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

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Factors associated with patient outcome after transforaminal epidural injection for lumbar disc herniation and stenosis: a systematic review of current literature

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Submitted

ABSTRACT

Purpose

Lumbar radicular pain is usually caused by a herniated disc (LDH) or spinal stenosis which instigates inflammatory and immunological responses. Transforaminal epidural injections (TEI) with steroids are aimed at reducing these responses in order to relieve pain symptoms and improve physical functionality. However, it is unknown which factors can differentiate between responders and non-responders. The purpose of this systematic review is to elucidate which demographical, clinical and radiological factors are associated with patient outcome after TEI.

Methods

The PubMed, Embase, Web of Science, Cochrane Library, Emcare and Academic Search Premier databases were searched for studies assessing the association between demographic, clinical and radiological variables, and clinical outcome after a unilateral, single-level TEI in patients with lumbar radiculopathy secondary to disc herniation or degenerative stenosis. Risk of bias was evaluated using an adjusted version of the Cowley risk of bias criteria. Outcome measures included patient-reported symptom relief, leg pain or physical functionality scores. A qualitative analysis of included studies was performed.

Results

A total of 36 studies were included assessing 37 different factors and their association with TEI outcome. Among demographic variables there was some evidence for an association between shorter duration of symptoms and superior outcome after TEI. For clinical factors there was limited evidence associating a positive Slump test with better patient outcome. Among radiological factors limited evidence was found for an association with stenosis rather than LDH, more centrally located LDH compared to more laterally locations of the herniation, the absence of transitional vertebrae and a higher degree of nerve root compression with a favorable outcome after TEI.

Conclusion

Several factors were identified that associated with TEI outcome possibly indicating some predictive power, although generally the evidence was limited. The small number of studies that assessed each factor and heterogeneity among studies precluded a quantitative analysis of the results. Additional studies are necessary to further substantiate these associations before strong conclusion can be drawn.

INTRODUCTION

Lumbar radiculopathy is generally caused by lumbar disc herniation or spinal stenosis secondary to degenerative changes located in the lateral recess or in the neuroforamen [1]. Due to an intricate interplay of physical compression, inflammatory and immunological processes, irritation of a nerve root arises which may result in symptoms of leg pain, sensory and motor deficits [2, 3]. Since these symptoms usually interfere with daily activities, lumbar radiculopathy is often considered strongly invalidating and patients seek for effective treatments to relieve symptoms [4]. For lumbar disc herniation current guidelines recommend starting conservative therapy during the first weeks to months before switching to more invasive options as this condition is generally self-limiting over time [5-7]. For spinal stenosis there is no full consensus on treatment strategies as some patients may experience spontaneous relief of symptoms despite the general idea that spinal stenosis has a more chronic character than disc herniation. As a result, clinical guidelines are more incongruous with each other [8-11]. Nevertheless, for both conditions there are treatment options aside from surgery for patients whose symptoms do not resolve naturally within reasonable time.

Transforaminal epidural steroid injections (TEI) is a treatment that has been offered to patients with (unilateral) lumbar radiculopathy due to disc herniation or stenosis for decades [12]. These steroid injections are aimed at reducing inflammatory cytokines and downregulating immunological reactions in order to relieve pain symptoms [13, 14]. They are assumed to have a temporary analgesic effect but may result in complete resolution of symptoms in some patients. In addition to the transforaminal route, epidural steroid injections can be administered through a caudal or interlaminar approach, but the transforaminal injection is considered to be the most selective one. Despite the wide use of TEI in patients with lumbar radiculopathy due to disc herniation or spinal stenosis its effectiveness remains a matter of debate. Studies have demonstrated contradictory results with large variation in efficacy and success percentages, but it remains unclear which determinants are of influence on the efficacy of TEI [10, 12, 15-18]. Some studies have suggested that TEI effectiveness may be affected by the etiology of lumbar radiculopathy (i.e., disc herniation or stenosis), whereas other studies propose alternative subgroups of patients that may benefit more from treatment with TEI. The varying effectiveness of TEI across studies and the uncertainty of which patient groups benefit more than others have led to discrepancies between clinical guidelines on the applicability and timing of TEI [5, 6, 8, 12, 15, 18-20]. Therefore, establishing predictive factors for treatment success with TEI could aid in tailoring treatment strategies for

patients with lumbar radiculopathy, possibly obviating the need for surgery or expediting the timing of surgical intervention. For this reason, we aim to provide a comprehensive overview of the current literature on demographic, clinical and radiological factors and their association with TEI efficacy in patients with unilateral lumbar radiculopathy due to disc herniation or stenosis.

METHODS

This systematic review was conducted in accordance with the PRISMA guidelines.

Search and selection

Six databases (PubMed, Embase, Web of Science, Cochrane Library, Emcare and Academic Search Premier) were searched from inception to 25 July 2025. A search strategy was constructed and adapted to every database by an expert librarian (Appendix 1). Full texts as well as meeting abstracts were included in the search. Strings were included for prospective and retrospective studies on patients with lumbar disc herniation or degenerative stenosis with unilateral symptoms. Acceptable outcome measures were the Numerical Rating Scale (NRS) or the Visual Analogue Scale (VAS) for pain scores and the Oswestry Disability Index (ODI) or the Roland Morris Disability Questionnaire (RMDQ) for physical disability scores. All results were screened by two reviewers (EV and NV) separately based on title and, consequently, on abstract. The remaining full texts were evaluated by two reviewers independently. Any discrepancies were resolved by discussion or consulting a third reviewer (CVL).

Inclusion and exclusion criteria

Studies analyzing the association between predictive factors and the success of TEI were included if they met the inclusion and exclusion criteria. Studies were eligible if the study design was a Randomized Controlled Trial (RCT), prospective cohort or retrospective cohort and patients had unilateral radicular pain. The choice to only include patients with unilateral symptoms was based on the idea that patients with bilateral complaints may not be sufficiently helped with a single transforaminal injection and pain and disability scores would not represent the treatment efficacy accurately. In addition, studies were eligible if patients had MRI confirmed LDH or degenerative stenosis (central, lateral recess and/or foraminal), they were injected on only one level on one side, received TEI containing any type of steroids, the outcome measure was based on symptom relief, leg pain, functionality scores or need for subsequent surgery, the cohort consisted of at least 20 patients, the follow-up was at least two weeks, and the

article was written in English. Studies were excluded if they presented a case report or series, systematic review or meta-analysis, included patients with previous back surgery, scoliosis or spondylolisthesis, allowed for administration of multiple injections, used an injection approach other than the transforaminal route, evaluated technical aspects of transforaminal injections, evaluated different types or concentrations of corticosteroids, used non-fluoroscopy guided injections, only measured back pain, or investigated a predictive factor derived from invasive examinations that are not part of routine work-up (e.g., not every patient with lumbar radiculopathy undergoes EMG).

Risk-of-bias assessment

Risk of bias assessment was performed by two reviewers separately (EV and NV), using an adjusted version of the Cowley risk of bias criteria (Appendix 2) [21]. Each study could be awarded a minimum of 0 and maximum of 10 points. Studies with a score above seven points were classified as low risk of bias, studies with 5-7 points as intermediate risk of bias and studies with fewer than 5 points as high risk of bias. Differences between the two assessors were resolved during a consensus meeting with a third reviewer (CVL).

Data extraction and analysis

From all included studies, data on methods (study design, cohort size), patients (inclusion and exclusion criteria, baseline characteristics, diagnostic characteristics), treatment, outcome variables and results were gathered by one reviewer with a second reviewer verifying the final data extraction. When patients were dichotomized based on treatment outcome the definition of treatment success was included. Results were based on data from text, tables or graphs and included raw data, whether an association was found and the conclusion the authors had drawn. For continuous outcome measures means and standard deviation (SD) or median value and range were retrieved, whereas for dichotomized outcomes absolute numbers, percentages, or odds ratios (OR) were gathered. A qualitative analysis was performed for all results.

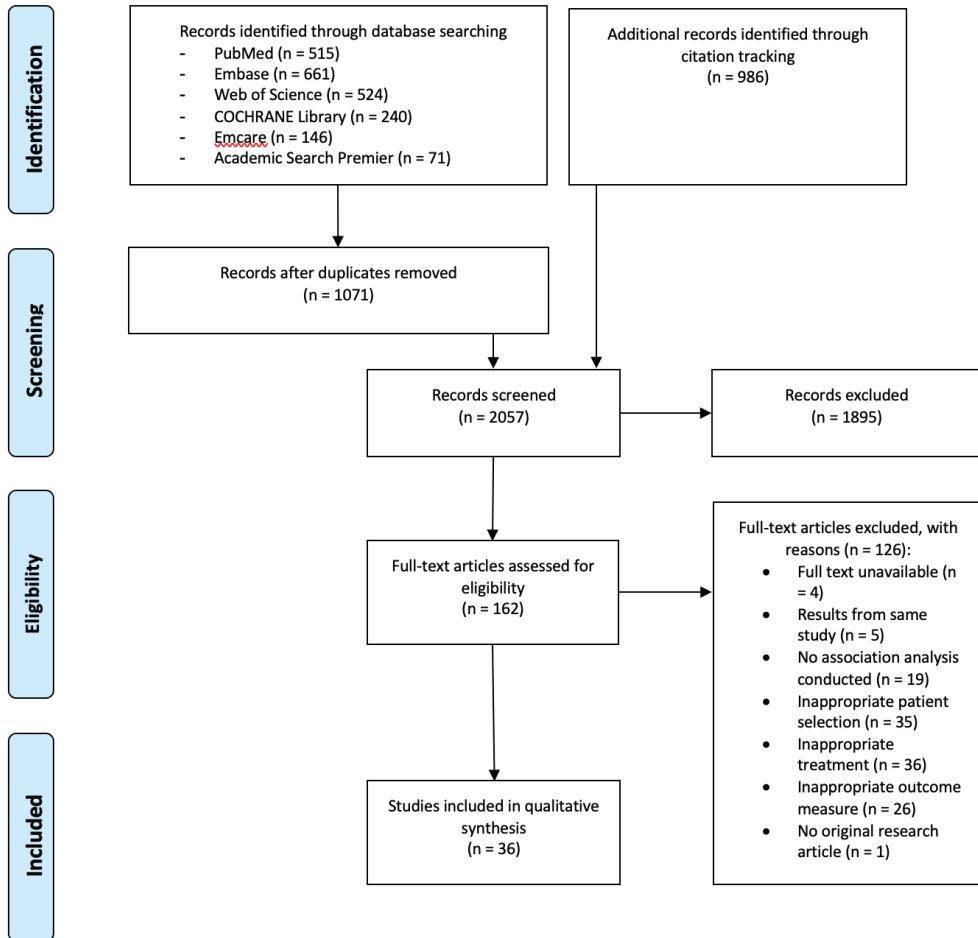
RESULTS

Article selection

The literature search yielded a total of 2057 unique articles of which 162 references were selected for full-text screening. Eventually, 36 articles were included for this review (Fig. 1) [22-57]. Twenty-two articles assessed patients with lumbar disc herniation, five articles evaluated patients with spinal stenosis and nine studies included both patient groups. Twenty-one studies were prospective,

and fifteen studies were conducted retrospectively. All studies were published between 2006 and 2025 and the patient population size ranged between 20 and 2024 patients. A more elaborate overview of study characteristics is given in Appendix 3.

Fig. 1 Flowchart of the article search and selection process. A total of 2057 records were screened of which 36 articles were included in this review.



Risk-of-bias assessment

Of the 36 reports, ten scored 8 or 9 out of ten points and were considered low risk of bias [28, 31, 32, 39, 45, 50, 52, 53, 55, 57]. A total of 22 reports were awarded 5 to 7 points and were categorized as intermediate risk of bias [22, 24-27, 29, 30, 35, 36, 38, 40-44, 46-49, 51, 54, 56]. Four studies scored four points or lower and were judged as high-risk of bias [23, 33, 34, 37] (Appendix 4).

Factors associated with patient outcome

In all studies, a total of 37 different factors were assessed for their association with patient outcome after treatment with a TEI. Of these 37 factors, eight variables were demographic, ten were clinical and nineteen were radiological. Results are summarized in Table 1. All extracted data are provided in Appendix 5.

Table 1 An overview of all demographic, clinical and radiological variables studied for their association with TEI outcome. For each variable the number of studies that found an association and the number of studies that did not find an association are provided.

Variable	Number of studies that found an association	References	Number of studies that did not find an association	References
Demographic factors				
Age	1	[37]	8	[22, 24, 29, 36, 38, 41, 46, 50]
BMI	1	[37]	4	[36, 40, 46, 50]
Duration of symptoms	4	[29, 35, 37, 48]	6	[24, 36, 38, 41, 46, 50]
Injection level	0		6	[22, 24, 42, 50, 56]
Injection side	0		4	[24, 37, 38, 56]
MRI to block	0		1	[38]
Sex	1	[37]	6	[24, 36, 38, 41, 42, 50]
Smoking status	0		1	[36]
Clinical factors				
hsCRP	0		1	[44]
Positive Slump test	2	[31, 32]	0	
Pre-injection functional score	2	[36, 37]	1	[45]
Pre-injection pain score	1	[37]	5	[29, 36, 45, 46, 50]
Presence of HACS	1	[47]	0	
Presence of neurologic deficit	1	[36]	1	[31]
Presence of neuropathic pain	1	[51]	0	
Vitamin D deficiency	1	[43]	0	
Post-injection functional score	1	[36]	1	[45]
Post-injection pain score	1	[50]	2	[36, 45]

Table 1 An overview of all demographic, clinical and radiological variables studied for their association with TEI outcome. For each variable the number of studies that found an association and the number of studies that did not find an association are provided. (continued)

Variable	Number of studies that found an association	References	Number of studies that did not find an association	References
Radiological factors				
Facet tropism	1	[27]	0	
Gadolinium enhancement of nerve root	1	[54]	0	
IVD signal intensity	1	[56]	0	
Lesion level	0		3	[24, 29, 36]
Lesion severity	2	[28, 39]	3	[24, 33, 36]
Lesion side	0		1	[36]
Location of LDH	2	[32, 34]	3	[29, 36, 56]
Grade of facet degeneration	1	[49]	0	
Grade of nerve root compression	3	[31, 32, 56]	4	[26, 40, 46, 50]
Mean spinal nerve intensity	1	[38]	0	
Morphology of LDH	2	[36, 55]	1	[30]
Nerve-to-fat signal ratio	1	[38]	0	
Paraspinal muscle area	0		1	[46]
Presence of Modic changes	0		1	[57]
Presence of transitional vertebrae	3	[36, 52, 53]	1	[50]
Radiological etiology of symptoms	3	[24, 25, 42]	3	[29, 31, 41]
Type of disc degeneration	1	[32]	2	[36, 56]
Type of Gadolinium enhancement of nerve root	0		1	[54]
Type of transitional vertebrae	1	[53]	0	

BMI: Body Mass Index; HACS: human assumed central sensitization; hsCRP: high-sensitivity C-reactive protein; IVD: intervertebral disc; LDH: lumbar disc herniation; MRI: Magnetic Resonance Imaging

Demographic factors

One high risk-of-bias study reported that age was positively associated with improvement in pain and disability scores following TEI [37], whereas eight others did not demonstrate a relationship [22, 24, 29, 36, 38, 41, 46, 50]. Duration of symptoms was negatively associated in four out of ten studies in terms of pain and functionality scores [29, 35, 37, 48], including one high-risk-of-bias study [37].

Sex was evaluated in seven studies [24, 36-38, 41, 42, 50], but only one (high risk of bias) observed better outcomes in men at two months follow-up [37]. Among five studies investigating body mass index (BMI) [36, 37, 40, 46, 50], only a single high-risk-of-bias report found a marginal positive association with short-term functional improvement but not with pain or longer-term results [37].

For injection level [24, 38, 42, 50, 56], injection side [24, 37, 38, 56], the number of days between MRI and TEI treatment [38] and smoking status [36], no association was found in any of the studies.

Clinical factors

Six studies assessed pre-injection pain scores [29, 36, 37, 45, 46, 50] and three pre-injection functional scores [36, 37, 45]. Only one high-risk of bias study found an association between pre-injection pain scores and better short-term outcome [37]. That same study, along with another [36], reported an association between baseline functional scores and post-injection outcomes.

High-sensitivity C-reactive protein levels were not associated with TEI outcome [44]. One study showed that patients with neuropathic pain experienced greater functional improvement at three months than those without [51]. A positive Slump test correlated with greater reductions in pain and disability at three weeks [31, 32], whereas vitamin D deficiency and the presence of central sensitization were negatively associated with outcome [43, 47]. One study found no association between neurological deficit and treatment effect [31], while, contrastingly, another reported poorer outcomes in patients with sensory symptoms [36].

Pain reduction one hour post-injection predicted three-month success in one study [50], although two other studies found no such association [36, 45]. However, one of these did find an association between higher functionality at three weeks and one-year outcome [36].

Radiological factors

Three of six studies demonstrated an association between the radiological etiology (LDH or stenosis) and treatment effect [24, 25, 29, 31, 41, 42]. Patients with lumbar stenosis achieved greater immediate post-injection improvement than those with LDH in one study [24], whereas another reported superior long-term results for foraminal stenosis compared to LDH or spinal/lateral recess stenosis [42]. Contrastingly, the third study demonstrated better pain reduction in LDH than LSS at four weeks [25].

Type of disc degeneration (i.e., bulging, protrusion, extrusion) was assessed in three studies [32, 36, 56], but only one found greater short-term functional improvement for disc extrusion compared to disc protrusion [32]. Two of three studies evaluating disc morphology reported an association with TEI outcome, though one was high risk-of-bias [23, 55].

Findings on LDH location were inconsistent: three studies found no correlation [29, 36, 56], whereas two other studies suggested better outcomes for central/subarticular or paramedian herniations compared with foraminal/extraforaminal lesions [32, 34], one of which had high risk of bias.

Three studies investigated MRI signal characteristics. Increased nerve-to-fat signal ratio and mean spinal nerve intensity on axial T2-weighted images predicted better post-injection outcomes in one study [38], and gadolinium enhancement of the nerve root was also associated with improvement in another, independent whether the post-dorsal root ganglion enhanced [54]. High signal intensity zones within the intervertebral disc were associated with lower pain scores at two weeks, but not for success rates or for three-month post-injection outcomes [56].

Lesion level and side were not associated with TEI outcome [24, 29, 36]. Lesion severity (grading of LDH or stenosis) was examined in five studies using various grading scales [24, 28, 33, 36, 39]. Four categorized lesion severity as mild, moderate or severe: two reported better outcomes for mild-moderate or moderate stenosis compared to severe cases [28, 39], whereas two studies found no association for either LDH or stenosis patients [24, 33], though the latter study had a high risk of bias. Another study also found no correlation between Pfirrmann grade and post-injection outcome [36].

Seven studies evaluated the degree of nerve root compression using different grading systems. Three demonstrated outcome differences by compression grade. In two studies, high-grade subarticular compression was associated with

greater short-term functional improvement compared to high-grade foraminal or low-grade (subarticular) compression, whereas pain scores and outcomes between low- and high-grade foraminal compression did not differ [31, 32]. A third study reported lower pain scores at three months in patients with any compression versus none, but not at two weeks or in success-rate analyses [56]. By contrast, three studies using the (modified) Pfirrmann scale and one dichotomizing discoradicular contact found no association between compression grade and TEI outcome [26, 40, 46, 50].

Four studies assessed the presence of transitional vertebrae of which three found a negative association with TEI outcome [36, 52, 53]. Specifically, sacralization was associated with worse results than lumbarization or absence of transitional vertebrae [53]. Facet tropism and high-grade facet degeneration were associated with less favorable TEI responses [27, 49]. No associations were demonstrated for paraspinal muscle area or the presence of Modic changes [46, 57].

DISCUSSION

This systematic review summarizes the current literature on demographic, clinical and radiological variables, and their association with patient outcome after TEI. For demographic variables, there is some evidence for an association between duration of symptoms and outcome after TEI, with four out of ten studies indicating worse patient outcome when symptom duration was longer. Chronicity of inflammatory processes can result in pain perception and conduction alterations, and, therefore, may render local treatment with corticosteroids less effective [29, 37, 58, 59]. However, of these studies, three had an intermediate and one had a high risk of bias. Of the studies that found no association, five were intermediate and one was low risk of bias. As a result, there is no convincing evidence that can fully sustain this association and, thus, no implication that patients with chronic radicular symptoms should be advised against treatment with TEI.

In terms of clinical factors, a positive Slump test was positively associated with TEI outcome. A possible explanation for the positive association may be that this test makes a distinction between lumbar radiculopathy and leg pain symptoms without neural compromise, while TEI is only aiming to relieve radicular pain. However, the evidence was limited with only two studies reporting on this variable. In addition, five out of six studies found no association with pre-injection

pain score, indicating that both patients with mild and severe radicular pain may benefit from TEI.

Similarly, there was limited evidence for the association between stenosis rather than LDH patients and improved outcome after TEI. This appears to contrast with the results related to symptom duration in some studies, since, in general, patients with lumbar stenosis tend to suffer from chronic symptoms more frequently than LDH patients. However, it is possible that the inflammatory component plays a more significant role in stenosis patients compared to LDH patients. Some evidence was available for the association between the presence of transitional vertebrae and inferior TEI results. This association may be due to a more challenging identification of the affected nerve root to aim for with TEI, or to the technically more complicated procedure in applying TEI. Furthermore, there was limited evidence suggesting that more centrally located LDH are associated with better outcomes following TEI compared to more lateral locations. Central or paramedian herniated discs may be larger, potentially eliciting a higher release of inflammatory cytokines. Although this would also result in more compression, lateral herniations may actually exert greater physical impingement due to the restricted space available for the nerve root within the foramen. Hence, in the case of central and paramedian disc herniations, the inflammatory component rather than mechanical compression may affect the nerve root more, leading to a higher response to TEI. Conversely, three out of seven studies demonstrated a positive correlation between higher grades of nerve root compression and superior TEI outcomes. This finding appears counterintuitive, as patients with less physical compression are generally thought to have a larger inflammatory or immunological component and would therefore be expected to respond better to TEI. However, the reliability of this association is limited: it was observed in fewer than half of the available studies and only for functional improvement, not for pain scores [31, 32]. Moreover, one study included only patients with either marked (≥ 10 -point) improvement in ODI or no response, thereby excluding those with intermediate outcomes [31], while another found a statistically but not clinically significant difference [56].

A strength of the current review is that strict inclusion and exclusion criteria were applied during the literature search. Only studies that described treatment with a single transforaminal epidural steroid injection were eligible for inclusion in order to maximize the comparability between treatments. Moreover, only studies on patients with unilateral radiculopathy could be included as it was hypothesized that TEI may not be as effective in patients with bilateral complaints due to its route of administration, hence our results would be confounded by this. Furthermore, reports using outcome instruments for pain symptoms other

than NRS and/or VAS, or for functional disability other than ODI and/or RMDQ scores were excluded for comparability purposes. However, our strict inclusion and exclusion criteria may have resulted in the omission of articles that held interesting results but not fully met our criteria. Another limitation is that comparability of studies may be restrained by the diversity of steroids, volumes and dosages used for TEI, and the variety in follow-up moments across studies. This may have affected the results from our review.

To our best knowledge, only three other reviews have been published before that evaluated the association of factors with outcome after epidural steroid injections [60-62], though they had different approaches than we chose for the current paper. One review focused on RCTs of epidural steroid injection versus placebo, different epidural injection approaches, different type and dose of corticosteroids, and yielded only limited evidence for epidural corticosteroid efficacy, without appointing clear prognostic factors [60]. Another review considered laboratory markers and imaging characteristics as predictive tools for epidural steroid injection efficacy [61], and concluded that there is some evidence for an association of more pain relief in patients with more nerve root compression. Additionally, they reported that IFN- γ obtained from epidural lavage fluid predicts short-term pain reduction, although it was mentioned that the use of this assay is challenging and expensive in a clinical setting. Yet, for that particular review studies on all epidural techniques and both patients with cervical and lumbar radicular pain were included. A more recent review on prognostic factors in disc-related sciatica reported findings consistent with ours, demonstrating some evidence of a negative association between symptom duration and TEI outcome, as well as for the degree of nerve root compression, for which our review provided only limited support [62]. However, the authors accepted studies on patients with bilateral sciatica, all three epidural techniques with or without image-guidance, multi-level injections, they did not include the PubMed database, excluded stenosis patients and included fewer prospective studies.

The heterogeneity with regard to design and methodology between studies complicates the comparability of findings and may explain that some results are contradictory. In order to identify subgroups of LDH and stenosis patients that benefit more from TEI treatment, future studies should be specifically designed for development of a prediction model for TEI success. Moreover, future studies should focus on predictive factors for the effect of a single injection rather than a series of injections.

Overall, there is no strong evidence for any association between the assessed variables and TEI outcome based on the studies in this review. There is limited support that duration of symptoms, positive Slump test, radiological etiology of symptoms, location of LDH, transitional vertebrae and nerve root compression may influence TEI efficacy, but these associations need to be further substantiated in future studies before firm conclusions can be drawn.

Appendices will be available online after publication.

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