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EVIDENCE-BASED REVIEW

Update of Evidence-Based Interventional Pain Medicine according to Clinical Diagnosis

1. Lumbosacral radicular pain

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Abstract

Introduction: Patients suffering lumbosacral radicular pain report radiating pain in one or more lumbar or sacral dermatomes. In the general population, low back pain with leg pain extending below the knee has an annual prevalence that varies from 9.9% to 25%.

Methods: The literature on the diagnosis and treatment of lumbosacral radicular pain was reviewed and summarized.

Results: Although a patient's history, the pain distribution pattern, and clinical examination may yield a presumptive diagnosis of lumbosacral radicular pain, additional clinical tests may be required. Medical imaging studies can demonstrate or exclude specific underlying pathologies and identify nerve root irritation, while selective diagnostic nerve root blocks can be used to confirm the affected level(s). In subacute lumbosacral radicular pain, transforaminal corticosteroid administration provides short-term pain relief and improves mobility. In chronic lumbosacral radicular pain, pulsed radiofrequency (PRF) treatment adjacent to the spinal ganglion (DRG) can provide pain relief for a longer period in well-selected patients. In cases of refractory pain, epidural adhesiolysis and spinal cord stimulation can be considered in experienced centers.

Conclusions: The diagnosis of lumbosacral radicular pain is based on a combination of history, clinical examination, and additional investigations. Epidural steroids can be considered for subacute lumbosacral radicular pain. In chronic lumbosacral radicular pain, PRF adjacent to the DRG is recommended. SCS and epidural adhesiolysis can be considered for cases of refractory pain in specialized centers.

KEYWORDS

epidural adhesiolysis/epiduroscopy, epidural corticosteroids, evidence-based medicine, lumbosacral radicular pain, pulsed radiofrequency treatment, spinal cord stimulation

INTRODUCTION

This narrative review on lumbosacral radicular pain is an update of the 2010 article published in the series "Evidence-based Interventional Pain Medicine According to Clinical Diagnoses."[1]

Lumbosacral radicular syndrome (LRS) is characterized by radiating pain in one or more lumbar or sacral dermatomes; it may or may not be accompanied by other radicular symptoms or decreased sensory and/or motor function. In the literature, this disorder is also referred to as sciatica, ischias, or nerve root pain. A consensus approach toward standardization highlights huge differences in low back pain definitions and diagnosis, which make comparison of epidemiological data difficult.[2] The terms radicular pain and radiculopathy are sometimes used interchangeably, although they are not synonymous. Radicular pain refers only to pain radiating in a dermatomal distribution, while in the case of radiculopathy, objective sensory, motor, and/or reflex loss are usually present.[1] The word radiculopathy derives from the Latin term "radix," meaning "root," and the Greek term "patheia," which means "suffering" and is the basis for the term "pathology," so technically a person may have pathology of a nerve root that spares motor and sensory fibers. In this review, lumbosacral radicular pain is considered to be pain radiating into one or more dermatomes caused by nerve root inflammation and/or compression.

The annual prevalence of LRS in the general population, described as low back pain with leg pain traveling below the knee, varies from 9.9% to 25%. Although uncommon, it is important to note that sacroiliac joint, facet joint, and discogenic pain may also extend below the knee, depending on the levels involved and the magnitude of the stimulus[3]; hence, studies that seek to identify radicular pain based on symptoms without confirmatory tests may overestimate its prevalence. Because the point prevalence (1.6% to 13.4%) and lifetime prevalence (12% to 43%) are so high,[4] radicular pain may be among the most common forms of neuropathic pain.[5,6] The prevalence is highest in individuals between 45 and 64 years old.[7] The most important risk factors are male gender, obesity, smoking, history of lumbar pain, anxiety and depression, an occupation that requires lengthy periods of standing and bending forward, heavy manual labor, lifting heavy objects, and being exposed to vibration.[8]

The most common cause of radicular pain is lumbar disk protrusion or herniation, which can result in nerve root inflammation and/or compression.[9]

There is a lack of consensus regarding the evolution of radicular pain. From a practical standpoint, it is reasonable to define the period of acute pain as up to 1 month (in view of the high percentage of people who spontaneously recover during this period), subacute between 1 and 3 months, and chronic pain from 3 months onward (in view of reduced recovery after this period).[10] Pain completely or partially resolves in 75% of the patients within 3 months of onset, irrespective of visible nerve root compression on imaging.[11–13] This is confirmed in imaging studies, where most herniated discs retract or even completely resolve within 2 years of a repeat MRI in patients with LRS who have been treated conservatively. The extent of reduction is dependent on the type of protrusion such as sequestration, prolapse, or disk bulging with an intact annulus, which is less likely to recede.[14,15]

Despite spontaneous anatomical resolution in most protruded disks, about 25% of patients continue to experience pain after 3 months, which is consistent with the imperfect correlation between lumbar radicular symptoms and MRI findings after disk prolapse. Some studies have shown that females with LRS have worse outcomes compared to their male counterparts, with one randomized trial estimating the unadjusted odds for a long-term poor outcome as 3.3 times higher for female patients than for males.[16]

Degenerative spinal changes such as *spinal canal stenosis* can lead to radicular pain. The North American Spine Society (NASS) defines lumbar spinal canal stenosis (LSS) as a condition in which there is diminished space available for the neural and vascular elements in the lumbar spine secondary to degenerative changes in the spinal canal.[17] LSS can be classified based on the location of the stenosis (ie, central, lateral recess, or foraminal).[18] Radicular pain in LSS can be caused by a combination of mechanical compression, inflammation of nerve roots, and/or vascular congestion. It has been demonstrated that a decreased oxygen supply to the cauda equina and nerve roots, due to decreased blood circulation, can lead to radicular pain in patients with spinal stenosis.[19] Spinal ischemia can induce the activation of extracellular signal-regulated protein kinase (ERK), which is involved in pain sensation in superficial dorsal horn neurons.[20] A prospective study evaluating the long-term clinical course of LSS identified only severe intermittent neurogenic claudication (defined as a walking radius of <100 m) as being a significant risk factor for poor outcome.[21]

METHODOLOGY

This narrative review is based on the article "lumbosacral radicular pain" published in 2009.[22] In 2015, an independent company, Kleijnen Systematic Reviews (KSR), performed a systematic review of the literature for the period 2009–2015 based on existing systematic reviews (SRs) and randomized controlled trials (RCTs).[23,24] For the current article, an updated search was conducted with the PubMed, for the period 2015–2022, using "lumbar" OR "lumbosacral" AND "radicular" AND "pain," cross-referenced with interventional pain management techniques and terminology such as "epidural" AND

"steroid"; "pulsed radiofrequency"; "epidural lysis"; and "spinal cord stimulation." Additionally, the reference sections of all articles reviewed were searched to obtain missing publications.

DIAGNOSIS

History

The patient may experience radiating pain as sharp, piercing, shooting, or burning. Typically, leg pain is predominant over back pain, though most people with radicular pain experience axial pain as well since the pathology that leads to nerve root compression can also cause nociceptive pain. Pain caused by a herniated disc classically increases with sitting or coughing and can be attenuated by lying down or sometimes by walking.[7] Conversely, patients with central lumbar spinal canal stenosis (LSS) will typically report intermittent neurogenic claudication.[25] In patients with LSS, radicular pain as well as neurological signs (such as motor weakness or sensory loss) will progressively increase when walking, which often leads to significant functional deterioration. These symptoms often improve upon bending forward, including stopping to sit down.[26] Patients with LSS can be entirely asymptomatic at rest.[27]

In addition to pain, patients often report paresthesia in the affected dermatome. Since the dermatomal representation of Keegan contains several flaws, some guidelines recommend the figure by Lee et al.[28,29] (see Figure 1).

The distribution of pain along a dermatome can be indicative of the spinal level involved; however, there are large variations in radiation patterns with frequent overlap of dermatomes. Anatomical multisegmental innervation and overlap of dermatomes may complicate interpretation of the relationship between pain and involved nervous structures.[30]

The severity of pain as well as impact on quality of life, including work and sleep, should be evaluated. Pain severity (as measured on the Numeric Rating Scale [NRS]) can influence the threshold for different treatment modalities, though pain is inherently subjective and there is an imperfect correlation between pain and imaging findings in lumbosacral radiculopathy.[31] Patients with high disease burden are more likely to fail conservative and interventional treatments, which may be due to multifactorial reasons (eg, inability to participate in physical therapy, central sensitization, and greater psychiatric co-morbidity).[32]

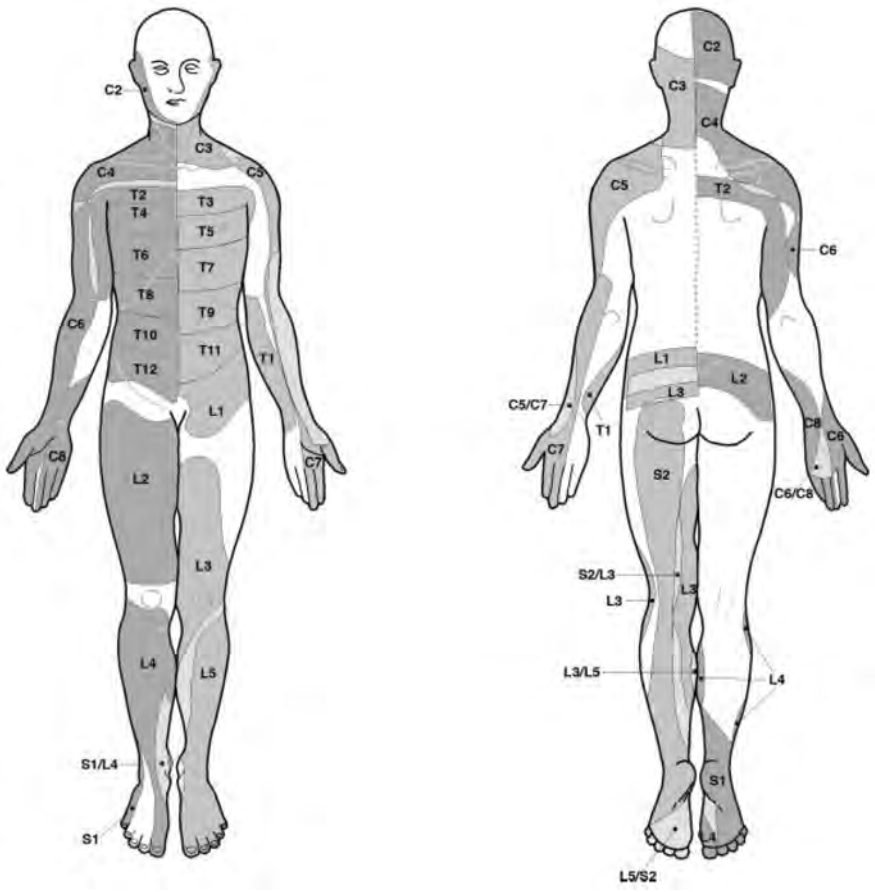

FIGURE 1 Evidence-based dermatome map representing the most consistent tactile dermatomal areas for each spinal dorsal nerve root. (From Lee et al.[29] with permission of the publisher).

Physical examination

The diagnostic value of anamnesis and physical examination is confounded by the absence of a gold standard. The most meaningful parameter from a patient's history is pain distribution, as not every patient will present with focal neurological sensory or motor findings.[33] The clinical test with the highest sensitivity for the lumbosacral radicular syndrome involving the lower lumbar nerve roots is the passive straight-leg-raising test (Lasègue test). If radicular pain can be elicited under 60°, there is a high likelihood that nerve root inflammation or compression is present. However, the accuracy of this test in the detection of lumbosacral radicular syndrome due to a herniated disc varies considerably: the global sensitivity is 0.92 with a specificity of 0.28.[34] This specificity drops even more when the test is positive above 60°. In contrast, the crossed straight-leg-raising test has high specificity (0.90), which comes at the expense of sensitivity (0.28).[34] Specificity of motor signs (muscle atrophy/paresis) and reflex abnormalities is high (Table 2). For the determination of the level of a possible herniated disc, dermatomal distribution is considered informative, though combining dermatomal distribution with motor, sensory, and reflex tests result in the greatest accuracy.[33,35] For identifying L2-4 radicular pain, the femoral stretch test has both high sensitivity (1.0) and high specificity (0.83) according to one systematic review.[36] This needs to be confirmed in high-quality clinical trials.

In practice, the presence of signs indicative of L4 (diminished patellar reflex or foot inversion) or S1 nerve root involvement (lessened Achilles' tendon reflex) is evaluated through neurological examination. An L5 motor paresis will often present clinically with "foot stomping" or "foot drop" and decreased ankle dorsiflexion and/or extension of the toes, while an S1 paresis can cause decreased plantar flexion.[26] If suspected, cauda equina and other[36] neurological disorders (eg, cervical myelomalacia) should be ruled out.

In summary, a diagnosis of lumbosacral radicular syndrome appears justified if the patient reports radicular pain, usually unilateral, combined with one or more positive neurological signs that indicate nerve root irritation or neurological loss of function.[11] A screening tool that can be used to distinguish axial from radicular back pain is the StEP (Standardized Evaluation of Pain questionnaire), which integrates history taking and physical examination.[37,38]

A peripheral vascular examination, including evaluation of pedal pulses, should be performed in patients who report a history of neurogenic claudication. Peripheral vascular disease can lead to a disease state called "vascular claudication," which presents similarly to neurogenic claudication caused by LSS.[19] The Van Gelderen bicycle test, ankle-brachial index, and a thorough neurological and vascular exam can all be useful in distinguishing vascular from neurogenic claudication.[39]

An overview of the accuracy of findings of clinical assessment for diagnosis of nerve root compression due to a herniated disc according to either MRI or surgical findings is provided in Table 1.

Additional tests

Imaging studies

In view of the favorable natural evolution of lumbosacral radicular pain in about three-quarters of patients, additional examinations have little value in the acute phase in the absence of serious or progressive neurological findings.[42,43] When imaging is indicated, magnetic resonance imaging (MRI) is preferred because of its better visualization of soft tissues and absence of radiation exposure.[11] In patients with the clinical diagnosis of LRS, a herniated disc can be found at the concordant level in 65% to 83% of cases.[44–46]

The specificity of MRI, however, is low. This is illustrated by the observation that a herniated disc on MRI or computer tomography (CT) can be identified in 20%–36% of asymptomatic individuals.[47] There is also little correlation between the severity of a pain and the magnitude of a spinal disk herniation, with approximately one-third of patients with clinical LSR showing no nerve root compression on imaging. The symptoms of radicular pain can also disappear after conservative therapy without a corresponding decrease in the volume of the herniated disc.[48–50] Similarly, only weak correlations exist between the severity of central and lateral recess stenosis, and pain and functional disability,[51] which is confirmed by the Minimal Invasive Spine Treatment (MIST) guidelines.[52] If the clinical picture is unclear or there is a lack of radiological correlation, electromyography (EMG) and nerve conduction studies (NCS) can be performed to differentiate lumbar radicular syndrome from peripheral neuropathy (sensitivity 0.45 to 0.65).[53]

Selective segmental nerve blocks

Selective spinal segmental nerve blocks, also called selective spinal nerve root blocks (SNRB), may be indicated to evaluate atypical extremity pain, when imaging and clinical presentation do not correlate, when MRI or electrodiagnostic studies are non-corroborative, in patients with transitional anatomy, and to assess anomalous innervation (eg, conjoined nerve roots). In a lumbosacral radicular syndrome without clear signs of a focal neurological deficit, variable hypesthesia is often present in patients selected for diagnostic

TABLE 1 Accuracy of findings on clinical assessment for diagnosis of nerve root compression due to a herniated disc, according to either MRI or surgical findings.[a34] (with permission of the publisher).

Assessment and finding	Patient sample	Reference standard	Sensitivity	Specificity	Positive predictive value	
					10% prevalence	50% prevalence
Clinical history[b]						
Leg pain worse than back pain	Referred from primary care to neurology	MRI	82	54	17	64
Typical dermatomal pattern of symptom distribution	Referred from primary care to neurology	MRI	89	31	12	56
Pain worsened by coughing, sneezing, or straining	Referred from primary care to neurology	MRI	50	67	14	60
Physical examination[c]						
Positive ipsilateral straight leg-raising test	Primary care	MRI	64	57	14	60
	Referred for surgery	Surgical findings	92	28	13	56
Positive crossed straight-leg-raising test	Referred for surgery	Surgical findings	28	90	24	74
Paresis	Primary care	MRI	27	93	30	79
Muscle atrophy	Referred for surgery	Surgical findings	15–38	50–94	3–41	23–86
Impaired reflexes[d]	Primary care	MRI	15	93	19	68
Neurologist's assessment based on clinical history and physical examination[b]	Referred from primary care to neurology	MRI	81	52	16	63

[a] Estimates vary substantially among studies, in part because of variations in patient selection criteria and procedures. The prevalence of a herniated disc as the cause of back and leg pain may be approximately 10% in primary care and 50% in specialty care populations. MRI denotes magnetic resonance imaging.

[b] Data on clinical history are calculated from a study by Vroomen et al.,[40] which included patients with back and leg pain. MRI showed herniated disc and nerve root compression in 152 patients, with 122 having other diagnoses.

[c] Estimates are based on data from a systematic review of multiple studies by van der Windt et al.[41]

[d] The L5 nerve root affects neither the Achilles tendon nor the patellar reflex but is one of the two most commonly affected nerve roots. The tibialis posterior, tibialis anterior, and medial hamstring reflexes have been used to identify L5 nerve root pathology but are characterized by relatively low sensitivity and specificity. Thus, in a person with suspected L5 radicular syndrome, normal reflexes convey limited information.

TABLE 2 Red flags (adapted from Knezevic et al.[3]).

Patient history
Neoplasms
Physical traumas
Advanced age:
• >50 years (cancer risk)
• >70 years (fracture risk)
Unintentional weight loss
Immunodeficiency
• Tuberculosis exposure
• Indwelling catheters
Osteoporosis
Medication history
Intravenous drug abuse
Corticosteroid use or other immunosuppressive drug use
Signs and symptoms
High fever (>38°C)
Worst pain at rest or at night
Saddle anesthesia
Weakness in lower limbs
Bladder or bowel dysfunction (eg, overflow incontinence and urinary retention)
Gait disturbance
Abrupt, unexplained weight loss
Night sweats
Inflammatory back pain[61]

SNRB.[54] These changes in sensory function can fluctuate in time and location. This is important because studies by Wolff et al. found that selective nerve root blocks may be less informative in patients with long-standing, non-dermatomal sensory changes, and that pain reduction is less common than hypesthesia, which can vary significantly.[30,55]

An intraforaminal segmental nerve block may simultaneously anesthetize the nervus sinuvertebralis, responsible for afferent input from the nearby disci intervertebrales (superficial annulus fibrosus), the ligamentum longitudinale posterius, and the ventral dura mater and nerve root sleeve. This undermines specificity and increases the risk of a false-positive result. The ganglion spinale (dorsal root ganglion, DRG) is also usually blocked, including the sensory nerve fibers of the ramus dorsalis of the segmental nerve, which innervate lumbar spinal muscles and nearby facet joints. It has been shown that pain can be reduced by a peripheral nerve block when the etiology of the pain is located proximal to the nerve. Thus, a peripheral nerve block may affect pain from proximal spinal nerve root irritation causing corresponding pain in the leg and back.[56,57] The specificity of a single-level diagnostic block is influenced by the injectate volume. In one study, 78.8% of nerve root blocks were selective for the specified nerve root after injecting 0.2 mL of dye, while 0.5 mL of contrast extended to an adjacent level in 30% of cases, and 1.0 mL diffused to an adjacent segment in 67% of cases, rendering the injections non-specific.[58] Another study found that when pain was reproduced with stimulation and relieved with anesthetic injection, a selective nerve root block successfully predicted the level of surgical pathology in over 95% of cases; when pain was reproduced during injection but not relieved, multiple nerve roots tended to be involved; and when pain was relieved by local anesthetic injection but not reproduced during injection, the block was unhelpful in identifying surgical pathology.[59] There has been discussion in the literature regarding dermatome mapping, but this technique requires validation.

Overall, the evidence suggests that a negative selective nerve root block has greater predictive value than an isolated positive block.[30] The sensitivity of SNRB (0.80–0.91) is greater than the specificity (0.17–0.33), with low-volume blocks being more specific than high-volume blocks. These findings make routine SNRB unsuitable as preoperative surgical prognostic tests, though studies have found them helpful to identify candidates for pulsed radiofrequency treatment (PRF).[60]

Differential diagnosis

In cases of acute low back pain with radicular symptoms, serious underlying pathology or physical abnormalities, which can account for the complaints (ie, "red flags"), should be ruled out (Table 2 lists the red flags).

The value of red flags is limited. 80% of patients with acute low back pain present with at least 1 red flag, but <1% are found to have a serious underlying disease.[62] Most red flags are non-specific and have limited utility in facilitating faster detection of a serious underlying disease. In fact, the low specificity of red flags often results in unnecessary referrals, imaging, and other diagnostic evaluations.[62–64] The presence of radiculopathy may also increase the reporting of red flag symptoms such as gait disturbances and intense pain not relieved at night. Nonetheless, a combination of different red flags, or red flags corroborated by multiple signs or symptoms, warrants further investigation.

When making a differential diagnosis, neurological disorders and inflammatory/metabolic causes (Lyme disease, diabetes, ankylosing spondylitis, Paget's disease, arachnoiditis, and sarcoidosis) must be considered and ruled out.[26] The differential diagnosis in patients with lumbar spinal canal stenosis includes discogenic pain, spondylolisthesis, sacroiliitis, and facet syndrome. Often these degenerative conditions coincide and complicate reaching a definitive diagnosis.[65]

A large, central disk herniation that compresses the low lumbar and sacral nerve roots may result in acute *cauda equina syndrome*. This can provoke significant bowel and micturition dysfunction with saddle anesthesia and diminished anal sphincter tone. Involvement of

the lumbar nerve roots leads to weakness in the legs that may progress to paraplegia. Rapid recognition of these symptoms and referral for emergency surgery is strongly recommended.[26]

TREATMENT OPTIONS

Conservative management

(Sub)acute radicular complaints (0–12 weeks)

There is no strong evidence for the effectiveness of conservative treatments for lumbosacral radicular syndrome.[66] A recent guideline recommends providing *information to the patient* about the causes and prognosis of lumbosacral radicular syndrome, and encouraged them to continue with normal activities.[67]

There is no difference between the advice for *bed rest* and the advice *to remain active*.[68]

The use of *NSAIDs (Non-Steroidal Anti-Inflammatory Drugs*) showed positive results in three randomized trials for acute radicular pain compared to placebo.[69,70] However, a more recent systematic review found that NSAIDs were no more effective than placebo in reducing pain or disability but did find a statistically significant global improvement associated with NSAIDs compared with placebo at short-term follow-up (up to 3 weeks).[71] In general, guidelines do not recommend NSAIDs for neuropathic pain, and they are widely acknowledged to be more effective for nociceptive pain.

Systemic corticosteroids

A 2012 meta-analysis[72] shows moderate-quality evidence favoring corticosteroids over placebo in reducing pain after 2 weeks and up to 3 months. In two later trials, the results were less favorable. One of these trials[73] reported pain relief at 24 h but not at 6 weeks. Another large trial[74] showed a small reduction in disability (but no improvement in pain) in favor of corticosteroids at 3 weeks and 1 year.

Benzodiazepines

An RCT comparing diazepam with placebo for subacute pain demonstrated 50% or more pain reduction after 7 days in 41% of the patients in diazepam group and in 79% of the patients in the placebo group.[61] The authors concluded that benzodiazepines should not be used in patients with subacute radicular pain.

Anticonvulsants

An RCT comparing pregabalin with placebo for leg pain included 80% presenting with subacute LRS.[75] After 8 weeks, there was no significant difference between both groups. Anticonvulsants therefore do not seem effective in the acute phase of LRS; moreover, there is a growing concern of the role these agents play in overdose deaths.[76]

Opioids

An RCT comparing morphine to placebo for patients with radicular pain found no benefit from morphine in the reduction of pain and disability at 10-day follow-up.[77] Currently, there is scant evidence supporting long-term opioids in patients with subacute LRS. In view of the opioid crisis, caution is advised regarding opioids for subacute lumbosacral radicular pain.

Exercise therapy is often considered a first-line treatment. There is, however, a lack of evidence supporting this intervention.[33,66] A randomized study was able to demonstrate a better outcome after 52 weeks in patients who received physiotherapy in the form of exercise therapy combined with conservative therapy from a general practitioner in comparison with patients who received only conservative therapy (79% versus 56% Global Perceived Effect, respectively). However, this intervention does not appear to be cost-effective.[78]

In summary, there is low-quality evidence that exercise is better than no treatment in the short-term, but evidence for a long-term effect is lacking.[79]

Chronic radicular complaints (>12 weeks)

The role of physiotherapy in patients with chronic radicular pain is also unclear since there are few randomized studies available.[80] In one systematic review that included six studies, different forms of manual therapy were found to be more effective than various active controls, though only one trial was identified as high quality.[81] For chronic lumbosacral radicular pain, a trial period with *tricyclic antidepressants* (TCAs) such as amitriptyline is often initiated.[82] However, the evidence supporting TCA for chronic lumbosacral radicular pain is limited.[77,83]

Anticonvulsants are a possible alternative for the treatment of neuropathic pain. In chronic radicular pain, however, most trials do not demonstrate significant benefit.[71,75,84]

Opioids often were used as a last resort for therapy-resistant chronic pain for select patients, but it is uncertain whether morphine leads to a greater pain reduction compared with placebo for chronic lumbosacral radicular pain. In a placebo-controlled 4-phase crossover study, neither morphine, nortriptyline, nor the combination was found to be effective compared to placebo.[77] In view of the opioid crisis, caution is advised regarding chronic opioid therapy for lumbosacral radicular pain.[85]

Neurogenic claudication

Few high-quality randomized controlled trials regarding conservative management in patients with lumbar spinal canal stenosis have been published.[86] Options include pharmacological treatment, exercise therapy, and multidisciplinary rehabilitation.

No benefit has been demonstrated for opioids or NSAIDs compared to paracetamol in patients with spinal canal stenosis.[87,88]

A recent clinical practice guideline reported that a trial of serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants can be considered based on very-low-quality evidence, but recommended against the use of NSAIDs, paracetamol, gabapentinoids, muscle relaxants, and opioids.[89]

A narrative review reported that short-term clinical improvement can be achieved with PGE1-treatment in patients with LSS.[90]

Exercise therapy is often proposed in patients with neurogenic claudication, yet evidence for this treatment modality is scarce. A systematic review found low-quality evidence that physical therapy is beneficial.[91] A post hoc analysis of the Spine Patient Outcomes Research Trial (SPORT) found a positive association between physical therapy and long-term outcomes in patients with LSS.[92] A randomized trial demonstrated that similar results were achieved with physical therapy compared to surgical decompression.[93] A more recent RCT showed long-term improvement in patients with neurogenic claudication with medical care, group exercise, and manual therapy/individualized exercise.[94] Outcome measurements included self-reported symptoms and walking capacity. The greatest short-term effect in this study was achieved with the combination of manual therapy and individualized exercise.

Interventional management

Interventional techniques are indicated for patients with persistent radicular pain despite conservative management. Epidural administration of corticosteroids may provide a beneficial effect for up to 3 months after a single injection, with some studies demonstrating better results in patients with a shorter duration of pain.[95–97] Epidural corticosteroid administration is therefore indicated in cases of subacute radicular pain. In patients with chronic radicular complaints, epidural corticosteroids generally do not provide any long-term improvement, though some studies demonstrate benefit with repeat procedures.[98,99] Pulsed radiofrequency (PRF) treatment is another treatment option for chronic radicular pain. Adhesiolysis, either as a standalone treatment or in combination with epiduroscopy, is predominantly used for eliminating scar tissue in the epidural space, though individuals without suspected scar tissue may also benefit.[100,101] Spinal cord stimulation (SCS) is documented to be effective in the treatment of patients with persistent spinal pain syndrome type 2 (PSPS type 2),[102] though some literature also supports its use non-operated patients. Recently, growing attention has been directed toward regenerative medicine.

Epidural corticosteroid administration

Herniated discs

The rationale for epidural corticosteroid administration rests on the anti-inflammatory effect on the ganglion spinale/dorsal root ganglion (DRG), suppression of ectopic discharges from injured nerve fibers, and inhibition of prostaglandin synthesis.[103] In patients with a herniated disc, when local anesthetics are added, they enhance blood flow to ischemic nerve roots. There are three approaches for epidural corticosteroid administration: interlaminar, transforaminal, and caudal.

Transforaminal corticosteroids. Transforaminal administration allows for the more precise application of corticosteroids at the level of the inflamed nerve root. There have been several systematic reviews published on this subject in recent years, with direct and indirect findings suggesting superior pain relief compared to interlaminar epidural steroid injections.[104–108]

Caudal corticosteroids. In a comparative study, the effectiveness of caudal, interlaminar, and transforaminal corticosteroid administration in the epidural space was compared in patients with radicular pain due to disk herniation. The transforaminal approach provided the best clinical results.[109]

Special attention has been devoted by societies and government regulatory bodies to prevent neurological complications from transforaminal administration and high-volume caudal administration. To allow for rapid imaging and treatment in the event of a potential neurological complication, it is advisable to limit the amount of local anesthetic since lower doses generally allow rapid neurological resolution.[110,111] Since caudal infiltration requires larger amounts of local anesthetic in larger volumes to be effective, this technique is less ideal from a safety point of view. High volumes rapidly injected epidurally have been associated with blindness.[112]

Interlaminar corticosteroids. The available evidence concerning interlaminar corticosteroid administration has been studied in systematic reviews. Interlaminar injections provided less leg pain relief compared to transforaminal injections and possibly the caudal approach, which may be related to the higher volumes required with the latter, though this can also dilute the concentration of medication reaching the area(s) of pathology[113,114]; hence, a midline interlaminar approach has become less common over recent years. In view of the higher risks for catastrophic complications with transforaminal steroid delivery, the parasagittal interlaminar approach has gained popularity, with randomized studies finding superior results compared to midline interlaminar epidural steroids and comparable results to transforaminal delivery.[115,116] The less auspicious results with midline interlaminar injections are ascribed to the fact that there is no guarantee that the medication reaches the ventral epidural space and DRG, which are likely sites of inflammation.[117]

Reviews on effectiveness. In general, reviews on epidural steroid injections (ESI) have yielded mixed results, with one review finding that studies and evidence-based reviews performed by pain practitioners were more likely to yield positive findings.[118] These reviews can be summarized as follows: Epidural steroid infiltrations (ESI) are more effective for alleviating lumbosacral radicular pain than *conservative treatments* in terms of short- and intermediate-term benefit.[119]

Regarding placebo-controlled studies, ESI are probably more effective *compared to active control* (local anesthetic and/or saline) in reducing leg pain at short-term follow-up, and probably slightly more effective in reducing disability at short-term follow-up. At intermediate-term follow-up after 6 weeks, the effects favoring epidural steroid injections wane.[120]

Systematic reviews have shown that most of the very short-term effects from epidural steroid injections derive from the injection itself rather than the steroids.[121] One systematic review found moderate-quality evidence that epidural corticosteroid with or without local anesthetic administration reduces leg pain better than sham injection up to 3 months after the intervention in the treatment of lumbosacral radicular pain refractory to conservative treatment.[24]

In summary, multiple randomized controlled trials and high-quality observational studies provide varying degrees of evidence supporting the efficacy of ESI compared to placebo in reducing pain, improving function, and reducing reliance on other health care in patients with radicular pain due to disk herniation,[122] with the effect size being modest, and transforaminal and parasagittal interlaminar ESI providing better outcomes than interlaminar injections.

Surgery-sparing effect. In a randomized double-blind study, patients scheduled for surgery received a transforaminal epidural injection with local anesthetic only or local anesthetic with corticosteroid. At 13 to 28 months of follow-up, 20/28 patients in the local anesthetic with corticosteroid group decided not to undergo surgery, compared to 9/27 patients receiving local anesthetic alone.[123] The majority (81%) of patients who had not had surgery 1 year after infiltration were able to avoid surgery after 5 years.[124] A systematic review evaluating the ability of ESI to prevent surgery found a small surgery-sparing effect in the short-term (<1 year), but not long-term.[125]

Spinal canal stenosis

Epidural infiltration of local anesthetics in combination with corticosteroids is often proposed in patients with neurogenic claudication to provide pain relief by reducing local inflammation and nerve root ischemia, which can be caused by the stenosis.[25] An RCT demonstrated significantly greater pain reduction after bilateral transforaminal epidural corticosteroid injections compared to interlaminar epidural corticosteroid injections.[126] A meta-analysis found that epidural corticosteroid injections provide limited short- and long-term improvement in pain and walking distance in patients with LSS.[127]

Recent clinical practice guidelines recommend against the use of epidural steroid injections in patients with spinal canal stenosis.[24,89] This recommendation was formulated to a large extent based on a randomized controlled trial, which showed that in the treatment of lumbar spinal canal stenosis, epidural injection of corticosteroids with local anesthetic offered minimal benefit at 6 weeks and 1 year as compared with injection of local anesthetic alone.[128,129] Interestingly, among patients in whom there was reduced pain and improved function 6 weeks after the initial injection, these outcomes were maintained at 12 months. Although no significant benefit for corticosteroid injection was demonstrated, there was no sham injection group. Therefore, the effectiveness of epidural infiltration of lidocaine alone, which contain therapeutic effects independent of steroids,[121,130,131] cannot be disregarded. Repeated injections in either group offered no additional benefit if the initial injection did not reduce pain or improve function.

In summary, transforaminal epidural corticosteroid administration may be more efficacious than interlaminar approaches. In practice, however, due to rare but potentially catastrophic neurological complications associated with the transforaminal approach, the interlaminar and caudal approaches should also be considered, particularly in individuals with bilateral symptoms.

(Pulsed) radiofrequency treatment

The application of conventional radiofrequency (RF) treatment (>67°C) adjacent to the lumbar ganglion spinale (dorsal root ganglion, DRG) has lost interest because no added value could be demonstrated in comparison with a sham procedure in a randomized, double-blind, sham-controlled study.[132]

Yet, pulsed radiofrequency (PRF) has gained interest in recent years, though reimbursement issues in some countries limit widespread utilization. In a systematic review and meta-analysis, 4 of 6 RCTs found PRF treatment resulted in greater reductions in pain scores after 12 weeks compared to the control groups.[133] PRF is therefore recommended in patients with chronic radicular pain, defined as pain lasting for more than 3 months.[134]

In one RCT, PRF with transforaminal steroid and local anesthetic injections was found to provide better pain relief, but not functional improvement, compared to sham PRF with transforaminal injections in patients with lumbar spinal stenosis.[135] Reports of complications with PRF are rare.

Epidural adhesiolysis/epiduroscopy

Epidural adhesiolysis aims to mechanically dissolve epidural scar tissue to alleviate radicular pain and facilitate the spread of analgesic substances to possible areas of pain generation. There is currently no consensus on the method, the solution to be used or the duration of administration. Heavner and colleagues compared the use of 0.9% NaCl with 10% NaCl with or without hyaluronidase in 59 patients with a lumbosacral radicular pain, with a catheter left in place for 3 days.[136] Although there were no significant differences between groups, the two groups that received hypertonic saline required less treatments than the two that received normal saline. Other investigators have same-day protocols to be more effective than standard medical management.[137]

The use of video imaging of the epidural space, called epiduroscopy, allows visualization and identification of adhesions or lesions, enabling targeted adhesiolysis.[138] Although these are two different procedures, the results in the literature are often reported together, which makes interpretation challenging. Possible mechanisms of action include the washing out of inflammatory cytokines, increasing perfusion to ischemic nerve roots, mechanically disrupting scar tissue that may be contributing to pain, and enhancing the flow of steroids and local anesthetic to pain-generating tissue.[100,101]

Clinical trials for herniated disc, spinal stenosis, and FBSS/PSPS have shown superiority of epidural adhesiolysis over conventional medical management, traditional ESI, and sham ESI. Gerdesmeyer published a 10-year follow-up[139] of his RCT comparing percutaneous adhesiolysis with placebo.[140] This study included operated and non-operated patients and showed significant improvement in the active group after 12 months. During the 10-year follow-up, an effect was still observed in the group treated with adhesiolysis; however, the generalizability is limited by the multiple other co-interventions patients received during this time frame. Systematic reviews on this topic provide conflicting results: in one systematic review, three reports suggested that adhesiolysis was effective for pain and disability. However, two of these studies contained serious methodological flaws. 58 adverse events were reported among 130 patients undergoing endoscopic adhesiolysis, and 19 among the 110 undergoing percutaneous adhesiolysis. They concluded that quality evidence supporting the efficacy and cost-effectiveness of adhesiolysis for treating FBSS was nonexistent, whereas the evidence on its effectiveness and safety was insufficient.[141] However, another systematic review was very positive: Based on nine RCTs, the authors found an evidence level of I to II and provided a recommendation for percutaneous adhesiolysis in managing low back and lower extremity pain.[142]

A systematic review on epiduroscopy found a clinically relevant reduction in pain and disability scores at 6 to 12 months after mechanical adhesiolysis in FBSS/PSPS patients. The quality of evidence was moderate, and the level of recommendation was weak. Practitioners should consider the benefits of epiduroscopy only after carefully weighing the risks and benefits in individual patients with FBSS or other reasons for suspected epidural scar tissue.[143]

Spinal cord stimulation

Spinal cord stimulation (SCS), also referred to as dorsal column stimulation (DCS), is an established interventional treatment modality reserved for patients with pain refractory to conservative therapy. SCS consists of the introduction of electrodes in the epidural space – either percutaneous or through laminectomy – with the purpose of electrical stimulation of the dorsal aspect of the spinal cord to modulate neural function and reduce pain. The rationale for this technique finds its origin in the gate control theory, first described by Melzack and Wall.[144] This theory proposes that selective activation of large, non-nociceptive nerve fibers can "close the gate" of nociceptive signals in the spinal cord. Since the first report of the clinical effectiveness of SCS by Shealy et al. in 1967,[145] major technological advancements have been made including new insights on the working mechanisms.[146] Although the gate control theory has played an important role in our understanding of pain transmission and the general principle of classic tonic SCS, several of these new insights illustrate that this theory is oversimplified with more complex neural interactions and cell types being implicated in the working mechanism of this treatment. Furthermore, multiple novel stimulation paradigms have emerged in the past decade, each with a distinct stimulation waveform.[147] These novel waveforms were developed to overcome limitations of paresthesia-based tonic stimulation that persist despite considerable improvements since its inception.

Pain relief with *tonic SCS* is postulated to be mediated by both spinal and supraspinal mechanisms. On the spinal level, tonic SCS directly stimulates large non-nociceptive A-beta fibers localized in the dorsal column. According to the gate control theory, this segmental antidromic stimulation leads to an inhibition of nociceptive signals entering the dorsal horn through small A-delta and C fibers. Concurrent orthodromic stimulation of these A-beta fibers causes paresthesia in the dermatomes innervated by the stimulated nerve fibers. This notion illustrates the requirement

of meticulous overlap between the paresthesia and the painful area with tonic SCS to maximize the pain relief.[148] Supraspinal mechanisms involve the activation of multiple brainstem nuclei by tonic stimulation including the locus coeruleus, the nucleus raphe magnus, and the rostral ventromedial medulla. This activation causes modulation of spinal nociceptive transmission by descending inhibitory projections. *High-frequency SCS* (HF-SCS) refers to the stimulation paradigm whereby the frequency of the stimulation waveform is higher than 1000 Hz. In stark contrast to tonic SCS, where the presence of paresthesia in the painful dermatome is a prerequisite for pain relief, stimulation in the HF-SCS paradigm is administered below the sensory threshold. Animal studies confirm that there is neither activation of A-beta fibers in the dorsal column nor a reduction of evoked responses in the gracile nucleus with this subthreshold stimulation paradigm.[149] *Burst SCS* refers to a stimulation paradigm whereby the waveform consists of multiple "bursts" containing five closely spaced pulses (with a certain "intraburst" frequency). These bursts are delivered with a certain "interburst" frequency. The rationale for burst SCS is to mimic physiological thalamo-cortical neural burst firing patterns, with proposed enhanced synaptic connectivity.[150] Similar to HF-SCS, burst SCS can produce pain relief without the need for paresthesia, which implies that activation of dorsal column A-beta fibers is not the main mechanistic contributor of this stimulation paradigm. *Differential target multiplexed (DTM) SCS* is a stimulation paradigm that consists of multiple waveforms that are different in frequency, pulse width and amplitude. The rationale for this paradigm stems from the finding that tonic SCS modulates gene expression at the target level of the spinal cord as well as the DRG of the corresponding nerve involved in neuropathic pain.[151]

The effectiveness of SCS, including tonic stimulation as well as other stimulation paradigms, has been demonstrated in multiple randomized controlled trials.[152] A systematic review of the evidence for SCS in patients with refractory low back pain who did not have prior spine surgery found 10 studies that showed favorable outcomes on pain, functionality, and quality of life. However, not all studies reported statistical significant findings, and one review found large discrepancies between industry-sponsored and non-industry-sponsored studies.[153,154]

In another systematic review comparing the effect of SCS and paresthesia-free high-frequency SCS, burst SCS, and subperception SCS involving 13 RCTs, the results between treatment groups were comparable.[155]

Patient preference is highly individualized and may be activity dependent. A recent systematic review that included 11 RCTs found that novel waveforms were superior to tonic SCS or placebo in leg and back pain and health-related quality of life. The authors concluded that there is low certainty evidence for considering novel SCS wave forms as a complement to usual care.[156,157]

The two most important determinants for long-term outcome in SCS are assumed to be appropriate patient selection and a SCS trial before final implantation.[158] Clinical screening should include evaluation of psychosocial factors. Of note, depression is significantly correlated with poorer long-term outcome. Untreated major psychiatric disorders and active substance abuse are considered absolute contraindications for SCS implantation. A SCS trial has important diagnostic value, but the cost-effectiveness has not yet been proven.[159]

DRG stimulation

The dorsal root ganglion (DRG) has emerged as a promising anatomical target for neuromodulation due to its unique characteristics, including somatotopic organization.[160] DRG stimulation may provide added value compared to SCS for focal neuropathic pain syndromes, including lumbosacral radicular pain.[161] DRG stimulation has been touted as a treatment in a growing number of indications, though best-practice guidelines are still being refined.

Surgery

For a well-selected population, a surgical intervention results in a more rapid reduction of (sub)acute *radicular complaints* compared to conservative care, but outcomes after 1 to 2 years are generally equivalent.[10,42,162,163]

It is unclear what effect surgery has on the natural course of herniated disc disease, and there is no consensus on the optimal timing of surgery.[164] This is the reason for the uncertainty regarding the benefit of surgery on patients with radicular pain of long duration. A recent RCT with long-term follow-up in patients with radicular pain lasting 4 to 12 months reported better outcomes for surgery compared to a conservatively treated group at 6 and 12 months.[165,166]

For patients with an acute and significant neurological loss of motor function due to a herniated disc (Medical Research Council grade 3 or less), immediate surgical treatment is usually recommended. The initial loss of function can still regress after surgery (ie, in up to 50% of patients).[167,168] It can therefore be surmised that the outcomes for neurological deterioration in cases of herniated disc are determined more by the severity of disease at outset than by the timing of the intervention.[169–171]

Spinal canal stenosis

Surgery is often proposed when neurogenic claudication symptoms deteriorate, and conservative management fails. Spinal stenosis is the most common indication for

spine surgery in patients older than 65 years, with a 15-fold increased utilization observed between 2000 and 2007.[172] A systematic review failed to definitely determine whether surgical or nonsurgical treatment is better for patients with LSS, mainly due to a lack of well-designed studies.[173]

In patients with spinal canal stenosis who present with secondary neurological loss of function after surgical decompression, reflex disturbances and sensory and motor deficits are likely to be permanent or only resolve partially. Up to 70% of patients will continue to have residual neurological abnormalities after decompression,[170] and the risk of permanent neuropathy is greater in patients with central spinal canal stenosis than in those with lateral recess stenosis.[171]

Considerations

Minimally invasive surgeries

In view of the low quality of life of patients with *radicular pain* and failed back surgery syndrome,[174] the high recurrence rate,[175] and the limited evidence supporting conservative treatment, there is a need for interventions to bridge the period until natural recovery occurs or surgery becomes necessary. Minimally invasive lumbar decompression (MILD) is a procedure used to widen the spinal canal in individuals with ligamentum flavum hypertrophy, while interspinous spacers purport to unload intervertebral discs and widen the spinal canal and foramina. In a subset of patients with central spinal stenosis who failed conventional ESI, evidence-based reviews have reported modest benefit for MILD and interspinous spacers based on mostly low-quality studies.[176]

Regenerative medicine

Although regenerative medicine treatments have been anecdotally reported to provide benefit for radiculopathy, the strongest evidence exists for nociceptive, degenerative conditions, which may predispose individuals to radicular pain.

COMPLICATIONS OF INTERVENTIONAL MANAGEMENT

Complications and side effects of epidural corticosteroids

Interlaminar epidural corticosteroids

Dural puncture with or without transient headache [post-dural puncture headache, PDPH] is reported in 2.5% of interlaminar epidural injections.[177] In 5.2% of individuals, minor complications such as blood during needle placement occur. In approximately 4% of patients, the appearance of new neurological symptoms lasting longer than 24 hours after infiltration has been reported. These side effects last for a median duration of around 3 days (1–20 days).[178] More serious complications include arachnoiditis and conus medullaris syndrome, which are more likely to occur after multiple, unrecognized subarachnoid injections. Blindness has been reported and is attributed to retinal hemorrhage that occurs secondary to a rapid increase in retinal venous pressures from the rapid injection of large volumes.[112] Epidural abscesses, bacterial and fungal meningitis that can occur following inadvertent contaminated intrathecal spread, and aseptic meningitis hives also been reported.[179]

Transforaminal epidural corticosteroids

Transforaminal epidural steroid administration should always be performed under fluoroscopy with real-time contrast injection or digital subtraction angiography. The use of X-rays involves a small amount of radiation exposure.

With transforaminal epidural corticosteroid injections, the most frequently reported complications are headache, with or without temporary increase in back and leg pain and temporary loss of muscle strength and sensation.

In a series of 207 patients who received a total of 322 injections, headache occurred in 2–4%, while 0.6% of the patients reported increased pain in the leg.[180] A prospective observational study evaluating 1305 transforaminal epidural steroid injections in 562 patients reported no major complications.[181] Minor complications were reported in 11.5% of cases, with vasovagal reaction being the most frequent side effect (7.4%).

Table 3 provides an overview of reported complications.

Serious neurological complications, though rare, can be catastrophic. Spinal cord infarct can result in paraplegia in the lumbar spine, with the most likely mechanism being injury to, spasm, or particulate steroid embolization in a radiculomedullary artery.[196] The largest radicular artery is the arteria radicularis magna (artery of Adamkiewicz), supplying the anterior spinal artery. In more than 80% of the population, this artery is present in the spinal canal between T9 and L2. However, in a minority of cases, it is present between T7 and L4, and rarely as caudal as S1,[208,209] which results in the possibility that the artery is in the vicinity of the needle during the transforaminal approach. Depot steroid injections can aggregate and embolize if an injection is intravascular; when this occurs in a

TABLE 3 Overview of published case reports on serious side effects and complications.

Author year ref	Type of complication	Number of cases	Classification	Remarks
Young 2002[182]	Transient blindness	1	Blindness	Article mentions 9 previous published cases
Gozal 2016[183]	Oculomotor nerve palsy	1	Eye	Diabetic patient
Bilir 2006[184]	Cauda equina	1	Cauda equina	Resolved spontaneously
Goodman 2007[185]	Dural puncture and subdural injection	2	Dural puncture	
Karppinen 2001[186]	Retroperitoneal hematoma	1	Hematoma	
Desai 2014[187]	Nerve root hematoma	1	Hematoma	
Gungor 2017[188]	Epidural hematoma on contralateral side	1	Hematoma	Severe spinal stenosis
Kim 2019[189]	Epidural hematoma	1	Hematoma	Hematoma at T11-L1, injection at L2-L3
Kabbara 2004[190]	Epidural abscess	1	Infection	MRSA
Hooten 2006[191]	Discitis	1	Infection	
Simopoulos 2008[192]	Vertebral osteomyelitis	1	Infection	MRSA
Eisenberg 2019[193]	Adhesive arachnoiditis	2	Infection	
Finn 2005[194]	Intradiscal injection	1	Intradiscal	
Trinh 2016[195]	Intradiscal injection	1	Intradiscal	Using the Kambin triangle
Houten 2002[196]	Paraplegia	3	Neurological	Distal edema at thoracic level
Huntoon 2004[197]	Paraplegia	1	Neurological	Acute vascular infarct
Glaser 2005[198]	Paraplegia	1	Neurological	Thoracolumbar infarct
Somayaji 2005[199]	Paraplegia	1	Neurological	Thoracic and conus spinal infarction
Quintero 2006[200]	Paraplegia	1	Neurological	MRI showed no spinal cord abnormalities
Kennedy 2009[201]	Paraplegia	2	Neurological	Fluoroscopy and CT guided, spinal cord infarction
Lyders 2009[202]	Paraplegia	1	Neurological	Spinal cord infarction
Thefenne 2010[203]	Paraplegia	1	Neurological	Medullary ischemia
Chang Chien 2012[204]	Paraplegia	1	Neurological	Occurred with proof dose of local anesthetic, injection was performed under DSA
Jeon 2021[205]	Paraplegia	1	Neurological	Cauda equina
Gharibo 2016[206]	Conus medularis infarction	1	Neurological	With non-particulate steroid
Wong 2018[207]	Spinal myoclonus	1	Neurological	Occurred with ropivacaine

critical artery supplying the anterior spinal artery, spinal cord ischemia may result.[210]

Intradiscal injections may occur, especially in patients with far lateral disk herniations with anterior needle placement, with a reported incidence ranging from 0.17% to over 2%.[112,211,212]

The reported cases of serious complications with transforaminal injections warrant a cautious approach. Guidelines have recommended performing transforaminal infiltrations with particulate corticosteroids only below the L3(−L4) level, to administer the injectate fluid during real-time fluoroscopy or digital subtraction angiography, to administer a local anesthetic before injecting depot steroid, and to use only short-acting local anesthetics to enable a rapid neurological evaluation if necessary.[111,213] When proper technique is followed and sedation is avoided, neurological complications are rare.

Endocrine side effects

Cushing's syndrome has been reported in a prospective study evaluating epidurally administered betamethasone dipropionate and betamethasone sodium phosphate.[214] Hyperaldosteronism, hyperglycemia, weight gain, and fluid retention are infrequent indirect complications caused by glucocorticosteroid administration.[180,215] According to a recent literature review, serious side effects and complications are rare and only documented in case reports.[216]

Side effects and complications of radiofrequency treatments

Pulsed radiofrequency treatment (PRF)

In an extensive review of the literature on the use of PRF, no treatment-related neurological complications were identified.[217] For both RF and PRF, generic complications can include tissue burns from equipment malfunction or inappropriate placement of the electrical dispersive pad, and interference with implanted electromagnetic devices. The most common side effect is transient pain over the treated dermatome.

Side effects and complications of epidural adhesiolysis/epiduroscopy

The most commonly reported complications of epidural adhesiolysis are dural puncture, catheter shearing, and infection. Other potential complications include intravascular injection, vascular injury, cerebral vascular or pulmonary embolus, reaction to the injected fluid or medication (steroids, hypertonic saline, hyaluronidase, among others), and administration of high volumes of fluid potentially resulting in excessive epidural hydrostatic pressures, blindness, brain damage, or even death.[218]

Side effects and complications of spinal cord stimulation

Two broad categories of SCS complications can be distinguished: technical or hardware-related complications and biological complications.

Technical complications

Hardware-related complications are more common than biological complications.[219] Lead-related complications are the most prevailing technical complications related to SCS and are reported to be the most common cause for revision surgery due to SCS malfunction.[220] Lead migration can occur in a cranio-caudal direction or a horizontal direction. There seems to be a significant higher risk for lead migration with cervical lead placement compared to thoracic placement, the site for lumbosacral radiculopathy.[221] The reported incidence of lead migration varies from 13.2% to 27%.[219] Lead migration will present as sudden loss of efficacy and paresthesia, or the occurrence of paresthesia in other dermatomes with tonic SCS. The diagnosis can easily be confirmed by performing medical imaging: a plain radiograph of the thoracic (or cervical) spine will demonstrate a shifted lead tip position in most cases compared to periprocedural plain radiographs. Although in some instances the loss of efficacy can be restored by reprogramming, most cases of lead migration will require (minor) revision surgery to reposition the lead tip to its original position and regain the therapeutic effect.

Lead fracture is another possible complication. The reported incidence varies from 5.9% to 9.1%.[221] The most common site seems to be distal to the fixation point in the deep fascia, specifically where the lead enters the epidural space. Lead fracture will present as loss of efficacy or loss of paresthesia (in tonic SCS) and can be easily diagnosed using plain radiography demonstrating a kink or fracture. An abnormally high impedance will be seen when evaluating the stimulation parameters. Revision surgery is often be necessary to restore the therapeutic effect. The incidence of lead fracture and migration is postulated to decrease due to improved anchoring techniques and implant advances.[152] Battery depletion is a side effect inherent to SCS with surgery required to replace a depleted battery. However, it is considered a complication if revision surgery is necessary to replace a battery before the expected date of depletion. Data on the incidence of premature battery depletion are sparse; a literature review reported an incidence of 1.7% in 2004.[222] Rechargeable batteries have been introduced to tackle this issue by increasing the battery lifespan to approximately 9 years. Yet, evidence regarding their cost-effectiveness remains limited.[223] A notification on the handheld device of the SCS will warn the patient of imminent battery depletion, which presents as loss of therapeutic effect. SCS malfunction can also occur due to a change of position of the implantable pulse generator (IPG) or loss communication between the handheld device and the IPG. Patient education on the use of the external handheld device is crucial to avoid patient dissatisfaction. A potential side effect of recharging a SCS is an unpleasant heating sensation perceived over the IPG. This could lead to interrupted charging sessions in extreme cases. Unwanted or unpleasant stimulation occurs in 2.4% of patients with tonic SCS and could lead to patient dissatisfaction or even explant surgery.[222]

Biological complications

Neurological damage is one of the most feared and serious complications of SCS implantation because of potentially permanent morbidity. Immediate damage can be caused by direct needle trauma to the spinal cord and/or nerve roots or by inadvert intramedullary placement of the SCS lead.[152] The incidence of motor damage without epidural hematoma or infection is

reported to be 0.13% with paddle lead implantation by laminectomy.[224] Delayed damage can be caused by compression of the spinal cord and/or nerve roots by the formation of an epidural hematoma, epidural abscesses, or delayed scarring around the epidural electrode. The incidence of epidural hematoma after SCS implantation is reported to be 0.25%–0.3%.[222] Neurological damage can present as new-onset paresthesia, radicular pain, axial low back pain, motor weakness, sensory loss, or autonomic dysfunction. An epidural hematoma can present as a cauda equina syndrome. The use of anticoagulants or anti-platelet drugs is a risk factor for bleeding complications after SCS implantation. Guidelines have been published to guide practitioners in stopping or bridging these medications and to decrease the risk of epidural hematoma.[225] Inadvert dural puncture can occur during percutaneous epidural needle placement, possibly resulting in post-dural puncture headache (PDPH) or cerebrospinal fluid (CSF) leakage into the epidural space or even the surgical wound. The incidence of dural puncture is reported to be 0.3% after percutaneous lead placement and 0.05% after paddle lead placement.[219] PDPH can present as new-onset positional headache, axial (neck) pain, photophobia, or tinnitus. Fluid accumulation at the surgical site can be indicative of CSF leakage. In most cases of PDPH, conservative management with bed rest and analgesics will suffice. Severe cases may necessitate an epidural blood patch to alleviate symptoms.[226] Infection is one of the major complications of SCS implantation and can present as a superficial wound infection, a deep infection, or an epidural abscesses. Superficial wound infections occur within 30 days post-implantation and involve the skin and subcutaneous tissues. Deep infections involve the IPG pocket or the lead track. The incidence of infection is reported to be as high as 10% according to one RCT, while two systematic reviews report infection rates of 3.4% and 4.6%, respectively.[220,222,227] The majority of SCS-related infections are superficial wound infections, with only 0.1% being deep.[220] The most common culprit is the staphylococcus species with positive cultures in 48% of cases.[228] Infection can present with constitutional symptoms including fever, chills, nausea, vomiting, general malaise, or muscle pain. Superficial infections can present as swelling, redness, warmth, and pain at the surgical site. Workup needs to include laboratory testing including inflammatory markers, as well as wound or blood cultures. Prevention is essential and includes prophylactic antibiotics during the perioperative period, adequate skin preparation, strict sterile technique in the operating room, and satisfactory wound hemostasis. Treatment of infection includes antibiotic therapy guided by the microbial report and cultures. In many cases, explant surgery is necessary because partial or no device removal is associated with lower success rates of antibiotic therapy and higher infection relapse rates. Skin erosion due to the hardware, in most cases the IPG, is a rare complication with a reported incidence of 0.2%.[222] The patient will complain of pain at the surgical site or the IPG pocket. In case of deep infections, removal of the hardware is usually necessary. A frequent side effect of SCS is device-related pain or discomfort, often at the IPG pocket or surgical lead-anchor site. The incidence in the literature varies from 0% to 12% and is potentially related to the size of the IPG.[219] In rare cases, explant surgery is necessary to alleviate symptoms. Hypersensitivity reactions ranging from contact dermatitis to IgE-mediated allergic reactions are infrequently reported. These can present as new-onset pain, dysesthesia, rash, or erythema at the IPG pocket or implantation site. An infection must be ruled out in case of suspected hypersensitivity. In the literature, explant surgery successfully resolves the complaints.

Evidence for interventional management

Table 4 gives a summary of the evidence for interventional pain management techniques for lumbosacral radicular pain according to the systematic reviews.

RECOMMENDATIONS

Based on the evidence available regarding effects and complications, we recommend the following techniques for the treatment of LRS, summarized in Figure 2.

- Transforaminal (or parasagittal) epidural corticosteroid injections are recommended for patients with subacute unilateral radicular pain symptoms.
- At L3(−L4) and below, epidural injections can be performed with particulate or non-particulate steroids.
- Above the level of L3(−L4), only non-particulate corticosteroids are recommended for the transforaminal approach.
- In patients with spinal canal stenosis, epidural local anesthetic injections (without steroids) could be used in those at high risk for steroid-related complications. A repeat injection can be considered if there was initial improvement during the first 6 weeks.
- Radiofrequency treatment adjacent to the ganglion (DRG) is not recommended. Pulsed radiofrequency (PRF) treatment adjacent to the ganglion spinale (DRG) can be considered in those with chronic LRS.
- Adhesiolysis or epiduroscopy can be considered in those who do not respond to conventional epidural injections but the risk: benefit ratio is unclear.
- Spinal cord stimulation (PB) is effective in approximately 50% of well-selected patients.

Clinical practice algorithm

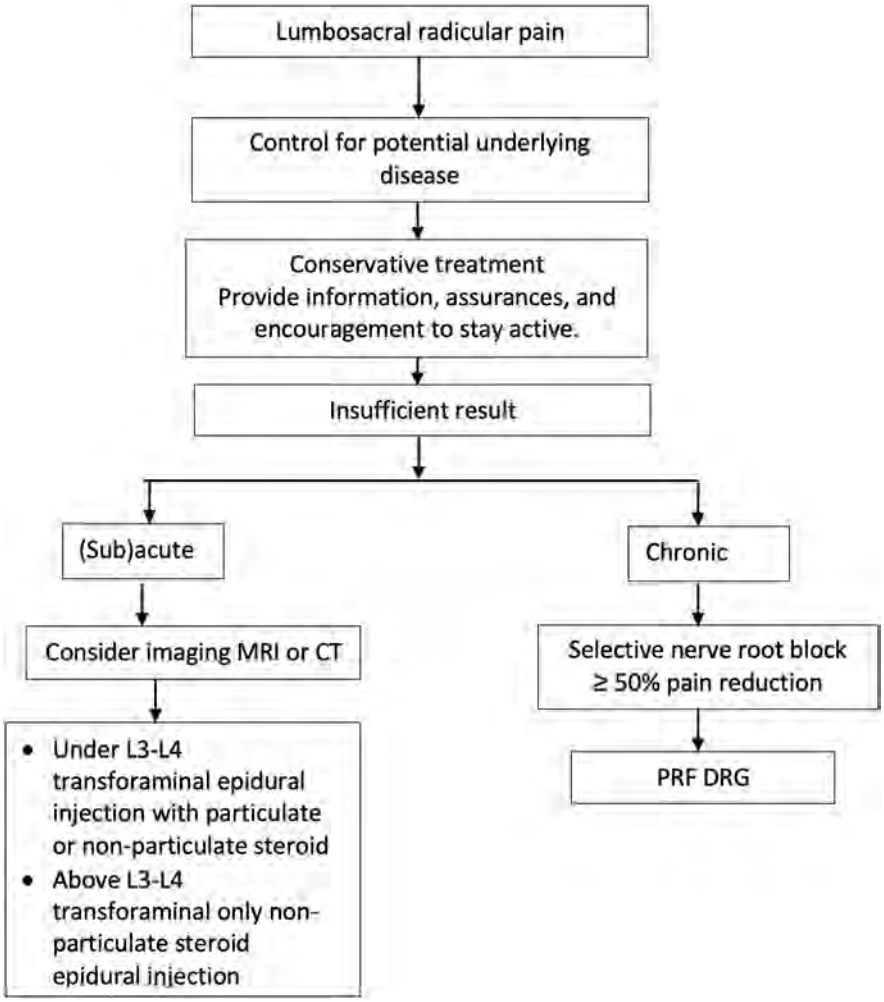

FIGURE 2 Clinical practice algorithm for the management of lumbosacral radicular pain.

TECHNIQUES

Depending on the interventionalist's experience and training, different techniques may be used. We describe here the techniques preferred by the authors.

For alternative techniques, we refer readers to "Interventional Pain. A step-by-step guide for the FIPP Exam."[229] Ultimately, physicians should use the techniques they feel most comfortable with.

Practical recommendations epidural corticosteroid administration

Although it is likely that particle size and aggregability of the depot corticosteroid are related to reported neurological complications, the literature concerning this is inconclusive.[230] There are also two publications and numerous unpublished reports in the U.S. FDA database on serious neurological complications with the transforaminal administration of non-particulate corticosteroid.[206,231,232] In one study, dexamethasone was found to have similar short-term clinical effectiveness compared to triamcinolone, although more injections were required.[233] In more recent RCTs, particulate corticosteroids were reported to be associated with significantly better outcomes compared to dexamethasone.[234,235] At this time, there is no evidence that a corticosteroid dosage higher than an equivalent of 40 mg of depot methylprednisolone or triamcinolone produces a superior clinical effect,[236] yet the risk of endocrine side effects is substantially higher. Therefore, using the lowest effective dose of depot corticosteroid is recommended.

With regard to the number of infiltrations, there are no studies that have shown that a series of three infiltrations results in better outcomes, and performing a series of rote injections with regard to outcome is antithetical to personalized medicine.[237] Based on RCTs published on transforaminal epidural corticosteroids,

TABLE 4 Summary of the evidence according to the systematic reviews.

Author date ref	Technique	Quality of evidence	Conclusion	Recommendation
Verheijen 2021[100] Epidural steroid administration in sciatica patients	Interlaminar, transforaminal, caudal epidural steroids	Syst. Rev 17 trials: 5: low risk of bias, 2: raised concern, 10: high risk of bias	ESI superior to epidural placebo for reduction of leg pain at 6 weeks. Caudal and TF superior to IL	ESI can be recommended for short-term pain management. MCID was not met
Yang 2020[106] Epidural steroid vs. conservative treatment in sciatica patients due to herniated disc or spinal stenosis	Epidural steroids: no administration route specified	Syst rev with 6 RCTs and low overall risk of bias	ESI superior to conservative treatment for pain relief up to 3 months. No difference at 6 months No difference in functional improvement	ESI is preferred over conservative treatment for short- to intermediate-term pain relief
Oliviera 2020[107] Cochrane review epidural steroid vs placebo injections in patients with lumbosacral radicular pain (central spinal canal stenosis excluded)	Interlaminar, transforaminal, caudal epidural steroids	Syst rev 25 studies. 8 trials of high quality Moderate quality of evidence (downgraded because of bias)	Epidural steroids are probably slightly more effective than placebo in reducing leg pain in the short term Epidural steroids are probably slightly more effective than placebo in reducing disability in the short term	Limited support for the epidural injection of steroids in the lower spine for the treatment of sciatica as the benefit is small and of short duration
Smith 2020[110] Comprehensive review Transforaminal epidural steroids In patients with radicular pain due to disk herniation or spinal stenosis	Transforaminal epidural	32 observational, pragmatic and explanatory studies RCT's provided high-quality evidence Observational studies: high quality	TFESI are effective for lumbosacral radicular pain due to disk herniation Evidence supporting TFESI for LRS due to spinal canal stenosis of lower quality but suggestive for beneficial effect TFESI with non-particulate and particulate steroids confer equal effectiveness	There is strong evidence that lumbar transforaminal injection of steroids is an effective treatment for pain due to disk herniation
Marliana 2021[134] PRF DRG in lumbar herniated nucleus pulposus	PRF DRG	Syst rev of 6 RCT's Risk for bias low	PRF effect was not significant at 4 and 8 weeks, but had a significant effect on pain at 12 weeks	PRF can be used for the management of lumbar HNP
Brito-Garcia[141] Systematic review epidural adhesiolysis in FBSS	Epidural adhesiolysis and endoscopic adhesiolysis	Syst rev of 10 reports with high risk of bias	Adhesiolysis effective in pain relief and disability Several side effects	Adhesiolysis should be reserved for refractory patients treated in a specialized center in a trial
Manchikanti[142] Systematic review epidural adhesiolysis in FBSS, Spinal Stenosis and disk herniation	Epidural adhesiolysis	Syst rev of nine studies follow-up 1 year	Improvement in pain and function and decrease in opioid consumption	Level I or II evidence
Eckermann[153] Systematic review of spinal cord stimulation in patients without prior surgery	Spinal cord stimulation	Syst rev of 10 studies	Pain reduction improvement in functionality, quality of life	SCS is an acceptable alternative for chronic low back pain without prior surgery
Head[155] Systematic review of different wave forms SCS	Paresthesia-based SCS paresthesia-free high-frequency SCS, burst SCS, and subperception SCS	Syst rev of 13 RCTs	PB-SCS better than reoperation and than conventional treatment HF-SCS significantly better than PB-SCS Burst SCS preferred by patients SP SCS at 5 kHz better than sham	Investigation into the optimal choice of stimulation frequency is needed

Abbreviations: DRG, dorsal root ganglion; ESI, Epidural steroid injection; HNP, herniated nucleus pulposus; IL, interlaminar; MCID, minimal clinical important difference; PB, paresthesia-based; PRF, pulsed radiofrequency; RCT, randomized controlled trial; SP, subperception; Syst. Rev., systematic review; TF, transforaminal; TFESI, transforaminal epidural steroid injection.

1–2 injections are typically performed. Considering the potential endocrine side effects, adhering to an interval of at least 2 weeks between infiltrations is recommended.

In the event of a documented contrast allergy, earlier guidelines recommended using preservative-free dexamethasone[111,238,239] More recent multispecialty guidelines recommend the consideration of pretreatment with glucocorticosteroids, sometimes with antihistamine, in individuals with a mild documented contrast allergy and injection with a different, low-osmolar non-ionic contrast agent. In those with documented moderate or severe hypersensitivity reactions, pretreatment and injection with a different, low-osmolar non-ionic agent can be considered for those with a contraindication to gadolinium.[240]

A recent cohort study conducted in the Medicare population on serious spinal adverse events of epidural corticosteroid injections failed to demonstrate that non-particulate corticosteroids had lower event rates than particulate steroids.[232] Alternatively, a parasagittal injection can be considered when a transforaminal injection is deemed too risky.

Interlaminar epidural corticosteroid administration

This technique can be carried out with the patient in a prone position, lying on the side or sitting; in the two latter postures, place the patient in flexion or in the "fetal" position.[241]

Determination of the correct level can occur with reference to the iliac crest, which is usually located at the L4 level, or preferably via fluoroscopy as the landmark approach to identify spinal levels is frequently inaccurate.[242] In the *medial approach*, a local anesthetic (eg, Xylocaine 1%) is infiltrated in the middle of the processi spinosi. Thereafter, the subcutaneous tissue and the ligamentum supraspinosum are approached with a Tuohy epidural needle. A loss-of-resistance (LOR) syringe, filled with air or preferably a low volume of physiologic solution, is then connected to the needle, and the needle is slowly advanced using the LOR technique. Using loss of resistance to saline reduces the likelihood of pneumocephalus in case of accidental dural puncture. Subsequently, the needle enters the ligamentum interspinosum and the ligamentum flavum, which both provide additional resistance. A false sensation of loss of resistance may occur upon entering the space between the ligamentum interspinosum and the ligamentum flavum. The ligamentum flavum provides the greatest resistance to the epidural needle since it is almost entirely composed of collagenous fibers. Breaking through this ligament to the epidural space is accompanied by a significant loss of resistance. The injection of contrast agent should be used to verify correct positioning in the epidural space on fluoroscopy. When injecting medication into the epidural space, normally no resistance should be felt since it is filled with fat, blood vessels, lymphatic, and connective tissue. Fluoroscopy with spot or real-time contrast injection in the antero-posterior and lateral (or contralateral oblique) views is recommended for the interlaminar approach at lumbar levels.[111] For parasagittal interlaminar injections, the needle tip should be located in the lateral fifth of the interlaminar lucency. In the case of suboptimal contrast spread or aspiration of blood, the needle must be reoriented.

Transforaminal epidural corticosteroid administration

This procedure is carried out with the patient in prone position. With a transforaminal approach, the C-arm is adjusted from an anterior–posterior (A-P) view in such a way that the X-ray beam runs parallel to the endplates of the targeted level. Thereafter, the C-arm is rotated in the oblique direction until the processus spinosus projects over the contralateral facet column. With the C-arm in this projection, the injection point is found by placing a metal marker underneath the pedicle. If there is a superimposition of the processus articularis superius (superior articular process, SAP) on the underlying joint, the C-arm must be rotated cranially.

A 10-cm long, 25-G, or 22-G radiopaque needle with connecting tubing, or one that is first flushed with contrast medium, is inserted in co-axial direction parallel to the radiation beam (Figure 3). Thereafter, the direction is corrected such that the needle tip is superimposed over the bevel (tunnel view or co-axial view). The depth of the needle tip is then checked in a lateral view.

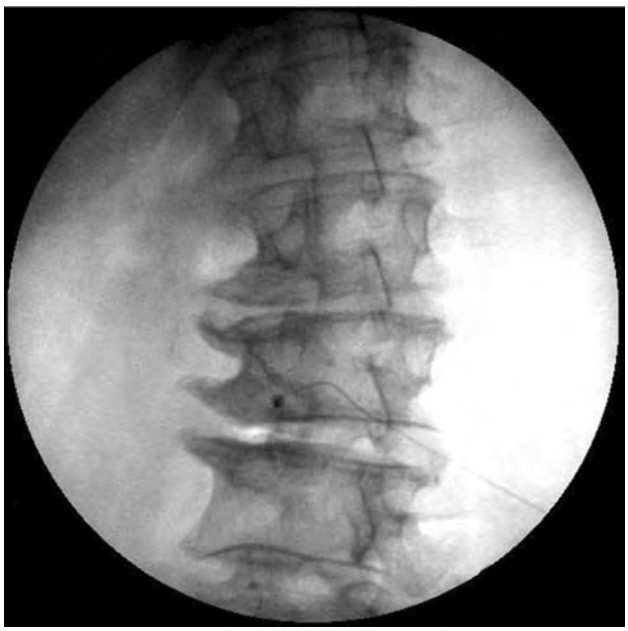

FIGURE 3 Lumbar transforaminal epidural injection: injection point (oblique insertion).

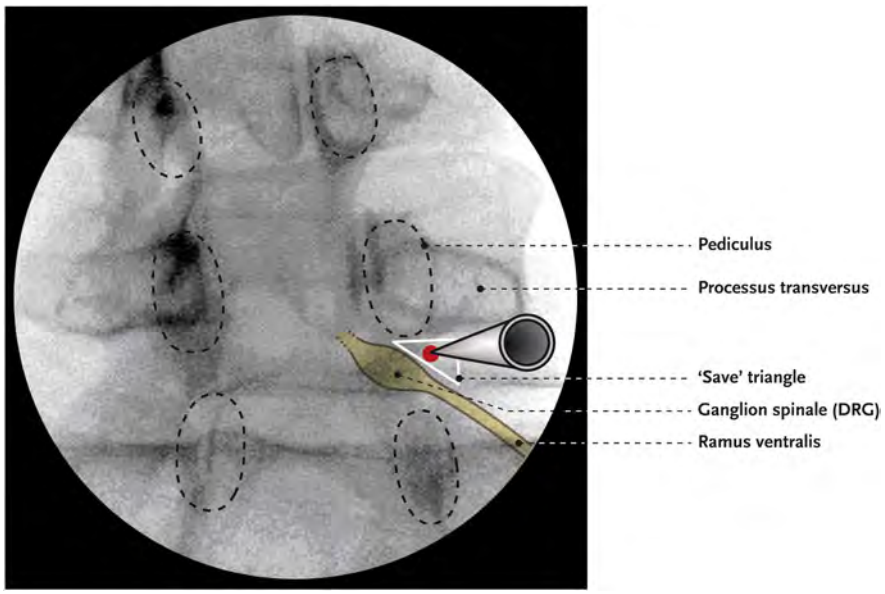

FIGURE 4 Safe triangle for the insertion of the needle in transforaminal epidural injection. (Illustration: Rogier Trompert Medical Art. http://www.medical-art.eu).

A classic approach is to have the needle tip positioned in the dorsocranial quadrant of the foramen intervertebrale, though more ventral positioning may be necessary to obtain ventral epidural spread. The direction of the radiation beam is then switched back to the antero-posterior (A-P) view. As a result, the needle tip should ideally be located beneath the mid-portion of the pedicle.[243] After the injection of a small quantity of contrast agent during real-time imaging, the spinal nerve root should be visible, with proximal epidural spread. If nerve root but not epidural spread is visible, the needle may need to be positioned deeper toward the ganglion spinale (dorsal root ganglion, DRG). The execution of this procedure using real-time contrast injection allows for the detection of intrathecal, intravascular, and intradiscal uptake.

We recommend avoiding injection when pain or paresthesia is elicited, as injecting a substance intraneurally may lead to irreversible nerve damage. In addition to being unpleasant and possibly limiting the amount of injectate that can be administered, segmental medullary blood vessels adjacent to spinal nerve roots may be encountered.[180,197] Some have recommended targeting the "safe triangle" (Figure 4). This triangle is formed cranially by the underside of the upper pediculus, laterally by a line drawn between the lateral edges of the upper and lower pediculus, and medially by the spinal nerve root (as the tangential base of the triangle). A needle tip in this zone may be less likely to contact a nerve, but does not prevent violation of radiculomedullary arteries, which are concentrated superiorly and anteriorly in the foramen.[244,245] For this reason, it may be advantageous to position the needle tip posteriorly in the neuroforamen provided ventral epidural spread is observed. Fluoroscopy with contrast under real-time imaging is compulsory. Digital subtraction angiography (DSA) is more sensitive for detecting intravascular uptake but is optional depending on availability and concerns for increased radiation exposure.[246,247] Even using DSA, it is impossible to completely rule out inadvertent intravascular uptake. It is therefore recommended to use a short-acting, low-dose local anesthetic such as 1 mL of preservative-free xylocaine 1% to enable a rapid neurological evaluation (eg, to ensure the patient is able to move their ipsilateral leg).[197,210] Once correct positioning is confirmed, the corticosteroid can be injected.

S1 transforaminal epidural procedure

The technique used at the S1 nerve root level is analogous with the transforaminal technique used for lumbar levels except that the needle is positioned through the foramen sacrale dorsale of S1 on the S1 pedicle. For this technique, the target lies on the caudal edge of the S1 pediculus on a location homologous to that used for lumbar transforaminal injections. Despite anatomical differences between the foramen sacrale dorsale (small and round) and foramen sacrale ventrale (larger and semilunar), they cannot always be reliably distinguished on fluoroscopy. However, by reorienting the C-arm cephalo-caudally and rotating it ipsilaterally, the foramen sacrale ventrale and the foramen sacrale dorsale of S1 will overlap, creating a visually apparent target. The puncture point is chosen in the center of the foramen sacrale dorsale of S1. A 10-cm long, 25-G, or 22-G needle with connection tubing is then advanced in a coaxial ("tunnel") view until it has reached the foramen sacrale dorsale. The depth of the needle is then verified in a lateral view. In an optimal position, the needle tip

is positioned approximately 5 mm from the floor of the canalis sacralis in a lateral view. Visualization of the S1 nerve root with epidural uptake upon contrast injection using real-time imaging in an A-P view confirms correct placement.

(Pulsed) radiofrequency treatment

Diagnostic block

To perform a diagnostic block, the patient is placed in prone position, and the C-arm is adjusted from A-P view in such a way that the X-rays run parallel to the endplates of the targeted level. Thereafter, the C-arm is rotated obliquely until the processus spinosus projects over the contralateral facet column. The injection point is then marked by placing a metal marker over the *lateral part* of the foramen intervertebrale. A 10-cm long, 22-G needle with connection tubing is inserted co-axially in the trajectory of the X-ray beam (Figure 4). The image intensifier is then switched to a lateral view, and the needle inserted until the tip is situated in the dorsocranial part of the foramen intervertebrale (Figure 5).

Regardless of the approach, a small amount of contrast agent is injected with real-time imaging in an A-P view (Figure 6). The contrast in a selective nerve root block should outline the targeted nerve without proximal epidural uptake that could undermine validity. Finally, a volume ranging between 0.5 mL and 1 mL of lidocaine depending on the contrast spread pattern is injected, with studies, demonstrating that lower volumes and more lateral needle position enhance specificity.[58]

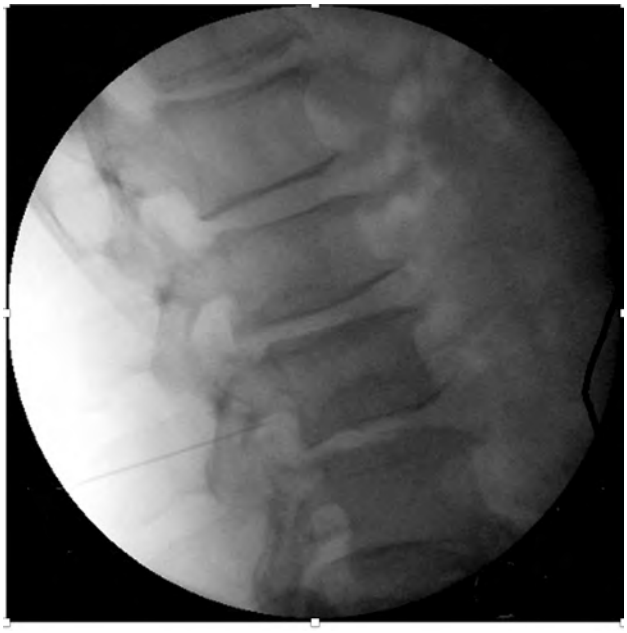

FIGURE 5 Diagnostic spinal nerve root block: lateral view with needle tip in dorsocranial quadrant of the neuroforamen.

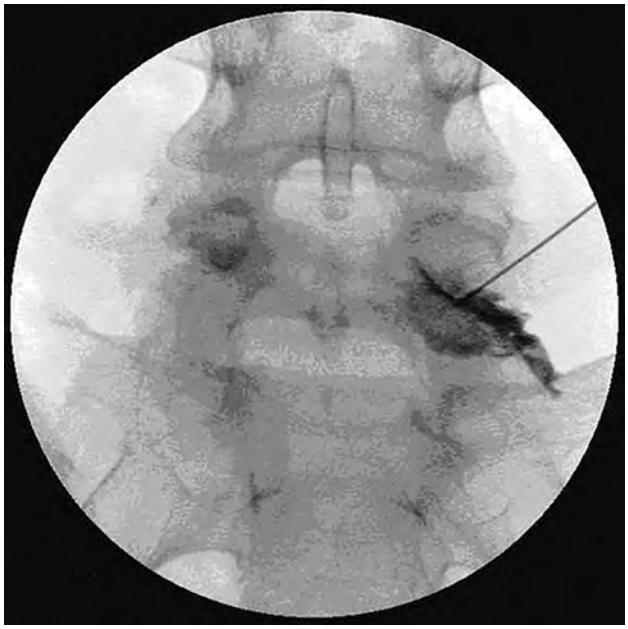

FIGURE 6 Diagnostic spinal nerve root block: after real-time injection of contrast agent.

A prognostic block is considered positive if there is a 50% or greater reduction in radicular pain 10–30 minutes after the intervention. The level(s) that provide the greatest reduction in radicular pain is chosen for PRF treatment.

Lumbar percutaneous pulsed radiofrequency treatment

The insertion point for PRF treatment is determined in the same way as for the diagnostic block, except that the projection angle is maintained as *medial* as possible to reach a position sufficiently proximal to the ganglion spinale (dorsal root ganglion, DRG). The cannula is inserted co-axially in the direction of the radiation beam so that the needle tip is superimposed over the needle hub in a co-axial or tunnel view. Thereafter, the cannula is carefully advanced until the needle tip is situated in the middle of the foramen intervertebrale in a lateral view.

The stylet is removed and exchanged for a radiofrequency thermocouple probe. The impedance is checked, and thereafter, sensory stimulation at 50 Hz is performed. The patient should ideally feel tingling in the distribution of their pain at a voltage of <0.5 V to ensure the needle tip is sufficiently close to the DRG to be captured by the electrical field.

Once these criteria are met, the position of the cannula is recorded in two planes. Some practitioners opt to pre-inject local anesthetic (eg, lidocaine) to prevent pulsations, reduce high impedances, and possibly to enhance the size of the electrical field created. Thereafter, a pulsed current (routinely 20 ms current and 480 ms without current) is applied for 2 to 6 minutes at an output of

45 V.[133,135] During the procedure, the temperature at the tip of the electrode should not exceed 42°C.

Adhesiolysis and epiduroscopy

For description of the technique, we refer to Interventional Pain. A step-by-step guide for the FIPP Exam, chapter 21 p 155–162.[248]

Spinal cord stimulation

The technique of SCS is described in the chapter persistent spinal pain syndrome.

CONCLUSIONS

Lumbosacral radiculopathy is a common, debilitating condition, which may have several etiologies that all result in irritation of spinal nerve roots. Conservative management is recommended by many guidelines, though the evidence for physical therapy, exercise, and adjuvants such as antidepressants is weak and conflicting. Epidural steroid injections may provide intermediate-term benefit in well-selected patients, with herniated disc responding better than spinal stenosis. In carefully selected patients, pulsed radiofrequency of the DRG may provide intermediate-term benefit, and in cases of refractory pain, epidural adhesiolysis/epiduroscopy, or spinal cord stimulation can be considered by experienced practitioners. Decompression surgery is recommended in cases of severe or progressive neurological deficits, but the evidence for long-term benefit compared to conservative therapy is weak.

AUTHOR CONTRIBUTIONS

Laurens Peene performed the literature search and wrote the manuscript. Jan Van Zundert and Koen Van Boxem assisted in the selection of the literature and revised the manuscript. Koen Van Boxem is the final responsible for this manuscript. Steven P. Cohen, Jan Willem Kallewaard, Andre Wolff, Frank Huygen, Antal van de Gaag, Steegers Monique, Kris Vissers, and Chris Gilligan revised and edited the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

This narrative review is based on the existing literature; therefore, data on the used publications are available through PubMed and libraries.

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