.[8] Of the corticosteroids, methylprednisolone is the largest in size while betamethasone is the smallest.[8]

The evidence for the three types of epidural steroid injections and analysis of the literature will serve as the foundation to provide recommendations and guidelines for each type of injection. There have been 48 systematic reviews and 42 RCTs examining the efficacy of epidural steroid injections in the management of chronic spinal pain.[9] These studies have suggested that epidural steroid injections have clear but often not long-lasting reduction in chronic spinal pain.[9] The most recent and authoritative of these systematic reviews was performed by Manchikanti et al. This review outlined the efficacy and the evidence-based recommendations for conditions treated with epidural injection therapy. Additionally, this review comprehensively evaluated the efficacy of each epidural treatment approach (caudal, interlaminar, transforaminal) for given spinal indications (disc herniation, lumbar spinal stenosis, etc.). Given the comprehensive nature and recency of that review, we will

briefly summarize the results from that manuscript as: 1) no new studies were identified in our search process and 2) there have been numerous authoritative reviews of this modality.

Interlaminar Epidural Steroid Injection

The Manchikanti review identified 13 high-quality RCTs evaluating the efficacy of interlaminar steroid injections. Ten studies were rated as high quality. The review concluded that there is Level I evidence treatment of lumbar disc herniation with interlaminar epidural steroid injections and Level II evidence for the treatment of lumbar spinal stenosis and axial/discogenic pain. The manuscript also suggests that overall the treatment effect has been rated as significant with the exception of systematic reviews with methodological flaws. These reviews were not specified. No new or additional studies were identified in our review process in the interval between publication of the Manchikanti study and the preparation of this manuscript.

Transforaminal Epidural Steroid Injection

In the Manchikanti review, there were 13 high-quality RCTs evaluating the efficacy of transforaminal epidural steroid injections. The majority of the studies examined the efficacy of transforaminal approaches in the setting of disc herniation. The evidence synthesis suggested Level I evidence for transforaminal injections in the setting of disc herniation and Level II evidence in the setting of lumbar spinal stenosis.

Caudal Epidural Steroid Injection

In the Manchikanti review, there were ten high-quality RCTs meeting inclusion criteria. Two compared caudal epidural injections to interlaminar and transforaminal injections in the management of disc herniation, while one study compared transforaminal injections to caudal injections in the management of lumbar disc prolapse. The remaining studies evaluated treatment of spinal stenosis, axial back pain or post-surgery syndrome. None of the RCTs were placebo controlled. Using the criteria methodology from that review the following conclusions were drawn concerning caudal epidural steroid injections: Level III evidence that caudal and interlaminar approaches are equivalent, Level II–III evidence for treatment of lumbar spinal stenosis with caudal approaches, Level II in post-surgery syndrome, Level III evidence that transforaminal approaches are superior to caudal approaches.[9]

Evidence Summary

For epidural interventions, RCTs and observational studies with functional status improvement measures were included. Short-term relief was defined as less than six months whereas greater than six months was considered long-term relief. The ASPN consensus guideline committee reviewed the 36 RCTs mentioned above as being of high quality. No additional studies were identified in our search process. For epidural interventions, there was sufficient evidence in the form of RCTs (Table 3), for the committee to make recommendations. Table 4 summarizes those recommendations.

Trigger Point Injections

For trigger point interventions, there was sufficient evidence in the form of RCTs for the committee to make recommendations. A review of RCTs regarding TPIs has revealed 25 studies investigating the efficacy of these injections for myofascial pain syndrome (MPS) with diverse medications. Over 40 RCTs were found through a PubMed literature search for "trigger point injection" that studied trigger point injections (technical variations, adjuncts for MPS treatment, and in comparison to other treatments for MPS). Given the volume of RCTs available, a focus was placed on literature published within the past five years with a focus on further studies outside this time frame to evaluate and clarify points made.

MPS is a soft tissue pain condition, characterized by a localized taut band of muscle that can cause acute or chronic pain.[10] This condition is clinically diagnosed by identification of the characteristic taut bands on physical exam and a history indicative of myofascial pain, although objective means for diagnosis are often costly and not widely available. Diagnostic criteria defined by Simons et al are often referenced when describing the features of trigger points including the presence of taut bands, tenderness from taut bands, reproducibility of pain, local twitch response, restricted range of motion, autonomic symptoms, and referred pain.[11] Palpation of an active trigger point can cause referred pain through

Table 3 Evidence Summary for Epidural Steroid Injections

Study author	Study type	Study size	Endpoints	Evidence level	Notes
Ghai et al[7]	RCT	69	NRS	I-A	Comparing lidocaine versus lidocaine Mixed with methylprednisolone
Manchikanti et al[408]	RCT	70	NRS	I-A	Comparing local anesthetic only or with local anesthetic mixed with non-particulate betamethasone
Gharibi et al[409]	RCT	42	NRS	I-A	Comparing interlaminar versus transforaminal epidural steroid injections
Ng et al[410]	RCT	86	NRS	I-A	Comparing bupivacaine versus bupivacaine and methylprednisolone
Manchikanti et al[411]	RCT	120	NRS	I-A	Testing effectiveness of transforaminal epidural injections of local anesthetic with or without steroids
Iversen et al[412]	RCT	461	NRS	I-A	Interventions Subcutaneous sham injections of 2 mL 0.9% saline, caudal epidural injections of 30 mL 0.9% saline, and caudal epidural injections of 40 mg triamcinolone acetonide in 29 mL 0.9% saline. Participants received two injections with a two-week interval.
Nandi et al[413]	RCT	93	VAS	I-A	Comparing steroids versus conservative treatment
Cohen et al[414]	RCT	145	NRS	I-A	Comparing steroids versus conservative treatment
Vad et al[415]	RCT	48	VAS	I-A	Comparing steroids versus conservative treatment
Buchner et al[416]	RCT	40	VAS	I-A	Comparing steroids versus conservative treatment

Abbreviations: RCT, randomized controlled trial; NRS, numeric rating scale; VAS, visual analog scale.

Table 4 ASPN Back Consensus Group Recommendations for Epidural Steroid Injections

Recommendation	Grade	Level	Level of certainty Net benefit
Interlaminar epidural injections for treatment of low back and radicular pain originating from disc disease, spinal stenosis and for chronic back/leg pain after surgical intervention	A	I-A	High
Transforaminal epidural injections for treatment of low back and radicular pain originating from disc disease, spinal stenosis and for chronic back/leg pain after surgical intervention	A	I-A	High
Caudal epidural injections for treatment of low back and radicular pain originating from disc disease, spinal stenosis and for chronic back/leg pain after surgical intervention when interlaminar or transforaminal approaches are not feasible	A	I-A	High
Use of either steroid or local anesthetic or the two classes of medication in combination for use in epidural injections for treatment of low back and radicular pain originating from disc disease, spinal stenosis and for chronic back/leg pain after surgical intervention	A	I-A	High

activation of the central nervous system along with the distribution of the nerve innervating the muscle that is activated.[12] Once diagnosed, MPS is treated by a variety of modalities including pharmacologic therapies (namely nonsteroidal anti-inflammatory drugs), therapy (including dry needling and acupuncture), and trigger point injections (TPIs).

Indications and Contraindications

TPIs should be considered in patients after thorough evaluation has ruled out other causes of back pain including muscle strain, facetogenic back pain, discogenic back pain, vertebrogenic back pain, spinal cord stenotic disease, vertebral body disease (including fracture), and radicular back pain. Once MPS has been diagnosed with the criteria outlined by Simons et al,[11] patients can be trialed with conservative management, including pharmacologic therapy and physical therapy. If MPS persists

and taut bands are identified, it is reasonable to perform TPIs. Contraindications for the procedure include patient refusal, infection overlying the site of injection and concurrent use of specific anticoagulants and anti-platelet medications.[13]

Safety/Complications

Though relatively safe as TPIs are generally performed with large gauge short needles by anatomic technique through identification of taut bands by physical examination, they are occasionally associated with complications specific to the region at which the injections are performed, namely the cervical and thoracic region. A 2004 study by Fitzgibbon et al characterized 5475 claims from the American Society of Anesthesiologists Closed Claims Project between 1970 and 1999 for chronic pain, with the authors determining that 284 pain management-specific claims (5.1%) were made with 276 of these claims (5.0% of total claims, 97.1% of pain management claims) were for invasive procedures.[14] Of those claims, 138 (50%) involved injections (50%), including 17 claims for TPIs (6.1% of pain management claims, 12.3% of injection-specific claims). Interestingly, when assessed for complication type, 18 incidences of pneumothorax were reported with injections out of 59 total from all of the pain management associated claims (30.5%), of which 15 were associated with TPIs (83.3% of all injection associated pneumothoraxes; 88.2% of all TPI-associated claims).[14]

A review of the literature regarding complications of TPIs reveals a general dearth of publications, although a number of reports of complications associated with dry needling and acupuncture have been published. One of the first articles addressing TPI-associated complications of pneumothorax was published by Shafer in 1970.[15] Subsequently, several additional case reports have been published, including one by Ahiskalioglu et al, in which a patient developed pneumothorax following cervical and thoracic TPIs.[16] In their report, a 25-year-old 45 kg female received TPIs to her trapezii, supraspinatus, levator scapulae, and rhomboideus muscles with subsequent development of pneumothorax.[16] Fortunately, this episode was self-resolving through conservative care and close follow-up. Paik et al published a case report in which a CT-guided aspiration was required for a 25-year-old female who developed a right-sided pneumothorax following a right trapezius TPI.[17]

Local anesthetics are often used for TPIs, and there is also a risk of reversible myotoxicity. In a review by Zink et al examining reports of histologic changes of skeletal muscle upon exposure to various local anesthetics (procaine, carbocaine, lidocaine tetracaine, chloroprocaine, bupivacaine) suggested that all local anesthetics studied resulted in some degree of reversible myotoxic effects in experimental models. However, few reports of clinical myotoxic reports have been published.[18] No incidences of bowel perforation or pneumoperitoneum associated with TPIs were found through a thorough literature review. TPIs are considered a low-risk procedure and one should abide by the multi-specialty, multi-organizational guideline publication on peri-procedural antiplatelet and anticoagulant management for interventional spine and pain procedure when performing these injections.[13]

Evidence Summary

A review of RCTs regarding TPIs has revealed several studies investigating the efficacy of these injections for MPS with diverse medications. Over 40 RCTs were found through a PubMed literature search for “trigger point injection” that studied trigger point injections (technical variations, adjuncts for MPS treatment, and in comparison to other treatments for MPS). A focus was placed on literature published within the past 5 years with a focus on further studies outside this time frame to further evaluate and clarify points made by recent studies (Tables 5 and 6).

Facet Interventions

Facet interventions have a long history of clinical effectiveness, and there are multiple systematic reviews examining the efficacy of the technique. The current section will review recent efficacy studies with an eye toward answering several relevant clinical questions concerning facet intervention such as the role of articular injections vs RFA, facet intervention and medical management, risk mitigation for intra-arterial injection and prognostic value of diagnostic blocks.

Lumbar facet joint pain is one of the most common types of axial back pain. Its prevalence varies greatly in the literature, with estimates of prevalence ranging from as low as 4.8% to over 50%.[19–22] Many of the studies investigating prevalence have been methodologically flawed. The wide disparity in reported prevalence demonstrates the need for standardized criteria on how to properly diagnose lumbar facet pain. In addition, there is a poor correlation between

Table 5 Evidence Summary for Trigger Point Injections

Study author	Study type	Study size	Endpoints	Evidence level	Notes
Roldan et al[417]	RCT	48	NRS	I-A	Comparing local anesthetic and steroid TPI to saline TPI in ED patients. Resulted in similar change in pain relief in both groups.
Sakalys et al[418]	RCT	50	VAS	I-A	Comparing platelet rich plasma injection versus TPI for myofascial pain. Better pain relief 4 weeks out with platelet rich plasma injection.
Moon et al[419]	Double blind RCT	136	VAS, 5-point Likert Scale	I-A	Comparing TPI with and without vibration therapy. Vibration therapy during TPI decreased pain during injection compared to without vibration therapy
Dessie et al[420]	Double blind RCT	59	VAS, PFDI-20	I-A	Comparing saline or Botox TPI for abdominal MPS in pelvic pain. No difference between groups
Ata et al[421]	RCT	76	VAS, SF-12	I-A	Determining if kinesiology tape prolonged TPI effects. Study found that it did prolong TPI relief.
Pecos-Martin et al[422]	Double blind RCT	72	VAS, NPQ, PPT	I-A	Comparing dry needling near a trigger point or directly into a trigger point. Dry needling into a trigger point is more beneficial.
Kwanchuay et al[423]	Double blind RCT	33	VAS, PPT	I-A	Comparing Botox to saline TPI. No difference between the two groups.
Choi et al[424]	RCT	21	VAS, PPT, SF-MPQ	I-A	Determining if transcranial direct current stimulation worked in making TPI more effective. Study indicates that it does.
Seo et al[425]	Double blind RCT	76	VAS, NPAD, GAS, PPT	I-A	Comparing performing Botox TPI with motor electrical stimulation or sensory stimulation guidance. Sensory stimulation found to be more helpful.
Yoon et al[426]	RCT	77	VAS, NDI, SF-36	I-A	Comparing needle sizes on injection pain. No difference noted between sizes of needles used.
Ga et al[427]	RCT	39	VAS, FACES, PPI, GDS-SF	I-A	Comparing TPI with acupuncture for MPS. No difference seen between groups.
Zaralidou et al[428]	RCT	68	-	I-A	Comparing ropivacaine to levobupivacaine for TPI, no significant differences found between groups.
Qerama et al[429]	Double blind RCT	30	NRS, PPDT, PPTT	I-A	Comparing Botox TPI to placebo. No difference in pain relief between groups, but Botox caused decreased electromyography activity.
Göbel et al[430]	Double blind RCT	145	PS	I-A	Comparing Botox to normal saline TPI. Botox was better between weeks 5–8 in this study.

Kamanli et al[431]	Single blind RCT	29	PPT, PS, VAS, NHP	I-A	Comparing Botox TPI to dry needling to bupivacaine TPI. TPI in general found to have better benefit than dry needling. Authors note bupivacaine was best for TPI as it was fast acting meanwhile Botox TPI should be used in medically refractory cases
Iwama et al[432]	RCT	21	PS	I-A	Testing injection pain with dilute local anesthetic in volunteers as well as using dilute local anesthetic doses in patients with MPS. Less pain with dilute local injections. Duration relief in MPS patients not affected by using dilute local at low enough doses.
Iwama et al[433]	RCT	20	PS	I-A	Comparing 0.25% to 1.0% lidocaine for TPI. 0.25% had less injection pain and better efficacy.
Krishnan et al[434]	RCT	30	VAS	I-A	Comparing injection pain of bupivacaine, ropivacaine, bupivacaine with steroids, ropivacaine with steroids, and just needle insertion. Ropivacaine was less painful (alone) compared to bupivacaine or either local anesthetic in combination with steroids.
Wheeler et al[435]	Double blind RCT	33	NPAD, PS	I-A	Comparing 50 U Botox, 100 U Botox, and normal saline TPI. All 3 groups improved pain. No statistically significant benefit of one injection type to the others.
Tschopp et al[436]	RCT	107	PS	I-A	Comparing 0.25% bupivacaine to 1.0% lidocaine to saline TPI. No difference in relief between groups so long as needle hits muscle belly.
Hong et al[437]	RCT	58	PTM	I-A	Local anesthetic TPI compared to dry needling to evaluate need for twitch response. Significant improvement in patients with twitch response compared to those without upon needle insertion
Garvey et al[438]	Double blind RCT	63	NRS	I-A	Comparing local anesthetic TPI, local anesthetic with steroid TPI, acupuncture, and cool spray with acupuncture. No difference between types of procedural techniques noted.
Hameroff et al[439]	Cross over double blind RCT	15	PS	I-A	Comparing bupivacaine to etidocaine to saline for TPI. Local preferred to saline alone.
Kocak et al[440]	RCT	54	VAS	I-A	Comparing NSAID and TPI for low back MPS; TPI was superior to NSAIDs when assessed with pain relief within the first hour of intervention.
Mitidieri et al[50]	RCT	35	VAS, NCS, MPQ	I-A	Comparing acupuncture to TPI for pelvic pain from abdominal MPS, no difference seen between outcomes when analyzed at 1 week, 1 month, 3 months, and 6 months out except for MPQ differences at 1 week.

Abbreviations: NRS, numeric rating score; VAS, visual analogue score; PFDI-20, Pelvic Floor Distress Inventory-20; SF-12/36, 12- or 36-Item Short Form Health Questionnaire; NPQ, Neck Pain Questionnaire; PPT, pressure-pain threshold; SF-/MPQ, Short Form/McGill Pain Questionnaire; NPAD, Neck Pain and Disability Scale; GAS, Global Assessment of Improvement Scale; NDI, Neck Disability Index; FACES, Wong-Baker FACES Pain Scale; PPI, pressure pain intensity scores; GDS-SF, Geriatric Depression Scale-Short Form; PPDT, pressure pain detection thresholds; PPTT, pressure pain tolerance thresholds; NHP, Nottingham Health Profile; PS, pain score (internal system); PTM, pressure threshold meter; NCS, numeric categorical scale; TPI, trigger point injections; NSAID, nonsteroidal anti-inflammatory drug.

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Table 6 ASPN Back Consensus Group Recommendations for Trigger Point Injections

Recommendation	Grade	Level	Level of certainty Net benefit
The type of medication for TPI does not make a significant difference in pain outcomes	A	I-A	Strong
Eliciting a localized twitch response for needle placement predicts best outcomes	A	I-A	Strong
In medically refractory cases, TPI with BTXA may be of benefit	C	I-B	Moderate
Dilute local anesthetic concentrations may result in less injection pain	I	II	Weak
Novel injectables may be of benefit for MPS	I	II	Weak
Adjunct therapies may be of use to prolong the relief of TPI for MPS	I	II	Weak

Abbreviations: TPI, trigger point injections; BTXA, botulinum toxin type A; MPS, myofascial pain syndrome.

lumbar facet joint pathology on imaging and LBP.[23] Numerous questions have been raised regarding the ideal cutoff for determining whether a diagnostic block is positive, how many blocks should be performed before considering radiofrequency ablation (RFA) and the volume of local anesthetic that should be injected.[24–29] Lumbar facet interventions are the second most commonly performed procedures for chronic pain, yet there is still controversy regarding their effectiveness.[30,31] While most reviews concluded that RFA is effective for lumbar facet joint pain,[32–35] some studies dispute this.[31,35] Facet blocks, including intra-articular and medial branch blocks, are frequently used prior to radiofrequency ablation. Cohen et al[36] in the *FACTS*, RCT discussed effectiveness of lumbar facet joint blocks and predictive value prior to the procedure. This randomized study established the lack of long-term therapeutic benefit for intra-articular and medial branch facet blocks but suggested the possibility that when used as prognostic tools, these injections may provide superior outcomes prior to RFA on some measures compared to control blocks. For intra-articular injections, most reviews have concluded that the injections are ineffective,[31,32,34,37,38] although some studies indicate they may provide some benefit compared to sham and conservative treatment.[39–41]

Consensus practice guidelines on interventions for lumbar facet joint pain developed by a multispecialty, international working group[42] concluded that lumbar medial branch RFA may provide benefit to well-selected individuals, with medial branch blocks (MBB) being more predictive than intra-articular (IA) injections. More stringent selection criteria are likely to improve denervation outcomes, but at the expense of more false-negatives,[42] potentially missing many patients that could benefit from RFA procedures. Physical examination signs such as tenderness over the facet joints, lumbar paraspinal tenderness and increased pain with trunk extension can help improve diagnostic accuracy. However, most reviews and guidelines do not support positive physical examination requirements for a diagnosis of lumbar facet pain,[43,44] but rather favor diagnostic injections as the only reliable means for diagnosing it. Physical examination such as palpation of the lumbar spine under fluoroscopy and recognizing pain referral patterns can help determine the levels at which a diagnostic block can be performed. Regarding imaging studies such as scintigraphy, magnetic resonance imaging (MRI) and CT, there is weak or no evidence supporting the use of these imaging modalities for identifying painful lumbar facet joints prior to MBB or IA facet joint injections.[45,46] Although there is insufficient evidence regarding the optimal timing of facet joint blocks for chronic LBP, or the duration of conservative treatment prior to consideration of facet injections, 3 months of conservative therapy prior to considering facet interventions is typically considered acceptable Compared with saline controls, both IA and medial branch injections with a local anesthetic (LA) provide better predictive information for medial branch RFA.[36] Despite the lack of large prospective studies comparing the prognostic value of MBB and intra-articular facet injections as a screening procedure prior to RFA, some studies[32,47,48] concluded that medial branch blocks are superior to intra-articular facet injections in predicting the success of RFA and should be the preferred screening method. Intra-articular injections of corticosteroids may, however, be used as a therapeutic injection for certain patients with suspected inflammatory pain, and in those who want to avoid ablative therapies, such as young athletes.[49,50]

The volume of the injectate for MBB and IA facet injections remains a subject of debate. Injecting excessive volumes can lead to spread of the injectate to adjacent structures such as the epidural space, spinal nerves, musculature and ligaments, undermining the specificity and positive predictive value of RFA. In addition, injecting insufficient volumes can lead to capsule

distension and rupture in cases of IA injections. There are no studies evaluating the prognostic effect of the injectate volume on RFA outcomes. For MBB, there are several studies evaluating the efficacy of lumbar facet MB RFA using different volumes[36,51–53] such as 0.3 mL, 0.5 mL, 0.75 mL and 1 mL with no difference in outcomes based on injectate volume. For IA injections, the joint capsule volume ranges from 1mL to 2 mL.[54] Different volumes have been used in different RCTs examining the prognostic value and efficacy of IA injections. Large injectate volumes may result in rupture of the joint capsule and inadvertent spread to other potential pain generators, thereby undermining specificity. On the other hand, insufficient volumes may fail to anesthetize the joint, leading to false-negative blocks. In short, the accepted consensus is to use a volume of 0.5 mL–1.0 mL for MBB to reduce spread to adjacent structures and a volume of less than 1.5 mL for IA injections to prevent capsular rupture and spread to adjacent structures. Adding steroids to the injectate for MBB and IA injections for diagnostic purposes should be avoided. Many studies provide evidence against the use of intra-articular steroids.[36,55,56]

In Phase I of a three-arm double-blind study that compared IA LA and steroid lumbar facet injections, MBB with LA and steroid, and saline control blocks, Cohen et al[36] found no significant differences in any outcome measure at any time point in the 6-month follow-up. Based on a review of evidence, the routine use of therapeutic facet injections is not recommended. However, there are a few exceptions, such as patients who may be at risk of complications from RFA (young athletes, older individuals on anticoagulation therapy or with implantable cardiac devices). In those cases, it is reasonable to add steroids to a block for possible intermediate-term relief. The number of diagnostic MBBs before RFA remains a subject of controversy. The American Society of Interventional Pain Physicians (ASIPP) and the Spine Intervention Society (SIS) advocate for the use of two diagnostic blocks prior to RFA[19,44] to minimize placebo effects and false-positive results. False-positive results can also be contributed to spilling of the injectate into surrounding structures, use of sedation, use of copious superficial anesthesia and resting while not performing normal activities following the block.[32,57] There are several reasons for false-negative blocks, including intravenous uptake, failure to anesthetize the target nerve, inability to access the joint for IA injections, aberrant anatomy, procedure-related pain such as muscle soreness and spasm and opioid-induced hyperalgesia. The decision whether to perform a single block, double block or no blocks is based on weighing false-positive versus false-negative results. There exists evidence that the success rate for medial branch RFA will increase with the number of blocks, but this will occur at the expense of missing out on some patients with false-negative results who could have benefited from the RFA. The multispecialty, international working group[42] advocates for the use of a single block prior to RFA. They concluded that dual blocks result in a higher subsequent success rate for medial branch RF, but that the use of no diagnostic MBB results in the highest overall number of patients with a positive response to the RFA, thereby making a single block the "middle ground" option. They concluded that the decision to either proceed straight to RFA, performing a single block or double blocks can be tailored to the clinical scenario. Another debatable subject is the cutoff that should be used to consider a block as successful. Several studies compared outcomes of RFA based on percentage of relief from MBB, using different cutoffs including 50%, 80% and 70%.[24,48,58–63] A 50% or greater cutoff is generally the most accepted model. In addition, other parameters to measure functional improvement should be considered when assessing the success of a diagnostic block.

Indications and Contraindications

Lumbar facet MBBs and intra-articular facet injections are indicated in the diagnosis and possible treatment of LBP due to lumbar facet joint pathophysiology. Chronic facet pain due to osteoarthritis (OA) has been associated with degenerative disc disease (DDD). DDD results in concomitant changes in the facet joints, and the reverse is also true: degeneration and motion abnormalities of the facet joints can accelerate disc degeneration. DDD usually precedes facet joint arthritis, and it is well noted that facet arthropathy is more prevalent at spinal levels with advanced DDD. Other conditions other than facet OA may cause facet-induced pain. Inflammatory arthropathies such as rheumatoid arthritis, ankylosing spondylitis and reactive arthritis can use lumbar facet pain. Other less common conditions such as pseudogout, synovitis, chondromalacia facetae and infection can also cause facet pain. Facet synovial pseudocysts can cause axial back pain as well as possible radicular pain due to compression of adjacent structures. Severe trauma such deceleration injuries and motor vehicle accidents can cause dislocation of the lumbar facet joints and lumbar facet pain following the trauma. Contraindications include patient refusal, ongoing active infection, and allergy to the medications used. Coagulopathy and patients on anticoagulants should be assessed prior to performing these interventions. Benefit versus risk analysis should be performed for those patients prior to proceeding with the injection.

Complications

The risks and complications from lumbar facet injections can be due to vascular penetration and injury, injection, procedure-related pain and injury to non-target neural structures. The incidence of vascular penetration and positioning of the needle intravascularly varies from 3.6% to 20%.[64–69] A multispecialty, international working group[42] and other societies such as SIS recommend checking for intravascular placement of the needle tip by aspirating and visualizing the spread of contrast on fluoroscopy in real-time prior to performing MBBs to reduce false-negative results. This should ideally be done in a manner such that the total injectate dose (LA and contrast) is kept as low as possible to minimize the effect on local anesthetic dispersion.[42] Most societies recommend continuation of non-heparin anticoagulants prior to lumbar facet MBBs, as the risk of discontinuation of those medications such as development of thromboembolic events outweighs the benefits. Post-procedural pain can lead to false-negative results for the prognostic MBB, particularly in patients experiencing opioid-induced hyperalgesia. Manchikanti et al[68] found that irritation of the nerve roots occurred in 0.1% of patients but found no long-term neural deficits out of 3162 MBBs performed. Proper use of fluoroscopic or CT guidance is recommended for MBBs and IA facet injections, although ultrasound guidance can be used by physicians highly skilled and experienced in ultrasound. Proper formal training in interventional pain procedures is recommended for physicians performing MBBs and IA facet injections to avoid complications and improve outcomes.

Evidence Summary

A review of RCTs for facet joint injections reveals several studies investigating the efficacy of these injections for LBP. A PubMed literature search yielded 11 RCTs evaluating lumbar facet injections and/or medial branch blocks for LBP during the literature review time period warranting inclusion. The focus was placed on literature published during this time period. Other landmark studies published outside of this time frame were also evaluated to clarify and support data from more recent studies. For facet interventions, there was sufficient evidence in the form of RCTs (Table 7), for the committee to make recommendations. Table 8 summarizes those recommendations.

Two of the main questions regarding intra-articular facet joint injections are 1) do they replace radiofrequency ablation, and 2) do they delay the need for radiofrequency ablation.[56,70] Most of the data suggests that intra-articular facet joint injections are not therapeutic, and they do not replace or delay the need for radiofrequency ablation.[36,56,70] However, there are several studies that suggest otherwise. For example, Wu et al demonstrated that both autologous platelet-rich plasma and intra-articular steroid injections were effective for treating lumbar facet joint syndrome.[71] In addition, Sae-Jung et al determined that methylprednisolone facet joint injections were effective for facet-mediated LBP but augmented with the addition of diclofenac.[72]

Intradiscal Regenerative Therapies

The intervertebral disc plays a crucial role in the health of the spine complex. Several pathologies of the disc itself, including internal disc disruption, tears, degeneration, and loss of height can all predispose patients to discogenic back pain and its sequelae. The disc is a central part of the interconnected biomechanical system of the spine, which allows for mobility and distribution of stress. Degeneration often correlates with loss of disc height that can lead to excess motion and instability. While this review will focus on treating pain originating from the disc itself, damage to the disc may lead to excess forces and subsequent damage throughout the spine.

The disc is a sensitive environment as it depends on diffusion for nutrients and waste movement due to its avascular nature at baseline. This diffusion capacity is relatively poor and worsens with both increasing age and pathology. In healthy discs, nerve endings are limited to the outer one-third of the disc and are not found in the inner annulus or nucleus pulposus region.[73] In degenerated discs, nociceptive nerve fibers along with vasculature may migrate into the central disc regions.[74] It is theorized that neurotransmitters together with changes within the extracellular matrix itself and the release of cytokines regulate this nerve ingrowth. In addition, pain-related peptides and proinflammatory cytokines are increased.

A common cause of disc failure is overloading in which forces may lead to desiccation of the disc and annular tears. The disc itself has a limited compression capacity which worsens with decreasing fluid content. To improve disc failure, the premise is to regain or maintain disc height to reduce the axial nerve compression and to restore the tissue dynamics (fluid content) of the annulus. A second goal is to possibly reconstitute the central nucleus with a matrix environment that

Table 7 Evidence Summary for Intra-Articular Facet Joint Injections

Study author	Study type	Study size	Endpoints	Evidence level	Notes
Snidvongs et al[441]	Blinded parallel two-arm pilot RCT.	8		Unable to recruit enough patients, no conclusions.	To evaluate the clinical effectiveness and cost-effectiveness of lumbar facet-joint injections compared with a sham procedure in patients with non-specific LBP of > 3 months' duration.
Kennedy et al[56]	Double-blind, prospective, randomized, placebo-controlled trial	28		1-A	No statistically significant difference in the need for radiofrequency neurotomy (radiofrequency neurotomy) between the groups. There is no difference in mean time to radiofrequency neurotomy between saline (6.1 wks) and corticosteroid (6.5 wks) groups. There is a need for radiofrequency neurotomy.
Cohen et al[36]	RCT	229	NRS	1-A	This study establishes that facet blocks are not therapeutic. The higher responder rates in the treatment groups suggest a hypothesis that facet blocks might provide prognostic value before radiofrequency ablation.
Karkucak et al[442]	RCT	47	VAS, ODI, STAI	1-A	The ultrasound-guided local injections offer better clinical outcome in the treatment of facet syndrome compared to blind injection.
Ye et al[443]	RCT	10		1A	The lumbar facet joint space can be accurately demonstrated by ultrasound. The ultrasound-guided facet joint injection in the lumbar spine obtained almost the same satisfactory feasibility, accuracy and clinical efficiency compared with low dose CT. Ultrasound technique could provide the real-time monitoring.
Wu et al[71]	RCT	46	VAS, RMQ, ODI	1A	Both autologous PRP and LA/corticosteroid for intra-articular injection are effective, easy, and safe enough in the treatment of lumbar facet joint syndrome. However, autologous PRP is a superior treatment option for longer duration efficacy.
Ellard et al[444]	RCT	26	VAS		No analysis due to difficulty in recruitment
Sae-Jung et al[72]	RCT	99	ODI, VAS		This prospective randomized trial is to determine the effectiveness of treating lumbar facet syndrome with oral diclofenac, methylprednisolone facet joint injection or both. The combined treatment was more effective in reducing lumbar facet pain and improving the functional index than either treatment alone. This approach should be the preferred treatment.

(*Continued*)

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Table 7 (Continued).

Study author	Study type	Study size	Endpoints	Evidence level	Notes
Do et al[445]	RCT	60	NRS		Six months after treatment, about half of patients in both groups reported successful pain relief (pain relief of ≥50%). both IA pulsed radiofrequency (PRF) stimulation and IA corticosteroid injection (ICI) into the lumbar facet joint (LFJ) significantly relieved LFJ pain. Their effects persisted for at least 6 months after the procedure. Thus, IA PRF is a useful therapeutic option for the management of LFJ pain.
Kennedy et al[70]	Randomized, double blind, placebo-controlled study	56	Time to RFA, need for RFA		Intra-articular corticosteroids were not effective in reducing the need for or the time to a radiofrequency ablation of the medial branches in those with dual MBB-confirmed lumbar z-joint pain.
Joo et al[69]	Prospective RCT	126	Vascular uptake		A Quincke needle was related to positive IV injection at a 1.898-fold higher rate than was use of a Whitacre needle. Whitacre needles can be considered to reduce the risk of IV injection during L-MBB.

Abbreviations: RCT, randomized controlled trial; LBP, low back pain; NRS, numeric rating scale; ODI, Oswestry Disability Index; STAI, State-Trait Anxiety Inventory; VAS, visual analog scale; RMQ, Roland-Morris Disability Questionnaire; CT, computed tomography; PRP, platelet-rich plasma; LA, local anesthetic; IA, intra-articular; PRF, pulsed radiofrequency; ICI, IA corticosteroid injection; LFJ, lumbar facet joint; RFA, radiofrequency ablation; MBB, medial branch blocks.

Table 8 ASPN Back Consensus Group Recommendations for Intra-Articular Facet Injections

Recommendation	Grade	Level	Level of certainty Net benefit
Intra-articular facet steroid injections do not replace or delay the need for RFA.	C	I-A	Strong
Intra-articular facet steroid injections can be prognostic for RFA	C	I-A	Strong
In acute cases of facet mediate pain, facet steroid injections may help due to possible inflammatory component	C	I-B	Moderate
Combining facet steroid injections with oral NSAIDs can be more effective than injection therapy alone	B	II	Moderate
Image guided facet steroid injections are more effective than blind injections	A	I-A	Strong
Do not use intra-articular facet joint steroid injections as sole therapy for facet-mediated pain.	B	I-A	Strong
Whitacre needles can reduce the risk of IV injection during MBB	C	I-A	Moderate
Lumbar Medial Branch Blocks can be prognostic for RFA	A	I-A	Strong

Abbreviations: RFA, radiofrequency ablation; NSAIDs, nonsteroidal anti-inflammatory drugs; IV, intravenous; MBB, medial branch blocks.

can hold fluid and improve nutritional flow. Using regenerative medicine, the hope is to improve the damaged internal environment of the disc by reconstituting a matrix that may improve and return disc function.[75]

Indications

Intradiscal regenerative medicine has primarily been studied in patients with intractable chronic LBP for at least 3–6 months despite failure of a multi-modal treatment approach including indicated medications, physical therapy, and other interventional procedures as per recommendation guidelines. Patients should have history, physical exam, and radiologic findings consistent with their symptomatic lumbar intervertebral discogenic pain. Provocative discography can further specify the source of pain and the precise level(s) to treat.

Safety and Complications

The overall safety profile of regenerative therapies is excellent and comparable to standard intradiscal procedures. Rare adverse events may include LBP, muscle spasms, and discitis. Standard intradiscal precautions should be taken with an emphasis on sterile technique in both the preparation of the injectate and the intradiscal procedure itself. To further illustrate this significance, a case of spondylodiscitis with positive *Cutibacterium acnes* culture has been reported subsequent to platelet-rich plasma (PRP) intradiscal injections. The authors stressed the importance of appropriate sterile technique and risk-stratification of patients with high infection potential, as well as better understanding of intradiscal biologic therapies and the intradiscal environment.[76] Traditional antibiotic therapy protocols for intradiscal interventions may benefit from further review specifically regarding regenerative medicine.

Evidence Review with Evidence Level Designation: Intradiscal Regenerative Therapies

It is important to understand that not all biologics used in regenerative medicine are equivalent. For instance, factors at a minimum that can affect the final PRP product include volume of blood aspirated, baseline platelet count, patient health status and comorbidities, patient medications, anticoagulant of choice, centrifugation parameters, and inclusion/exclusion of leukocytes. Similarly, mesenchymal stem cells (MSCs) are found in most tissues of the human body but primarily sourced for reimplantation from the bone marrow and adipose due to ease of access. Volume of aspirate, patient health status and comorbidities, patient medications, harvesting protocol parameters and technique can all affect the final MSC product. Not distinguishing this heterogeneity, we have summarized the gross clinical evidence evaluating regenerative medicine for LBP from discogenic pathology, including prolotherapy, protein-rich plasma (PRP), cellular therapy, and other intradiscal injectates (Table 9).

Table 9 Evidence Summary for Intradiscal Regenerative Therapies

Study author	Study time	Study size	Endpoints	Authors conclusion	Study analysis and notes
Miller et al, 2006[446] [prolo-therapy]	Prospective	76	NRS	Reductions in pain NRS were maintained in patients with uniformly moderate to severe disc desiccation at an average of 18 months. Those patients who experienced no appreciable improvement from the treatment were not worse in any sustained way	Level I-B
Akeda et al, 2017[447] [PRP Releasate]	Prospective	14	Change in imaging	Lumbar radiographs no significant change in disc height. No change in T2 imaging of AF and NP. No negative affect on the matrix of degenerated IVDs. No persistent neurologic deficits.	Level I-B
Levi et al, 2016[448] [PRP]	Prospective trial	22	VAS and ODI	Encouraging preliminary 6-month findings, using strict categorical success criteria, for intradiscal PRP as a treatment for presumed discogenic LBP. Randomized placebo-controlled trials are needed to further evaluate the efficacy of this treatment.	Level I-B
Tuakli-Wosornu et al, 2016[77] [PRP]	RCT	47	NRS, NASS outcome questionnaire, SF-36	Those who received PRP maintained significant improvements in FRI scores through at least 1 year of follow-up.	Level I-B
Cheng et al, 2019[78] [PRP]	5- to 9-year follow-up of previous RCT (Tuakli-Wosornu et al, 2016).	21	NRS, NASS outcome questionnaire, SF-36	This study shows improvements in pain and function post intradiscal injection of PRP were sustained for follow-up periods of 5–9 years following intradiscal PRP treatment for moderate-severe lumbar discogenic pain.	Level I-C
Jain et al, 2020[449] [PRP]	Prospective	25	NRS, ODI	This study shows a positive correlation between platelet concentration for PRP with improvement in pain and functional status in patients receiving intradiscal PRP for chronic discogenic LBP. The authors recommend use of intradiscal PRP for treatment of discogenic pain with preferably a higher platelet count to elicit a favorable response.	Level I-C
Navani et al, 2018[450] [PRP or MSCs]	Prospective case series	20	NRS, SF-36	This study supports the safety of a single intradiscal biologic injection and provides addition evidence for the efficacy in management of lumbar discogenic pain, with improvements in both pain and function, and decreased utilization of medications and medical services thereby decreasing health care costs.	Level I-C
Ju et al, 2020[83] [growth factor, fibrin sealant, or stem cells]	Post hoc comparison using single-site data from 4 multicenter RCTs.	50	VAS and disability scores.	There was no difference in outcomes between therapeutic intradiscal agents (growth factor, fibrin sealant, or stem cells) and control saline groups. In all groups, patient reported pain and disability score improvements. Saline control patients demonstrated significant improvements in pain and disability at 1 year follow-up post injections. Suggests that perhaps saline injection has a therapeutic effect possibly by diluting pro-inflammatory mediators within the degenerated intervertebral disc, or decreasing of intradiscal pressure, or a combination of the placebo effect.	Level I-C

Orozco et al, 2011[451] [MSCs]	Case-series pilot Phase I n=10	10	VAS, ODI, SF-36	MSC therapy may be a valid alternative treatment for chronic back pain caused by DDD. Advantages over current gold standards include simpler and more conservative intervention without surgery, preservation of normal biomechanics, and same or better pain relief. This outcome compares favorably with spinal fusion or total disc replacement.	Level II
Elabd et al, 2016[452] [bone marrow derived MSC]	Long-term follow-up study.	5	Physical examination, low back MRI, and quality of life questionnaire.	This early human clinical data suggests the safety and feasibility of the clinical use of hypoxic cultured bone marrow derived MSCs for the treatment of LBP due to DDD and support further studies. A larger double-blind, controlled, randomized clinical study with significant number of patients and implementation of validated endpoint measurements are next steps in order to demonstrate efficacy of this biologic.	Level II
Pettine et al, 2017[453] [BMC]	Prospective, open-label, non-randomized	26	ODI, VAS	There were no adverse events related to marrow aspiration or injury and this study provides evidence of safety and feasibility of intradiscal BMC therapy. No radiologic evidence of worsening. Pt. improvement and satisfaction with this surgical alternative supports further study of the therapy.	Level I-B
Centeno et al 2017[454] [autologous cultured MSC]	Prospective	33	NRS, SANE, FRI, measurement of the intervertebral disc posterior dimension, and adverse events	Patients treated with autologous cultured MSCs for lower back pain with radicular symptoms in the setting of DDD reported minor adverse events and significant improvements in pain, function, and overall subjective improvement through 6 years of follow-up. 3 patients reported pain related to procedure that resolved. No serious adverse events (ie, death, infection, or tumor) with the procedure.	Level I-B
Noriega et al, 2017[455] [allogeneic MSCs]	RCT	24	VAS, ODI	Feasibility and safety were confirmed, and indications of clinical efficacy were identified. Allogeneic MSC therapy may be a valid alternative for the treatment of DDD that is more logistically convenient than the autologous MSC treatment. The intervention is simple, does not require surgery, provides pain relief, and significantly improves disc quality.	Level I-B
Bae et al, 2014[456] [allogeneic MPCs]	Prospective, multicenter, RCT.	100	VAS, ODI	Allogeneic MPCs were well tolerated, showed improvements in pain and functional improvement and reduced interventions compared to controls. Needs randomized Phase 3 studies. When compared to HA results did not reach statistical significance	Level I-B
Kumar et al, 2017[457] [AT-MSCs and HA derivative]	Single-arm, open-label, phase I clinical trial	10	VAS, ODI, SF-36	Combined implantation of MSCs and HA derivative in chronic discogenic LBP is safe and tolerable. However, the efficacy of combined AT-MSCs and HA should be investigated in an RCT in a larger population. No procedure or stem cell-related adverse events or serious adverse events during the 1-year follow-up period.	Level I-B

(*Continued*)

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Table 9 (Continued).

Study author	Study time	Study size	Endpoints	Authors conclusion	Study analysis and notes
Comella et al, 2017[458] [SVF]	Open label study.	15	VAS, PPI, ODI, BDI, DPQ, and SF-12.	Stromal vascular fraction (SVF) proved promising, however a true evaluation of efficacy and safety would require larger phase II/III studies.	Level I-B
Wolff et al, 2020[459] [intradiscal cBMA]	Retrospective analysis	33	VAS, ODI, SF-36	Intradiscal cBMA injections may be effective to reduce pain and improve function. Patients with relatively higher initial pain may have potential for greatest improvement.	Level I-C
Amirdelfan et al, 2021[460] [MPCs]	Multicenter, randomized, controlled study	100	VAS, ODI, SF-36, Radiographs, Productivity and Activity Index	Results provide evidence that intradiscal injection of MPCs could be a safe, effective, durable, and minimally invasive therapy for subjects with chronic LBP associated with moderate degenerative disc disease. There were no significantly increased rates of adverse events in the MPC groups compared to control groups up to 36 months post injection of intradiscal MPCs.	Level I-B
Haufe et al, 2006[461] [HSCs]	Prospective case report	10	VAS	Even though MSCs have been suggested as a possible treatment for degenerative discs, this study reveals that HSCs, which are similar precursor cells, are of no benefit in living human subjects. Possibly the HSCs cannot survive in the oxygen-poor environment of the disc, even with hyperbaric oxygen therapy.	Level I-B
Yin et al, 2014[82] [Fibrin]	Prospective Multicenter Pilot Study	15	VAS, RMDQ	Intradiscal injection of fibrin appears safe and may improve pain and function in selected patients with discogenic pain. There were 2 instances of low back muscle spasm and one case of discitis were considered related to the procedure or product	Level I-B
Peng et al, 2010[81] [methylene blue]	Randomized placebo-controlled trial	72	NRS, ODI	The current clinical trial indicates that the inj. of methylene blue into the painful disc is a safe, effective and minimally invasive method for the treatment of intractable and incapacitating discogenic LBP.	Level I-B
Beall et al, 2021[80] [viable disc allograft]	Prospective, multicenter, blind, randomized clinical trial	182	VASPI, ODI	Viable disc allograft injection into painful degenerated discs demonstrated improvements in pain and function scores, with excellent safety profile.	Level I-B

Abbreviations: NRS, numeric rating scale; AF, annulus fibrosus; NP, nucleus pulposus; IVD, intervertebral disc; PRP, platelet-rich plasma; VAS, visual analog scale; ODI, Oswestry Disability Index; LBP, low back pain; NASS, North American Spine Society; FRI, Functional Rating Index; MSCs, mesenchymal stem cells; RCT, randomized controlled trial; SF-36, short form 36 questionnaire; DDD, degenerative disc disease; MRI, magnetic resonance imaging; BMC, bone marrow concentrate; SANE, single assessment numeric evaluation; MPC, mesenchymal precursor cell; HA, hyaluronic acid; SVF, stromal vascular fraction; HSC, hematopoietic stem cells; RMDQ, Roland-Morris Disability Questionnaire; VASPI, visual analog scale of pain intensity.

Evidence Review with Evidence Level Designation: Prolotherapy and Platelet Rich Plasma

Prolotherapy is among the earliest studied regenerative medicines. There have been several prospective and retrospective trials and case reports studying PRP, although only one published RCT. A prospective, double-blind, randomized controlled trial by Tuakli-Wosornu et al in 2016 investigated intradiscal PRP for treatment of chronic moderate to severe lumbar discogenic pain unresponsive to conservative treatment and confirmed with discography. Twenty-nine patients received intradiscal PRP with the control group consisting of 18 patients who received only intradiscal contrast. Over 8 weeks of follow-up, there were significant improvements in participants who received the intradiscal PRP with regard to pain, function, and patient satisfaction compared with the controls.[77] Furthermore, those who received PRP were able to maintain significant improvements in the Functional Rating Index for at least 1-year follow-up. In 2019, Cheng et al performed a 5-to-9-year follow-up on the same patients from the aforementioned RCT by Tuakli-Wosornu et al. From the PRP intervention group, 21 of the 29 original patients were able to be included in this follow-up study. Seventy-one percent were classified as successes as they demonstrated both clinical and significant improvements in pain and function. The remaining 29% of patients required spinal surgery and were classified as failures. This study further supports improvements in pain and function post-intradiscal injection of PRP sustained for follow-up periods of 5–9 years following intradiscal PRP treatment for moderate-severe lumbar discogenic pain.[78]

Cellular Therapy

Several case series and prospective studies have investigated the use of intradiscal autologous stem cells for lumbar discogenic pain. Overall, there is moderate evidence, including that from two relatively small size RCTs, supporting intradiscal allogeneic mesenchymal stem cells in the treatment of discogenic LBP. Regarding human umbilical cord tissue-derived mesenchymal stem cells, there is a single study of small sample size producing low evidence in its support.

In 2021, Beall et al published one-year results of the *VAST* RCT investigating the clinical relevance of treating painful intervertebral disc tissue by supplementary transplantation of viable cellular allograft disc matrix. This structural allograft is prepared from human nucleus pulposus allograft that contains allogeneic viable cells. A minimum of 6×10^6 cells were suspended in each allograft matrix suspension. This prospective, randomized, parallel-arm, multicenter study enrolled a total of 218 subjects who demonstrated clinical disc degeneration of 1 or 2 vertebral levels from L1 to S1 and Pfirrmann levels 3 through 6 on MRI. The cellular allograft group was compared to saline placebo or continued treatment with nonsurgical management in a 3.5:1:1 randomization. At 12 months with a total of 182 subjects completing the study, clinically meaningful improvements in mean visual analog scale of pain intensity (VASPI) and ODI scores were achieved in both the investigational allograft and saline groups. A responder analysis demonstrated a clinically meaningful reduction in ODI of ≥15 points at 12 months that was statistically significant in favor of the allograft group (76.5%) compared to the saline group (56.7%). The supplementation of the disc with viable allograft was able to produce a marked reduction in pain, an improvement of function, and a safety profile similar to traditional discography. Although the saline control placebo group also was able to demonstrate improvements, as previously suggested in prior studies, intradiscal saline may have some therapeutic advantage in itself and thus likely is an active comparator rather than a neutral placebo control.[79,80]

Cellular Therapy: Other Intradiscal Injectates

Methylene blue has been studied by an RCT by Peng et al in 2010. Seventy-two subjects with discogenic LBP were randomized: 36 of whom received 1 mL of 1% methylene blue followed by 1 mL of 2% lidocaine, and 36 in the placebo group received 1 mL of isotonic saline followed by 1 mL of 2% lidocaine. The authors of this single study concluded that the injection of methylene blue into the painful disc is a safe effective and minimally invasive method for the treatment of intractable and incapacitating discogenic LBP.[81]

Fibrin is another injectate that has been trialed to treat discogenic pain. In 2014, Yin et al reported on 15 adults with confirmed discogenic pain who underwent intradiscal injection of a fibrin sealant. Eighty-seven percent of the subjects achieved at least a 30% reduction in low back pain VAS compared with baseline at the 26-week primary end point without significant adverse events. Although this was not an RCT and only evaluated 15 patients, fibrin may provide benefits in certain patients. Fibrin is composed of purified prothrombin and fibrinogen and reconstituted with aprotinin and calcium. When injected into the annular tears, it has the ability to form a matrix sealant that protects the nucleus pulposus.[82]

In an attempt to further define the evidence for intradiscal treatments, a post hoc comparison in 2020 by Ju et al aggregated single-site data from 4 separate multicenter RCTs [Study A: Growth factor BMP-7 (n = 15); Study B: active fibrin sealant (n = 10); Study C: Growth Factor rhGDF-5 (n = 3); Study D: cell-based stem cell treatment MPC-06-ID in HA (n = 10); and saline control group (n = 12)]. While there was both a significant decrease in VAS pain and an improvement in patient reported disability scores, the authors concluded there was no significant difference between the investigational group of biologics and the saline control group. The authors suggested that perhaps saline injection itself has a therapeutic effect, possibly by diluting pro-inflammatory mediators within the degenerated disk, decreasing intradiscal pressure, or a combination of the placebo effect. The small sample sizes and heterogeneity of combining multiple studies make it difficult to draw conclusions from this study[83] (see Table 9 for evidence summary).

Therapy Grading

Intradiscal regenerative therapy is burgeoning area of research and intervention. Different than interventions in the previous sections that have established histories with decades of experience, this intervention category is relatively recently introduced into the lexicon of therapeutic intervention. As a result, there is one RCT and several observational studies and case series which are utilized to form recommendations. Table 9 summarizes the current literature on this family of interventions and Table 10 summarizes those recommendations. There is evidence for the use of intradiscal PRP in the form of a single RCT, and several prospective observational studies and case series for both autologous bone marrow and adipose tissue-derived mesenchymal stem cells, as well as allogeneic mesenchymal stem cells and cellular allograft disc matrix for the treatment of persistent lumbar discogenic back pain. It is important to discern that the primary patient populations studied have previously failed the multidisciplinary standard of care. Regenerative Medicine holds the potential to provide an alternative intervention for these patients whose pain persists despite the recommended conservative management. In these selected patients, intradiscal biologics may improve pain and function without the need for advanced surgical treatments that can impair the spine's native biomechanics (Table 10).

Sacroiliac Joint Injections

The sacroiliac joint (SIJ) is a diarthrodial synovial joint with abundant innervation from the lumbosacral nerve roots.[84,85] The joint itself is approximately two-thirds synovial and one-third ligamentous, with the synovial portion extending anterior and inferiorly and reinforced at its posterior and superior aspect by syndesmotic ligament.[86] The sacroiliac joint is accepted as a relatively common source of low back and/or buttock pain with or without lower extremity pain. The sacroiliac joint has been implicated as the primary pain generator in 10% to 27% of low back pain cases.[87,88] SIJ dysfunction more commonly occurs with degenerative conditions or with an imbalance between the two SI joints; therefore, patients at increased risk for SIJ pain include those with leg length discrepancy, advanced age, inflammatory arthritis, pregnancy, trauma, and previous spine surgery.[89]

There are no definite historical, physical, or radiological features to provide a definite diagnosis of sacroiliac joint pain.[90–92] A systematic review by Szadek et al evaluated the diagnostic validity of the International Association for the Study of Pain (IASP) criteria for sacroiliac joint pain and concluded that the thigh thrust test, the compression test, and 3 or more positive stressing tests contain sufficient discriminative power for diagnosing sacroiliac joint pain.[93]

Table 10 ASPN Back Consensus Group Recommendations for Regenerative Therapies

Recommendation	Grade	Level	Level of certainty Net benefit
Intradiscal PRP in the treatment of discogenic LBP	I	I-B	Low
Intradiscal allogeneic mesenchymal stem cells in the treatment of discogenic LBP	I	I-B	Low
Intradiscal bone marrow derived MSCs	I	I-B	Low
Intradiscal adipose tissue derived MSCs	I	I-C	Low

Note: While these small moderate quality studies look promising, there is much yet to do in this space.
Abbreviations: LBP, low back pain; MSCs, mesenchymal stem cells.

There are many therapies for SIJ dysfunction, with the most common and often first step in therapy algorithms being SIJ intra-articular injections, which can be utilized both diagnostically and therapeutically.[94]

Indications and Contraindications

Diagnostic intra-articular SIJ blocks and therapeutic intra-articular SIJ blocks have their own specific roles in the diagnosis and therapy of SIJ-mediated pain. A thorough history and physical examination including provocative tests are performed for an accurate diagnosis. Typically, if a patient has a positive response to 3 or more SI joint provocative tests, a positive outcome of a diagnostic SI joint block can be predicted.[93] However, SIJ diagnostic injection is then indicated, as it is a true confirmatory test.[95,96] In diagnostic blocks, an anesthetic is injected into the posterior SIJ under fluoroscopic guidance, and if there is a certain degree of pre-defined pain relief following the diagnostic injection for the duration of the anesthetic, then the diagnosis of SI joint dysfunction can be established.[97,98]

Therapeutically, a local anesthetic is combined with a corticosteroid medication to provide pain relief in the SI joint. Therapeutic SI joint injections can be intra-articular or periarticular, and a growing body of research suggests that intra-articular therapeutic injections are superior to periarticular injections.[98,99] Absolute contraindications of SI joint injections include patient history of allergy to cortisone injections, and local malignancy. Relative contraindications include coagulopathy, current, uninterrupted use of blood thinning agents, pregnancy, systemic infection, septic joint, osteomyelitis, and poorly controlled diabetes.[100–102]

Safety and Complications

The largest study to date on SIJ adverse events indicated that there were very low numbers of adverse effects secondary to SIJ injections, with 3% (5/191) of patients experiencing immediate transient reactions and 24% (32/132) with delayed adverse reactions, the most common being increased pain.[103] There are rarer but more serious complications reported in the literature including trauma to the nerves, accidental intervertebral foraminal injection, hematoma, sciatic palsy, meningitis, abscess, and systematic infection.[104–106] Another study determined that 2.5% of 525 SIJ injection resulted in a vasovagal reaction, and there have been case studies illustrating very rare complications such as herpes reactivation or pyogenic sacroiliitis.[107–109] Temporary sciatic palsy was reported in two studies, with 3/67 cases in one and 5/60 in the other.[110,111] One of the major complications of the procedure is that many were technically unsuccessful, with rates of 10–20%.[112]

The most recent data on SIJ blocks, both diagnostic and therapeutic, was compiled to guide the below best practice guidelines. Image guidance for SIJ injections has been found to be very important in multiple studies.[113–116] A study determined that in patients who underwent SIJ injections without image guidance, intra-articular needle placement was confirmed in only 22% in subsequent computed tomography (CT) scans.[113] In another study of "blind" injections, only five of 60 needles closely approximated the joint, and none had proper intra-articular placement.[114] Ultrasound and CT can also be used for image guidance.[115] However, ultrasound cannot verify intra-articular placement of the injectate, and was found to be inferior to fluoroscopic guidance in a prospective, randomized, single-blinded study.[116] CT guidance can also be utilized but has been found to be less effective than fluoroscopy at capturing the escape of injectate from the joint to adjacent structures, and neither ultrasound nor CT guidance can rule out concurrent intravascular flow.[113]

Diagnostic intra-articular SIJ blocks remain the gold standard for establishing a diagnosis of SIJ pain.[114] The positive response of intra-articular diagnostic injections is a complete or near complete relief of pain. Various studies have set different levels of pain relief as the threshold needed for a positive test, ranging from >70% pain relief to >50% pain relief from the diagnostic block.[93,115,117,118] The studies that utilized >70% pain relief as the threshold for an accurate diagnostic block had a smaller number of subjects and therefore were more specific for diagnosis for SIJ-mediated pain.[119] The most important criteria, however, found across multiple studies, was the use of a single positive, diagnostic block versus dual positive, diagnostic blocks.[109,120–126] Utilizing dual controlled blocks significantly decreases the positive response rate, with dual blocks reporting rates of positive SIJ pain diagnosis from 10 to 40% whereas single control blocks produced 29–63% positivity rates of SIJ pain.[109,120–126] Therefore, it has been demonstrated that diagnostic accuracy is at Level II for dual diagnostic blocks, with at least 70% pain relief as the criterion standard and Level III for single diagnostic blocks, with at least 75% pain relief as the criterion standard.[109,120–126]

There have been only two randomized controlled trials, one in which therapeutic SIJ injection was completed utilizing a steroid versus utilizing saline in patients with ankylosing spondyloarthropathy. Those receiving a steroid experienced a mean VAS score decrease from 6.8 to 1.3 compared to the decrease in saline VAS score from 7.0 to 5.2, with a 50% decrease in NSAID use in the steroid group and 14% relief in the saline group, as well as 1 month pain relief sustained in 5/6 patients in the steroid group and 1/6 in the saline group.[110] While of small sample size, these data demonstrated statistically and clinically significant improvements with steroid injection versus placebo. However, Kim et al, who compared prolotherapy to therapeutic SIJ injection, found that 27.2% of subjects achieved 50% pain relief in the steroid group at 6 months and 63.6% of those in the prolotherapy group achieved 50% pain relief. This was repeated at 15 months, with 10.2% in the steroid group achieving significant pain relief compared to the prolotherapy group, in which 58.7% of patients experienced sustained pain relief.[127] However, the study is significantly flawed, and confounded in that many subjects received varying numbers of injections that were not reported.[128] The remainder of studies focused on therapeutic SIJ injections were all observational, either prospective or retrospective. Three studies utilized the criteria of 2 positive diagnostic blocks to select patients who received the therapeutic steroid SIJ injection. In these 3 investigations, 45–67% of study participants reported at least 50% pain relief at 4 weeks.[129–131] There have been numerous studies in which patients were selected for therapeutic SIJ injections after one positive diagnostic block. These results varied far more significantly likely due to these studies utilizing a heterogonous set of diagnostic criteria, follow-up times, and outcome measures. As mentioned above, patients diagnosed with SIJ pain based on the results of only a single diagnostic block demonstrated greater variability in their responses than those diagnosed via dual controlled blocks.[109,120–126] The studies utilizing single blocks as diagnostic criteria reported an average duration of pain relief from their therapeutic injections ranging from 76 to 94.4 days, with the percentage of patients receiving relief from their therapeutic injections ranging from 23% to 78%.[110,127–131]

Evidence Summary

For sacroiliac joint literature, there was sufficient evidence in the form of 2 RCTs and several observational studies (Table 11), for the committee to make recommendations. Table 12 summarizes those recommendations. SIJ dysfunction is a complex pain process with numerous proposed therapy options ranging from physical therapy to invasive surgery on the procedural continuum, SIJ injections are usually the first line in both diagnostic and therapeutic care.

Minimally Invasive Spine Procedures

Percutaneous Image-Guided Minimally Invasive Lumbar Decompression

Lumbar spinal stenosis (LSS) is a widely prevalent condition commonly seen in the elderly population.[132] These patients typically present with myriad symptoms classified as neurogenic claudication. These symptoms may include lower back and leg pain/paresthesias, worsened by walking and usually relieved after rest.[133] While most patients remain asymptomatic, it is estimated that approximately 10% population over the age of 70 will suffer from symptoms secondary to LSS.[134] These chronic and disabling symptoms lead to impairment of patients' quality of life. Among the several factors that may contribute to LSS, ligamentum flavum hypertrophy (LFH) is regarded as one of the most common causes in the elderly.[135] Conservative measures including physical therapy, NSAIDs, and epidural steroid injections have demonstrated limited benefit in providing long-term symptomatic relief in these patients.[136–139] Therefore, the treatment of spinal stenosis historically has been limited to open laminectomy with or without fusion, which can expose the patient to increased complications and an extended hospital stay. Percutaneous image-guided lumbar decompression (PILD) for lumbar spinal stenosis is a procedure in which specially designed instruments are used to percutaneously remove a portion of the lamina and debulk the ligamentum flavum. The procedure is performed under fluoroscopic guidance without direct visualization of the surgical area.

Indications

The PILD procedure is currently only indicated for the treatment of lumbar spinal stenosis secondary to ligamentum flavum hypertrophy. The following criteria should be met before a patient is considered a candidate for PILD:

Table 11 Evidence Summary for Sacroiliac Joint Injections

Study author	Study type	Study size	End point	Evidence level	Notes
Maugars et al, 1996[130]	Prospective RCT double blind saline vs steroid for SIJ	10	NRS, NSAID use, pain relief at 1 month	I-A	Comparing VAS decrease in steroid injections 6.8 to 1.3 to saline 7.0 to 5.2, decrease in NSAID use in steroid injections (50%) vs saline (14%) injections and pain relief at 1 month, saline 1/7 and steroid 5/6.
Kim et al, 2010[131]	Prospective RCT comparing prolotherapy vs SIJ injection	48	>50% pain relief in two groups and sustained pain relief at 15 mo	I-A	>50% improvement: SIJ steroid group: 27.2%, prolotherapy: 63.6%. pain relief at 15 months: SIJ steroid: 10.2%, prolotherapy: 58.7%
Jee et al, 2014[115]	Prospective observational: IA injection fluoroscopic vs ultrasound guidance	110	VAS decrease at 2 weeks and 12 weeks	I-B	Intra-articular injection with fluoroscopic vs ultrasound guidance, effectiveness data also collected with mean pain (NRS) decrease at 2 weeks, 6.45 to 3.14 (51.3% reduction) and 6.45 to 2.56 at 12 weeks
Liliang et al, 2011[123]	Prospective observational	58	>50% pain relief at 6 weeks	I-B	Used dual + blocks as selection criteria for therapeutic injection. Amount of patients who underwent SIJ injection with steroid and local anesthetic and assessed who had >50% pain relief at 6 months, 67%
Chou et al, 2004[111]	Retrospective	54	Percent of patients with 80% at 2 weeks	I-C	Used dual + blocks as selection criteria for therapeutic injection. Pain relief of >80% at 6 weeks was found to be 28% (95% CI: 16–40%)
Irwin et al, 2007[462]	Retrospective	42	>50% pain relief at 1 month	I-C	Used dual + blocks as selection criteria for therapeutic injection. Pain relief of >50% at 1 month found in 43% of patients (18/42)
Hawkins et al, 2009[463]	Retrospective	120	Significant pain relief of 50% or more	I-C	77% of patients with >50% pan relief at 3, 6, 12 months
Borowsky et al, 2008[464]	Retrospective	120	Change in VAS pain scores and patient self- reported ADLs at 3 weeks and 3 months	I-C	12.5% for intra-articular SIJ injection versus 31.25% for combined intra-articular and peri-articular injection at 3 months
Maugars et al, 1992[465]	Prospective	42	% improvement maintained 1 month	I-B	Diagnosis of sacroiliitis with a sero-negative spondyloarthropathy, % improvement maintained for at least 1 month: 100% improvement: 26.2%, 80–90% improvement: 40.5%, 70–80% improvement: 14.3%, 50–70% improvement: 4.8%.
Visser et al, 2013[466]	Prospective	18	Patients with pain relief (>NRS 2/10 decrease) 12 weeks compared to baseline	I-B	Pain relief of at least VAS decrease 2/10, at 12 weeks compared to baseline: 50% (95% CI: 27–73%) of patients

Abbreviations: RCT, randomized controlled trial; SIJ, sacroiliac joint; NRS, numeric rating scale; NSAID, non-steroidal anti-inflammatory drug; VAS, visual analog scale; 95% CI, 95% confidence interval; ADLs, activities of daily living.

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Table 12 ASPN Back Consensus Group Recommendations for Sacroiliac Joint Injections

Recommendation	Grade	Level	Level of certainty Net benefit
Sacroiliac joint injections have been associated with positive predictive value in diagnosis of SIJ dysfunction	A	I-A	Strong
Sacroiliac joint injections demonstrate short term relief of SIJ dysfunction	B	I-B	Moderate

- The patient has symptomatic LSS, ie, presence of neurogenic claudication.
- Confirmation of central/foraminal LSS secondary to LFH on imaging (MRI/CT).
- LFH $\geq$ 2.5mm.

Safety and Complications

The PILD procedure was designed as a minimally invasive procedure for the treatment of lumbar spinal stenosis secondary to ligamentum flavum hypertrophy. The efficacy and safety of the PILD procedure has been demonstrated in several level 1 clinical studies (Table 13), with recommendations in Table 14.

Almost all clinical studies of PILD assessed patients for procedure-related complications including dural tears, nerve root injuries, bleeding, infections, and rehospitalization post-procedure. None of the studies identified any serious procedure/device-related complications. Minor procedure-related complications that were reported included soreness at the surgical site,[140] minor post-operative bleeding,[141] and minor intra-operative bleeding that was controlled with gel foam.[142] All clinical studies demonstrated that the safety profile of the PILD procedure was equivalent to that of epidural steroid injections. Levy et al published the results of a multicenter systematic analysis conducted to evaluate the safety of PILD procedure.[143] This review included 373 patients who underwent a PILD procedure. There were no major procedure- or device-related events reported. Schomer et al published the results of a meta-analysis conducted to compare safety and efficacy of PILD procedure to open lumbar decompression in patients suffering from lumbar spinal stenosis.[144] SPORT (Spine Patient Outcomes Research Trial) surgical cohort patients were analyzed for efficacy and safety of standard lumbar decompressive laminectomy and were compared to PILD patients. While no significant differences were found between the two procedures in terms of efficacy, the complication rate in surgical cohort was significantly higher. To date, there have been no reports of serious device or procedure-related complications with the PILD procedure. In contrast, the SPORT surgical cohort reported complications in 9.9% patients, which included dural tears in 9.2% of patients, 9.5% patients required intraoperative blood transfusions, and 4.9% required postoperative blood transfusions. The study concluded that as a minimally invasive alternative to decompression surgery, PILD procedures yielded comparable patient outcomes with shorter procedure times, less blood loss, shorter hospital stays, and significantly better safety.

Evidence Summary

For percutaneous image-guided lumbar decompression, there was sufficient evidence in the form of three RCTs and several prospective observational studies (Table 13), for the committee to make recommendations. Table 14 summarizes those recommendations.

Stand-Alone Interspinous Spacers, Indirect Decompression

The first interspinous implant for the lumbar spine was developed in the 1950s by Knowles. Owing to flaws in design, material, surgical technique, and applied indications, its use was abandoned. The first modern interspinous device, the Wallis system, was developed by Abbot Spine in 1986 and was used primarily in patients with recurrent disc herniation.[145] Since that time, many adaptations have been introduced to the market as either combination treatment with other surgical procedures or as stand-alone approaches. Traditionally, these interspinous implants were designed to be utilized via open techniques. In 2016, a stand-alone interspinous spacer for the indirect decompression of the lumbar spine was introduced commercially. The Superion device (Vertiflex, Inc., San Clemente, CA; percutaneous interspinous process device [IPD]) is

Table 13 Evidence Summary for PILD in Spinal Stenosis

Study	Study type	Study size	Endpoints	Results	Evidence
Chopko et al, 2010[141] MIDAS I	Prospective clinical study	N=78 Outcomes assessed at baseline and 6 weeks	VAS, ODI, ZCQ, SF-12 Health Survey.	At Baseline- VAS =7.3(3–10) ODI =47.4(16–84) At 6-week follow-up VAS = 3.7(0–10) (p<0.0001) ODI= 29.5 (0–72) (p<0.0001) ZCQ- Patients had statistically significant improvement in both pain and neuroischemic domain at 6-week follow-up. (p<0.001) Health of the patients showed statistically significant (95% CI) improvement in SF-12v2 survey for all but the general health survey scale.	I-C
Basu et al, 2011[467]	Prospective case series	N=27 Patient outcomes assessed at baseline and 6 months	VAS, ODI, ZCQ	Baseline- VAS = 9.1(95% CI ± 0.59) ODI =55.1 (95% CI ± 6.34) At 6 months- VAS = 3.9 (95% CI ± 2.25) (p<0.0001) ODI=31.1 (95% CI ± 9.29) (p<0.0004) ZCQ showed significant improvement in both pain and neuroischemic domains. No device/procedure related complications were reported.	I-C
Deer et al, 2012[468]	Prospective clinical study	N=46 Outcomes assessed at baseline, 12 weeks, 6 months, and 12 months	VAS, ODI, ZCQ	At Baseline - VAS = 6.9 (95% CI ± 0.6) ODI = 49.4 (95% CI ± 2.5) At 12 weeks- VAS = 4.2 (95% CI ± 1.0) (p<0.01) ODI= 35.1 (95% CI ± 5.6) (p<0.01) At 6 months- VAS= 4.4 (95% CI ± 1.0) (p<0.01) ODI= 35.0 (95% CI ± 5.5) (p<0.01) At 12-month follow-up- VAS=4.0 (95% CI ± 1.0) (p < 0.0001) ODI=32.0 (95% CI ± 5.8) (p < 0.0001) Statistically significant improvements were achieved in all ZCQ domains, including Symptom Severity, both Symptom Severity sub-domains (Pain and Neuro-Ischemic) and Physical Function (paired *t*-test; P < 0.0001).	I-B

(*Continued*)

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Table 13 (Continued).

Study	Study type	Study size	Endpoints	Results	Evidence
Brown et al, 2012[469]	Prospective randomized clinical trial	N=38 Outcomes assessed at baseline, 6 and 12 weeks	VAS, ODI, ZCQ	In the PILD treatment group: At Baseline- VAS = 6.3 (95% CI ± 0.7), ODI = 38.8 (95% CI ± 4.2) At 6 weeks- VAS=3.8 (95% CI ± 1.3) ODI=27.4 (95% CI ± 7.0) At 12 weeks- VAS= 3.4 ODI=18.6 The change in VAS from baseline to week 6 and baseline to week 12 was significant ($p< 0.01$), but the change from week 6 to week 12 was not significant. The change from baseline to 6-weeks post PILD and baseline to 12-weeks post PILD was significant ($p < 0.05$), but the change from 6-weeks to 12-weeks was not significant, ($p>0.05$). In the ESI treatment group- At Baseline- VAS = 6.4 (95% CI ± 1.0) ODI = 40.5 (95% CI ± 5.9) At 6 weeks- VAS= 6.3 (95% CI± 1.4) ($p > 0.05$). ODI =34.8 (95% CI ± 8.2) ($p>0.05$) ZCQ score showed significant improvement at 6 and 12 weeks for PILD treatment group.	I-A
Mekhail et al, 2012[133]	Prospective case series study	N=40 Outcomes assessed at baseline and 1 year.	PDI, RMQ	At Baseline Mean PDI score = 41.4 (95% CI ± 4.6) Mean RMQ= 14.3 (95% CI ± 2.1) VAS= 7.1(95% CI ± 0.8) At 1 year Mean PDI= 18.8 (95% CI ± 4.9) ($p<0.0001$) Mean RMQ= 6.6 (95% CI ± 2.0) ($p<0.0001$) VAS= 3.6 (95% CI ± 0.9) ($p<0.0001$) Standing Time improved from a baseline of 8 to 56 minutes at 12-month follow-up. (ANOVA, $p<0.00001$) Walking Distance improved from a baseline mean of 246 feet to 3956 feet at 12-month follow-up. (ANOVA, $p<0.00001$)	I-B

Benyamin et al, 2016[142] MiDAS ENCORE I	Prospective, multicenter, RCT	N=302 Outcomes assessed at baseline, 6 months, and 1 year	ODI, NPRS, ZCQ	At 6 months responder rate- ODI PILD vs ESI = 62.2% vs 35.7% (95% CI ± 26.6%) (p<0.001) NPRS PILD vs ESI = 55.9% vs 33.3% (95% CI ± 22.6%) (p<0.001) At 1 year- ODI PILD vs ESI = 58% vs 27.1% (95% CI ± 30.9%) (p<0.001) NPRS PILD vs ESI = 57.3% vs 27.1% (95% CI ± 30.2%) (p<0.001) Statistically significant improvements were seen with PILD over ESI in all three domains of ZCQ at 6 months and 1 year. (p<0.001).	I-B
Staats et al, 2018[470] MiDAS ENCORE II	2-year follow-up data for PILD procedure arm of MiDAS ENCORE study	N=143 6-months, 1 year and 2 years	ODI, NPRS, ZCQ	At 2 years- ODI improved by 22.7 points (95% CI, 18.5–26.9), NPRS improved by 3.6 points (95% CI, 3.1–4.2), and ZCQ symptom severity and physical function domains improved by 1.0 (95% CI, 0.8–1.2) and 0.8 points (95% CI, 0.6–0.9), respectively. Improvements in all domains were statistically significant. There were no serious device related adverse events	I-A

(*Continued*)

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Table 13 (Continued).

Study	Study type	Study size	Endpoints	Results	Evidence
Deer et al, 2022[19] The MOTION study	Prospective, multicenter, randomized controlled clinical study	N=155 Patients evaluated at baseline, 6 months, and 1 year	ODI, NPRS, ZCQ	At Baseline- CMM alone vs PILD+ CMM ODI= 51.7 ± 14.8 vs 55.3 ± 14.3 (p=0.129) NPRS= 7.8 ± 1.5 vs 7.5 ± 1.4 (p=0.259) ZCQ Symptom Severity= 3.56 ± 0.59 Vs 3.58 ± 0.61 (p= 0.887) ZCQ Physical Function = 2.78 ± 0.46 Vs 2.84 ± 0.50 (0.425) At 6 months- outcome measures with mean improvement ± SD CMM alone vs PILD+ CMM ODI= 3.8 ± 11.1 vs 16.3 ± 18.0 (p<0.001) NPRS Back= 0.6 ± 1.7 vs 2.4 ± 2.6 (p<0.001) NPRS Leg= 0.9 ± 2.0 vs 2.5 ± 3.0 (p<0.001) ZCQ Symptom Severity= 0.11 ± 0.48 Vs 0.72 ± 0.85 (p= <0.001) ZCQ Physical Function = 0.05 ± 0.35 Vs 0.48 ± 0.65(p<0.001) At 1 year- outcome measures with mean improvement ± SD CMM alone vs PILD+ CMM ODI= 2.0 ± 11.7 vs 16.1 ± 19.0 (p<0.001) NPRS Back= 0.4 ± 1.3 vs 1.4 ± 2.1 (p<0.001) NPRS Leg= 1.4 ± 2.1 vs 3.6 ± 3.1 (p<0.001) ZCQ Symptom Severity= 0.12 ± 0.46 Vs 0.64 ± 0.83 (p= <0.001) ZCQ Physical Function = 0.04 ± 0.38 Vs 0.43 ± 0.70 (p<0.001) PILD with CMM was superior to CMM alone across all measures in treating patients with neurogenic claudication.	I-A

Abbreviations: ZCQ, Zurich Claudication Questionnaire; ESI, epidural steroid injection; VAS, visual analog scale; ODI, Oswestry Disability Index; SF-12, Short Form Health Questionnaire; 95% CI, 95% confidence interval; PDI, Pain Disability Index; PILD, percutaneous image-guided minimally invasive lumbar decompression; RMQ, Roland-Morris Disability Questionnaire; ANOVA, analysis of variance; NPRS, numeric pain rating scale; CMM, conventional medical management.

Table 14 ASPN Back Consensus Group Recommendations for PILD Injections

Recommendation	Grade	Level	Level of certainty Net benefit
Percutaneous lumbar decompression for ligamentum flavum hypertrophy with the diagnosis of lumbar spinal stenosis	A	I-A	Strong

a low-profile evolution of previous IPD systems that can be implanted percutaneously between symptomatic vertebral levels on an outpatient basis. This technique has a number of potential advantages and imparts results that parallel the open technique.[146] Interspinous spacers have been designed to provide an alternative to open surgical decompression surgery with minimal surgical dissection. Indirect decompression of the spinal canal using an interspinous spacer is a minimally invasive procedure that can be performed in an ambulatory surgery center and has been shown to provide comparable clinical performance to decompressive laminectomy for management of symptoms of spinal stenosis.[147,148]

Indications and Contraindications

The effective utilization of the interspinous spacer relies upon the appropriate diagnosis of LSS. This should begin with a proper history and physical examination to rule out other sources of back pain. Patients must report symptoms of neurogenic claudication that abate with sitting down or leaning forward, referred to as the "shopping cart sign". To confirm clinical suspicion of LSS, MRI or CT myelogram studies are required.[149] In addition, lumbar x-rays including flexion/extension views should be performed in order to assess for spondylolisthesis and segmental instability.

The initial treatment of LSS consists of various nonoperative approaches including physical therapy, pain medications (NSAIDs, mild opioids), and epidural steroid injections, referred to as conservative care.[150] Conservative treatment is generally recommended for 6 months prior to initiating more invasive treatments. Patients with symptoms refractory to sustained conservative medical management warrant surgical consideration.[150] As mentioned, open decompression surgery has been associated with significant post-operative complications.

Standalone lumbar interspinous spacers are indicated to treat skeletally mature patients suffering from painful walking, numbness, and/or cramping in the legs (neurogenic claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, as confirmed by advanced radiographic imaging. They are indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, numbness, and/or cramping, with or without back pain, and who have undergone at least 6 months of non-operative treatment. Interspinous spacers may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5.

For this intended use, moderate degenerative lumbar spinal stenosis is defined as follows:

- 25% to 50% reduction in the central canal and/or nerve root canal (subarticular, neuroforaminal) compared to the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:

- Evidence of thecal sac and/or cauda equina compression,
- Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements,
- Evidence of hypertrophic facets with canal encroachment.

And associated with the following clinical signs:

- Presents with moderately impaired physical function defined as a score of ≥2.0 on the Zurich Claudication Questionnaire (ZCQ),
- Ability to sit for 50 min without pain and to walk 50 feet or more.[151]

The interspinous spacers may be contraindicated in the following situations:

- Severe spinal stenosis with neurological deficits
- Multilevel (more than 2 levels of spinal stenosis)
- Spinal instability (>3mm of translation)
- Osteoporosis (high risk for spinous process fracture)
- Scoliosis (Cobb angle >17 degrees)
- Baastrup's disease
- Greater than grade I spondylolisthesis
- Previous lumbar surgery at the affected level
- Symptoms not relieved with forward flexion[20]

Safety/Complications

The device and device-related adverse effects (AEs) as reported during the RCT, post hoc analyses, and clinical registries performed to date are quite minimal. The most commonly reported minor, self-limiting post-procedure adverse events included incisional pain and transient worsening of back pain. The following device- or procedure-related events have been reported:

- 23 spinous process fractures
- 10 wound complications
- 2 infections
- 50 reoperations/revisions

Literature Summary

A review of literature revealed that there are 28 published peer-reviewed articles and 6 clinical studies published to date with direct patient data regarding the clinical efficacy of stand-alone interspinous spacers for LSS. The clinical studies include one RCT, 2 post hoc analyses of RCTs, an open-label follow-up on RCT study arms, and 2 prospective single-arm studies.

In 2015, Patel et al[152] published results from a prospective, multicenter, randomized, controlled, investigational device exemption noninferiority trial. A total of 391 randomized patients were implanted with Superion (n = 190) or control (n = 201) spacers at 29 sites in the United States between August 2008 and December 2011. These patients returned for visits at 6 weeks and 3, 6, 12, 18, and 24 months. The primary endpoint of this study was a composite treatment success outcome at the 2-year follow-up visit, defined as (1) clinically significant improvement in at least 2 of 3 ZCQs, (2) freedom from reoperation, revision, removal, or supplemental fixation at the index level, (3) freedom from epidural steroid injection or nerve block at the index level within 12 weeks of the 2-year visit, (4) freedom from rhizotomy or spinal cord stimulator at any level, and (5) freedom from major implant or procedure-related complications. Secondary outcomes included leg and back pain severity assessed on a 100-mm visual analogue scale, ODI, patient satisfaction questions and adverse events classified by seriousness and relationship to the device and/or procedure. The primary composite endpoint of this study was met, which demonstrated that the Superion spacer was noninferior to the X-Stop spacer. Leg pain, the predominant patient complaint, decreased in severity by 70% during 2 years in each group. Most (77%) patients achieved leg pain clinical success (improvement ≥20 mm) at 2 years. Back pain clinical success (improvement ≥20 mm) was 68%, with no differences between groups. ODI clinical success (≥15% point improvement) was achieved in 65% of patients. The rates of complications and reoperations were similar between groups.[152]

Other peer-reviewed publications include literature reviews, a clinical registry, and a cadaveric biomechanical study. The literature reviews include topics such as cost-effectiveness, use in levels adjacent to the previous surgery, and algorithms for LSS treatment. For interspinous spacers, there was sufficient evidence in the form of RCTs and prospective observational studies (Table 15), for the committee to make recommendations. Table 16 summarizes those recommendations.

Table 15 Evidence Summary for Interspinous Spacers, Indirect Decompression

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Nunley et al, 2018[471]	Post hoc analysis of RCT	190	I-B	Opioid Use	Opioid use: -50% at baseline after procedure -25.2% at 12 months -13.3% at 24 months -7.5% at 60 months.
Nunley et al, 2018[472]	Post hoc analysis of RCT	190	I-B	SF-12	-Physical Component Summary (PCS) score: 29.4 ± 8.1 Pre- operative to 43.8 ± 11.6 at 5 years (49%). -Mental Component Summary (MCS) score: from 50.0 ± 12.7 Pre-operative to 54.7 ± 8.6 at 5 years -Improved Quality of Life at 60 months
Nunley et al, 2017[473]	Open-label follow-up study on RCT treatment arm	88	I-B	ODI, VAS, ZCQ	-65% of patients demonstrated success in ODI -80% of patients showed successful improvements in VAS -84% of patients demonstrated clinical success in at least 2 of 3 ZCQ domains
Patel VV et al, 2015[152]	Multicenter, RCT	391	I-A	ODI, VAS, ZCQ	-63% patients improved ODI -76% patients improved leg pain -65% patients improved back pain -84% of patients demonstrated clinical success in at least 2 of 3 ZCQ domains
Bini W et al, 2011[474]	Prospective, single-arm	104	I-B	NRS, ODI, SF-12	-86% improvement in extremity pain -76% improvement in LBP -64% improvement in ODI -41% improvement in PCS -22% improvement in MCS
Shabat S et al, 2011[475]	Prospective, single arm	53	I-B	NRS, ZCQ, ODI, SF-12	-54% improvement in axial and extremity pain -43% improvement in ZCQ(ss) -44% improvement in ZCQ(pf) 75% of patients had clinically successful improvements in ODI (defined as a 30% improvement in score) -40% improvement in PCS and MCS

Abbreviations: RCT, randomized controlled trial; PCS, physical component summary; MCS, mental component summary; ODI, Oswestry Disability Index; VAS, visual analog scale; ZCQ, Zurich Claudication Questionnaire; NRS, numeric rating scale; SF-12, Short Form Health Questionnaire; LBP, low back pain.

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Table 16 ASPN Back Consensus Group Recommendations for Interspinous Spacers, Indirect Decompression

Recommendation	Grade	Level	Level of certainty Net benefit
Stand-alone interspinous spacers for indirect decompression are safe and effective for the treatment of mild to moderate lumbar spinal stenosis if no contraindications exist	A	I-A	High

Percutaneous and Endoscopic Disc Procedures

Lumbar intervertebral discs provide a cushion between the vertebral bodies to allow the spinal column to tolerate a particular amount of compression on a regular basis. Despite their structural benefit, lumbar disc herniations (LDH) can be particularly problematic due to their predilection for nerve root compression based on anatomic location. These often manifest as an acute radiculopathy in a sciatic distribution with or without acute LBP. The prevalence of LDH is approximately 1–3%.[153] Those who undergo 6 weeks of conservative therapy without significant improvement in symptoms are recommended to undergo surgical intervention to remove the herniated portion of the disc.[154] The most common procedure to accomplish this task is the classic open microdiscectomy (MD). In this procedure, the lamina of the affected levels are exposed, a small laminotomy is made and a discectomy is performed with the aid of intraoperative microscopy. This procedure produces excellent short-term outcomes in a majority of patients.[155,156] However, this procedure also has its potential pitfalls. As many as 10% of patients undergoing MD will experience a re-herniation of the remaining disc material.[157] In addition, approximately 30% of patients experience LBP after surgery and 20% ultimately require a revision surgery.[158,159]

In an effort to reduce pain and complications associated with open MD, minimally invasive procedures have been developed over the years in hopes of achieving similar results. One of the first generations of minimally invasive surgery was percutaneous laser disc decompression. While this achieved good clinical results, further developments in technology have witnessed this technology's use reduced over time.[160–162] These developments in technology have mostly been with regard to that of visualization or approach techniques. In reference to visualization, this has typically involved an endoscope as opposed to a traditional microscope. Compared to the traditional open procedure, both percutaneous and tubular approaches have been developed in an effort to spare painful muscle dissection.[163–168] As these new approaches have been developed, they have been tested against the gold standard of MD for both clinical results and complications.

This section discusses the available percutaneous, endoscopic and other minimally invasive options for lumbar discectomy and how they compare to the clinical outcomes and complication rates achieved in traditional MD.

Indications and Contraindications

Lumbar discectomy, in both its minimally invasive and more traditional open forms, is a procedure which targets the removal of a portion of an intervertebral lumbar disc which is herniated through the disc annulus or causing the annulus to bulge, ultimately leading to pressure on the traversing and/or exiting nerve root at this level. In the traditional open procedure, a laminotomy is usually created at the more cranial level of the disc herniation. The thecal sac and traversing nerve root are then retracted medially, and the herniated or bulging disc fragment is removed under microscopic magnification. In the more minimally invasive techniques, bony removal is often limited, if necessary at all. Visualization is often provided by an endoscope in an effort to limit the opening needed to perform such a procedure.

Lumbar discectomy is indicated in the following situations:

- Diagnostic testing (MRI, CT myelogram) which shows a herniated/bulging lumbar disc causing compression of the traversing nerve root, exiting nerve root or cauda equina
- Significant pain, weakness, numbness or paresthesias in an expected distribution based on the compressed nerve root
- Radiculopathy symptoms that are more significant than LBP symptoms
- Symptoms have not improved with upwards of 6 weeks of conservative management (NSAIDs, oral steroids, epidural steroid injections, physical therapy, etc.)

- Symptoms consistent with cauda equina syndrome (bilateral leg weakness, sensory disturbances in the genital and saddle region, loss of bowel/bladder control)

While multiple different interventions are possible with regard to lumbar discectomy, all of these procedures and devices have received approval from the FDA. Regarding contraindications to lumbar discectomy, the most significant is related to spinal instability. In patients with evidence of underlying instability, decompression alone can lead to worsening of this instability and further morbidity. Other contraindications which have been noted in the literature include calcified discs, painless weakness and pyogenic spondylodiscitis or other severe disc space infections. Specifically, endoscopic discectomy can be contraindicated in the setting of cauda equina syndrome and severe fibrotic adhesions. Also, regarding endoscopic discectomy, tubular discectomy and other percutaneous techniques, surgeon experience and level of training must be considered prior to proceeding.[169]

Safety and Complications

Most studies that have compared minimally invasive techniques for discectomy to more traditional open procedures have studied rates of complications between these two techniques. While minimally invasive techniques may lead to less post-operative pain for the patient, subjecting them to increased risk as a result of that technique would potentially reduce any benefit gained. Thus, careful investigation of differences in complications between these groups is of paramount importance.

In microendoscopic discectomy techniques, a number of studies have been completed with monitoring of peri-operative complications. Two particular complications which have been carefully monitored include reherniation of the disc and dural tear. Teli et al found higher incidence of both dural tears (8.7% v. 3%) and reherniation (11.4% v. 3.5%) in microendoscopic discectomy as compared to open procedures.[170] However, other studies in which microendoscopic techniques were used have not yielded such results. In these other studies, similar rates of dural tears (approximately 7% in each group) and reherniations (approximately 2% in each group) were noted between microendoscopic techniques and more traditional open discectomies.[171,172]

Other studies which have reviewed microendoscopic, percutaneous and open discectomy techniques have identified minimal complications that were mostly transient in nature. These include dysesthetic pain, motor weakness, paresthesias and urinary retention. In all of the studies reviewed, the individual rate of these complications did not exceed 5% with regard to any of the above techniques. In addition, no serious adverse events, such as post-operative discitis, were noted.[162,173–178] Overall, based on the available data, the procedures performed for lumbar discectomy can be performed safely, regardless of the technique used.

Evidence Review with Evidence Level Designation

A number of studies have been performed assessing discectomy procedures, as well as several reviews. Some studies have compared microendoscopic discectomy to open techniques.[170–172] Others have compared microendoscopic techniques to percutaneous methods.[173,174] Still, others have compared percutaneous techniques to open procedures[175,176,179] and tubular methods to open procedures, as well.[162,177,178] A number of systematic reviews and meta-analyses have also been completed which compared the above techniques, some focusing on efficacy while others on complications.[180–183] While many studies of these procedures are available, for the purposes of this guideline, we limited our use to the most recent data available in an effort to provide the most accurate and up-to-date recommendation.

In summary, percutaneous and endoscopic disc procedures have a favorable safety and efficacy profile in terms of lumbar disc herniation with persistent radicular symptoms. Further research is needed to examine complication rates in regard to dural tears and re-herniation and evaluating methods to further decrease these rates of incidence for these techniques to supplant MD as standard of care. For percutaneous and endoscopic disc procedures, there was sufficient evidence in the form of RCTs (Table 17) for the committee to make recommendations. Table 18 summarizes those recommendations.

Table 17 Evidence Summary for Percutaneous and Endoscopic Procedures

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Teli et al, 2010[170]	Prospective, randomized, single center	212	I-A	VAS (leg and back), ODI, SF-36 (mental and physical health)	No difference in VAS, ODI or SF-36 scores throughout follow up between groups, all improved significantly within groups
Garg et al, 2011[171]	Prospective, randomized, single center	112	I-B	ODI	Mean ODI change of 12.76 in MED, 6.97 in OD at 1 week, Continued improvement over 12 months but not statistically significant in either group
Hussein et al, 2014[172]	Prospective, randomized, single center	185	I-B	NRS (leg and back), ODI	Mean NRS leg change 7.8 (MED) v. 6.6 (OD), Mean NRS back change 1.9 (MED) v. 4.4 (OD), Mean ODI change 51.2% (MED) v. 11.17% (OD), McNabb's criteria Excellent outcome 92.6% (MED) v. 42.2% (OD), Good outcome 4.2% (MED) v. 28.9% (OD), Fair outcome 1.1% (MED) v. 24.4% (OD), Poor outcome 2.1% (MED) v. 4.4% (OD)
Chen et al, 2018[173]	Prospective, randomized, single center	153	I-A	VAS (leg and back), ODI, SF-36 (mental and physical health)	No difference in ODI, VAS or SF-36 scores between groups, significantly improved from preoperative in both groups
Ruetten et al, 2008[174]	Prospective, randomized, single center	200	I-A	VAS (leg and back), ODI, NASS	VAS, ODI and NASS significantly decreased from preoperative to postoperative, No difference between the two groups, 2 years 79% v 89% with no leg pain
Pan et al, 2014[175]	Prospective, randomized, single center	20	I-B	VAS	VAS improved in both groups with no statistical difference between groups (OD 7.5 to 1.9, PELD 7.5 to 1.8); Blood loss (99 v. 8), hospital stay (5.6 v. 1.9) and wound size (4.9 v. 0.51) significantly less in PELD group
Pan et al, 2016[179]	Prospective, randomized, single center	106	I-B	VAS, JOA and ODI	VAS scores statistically significantly better at all time points up to 12 months ($p < 0.05$), no difference noted between groups at 12 months; JOA and ODI with no difference throughout; incision size (0.8 v. 3.7), blood loss (13.8 v 87.2), hospital stay (7.2 v 12.8) significantly better in PELD ($p < 0.05$)
Ding et al, 2017[176]	Prospective, randomized, single center	100	I-B	VAS and ODI	VAS and ODI decreased in each group pre to post op but no difference between the groups; Incision length (3 v. 0.5) and hospital stay (10.2 v. 7.6) significantly decreased in PELD
Ryang et al, 2008[177]	Prospective, randomized, single center	60	I-B	VAS, ODI, SF-36	VAS and ODI decreased in each group but no statistical difference between groups at postop (2.1 v. 2.1, 12 v 12), SF-36 improved in both (no difference in physical score (47.5 v 47.6), improved mental score in OD (51.9 v 44)), no difference in operative time, blood loss or hospital stay
Franke et al, 2009[178]	Prospective, randomized, multicenter	100	I-A	VAS, ODI	VAS and ODI improved in both groups and both centers but no difference between the groups
Arts et al, 2011[476]	Prospective, randomized, multicenter	325	I-A	VAS, RDQ	VAS leg, VAS back and RDQ similar between two groups

Abbreviations: VAS, visual analog scale; ODI, Oswestry Disability Index; SF-36, Short Form Health Questionnaire; MED, microendoscopic discectomy; NRS, numeric rating scale; OD, open discectomy; NASS, North American Spine Society questionnaire; PELD, percutaneous endoscopic lumbar discectomy; JOA, Japanese Orthopedic Association; RDQ, Roland-Morris Disability Questionnaire.

Table 18 ASPN Back Consensus Group Recommendations for Percutaneous and Endoscopic Procedures

Recommendation	Grade	Level of evidence	Level of certainty Net benefit
Microendoscopic Discectomy	B	I-a	High
Percutaneous Endoscopic Discectomy	B	I-a	High
Tubular Discectomy	B	I-a	High

Interspinous/Interlaminar Fusion Devices

Degenerative lumbar spinal stenosis has many etiologies that can include hypertrophied ligamentum flavum, osteophytes, facet joint hypertrophy and degeneration of the disc space.[184] Lumbar spinal stenosis and lumbar degenerative disc disease are often seen in conjunction and are largely products of each other.[185] Treatment options for those with spinal stenosis and degenerative changes include conservative measures such as physical therapy, medications, and epidural steroid injections.[186] The most common surgical options can include open laminectomy or decompression with or without transpedicular screw fixation.[187] There are several limitations to these spinal surgical procedures including extended recovery and chronic back pain associated with post-laminectomy syndrome. These surgeries have also been associated with a higher incidence of adverse events such as cerebrospinal fluid leak, nerve injury, deep wound infections, misplaced hardware, and hardware failures.[188,189] Lastly, there is concern regarding adjacent segment disease from altered biomechanics.[190] Many of these factors limit the use of these procedures in those patients of advanced age, those with medical comorbidities, and those with mild or moderate findings. Minimally invasive approaches with reduced procedural risks become a viable option for those patients.

Although indirect decompression with the use of interspinous process spacers (IPS) has demonstrated positive outcomes, its implementation is limited in those patients with degenerative changes, spondylolisthesis, and multiple pain generators such as disc degeneration and facet joint hypertrophy. This has led to the development of minimally invasive devices for interspinous or interlaminar fixation (ISF) which can address both the stenosis and degeneration and provide the ability to stabilize adjacent spinous processes, decompress neural structures by blocking extension, and minimize overload on adjacent spinal levels. Biomechanically, they have been demonstrated to deliver immediate flexion-extension balance and provide effective stabilization for arthrodesis while preserving motion.[191,192] Advantages include small skin incisions, minimally invasive nature, minimal muscle dissection, shorter operative times, and favorable efficacy.[193] It is these features that make it a suitable option to those patients not suited for pedicle screw fixation, non-surgical candidates, and those early in the treatment paradigm. This has specifically been demonstrated in an elderly cohort demonstrating significant improvement in VAS with reliable fusion rates.[194]

The use of ISF in isolation as a treatment was performed by Postacchini et al, who demonstrated in a prospective study that a stand-alone ISF, with minimally invasive decompression in stenotic patients with degenerative spondylolisthesis, provided fusion and highly significant improvement in all outcome measures at a two-year follow-up.[195] This finding was supported in a multicenter RCT directly comparing ISF with decompression to decompression alone.[196] Two-year follow-up was performed on moderate to severe spinal stenosis with the primary endpoint being superior for the ISF with decompression group, as well as patients in the decompression alone group being more likely to undergo a secondary intervention or injections. ISF with decompression vs decompression with pedicle screw fusion was also assessed in a multicenter RCT with five-year follow-up.[197] The majority of ISF with decompression group patients (50.3%) met all composite endpoints, while only 44% in the pedicle screw fusion group did so. The two groups were similar in reoperation rates, as well as improvement in ODI, and VAS. This finding further supports the utility of ISF.

Chin et al performed a retrospective review of prospectively collected data on patients undergoing open decompression and distraction of the spinous processes at L4-L5 using an interspinous device. Procedures were performed in an outpatient setting with a follow-up period of over 5 years.[198] There were a total of 56 patients who met criteria for inclusion. The authors found significant improvements in both VAS pain scores and ODI. There was one case that

underwent the removal of the device and converted to a hemilaminectomy. Lastly, there were no complications. An additional retrospective study utilizing the same device collected data on 13 patients with a median follow-up of 19 months, demonstrating a statistically significant improvement in pain scores without reoperation or complications.[199] These studies demonstrate both the safety and efficacy of ISF when used as a stand-alone device. Another study specifically looked at the use of ISF without decompression as a stand-alone device.[200] The study was retrospective, with a sample of 32 patients followed for three months with the Aurora Zip (Aurora Spine, Carlsbad, CA) ISF device used at four sites to evaluate the safety and efficacy of the treatment of lumbar spinal stenosis and degenerative disease. The study determined that subjects experienced a 67% reduction in VAS pain scores while having no complications.

There are several ISF devices on the market which vary in their application and patient selection. Some of the variability is due to its use with vs without a decompression, as well as with or without coinciding anterior spinal fusion. Ultimately, the use of bone graft material is a defining factor in the labeling of ISF, as well as being able to properly decorticate and prepare bone for arthrodesis.

Evidence and Therapy Grading

For interspinous/interlaminar fusion devices, there were no RCTs to guide recommendations; however, there was sufficient evidence in the form of prospective studies (Table 19) for the committee to make recommendations. Table 20 summarizes those recommendations.

Table 19 Evidence Summary for Interspinous/Interlaminar Fusion Devices

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Postacchini et al, 2016[195]	Prospective cohort, multicenter	25	I-B	Rates of Fusion, NRS (leg and back), ODI, SF-36 (mental and physical health)	Provided fusion and highly significant improvement in all outcome measures at a two-year follow-up
Schmidt et al, 2018[196]	Prospective, randomized, multi center	230	I-A	ODI	Primary endpoint being superior for the ISF with decompression group, as well as patients in the decompression alone group being more likely to undergo a secondary intervention or injections
Musacchio et al, 2016[197]	Prospective, randomized, multi center	215	I-A	ODI	ISF with decompression group had 50.3% of the patients meeting all composite endpoints, while it was at 44% in the pedicle screw fusion group. The two groups were similar in reoperation rates, as well as improvement in ODI, and VAS
Chin et al, 2020[198]	Retrospective review of prospective data	56	III	VAS (leg and back), ODI	There were significant improvements in both VAS pain scores, as well as ODI

Abbreviations: NRS, numeric rating scale; ODI, Oswestry Disability Index; SF-36, Short Form Health Questionnaire; ISF, interspinous fixation; VAS, visual analog scale.

Table 20 ASPN Back Consensus Group Recommendations for Interspinous/Interlaminar Fusion Devices

Recommendation	Grade	Level	Level of certainty Net benefit
ISF can be used as a stand- alone device for decompression.	B	I-B	Moderate
ISF can be used as a stand- alone device for spinal fusion	C	I-B	Moderate
ISF is a suitable option to those patients not suited for pedicle screw fixation, non- surgical candidates, and those early in the treatment paradigm	B	I-B	Moderate

Minimally Invasive Sacroiliac Fusion

Sacroiliac joint dysfunction denotes abnormal biomechanics between the sacrum and ileum, typically as a result of hypermobility. With pathological movement or laxity of the sacral ligaments, movement may result in sacroiliitis (inflammation within the sacroiliac joint) and sacroiliac joint pain. Normal movement of the sacroiliac joint is typically limited to 2 to 4 degrees of movement due to the bony architecture and ligamentous structures surrounding the joint. However, if the anatomy is disrupted or degenerative, excessive or limited nutation and counter-nutation may occur.[201] Nutation refers to the anterior-inferior movement of the sacrum, while the coccyx moves posteriorly relative to the ilium; and counter-nutation refers to the posterior-superior movement of the sacrum, while the coccyx moves anterior relative to the ilium. In established cases of SIJ dysfunction, there may be either resultant elements of ankyloses or arthrosis within the joint.

Diagnostic imaging in the form of CT scans, MRIs, and plain film radiographs may provide evidence of degenerative changes within the sacroiliac joints but does not always coincide with the joint as the etiology of pain symptoms. This eventually led to the adoption of diagnostic sacroiliac joint injections. The use of image-guidance substantially improved the accuracy of the injections. To date, diagnostic SIJ injection with image guidance is the most reliable method for diagnosing sacroiliac joint dysfunction.[102]

Indications

Although there is a diagnostic methodology for SIJ dysfunction, the treatment algorithm has only been more recently defined and continues to evolve.[103] Conservative treatments included bracing, medications, activity modification, manual therapy, chiropractic manipulation, physical therapy, and intra-articular SIJ injections.[202] In the past decade, sacroiliac joint stabilization/fusion has been presented as an option for recalcitrant cases of sacroiliac joint pain. Historically, arthrodesis was performed as an open procedure and used sparingly due to its invasive nature. Surgical stabilization and/or fusion may now be performed via a minimally invasive approach. There are multiple options for sacroiliac joint stabilization/fusion, with the most common being: 1) the lateral approach, and 2) the posterior approach. In the past decade, the use of a minimally invasive transiliac or transarticular (lateral) approach became recognized with multiple high-level studies providing empirical support.[203–211] The use of the posterior approach has been recently proposed as a less invasive and safer procedure. Specifically, the posterior approach avoids the neurovascular bundle.[212,213]

With certain posterior sacroiliac joint systems, an allograft transfixation implant(s) are placed to stabilize the joint for arthrodesis. This is not a new concept, as it was used in a previous study by McGuire et al.[214] Cranial and caudal fibular dowel grafts, harvested from the posterosuperior iliac spine, were demonstrated to be effective in successful fusion of the SIJ. Newer posterior systems include a cortical allograft and therefore negate the need for harvesting of bone. Further distinguishing it is that the procedure is performed minimally invasively, which allows it to be performed on an outpatient basis and does not require weight-bearing restrictions.[215]

Safety and Complications

Minimally invasive SIJ fusion is a relatively safe procedure but is not without certain risks. Shamrock et al performed a recent review on the safety of transiliac sacroiliac joint fusion. They reported on fourteen studies of a total of 720 patients (499 females/221 males) with a mean follow-up of 22 months.[216] There were 91 reported procedural-related complications (11.11%) with the most common adverse event being surgical wound infection/drainage (n = 17). Twenty-five adverse events were attributed to be secondary to placement of the implant (3.05%) with nerve root impingement (n = 13) being the most

common. The revision rate was 2.56%. Consistent with their report, Heiney et al reported surgical wound infection as the most common complication associated with the transiliac sacroiliac joint fusion in a systematic review of 432 subjects.[217]

There is evolving scientific literature studying the overall number of complications for the posterior approach for minimally invasive sacroiliac joint fusion.[218] Non-union was the most common complication noted but has not been consistently tracked in the studies with post-procedure imaging. Rajpal et al reported two hematomas and one infection as a result of a posterior sacroiliac screw fixation.[219] There have been no reported serious complications as a result of percutaneous posterior allograft sacroiliac joint fusion/stabilization. Sayed et al published multicenter outcomes with a novel posterior approach on 50 patients and reported a 0% serious adverse event (SAE) rate.[218]

Evidence Review and Therapy Grading

A prospective observational study reported on 171 patients who underwent sacroiliac arthrodesis using a hollow-threaded fusion cage (DIANA cage, Signus, Alzenau, Germany).[220] There were significant improvements in ODI, SF-MPQ, and both the physical and mental components of the SF-12. VAS scores decreased from 74 to 37 mm. The rate of SI joint fusion, confirmed by CT scan, was low. However, the authors attributed the low percentage of radiographic fusion to the early (6 months) stage at which patients received CT scans; inadequate preparation of the recess or deposit of bone (substitute) material; poor positioning of the implant; and osteoporosis.

In a retrospective case series, 24 patients underwent a unilateral (22) or bilateral (2) SIJ fusion utilizing the posterior oblique approach with cylindrical-threaded implants (Medtronic, Minneapolis, Minnesota).[219] A statistically significant reduction in LBP scores was noted from an average VAS baseline score of 6.6 ± 2.4 to 3.7 ± 3.3 postoperatively. Leg pain scores decreased from 4.8 ± 3.8 to 1.5 ± 2.9. The mean total satisfaction score was 79% ± 27.6%.

In a recent retrospective multicenter observational study, patients with posterior minimally invasive SIJ fusion (PainTEQ, Tampa, FL, USA) were followed for at least 12 months post-implantation.[28] Based on inclusion criteria, a retrospective review was performed on 50 of 110 charts. An NRS reduction of 66.5% was noted overall. In a subanalysis, the percentage of NRS reduction was calculated in cohorts of patients that had undergone previous lumbar surgery versus those who had not done so. There was a 66.8% NRS reduction in patients with histories of lumbar fusion versus a 59.6% reduction in NRS in those without such.

The use of posterior minimally invasive SIJ fusion (SIJF) (PainTEQ, Tampa, FL, USA) was lastly studied as a means of "salvage therapy". In a multicenter retrospective observational study, 111 patients had undergone posterior SIJ fusion for refractory SIJ-related pain following previous spinal cord stimulation (SCS), interspinous spacer (ISS), intrathecal drug delivery system (IDDS) implantation, and/or PILD. The totals for each of these prior procedures included 76 SCS (68.5%), 39 ISS (35.1%), 3 IDDS (2.7%), and 2 PILD (1.8%). Nine patients (8.1%) had undergone multiple prior procedures (7 patients had SCS+ISS, 2 patients had SCS+IDDS). The mean time between SIJ allograft implantation and the last follow-up was 290.9 ± 195.7 days. At the final follow-up, the mean overall patient reported pain relief (0–100%) was 67.6% ± 28.9%. One hundred and two patients (91.9%) reported pain relief post-operatively of ≥30%. Fifty-two patients (46.8%) reported pain relief of ≥80%.[221] More recently, a prospective multicenter study on this same SI fusion approach was published on 69 patients at 6 months with an average mean improvement in VAS of 34.9, ODI reduction of 17.7 and 0 device-related adverse events.[222]

Minimally Invasive Lateral Sacroiliac Fusion Evidence

The lateral approach to minimally invasive SIJ fusion involves dissection through the lateral gluteus muscles down to the ilium, where a device is used to transfix the ilium to the sacrum.[223] The majority of evidence for minimally invasive lateral sacroiliac fusion and the highest level of evidence – two level-I prospective studies – comes from studies of a triangular titanium implant (SI Bone iFuse system; Santa Clara, CA) (Table 21, with recommendations in Table 22). There are currently 11 published level-IV retrospective studies, two level-II prospective cohort studies, and two level-I prospective studies of this technology. The RCT of minimally invasive lateral sacroiliac fusion versus nonoperative care by Polly et al determined that 82% of surgical patients and 26% of nonoperative patients achieved success which was defined by a composite score, and surgical patients received higher clinical benefit as measured by the VAS SIJ pain

Table 21 Evidence Summary for Minimally Invasive Sacroiliac Fusion

Source, year	Design	Study size	Endpoints	Notes	Level of evidence
Endres et al, 2013[477]	Case series	19	ODI, VAS	VAS reduction from 8.5 at baseline to 6 (2 points, 29.4% pain reduction). Mean ODI score decreased from 64.1 at baseline to 57 at follow-up. Fusion was seen in 79% of joints.	II
Fuchs and Ruhl, 2018[220]	Retrospective observational study	171	VAS, ODI, SF-12, SF-MPQ	ODI improved from 51 to 33, the SF-MPQ decreased from 50% to 31%, the SF-12 physical component rose from 22% to 41%, the mental component summary increased from 40% to 55%, and VAS decreased from 74 to 37 mm.	I-C
Wise and Dall, 2008[478]	Case Series	13	VAS	Improvements were seen in the LBP score on a VAS, with an average improvement of 4.9 cm. Leg pain improved an average of 2.4 cm, and dyspareunia pain improved an average of 2.6 cm. The overall fusion rate was 89% (17 of 19 joints) as assessed by postoperative CT scan obtained 6 months after the procedure.	II
Rajpal et al, 2019[219]	Retrospective observational study	24	NRS, self-reported patient satisfaction	Statistically significant reduction in LBP scores from an average baseline score of 6.6 to 3.7 postoperatively. Leg pain scores decreased from 4.8 to 1.5. The mean total satisfaction score was 79.0%.	I-C
Patterson et al, 2018[479]	Case series	21	NRS, activity level and overall satisfaction	NRS reduction at 12 weeks was 6.29. 73.2% avg pain reduction at 10–12 weeks. 81.8% patients reported at least 60% reduction in pain. Overall satisfaction with procedure was an average of 4.95 (0–5 scale).	II
Mann et al, 2019[480]	Case series	10	NRS, activity level and overall satisfaction	NRS reduction was 4.6 (62.3% avg pain reduction) at 12 weeks. NRS reduction was 6.1 (79.2% avg pain reduction) at 12 months. 80% patients reported at least 60% reduction in pain with 7 of those patients having complete resolution of pain at 12 months.	II
Pyles et al, 2020[481]	Case series	7	NRS, % pain relief	Average NRS was 6.9 pre-fusion, 0.8 post-fusion, and 0.4 at most recent follow-up (average NRS reduction of 6.5, 94.2% pain reduction).	II
Pyles 2019[482]	Case series	20	% pain relief	SIJF in previous SCS implanted patients. 55% of the patients (11/20) received 100% pain relief with the average percentage improvement of pain being 72% at less than 6 months follow-up.	II
Kim et al, 2019[483]	Case series	16	Opioid use, NRS, % pain relief	Average pre-fusion NRS was 7.15 ± 1.76 and average post-fusion NRS at latest follow-up was 0.90 + 1.97. Mean decrease of 5.9 cm in NRS (88% pain reduction). Average improvement following fusion was 89.50%.	II
Calodney et al, 2022[222]	Prospective, Multicenter	69	VAS, ODI, PROMIS 29, adverse events	Average mean improvement in VAS of 34.9, ODI reduction of 17.7 and 0 device related adverse events.	I-B

(*Continued*)

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Table 21 (Continued).

Source, year	Design	Study size	Endpoints	Notes	Level of evidence
Lam et al, 2020[484]	Retrospective observational study	75	% pain relief, opioid use	Average percent relief at 3 months follow-up was 83.3%. Twelve out of the 45 patients (26.7%) reported decreased opioid use. 30 patients (43.5%) reported near complete resolution at 3 months.	I-C
Sayed et al, 2021[218]	Retrospective observational study	50	NRS, % pain relief	The overall average pre SIJ fusion NRS was 6.98 (95% CI [6.26, 7.70]). The overall average NRS at last follow up was 3.06 (95% CI [2.35, 3.77]) with an average overall percent relief of 66.5%. Sub-analysis conducted for those patients with and without history of lumbar fusion.	I-C
Deer et al, 2021[221]	Retrospective observational study	111	% pain relief	At the last follow-up, the mean overall patient reported pain relief was 67.6% ± 28.9%. One hundred and two patients (91.9%) reported pain relief post-operatively of ≥30%. Fifty-two patients (46.8%) had a patient reported pain relief of ≥80%	I-C
Duhon et al[205]	Prospective observational study	172	VAS, ODI	VAS decreased from 79.8 to 26.0 at 24 months ($p<0.001$) and ODI decreased from 55.2 to 30.9 ($p<0.001$). Percent of patients taking opioids decreased from 76.2% to 55%.	I-B
Darr et al[485]	Prospective observational study	103	VAS, ODI, EQ-5D	Mean improvement in SI joint pain of 55 points (0–100), mean improvement in ODI of 28 points, improvement in EuroQOL-5D of 0.3 points ($p<0.0001$).	I-B
Polly et al[224]	RCT	102 surgery, 46 conservative	VAS, ODI, EQ-5D, SF-36	At 24 months, 82% of SI joint fusion group received substantial clinical benefit in VAS and 66% received substantial clinical benefit in ODI score.	I-A
Dengler et al[203]	RCT	52 surgery, 51 conservative	VAS, ODI, ASLR, EQ-5D-3L, walking distance, satisfaction	Mean LBP improved in the SI joint fusion group by 43.3 points vs.5.7 points in conservative group ($p<0.0001$). Mean ODI improved by 26 points in surgical group vs 6 points in nonsurgical group ($p<0.0001$).	I-A
Araghi et al[228]	Prospective observational study	50	VAS, ODI, opioid use	SI joint pain decreased from 76.2 to 35.1 ($p<0.0001$) and ODI decreased from 55.5 to 35.3 ($p<0.001$). Opioid use was reduced from 66 to 30%.	I-B
Al-Khayer et al[486]	Case Series	9	VAS, ODI	Mean ODI decreased from 59 to 45 ($p<or+0.005$) and mean VAS was reduced from 8.1 to 4.6 ($p<or=0.002$). Mean patient satisfaction 6.8	II
Khurana et al[487]	Case Series	15	SF-36, Majeed scoring system	Mean SF-36 improved from 37 to 80 for physical function and 53 to 86 for general health ($p=0.037$) and mean Majeed score increase from 37 to 79 ($p=0.014$).	II

Mason et al[229]	Prospective observational study	55	VAS, SF-36, Majeed scoring system	VAS SI joint pain improved from 8 to 4.5, SF-36 improved from 26.6 to 42.9, Majeed score increased from 36.9 to 64.8.	I-B
Rappoport et al[227]	Prospective observational study	32	VAS, ODI	Mean VAS back and leg pain scores decreased significantly by 12 months postop ($p<0.01$).	I-B
Patel et al[488]	Prospective observational study	51	ODI, SI joint pain score	ODI decreased from 52.8 to 27.9 ($p<0.001$) and SI joint pain score improved from 78 to 21 ($p<0.0001$). Proportion of subjects taking opioids decreased from 57% to 22% and 3 physical function tests improved	I-B

Abbreviations: ODI, Oswestry Disability Index; VAS, visual analog scale; SF-12, Short Form Health Questionnaire; MPQ, McGill Pain Questionnaire; LBP, low back pain; CT, computed tomography; NRS, numeric rating scale; SIJF, sacroiliac joint fusion; SCS, spinal cord stimulation; ASLR, active straight leg raise; EQ-5D, EuroQOL Health Questionnaire.

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Table 22 ASPN Back Consensus Group Recommendations for Minimally Invasive Sacroiliac Joint Fixation

Recommendation	Grade	Level	Level of certainty Net benefit
Minimally Invasive Sacroiliac Fusion	A	I-A	High

scores, ODI, SF-36, and EQ-5D. A total of 148 patients were randomly assigned to surgical versus nonsurgical care, and crossover from non-surgical to surgical care was allowed after 6 months.[224]

Complication rates for minimally invasive lateral sacroiliac fusion have been relatively low, and the most concerning complication is nerve impingement, which may require removal or repositioning of the device. In an analysis of implants from a manufacturer's database, Miller et al reported a nerve impingement rate of 0.9% and a 1.4% rate of improper device placement.[225] The lateral approach may injure the L5, S1, or S2 nerves if the implant is malpositioned, and some have argued that navigation may be useful to reduce the risk of nerve injury.[223] There is also some evidence that intraoperative neuromonitoring with EMG may also reduce the risk of nerve injury during minimally invasive SIJF.[226]

Other technologies for minimally invasive lateral sacroiliac fusion have been studied. Rappoport et al published 24-month outcomes of patients undergoing SIJF with a hydroxyapatite coated screw (Globus Medical; Audubon, PA) and reported that leg and back pain VAS scores both statistically improved at 12 months with surgery.[227] Another lateral sacroiliac fusion technology – SImmetry (Surgalign Spine Technologies; Deerfield, IL) – adds SI joint decortication and bone graft delivery steps prior to implant placement. A lone level 2 prospective study has been published. In this study, Araghi et al analyzed 50 patients who underwent SImmetry fusion and reported statistically significant reductions in SI joint pain and ODI at 6 months in addition to reduced opioid use. There was one revision (2%) for nerve impingement reported in this series.[228] Finally, there are several publications utilizing hollow modular anchorage screws filled with demineralized bone matrix putty and local bone. The largest prospective study involving 55 patients determined that VAS SI joint pain, SF-36 PCS, and Majeed scores improved with surgery.[229]

Summary of Evidence Review and Recommendations

For minimally invasive sacroiliac fusion, there was sufficient evidence in the form of 2 RCTs and several prospective observational and case studies (Table 21) for the committee to make recommendations. Table 22 summarizes those recommendations.

Sacroiliac joint dysfunction accounts for a substantial amount of reported lower back pain. Surgical stabilization and/or fusion of the SIJ may be considered when a patient has persistent moderate to severe pain, functional impairment, and failed intensive non-operative care. Overall, the evidence for minimally invasive lateral sacroiliac fusion has been Grade B, ie, moderate level of certainty for net-benefit.

Based on the efficacy and safety of minimally invasive sacroiliac fusion in properly selected patients, the authors give this therapy a grade A, ie, high level of certainty of benefit based on multiple level 1-A and 1-B studies. The authors recognize that there is a considerable need for further research for all SIJ fusion systems regardless of type or approach as well as no current evidence to support one technique over another.[218] The ASPN Back Group also applies this therapy grade only to sacroiliac fusion systems and techniques with high quality peer-reviewed studies.

Vertebral Augmentation

Vertebral compression fractures (VCFs) may be classified as osteoporotic, pathologic or traumatic. In the United States, there are approximately 1 million osteoporotic VCFs reported per year along with 160,000 neoplastic fractures and 50,000 traumatic fractures.[230–238] Overall, VCFs occur in 30–50% of individuals over 50 years of age[239,240] and may be associated with significant debilitating pain, poor quality of life (QOL), and decreased function and are prone to progression over time leading to worsening pain, compensatory structural changes that may predispose to adjacent fractures, worsening disability and increased morbidity and mortality.[241–244] Vertebral compression fractures create a heavy financial burden in the healthcare industry with costs well over $1 billion dollars yearly, and treatment optimization is essential to improve patient outcomes and healthcare utilization reduction.[245] Although some VCFs may be

managed conservatively, those associated with significant vertebral height loss, kyphotic deformity, debilitating pain-limiting function, progression of vertebral height loss, evolution of symptoms and advanced imaging findings of a VCF may warrant vertebral augmentation.[246,247]

This section will focus on specific vertebral augmentation methods, such as percutaneous vertebroplasty (PVP), percutaneous balloon-kyphoplasty (PBK) and implantable vertebral augmentation devices for the management of symptomatic VCFs when clinically indicated as described below.

The ASPN Back Group opines that vertebral augmentation is indicated when the following criteria are present:

- Urgent/emergent/hospitalized:
  - Primary metastatic neoplasia with pathological fractures associated with severe pain (conservative treatment trial not indicated);
  - Non-ambulatory patient secondary to VCF with severe pain preventing ambulation for more than 24–48 hours despite aggressive medical management;
- Non-urgent/non-emergent/non-hospitalized in the following situations:
  - Acute (<6 weeks) painful VCF confirmed by advanced diagnostic imaging within 30 days;
  - Sub-acute (<6 months) painful VCF confirmed by advanced diagnostic imaging;
  - Presence of debilitating severe pain and functional deficits related to a vertebral fracture;
    - Severe pain on a daily basis, defined as >6/10 on a visual analog scale or numeric pain;
    - Significant functional impairment and inability to perform ADLs, such as non-ambulatory or limited ambulation, limited transfers, bathing, self-care, etc.;
  - Lack of satisfactory improvement with at least 4 weeks of NSM as defined above.
  - Absence of alternative causes for pain, such as discitis, disc herniation, spinal cord compression, etc.

Contraindications to vertebral augmentation may be classified as relative or absolute. Safety and complications are detailed below (not an all-inclusive list; other contraindications may exist).

- Absolute contraindications
  - active systemic infection
  - other localized infection within the procedural field
- Relative contraindications
  - coagulopathy, thrombocytopenia
  - allergy to bone cement/PMMA
  - retropulsion of vertebral body fragments causing central canal stenosis with neurological deficit
  - spinal instability
  - pregnancy
  - spinal cord compression/myelopathy
  - neurological deficits

However, not every contraindication should preclude the procedure. The two absolute contraindications that have been agreed upon by a multidisciplinary group of experts include the presence of active infection at surgical site or an untreated blood-borne infection. It is important to note that osteomyelitis is a strong, but not absolute, contraindication. In very rare instances, vertebral augmentation may be necessary in the setting of continuous antibiotic suppression therapy in patients with few or no other options. Relative contraindications should be approached on a case-by-case basis as some of them can be avoided (ie, substituting a non-allergic filling material for a filling material in a patient with a known allergy to it) while others cannot (ie, spinal instability). Fracture retropulsion was historically considered one of the traditional contraindications but should now no longer be a contraindication, with current recommendations suggesting that vertebral augmentation increases fracture reduction and pulls the retropulsed fracture forward via ligamentotaxis of the posterior longitudinal ligament.[246,248,249]

Safety and Complications

Vertebral augmentation methods have an excellent safety profile and are considered safe by numerous society guidelines and landmark review studies, with a low risk of complications, post-treatment re-fractures and adjacent fractures.[250–253] It is important to consider complications of both vertebral augmentation and NSM when evaluating treatment options for patients with painful VCFs. It should be kept in mind that NSM is not without complications. In the elderly population, bed rest and limitations on activity levels can be quite detrimental especially in conjunction with concurrent opioid therapy. This was demonstrated in the safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (*VAPOUR*) trial, which showed that the NSM patient cohort was associated with more SAEs compared to the vertebroplasty cohort including a case of paralysis and another case of a patient with neurologic compromise necessitating surgical decompression.[251] Neither of these patients that experienced the SAEs had substantial fracture retropulsion at the time of enrolment.[251]

Vertebral augmentation is a minimally invasive intervention yet does present some risks. Most of these risks, however, are not clinically significant in approximately 99% of cases.[254] Perhaps, vertebroplasty has a slightly higher risk compared to the newer vertebral augmentation methods, particularly related to cement extravasation into the surrounding tissue, including leakage intradiscally or into the spinal canal or adjacent vasculature. Safety can be optimized, and complications can be reduced by proper patient preparation and careful risk factor analysis. Patients with intravertebral cleft and cortical disruption are at higher risk of cement leakage and low cement viscosity and high volume of injected cement can increase the risk of cement leakage during vertebral augmentation. These factors, therefore, should be taken into consideration when planning the patient's vertebral augmentation. Interestingly, age, sex and fracture type, and surgical approach were not significant risk factors for significant adverse events.[254–256] Reported complications included such minor issues as mild superficial tissue infection and small amounts of bleeding to more serious complications such as pneumothorax, rib fracture, cord compression, nerve root injury and pulmonary embolism from cement leakage. These more serious complications, however, are rare events. Cement leakage is a common occurrence and is even more common in malignant lesions, likely because the cortex of the vertebral body is commonly destroyed and there are frequently increased levels of vascularity and neovascularity.[254,257]

Taking into account all of the available data regarding the safety profile, low complication rate and relative clinical insignificance of side effects, as well as clinical efficacy compared with NSM described below, we believe that vertebral augmentation outweighs the possible risks and should be considered in selected patients that meet the above-cited criteria. It is imperative to discuss the risks and benefits of VA with the patient during the informed consent process, especially as compared to the risks and benefits of NSM.

Evidence Review

As of July 2021, more than 1800 search results on PubMed were related to vertebral augmentation studies, with at least 15 level I-A RCTs published within the past decade and numerous other level I-B well-designed, controlled clinical studies. Since the two controversial and subsequently downgraded RCT studies published in 2009, the evidentiary landscape regarding the use of vertebral augmentation has evolved, with the majority of the data demonstrating positive benefits of pain relief and improvement in function when utilized alone and when compared to sham/placebo or to NSM.[250,251,258–273]

Based on the body of evidence, vertebral augmentation is a safe and effective treatment with multiple level I-A studies supporting its use when the proper clinical scenario described above is met.

Since VCFs are very commonly associated with severe debilitating pain, functional impairments and increased mortality risk, based on the abundance of high-quality level I-A studies, multiple meta-analyses and systematic reviews, we favor the use of vertebral augmentation in the treatment of patients with painful VCFs. For vertebral augmentation, there was sufficient evidence in the form of 15 RCTs and several prospective observational and case studies (Table 23) for the committee to make recommendations. Table 24 summarizes those recommendations.

Table 23 Evidence Summary for Vertebral Augmentation

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Wang et al, 2021[489]	RCT	72	Bilateral percutaneous kyphoplasty (PKP) vs percutaneous curved kyphoplasty (PCKP)	I-A	6 months	Fluoroscopy time, total surgical time, cement volume, anterior vertebral height, Cobb angle, VAS, and ODI	VAS and ODI at 24 hours and 6 months: • Improvement in both groups without statistical significance Total Surgical and Fluoroscopy Times: • PCKP group had significantly lower times than PKP ($p<0.05$) Cement Volume: • Higher cement perfusion volume in the PKP group (4.78±0.67mL) compared to PCKP (3.84±0.55mL) Vertebral Height: • Both groups produced an increase in height without a statistical significant difference. Cobb Angle: • Both groups resulted in decreased Cobb angle without a statistical significant difference	Bone Leakage: 3 in PCKP and 8 in PKP

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Griffoni et al, 2020[271]	Prospective, RCT	139	Percutaneous vertebroplasty vs Balloon kyphoplasty	I-A	12 months	VAS, WHOQoL, ODI, imaging indices	VAS: • Reduced VAS scores in both groups. No statistically significant difference. ODI: • Significantly reduced scores in both groups but no statistically significant difference between them. WHOQoL5D: • Scores significantly increased in both groups without statistical difference between them. Imaging Indices: • No statistical difference between either group in regard to wedge angle reduction or sagittal index.	Rate of cement leakage 4.5% 40 new fractures reported during follow-up in 113 patients. 12 were at adjacent level

Noriega et al, 2020[490]	Prospective, parallel group, controlled comparative randomized study	152	Titanium implantable vertebral augmentation device vs balloon kyphoplasty (BKP)	I-A	12 months	Responder rate VAS, ODI, EQ-5D	Responder Rates for Primary Composite: • TIVAD - 89.8% (95% CI 82.1%-97.5%) • BKP - 87.3% (95% CI 78.5%-96.1%) Bayesian Analysis of Primary Composite: • TIVAD non-inferior to BKP 1 year after surgery VAS and EQ-5D: • Sustained improvement over all time points favoring TIVAD ODI: • Progressive improvement between both groups	Lumbar and thoracic vertebral fractures in both groups Non-serious rib fracture in TIVAD group
Beall et al, 2019[260]	Prospective, clinical trial, multicenter	350	Balloon kyphoplasty	I-B	12 months	NRS, ODI, SF-36v2 PCS, EQ-5D,	Statistically significant improvement at 3 months: • NRS – improved 6 points ($p<0.001$) • ODI – improved 35.3 points ($p<0.001$) • SF-36v2 PCS – improved 12.4 points ($p<0.001$) • EQ-5D – improved 0.351 points ($p<0.001$) Statistically significant improvement noted at all time points	1 asymptomatic balloon rupture 1 subject with rib pain beginning intraoperatively ending <6 months 1 new adjacent VCF at 25 days postoperatively 1 aspiration pneumonia with prolonged hospital stay 1 myocardial infarction at 105 days postoperatively

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Liu et al, 2019[491]	RCT	100	Percutaneous kyphoplasty vs Percutaneous vertebroplasty	I-A	1 month	BGP, B-CTX, BALP, TRACP, malondialdehyde (MDA), total antioxidant capacity (TAC), superoxide dismutase (SOD), VAS scores, ODI values, Cobb's angle	Bone Markers: • BGP higher in observation group • B-CTX, BALP, and TRACP lower in observation group • MDA lower in observation group • TAC and SOD higher in observation group ODI and VAS: • No significant difference Cobb's angle: • Smaller angle in observation group	None reported
Lui et al, 2019[492]	RCT	116	Balloon kyphoplasty vs Conservative Therapy	I-A	NR	Percentage of trailing, leading, and midcourt height Degree of upper thoracic kyphosis VAS and Barthel Index	Trailing Edge (%) • Observation: 10.14±3.19 • Control: 1.84±0.67 Leading Edge (%) • Observation: 15.13±4.21 • Control: 0.74±0.47 Midcourt Line Height (%) • Observation: 14.72±3.25 • Control:1.73±0.53 Upper Thoracic Kyphosis(°) • Observation: 13.17±2.67 • Control:1.69±0.83 VAS (after treatment) • Observation: 2.25±0.21 • Control: 4.54±0.28 Barthel Index • Observation: 24.34±4.53 • Control: 31.57±4.25	Observation Group: 1 case of cement leakage Rate of complication of 1.72% Control Group: 1 case of venous embolism 4 cases of decubitus ulcers 4 cases of infection Rate of complication was 15.52% Observation had significantly lower rates of complications ($p<0.05$)

Firanescu et al, 2018[493]	RCT	180	Vertebroplasty vs sham control	I-A	12 months	VAS, QUALEFFO, RMDQ	Mean VAS reduction at 12 months): • Vertebroplasty: 5.00 (95% CI 4.31–5.70) • Sham: 4.75 (95% CI 3.93–5.57) • Group Difference: 0.13(95% CI −0.41 to 0.66) Mean QUALEFFO reduction at 12 months: • Vertebroplasty: 18.32 (95% CI 18.32 to 23.61) • Sham: 18.61 (95% CI 13.02 to 24.2) • Group Difference: −0.14 (95% CI −3.04 to 2.76) Mean RMDQ reduction at 12 months: • Vertebroplasty: 7.71 (95% CI 5.87 to 9.55) • Sham: 7.47 (95% CI 5.56 to 9.38) • Group Difference: 0.12 (95% CI −1.11 to 1.35)	1 patient with chronic pulmonary obstructive disease developed respiratory insufficiency 1 patient had a vasovagal reaction

(*Continued*)

Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Hansen et al, 2016[494]	Double blind, placebo-controlled, RCT	46	Percutaneous vertebroplasty vs Sham	I-A	12 months	VAS, SF-36 PCS, SF-36 MCS, EQ-5D	Mean VAS (standard error) at 12 months: • PVP: 28.35 (5.16) • Sham: 30.67 (4.65) • No statistical difference between groups Mean SF-36 PCS (standard error) at 12 months): • PVP: 31.90 (9.19) • Sham: 35.15 (11.92) • No statistical difference between groups Mean SF-36 MCS (standard error) at 12 months: • PVP: 48.60 (10.75) • Sham: 53.60 (10.29) • No statistical difference between groups Mean EQ-5D (standard error) at 12 months: • PVP: 0.67 (0.27) • Sham: 0.74 (0.22) • No statistical difference between groups	NR

Clark et al, 2016[251]	Randomized, double-blind, placebo-controlled RCT, multicenter	120	Vertebroplasty vs Placebo	I-A	6 months	NRS, RMDQ, VAS, QUALEFFO, EQ-5D	NRS: • Mean reduction ratio for vertebroplasty to placebo 1.3 (95% CI 0–2.6, p=0.043) VAS: • Lower score with vertebroplasty at 14 days but not at 6 months (11, 95% CI 0–23, p=0.050) RMDQ: • Mean reduction greater in vertebroplasty group. Maximum difference at 6 months of 4.2 (95% CI 1:6 to 6:9, p=0.0022) QUALEFFO: • Lower in vertebroplasty group with mean difference at 6 months of 7 (95% CI 1–13, p=0.032) EQ-5D • Higher score at 1 and 6 months (−0.06, 95% CI −0.10 to −0.01, p=0.012)	3 patients in each group died from unrelated causes Vertebroplasty Group: 1 respiratory arrest after sedation (resuscitated and underwent procedure 2 days later) 1 supracondylar humerus fracture during Placebo Group: 2 cases of spinal cord compression from interval collapse and retropulsion
Leali et al, 2016[495]	Prospective, multicenter, RCT	400	Percutaneous vertebroplasty vs conservative therapy	I-A	6 months	VAS, ODI, pain medication	Mean VAS: • 2.3 points (post-op), 4.8 (pre-op), p=0.023 Mean ODI: • 31.7% (post-op), 53.6% (pre-op), p⊆0.012 Analgesia: • 120 (65%) able to stop analgesia after 48 hours (p⊆0.0001)	1 fracture of transverse process 1 psoas muscle bleed 3 patients had new vertebral fractures during follow up

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Wang et al, 2016[496]	Prospective, RCT	206	Percutaneous vertebroplasty vs Image-guided facet joint blocks	I-A	12 months	VAS, ODI, RMDQ, SF-36 PCS, SF-36 MCS	• Statistically significant lower VAS, ODI, and RMDQ in PVP group compared to FB group at 1 week ($p<0.05$). • No statistical significance between groups for VAS, ODI, SF-36 at 12 months ($p>0.05$)	NA
Yang, et al, 2016[497]	Prospective, RCT	135	Percutaneous vertebroplasty vs conservative therapy	I-A	12 months	VAS, ODI, QUALEFFO	Statistically significant improvement for VAS, ODI, and QUALEFFO at 12 months ($p<0.0001$)	NA
Hartmann et al, 2015[498]	Retrospective Study	18	NA	II	NR	VAS, ODI, SF-36, Radiologic Evidence	• ODI and SF-36 showed moderate limitations • Restored vertebral kyphosis by 3.2° • Restored segmental kyphosis by 5°	2 asymptomatic cement leakages
Tutton et al, 2015[499]	Prospective, randomized, non-inferiority study	300	Kiva vs Balloon Kyphoplasty	I-A	12 months	VAS, ODI, device related injuries	VAS Mean Improvement: • Kiva: 70.8 points • BK: 71.8 ODI Mean Improvement: • Kiva: 38.1 • BK: 42.2 Primary endpoint showed noninferiority of Kiva to BK	No serious adverse events
Chen et al, 2014[500]	RCT, comparative study	96	Percutaneous vertebroplasty vs conservative therapy	I-A	12 months	VAS, ODI, RMDQ	• VAS, ODI, RMDQ significantly better at 12 months in PVP group ($p\leq0.001$) • 39 PVP patients experienced complete pain relief compared to 15 CT patients ($p\leq0.001$)	NA

Diel et al, 2013[501]	Retrospective Review of RCT	100	NA	I-C	NR	Vertebral height, Beck Index, Alternate Beck Index, Local kyphotic angle,	Mean Post-Op Ant., Mid., and Post. Vertebral Height (mm): • 24.5, 24.6, 30.4 Mean Post-Op Local Kyphotic Angle: • Reduced to 8.9° Mean Post-Op Beck Index: • 0.81 Mean Post-Op Alternative Beck Index: • 0.82	NR
Korovessis et al, 2013[502]	Prospective RCT	190	BKP vs Kiva implantation	I-A	Average of 14 months (range of 13–15 months)	AVBHr, PVBHr, MVBHr, wedge angle, VAS, SF-36 (PF and MH), ODI	AVBHr % Correction: • Kiva – 24.3±45 • BKP – 23±63 PVBHr % Correction: • Kiva – 5.92±16 • BKP – −1.26±8 MVBHr % Correction: • Kiva – 30.5±47 • BKP – 21.9±26 Wedge Angle (°): • Kiva – 5±3.5 • BKP – 6±5 VAS: • Kiva – 8.2±1.4 (Pre); 2.7±3 (Post) • BKP – 7.8±1.2 (Pre); 2.5±3 (Post) SF-36 (%) improvement: • Kiva – 51 (PF); 34 (MH) • BKP – 59 (PF); 34 (MH) ODI: • Kiva – 64±19 (Pre); 31.7±19 (Post) • BKP – 62±14 (Pre); 26.3 ±15.7 (Post)	Cement leakage in 4 (0.03%) Kiva and 12 (0.098%) BKP. No intracanal leakage in Kiva. 2 (2.3%) intracanal leakage in BKP. 10 (12.2%) new fractures in Kiva and 11 (13%) in BKP

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Otten et al, 2013[503]	Prospective comparison study	52	Balloon kyphoplasty vs Kiva	I-B	6 months	VAS, ODI	Kiva demonstrated greater pain improvement Kiva had less adjacent level fractures and cement leakage	NR
Werner et al, 2013[504]	RCT, comparative study	65	Balloon Kyphoplasty vs Vertebral Body Stenting	I-A	NR	Change in kyphotic angle	Change in Kyphotic Angle: • BKP: 4.5±3.6 • VBS: 4.7±4.2 • p=0.972	9 cases of major cement leakage 10 intraoperative complications
Blasco et al, 2012[505]	Prospective, RCT	125	Vertebroplasty vs conservative therapy	I-A	12 months	VAS, QUALEFFO, analgesia, new fractures	VAS at 2 months: • 42% mean reduction with PVP group compared to only 25% in CT group QUALEFFO: • PVP group had significant improvement at all time points compared to CT only at 6 and 12 months Analgesia: • No significant difference between two groups New Fractures: • 2.78-fold more risk of new fracture in PVP group	NR
Vanni et al, 2012[506]	Prospective RCT	300	Balloon kyphoplasty vs SpineJack	I-A	12 months	VAS, ODI, radiographic evidence	VAS and ODI: • No statistical difference between groups SpineJack had greater improvement in vertebral height compared to BKP	20 cement leakages in BKP group

Boonen et al, 2011[264]	RCT	232	Balloon kyphoplasty vs nonsurgical management	I-A	24 months	SF-36, EQ-5D, RMDQ, VAS, Likert Scale	SF-36: • Significant improvement in pain (3.24 points, 95% CI 1.47–5.01, p = 0.0004) EQ-5D: • Significant improvement in QoL (0.12 points, 95% CI 0.06–0.18, p = 0.0002) VAS: • Significant reduction in back pain (−1.49 points, 95% CI −1.88 to −1.10, p<0.0001) RMDQ: • -3.01-point difference in reduction of disability (95% CI −4.14 to −1.89, p<0.001) Likert Scale: • Patients more satisfied (3.09 points, 95% CI 2.26–3.92, p<0.0001)	Similar frequency of adverse events and serious adverse events between two groups 1 hematoma at surgical site 1 recurrent UTI within 2 days of surgery. This patient also developed spondylitis 23 deaths (12 in observation group and 11 in control group) that were all unrelated to treatment
Farrokhi et al, 2011[507]	RCT, comparative study	105	Percutaneous vertebroplasty vs optimal medical therapy	I-A	36 months	VAS, ODI, radiologic evidence	VAS Mean Difference: • -1.5 (−9.85 to 6.85, p<0.81) ODI Mean Difference: • -14.0 (−14.91 to −13.09, p<0.01) Vertebral Height Mean Difference (cm): • 2.0 (1.5 to 0.44, p<0.01) Sagittal Index Mean Difference (°): • -14.0 (−14.96 to −13.05, p<0.011)	1 patient with epidural cement leakage
Muto et al, 2011[508]	Prospective Study	20	Vertebral body stenting system	II	12 months	VAS, ODS, radiological evaluation	Improved pain and disability scores. Improved vertebral body height: 1.5mm on average	No complications

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Klazen et al, 2010[509]	RCT, multicenter, comparative	202	Vertebroplasty vs conservative treatment	I-A	12 months	VAS, EQ-5D, QUALEFFO, RMQD	VAS at 1 Month: • Vertebroplasty – −5.2 (95% CI −5.88 to −4.72) • Conservative – −2.7 (95% CI −3.22 to −1.98) • Difference – 2.6 (95% CI 1.74–3.37, p<0.0001) VAS at 1 year: • Vertebroplasty – −5.7(95% CI −6.22 to −4.98) • Conservative – −3.7 (95% CI −4.35 to −3.05) • Difference – 2.0 (95% CI 1.13–2.80, p<0.001) EQ-5D: • 1 month - favored vertebroplasty with difference of 0.010 (95% CI 0.014–0.006) • 1 year - favored vertebroplasty with difference of 0.108 (0.177–0.040) QUALEFFO and RMQD: • Vertebroplasty had greater improvement (and quicker) over time	No serious complications or adverse events were reported
Rousing et al, 2010[510]	RCT	50	Percutaneous vertebroplasty vs Conservative therapy	I-A	12 months	VAS	VAS: • 7.9 (Pre-Op) and 2.0 (Post-Op) for the PVP group. • No statistical difference between groups at 3 and 12 months	2 adjacent fractures in PVP group

Buchbinder et al, 2009[262]	Multicenter, randomized, double-blind, placebo-controlled trial	71	Percutaneous vertebroplasty vs Sham	I-A	6 months	Pain score, QUALEFFO, Assessment of Quality of Life (AQoL), RMDQ, EQ-5D	Change in Pain Score: • PVP: 2.4±3.3 • Sham: 2.1±3.3 • Difference: 0.1 (95% CI −1.2 to 1.4) Change in QUALEFFO Score: • PVP: 6.4±13.4 • Sham: 6.1±13.4 • Difference: 0.6 (95% CI −5.1 to 6.2) Change in AQoL Score: • PVP: 0.0±0.3 • Sham: 0.1±0.3 • Difference: 0.1 (95% CI −0.1 to 0.2) Change in RMDQ Score: • PVP: 4.1±5.8 • Sham: 3.7±5.8 • Difference: 0.0 (−3.0 to 2.9) Change in EQ-5D Score: • PVP: 0.2±0.4 • Sham: 0.2±0.4 • Difference: 0.0 (−0.1 to 0.2)	7 new vertebral fractures 3 new rib fractures 1 case of osteomyelitis
Kallmes et al, 2009[261]	Multicenter, RCT	131	Percutaneous vertebroplasty vs Sham	I-A	1 month	Pain intensity, RMDQ	RMDQ: • PVP: 12.0±6.3 • Sham: 13.0±6.4 • Treatment Effect: 0.7 (95% CI −1.3 to 2.8, p=0.49) Pain Intensity: • PVP: 3.9±2.9 • Sham: 4.6±3.0 • Treatment effect: 0.7 (−0.3 to 1.7, p=0.19)	1 thecal sac injury 1 patient admitted with tachycardia and rigors

(*Continued*)

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Table 23 (Continued).

Source, year	Design	Sample size	Treatment arms	Level of evidence	Follow-up	Outcome measures	Results	Complications
Wardlaw et al, 2009[250]	RCT, comparative study	300	Balloon kyphoplasty vs nonsurgical care	I-A	12 months	SF-36 PCS	SF-36 PCS Improvement at 1 month: • BKP: 7.2 (95% CI 5.7–8.8) • NSM: 2.0 (95% CI 0.4–3.6) • p<0.0001	1 hematoma 1 UTI
Voormolen et al, 2007[511]	RCT, comparative study	34	Percutaneous vertebroplasty vs optimal pain medication (OPM)	I-A	2 weeks	VAS, analgesic use, QUALEFFO, RMDQ	Change in VAS: • PVP: −2.1 • OPM: −1.1 • Difference: −1.5 (95% CI −3.2 to 0.2) Change in Analgesic Use: • PVP: −0.7 • OPM: +0.9 • Difference: −1.5 (95% CI −2.3 to −0.8) Change in QUALEFFO: • PVP: −6.8 • OPM: −0.7 • Difference: −6.1 (95% CI −10.7 to −1.6) Change in RMDQ: • PVP: +19 • OPM: −2 • Difference: 21 (95% CI 0.07 to 0.35	2 patients with new VCFs

Abbreviations: RCT, randomized controlled trial; VAS, visual analog scale; ODI, Oswestry Disability Index; PKP, percutaneous kyphoplasty; PCKP, percutaneous curved kyphoplasty; WHOQoL, World Health Organization quality of life health questionnaire; EQ-5D, EuroQOL Health Questionnaire; TIVAD, titanium-implantable vertebral augmentation device; 95% CI, 95% confidence interval; BKP, balloon kyphoplasty; NRS, numeric rating scale; SF-36, Short Form Health Questionnaire; PCS, physical component summary; MCS, mental component summary; VCF, vertebral compression fracture; B-CTX, carboxyl-terminal collagen I crosslinks; BALP, bone alkaline phosphatase; TRACP, tartrate-resistant acid phosphatase; MDA, malondialdehyde; TAC, total antioxidant capacity; SOD, superoxide dismutase; QUALEFFO, quality of life questionnaire in patients with vertebral fractures; RMDQ, Roland-Morris Disability Questionnaire; AVBHr, anterior vertebral body height ratio; PVBHr, posterior vertebral body height ratio; MVBHr, midline vertebral body height ratio; BKP, balloon kyphoplasty; VBS, vertebral body stenting; PVP, percutaneous vertebroplasty; AQoL, Assessment of Quality of Life; OPM, optimal pain medication.

Table 24 ASPN Back Consensus Group Recommendations for Vertebral Augmentation

Recommendation	Grade	Level of evidence	Level of certainty Net benefit
Vertebral Augmentation	A	I-A	High

Neuromodulation

Spinal Cord Stimulation (SCS)

SCS is a well-established treatment option for patients who experience chronic refractory pain, including LBP from a multitude of etiologies. As the field of neuromodulation is rapidly evolving with new technology and programming options, it is increasingly important to perform well-designed, high-quality studies to ensure optimized patient outcomes.

The studied indications for SCS in the treatment of lumbar spine pathology include failed back surgery syndrome (FBSS), nonsurgical refractory back pain, and lumbar spinal stenosis. The quality of evidence varies for each of these indications and recommendations have been provided separately based on the specific indication.

Though SCS has been considered to be a safe and minimally invasive procedure, variable complication rates have been reported. These can be divided primarily into those that can be attributed to biologic factors and those that are device (hardware)-related. Device-related complications consist of lead migration, lead breakage, lack of effective stimulation, hardware malfunction, loose connections, battery failure, and failure to communicate with the generator. Biologic complications consist of epidural hemorrhage, seroma, CSF leakage, allergic reaction, pain over implant site, and skin breakdown.[274,275]

Safety: Hardware Complications

The majority of device failures are related to the hardware and more specifically the leads. Lead fractures and disconnects have been reported to occur in 5.9–9.1% of cases and are typically discovered through imaging and impedance checks.[275,276] Lead migration rates have been reported anywhere between 13.2 and 22.6% based on past literature reviews.[274,277] Regarding lead migration, additional issues that may arise include potential loss of efficacy with need for revision and possible replacement, all of which puts additional strain on SCS therapy delivery. Though paddle electrodes have been deemed an alternative approach to address lead migration, they also present with their own set of potential complications, including neurologic injury and possible epidural hematoma.[278]

Safety: Non-Hardware Complications

Though non-hardware complications occur at a lower rate than hardware complications, these can include neurologic injury, epidural hematoma, skin erosion, epidural fibrosis, dural puncture, pain, and allergic reactions to the device components.[274,279] The most common site for infections has been at the pocket site, with incidence ranging between 2 and 10% of implants. This was further analyzed by Hoelzer et al in over 2737 cases in which an overall infection rate of 2.45% was identified.[279,280] In their analysis, it was determined that post-operative dressings and antibiotic coverage were important in decreasing infection rates. Another low-frequency complication is epidural hematoma with an incidence of 0.25–0.3%.[274,281] Another potential complication is neurologic injury (incidence of 0.03–0.25%) that can involve the motor, sensory or autonomic nervous systems and may result from direct trauma from the needle or lead, in both percutaneous and paddle variations.

The impact of neuromonitoring in reducing central nervous system (CNS) injury with various levels of periprocedural sedation is important to consider and review.[282,283] Although SCS is a viable, generally safe, non-pharmacologic approach to pain management, we must keep in mind that there are potential hardware and non-hardware complications that can occur.

Evidence Review

The evidence for SCS in the treatment of FBSS is supported by six randomized, controlled trials with significant enrollment volumes over time periods greater than six months. The evidence for SCS in the treatment of nonsurgical LBP

consists of two prospective case series and small cohorts of patients within larger studies. Compared to FBSS and nonsurgical LBP, there is a dearth of evidence describing the use of SCS for lumbar spinal stenosis (LSS)-related back and leg pain. For SCS, there was sufficient evidence in the form of six RCTs and several prospective observational and case studies (Table 25) for the committee to make recommendations. Table 26 summarizes those recommendations.

Intrathecal Drug Delivery

Given the many thousands who died of prescription opioid overdoses during the first decade of this millennium, traditional opioid analgesia has become a less comfortable mode of treatment for chronic LBP in recent years. However, IDDS is established as a safe, effective, and economical treatment option for the management of a wide range of refractory chronic pain.[284–290] Yet, its clinical utility specific to back pain remains limited by the lack of high-quality RCTs.[291,292] This subsection will review current literature on the role of IDDS for LBP and present clinical guidance.

Indications

Prior to discussing disease-specific indications, it is important to establish and understand the definition of refractory pain. Deer et al proposed that pain is defined as refractory, regardless of etiology, when 1) multiple evidence-based biomedical therapies used appropriately have failed to reach treatment goals or have resulted in intolerable adverse effects, and 2) psychiatric disorders and psychosocial factors that could influence pain outcomes have been optimized.[293] The FDA has indicated IDDS for a variety of noncancer pain conditions in cases in which more conservative therapies have failed.[294–296] The majority of patients with IDDS implanted for noncancer pain have back pain with or without leg pain, with the most common diagnosis being FBSS or post-laminectomy syndrome (PLS).[297,298]

Patient selection is crucial. A complete evaluation including physical examination, medication review, comorbidity assessment, and psychosocial evaluation is recommended.[295,299] Patients considered for this therapy must also have a clear diagnosis and source for their chronic back pain. They must be refractory to conservative medical management or other less invasive procedures; however, it should not be considered as a salvage therapy but rather as a distinctly different therapy.[295,300] The 2017 Polyanalgesic Consensus Conference (PACC) guidelines, in fact, suggest IDDS within the same line as SCS and before the escalation of long-term systemic opioid therapy (Table 27).[295] Currently, it is recommended to consider IDDS for diffuse pain pattern that may not be adequately covered by SCS.[295] Key considerations for patient selection are outlined in Table 28.

The medication choice for intrathecal administration has been well established in the literature. It is based on the level of evidence and consensus with stratification based on diagnosis and pain characteristics.[295,297] Morphine and ziconotide are the only two FDA-approved intrathecal medications. Ziconotide is the first-line choice for localized noncancer neuropathic or nociceptive pain in the absence of history of psychosis or renal disorder.[301] Morphine is preferred in patients with diffuse pain on more than 120 morphine equivalents in daily use.[295,301] Second-line agents for localized and diffuse pain are fentanyl and hydromorphone, respectively, with or without bupivacaine.[295] Other agents for tertiary and quaternary uses include admixtures of first- and second-line drugs with clonidine, sufentanil, or baclofen. The 2017 PACC guidelines summarize an algorithmic approach with recommended starting doses and titration.[295]

Safety and Complications

Some authors have challenged the safety of IDDS.[302–305] Coffey et al demonstrated higher mortality associated with IDDS compared with SCS or lumbar laminectomy and raised concerns regarding opioid overdose and critical device-related issues.[303] However, there exists an abundance of literature supporting IDDS as a safe and effective treatment option for different types of chronic, noncancer back pain.[284–290,306–321] The 2017 PACC guidelines also suggested that the risk-benefit profile of IDDS makes it a relatively safe therapy, especially when compared to chronic systemic opioid therapy.[297] It is imperative for clinicians to not only implement risk-mitigating strategies but also understand the intrathecal physiology and anatomy, pharmacokinetic and pharmacodynamic properties of medications, and all potential complications.

Table 25 Evidence Summary for Spinal Cord Stimulation

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
FBSS					
North et al, 2005[512]	Randomized controlled trial	60	I-A	Success defined as >50% pain relief and patient satisfaction	At six months, 47.4% of FBSS patients had successful outcome with SCS versus 11.5% of the reoperation cohort
Kumar et al, 2008[513,514]	Randomized controlled trial	100	I-A	Success defined as >50% pain relief	At 24 months, 47% of FBSS patients had successful outcome with SCS versus 7% of the conventional medical management cohort
Kapural et al, 2016[515,516]	Randomized controlled trial	198	I-A	Success defined as >50% pain relief	At 24 months, ≥50% pain reduction of LBP was seen in 76.5% of 10 kHz SCS patients compared to 49.3% in the paresthesia-based arm ($p<0.001$). Also, responder rate was 72.9% in the 10 kHz SCS arm versus 49.3% in the paresthesia-based arm for leg pain ($p<0.001$).
De Andres et al, 2017[517]	Randomized controlled trial	60	I-A	VAS (leg and back)	At 12 months, the authors reported that pain scores did not differ between the two arms. This was also true of the other primary outcome measures
Deer et al, 2018[518]	Randomized controlled trial	121	I-A	Mean daily VAS score, responder rate (defined as ≥30% pain relief)	Superiority of burst stimulation over paresthesia-based stimulation was achieved ($p < 0.017$). Also, 60% of patients were responders to burst stimulation versus 51% with tonic stimulation.
Mekhail et al, 2020[519]	Randomized controlled trial	134	I-A	Success defined as >50% pain relief	At 12 months, 83.1% of the ECAP-controlled arm had >50% pain relief versus 61% of the control arm.
Non-operated back pain					
Al-Kaisy et al, 2018[520]	Prospective case series	20	I-B	Pain relief, disability, opioid use	Reductions in VAS (79±12 mm to 10±12mm), disability (ODI; 53±13 to 19.8±12), and opioid use were seen at 36 months.
Baranidharan et al, 2021[521]	Prospective case series	25	I-B	Pain relief, disability, quality of life, opioid use	At 12 months, back pain VAS scores improved by 4.6 points and leg pain VAS scores improved by 2.7 points. ODI was reduced by 22.1 points. EQ-5D-5L was increased by 23 points. Opioids were discontinued in 42.8% of patients.
Lumbar spinal stenosis					
Costantini et al, 2010[522]	Retrospective case series	69	I-C	Pain relief, disability, medication usage	VAS improved from baseline 7.4±2.3 to 2.8±2.4 ($p<0.05$). Opioid use decreased from 29% of patients to 13%, NSAIDs from 75% to 49%, antidepressants from 33% to 20%, and antiepileptics from 32% to 9% ($p<0.05$). ODI decreased from 34.3±7.6 to 15.7±13.1 ($p<0.05$)
Kamihara et al, 2014[523]	Retrospective case series	41	I-C	Success defined as continued SCS use for one year or more after implantation	95.1% of patients continued to use their SCS for one year or more after implantation

Abbreviations: FBSS, failed back surgery syndrome; SCS, spinal cord stimulation; LBP, low back pain; VAS, visual analog scale; ECAP, evoked compound action potential; ODI, Oswestry Disability Index; EQ-5D, EuroQOL Health Questionnaire; NSAID, nonsteroidal anti-inflammatory drug.

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Table 26 ASPN Back Consensus Group Recommendations for Spinal Cord Stimulation

Recommendation	Grade	Level of evidence	Level of certainty Net benefit
SCS following lumbar spinal surgery	A	I-A	Strong
SCS in the treatment of non-surgical LBP	B	I-C	Moderate
SCS in the treatment of patients with predominate lumbar spinal stenosis	C	I-C	Moderate

Abbreviation: LBP, low back pain.

Table 27 Disease Indications for Intrathecal Drug Delivery

Axial neck or back pain (not a surgical candidate)
• Multiple compression fractures • Discogenic pain • Spinal stenosis • Diffuse multiple-level spondylosis
Failed back surgery syndrome/Post-laminectomy syndrome
Trunk pain • Postherpetic neuralgia • Post-thoracotomy syndromes
Abdominal/pelvic pain • Visceral • Somatic
Extremity pain • Radicular • Joint
Complex regional pain syndrome (CRPS)
Cancer pain, primary invasion, metastasis, and treatment (chemotherapy, radiation)-related
Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

Note: Data from these studies.[23,24]

Table 28 Key Considerations for Patient Selection

Contraindications	Indications
• Immunocompromised patients or active infection • Severe psychological conditions, including untreated significant addiction; active psychosis; major uncontrolled depression or anxiety; active suicidal or homicidal behavior; severe cognitive deficits; severe sleep disturbances • Inability to comply with medication refill schedule • Current or anticipated lack of insurance coverage or mean to pay for ongoing management of the pump	• Chronic pain with a clear, appropriate diagnosis resulting in significant interference with of ADLs including ability to work and overall QOL • Has tried and failed to achieve sufficient analgesia with less invasive therapies • Optimization of all preexisting comorbidities • Absence of severe or uncontrolled psychological conditions • Patients in which oral opioid therapy is contraindicated

Abbreviations: ADL, activities of daily living; QOL, quality of life.

IDDS complications can be technical including catheter or pump malfunction, pharmacological, or procedural (Table 29).[25,60–62,297,322–324] The most common complications were drug-related (reportedly up to 77% of all complications), followed by hardware malfunctions and procedural-related issues.[297,305,325] While the majority of complications are transient and minor, serious complications can occur. An increased mortality associated with intrathecal opioid therapy in noncancer patients (0.088% at 3 days after implantation, 0.39% at 1 month, and 3.89% at 1 year) has been reported.[303] Other rare but serious complications include sudden drug withdrawal or overdose, epidural or spinal

Table 29 Complications Associated with IDDS

Catheter-related
• Catheter damaged/severed/nicked/broken/fractured
• Catheter kink/twisting
• Catheter migration
• Catheter occlusion
• Catheter disconnection
• Fluid collection around the catheter
Pump-related
• Motor stall
• Corrosion
• Gear wear
• Pump flipped
• Pump empty/low volume
• Premature battery depletion
• MRI compatibility issues
Drug-related
• Drug withdrawal
• Drug overdose
• Nausea/vomiting
• Diaphoresis
• Pruritus
• Sedation/somnolence/lethargy
• Cardiovascular events
• Respiratory depression
• Edema of lower limbs
• Urinary retention/incontinence
• Sexual dysfunction/hypogonadotropic hypogonadism
• Osteoporosis
• Neuroendocrine dysfunction
• Constipation
• Hyperalgesia or allodynia
• Neuropsychiatric events
Procedural/Biological causes
• Granuloma
• Bleeding/epidural hematoma/spinal hematoma/pocket hematoma
• Meningitis
• Infection/erosion
• CSF leak/hygroma/post dural puncture headache
• Intracranial hypotension
• Seroma
• Allergic reaction
• Pump site discomfort

Note: Data from these studies.[297,322–324]
Abbreviations: MRI, magnetic resonance imaging; CSF, cerebrospinal fluid.

hematoma, meningitis, and catheter tip granulomas likely related to higher doses and concentrations of opiates except for fentanyl.[297,322,326] The administration of the lowest effective drug dose and concentration is recommended to prevent granulomas.[297]

Drug-related complications are most studied with intrathecal opioids, most commonly morphine. Intrathecal opioids have been associated with adverse effects including respiratory depression, nausea, vomiting, diaphoresis, pruritus, sedation or change in mental status, urinary retention, and sexual dysfunction.[297,299,305] Intrathecal ziconotide has been associated with cognitive and neuropsychiatric adverse events, especially when titrated rapidly.[297,327,328] It should also be avoided in patients with renal disorders due to the risk of renal toxicity and rhabdomyolysis.[299,329,330] Bupivacaine may result in sensorimotor loss or cardiotoxicity in higher doses.[297] Clonidine has also been associated with cardiovascular side effects, from peripheral edema to potential life-threatening hypertensive crises and stress-induced cardiomyopathy.[299]

Although it is largely a safe therapy especially with recent advancement in technology and understanding of intrathecal drugs, IDDS may carry a higher risk than other interventional pain procedures. Therefore, IDDS should be implanted and managed by experienced multidisciplinary teams, with expertise in patient selection, medication selection, surgical techniques, and long-term management with understanding of all potential complications.

Evidence Review with Evidence Level Designation

It is generally accepted that intrathecal delivery of medications has clinical value; therefore, the questions that confront the therapy today concern the evidence surrounding applications of medications and medication combinations as well as guidance from pan societies concerning clinical application of the therapy. For example, IDDS has been criticized regarding the lack of high-quality RCTs with long-term follow-ups for many medications, although RCTs do exist to support the use of ziconotide. Some authors such as Hayes et al stressed the lack of consistency in the clinical use of IDDS in chronic noncancer pain.[331] Brown et al also highlighted the complexity of intrathecal opioid therapy.[332] Their study suggested that despite some therapeutic benefit of IDDS, patients continue to suffer from substantial physical impairment.[332] As a result of these suggestions, the PACC was created to fill the void regarding clinical questions that persist with consensus opinion and evidence accumulation.[294,295,297] However, there exist several retrospective trials and three prospective observational trials supporting the therapy (Table 30).

Numerous systematic reviews of IDDS have been performed by several groups.[292,314,316,324,333–335] Although review methodologies vary, all of the reviews report a gap in our current literature supporting IDDS for noncancer pain, including chronic LBP (Tables 28–30). Based on our literature search and evidence review, the evidence of IDDS for chronic noncancer back pain is moderate. Based on the USPSTF criteria[1] modified for interventional spine procedures, the therapy grading for IDDS is limited to grade B for noncancer back pain. Evidence is presented in Table 30, and recommendations may be found in Table 31.

Peripheral Nerve Stimulation for Low Back Pain–Multifidus Activation via Medial Branch Nerve Stimulation

The majority of CLBP patients suffer from mechanical (musculoskeletal) pain that is predominantly nociceptive in nature; however, neuropathic or mixed patterns are also commonly seen. Patients with CLBP often endure impaired quality of life, depression, anxiety, and sleep disturbance. Patients suffering from CLBP learn to balance activity with pain on an individual level. Some will tolerate a certain amount of pain to increase their activity level. Others are less tolerant to pain and will minimize any perceived activity that may aggravate their pain, initially leading to inactivity, guarding, and kinesiophobia. Persistent back pain-induced inhibition and disruption of proprioceptive signaling has also been correlated with long-term motor cortex reorganization. Ultimately, this results in impaired neuromuscular control and functional instability from degeneration and atrophy of the lumbar multifidus muscle, the most important stabilizer muscle of the lumbar spine.

Recently, interest has been drawn to incorporating peripheral nerve stimulation (PNS) for CLBP. These treatments have been demonstrated not only to improve pain and function but also to decrease the need for multiple interventions to treat CLBP, many of which are unsuccessful.[336,337] Targeting the medial branch nerve of the dorsal rami of the lumbar spine, which innervates the fascicles of the multifidus muscles, results in activation. These muscles originate at the

Table 30 Evidence Summary for Intrathecal Drug Delivery Systems

Author, year	Intervention, patient type, sample size	Study type, level of evidence	Key findings
Ade et al, 2020[524]	Intrathecal (IT) hydromorphone + bupivacaine (n=30) vs IT fentanyl + bupivacaine (n=28) in patients with FBSS.	Retrospective comparative analysis, I-C	Fentanyl admixture with bupivacaine showed similar efficacy to hydromorphone + bupivacaine. Lower rate of opioid escalation was noted in the fentanyl group.
Anderson et al, 1999[525]	IT morphine in 30 patients with chronic noncancer pain (n=14 FBSS, n=1 chronic LBP).	Prospective, I-B	IT morphine is safe and effective for the management of severe, noncancer pain. Long-term improvement in daily function was also noted.
Atli et al, 2010[526]	IT opioids in 57 patients with chronic refractory pain including 28 FBSS and more patients with neuropathic/radicular or axial back pain.	Retrospective, I-C	Reduction of VAS and oral opioid consumption through 3-year follow-up. Noted 20% complication rate.
Deer et al, 2002[313]	IT opioid (pre) vs IT opioid + bupivacaine (post) in 109 patients (n=84 with FBSS, n=25 with metastatic cancer pain of spine).	Retrospective, I-C	IT bupivacaine provided additional analgesic benefit and reduction of oral opiate when added to IT opiate.
Deer et al, 2004[288]	IT morphine in 136 patients with LBP.	Prospective, I-B	Significant pain reduction, improvement in QOL, and patient satisfaction reported at both 6- and 12-month follow-up.
Doleys et al, 2006[527]	IT opioids (n=50) vs oral opioids (n=40) vs pain Rehabilitation program (n=40) in FBSS.	Retrospective, I-C	IT opiate group appeared to statistically significantly superior in numerical pain rating improvement.
Duse et al, 2009[315]	IT morphine in 30 patients with refractory noncancer pain, including 14 who presented with osteoporosis-related back pain, FBBS, or spinal arthrodesis	Prospective, I-B	IT morphine therapy effectively improved psychosocial function in patients with refractory pain that had failed to respond to standard multimodal therapy.
Galica et al, 2018[528]	IT hydromorphone and bupivacaine in FBBS (n=54).	Retrospective, I-C	Combination therapy with IT hydromorphone and bupivacaine improved pain intensity scores in patients with FBSS at 12 and 24 months.
Grider et al, 2016[529]	Low-dose intrathecal opioid in 58 patients with analysis by age, gender, diagnosis and pre-implantation opioid dosage	Prospective I-B	Significant sustained 3 year reduction in VAS at less than 0.5 mg per day opioid
Hamza et al, 2012[306]	IT opioid in 58 patients with chronic noncancer pain including 35 FBSS and 16 LBP patients.	Prospective, I-B	Statistically significant reduction in both worst and average pain through a 36-month follow-up (6, 12, 18, 24, 36 months follow-ups)
Hayek et al, 2016[530]	IT hydromorphone + bupivacaine in 57 patients with FBSS	Retrospective, I-C	Patient-controlled delivery of IT hydromorphone and bupivacaine are effective in treating chronic pain due to FBSS. IT dose escalation was noted.
Ilias et al, 2008[531]	Patient controlled analgesia IT therapy using personal therapy manager device (opioids with or without clonidine, bupivacaine, baclofen, and/or midazolam) in 168 patients with existing IDDS for chronic refractory pain (92% noncancer; most commonly FBSS, 8% cancer).	Prospective, I-B	A significant reduction of the overall average VAS at 12 months.

(*Continued*)

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Table 30 (Continued).

Author, year	Intervention, patient type, sample size	Study type, level of evidence	Key findings
Kanai et al, 2019[308]	IT bupivacaine (0.5, 1.0, and 1.5mg at 1-week intervals) for chronic LBP and lower extremity, n=70.	Prospective, I-B	IT bupivacaine was safe and effective at least through 12 months, with 1.0 mg as the optimal dose.
Rainov et al, 2001[310]	IT combination therapy (morphine admixed with bupivacaine, clonidine, or midazolam) in 26 patients with chronic noncancer back and leg pain due to degenerative lumbar spinal disorder.	Prospective, I-B	IT combination therapy can have a favorable and sustained efficacy in patients with chronic refractory pain of spinal origin. No drug-related complications noted through up to 27 months.
Rauck et al, 2006[532]	IT ziconotide (n=112) vs placebo (n=108).	RCT, I-A	IT ziconotide group showed statistically significant improvement in VASPI.
Rauck et al, 2013[533]	IT gabapentin in 170 chronic noncancer patients including 116 patients with back pain with or without leg pain.	Multicenter RCT, I-A	IT gabapentin was as safe as oral gabapentin without statistically significant analgesic effect. Study length = 22 days.
Rauck et al, 2010[534]	IT morphine in 110 patients (60 FBSS, 6 compression fractures). 8 patients later excluded.	Prospective, I-B	Decrease in pain and disability in 68.4% of patient visits for up to 6 months. 28 patients with "serious" adverse events.
Raphael et al, 2002[311]	IT opioid in 36 patients with chronic LBP.	Retrospective, I-C	Retrospective patient questionnaire revealed significant improvement in pain and QOL.
Roberts et al, 2001[318]	IT morphine in 88 patients with chronic noncancer pain (n=64 with back pain; 55 with FBSS, 6 with back pain without surgery, 3 with compression fracture).	Prospective, I-B	A majority of patients had significant pain relief, improved physical activity levels, and reduction in oral medications through average of 36 months.
Shaladi et al, 2007[535]	IT morphine in 24 patients with chronic vertebral compression fractures	Prospective, I-B	IT morphine resulted in significant improvement of pain and all variables of QUALEFFO including quality of daily life, domestic work, ambulation, and perception of health status at 12 months.
Staats et al, 2007[536]	IT opioid therapy with or without adjunct agents in 101 patients with chronic noncancer back pain.	Retrospective, I-C	Patients with noncancer LBP can be maintained with constant flow rate pump throughout treatment.
Veizi et al, 2011[317]	IT opioids (59% FBSS) vs IT opioid + bupivacaine (50% FBSS). Total n = 126.	Retrospective, I-C	Both groups with significant reduction in pain intensity and oral opioid consumption. Adjunct therapy with bupivacaine blunted IT opioid dose escalation.
Wallace et al, 2008[320]	IT ziconotide as adjunct to IT morphine in 26 patients with chronic refractory noncancer pain (n=23 FBSS).	Prospective, I-B	Addition of IT ziconotide as adjunct to IT morphine increases analgesic efficacy and reduce oral opioid dosage at 18 months.
Winkelmuller et al, 1996[537]	IT morphine with various adjunct therapies (buprenorphine, clonidine, fentanyl, bupivacaine, or NaCl) in 120 patients with FBSS.	Retrospective, I-C	Patients continued to report pain reduction through variable follow-up periods, from 6 months to 5.7 years.

Abbreviations: FBSS, failed back surgery syndrome; LBP, low back pain; IT, intrathecal; QUALEFFO, Questionnaire of the European Foundation of Osteoporosis; VASPI, Visual Analogue Scale of Pain Intensity; VAS, visual analog scale; QOL, quality of life; RCT, randomized controlled trial.

Table 31 ASPN Back Consensus Group Recommendations for Intrathecal Drug Delivery Systems

Recommendation	Grade	Level	Level of certainty Net benefit
Intrathecal drug delivery is safe and effective in chronic refractory pain of spinal origin.	B	I-B	Moderate
Intrathecal drug delivery is safe and effective in refractory failed back surgery syndrome.	A	I-A	High
Intrathecal ziconotide is safe and effective for chronic non-cancer pain management.	A	I-A	High
Intrathecal opioids are safe and effective in chronic non-cancer pain management.	B	I-B	Moderate
Intrathecal bupivacaine is safe and effective for chronic non-cancer pain management.	B	I-C	Moderate
Intrathecal drug delivery can help minimize medication utilization through oral route	B	I-B	Moderate
Intrathecal combination drug therapy is effective in chronic refractory pain of spinal origin.	B	I-C	Moderate
Intrathecal drug therapy can help improve function and quality of life in chronic refractory pain of spinal origin.	B	I-C	Moderate
Intrathecal ziconotide can augment opioid analgesic effect	B	I-B	Moderate
Intrathecal combination (opioids + local anesthetic ± ziconotide) therapy can prolong the development of intrathecal opioid tolerance	C	I-C	Moderate
Shared decision making should be utilized if contemplating intrathecal drug therapy in patients with multiple co-morbidities affecting cardiopulmonary function, hematopoietic function, or central nervous function.	A	I-C	Moderate

posterior sacrum, superior iliac spine, and mammillary processes of the lumbar vertebrae. They insert on the spinous processes of the vertebrae in the lumbar spine, 2–4 bones above the origin. This muscle group plays a critical role in providing segmental stability in response to changes in posture and protection against sudden movements.

Indications

After a comprehensive history and focused neurologic and musculoskeletal physical examination, assessment of CLBP should include an individualized, phasic, comprehensive, and multi-modal treatment plan, avoiding surgery if not indicated. Initial options may include the use of adjuvant non-opioid medications to facilitate a rehabilitative paradigm focused on addressing impaired neuromuscular control from degeneration of the multifidus muscle to restore lumbar spine stability, decrease pain, and improve function. More advanced treatments such as PNS should be considered once more conservative options have failed and there is no indication for invasive surgery. Candidates for PNS therapy experience CLBP secondary to multifidus muscle dysfunction, which is often consistent with muscle atrophy. Atrophy can be confirmed via MRI and dysfunction via physical exam. The prone instability test and multifidus lift test are physical exam maneuvers used to assess weakness of the multifidi from atrophy. Currently, the literature and experience revolve around both short-term and permanently implanted techniques.

Safety and Complications

Thus far, safety and efficacy of the non-implanted 60-day system has been demonstrated in small, uncontrolled, prospective studies. In a 2019 investigation, most subjects in a small cohort of 11 patients experienced clinically significant reductions in average pain intensity, disability, as well as pain interference without any serious or unanticipated device-related adverse events. These findings are consistent with spinal cord stimulation therapies, which potentially include infection, as well as lead migration and fracture. In a 2021 study of PNS of the medial branch nerves in a cohort of patients with lack of long term relief from lumbar radiofrequency ablation, no serious adverse events where noted. The most common side effects were mild skin irritation and/or itching, and one case of superficial infection in the 15 subjects followed. A subsequent analysis of the literature revealed that percutaneous PNS leads with a coiled

design had a statistically significant lower infection risk than non-coiled leads.[338] Further studies of the safety and efficacy of non-implanted 60-day system are underway.

To date, safety and efficacy of the permanently implanted PNS system has been demonstrated in multiple publications. In the most recent trial, the primary safety outcome was to assess any serious device- or procedure-related adverse event at the 120-day visit following implant. All adverse events were otherwise documented and reported. This included observed rates through the one-year visit after implant; however, there were no actual statistical hypotheses tested in the safety assessment. Among the 204 randomized subjects, 8 SAEs were reported. Three occurred in the treatment group and 5 occurred in the control group for an overall related serious adverse event rate of 4% at the 120-day primary endpoint visit. There were no unanticipated SAEs related to the device or the procedure. Of the eight serious device- or procedure-related adverse events reported, all were procedure-related with the exception of one. The rates of adverse events are consistent with known SAE rates for spinal cord stimulation therapy; however, there was no finding of lead migration, an issue that affected previous design of electrodes used. This trial demonstrated clinical effectiveness as measured by substantial and durable improvements in pain, disability, and quality of life in a cohort of patients with a favorable benefit risk profile.[339,340]

Evidence Review with Evidence Level Designation

Thus far, evidence supporting the efficacy of the non-implanted 60-day system is developing, with an evidence level of II. The non-implanted 60-day system was studied in a 2019 case series, at which time the stimulator was granted Investigational Device Exemption status, by using a 30-day, percutaneous, non-surgical, open coil PNS array targeting the medial branch of the dorsal ramus.[341,342] Data demonstrated a reduction of pain intensity as well as in use of analgesic medications.

The highest level trial of the permanently implanted PNS system was an international, multi-center, prospective, randomized, active, sham controlled, blinded trial, which generated high, level I-A evidence supporting the significance of the treatment effect.[339,340] The study was conducted at 24 sites in the US, Australia, and Europe. A total enrollment of 204 subjects were implanted with the permanently implanted PNS system and randomized (1:1) to the treatment or control group. Subjects in the treatment arm had the permanently implanted PNS system programmed to deliver stimulation at a level appropriate to the individual subject. Subjects in the control group had the permanently implanted PNS system programmed to deliver low-level stimulation. The primary endpoint assessment occurred at the 120-day visit. After the 120-day visit, subjects in the control group were given the choice of having their IPG programmed to deliver individualized and appropriate stimulation (crossover group). A complete review of the available evidence for this medial branch stimulation is summarized in Table 32.

Therapy Grading

For PNS stimulation of medial branches, there was sufficient evidence in the form of six RCTs and several prospective observational and case studies (Table 32) for the committee to make recommendations. The ASPN Back Group recommends selectively offering the non-implanted 60-day system therapy to individual patients based on professional judgement and patient preferences. There is at least moderate certainty that the net benefit is small. The ASPN Back Group recommends offering the permanently implanted PNS system given that there is high certainty that the net benefit is substantial. Recommendations are summarized in Table 33.

Peripheral Nerve Field Stimulation

Since its initial documented use in 1965 by Drs. Wall and Sweet, peripheral nerve stimulation (PNS) has evolved dramatically. One of its derivatives known as peripheral nerve field stimulation (PNFS) is postulated to provide analgesic effects through a similar mechanism as PNS: stimulation of the Aβ afferent neurons leads to excitation of inhibitory dorsal horn interneurons, which block the potentiation of nociceptive signals from Aδ and C-fibers to wide dynamic range neurons and thus decreases the noxious signal sent to higher cortical regions.[343,344] Rather than providing electrical stimulation to a specific sensory nerve, which is the goal of PNS, PNFS targets more distal and smaller sensory branches as well as subcutaneous nerve endings.[345]

Table 32 Evidence Summary for Multifidus Activation via Medial Branch Nerve Stimulation

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Deckers et al, 2018[336]	Prospective, multi-center, single-arm, non-randomized trial	53	I-B	NRS (back), ODI, EQ-5D	The percentage of subjects at 90 days, 6 months, and 1 year with greater than or equal to MCID in single day NRS was 63%, 61%, and 57% respectively. The percentage of subjects with greater than or equal to MCID in EQ-5D was 88%, 82%, and 81% respectively. There were no unanticipated adverse events related to the device, procedure, or therapy.
Cohen, et al, 2019[337]	Case-series	9	II	Daily pain levels and analgesic medication consumption in weekly diaries and once weekly visits to assess pain, disability, and adverse events, ODI, BPI-9, PGIC	At one month, 67% of patients experienced highly clinically significant reductions in average BPI vs baseline. The mean reduction in average pain intensity in all subjects was 59% with average 76% reduction in non-opioids and 100% reduction in opioid, with 67% experiencing significant improvement in ODI and reduction in BPI.
Ilfeld et al, 2017[338]	Retrospective literature review	43	I-C	Rate of infection/1000 indwelling days; Rate of infection in the 1st 30 and 60 days	The risk of infection with non-coiled leads was estimated to be 25 times greater than with coiled leads. The infection rates were estimated to be 0.03 infections per 1000 indwelling days for coiled leads and 0.83 infections per 1000 indwelling days for non-coiled leads.
Gilligan et al, 2021[339]	Randomized, multi-center, active- sham-controlled clinical trial	204	I-A	Comparison of responder subjects with greater than or equal to 30% relief on VAS (LBP) without analgesic increase at 120 days; ODI, EQ-5D, PPR, PGIC, and LBP resolution	The primary endpoint comparing the responder proportions was inconclusive in superiority; however, prespecified secondary outcomes and analyses were consistent with a modest but clinically significant meaningful treatment benefit at 120 days.
Gilligan et al, 2021[340]	Open-label follow up of randomized, active-sham-controlled trial	204	I-C	VAS, ODI, EQ-5D-5L, opioid intake at 6, 12, and 24 months	At two years, 76% subjects experienced ≥50% CLBP relief and 65% reported CLBP resolution; 61% had a reduction in ODI of ≥20 points, 76% had improvements of ≥50% in VAS and/or ≥20 points in ODI, and 56% had these substantial improvements in both VAS and ODI.
Kapural et al, 2018[341]	Case report	2	II	BPI, ODI	2 subjects experienced clinically significant reductions in average BPI at end of therapy, which was sustained at 4 months with at least 50% reduction in ODI and 83% reduction in BPI, revealing the utility of minimally invasive neuromodulation therapy

(*Continued*)

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Table 32 (Continued).

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Gilmore et al, 2019[342]	Case Series	9	II	BPI-3, BPI-5	Among responders at four months, the mean reduction in average pain intensity (BPI-5) and worst pain intensity (BPI-3) was 84% and 78%, respectively. Subject-reported reductions in pain intensity were substantiated by concomitant and sustained reductions in analgesic medication usage. Subjects also reported clinically significant reductions in patient-centric outcomes of disability (ODI), pain interference (BPI-9), and PGIC.
Thomson et al, 2021[538]	Post-market prospective clinical follow-up	42	I-B	NRS, ODI, EQ-5D-5L	Among the 37 patients completing 2-year follow-up, NRS pain scores improved from 7.0 ± to 3.5 ± 0.3, ODI scores improved from 46.2 ± 2.2 to 29.2 ± 3.1, and health-related quality of life improved from 0.426 ± 0.035 to 0.675 ± 0.030. Additionally, 57% of patients experienced a greater than 50% reduction in pain, and 51% of patients benefited by a greater than 15-point reduction in ODI, both substantial improvements.

Abbreviations: NRS, numeric rating scale; ODI, Oswestry Disability Index; EQ-5D, EuroQOL Health Questionnaire; MCID, minimum clinically important difference; BPI, Brief Pain Inventory; PGIC, patient global impression of change; VAS, visual analog scale; PPR, percentage pain relief; LBP, low back pain.

Table 33 ASPN Back Consensus Group Recommendations for Multifidus Activation via Medial Branch Nerve Stimulation

Recommendation	Grade	Level	Level of certainty
The incidence of serious procedure or device related complications is favorable to other neuromodulation techniques	B	I-B	Moderate
Improvements in baseline are clinically significant at both 1 and 2 years after implant in a cohort of patients with severe, disabling chronic LBP	B	I-B	Moderate
Improvements in pain and disability increase the longer duration of treatment	B	I-B	Moderate
The infection rate of non-coiled leads is 25 times higher than rate for coiled leads	C	I-C	Moderate
Percutaneous 60 day PNS may provide sustained improvements in pain and function	C	I-C	Moderate
Percutaneous PNS may reduce or eliminate need for analgesics in individuals with chronic LBP	C	II	Low

Abbreviations: LBP, low back pain; PNS, peripheral nerve stimulation.

Various studies have demonstrated that in patients with axial LBP, lead depth placement of 10–12 mm maximizes activation of Aβ fibers while not being too superficial to raise concern for superficial erosion of leads or unintentional motor activation if placed too deep.[346] When considering PNFS, placement of the leads during the trial is critical as well. If the focal area of axial LBP is approximately 6 cm in diameter, then one lead is typically used with the intention of targeting the lead placement to the epicenter of this region to maximize the therapeutic effect. If the region of intense pain experienced by patients is larger, then placement of two leads at the periphery of the painful region is recommended. During this process, patients are asked to give feedback regarding the paresthesias experienced during active stimulation of the leads, and placement is adjusted to optimize pleasant paresthesias.[347] These trials are performed to optimize location and programing of the leads prior to permanent subcutaneous implantation of PNFS leads with an IPG.

Indications and Complications

The general indication for the use of PNFS is in patients with severe chronic neuropathic pain, without a clearly correctable underlying pathology, that persists despite various medical treatments.[348] With respect to its use in patients with LBP, PNFS can be used for treating either chronic unilateral or bilateral axial pain that may or may not be associated with failed back surgery syndrome following a multilevel spinal surgery.[349] In addition, some other important criteria when selecting patients include ensuring their pain is well localized to a specific region in the low back, the pain remains uncontrolled for more than 6 months despite guideline-based management, and the intensity of the axial LBP is more severe than radicular pain in situations in which both are occurring concurrently. Much like PNFS performed in other areas of the body, imaging prior to PNFS trialing should be performed to exclude any underlying reversible spinal pathology causing the patient's symptoms.[347]

The complications reported in PNFS are similar to those evidenced in PNS and include infection, lead migration, skin erosion, fracture/disconnection of the leads, and hardware malfunction. The propensity for certain complications to be more prevalent in PNFS than PNS may exist, particularly given the depth and technique utilized when anchoring the PNFS leads, but the lack of literature specifically evaluating complications of PNFS makes this distinction difficult to make.[348,349] Some of the various complications and complication rates seen in PNFS studies will be discussed in the following section.

Review of Evidence

When evaluating the evidence supporting the use of PNFS for the treatment of chronic LBP, there remains a paucity of literature that evaluates solely PNFS's role in treating LBP. Rather, some of the studies look at PNFS's use for the treatment of various regions of pain, and they incorporate statistically significant data from patients suffering from solely chronic LBP. Here, we will incorporate these statistically significant findings in addition to studies that isolate PNFS's role in treating solely axial chronic LBP. The literature is summarized in Table 34 and the therapy grade recommendations for PNFS for low back pain are highlighted in Table 35.

Table 34 Evidence Summary for Peripheral Nerve Field Stimulation

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Verrills et al, 2009[539]	Retrospective analysis	14 patients (13 patients responded)	I-C	- pre and post procedure VAS scores - employment, medication usage, and patient satisfaction	- Mean VAS score pre-treatment was 7.42, and post-treatment was 3.92. - 7/13 patients decreased pain medications - 10/13 satisfied with procedure outcome
Sator-Katzenschlager et al, 2010[540]	Retrospective multi-center analysis	111 patients	I-C	- pre-procedure NRS scores and post -procedure NRS scores (weekly for at least 3 months)	- FBSS patients: mean NRS score was 8.0 pre-implantation and 3.3 afterwards. - Chronic LBP patients: mean NRS score was 8.3 pre-implantation and 4.2 afterwards.
Yakovlev et al, 2011[541]	Retrospective analysis	18 patients	I-C	- pre and post procedure VAS scores - pre and post procedure opioid use	- Mean pre procedure VAS score = 7.4 - Mean post procedure VAS score = 1.7 (12 month follow up) - At 12 month follow up 11/18 patients stopped opioids entirely
Verrills et al, 2011[542]	Prospective observational study	100 patients	I-B	- pre and post PNFS implantation VAS scores - pre and post PNFS implantation ODI scores	- Average follow up for patients with lumbo-sacral pain = 7.2 months - Reduction in VAS by 3.3 ($p \leq 0.000$) - Statistically significant reduction in ODI ($p \leq 0.033$)
McRobers et al, 2013[543]	Prospective, multi-center, double-blinded, crossover RCT	32 patients were trialed and 23 patients had leads permanently implanted	I-B	- pre and post PNFS implantation VAS scores - SF-36 assessing quality of life, medication dosage and frequency	- Mean VAS scores decreased from 7.8 to 3.5 at 52 week follow up - At 52 weeks 16/23 patients still reported > 50% pain relief - SF-36 improved from 16.9 to 27.9 at 52 weeks ($p < 0.001$) - 43% of patients either decreased dose/frequency or stopped previous opiate medications
Kloimstein et al, 2014[544]	Prospective, multi-center, observational study	118 patients enrolled and 105 people implanted with PNFS	I-B	- VAS scores, ODI, BDI, SF-12	- Mean VAS pre-trial was 7.9, and 4.7 at 6 months post PNFS implantation ($p < 0.01$) - Improvement of ODI from 38.2 to 34.6 ($p < 0.01$) at 6 month follow up - Improvement of BDI from 17.8 to 15.1 (not statistically significant) - SF-12 score improvement from 4.29 to 3.67 ($p < 0.01$) at 6 months

Ishak et al, 2018[545]	Prospective, single center, observational study	26 patients enrolled and 13 had leads permanently implanted	I-B	- VAS scores, ODI, and EQ-5D-3L scores measuring quality of life - Pain medication usage at 24 months	- Statistically significant ($p < 0.01$) improvement in VAS, ODI and EQ-5D-3L scores pre-trial vs post implantation at 24 months - 77% decrease in NSAID use and 92% decrease in overall opioid use when compared to pre-implantation
Eldabe et al, 2019[546]	Prospective, multi-center, unblinded, RCT	116 patients	I-B	- VAS scores, ODI scores, EQ-5D-5L and SF-36 (quality of life evaluation)	- Statistically significant ($p < 0.0001$) improvement in VAS score after implantation at 9 months (68.8/100 decreased to 36.9/100), and also statistically significant improvement in ODI ($p < 0.0001$), EQ-5D-5L ($p = 0.0003$) and SF-36 ($p = 0.0062$)
van Gorp et al, 2019[547]	Prospective, multi-center, unblinded, RCT	52 patients enrolled (50 patients were implanted & completed 12 month follow up)	I-B	- VAS scores, ODI scores, HADS anxiety component score, MOSS scores, and MPQ scores	- Statistically significant improvement in VAS was noted at 12 months ($p < 0.001$) compared to baseline. - ODI score improvement from 57.1 to 40.4 at 12 months ($p < 0.05$). - Statistically significant improvement in HADS anxiety component score, MOSS scores, and MPQ scores at 12 month follow up ($p < 0.05$)

Abbreviations: VAS, visual analog scale; NRS, numeric rating scale; LBP, low back pain; PNFS, peripheral nerve field stimulation; ODI, Oswestry Disability Index; BDI, Beck Depression Inventory; SF-12/36, Short Form Health Survey; EQ-5D, EuroQOL Health Questionnaire; NSAID, nonsteroidal anti-inflammatory drug; HADS, Hospital Anxiety and Depression Scale; MOSS, Medical Outcomes Study-Sleep; MPQ, McGill Pain Questionnaire.

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Table 35 ASPN Back Consensus Group Recommendations for Peripheral Nerve Field Stimulation

Recommendation	Grade	Level	Level of certainty Net benefit
PNFS can be considered in patients with chronic axial low back, with and without radicular symptoms in their lower extremities, who have failed other treatment modalities.	C	I-B	Moderate

Ablative Therapies

Lumbar Radiofrequency Ablation Lumbar Spine

One of the most prevalent articulations of the lumbar spine is that of the zygapophyseal joint.[350] This joint is formed at each level of the lumbar spine and at the lumbosacral junction by the inferior articulating process of the level above in the superior articulating process of the level below. As in other parts of the human body, this joint is subject to degeneration of both primary and secondary causes leading to joint hypertrophy, joint stiffness, synovitis and hypomobility. Lumbar facet-mediated pain may likely result from repetitive stress and trauma to the joint and/or joint capsules causing chronic inflammation and capsular distention. Nonetheless, these pathological processes often lead to progressive and significant debilitating pain.[351]

The use of thermal destruction of neural tissue is simply based on the premise that pain that may be otherwise refractory to oral pharmacology or physical therapy is treated by destroying the sensation delivery pathway from the site of pain. Simply speaking, the destruction of the neural signal pathway is performed as the correction of the underlying cause from a surgical standpoint cannot be performed or does not exist.[352]

Conventional radiofrequency ablation (C-RFA), also known as radiofrequency thermocoagulation (RFTC) and radiofrequency neurolysis (as well as simply, "neurolysis"), is a treatment method utilizing radiofrequency current to create a thermal change in a defined, non-insulated area of an otherwise insulated conductive probe or needle. The conductance of energy to the tip of a radiofrequency needle creates a well-defined area of heat used for thermal ablation of a biological tissue. Commonly in medicine, thermal destruction is used when neural signaling is either aberrant or undesirable. Radiofrequency ablation exists as traditional, constant heat and for a defined time, thermal destruction. The level of heat typically is in the range of 60–90 degree Celsius. Pulsed RFA (P-RFA) parameters are similar to conventional RFA, albeit that output of the energy is delivered in short pulses. Shorter pulses reduce tissue target temperature with interval cooling permitted, therefore allowing for the use of radiofrequency interruption of neural signaling without diffuse tissue damage. A classic use of pulsed RFA is 20 millisecond pulses every 0.5 seconds with temperature not exceeding 42 degree Celsius.[353,354] Other forms of radiofrequency ablation include a "cooled" form of ablation with temperatures at or near 60 degree Celsius for a prolonged time period resulting in a larger circumference of a lesion.[355]

Indications

Indications for the use of lumbar RFA are largely related to intractable pain of the lumbar facet joints. Pain of nociceptive origin from the lumbar facet joints are treated using this therapy following pain for at least three months and the patient having tried and failed more conservative measures or these measures being contraindicated in that patient's specific medical state. Conservative measures include, but are not limited to, physical therapy, manual manipulation, psychological coping strategies, medically supervised exercise regimens and pharmacological management, typically most consistent with failure of non-steroidal anti-inflammatory medication, acetaminophen, and other therapies such as opioids. The latter pharmacological management strategy has generally fallen out of favor as a treatment option given the larger societal problem of opioid abuse. Lastly, RFA is typically preceded by diagnostic medial branch nerve blocks with local anesthetic solutions such as lidocaine, bupivacaine and ropivacaine followed by reassessment of pain reduction and functional improvement, if present.[35]

Safety and Complications

The overall safety profile related to the use of RFA is favorable. Some small retrospective studies exist and report complications; typically, these complications are self-limited and include common postprocedural issues such as pain

after injection, transient worsening of back pain, thermal injuries and infection. While complications may occur, the rate of complication is quite low,[356] although care must be taken to prevent heating of lumbar instrumentation, if present.[357] Similarly, the use of direct visualization through fluoroscopy and confirmation with sensory and motor testing also contributes to the low complication rate.

Review of the Evidence

There are several studies pertaining to the use of traditional RFA, pulsed RFA and cooled RFA in publication. The most substantial body of published data appears to be related to either traditional RFA in isolation or comparisons between traditional RFA and pulsed RFA.

Efficacy of Conventional, Continuous Radiofrequency Ablation

A C-RFA literature search revealed 3 randomized trials (one multicentered randomized, double blinded, sham lesion-controlled trial, two single-centered, randomized double-blind controlled trials), in addition to 1 single-centered sham-controlled trial, two large prospective observational outcome studies, 1 single-centered, prospective clinical audit, and 1 large single-center retrospective review. Table 36 presents an evidence summary, and recommendations appear in Table 37.

Sacroiliac Radiofrequency Ablation

Sacroiliac regional pain syndrome (SIRP) is a pain condition that is characterized by a localized pain below the posterior superior iliac spine and the buttock region. The pain arises from the densely innervated joint, joint capsule and the ligamentous structures in the posterior and the anterior aspects of the joint.[358] The prevalence of the SIRP pain depends on age of the patient, typically increasing with age, as the mechanics shift the weight from the anterior elements to the posterior elements. There is also a higher incidence in patients who have undergone adjacent segment fusion at the lumbosacral level. The importance of understanding the SIRP condition is that it accounts for many instances of lower back and buttock pain currently treated by the primary care providers and specialists.

Because of the transient and inconsistent results of sacroiliac injections (with local anesthetics, steroids) and prolotherapy, more definitive treatments have been sought. Since the advent of radiofrequency neurotomy, multiple authors have deployed a variety of different approaches to denervate the joint. There has been variability historically in outcomes attributable to patient selection, target selection, and procedural technique.

Pathophysiology and Innervation of the Sacroiliac Region

The SIJ is a 1–2 mm wide diarthrodial joint with an articular cartilage, synovial fluid, and a fibrous capsule. The joint has a strong ligamentous support structure that serves to stabilize the joint. The joint still has motion in two planes. The innervation of the intra-articular portion of the joint has been vigorously contested over the years. It appears that anteriorly, there is innervation from the lumbosacral trunks, obturator nerve, and gluteal nerves, and posteriorly from the lateral branches of the S1-S3 dorsal rami. Historically, there was a belief that there is also innervation from the L4 medial branch and the L5 dorsal ramus. Sacroiliac joint complex pain emanates from the extra-articular elements in addition to or separate from the intra-articular portion of the joint. This complex includes the articular portion of the joint, the joint capsule, overlaying dorsal ligaments, regional muscles, and nerves that supply these structures.

Diagnosis Pitfalls and Precautions

Pain and tenderness above the posterior superior iliac spine is less likely to be due to SIRP, whilst that at or below the sacral sulcus is more likely to be symptomatic of SIRP. The finger Fortin sign, whereby the patient points to the medial aspect of the sacral joint in the sulcus, has the greatest likelihood to be indicative of SIRP. Laslett et al and van der Wurff et al have thus posited that if 3/5 clinical signs are positive, there is high sensitivity and specificity of an SIRP diagnosis.[110,359]

Optimal diagnostic criteria for the sacroiliac joint, or more accurately the sacroiliac regional pain, have not been defined, in part due to the lack of agreement of the true pathophysiology of SIRP. Pain emanates from the joint as well as the surrounding soft tissues. Thus, a provocative injection of the joint or a pain-relieving local anesthetic injection that blocks the joint pain alone but missing the blockade of the soft tissues does not suffice. Likewise, a single clinical symptom ("I have buttock pain in the region of the sacroiliac joint") is not sufficient due to considerable overlap from other pain generators (such as annular

Table 36 Evidence Summary for Lumbar Radiofrequency Ablation

Study	Study type	Sample size	Outcomes measure(s)	Evidence level	Other
Van Wijk et al[548]	RCT	81	VAS, SF-36, global perceived effect	I-A	No difference from Sham – one diagnostic block
Van Kleef et al[51]	RCT	31	VAS, global perceived effect, ODI	I-A	Significant difference at 3,6,12; one block performed
Nath et al[52]	RCT	40	Pain Scores, global perceived effect, hip movement, SI joint test	I-A	3 diagnostic blocks performed; independent observer (orthopedic surgeon); Improvement in back pain and hip pain/movement
Leclaire et al[549]	Sham controlled	70	VAS, RMQ, ODI	I-A	Facet blocks prior to RFA; Sham RFA (no current) vs RFA. Results show short term relief, but efficacy not established
Gofeld et al[550]	Prospective audit	174 of 209 completed study	Questionnaire – total perceived pain reduction, reduction in pain medicine, functional improvement	I-B	Dual diagnostic medial branch blocks; Patient reported questionnaires at 6 weeks, 6,12,24 months. 68% showed at least 50% pain reduction from 6–24 months.
McCormick[62]	Single center, prospective outcomes	62	Percentage pain reduction, NRS score, MQS score	I-B	At least 1 diagnostic block with 75% pain reduction; > or = to 50% pain reduction and functional improvement; Median follow-up 39 months; 58% and 53% improved in function and pain reduction, respectively; RFA is a durable treatment
Yadav et al[551]	Single center, retrospective cohort	500	Responder >30% improvement in pain scores	I-C	Responders were > or = 30% pain reduction after diagnostic block; 1 year follow-up; patients with high preoperative opioid use were less responsive at 1 year
Tekin et al[53]	RCT	20 RFA, 20 Pulsed, 20 Sham	VAS, ODI	I-A	All groups reported a clinically significant reduction in pain from pre-procedure scores at 6 and 12 months
Kroll et al[552]	Prospective, Randomized, Double-blinded study	50, 26 on follow-up	VAS, ODI	I-B	Dual diagnostic blocks at least two levels; Randomized to C-RFA or P-RFA; No difference between groups in VAS or ODI; P-RFA no significant difference over time; C-RFA shows significant improvement over time
Cetin and Taktas[553]	Prospective, Double blinded; comparative	75 P-RFA; 43 C-RFA	VAS, Odom criteria	I-B	Follow-up months 1,3,4,12 and 24; C-RFA procedure more satisfied patients with less need for re-treatment compared to P-RFA
Colini-Baldeschi[554]	Observational	300	NRS	I-C	Single diagnostic block; 186 of 300 reported good pain relief at 6 months after P-RFA
Mikeladze et al[555]	Retrospective	83 of 114 with back pain	VAS	I-C	68 of 118 patients received pain relief following P-RFA and after a single diagnostic block; mixed study with both cervical and lumbar facet pain
Linder et al[556]	Retrospective with crossover	48	NRS	I-C	Single diagnostic block; crossover to C-RFA if P-RFA not successful at 1 month
McCormick et al[557]	Blinded, prospective comparative	43 total, cooled RFA 22, conventional 21	NRS at 6 months, NRS, ODI, PGIC	I-B	Single diagnostic block > 75% pain relief; 52%/42% experienced > or = 50% pain reduction; > or = 15 point or > or = 30% 62%/42% in cooled or conventional, respectively; Cooled RFA results in > or = 50% reduction in pain when single diagnostic block used.

Abbreviations: VAS, visual analog scale; SF-36, Short Form Health Questionnaire; ODI, Oswestry Disability Index; SI, sacroiliac; RMQ, Roland Morris Disability Questionnaire; RFA, radiofrequency ablation; NRS, numeric rating scale; MQS, Medication Quantification Scale; PGIC, patient global impression of change.

Table 37 ASPN Back Consensus Group Recommendations for Lumbar Radiofrequency Ablation

Recommendation	Grade	Level	Consensus
Conventional radiofrequency ablation is effective for low back pain	A	I-A	High
Conventional RFA is superior to pulsed RFA	B	I-B	Moderate
Pulsed RFA is not efficacious	D	I-B	Moderate
Conventional RFA and cooled RFA are equally efficacious	A	I-A	Strong

tears, herniations, facet arthropathy, neurocompressive stenosis, spondylolisthesis) that can masquerade as "sacroiliac pain". The importance of ruling out these other conditions is that there are definitive solutions for many of these conditions. Accurate prognostic and diagnostic information are also a prerequisite for optimal outcomes.

Imaging including sacroiliac degeneration again may suggest is the presence of pathophysiology, but this does not necessarily confirm that the joint is a painful one.

Prognostic Blockade for Radiofrequency Neurotomy

The construct of dual comparative anesthetic blocks with two separate local anesthetics as a prelude to radiofrequency neurotomy has been established for cervical and lumbar facet denervation,[52,360–362] although the extension of this paradigm to sacroiliac denervation has important limitations. First, sacroiliac innervation is inconsistent, second, the sacroiliac lateral branches are not always in the same tissue planes, and third, our understanding of the sources of innervation of the sacroiliac complex has been evolving. With respect to innervation, it was believed that the joint received innervation from the L4 medial branch, L5 dorsal ramus and the lateral S1, S2, and S3 lateral branches, leading Cohen et al in 2008[363] to include these nerves in their randomized prospective controlled trial. Subsequently, the L4 medial branch was believed not to contribute to the sacroiliac complex, leading Patel et al in 2012 to exclude the L4 medial branch from their RCT.[364,365] In both studies, the prognostic block technique differed. In the Cohen trial,[363] the patients were randomized to sham procedure or radiofrequency neurotomy if they reported >75% relief with one intra-articular corticosteroid and anesthetic injection 6 hours post-injection. In the Patel et al RCT, patients were eligible for study enrollment if they received >75% relief of their index pain with two sets of single-site, single-depth, anesthetic blocks of the L5 dorsal ramus and S1-S3 sacral lateral branches.[364,365]

Indications and Contraindications

Axial non-radicular pain is the most common clinical presentation in the contemporary pain clinic. Amongst this group of patients, mixed and nociceptive pain syndromes predominate with pain arising from the anterior and posterior elements, including facet joints, annular tears in the discs, and sacroiliac joints.[119,127,366,367] Lower back and buttock pain without distal radicular and neuropathic features must be carefully evaluated to precisely define the primary source of pain. The presence of pain should be corroborated with at least three positive clinical signs, subsequent to which prognostic dual comparative multi-site multi-depth anesthetic blocks with >75% relief with each block of the lateral S1, S2, S3 branches are the best indication for the sacral radiofrequency denervation procedure.

The procedure is contraindicated in anyone with localized infection, refusal and/or inability to provide informed consent, and pregnancy when fluoroscopy is indicated. Relative contraindications are poorly visualized anatomy and cases in which limited visualization of the sacral foraminal precludes adequate placement of the radiofrequency cannulas.

Safety/Complications

Because the procedure involves defined bony landmarks and end points, SIRP is safe, with few if any real complications. In fact, none has been cited in the published literature. Nonetheless, transient post-procedure pain (neuritis) is a possible side effect, as is possible infection, although both are easily addressed with analgesics (gabapentin) and antibiotics, respectively.

Evidence Summary for Sacroiliac Radiofrequency Neurotomy

Many prospective studies for the treatment of SIRP exist. Three sham-controlled studies demonstrated efficacy,[363–365,368] and four further pragmatic effectiveness trials, and eight observational studies have been published (Table 38). In these investigations, there was extensive variation in terms of selection criteria, targeted nerve branches, procedure techniques and technologies deployed. Table 39 contains the recommendations for SI joint lateral branch ablation.

Basivertebral Radiofrequency Ablation

The basivertebral nerve (BVN) is a branch of the sinuvertebral nerve responsible for carrying nociceptive information from damaged vertebral endplates. The sinuvertebral nerve arises bilaterally from the ventral ramus of each spinal nerve immediately distal to the dorsal root ganglia and travels to join a branch of the grey ramus communicants responsible for sympathetic fibers. The nerve then takes a recurrent course and re-enters the spinal canal through the basivertebral foramen towards the midline of the vertebral body, where these fibers become the BVN. Although there is some anatomical variability, the BVN travels in a posterior to anterior direction approximately 30–50% into the vertebral body, forming a central nerve trunk, where it bifurcates towards the superior and inferior endplate. This is the anatomical target for the ablative procedure of the BVN for vertebral pain discussed in this section.[369–371]

Historically, other structures such as intervertebral discs, facet joints, ligaments and muscles have been studied as the source of axial LBP. Recently, a shift towards damaged vertebral endplates has been proposed as a potential contributory etiology of LBP.[372,373] Numerous studies have postulated that axial LBP may have a vertebral etiology component, and there is growing evidence that damaged vertebral end plates with nociceptive pain carried by the BVN can be perceived as LBP through substance P and calcitonin gene-related peptide (CGRP), which has been confirmed with protein gene product (PGP) 9.5 positive histochemical marker visualized under microscopy.[371–377]

Vertebral endplates are highly vascularized and innervated structures susceptible to post-traumatic degenerative changes, inflammation, and intraosseous edema, which tend to manifest in MRIs as Modic changes (MC) which may

Table 38 Evidence Summary for Sacroiliac Radiofrequency Ablation

Author	Study type and size	Outcome measures	Key findings	Level of evidence
Cohen et al 2008[363]	RCT N=28 Sham controlled	>75% relief NRS	Radiofrequency is superior (79%) to sham (14%) at 1 month	I-A
Patel et al 2012[364]	RCT N=51 Sham Controlled	>75% Relief NRS	Radiofrequency is superior (47% responder rate [RR]) to sham (12% RR) at 3 months	I-A
van Tilburg et al, 2016[368]	RCT N=60 Sham controlled	>2 point NRS decrease after sacroiliac joint injections	Radiofrequency is not superior to sham	I-A
Salman et al, 2016[558]	RCT N=30 Steroid versus RF	>75% relief NRS	Radiofrequency is superior (53% RR) to single shot steroid injection (20% RR)	I-A
Juch et al, 2017[559]	RCT N-228, RF+ Exercises compared to Exercise alone	>50% relief NRS	>30% NRS improvement in 51% in RF and 49% exercise group. No significant difference	I-A

Abbreviations: RCT, randomized controlled trial; NRS, numeric rating scale; RR, responder rate; RF, radiofrequency.

Table 39 ASPN Back Consensus Group Recommendations Sacroiliac Radiofrequency Ablation

Recommendation	Grade	Level of evidence	Level of certainty Net benefit
SI joint denervation/ablation is effective in treatment of SI joint dysfunction pain and is superior to sham in RCT	B	I-A	Strong

present clinically inconsistently from other potential etiologies.[373,376–382] Identifying the etiology of LBP is a common challenge in clinical practice. Eighty percent of cases are diagnosed as non-specific LBP, and only 20% of LBP cases can be attributed to a pathoanatomical entity. Jensen et al reviewed 82 studies and determined that MCs were reported in up to 43% of patients with nonspecific LBP; a positive association between MCs and nonspecific LBP was found in 7 of 10 studies. Therefore, the identification and diagnosis of this subset of patients with pathoanatomical changes is crucial to optimize patient outcomes.[382–385]

LBP associated with MCs presents clinically differently than other etiologies. The clinical presentation may vary widely in the population, but it is generally described as a deep, aching, midline (up to 70% of cases), burning pain of progressive nature that is potentially more severe at night. There is generally no radicular expression (in only approximately 6% of cases reported), no lower extremity weakness or sensory deficits, and symptoms tend to be worse with spinal flexion, sitting, and standing, in contrast to extension. Type I MCs are positively associated with higher LBP intensity and worse ODI scores. These patients tend to present with significant functional impairments, and those with MCs reported a greater frequency and duration of symptoms, seeking care more often than those without MCs.[372,380,381,384,386] Among the three types of MCs, Type I is known to be the one strongly associated with LBP, in contrast to Type II or Type III, which have been shown to be more stable and demonstrate less refractory pain. Type I MCs are described as vertebral endplate disruptions, degeneration and fissuring with areas of granulation under histological analysis, and present as bone marrow edema, increased vascularity and inflammation within the vertebral endplates, perceived as decreased signal in T1-weighted MRI and increased signal in T2-weighted MRI.[382,387,388]

Treatment options for LBP associated with MCs are similar to those recommended for LBP of other etiologies, starting with a conservative approach to minimally invasive surgical options; however, conservative care is generally not effective.[389] With advancements in the pathoanatomical understanding of vertebral endplate damage, the association of MCs with LBP severity, and the BVN role in providing sensory innervation to vertebral endplates described above, it is feasible to presume that RFA or neurotomy of this nerve may interrupt nociceptive signaling and potentially reduce LBP of vertebral etiology by directly targeting the potential pain generator.[390]

Indications and Contraindications

Intraosseous BVN ablation or neurotomy is a minimally invasive procedure performed under fluoroscopic or CT-guidance. The procedure involves unilateral transpedicular or transforaminal endoscopic extrapedicular access, with the use of bipolar electrodes to deliver high frequency alternating current, resulting in BVN neurotomy and the interruption of pain transmission from damaged vertebral endplates.[85,390–393]

Medical necessity to support this intervention should include a detailed history and physical exam, in addition to diagnostic studies and treatment history to support the rationale for the procedure.

BVN ablation at the L3 through S1 vertebrae is indicated when patients meet the following indication criteria:

- Chronic axial LBP (greater than 6 months of duration).
- Pain refractory to conservative nonsurgical treatment for at least 6 months of duration.
- Evidence of vertebral endplate changes on MRI as below:
  - Modic Type I and/or Modic type II changes.
  - Vertebral endplate changes with inflammation, edema, disruption and/or fissuring.
  - Fibrovascular bone marrow changes (hypointensive signal for Modic type I changes).
  - Fatty bone marrow replacement (hyperintensive signal for Modic type II changes).

BVN ablation is clinically indicated using an FDA-cleared device for the procedure when the above criteria are met.

Studies published to date on the use of BVN ablation for vertebral pain also fulfilled other inclusion criteria, which were variable based on each study. These included confirmed skeletal maturity on diagnostic images, significant limitations in function and ADLs with a minimum of at least 30 points on the ODI and of 4 cm on the VAS, and all other reasonable sources of pain have been ruled out. Regardless, the patient population of all published studies on BVN

ablation has met the 3 main inclusion criteria noted above. General contra-indications to the procedure include active systemic infections, pregnancy, histories of spine surgery at the treatment level, type III MCs, tumors, metastatic disease, osteoporosis, and implantable pulse generators. Other contra-indications or exclusion criteria reported by some of these studies included compression fracture at the treatment level, symptomatic spinal stenosis, radicular pain, body mass index greater than 40, addictive behavior, three or more Waddell's signs, Beck Depression Inventory (BDI) score greater than 24, thrombocytopenia, and coagulopathy.[394,395]

Safety and Complications

The device- and procedure-related AEs reported in the 473 clinical trial procedures (including 78 sham procedures) performed to date are quite low and had a median time to resolution of 66.5 days. The most commonly reported minor, self-limiting post-procedure adverse events included incisional pain and transient worsening of back pain. The following device- or procedure-related events have been reported:

- 1 case of a nerve root injury.
- 2 cases of lumbar/lumbosacral radiculopathy.
- 4 cases of motor/sensory deficits.
- 17 cases of transient radiculitis successfully treated with oral medications.

Serious AEs reported in the post-market surveillance for commercial cases FDA database through February 2021 include 1 case of vertebral compression fracture in a sham procedure in a patient undergoing hormonal therapy and 1 case of a retroperitoneal hemorrhage. Post-procedure MRIs at variable follow-up intervals did not reveal any signs of avascular necrosis, spinal cord injury or accelerated disc degeneration. In addition, there were no reports of thermal injuries, post-procedure infections, or broken devices. Although AEs are considered relatively rare in the studies published to date, future larger scale studies are needed, nonetheless, based on the studies available, BVN ablation seems to be safe and well tolerated by most patients when proper patient selection and procedural technique are applied.[85,390,391,393,394,396]

Evidence Review with Evidence Level Designation

There have been numerous clinical studies published to date with direct patient-data regarding the clinical efficacy of BVN ablation for axial LBP of vertebrogenic nature.[370,391,392,395,397–403] In addition, clinical and systematic reviews recently have been published discussing different aspects of this intervention in chronic axial lower back pain management, analyzing common data points among similar studies, as well as published society guidelines.[85,390,393,394,396,404–407] Table 40 provides a summary of available clinical studies, outcome measures utilized, level of evidence (according to USPSTF criteria[1]) and comments on each study. Studies published to date reported functional outcomes with the ODI and pain assessment utilizing the VAS, while quality of life measurements were reported utilizing the SF-36 and/or the EQ-5D-5L questionnaire. Patient satisfaction has been analyzed utilizing the MacNab criteria, and opioid utilization was also reported as an outcome measurement in several studies.

Evidence and Therapy Grading

For basiventral nerve ablation, the evidence is summarized in Table 40. Based upon 11 studies meeting search criteria for inclusion in the review, the recommendation for basivertebral nerve ablation is Grade A with Level of Certainty 1a based upon 4 RCTs (Table 41).

Conclusions

The ASPN Back Guideline provides a comprehensive framework for the safe and effective utilization of interventional treatments for lumbar disorders. Interventional treatments should be utilized based on the published efficacy and relative risk data. Over the last several years, many novel techniques and procedures for lower back disorders have been developed. The authors of ASPN Back believe that this guideline will help identify gaps in the literature and provide guidance on future evidence development. Given the broad scope of interventional treatments for lower back pain, many

Table 40 Evidence Summary for Basivertebral Radiofrequency Ablation

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Smuck et al, 2021[560]	Prospective, multicenter, open label RCT	140	I-B	ODI, VAS	Mean ODI reduction, difference between arms of −20.3 (CI −25.9 to −14.7 points; $p < 0.001$) Mean VAS pain improvement (difference of −2.5 cm between arms (CI −3.37 to −1.64, $p < 0.001$)
Koreckij et al, 2021[561]	Prospective, open label, single-arm RCT	140	I-B	ODI, VAS, SF-36, EQ-5D-5L, responder rates	Improvements in ODI, VAS, SF-36 and EQ-5D-5L were statistically significant at 24-month follow up Mean ODI change improved 28.5±16.2 points (from baseline 44.5; $p < 0.001$) Mean VAS change improved 4.1±2.7 cm (from baseline 6.6; $p < 0.001$ Responder Rates: A combined responder rate of ODI≥15 and VAS≥2 was 73.7% A ≥50% reduction in pain was reported in 72.4% of patients and 31.0% were pain-free at 2 years At 24 months, only 3(5%) of patients had BVNA-level steroid injections, and 62% fewer patients were actively taking opioids
Macadaeg et al, 2020[395]	Prospective, open-label, single-arm, multicenter	47	I-B	ODI, VAS, Responder Rates, SF-36, EQ-5D-5L	Mean ODI change of −32.6 Mean VAS change of −4.3 Responder Rates: 15-point ODI reduction – 88.9% 20-point ODI reduction – 88.4% 2.0 cm VAS reduction – 80.0% SF-36 Total Score increase of 26.3 EQ-5D-5L increase of 0.22
De Vivo et al, 2020[403]	Prospective uncontrolled trial	56	I-B	ODI, VAS, Responder Rates	Mean ODI change of −32.4 Mean VAS change of −4.3 Responder Rates: 10-point ODI reduction - 96.4% 2-point VAS reduction - 96.4%

(*Continued*)

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Table 40 (Continued).

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Fischgrund et al, 2020[402]	Open-label follow-up study of RCT treatment arm	100	I-B	ODI, VAS, Responder Rates, Opioid Use	Mean ODI change of −25.9 Mean VAS change of −4.4 Responder Rates: 15-point ODI reduction - 77% 2-point VAS reduction - 88% Combined (ODI ≥ 15 and VAS ≥ 2) - 75% In patients on opioids at baseline: Stopped use – 73.3%
Kim et al, 2020[370]	Prospective case series	30	I-C	ODI, VAS, MacNab criteria	Mean ODI change of −52.7 Mean VAS change of −5.7 MacNab criteria: Excellent outcomes – 56.7% Good outcomes – 36.7% Fair outcomes – 6.7%
Markman et al, 2020[401]	Post-hoc analysis of sham-controlled trial	69	II	ODI, Opioid Use	Treatment arm: Decreased opioid use (n=27) mean ODI change −24.9 Increased opioid use (n=18) mean ODI change −7.3 Sham arm: Decreased opioid use (n=19) mean ODI change −17.4 Increased opioid use (n=5) mean ODI change −1.2
Khalil et al, 2019[400]	Prospective, randomized, multicenter	104	I-A	ODI, VAS, Responder Rates, SF-36, EQ-5D-5L, Opioid Use	Mean ODI change of −25.3 (treatment) vs −4.4 (control) Mean VAS change of −3.5 (treatment) vs −1.0 (control) Responder Rates: 20-point ODI reduction – 62.7% (treatment) vs 13.5% (control) 2-point VAS reduction – 72.5% (treatment) vs 34.0% (control) SF-36: PCS – increase 14.02 (treatment) vs 2.114 (control) MCS - increase 2.615 (treatment) vs 2.786 decrease (control) EQ-5D-5L Increase 0.1803 (treatment) vs 0.0135 (control) No change in opioid use in either arm at 3 months

Fischgrund et al, 2019[399]	Open-label follow-up study	106	I-C	ODI, VAS, Responder Rates, SF-36, Opioid Use	Mean ODI change of −23.4 Mean VAS change of −3.6 Responder Rates: 10-point ODI reduction - 76.4% 20-point ODI reduction – 57.5% 1.5 cm VAS reduction – 70.2% SF-36 PCS increase of 11.84 In patients on opioids at baseline: Reduced use – 60.7% Stopped use – 46.4%
Truumees et al, 2019[398]	Prospective, open-label, single-arm, multicenter	28	I-B	ODI, VAS, Responder Rates, SF-36, EQ-5D-5L	Mean ODI change of −30.1 Mean VAS change of −3.5 Responder Rates: 10-point ODI reduction – 92.9% 20-point ODI reduction – 75.0% 2.0 cm VAS reduction – 75.0% SF-36 PCS increase of 15.78 SF-36 MCS increase of 4.23 EQ-5D-5L increase of 0.198 50% (4/8) patients taking extended-release narcotics had stopped by 3 months post procedure.
Kim et al, 2018[392]	Single center retrospective observational	14	I-B	VAS, MacNab criteria	Mean VAS change of −5.4 MacNab criteria: Excellent outcomes – 50.0% Good outcomes – 42.9% Fair outcomes – 7.1%

(*Continued*)

https://doi.org/10.2147/JPR.S386879

Table 40 (Continued).

Source, year	Design	Sample size	Level of evidence	Outcome measures	Results
Fischgrund et al, 2018[397]	Prospective, randomized, double-blind, sham-controlled, multicenter	225	I-A	ODI, VAS, Responder Rates, SF-36	3 Month Primary Endpoint (per protocol): Mean ODI change of −20.3 (treatment) vs −15.4 (control) Mean VAS change of −2.9 (treatment) vs −2.5 (control) 12 Month Primary Endpoint (per protocol): Mean ODI change of −19.8 (treatment) vs −15.9 (control) Mean VAS change of −2.8 (treatment) vs −2.2 (control) Responder Rates 3 Month (per protocol): 10-point ODI reduction – 75.6% (treatment) vs 55.3% (control) SF-36 - 3 Month (per protocol): PCS – increase 9.74 (treatment) vs 9.05 (control) MCS - increase 2.24 (treatment) vs 0.78 (control) SF-36 - 12 Month (per protocol): PCS – increase 9.17 (treatment) vs 7.63 (control) MCS - increase 1.13 (treatment) vs 1.46 decrease (control)
Becker et al, 2017[391]	Prospective, single-arm, multicenter pilot	16	I-B	ODI, VAS, Responder Rates, SF-36	Mean ODI change of −29 Mean VAS change of −16 mm Responder Rates: 10-point ODI reduction – 81% SF-36 PCS increase of 7.2

Abbreviations: RCT, randomized controlled trial; ODI, Oswestry Disability Index; VAS, visual analog scale; CI, 95% confidence interval; SF-36, Short Form Health Questionnaire; PCS, physical component summary; MCS, mental component summary; EQ-5D, EuroQOL Health Questionnaire; BVNA, basivertebral nerve ablation.

Table 41 ASPN Back Consensus Group Recommendations for Basivertebral Nerve Ablation

Recommendation	Grade	Level of evidence	Level of certainty Net benefit
Basivertebral nerve ablation	A	I-A	High

less established interventions were not included. This represents a limitation of this guideline and provides an opportunity to make future guidelines even more robust. The ASPN Back Guideline will be updated at regular intervals to include new therapies and evidence.

Abbreviations

β-CTX, Carboxyl-terminal collagen I crosslinks; 95% CI, 95% confidence interval; ADLs, Activities of daily living; AE/SAE, Adverse event/Serious adverse event; AF, Annulus fibrosus; ANOVA, Analysis of variance; AQoL, Assessment of Quality of Life; ASA, American Society of Anesthesiologists; ASIPP, American Society of Interventional Pain Physicians; ASLR, Active straight leg raise; ASPN, American Society of Pain and Neuroscience; ASRA, American Society of Regional Anesthesia and Pain Medicine; AVBHr, Anterior vertebral body height ratio; BALP, Bone alkaline phosphatase; BDI, Beck Depression Inventory; BGP, Bone gla protein; BKP, Balloon kyphoplasty; BMC, Bone marrow concentrate; Botox, Botulinum toxin; BPI, Brief Pain Inventory; BTXA, Botulinum toxin type A; BVN, Basivertebral nerve; CDC, Centers for Disease Control; CEI, Caudal epidural injections; CGRP, Calcitonin gene-related peptide; CLPB, Chronic low back pain; CMM, Conventional medical management; CNS, Central nervous system; C-RFA, Conventional radiofrequency ablation; CRPS, Complex regional pain syndrome; CT, Computed tomography scan; DBM, Demineralized bone matrix; DDD, Degenerative disc disease; DIANA cage, Hollow threaded fusion cage for SIJ fusion; ECAP, Evoked compound action potential; ED, Emergency Department; EMG, Electromyography; EQ-5D, EuroQOL Health Questionnaire; ESI, Epidural steroid injection; FACES, Wong-Baker pain scale; FBSS, Failed back surgery syndrome; FRI, Functional Rating Index; GAS, Global Assessment of Improvement Scale; GDS-SF, Geriatric Depression Scale – Short Form; GIC/PGIC/CGIC, Global Impression of Change (patient-, clinician-); HA, Hyaluronic acid; HADS, Hospital Anxiety and Depression Scale; HCPCS, Healthcare Common Procedure Coding System; HSC, Hematopoietic stem cell; IA, Intra-articular; IASP, International Association for the Study of Pain; ICD, International Classification of Diseases; ICI, Intra-articular corticosteroid injection; IDDS, Intrathecal drug delivery; IPD, Interspinous process device; IPG, Implanted pulse generator; IPS, Interspinous process spacers; ISF, Interspinous fixation; ISS, Interspinous spacer; IT, Intrathecal; ITT, Intent to treat; IV, Intravenous; IVD, Intervertebral disc; JOA, Japanese Orthopedic Association; LA, Local anesthetic; LBP, Low back pain; LDH, Lumbar disc herniations; LFH, Ligamentum flavum hypertrophy; LFJ, Lumbar facet joint; LSS, Lumbar spinal stenosis; LTR, Localized twitch responses; MAC, Monitored anesthesia care; MBB, Medial branch blocks; MC, Modic change; MCID, Minimum clinically important difference; MCS, Mental component summary (SF-12, −36); MD, Microdiscectomy; MDA, Malondialdehyde; MED, Microendoscopic discectomy; MME, Milligram morphine equivalent; MOSS, Medical Outcomes Study-Sleep; MPC, Mesenchymal precursor cell; MPQ, McGill Pain Questionnaire; MPS, Myofascial pain syndrome; MQS, Medication Quantification Scale; MRI, Magnetic resonance imaging; MSC, Mesenchymal stem cells; MSMD, Multisite, multidepth; MVBHr, Midline vertebral body height ratio; NACC, Neurostimulation Appropriateness Consensus Committee; NASS, North American Spine Society; NCS, Numeric Categorical Scale; NDI, Neck Disability Index; NHP, Nottingham Health Profile; NICE, National Institute of Health and Clinical Excellence; NNT, Number-needed-to-treat; NP, Nucleus pulposus; NPAD, Neck Pain and Disability Scale; NPQ, Neck Pain Questionnaire; NRS, NPRS, Numeric rating scale, numeric pain rating scale; NS, Normal saline; NSAID, Nonsteroidal anti-inflammatory drug; NSM, Non-surgical management; OA, Osteoarthritis; OD, Open discectomy; ODI, Oswestry Disability Index; OMM, Optimized medical management; OPM, Optimal pain medication; PACC, Polyanalgesic Consensus Conference; PBK, Percutaneous balloon kyphoplasty; PCKP, Percutaneous curved kyphoplasty; PCS, Physical component summary (SF-12, −36); PDI, Pain Disability Index; PDQ, Pain Detect Questionnaire; PEEK, Polyether ether ketone; PELD,

Percutaneous endoscopic lumbar discectomy; PFDI-20, Pelvic Floor Disability Index; PGP, Protein gene product; PILD, Percutaneous image-guided minimally invasive lumbar decompression; PKP, Percutaneous kyphoplasty; PLS, Post-laminectomy syndrome; PMMA, Polymethyl methacrylate; PNFS, Peripheral nerve field stimulation; PNS, Peripheral nerve stimulation; PPDT, Pressure pain detection thresholds; PPI, Pressure pain intensity scores; PPR, Percentage pain relief; PPT, Pressure-pain threshold; PPTT, Pressure pain tolerance thresholds; PRF, Pulsed radiofrequency; P-RFA, Pulsed radiofrequency ablation; PRGF, Plasma rich growth factor; PRP, Platelet-rich plasma; PS, Pain scale; PTED, Percutaneous transforaminal endoscopic discectomy; PTM, Pressure threshold meter; PVBHr, Posterior vertebral body height ratio; PVP, Percutaneous vertebroplasty; QoL, Quality of life; QUALEFFO, Questionnaire of the European Foundation of Osteoporosis; RCT, Randomized controlled trial; RFA, Radiofrequency ablation; RFTC, Radiofrequency thermocoagulation; rhBMP-2, Bone morphogenetic protein-2; RMQ/RMDQ, Roland-Morris Disability Questionnaire; RR, Responder rate; SANE, Single assessment numeric evaluation; SCS, Spinal cord stimulation; SD, Standard deviation; SF-12, SF-36, Short Form questionnaire; health-related quality of life (12-, 36-item); SI, Sacroiliac; SIJ, Sacroiliac joint; SIJF, Sacroiliac joint fusion; SIRP, Sacroiliac regional pain syndrome; SIS, Spine Intervention Society; SLBB, Sacral lateral branch block; SLBRFA, Sacral lateral branch radiofrequency ablation; SOD, Superoxide dismutase; SPORT, Spine Patient Outcomes Research Trial; SQS, Subcutaneous nerve stimulation; SSSD, Single site, single depth; STAI, State-Trait Anxiety Inventory; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; SVF, Stromal vascular fraction; TAC, Total antioxidant capacity; tDCS, Transcranial direct current stimulation; TFESI, Transforaminal epidural steroid injection; TIVAD, Titanium-implantable vertebral augmentation device; TPI, Trigger point injections; TRACP, Tartrate-resistant acid phosphatase; TSQ, Treatment Satisfaction Questionnaire; USPSTF, United States Preventive Services Task Force; VA, Vertebral augmentation; VAPOUR, Vertebroplasty for acute painful osteoporotic fractures; VAS, Visual analog scale; VASPI, Visual analog scale of pain intensity; VBS, Vertebral body stenting system; VCF, Vertebral compression fractures; WBC, White blood cell; WHO, World Health Organization; WHOQoL, World Health Organization quality of life health questionnaire; ZCQ, Zurich Claudication Questionnaire.

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