Optimizing care in lumbar radiculopathy and neurogenic claudication: from injection to inference, and from clinician to algorithm

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The outcome of epidural injections in lumbar radiculopathy is not dependent on the presence of disc herniation on magnetic resonance imaging: assessment of short term and long-term efficacy

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ABSTRACT

Objective

Lumbar radiculopathy is a condition with major physical, social, and economic consequences. Despite its favorable prognosis, the burden can be significant. In this study, we aimed to determine the value of magnetic resonance imaging (MRI) and the efficacy of transforaminal epidural injections (TEIs) in patients with lumbar radiculopathy secondary to lumbar disc herniation (LDH) and other causes (non-LDH).

Methods

Patients with lumbar radiculopathy were reviewed for radiologic diagnosis based on MRI. For patients receiving TEI therapy, response after 6–8 weeks (short-term) and 16 weeks (long-term), number of injections, subsequent surgery, and patient outcome were evaluated. Treatment response was assessed by patient-reported symptom relief and numeric rating scale pain scores.

Results

Overall, 66% of MRI examinations showed a clinically relevant LDH. A total of 486 of 1824 patients received TEI, of whom one third did not show LDH. Of patients, 70% reported a short-term effect with significant pain reduction and 44% reported a long-term effect. No significant differences were observed between the LDH and non-LDH groups. Of patients, 59% required multiple injections and reported similar efficacy compared with patients treated with a single injection.

Conclusions

A considerable part of MRI examinations in patients with lumbar radiculopathy do not show a clinically relevant LDH. Regardless of the radiologic diagnosis, most patients treated with TEI benefit in both the short-term and the long-term after a single-injection or multiple-injection regime. Subsequent injections are advisable if the effect from the first injection is unsatisfactory or wears off. MRI examination before TEI therapy may be redundant, which allows for expedition of this treatment.

INTRODUCTION

Lumbar radiculopathy is a common spinal condition characterized by radicular pain toward the lower extremity.[1] Although lumbar disc herniation (LDH) is the most prevalent cause, a variety of degenerative spinal disorders can instigate unilateral radicular symptoms originating from the lumbar spine.[2] It is assumed that the origin of lumbar radiculopathy is multifactorial, involving a complex interplay of physical impingement, inflammatory processes, and immunologic responses resulting from degenerative spinal changes, which, consequently, induce lumbosacral nerve root irritation.[3,4] Patients often present with severe leg pain, paresthesia, and other neurologic deficits that seriously impede their daily functioning and decrease their quality of life.[5]

Despite the severity of symptoms, most patients with lumbar radiculopathy spontaneously recover within 1 year.[6,7] Therefore, patients are initially treated conservatively for several weeks before consultation with a neurologist and extensive radiologic imaging,[8] considering the absence of warning signs that require immediate attention. After referral, surgical options can be discussed with the neurosurgeon, but generally, patients are encouraged to prolong conservative therapy up to 16 weeks.[9] Nevertheless, the physical and mental burden while awaiting natural resolution can be intolerable.

Transforaminal epidural injection (TEI) therapy is a widely used treatment to create a more bearable situation for these patients.[10,11] A small amount of local anesthetic and corticosteroid is administered in the vicinity of the affected nerve root to alleviate symptoms by reducing the surrounding inflammatory processes.[12] Treatment with TEI is intended as a temporary pain management strategy because the effect of a single injection may wear off after a couple of weeks to months. In part of the patients, this treatment is sufficient to await natural resolution of symptoms, obviating further treatment.[13]

Although TEI has been a long-established treatment for lumbar radiculopathy, controversy remains over its efficacy and the correlation with radiologic findings because of discrepancies between studies and a paucity of literature for causes other than LDH.[8,]14, 15, 16, 17, 18, 19, 20, 21 Moreover, it is still unclear whether multiple injections can produce equal long-term improvement compared with a single injection. In addition, it has been hypothesized that short-term response to TEI might predict long-term patient outcome, making it useful as a clinical decision-making tool.22, 23, 24

The main goal of this study is to retrospectively assess the correlation between the presence of a herniated disc on magnetic resonance imaging (MRI) and outcome of TEI in patients with lumbar radiculopathy in clinical practice. Second, the effect of a regimen of multiple injections, difference in surgery frequency, and patient outcome after treatment are evaluated.

METHODS

Patients

For this large retrospective cohort study, data from the Spaarne Gasthuis, Hoofddorp/Haarlem, the Netherlands, were used with consent from the medical ethical committee and the board of directors. The hospital's electronic patient record system was searched to select all patients who were diagnosed with lumbar radiculopathy between January 1, 2016 and September 1, 2017. The following inclusion criteria were used: 1) clinical diagnosis of lumbar radiculopathy by a neurologist or neurosurgeon, 2) radiologic examination of the lumbar and sacral spine with MRI, and 3) patient age of 18 years or older.

Data collection

For all patients data was collected concerning MRI examination and primary treatment choice. For patients treated with TEI, additional data were collected regarding demographics, cause of symptoms as deduced from MRI examination by the neurologist or neurosurgeon, history of back surgery, analgesic use, level of primary injection, additional injections, surgical intervention, and patient outcome after treatment. Response to TEI in the short-term was evaluated after 6–8 weeks after the first epidural injection by the anesthesiologist, neurologist, or nurse by telephone. Patients reported overall pain scores (numeric rating scale [NRS] ranging from 0 [no pain] to 10 [worst imaginable pain]) and whether they considered the treatment to be effective. Long-term response to TEI was evaluated at 16 weeks by patient-reported symptom relief. If patients were subjected to spinal surgery subsequent to TEI within these 16 weeks, TEI therapy was considered to have failed for the long-term. Patient outcome at the end of treatment was evaluated at the last hospital appointment for this episode of sciatic symptoms using a Likert scale with 3 categories, defined by "unsatisfactory", "satisfactory," and "good" outcome. Unsatisfactory was defined as no or only slight improvement compared with the patient's initial situation. A satisfactory outcome constituted significant improvement, but with the patient still experiencing some degree of pain or disability. A good outcome signified nearly complete or full recovery.

Treatment

Patients visited the outpatient clinic of the anesthesiology department to receive treatment with a TEI. The procedures were performed by several experienced anesthesiologists. The segmental level to be treated was chosen by the anesthesiologist based on MRI results and clinical findings. During the TEI procedure, the patient was positioned in a prone position on the table. After verification of the correct side and level, the skin was disinfected. Under fluoroscopic guidance with anteroposterior and lateral views, a spinal needle was inserted into the targeted neuroforamen. To confirm correct positioning of the needle, a contrast agent was injected, showing a neurogram. If the needle was mistakenly placed, it was repositioned and verified for epidural placement into the neuroforamen. A combination of a local anesthetic (lidocaine, chirocaine, or bupivacaine) and a corticosteroid (methylprednisolone 20–80 mg or dexamethasone 7.5–20 mg) was administered. The procedure lasted 15 minutes and afterward, the patient was monitored for half an hour in the recovery room by the nurse. If the first injection yielded an unsatisfactory outcome, a second injection was offered to the patient, either at the same or an adjacent level. Moreover, if the first injection was satisfactory but the effect gradually decreased, subsequent injections were offered. The injection regimen was continued until symptoms had sufficiently ameliorated, subsequent injections were unsuccessful to relieve symptoms, or the patient had decided to discontinue treatment. Patients were offered surgery by the neurosurgeon if conservative treatment failed and MRI showed a clinically relevant operable component.

Analysis

Patients were stratified according to findings derived from radiologic imaging. One group included patients with MRI-confirmed LDH concordant with clinical findings. Disc herniation was defined as a radiologically evident bulging disc, protrusion, or extrusion of an intervertebral disc in the lumbosacral spine. The non-LDH group comprised patients with LDH inconsistent with clinical findings, a degenerative cause of lumbar radiculopathy, or MRI examination without an evident cause. Consequently, patients were categorized based on primary treatment choice. For patients initially treated with TEI, treatment efficacy was extensively evaluated. Statistical analysis was performed using SPSS version 25 (IBM Corp., Armonk, New York, USA). Missing values were imputed adjusting for covariates. Continuous data were presented using mean and standard deviation and compared between groups with the unpaired *t* test and within groups with the paired *t* test. Percentages and exact numbers were used to present categorical data and the χ^2 test was used for comparisons. A *P* value <0.05 was considered statistically significant.

RESULTS

Patient population

A total of 1824 patients were diagnosed with lumbar radiculopathy and subjected to an MRI of the lumbar spine. In 66% (*n* = 1200), LDH concordant with the clinical condition was observed. In 53% (*n* = 630) of these patients with LDH, conservative treatment was prolonged, 19% (*n* = 233) underwent surgery, and 28% (*n* = 337) were referred to the anesthesiologist for TEI. Of 624 patients without radiologic evidence of a clinically relevant herniated disc, 69% (*n* = 430) continued conservative therapy, 7% (*n* = 45) were surgically treated, and 24% (*n* = 149) received TEI therapy.

A total of 486 patients were treated with 1 or multiple epidural injections at the anesthesiology outpatient clinic: 337 patients with a clinically important LDH and 149 patients without LDH. Patients received an average of 1.7 injections until 16 weeks follow-up. Demographic and clinical characteristics are shown in Table 1. Patients with LDH were on average 8.21 (95% confidence interval, 5.31–11.12) years younger, had less often chronic symptoms, and had less often been subjected to previous back surgery. Females were more represented in the non-LDH group. Baseline NRS for overall pain in the LDH group was comparable to the non-LDH group (0.2; 95% confidence interval, −0.6 to 0.3). Use of analgesic medication was equal between the 2 groups. However, when the type of analgesic was considered, patients with LDH-induced radiculopathy more frequently used nonsteroidal antiinflammatory drugs and opioids, although this latter type of medication was prescribed for a significant number of patients in both groups.

Table 1 Baseline characteristics

	LDH group (n = 337)	Non-LDH group (n = 149)	P-value
Age, yrs. (mean ± SD)	55.12 ± 15.28	63.34 ± 14.42	0.000
Sex: M/F	162 (48.1%) / 175 (51.9%)	51 (34.2%) / 98 (65.8%)	0.005
Duration of symptoms			0.006
≤ 3 months	91 (27.0%)	23 (15.4%)	
> 3 months	246 (73.0%)	126 (84.6%)	
Radiological diagnosis			0.000
LDH	337 (100.0%)	0 (0.0%)	
Degenerative stenosis	0 (0.0%)	97 (65.1%)	
Cyst	0 (0.0%)	11 (7.4%)	
Scar tissue	0 (0.0%)	11 (7.4%)	
Spondylolisthesis	0 (0.0%)	5 (3.4%)	

Table 1 Baseline characteristics (*continued*)

	LDH group (n = 337)	Non-LDH group (n = 149)	P-value
Inconclusive	0 (0.0%)	25 (16.8%)	
History of back surgery	63 (18.7%)	41 (27.5%)	0.029
Same level	47 (74.6%)	30 (73.2%)	0.798
Other level	16 (25.3%)	11 (26.8%)	
Level of injection			0.112
L1	1 (0.3%)	2 (1.3%)	
L2	4 (1.2%)	2 (1.3%)	
L3	27 (8.0%)	12 (8.1%)	
L4	52 (15.4%)	25 (16.8%)	
L5	167 (49.6%)	85 (57.0%)	
L6	3 (0.9%)	2 (1.3%)	
S1	83 (24.6%)	20 (13.4%)	
S3	0 (0.0%)	1 (0.7%)	
NRS overall pain (mean ± SD)	8.0 ± 1.4	7.8 ± 1.4	0.471
Pain medication use	307 (91.1%)	138 (92.6%)	0.511
Paracetamol	210 (62.3%)	102 (68.4%)	0.212
NSAIDs	168 (49.9%)	53 (35.6%)	0.003
Opioids	202 (59.9%)	75 (50.3%)	0.042
Antineuropathic drugs (gabapentin, pregabalin, amitriptyline)	71 (21.1%)	23 (15.4%)	0.157

Short-term efficacy of TEI

Of the 337 patients with LDH receiving TEI, 71% (*n* = 239) reported pain relief between 6 and 8 weeks after the first injection, whereas in the non-LDH group, 68% (*n* = 102) experienced a pain-reducing effect after treatment with an epidural injection. The mean NRS score decreased significantly after treatment to 4.7 ± 2.8 and 4.5 ± 2.6 for, respectively, the LDH group and non-LDH group compared with baseline. However, the difference in NRS reduction between groups was not statistically significant ($P = 0.868$) (Table 2).

Table 2 Outcome parameters at follow-up after TEI therapy between LDH and non-LDH patients

	LDH group (n = 337)	Non-LDH group (n = 149)	P-value
Short-term effect (y/n)	239 (71%) / 98 (29%)	102 (68%) / 47 (32%)	0.491
NRS overall pain (mean ± SD)			
At 8-week follow-up	4.7 ± 2.8	4.5 ± 2.6	0.469
Absolute change*	-3.2 ± 3.0	-3.3 ± 2.9	Intragroup: (<0.001 / <0.001) Intergroup: 0.868
Additional injections (y/n)	197 (58%) / 140 (42%)	90 (60%) / 59 (40%)	0.688
Long-term effect (y/n)	149 (44%) / 188 (56%)	63 (42%) / 86 (58%)	0.781
Surgery (y/n)	73 (22%) / 265 (79%)	18 (12%) / 131 (88%)	0.013
Likert treatment outcome (g/s/u)†	58 (17%) / 162 (48%) / 117 (35%)	13 (9%) / 72 (48%) / 64 (43%)	0.029

* Compared to NRS score at baseline
† g = good; s = satisfactory; u = unsatisfactory

Additional injections

Although 71% of patients in the LDH group experienced a relevant pain reduction after TEI, 59% of these patients (*n* = 140) required additional injections. Of patients in the LDH group who did not benefit from the first injection, 58% (*n* = 57) also received additional epidural injections (Figure 1). Similar results were found in the non-LDH group: 61% (*n* = 62) of patients responsive to the first TEI received subsequent injections, whereas this was true for 60% (*n* = 28) of patients unresponsive to the first epidural injection (Figure 2). Hence, a total of 58% (LDH) and 60% (non-LDH) received supplemental epidural injections, which was a nonsignificant difference (*P* = 0.688) (Table 2).

Long-term efficacy, surgery, and patient outcome at end of treatment

Long-term efficacy was assessed at 16 weeks follow-up (range, 13–18 weeks). Ten percent of patients in the LDH group (*n* = 33) and 6% in the non-LDH group (*n* = 8) underwent surgery before the 16-week follow-up moment. In these patients, TEI therapy was considered to have failed in the long-term (Figures 1 and 2). Of patients with LDH, 44% (*n* = 149) compared with 42% (*n* = 63) of patients without LDH reported a positive effect of TEI at 16 weeks (*P* = 0.203). More patients in the LDH group opted for surgery (*P* = 0.013). The outcome at the end of treatment using a 3-point Likert scale showed that a satisfactory or good outcome was more frequently observed in the LDH group (*P* = 0.029) (Table 2).

Patients with long-term effect after one or more epidural injections

Of the 337 patients with LDH, 239 (71%) initially experienced pain relief after the first injection in the short-term. In 24% of those patients (n = 57), this effect was still present at 16 weeks if treatment was restricted to a single injection. If additional injections were administered, another 29% (n = 70) reported improved symptoms in the long-term. Of the 98 patients with LDH not responding to the first injection, 22% (n = 22) indicated improved symptoms at 16 weeks after administration of additional injections. Therefore, 44% of patients with LDH (n = 149) showed symptom relief with a regimen of ≥1 injections at 16 weeks follow-up (Figure 1).

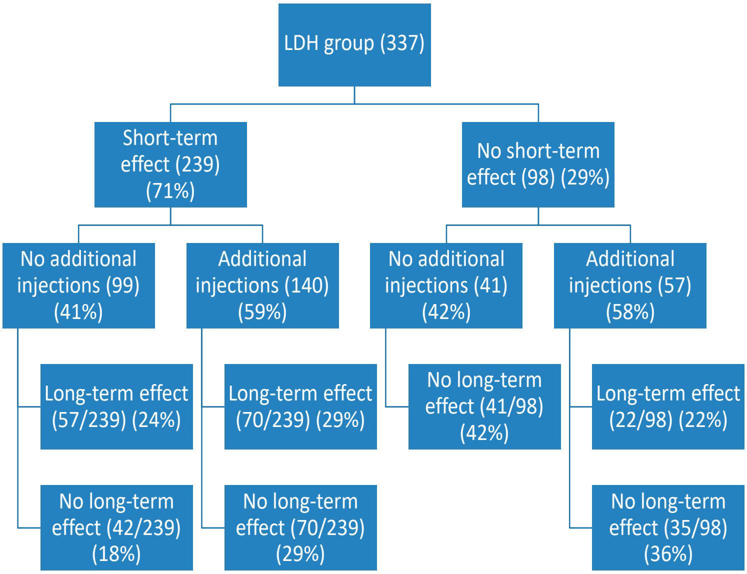

Fig. 1 Summary of transforaminal epidural injection results for patients with lumbar disc herniation (LDH).

Comparable results were observed in the group of 149 patients without LDH. A total of 102 patients (68%) initially experienced a pain-reducing effect after the first injection. If treatment was limited to that single injection, 23% (n = 23) reported a long-term effect. However, if patients required additional epidural injections despite a positive effect after the first injection, an additional 29% (n = 30) experienced an effect at 16 weeks. In the group of patients without LDH who lacked a response to the initial injection but were subjected to subsequent injections, 22% (n = 10) reported a long-term effect. Therefore, for all patients without LDH, 42% (n = 63) had improved symptoms at 16 weeks with ≥1 epidural injections (Figure 2).

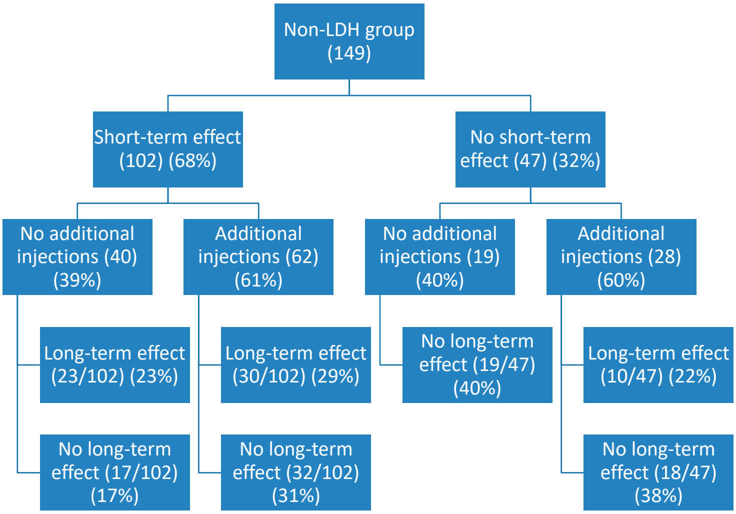

Fig. 2 Summary of transforaminal epidural injection results for patients without lumbar disc herniation (non-LDH).

DISCUSSION

The current study highlights that the efficacy of TEI in patients with lumbar radiculopathy is independent of the radiologic diagnosis. Comparable success rates and pain score reductions were observed in the LDH and non-LDH group for both short-term and long-term follow-up. These results indicate that nerve root compression secondary to a clinically concordant LDH is not a prerequisite for effective treatment with TEI. In the absence of nerve root compression or detectable disc herniation on MRI, inflammatory processes resulting from degenerative changes in other spinal structures may play a fundamental role.25, 26, 27, 28, 29, 30, 31 TEI therapy is assumed to target the inflammatory cascade directly and indirectly through multiple pathways, causing a decrease in nerve root inflammation, nociception of afferent fibers, and activity of proinflammatory cytokines.[3,]32, 33, 34, 35 Therefore, treatment with TEI can be effective in these patients as shown in our study for the non-LDH group.

Controversy exists over symptom improvement because of a placebo effect after TEI, as with other pain management strategies. An injection into the epidural space may achieve a washout of proinflammatory cytokines or result in lysis of inflammatory-mediated adhesions in some patients because injections with only a local anesthetic or saline have been shown to induce some degree of improvement.36, 37, 38 However, several studies have shown transforaminal steroid injections to be superior compared with placebo in the short-term, vindicating the addition of steroid for TEI.[16,36,39]

The literature on TEI for lumbar spinal conditions other than LDH is limited.[40] A study by Ng et al.[41] found no significant difference in pain reduction between patients with lumbar radiculopathy with LDH and patients with spinal stenosis at 6 weeks follow-up. In addition, Cohen et al.[42] reported that routine MRI before epidural injection had no additional value because equal efficacy after treatment was observed in 127 MRI-blinded and nonblinded patients with lumbar radiculopathy and physicians. These results are in line with results from our study.

A meta-analysis of studies comparing epidural steroid injections with conservative treatment in patients with lumbar radiculopathy[43] found that pain reduction was significantly greater after epidural steroid injections in the short-term. Because the cause of lumbar radiculopathy cannot be correlated with outcome results after TEI, pretreatment MRI examination may not always be necessary. Therefore, TEI therapy could be expedited with extensive imaging postponed to a later stage. Evidently, red flag indications need to be excluded by the general practitioner, concurring with local and national guidelines for treatment of lumbar radiculopathy and referring accordingly. Such a treatment strategy would allow for more adequate symptom management in an earlier stage of lumbar radiculopathy.

A previous study that compared early MRI or computed tomography with delayed imaging in patients with low back pain[44] reported no large effect on overall treatment results. Another trial[45] compared early examination of the lumbar spine with MRI with plain radiography in similar patients and found no significant benefit of MRI scans over radiographic imaging but stressed the higher financial costs of MRI. Hence, plain radiography may be sufficient to detect extreme abnormalities of the lumbar spine that can complicate TEI procedures at an early stage, and periprocedural safety in the absence of extensive imaging can be maintained with, for example, the use of fluoroscopic guidance. Expedition of TEI therapy could lead to improved maintenance of functionality, prevention of financial costs because of absenteeism, and reduction of oral analgesic intake, specifically of opioids, which are prescribed with rapidly increasing frequency despite the serious risk of drug dependence.[46]

Overall, 70% of patients in our study experienced short-term pain relief after a single TEI, with substantial pain reduction. These results are in line with related, although smaller, studies in the medical literature. In a report by Nandi et al.,[47] 47 patients with LDH received epidural steroid injections, of whom 68% were considered to show success at 4 weeks follow-up. Joswig et al.[23] studied 57 patients with LDH who received TEI, of whom 66.7% were identified as responders after 1 month.

Furthermore, 44% of patients reported long-term pain relief in the current study. Equal long-term effect size could be achieved after treatment with a regimen of multiple injections compared with a single injection in our study population. Additional TEIs were administered to 59% of patients, regardless of their initial response and were beneficial for most patients, resulting in 42%–44% of patients with a satisfactory long-term effect. Moreover, 22% of patients in the LDH group and non-LDH group experienced a good long-term effect after multiple TEIs despite an unsuccessful first injection.

Patients who required additional injections to have a satisfactory outcome at 16 weeks may not have received the primary injection at the appropriate lumbar level. Because the second injection was applied at the adjacent level in a few of these patients, identification of the correct nerve root can be ambiguous at first despite extensive radiologic imaging. Murthy et al.[48] investigated patients with radicular pain and inferred that repeat injections could have a similar effect to the primary injection. Furthermore, when administered within 3 months from the first injection, multiple injections could have a cumulative effect because pain reduction after a subsequent injection was larger than after previous injection(s).

In more recent years, it has been theorized that short-term response to TEI may be used as a predictor for the course of pain during follow-up.22, 23, 24 The rationale is that if the short-term response has predictive value for the severity of symptoms at 16 weeks (the time at which patients are eligible for surgical intervention), it can be used to predict the need for surgery. Early prediction results in surgery at an earlier stage after onset of symptoms. Because of the limited availability of data, it was not feasible to accurately determine whether prediction of long-term patient outcome based on short-term response is possible and this concept should be assessed in a prospective study.

The current study has a few limitations, including its retrospective nature. First, the type and amount of injection contents and exact moment of long-term follow-up varied among patients. Second, only NRS was systematically reported in the patients who received TEI. For all patients who were diagnosed with lumbar radiculopathy and subjected to an MRI of the lumbar spine, it would have been optimal if the clinical condition had been reported using the International

Consortium for Health Outcomes Measurement–dictated outcome measures (i.e., NRS, Oswestry Disability Index, and Quality of Life score [EQ-5D]). The 2 cohorts were not completely similar at baseline. The slightly higher age in the non-LDH group may be explained by the correlation between increasing age and a more degenerative state of the spine.49, 50, 51, 52

The findings of this study indicate that TEI is an effective treatment method to temporarily relieve symptoms for many patients with lumbar radiculopathy regardless of their radiologic diagnosis. MRI examination before TEI may not be necessary and TEI might be planned at an earlier stage, resulting in more adequate treatment of symptoms, reduction of opioid use, and avoidance of surgical intervention. For patients unresponsive or with recurring pain after a single epidural injection, multiple injections could be beneficial. To properly assess the efficacy of TEI in the acute phase of lumbar radiculopathy without extensive radiologic examination and determine the potential predictive value of epidural injections, a randomized controlled trial is required. Moreover, adverse events need to be registered to determine the safety of TEI without preceding MRI.

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