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Nagington, A; Foster, NE; Snell, K; Konstantinou, Kika; Stynes, S

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REVIEW ARTICLE

Prognostic factors associated with outcome following an epidural steroid injection for disc-related sciatica: a systematic review and narrative synthesis

Alan Nagington[1] · Nadine E. Foster[2,3] · Kym Snell[2] · Kika Konstantinou[1,2] · Siobhán Stynes[1,2]

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Abstract

Purpose Clinical guidelines recommend epidural steroid injection (ESI) as a treatment option for severe disc-related sciatica, but there is considerable uncertainty about its effectiveness. Currently, we know very little about factors that might be associated with good or poor outcomes from ESI. The aim of this systematic review was to synthesise and appraise the evidence investigating prognostic factors associated with outcomes following ESI for patients with imaging confirmed disc-related sciatica.

Methods The search strategy involved the electronic databases Medline, Embase, CINAHL Plus, PsycINFO and reference lists of eligible studies. Selected papers were quality appraised independently by two reviewers using the Quality in Prognosis Studies tool. Between-study heterogeneity precluded statistical pooling of results.

Results 3094 citations were identified; 15 studies were eligible. Overall study quality was low with all judged to have moderate or high risk of bias. Forty-two prognostic factors were identified but were measured inconsistently. The most commonly assessed prognostic factors were related to pain and function ($n=10$ studies), imaging features ($n=8$ studies), patient sociodemographics ($n=7$ studies), health and lifestyle ($n=6$ studies), clinical assessment findings ($n=4$ studies) and injection level ($n=4$ studies). No prognostic factor was found to be consistently associated with outcomes following ESI. Most studies found no association or results that conflicted with other studies.

Conclusions There is little, and low quality, evidence to guide practice in terms of factors that predict outcomes in patients following ESI for disc-related sciatica. The results can help inform some of the decisions about potential prognostic factors that should be assessed in future well-designed prospective cohort studies.

Keywords Prognostic factors · Epidural steroid injection · Sciatica · Systematic review

Background

Sciatica is a common variation of low back pain, presenting as sharp, shooting pain in the leg, often with numbness and muscle weakness [1]. In most cases (90%) [1] sciatica is caused by a lumbar disc herniation compressing the lumbar spinal nerve root(s), with associated inflammation [2]. Many patients improve but around 30% continue to suffer from pain and related disability after one year [3]. Guidelines recommend epidural steroid injections (ESI) for treating severe disc-related sciatica pain based on trial data that shows modest benefits in terms of pain reduction and avoidance of surgery [4, 5]. ESIs can be performed in a number of ways (caudal, interlaminar and transforaminal approaches), and with or without imaging to verify delivery of the injectile substance to the target level in the spine [6]. The term epidural steroid injection (ESI) is used throughout this paper to describe any type of spinal injection (including local anaesthetic and corticosteroid), used for disc-related sciatica for reducing leg pain.

✉ Siobhán Stynes
s.stynes@keele.ac.uk

[1] Midlands Partnership NHS Foundation Trust, Haywood Hospital, Stoke On Trent, Staffordshire, UK

[2] Primary Care Centre Versus Arthritis, School of Medicine, Keele University, Staffordshire, UK

[3] Surgical Treatment and Rehabilitation Service (STARS), Education and Research Alliance, The University of Queensland and Metro North Hospital and Health Service, Herston, QLD, Australia

There is considerable uncertainty about the effectiveness of ESI for sciatica. A recent Cochrane review update showing small, average, treatment effects raised questions about the value of ESIs [7], with similar findings in other reviews where very few studies detected clinically relevant effects, and the certainty of evidence was judged to be low [8, 9]. However, another recent review argued that these conclusions are flawed and their review which did not include active placebo (e.g. anaesthetic), showed strong evidence for the effectiveness of ESI for managing sciatica [10]. Clinical guidelines provide different recommendations; ESIs are recommended for those with severe sciatica in the UK [4] and Belgium [11], whereas they are not recommended in the Netherlands [12], ESIs are one of the most common interventional pain procedures in the USA [13]. In the UK National Health Service (NHS), the average cost for an ESI under image guidance is £711 [14] and on average 5.2% of patients receive three or more injections in a 12-month period (April 2015–March 2018). Around 9500 injections are repeated in under six months, with a total annual cost to the NHS of £6.7 m [15].

There appears to be wide variation in response to ESIs, with some patients improving to such a degree that spinal surgery is avoided whilst others do not improve [4, 7–10]. Little is known about which factors are associated with outcome from ESIs; patient characteristics, clinical assessment findings, imaging findings or other test results. Only one systematic review of prognostic factors associated with treatment outcomes for sciatica, limited to imaging and laboratory markers, concluded that nerve root compression grading on MRI (magnetic resonance imaging) scan and elevated inflammatory markers were promising predictors of outcome [16].

With the need to reduce low value healthcare [17] it would be helpful to be able to better identify patients who have a reasonable chance of benefiting from ESI. This would prevent unnecessary burden on healthcare services and unnecessary healthcare costs. The objectives of this systematic review were to identify what factors, from those that are routinely collected in clinical practice, are potentially associated with good or poor outcome after an ESI for sciatica.

Methods

This review followed the PRISMA statement for reporting systematic reviews [18]. The protocol was registered on PROSPERO (CRD42020225777).

Eligibility criteria

Study eligibility criteria were guided by the PICOTS framework [19], covering population, index prognostic factor, comparator prognostic factors, outcomes, timing and setting/study design (Table 1). Included studies reported results for adults with a diagnosis of disc-related sciatica confirmed with MRI scan (or CT (Computerised Tomography) myelogram) of any duration who received an ESI for their sciatica symptoms. Studies were excluded if they did not present any information, statistical or narrative, on the strength of association between prognostic factors and outcome(s). We did not include laboratory markers as prognostic factors as they are not routinely collected as part of usual healthcare for sciatica patients.

Search strategy and Study selection

Four electronic databases were searched (MEDLINE, EMBASE, CINAHL Plus, PsycINFO) from inception to November 2020. An updated search was carried out in February 2022. Reference lists of included full text studies were searched. The search strategy used subject headings and free text searching, combining terms for prognosis, epidural steroid injection and sciatica. The Medline search strategy is presented in Table 2.

The results of all searches were downloaded into EndNote X9 (available at https://endnote.com/) to remove duplicates. The remaining studies were transferred to an excel spreadsheet for initial title and abstract screening, aided by an eligibility criteria checklist (Table 3).

All titles and abstracts were screened independently by two authors (AN & SS). Any disagreement was resolved through discussion. Full texts were independently screened by two authors (AN and SS) with a third reviewer (KS or KK) being consulted in the case of disagreements.

Data extraction

One reviewer extracted data for all the studies (AN) which was thoroughly checked by a second reviewer (SS). Data extraction was guided by CHARMS-PF, a modification of the checklist for critical appraisal and data extraction for systematic reviews of prediction modelling studies that can be used for prognostic factors [19]. Prognostic factors identified were grouped into domains of patient socio-demographics, health and lifestyle, medication, work, onset of sciatica, pain and function (disability), psychological measures, clinical assessment findings, MRI scan findings, EMG (Electromyography) study findings, QST (Quantitative Sensory Testing) and level and number of injections.

Risk of bias

The Quality in Prognostic Studies (QUIPS) tool [20] was used by two authors independently (AN and SS) to assess the risk of bias for each study. It consists of six potential bias

Table 1 Criteria for inclusion and exclusion of studies

Population
Adults (aged 16 years and over)
Diagnosis of disc-related sciatica confirmed with MRI scan (or CT myelogram)
Epidural steroid injection (ESI) delivered via transforaminal, interlaminar or caudal approaches, with or without image guidance
Index prognostic factors
Prognostic factors collected/measured before the ESI intervention and analysed for their association with outcome
Prognostic factors include patient characteristics, clinical assessment findings, EMG study findings, MRI scan or other imaging findings
Comparator prognostic factors
n/a
Outcomes
Leg pain, measures of function / disability, time to recovery, health-related quality of life or progression to another injection or surgery
Timing
Any data collection time-point to reflect short-term (0 to 2 weeks), medium-term (up to 3 months) and longer-term (up to 1 year) outcomes
Setting/Study design
Any healthcare setting
Prospective and retrospective longitudinal cohorts, randomised controlled trials
Exclusion criteria
Population
Spinal injection for a back related condition that is not disc-related sciatica
Index prognostic factors
Laboratory markers (e.g. obtained from simple blood tests or from material harvested during the injection) measured as prognostic factors
Setting/Study design
Unpublished studies, conference proceedings, single case studies, pilot randomised controlled trials (RCT) and non-English articles

n/a not applicable; *MRI* magnetic resonance imaging; *CT* computerised tomography; *EMG* electromyography

domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting. Domains were rated as low, moderate or high [20]. If there was uncertainly or in the event a domain was considered not appropriate it was rated as unsure. Overall risk of bias classification was rated low, moderate or high risk. To achieve low overall risk of bias, each domain must score low in all the 6 domains.

Synthesis of results

Results extracted from studies, included unadjusted (or crude) and adjusted estimates of the association of the prognostic factor with the outcome and corresponding standard errors or confidence intervals (e.g. odds ratio) for each prognostic factor of interest [19]. Where possible, reporting of adjusted prognostic associations (from multivariable analyses), including odds ratios, and 95% confidence intervals and p values were stated. Study heterogeneity precluded statistical pooling of results. Therefore a narrative synthesis was developed to provide an overview of the evidence for each prognostic factor.

A guide to systematic review and meta-analysis of prognostic factor studies [19] was used as a guide to conduct the review and REMARK (reporting recommendations for tumour marker prognostic studies) [21] was used to guide the review reporting.

Results

Study selection

The search yielded 2726 citations after duplicates were removed. Following screening of titles and abstracts, the full texts of 130 studies were retrieved that satisfied the eligibility criteria outlined in Table 3. Studies unrelated to the topic of interest or not meeting the eligibility criteria were excluded. If after reading title and abstract the eligibility was unclear, full texts were retrieved and assessed. The updated search on 3rd February 2022 identified 368 additional titles and abstracts for screening. Four studies fulfilled the inclusion criteria therefore a total of 15 studies were included in the review (see the flowchart in Fig. 1).

Included studies

Fifteen studies, published between 1998 and 2021 (1606 participants) provided information about potential prognostic factors for patients with disc-related sciatica who had an

Table 2 Search strategy Medline

Search no	Search term	Results
1	Exp sciatic neuropathy/	7115
2	Sciatic*.tw,kf	29,750
3	Ischialg*.tw,kf	152
4	((disk* or disc*) adj3 (herniat* or prolapse* or slipped)).kf,tw	12,678
5	Intervertebral disc displacement/	18,774
6	Radiculopathy/	5165
7	Radicular.kf,tw	7787
8	((lumb* or sacr*) adj3 radicul*).kf,tw	2515
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	62,612
10	"Epidural*".kf,tw	42,886
11	(Nerve adj2 block*).kf,tw	13,719
12	"Injection*".kf,tw	579,321
13	Injections, Spinal/	12,609
14	Injections/	42,750
15	10 or 11 or 12 or 13 or 14	648,801
16	9 and 15	8775
17	Exp prognosis/	1,651,581
18	"Prognos*".kf,tw	626,383
19	"Predict*".kf,tw	1,614,105
20	Exp Cohort Studies/	2,042,708
21	Cohort.kf,tw	557,870
22	Exp disease progression/	182,669
23	Time factors/	1,192,326
24	Exp recurrence/	184,902
25	Exp morbidity/	564,505
26	Exp survival analysis/	300,604
27	'Natural history".kf,tw	49,189
28	Course.kf,tw	561,393
29	17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28	6,331,903
30	9 and 15 and 29	2874
31	Exp animals/ not humans/	4,744,209
32	30 not 31	2630

ESI for their symptoms [22–36] (see Table 4 for summary of included studies). Study designs included prospective ($n=6$ studies) and retrospective ($n=6$) longitudinal cohorts, RCTs ($n=1$), retrospective review of data from a previously published RCT ($n=1$) and data from an unpublished prospective cohort study ($n=1$). The sample size of included studies ranged from 17 to 390 with a median of 73 participants.

Study characteristics

Three studies included mixed populations of sciatica attributed to disc herniation or stenosis [22, 24, 27] but were included because they analysed results of diagnostic subgroups. All studies indicated concordance between clinical findings of nerve root pain/ radicular pain and imaging (MRI or CT) findings. It was less clear from most of the studies whether the clinically identified nerve root was the same as that reported on imaging.

Participants' age ranged from 17 to 88 years and female participants within studies ranged from 30 to 74%. The ESI routes of delivery were transforaminal ($n=7$), interlaminar ($n=2$) and caudal ($n=2$). One study included all three approaches [22]. Another two studies [26, 31] performed a selective nerve root block (SNRB), which is technically similar to a transforaminal ESI. The remaining study [25] did not clearly report the route of delivery. Fluoroscopic guidance (with contrast dye) was used in 11 studies (including all transforaminal ESI and SNRB studies and one interlaminar ESI study), ultrasound guidance was used for the caudal ESI [33, 35] and two studies did not use image guidance [24, 25]. Injectate solutions varied among the included studies, with differing use of corticosteroids (methylprednisolone acetate ($n=7$), triamcinolone acetonide ($n=7$) and dexamethasone ($n=1$)) and different local anaesthetic (bupivacaine ($n=8$), lidocaine ($n=5$), ropivacaine ($n=1$). One study, which did not report the ESI route of delivery, did not use anaesthetic and reported a total volume used of 7 ml [25]. The total injectate volumes varied between ESI routes of delivery. Transforaminal ESI and SNRB ranged from 1.5 to 4 ml, interlaminar ESI ranged from 3 to 9 ml and caudal ESI from 8 to 30 ml. One study did not report total volume used [26].

Characteristics of the individual studies are summarised in Table 4. Studies are grouped consistently in all tables according to the domains of the prognostic factor.

Prognostic factors

A total of 42 different prognostic factors were identified across the 15 studies (Table 5). The most assessed prognostic factors were related to pain and function ($n=10$ studies each), imaging features ($n=8$ studies), patient socio-demographics ($n=7$ studies), health and lifestyle ($n=6$ studies), clinical assessment findings ($n=4$ studies) and injection level ($n=4$ studies). Six of the 15 studies [23, 24, 26, 33, 34, 36] provided univariate/unadjusted analyses only.

Risk of bias

Nine of the 15 studies were judged as overall high risk of bias (RoB) and six studies were judged moderate RoB (Table 6 and Fig. 2). All high RoB studies had at least one domain judged as high RoB and the remaining domains were predominately moderate RoB. No study achieved low overall RoB, which required low risk ratings in all six domains [20]. In the individual domains of the QUIPS tool, low risk was most prevalent in the domain "outcome measurement".

Table 3 Title and abstract eligibility criteria checklist

Study eligibility	Yes	Unclear	No
Q1. *Population*: are the study participants adults (aged 18 +) with diagnosis of disc-related sciatica with imaging confirmation? Exclude non-specific LBP and sciatica not caused by disc herniation (e.g. stenosis)			
	Go to Q2		Exclude
Q2. *Population*: Is an epidural injection with steroid administered via transforaminal, interlaminar or caudal approaches?			
	Go to Q3		Exclude
Q3. *Index prognostic factor*: are prognostic factors collected/measured before ESI and analysed for their association with outcome? Do they include any of the following; Patient characteristics, Clinical assessment findings, EMG study findings, MRI/ other imaging scan finding?			
	Go to Q4		Exclude
Q4. *Outcome*: Is one or more pain, physical function and/or additional healthcare use measured?			
	Go to Q5		Exclude
Q5. *Timing*: Are data collection time-points included to reflect either short (0–2 weeks), medium (up to 3 months) and/or longer-term (3 months +) outcomes?			
	Go to Q6		Exclude
Q6. *Setting*: Is the study design a longitudinal cohort or RCT and published in English?			
Final decision	Include	Unclear	Exclude

LBP low back pain; *ESI* epidural steroid injection; *EMG* electromyography; *MRI* magnetic resonance imaging; *RCT* randomised controlled trial

Patient factors: demographics, health and lifestyle, medication, work and psychosocial factors

Seven studies investigated age [22, 24, 29, 31–33, 35] and six investigated gender [24, 29, 31–33, 35] but none found a statistically significant association with pain or disability outcomes following ESI. None of the health and lifestyle factors including body mass index (BMI) [29, 31, 35], smoking status [22, 31], type of previous surgery [24, 28] or comorbidities [31] showed a statistically significant association with pain or medication use outcomes. Three studies considered work-related characteristics [22, 28, 31]. White-collared office work [31] and increased physical demands of the job [28] were associated with poor outcomes in univariable analyses but neither remained significant in multivariable analyses. Secondary gain [22, 28] and history of an inciting event (e.g. lifting) [22, 31] were not found to be associated with outcome. Two studies using unadjusted analyses found higher levels of baseline depression to be associated with poorer outcomes of pain and the need for subsequent surgery [23, 26]. Medication use was investigated in two studies, neither found any association with pain reduction or changes in medication use after ESI [22, 28].

Sciatica related factors: onset of sciatica, pain and function

Of the two studies that investigated factors related to the onset of sciatica, no statistically significant association with pain outcomes were found for an inciting event [22, 31] or a previous sciatica episode versus a first episode [31]. For pain related factors, eight studies investigated pain duration [22, 24, 29–33, 35] and only one showed that pain duration less than 6 months was associated with better pain outcomes [35]. Only one [22] of seven studies [22, 24, 27–29, 31, 35] showed an association between higher baseline leg pain and a poorer pain outcome. Co-existing back pain [31], location of pain (calf, entire leg, thigh, gluteal) [31], bilateral sciatica [22] and side of sciatica (right or left) [31] showed no association with pain outcomes.

In unadjusted analysis, a study with 36 participants showed that pain not increased by walking was associated with poorer outcomes and pain that increased during coughing was associated with better outcomes (reduced pain) [24]. One [31] of the three studies [28, 31, 35] that investigated baseline disability scores, found higher baseline Oswestry Disability Index score was associated with minimal or no pain relief after ESI, but no multivariable analysis was carried out.

Clinical assessment findings

Four studies considered findings from the clinical assessment [24, 30, 31, 35]; lumbar flexion [35], straight leg raise test [24, 31, 35], and sensory, motor or reflex deficit [30, 31]. The only statistically significant association with poor pain outcomes, found in one study, was sensory deficit with pain relief (study did not report how pain was measured)

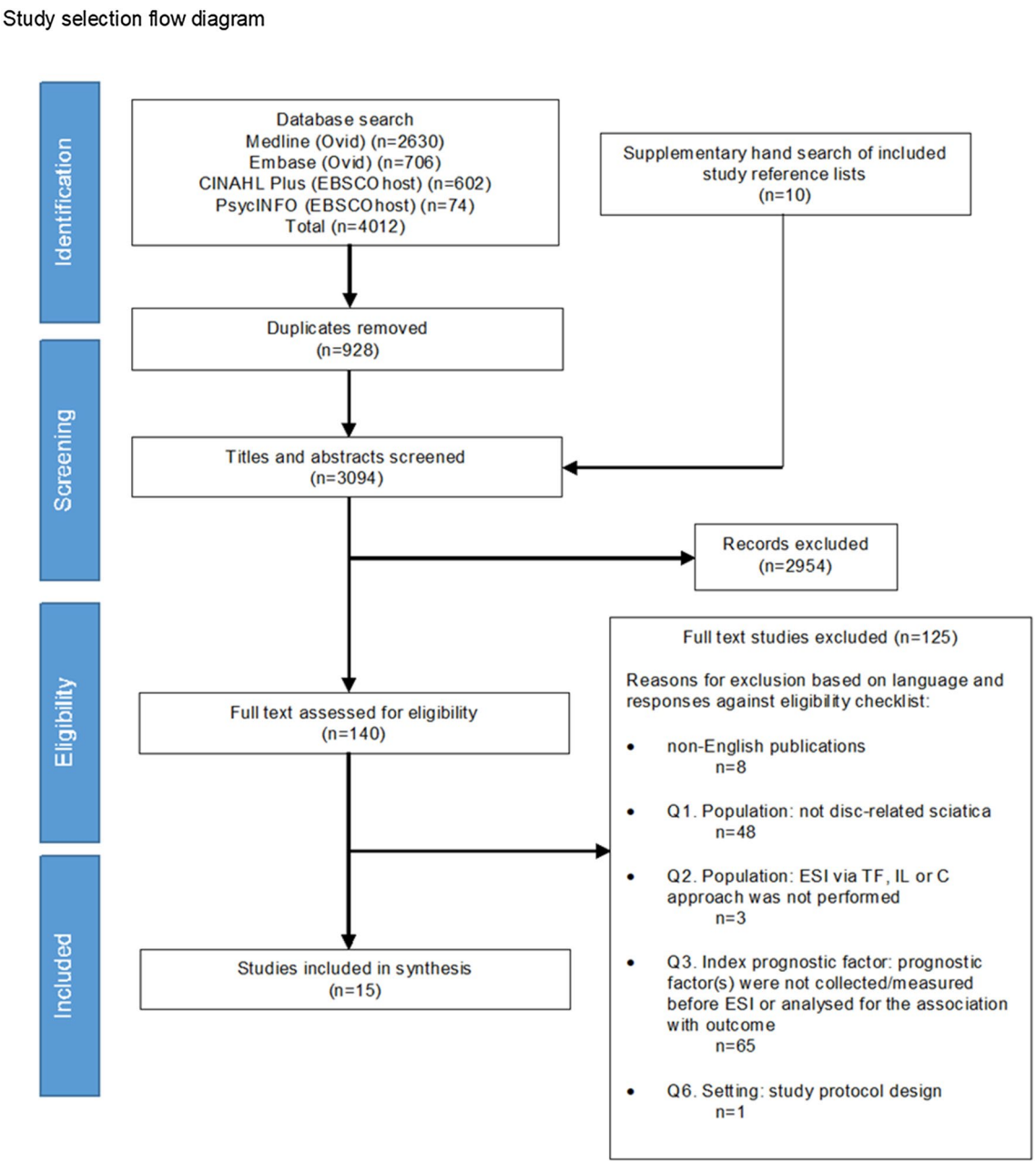

Fig. 1 PRISMA flow diagram showing identification and selection of included studies

in univariable analysis but it did not remain significant in multivariable analysis [31].

Investigation findings: MRI scans, EMG and QST

Eight studies considered various MRI scan findings as prognostic factors [29–36]. Following multivariable analysis, low-grade nerve root compression was associated with better pain outcomes in two studies [30, 32], the presence of a lumbosacral transitional segment was associated with poorer outcomes [31] and the location of disc herniation either centrally [32] or non-foraminal [35], was associated with better pain outcomes.

EMG findings were considered in two studies [27, 28]. In univariable analysis both showed an association between EMG evidence of sciatica and improved outcomes which remained significant in one of the two studies when adjusted for other baseline variables [27]. One small study considered QST, a test to measure mechanical and thermal sensations [25]. In adjusted analysis, greater dysfunction of Aδ-fibres (cold sensation) was associated with better

Table 4 Data extraction detailing study characteristics $n = 15$ studies

Author, year, country	Study design	Study population, sciatica diagnosis	Sampling methods	Sample size, completed cases	Baseline participants mean age years (SD), % female	ESI details
Engle et al. (2019) [22] America	Retrospective cohort	Adults > 18 years, clinical diagnosis of nerve root pain with concordant imaging (MRI) findings lumbosacral radiculopathy secondary to DH, spinal stenosis, or degenerative disc disease. Underwent ESI or epidural lysis of adhesions Exclusion: individuals with insufficient data, symptoms < 6 weeks	Medical records of patients who received ESI	$n = 390$, $n = 326$ (83%)	No baseline values for DH cohort $n = 390$. Total sample $n = 1242$ Age 53.8 (14.4), 58% female	TF, IL or C ESI fluoroscopic guidance + contrast Injectate solutions varied TF ESI: 40–80 mg methylprednisolone acetate, 1–2 ml 0.25% bupivacaine, 0–1 ml saline (total volume 3-4 ml) IL ESI: 40–80 mg methylprednisolone acetate, 1–2 ml 0.25% bupivacaine, 0–2 ml saline (total volume 3-5 ml) C ESI: 40-mg/ml 1.5–2 ml methylprednisolone acetate, 1–2 ml 0.25% bupivacaine or 1% lidocaine, 5–11 ml saline (total volume between 8 and 15 ml)
Bahar-Ozdemir et al. (2020) [23] Turkey	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Lumbar radiculopathy due to lumbar disc herniation, unresponsive to conservative treatments, duration < 3 months,	Patients scheduled for lumbar TF ESI	$n = 161$, $n = 103$ (64%)	Age 48.93 (13.39), 47% female	TF ESI fluoroscopic + contrast 40 mg/ml (2 ml) methylprednisolone acetate, 1 ml 0.5% Bupivacaine, 1 ml saline (total volume 4 ml)
Rivest et al. (1998) [24] America	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI or CT) findings. Low back pain with radicular symptoms, > 6 months duration, no previous spinal surgery, absence of neurological deficit or organic pathology requiring surgery	Patients selected from referrals	$n = 36$*, $n = 36$ (100%) *107 enrolled in study with disc herniation (DH) but only 36 had pre and post injection pain scores	No reported baseline values for $n = 36$ Baseline values for DH group $n = 107$. Age 42, 46% female	IL ESI non-image guided 3 ml (mg not recorded) (methylprednisolone acetate, 3 ml 0.5% lidocaine, 3 ml saline (total volume 9 ml)

Table 4 (continued)

Author, year, country	Study design	Study population, sciatica diagnosis	Sampling methods	Sample size, completed cases	Baseline participants mean age years (SD), % female	ESI details
Schiff, Eisenberg (2003) [25] Israel	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI or CT) findings. Lumbar radiculopathy, single dermatome, 1–24-month duration, presence of DH, confined to the spinal canal	Consecutive patients	$n=20$, $n=20$ (100%)	Age range 24–62 (median 41), 45% female	ESI non-imagine guided Route of delivery is unclear 80 mg (2 ml) methylprednisolone acetate, 5 ml 0.9% saline (total volume 7 ml)
Shaikh et al. (2021) [26] India	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Adults > 18 years with radicular leg pain and MRI evidence of lumbar DH	Consecutive patients	$n=50$, $n=50$ (100%)	Patients who avoided surgery median age 43 (range 19–69), patients who underwent surgery median age 36 (range 27–72) 30% female	SNRB fluoroscopic guided 40 mg/ml Triamcinolone, 0.25% bupivacaine (total volume not reported)
Batistaki et al. (2017) [27] Greece	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Unilateral radicular pain (> 3 months) due to DH or central spinal stenosis	All referrals	$n=20$, $n=20$ (100%)	No reported values for DH cohort. Total sample baseline values $n=39$ (DH $n=20$, stenosis $n=19$) Age 65.9 (12.52), 74% female	IL ESI fluoroscopic guidance + contrast 40 mg triamcinolone, 0.2% ropivacaine (total volume 6 ml)
Tong et al. (2003) [28] America	Retrospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI or CT) findings. Patients with lumbosacral radiculopathies treated with TF ESI	Consecutive patients	$n=76$, $n=76$ (100%)	Age 50.4 (14.8), 49% female	TF ESI fluoroscopic guided + contrast 80 mg/ml methylprednisolone acetate, 1 ml lidocaine (total volume 2 ml)

Table 4 (continued)

Author, year, country	Study design	Study population, sciatica diagnosis	Sampling methods	Sample size, completed cases	Baseline participants mean age years (SD), % female	ESI details
Sencan et al. (2020) [29] Turkey	Retrospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Adults 18–65 years, TF ESI due to unilateral L4, L5, or S1 nerve root compression, MRI confirming L3/4, L4/5, or L5/S1 subarticular/central DH, complete three-month follow-up data	Electronic medical records. Patients diagnosed with DH treated with TF ESI	$n=219$, $n=219$ (100%)	Age 43.65 (12.18), 54% females	TF ESI fluoroscopic guided + contrast 80 mg/ml methylprednisolone, 1 ml 0.5% bupivacaine, 1 ml saline (total volume 3 ml)
Ghahreman, Bogduk (2011) [30] Australia	Retrospective review of data from previously published RCT	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Adults with lumbar radicular pain caused by DH, assessed by a neurosurgeon as eligible for surgery, $n=6$ were inpatients, with intractable pain, remaining $n=65$ had radicular pain > 6 weeks, TF ESI either as their allocated treatment or rescue treatment. Clinically diagnosed (including SLR test) and MRI findings of DH*	Patients with adequate clinical and imaging data from previously published RCT*	$n=71$, $n=71$ (100%)	Age 48.2 years, 46% female	TF ESI fluoroscopic guided + contrast* 40 mg/ml (0.75 ml) triamcinolone, 1.75 ml 0.5% bupivacaine (total volume 2.5 ml)

Table 4 (continued)

Author, year, country	Study design	Study population, sciatica diagnosis	Sampling methods	Sample size, completed cases	Baseline participants mean age years (SD), % female	ESI details
Kanna et al. (2019) [31] India	Prospective cohort	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Patients with lumbar DH on MRI, unilateral radiculopathy, duration < 3 months, failed adequate conservative care (3 weeks), treated with SNRB	All referrals with acute unilateral sciatica	$n = 91$, $n = 91$ (100%)	Successful group age 40.39 (14.82), unsuccessful group age 37.3 (14.24) 40% female	SNRB fluoroscopic guided + contrast 80 mg (2 ml) triamcinolone, 1 ml 0.5% bupivacaine (total volume 3 ml)
Choi et al. (2007) [32] Korea	Retrospective cohort study	Clinical diagnosis of nerve root pain with concordant imaging (MRI or CT) findings. Adults, primarily leg pain, failed > 3 weeks conservative treatment	Patients referred for ESI	$n = 68$, $n = 68$ (100%)	Successful group age 43 years (range 19–78), 39% female Unsuccessful group age 41 years (range 20–67), 56% female	TF ESI fluoroscopic guided + contrast 40 mg/ml triamcinolone, 0.5 ml 0.5% bupivacaine (total volume 1.5 ml)
Cha et al. (2014) [33] Korea	Retrospective cohort study	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Patients hospitalised with lumbar radicular pain, failed > 2 weeks physical therapy, MRI (< 3 months prior to injection) confirming lumbar DH, expected to improve after C ESI	Patients hospitalised with sciatica	$n = 91$, $n = 91$ (100%)	Age range 17–79 years, 67% females	C ESI ultrasound guided 10 mg (2 ml) dexamethasone, 20 ml lidocaine, 8 ml saline (total volume 30 ml)
Paidin et al. (2011) [34] America	Retrospective review*	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. History and physical examination consistent with single-level, unilateral, lumbosacral radiculopathy (+ MRI)	Unclear	$n = 17$, $n = 17$ (100%)	Total sample n = 38, MRI images available for analysis n = 17 Age 44 years (range 23–81), 53% female	TF ESI fluoroscopic guided + contrast 40 mg/ml methylprednisolone acetate, 1 ml 2% lidocaine (total volume 2 ml)

Table 4 (continued)

Author, year, country	Study design	Study population, sciatica diagnosis	Sampling methods	Sample size, completed cases	Baseline participants mean age years (SD), % female	ESI details
Elashmawy et al. (2020) [35] Egypt	RCT	Clinical diagnosis of nerve root pain with concordant imaging (MRI) findings. Patients with radiculopathy caused by DH, failed > 6 weeks conservative treatment, refused surgery or were unfit for surgery	Consecutive patients	$n = 136$, $n = 121$ (89%)	C ESI ultrasound group Age 42.53 (10.30), 58% female C ESI fluoroscopic group Age 42.69 (10.48), 58% female	C ESI ultrasound guided or fluoroscopic guided + contrast 80 mg (2 ml) triamcinolone acetonide, 18 ml 0.5% lidocaine (total volume 20 ml)
Kwak et al. (2021) [36] Korea	Retrospective cohort study	Clinical diagnosis of nerve root pain with concordant imaging (MRI or CT) findings. Adults (20 years +) with lumbar DH on MRI, single-level unilateral radiculopathy, duration < 3 months, treated with TF ESI	Consecutive patients	$n = 160$, $n = 114$ (71%)	Age 50.9 (12.9), 42% female	TF ESI fluoroscopic guided + contrast 20 mg (0.5 ml) triamcinolone acetonide, 0.5 ml bupivacaine, 1 ml saline (total volume 2 ml)

SD standard deviation; *MRI* magnetic resonance imaging; *DH* disc herniation; *ESI* epidural steroid injection; *TF* transforaminal; *IL* interlaminar; *C* caudal; *SLR* straight leg raise; *CT* computed tomography; *RCT* randomised controlled trial; *SNRB* selective nerve root block

*Data from unpublished prospective study

Table 5 Prognostic factors investigated for association with outcome following an epidural steroid injection for disc-related sciatica, $n = 15$ studies

Prognostic factor domain	Prognostic factors included	Number of studies
Patient factors		
Demographics	Age [22, 24, 29, 31–33, 35]	7
	Gender [24, 29, 31–33, 35]	6
Health and lifestyle	Body mass index [29, 31, 35]	3
	Smoking status [22, 31]	2
	Past surgical history (all types) [24, 28]	2
	Comorbidities [31]	1
	Perceived health problem [24]	1
Medication	High-dose opioid use [22]	1
	Medication use (0 = nothing,1 = non-narcotic 2 = tramadol,3 = narcotic analgesic combination 4 = stronger narcotic medications [28]	1
Work	Work status [31]	1
	Physical demands of work [28]	1
	Litigation status [28]	1
	Secondary gain [22]	1
Psychological measures	Anxiety and Depression [23, 26]	2
Sciatica related factors		
Onset of sciatica	Onset (e.g. sudden vs gradual) [31]	1
	Inciting event (identified cause, e.g. work-related, motor vehicle collision, lifting event) [22]	1
	Previous episode of sciatica [31]	1
Pain and function (disability)	Pain duration [22, 24, 29–33, 35]	8
	Baseline pain intensity [22, 24, 27, 29, 31, 35]	6
	Pain experience (McGill Pain Questionnaire) [28]	1
	Location of pain (e.g. coexistent back pain, left/right leg, bilateral symptoms, calf, entire leg) [22, 31]	2
	Pain increased with activities (e.g. walking, sexual activities) [24]	1
	Function (Oswestry Disability Index, Pain Disability index) [28, 31, 35]	3
	Post-procedural 1-h NPRS score decrement* [29]	1
Clinical assessment factors		
Clinical assessment findings	Sensory deficit [30, 31]	2
	Motor deficit [30]	1
	Reflex deficit [30]	1
	Straight leg raise test [24, 31, 35]	3
	Lumbar flexion [35]	1
Investigation findings factors		
MRI scan findings	Level of disc herniation (e.g. L4/5, L5/S1) [30, 31, 33]	3
	Type of disc herniation (e.g. protrusion, extrusion) [31–33, 35, 36]	5
	Location of disc herniation (e.g. central, subarticular, foraminal) [30–33, 36]	5
	Grade of nerve root compression (e.g. abutment, displacement, entrapment) [29–34]	6
	Dimension/volume of herniation (e.g. ratio area of herniation and spinal canal) [30, 32, 33, 36]	4
	Presence of lumbosacral transitional vertebra [29, 31]	2
	Associated spinal stenosis/degenerative changes (at the segment affected by the herniation) [30, 32]	2
	Grade of disc degeneration (grade 1 (normal), 2, 3 vs grade 4, 5 (collapsed)) [33]	1
	Disc hydration (e.g. high, moderate or low) [32]	1
	Disc height loss (e.g. none, less than half, more than half) [33]	1
EMG findings	Evidence of radiculopathy (sciatica) on EMG [27, 28]	2
QST findings	Evidence of individual nerve fibre dysfunction: heat (C-fibre), cold (Aδ-fibre), vibration and touch (Aβ-fibre) [25]	1
Injection factors		
Injection factors	Injection level [29, 32, 35]	3
	Multilevel injections [22]	1

NPRS numerical pain rating scale; *MRI* magnetic resonance imaging, L4/L5 lumbar 4, lumbar 5; *EMG* electromyogram; *QST* quantitative sensory testing

Table 6 Methodological assessment according to six domains of potential bias (QUIPS)

Study	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Overall risk of bias
Engle et al. (2019) [22]	Moderate	Moderate	Moderate	High	Moderate	Low	High
Bahar-Ozdemir et al. (2020) [23]	Low	Moderate	Low	Moderate	High	Unsure	High
Rivest et al. (1998) [24]	Moderate	High	High	Moderate	Moderate	Moderate	High
Schiff, Eisenberg (2003) [25]	Moderate	Low	Low	Moderate	Moderate	Low	Moderate
Shaikh et al. (2021) [26]	Moderate	Low	Moderate	Moderate	High	High	High
Batistaki et al. (2017) [27]	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Tong et al. (2003) [28]	Moderate	Unsure	Moderate	Low	Moderate	Unsure	Moderate
Sencan et al. (2020) [29]	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Ghahreman, Bogduk (2011) [30]	Moderate	Moderate	Low	Unsure	Moderate	Moderate	Moderate
Kanna et al. (2019) [31]	Low	Low	Unsure	High	Moderate	Moderate	Moderate
Choi et al. (2007) [32]	Moderate	High	Moderate	Low	Moderate	Moderate	High
Cha et al. (2014) [33]	High	Low	Moderate	Unsure	High	Low	High
Paidin et al. (2011) [34]	High	High	Moderate	Low	High	Moderate	High
Elashmawy et al. (2020) [35]	Low	Moderate	Moderate	High	Moderate	Moderate	High
Kwak et al. (2021) [36]	Moderate	High	Low	Moderate	High	High	High

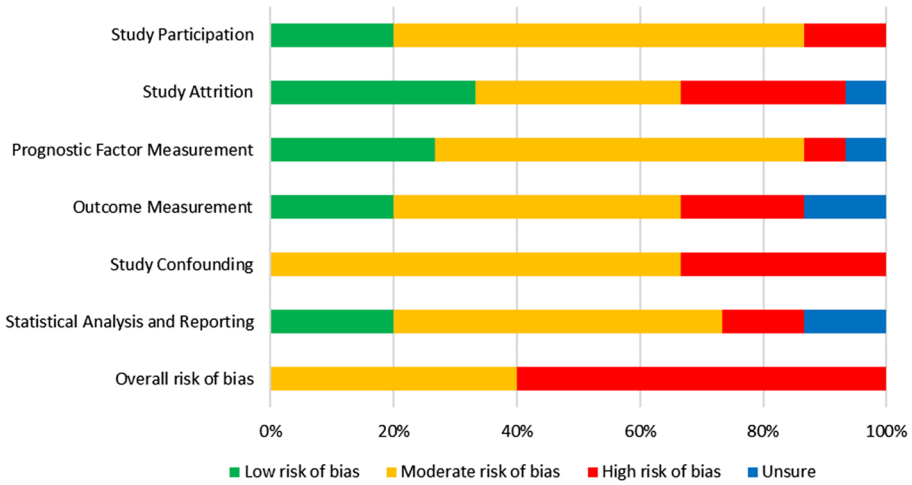

Fig. 2 QUIPS Risk of Bias summary: Review authors' judgement about each risk of bias domain presented as percentages across all included studies ($n-15$)

Table 7 Prognostic factors, results and conclusions of the 15 included studies

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Engle et al. (2019) [22]	*Demographic*: age *Health and lifestyle*: smoking status *Medication:* high-dose opioid use *Work:* secondary gain *Onset of sciatica*: inciting event *Pain and function*: duration, average baseline pain score, bilateral symptoms *Injection level:* multilevel injection	NPRS (P) ≥ 30% pain score reduction for ≥ 6 weeks without additional interventions	Unclear	Multivariable logistic regression	Adjusted prognostic effect Baseline pain score (OR 0.824, 95% CI 0.712–0.948), multilevel injection (OR 7.548, 95% CI 1.366–141.582)	High	Higher baseline pain score was associated with worse outcomes Multilevel injection was associated with better outcomes
Bahar-Ozdemir et al. (2020) [23]	*Psychological measures and perceptions:* depression, anxiety, somatisation levels	NPRS (P) ≥50% pain score reduction ODI (S)	1 h, 3 weeks and 3 months	Pearson correlation coefficient or Spearman rank correlation coefficient	Unadjusted prognostic effect Negative correlations between per cent reduction in the NRS and HADS-depression levels at 3 weeks ($r = -0.182$, $p = 0.022$) and 3 months ($r = -0.204$, $p = 0.037$)	High	Higher baseline depression score was associated with worse outcomes (reduction in pain)
Rivest et al. (1998) [24]	*Demographic:* age, gender *Health and lifestyle:* number of surgeries (all types) *Pain and function:* baseline pain intensity, duration, pain increased with walking/coughing, disturbances with sexual activities/chores *Psychological measures and perceptions:* perceived health problems *Clinical assessment findings:* SLR test	Change in VAS pain score (P)	2 weeks	Spearmen correlation coefficient (r) and Wilcoxon rank sum tests	Unadjusted prognostic effect Worse pre-injection VAS pain score ($r = .63$, $p < 0.001$), pain not increased by walking was associated with *worse* outcomes ($p < 0.005$), pain not increased by coughing was associated with *better* outcomes ($p < 0.005$)	High	Greater improvement in VAS pain scores at 2 weeks was associated with higher levels of pre-injection pain

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Schiff, Eisenberg (2003) [25]	*QST:* individual nerve fibre dysfunction: heat (C-fibre), cold (Aδ-fibre), vibration and touch (Aβ-fibre)	Change in NPRS pain score (P) SF-MPQ, SLR test, lumbar ROM (S)	Weekly, up to 4 weeks 2 and 4 weeks (secondary outcomes)	Stepwise regression, mixed model approach	Adjusted prognostic effect cold 0.23 ($p=0.046$), vibration − 0.22 ($p=0.0083$), touch − 1.00 ($p=0.017$) Secondary outcome: (SF-MPQ score): vibration 0.78 ($p=0.031$), touch − 4.39 ($p=0.024$)	Moderate	Patients with more dysfunction of Aδ-fibres (cold sensation) respond better to ESI, whereas those with more dysfunction of Aβ- fibres (vibration/touch) have poorer outcomes
Shaikh et al. (2021) [26]	*Psychological measures and perceptions:* depression, anxiety, stress	Number of patients who underwent surgery	3 months	Wilcoxon Signed Ranks test	Unadjusted prognostic effect Higher mean baseline DASS -depression score was associated with surgery not avoided, 10.8 (SD 7.5) vs 5.3 (SD 4.3) ($p=0.010$)	High	The presence of depression, not anxiety or stress, was associated with worse outcome necessitating surgery

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Studies investigating EMG study findings							
Batistaki et al. (2017) [27]	*EMG findings:* (assessing dysfunction of L5 and S1 nerve roots) expressed as MUR, SA (used to assess nerve root damage) and IP during maximal voluntary muscle contraction *Pain Intensity, Functional Status, Brief Pain Inventory Parameters, Stress and Anxiety Levels*	Change in VAS pain score (P) BPI, DN4 questionnaire, RMDQ, DASS, STAI (S)	6 and 12 months	Multivariate regression analysis	Adjusted prognostic effect Higher VAS and BPI baseline pain scores were associated with improvement in all dependant variables, between 33.4% and 71% ($r^2 = 0.344$ and $r^2 = 0.712$) *EMG:* MUR active right S1 root damage was associated with greater pain relief (BPI-severity: $r^2 = 0.313$, $p = 0.047$) and function (RMDQ: $r^2 = 0.335$, $p = 0.038$). MUR active left S1 root damage was associated with pain relief (VAS: $r^2 = 0.287$, $p = 0.032$, BPI-severity: $r^2 = 0.262$, p = 0.043, BPI-interference: $r^2 = 0.262$, $p = 0.043$), SA left S1 root was associated with pain relief (VAS: $r^2 = 0.277$, $P = 0.036$, BPI-severity: $r^2 = 0.261$, $p = 0.043$) and function (RMDQ: $r^2 = 0.286$, $p = 0.033$)	Moderate	MUR and SA (which form part of EMG assessment) are associated with better outcomes (pain relief)

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Tong et al. (2003) [28]	*Health and lifestyle*: past surgical history *Medication:* medication use *Work:* work physical demands, litigation status *Pain and function:* VAS pain severity, PDI, MPQ *EMG findings:* evidence of radiculopathy on EMG	Composite score of patients' pain severity and medication use (P) 0 = improved with pain severity and medication use, 1 = improved with either pain severity or medication use, 3 = worse with either pain severity or medication use, 4 = worse with pain severity and medication use	Mean follow-up 122 days (± 146.3)	Spearman rank order correlation analysis, ordinal regression analysis	Unadjusted prognostic effect Working at initial visit ($r = -0.31$, $p = 0.02$), SSDI or workers' compensation ($r = 0.43$, $p = < 0.001$), work with increased physical demands ($r = 0.44$, $p = 0.002$), EMG evidence of radiculopathy ($r = -0.25$, $p = 0.04$) Adjusted prognostic effect SSDI ($b = 1.96$, $p = 0.009$), physical work demands ($b = 0.56$, $p = 0.012$)	Moderate	Patients who have SSDI/workers' compensation and very heavy workloads are more likely to have unchanged pain severity and medication use
Studies investigating MRI scan findings							
Sencan et al. (2020) [29]	*Demographic:* age, gender *Health and lifestyle*: BMI *Pain and function*: duration, baseline NPRS scores, post-procedural 1-h NPRS scores *MRI findings:* presence of lumbosacral transitional vertebra, grade of nerve root compression* *Injection level:* level of ESI	NPRS (P) ≥ 50% pain score reduction at 3 months	1 h, 3 weeks, and 3 months	Univariate and multivariate regression analyses, multivariate binary logistic regression analysis	Adjusted prognostic effect Decrease pain scores 1 h after TF ESI was associated with treatment success ($p = 0.024$) and a significant predictor (OR 1.015, 95%, CI 1.003–1.026)^	Moderate	All prognostic factors measured before TF ESI were not associated with treatment outcomes Reduced pain scores 1 h after TF ESI was associated with treatment success

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Ghahreman, Bogduk (2011) [30]	*Pain and function*: duration *Clinical assessment findings:* sensory deficit, motor weakness or depressed reflex *MRI findings:* DH level, location, dimensions, degenerative changes at the segment affected by herniation, grade of nerve root compression**	VAS pain score (P) ≥ 50% pain score reduction lasting > 1 month	1 month	Two-sample t test, contingency table, chi-squared test, positive associations assessed by calculating sensitivity, specificity, and positive likelihood ratio	Adjusted prognostic effect *MRI findings*: Low-grade nerve root compression was associated with 75% (95% CI 62–88%) improvement and high-grade compression 26% (95% CI 12–38%) improvement ($p = 0.000$)	Moderate	Low-grade nerve root compression on MRI scans was associated with 75% success rate, compared to 26% for high-grade compression
Kanna et al. (2019) [31]	*Demographic:* age, gender *Health and lifestyle*: BMI, smoking status, comorbidities *Work:* work type *Onset of sciatica:* presence of inciting event, previous episode *Pain and function*: duration, side of pain, presence of LBP, location of pain, baseline VAS leg pain score, baseline ODI score *Clinical assessment findings:* sensory deficit, SLR test positivity *MRI findings:* DH level, position, type, grade of nerve compression, presence of lumbosacral transitional vertebra	Pain relief (not reported how pain was measured) (P)	Up to 1 year	Chi-square test, 2 × 2, multifactor contingency table. For multiple variables, logistic regression analysis	Unadjusted prognostic effect Non-manual work ($p = 0.01$), sensory symptoms ($p = 0.01$), higher mean baseline ODI score ($p = 0.02$), *MRI findings:* lumbosacral transitional segment ($p = 0.00005$) Adjusted prognostic effect *MRI findings*: lumbosacral transitional segment ($p = 0.0005$) associated with failed SNRB, odds ratio of 20.1	Moderate	Patients with non-manual work, high pre-injection ODI score, sensory symptoms and the presence of a lumbosacral transitional segment on MRI scans was associated with poorer outcomes

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Choi et al. (2007) [32]	*Demographic:* age, gender *Pain and function*: duration *MRI findings:* DH type, disc hydration, location***, DH size/volume, grade of nerve root compression, associated spinal stenosis *Injection level:* level of ESI	VAS pain score and patient satisfaction scale (0 = poor) to 4 = excellent) (P) Patient satisfaction score > two and a VAS pain reduction score > 50% at the last visit	mean follow-up 3.6 months	Chi-Square or Fisher's exact tests, Student's T test Logistic regression analysis	Unadjusted prognostic effect *MRI findings:* DH location and grade of nerve root compression were different between responder and non-responder groups ($p < 0.05$). Centrally located DH was more common in the responder group (27% vs 4%) Adjusted prognostic effect MRI findings: Grade 2 and 3 nerve root compression was associated with more unsatisfactory results compared to grade 1 compression (odds ratio: 7.43 and 25.9, respectively)	High	Central DH and minor grade 1 (abutment) nerve root compression seen on MRI scan is associated with successful outcomes
Cha et al. (2014) [33]	*Demographic:* age, gender *Pain and function*: duration *MRI findings*: DH level, type, zone***, volume, relationship between herniation and nerve root, disc height loss, disc degeneration grade	VAS pain score and RMDQ (P) > 50% pain score reduction or RMDQ improved by > 50%	Not clearly reported Follow-up < 6 weeks	Mann–Whitney U test and the chi-square test Logistic regression analysis	Unadjusted prognostic effect DH zone was related to effectiveness (VAS $p = 0.025$, RMDQ $p = 0.040$)	High	A centrally located DH, seen on MRI scan, was associated with successful outcomes

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Paidin et al. (2011) [34]	*MRI findings:* Grade of nerve root compression****	Change in NPRS score (P)	15 min (T1), 2 weeks (T2), 8 weeks (T3)	Repeated measures analysis of variance	Unadjusted prognostic effect grade I compression: T1 − 4.9 SE 0.78 ($p < 0.0001$) grade II compression: T1 − 4.2 SE 0.98 ($p = 0.0001$), T2 − 3.2 SE 0.98 ($p = 0.0022$), T3 − 2.6 SE 0.98 ($p = 0.0115$) grade III compression: T1 − 3.5 SE 1.1 ($p = 0.0027$), T2 − 3.3 SE 1.1 ($p = 0.0051$), T3 − 2.3 SE 1.1 ($p = 0.047$)	High	Higher grade of nerve root compression (grades II and III) was associated with pain reduction up to 8 weeks. In contrast, minor (grade I) nerve root compression was only associated with short-term (15 min) pain relief after TF ESI
Elashmawy et al. (2020) [35]	*Demographic:* age, gender *Health and lifestyle*: BMI *Pain and function*: duration, baseline VAS score, baseline ODI *Clinical assessment findings*: SLR, Modified Schober Test *MRI findings*: DH type *Injection level:* level of ESI	Change in VAS score (P)	1 and 3 months	Mann–Whitney U test and the chi-square test Logistic regression analysis	Unadjusted prognostic effect Age < 40 years (OR 2.67, 95% CI 1.09–6.55), Duration < 6 months (OR 3.16, 95% CI 1.40–7.15), Target level, not L2–3/L3–4 (OR 10.63, 95% CI 2.09–24.14), DH other than foraminal type, (OR 8.20, 95% CI 2.03–23.11) Adjusted prognostic effect Duration < 6 months (OR 2.25, 95% CI 1.04–4.71), Target level, not L2–3/L3–4 (OR 4.13, 95% CI 2.67–10.76), DH other than foraminal type (OR 3.78, 95% CI 2.05–7.84)	High	Duration < 6 months, target level not L2-3/L3-4 and DH other than foraminal type were significantly associated with successful outcomes after ultrasound and fluoroscopic guided C ESI

Table 7 (continued)

Author, year	Prognostic factors investigated	Primary (P) outcome (with categorisation if applicable) and secondary (S) outcomes	Measured time-points	Statistical analysis	Significant adjusted or unadjusted prognostic effects	QUIPS overall risk of bias	Conclusion
Kwak et al. (2021) [36]	*MRI findings*: DH location, type, size	Telephone interview (9 questions, e.g. presence of current pain)	At least 4 years	Chi-square test, independent t test and 1-way analysis of variance	Unadjusted prognostic effect More patients with extruded lumbar DH ($n=21$) required additional TF ESIs, compared with protruded lumbar DH ($n=9$), $p=0.026$	High	Most MRI findings (location and size) of DH was not associated with long-term outcomes of TF ESI. Higher rate of patients with extruded lumbar DH required additional TF ESIs

DH disc herniation; *NPRS* numerical pain rating scale; *OR* odds ratio; *CI* confidence intervals; *SF−36* short form 36; *ODI* Oswestry disability index; *HADS* hospital anxiety and depression score; *SLR* straight leg raise; *VAS* visual analogue scale; *QST* quantitative sensory testing; *SF−MPQ* short form McGill pain questionnaire, *ROM* range of movement; *EMG* electromyography; *MUR* motor unit pattern; *SA* spontaneous activity; *IP* interference pattern; *BPI* brief pain inventory; *RMDQ* Rolland Morris disability questionnaire; *DASS* depression anxiety stress scales; *STAI* state trait anxiety inventory; *MPQ* McGill pain questionnaire; *SSDI* social security disability insurance; *BMI* body mass index; *MRI* magnetic resonance imaging; *TF ESI* transforaminal epidural steroid injection; *SNRB* selective nerve root block; *SE* standard error

*Modified Pfirrmann grading system [37], Grade I: applies when the disc simply contacts the nerve root, Grade II: when the nerve root is displaced but with preservation of periradicular cerebrospinal fluid or fat, Grade III: when the periradicular CSF or fat is obliterated, Grade IV: when the nerve root is morphologically distorted

**System to grade foraminal root compression caused by a far lateral disc herniation, Grade I: applied when perineural fat was obliterated in two opposing directions (vertical or transverse), Grade II: was applied when perineural fat was obliterated in four directions without morphologic distortion of the nerve root, and Grade III was applied when distortion or other morphologic change in the nerve root was evident [38]

***Based on the classification system of Fardon and Milette [39]

****Pfirmann 3−tier classification system: Grade I: abutment of the disc to the nerve root, Grade II: displacement of the nerve root by the herniated disc, Grade III: entrapment of the nerve root between the herniated disc and lamina or facet joint at that level

pain outcomes and dysfunction of Aβ-fibres (vibration/touch) was associated with poorer outcomes (Table 7).

Injection factors

Of the three studies that considered the level the ESI was delivered (e.g. L5/S1) [29, 32, 35], one found that a target level other than between L2 and L4 was associated with better pain outcomes [35]. One study comparing multilevel injections (two or more) with single-level injections found a 7.5-fold increase in the odds of a better pain outcome favouring multilevel injections [22].

Discussion

This is the first systematic review to synthesise the literature investigating factors that can be routinely collected in clinical practice, as prognostic factors associated with outcomes following ESI for patients with disc-related sciatica. The review found 15 eligible studies, which explored 42 potential prognostic factors assessed before the ESI. Our review showed that no prognostic factor is consistently associated with patient outcomes, most studies found no association or conflicting results. Overall study quality was low with all judged to have moderate or high risk of bias and between-study heterogeneity precluded statistical pooling of results. Considering the frequent use of ESIs in clinical practice, the search results are surprising. It was anticipated that there would be more high-quality prognosis studies of this nature.

The most commonly assessed prognostic factors were patient demographics, health and lifestyle factors, leg pain related factors and MRI scan findings but even these were only included in, at most, six to eight of the studies. All but one of the studies used a measure of pain as a primary outcome but a variety of methods of measuring and defining a good or poor outcome was evident across studies.

Comparison of results to similar studies

To our knowledge, one systematic review has been published on prognostic factors associated with treatment outcomes for sciatica [16] but it only focused on imaging factors and laboratory inflammatory biomarkers. That review searched only one database and identified eight eligible studies with mixed populations (disc herniation and spinal stenosis) and ESIs for lumbar and cervical spine which makes it difficult to compare our results. For MRI imaging, the review concluded that nerve root compression grading, based on two studies, can predict short-term pain reduction after ESI. Our review, which included these two studies and four additional studies showed inconsistent results for grades of nerve root compression and their association with outcome. The review suggested elevated inflammatory biomarkers (obtained from simple blood tests or material harvested during the injection) seemed promising to predict outcomes. The evidence of the role of biomarkers in sciatica is not convincing [40]. Biomarkers were not included in this review as potential prognostic factors to inform a future prospective cohort study data collection as those specific to ESI are costly to perform and analyse and not routinely collected in clinical practice.

In the absence of similar reviews of ESIs for disc-related sciatica, we compared findings to reviews of prognostic factors in sciatica treatment outcomes. A review of factors associated with recovery following lumbar discectomy surgery for sciatica reported higher severity of pre-operative leg pain predicted better outcomes (reduced leg pain) at 2 and 7 years [41]. The review showed very low-level evidence that a lower pre-operative measure of health-related quality of life (measured by the EQ-5D) predicted better health-related quality of life at 2 years. There was low-level evidence to support duration of leg pain pre-operatively not being associated with outcome, and very low-quality evidence that supported other factors of pre-operative disability, duration and severity of back pain, ipsilateral SLR and forward bend not being associated with outcome. For non-surgically treated sciatica patients, there was positive association with strong evidence for leg pain intensity at baseline as a prognostic factor for subsequent surgery [42]. Overall, there is a lack of clear and consistent factors predicting outcomes in patients with sciatica [42–44] that has made it challenging to design prognostic models to guide treatment decision-making. A stratified care model developed for sciatica patients based on prognosis and factors associated with referral to spinal specialists was not superior to non-stratified usual care [45]. The authors of that trial recommended further research to identify factors associated with outcomes to help develop better predictive models for use in clinical decision-making.

Strengths and limitations of the review

The inclusion of a broad range of potential prognostic factors, treatment outcomes and study designs, consisting of RCTs, retrospective and prospective cohorts, strengthens the completeness of this review. But it could be argued that a more robust streamlined review was possible if only prospective study designs has been included, which are considered optimum for prognostic factor research [19, 46] and if we limited our eligibility criteria to a minimum sample of 100 participants as other prognostic factor systematic reviews have done [47]. Only four studies in the review used a prospective design and 10 of the 15 studies had a sample size with outcome follow-up data of less than 100 participants. It was anticipated that more high-quality prognosis studies would have been identified considering the popular use of ESIs. This raises the potential of publication bias and

selective reporting which is common in prognosis research [19].

Limitations of the review include the moderate to high risk of bias across the available studies. Therefore the conclusion of the review showing that no prognostic factor was consistently associated with patient outcome, may be in part due to the overall poor quality of the studies. Non-English studies were not included in the search strategy therefore potentially relevant studies may have been missed. The definition and diagnosis of sciatica was ambiguous in two of the included studies. It is possible therefore that not all subjects had disc-related sciatica. The diverse measured time-points and outcome measures used, ranging from pain outcomes (with differing definitions of what resulted in treatment success and failure), inconsistent disability outcomes and complex composite measures of pain severity and medication use, may also contribute to conflicting results. The review identified only four papers that focused on injection related factors as potential prognostic factors, three looked at the level of injection and one on multilevel injections versus single level. Other factors such as the injection approach, the type and dose of medication used were not considered in any of the papers we reviewed. This reflects current clinical practice where multiple types of ESI are performed, delivered through transforaminal, interlaminar or caudal approaches with varying steroid and anaesthetic types and dosages.

To consider injection related factors as potential prognostic factors would require a large cohort study, likely multicentre in nature to capture different practices and have enough numbers with different types of injections that could be used in the prognostic factor analysis. Alternatively, an individual participant data analysis would be needed, combining data and outcomes from existing trials and cohort studies to test injection factors as potential prognostic factors.

Conclusions and next steps

This systematic review highlights the continued uncertainty about prognostic factors in patients having ESI for sciatica. There is a clear need for a suitably powered, low risk of bias, prospective cohort to more carefully investigate factors that predict outcome following ESI. The results of this systematic review can help to inform at least some of the decisions about the predictors assessed in such a future cohort study. The variations in outcomes used across studies also highlights that there should be international agreement on the definition of treatment success that can be used consistently in future cohort studies and trials of ESIs.

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Conflict of interest The authors have no conflicts of interest to disclose.

References

1. Jensen RK, Kongsted A, Kjaer P, Koes B (2019) Diagnosis and treatment of sciatica. BMJ 367:l6273. https://doi.org/10.1136/bmj.l6273
2. Stafford MA, Peng P, Hill DA (2007) Sciatica: a review of history, epidemiology, pathogenesis, and the role of epidural steroid injection in management. Br J Anaesth 99(4):461–473. https://doi.org/10.1093/bja/aem238
3. Lequin MB, Verbaan D, Jacobs WC, Brand R, Bouma GJ, Vandertop WP, Peul WC et al (2013) Surgery versus prolonged conservative treatment for sciatica: 5-year results of a randomised controlled trial. BMJ Open 3(5):e002534. https://doi.org/10.1136/bmjopen-2012-002534
4. National Institute for Health and Care Excellence (2016) Low back pain and sciatica in over 16s: assessment and management. Manchester: National Institute for Health and Care Excellence. (NG59). Available: https://www.nice.org.uk/guidance/ng59/chapter/Recommendations
5. National Institute for Health and Care Excellence (2017) National Low Back and Radicular Pain Pathway. Including Implementation of NICE Guidance NG59
6. Lee J, Gupta S, Price C, Baranowski AP, British Pain Society (2013) Low back and radicular pain: a pathway for care developed by the British Pain Society. Br J Anaesth 111(1):112–20. https://doi.org/10.1093/bja/aet172
7. Oliveira CB, Maher CG, Ferreira ML, Hancock MJ, Oliveira VC, McLachlan AJ, Koes BW, Ferreira PH, Cohen SP, Pinto RZ (2020) Epidural corticosteroid injections for sciatica: an abridged Cochrane systematic review and meta-analysis. Spine (Phila Pa 1976) 45(21):E1405–E1415. https://doi.org/10.1097/BRS.0000000000003651
8. de Bruijn TM, de Groot IB, Miedema HS, Haumann J, Ostelo RWJG (2021) Clinical relevance of epidural steroid injections on lumbosacral radicular syndrome-related synptoms: systematic review and meta-analysis. Clin J Pain 37(7):524–537. https://doi.org/10.1097/AJP.0000000000000943

9. Verheijen EJA, Bonke CA, Amorij EMJ, Vleggeert-Lankamp CLA (2021) Epidural steroid compared to placebo injection in sciatica: a systematic review and meta-analysis. Eur Spine J 30(11):3255–3264. https://doi.org/10.1007/s00586-021-06854-9
10. Manchikanti L, Knezevic E, Knezevic NN, Sanapati MR, Thota S, Abd-Elsayed A, Hirsch JA (2021) Epidural Injections for lumbar radiculopathy or sciatica: a comparative systematic review and meta-analysis of Cochrane review. Pain Physician 24(5):E539–E554
11. Jonckheer P, Desomer A, Depreitere B, Berquin A, Bruneau M, Christiaens W, Coeckelberghs E et al (2017) Low back pain and radicular pain: development of a clinical pathway—Supplement. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). KCE Reports 295. D/2017/10.273/88
12. Verburg AF, Schaafstra A, Spinnewijn WE, Kroes BW, Bouma M, Burgers JS. Herziene NHG-standaard (2015) 'Lumbosacraal radiculair syndroom' [Revised NHG practice guideline 'Lumbosacral radicular syndrome']. Ned Tijdschr Geneeskd. 159:A9122. Dutch. PMID: 26246062
13. Manchikanti L, Pampati V, Soin A, Sanapati MR, Kaye AD, Hirsch JA (2021) Declining utilization and inflation-adjusted expenditures for epidural procedures in chronic spinal pain in the Medicare population. Pain Physician 24(1):1–15
14. Wilby MJ, Best A, Wood E, Burnside G, Bedson E, Short H, Wheatley D et al (2021) Microdiscectomy compared with transforaminal epidural steroid injection for persistent radicular pain caused by prolapsed intervertebral disc: the NERVES RCT. Health Technol Assess 25(24):1–86. https://doi.org/10.3310/hta25240
15. https://gettingitrightfirsttime.co.uk/wp-content/uploads/2019/01/Spinal-Services-Report-Mar19-L1.pdf
16. Benny BV, Patel MY (2014) Predicting epidural steroid injections with laboratory markers and imaging techniques. Spine J 14:2500–2508. https://doi.org/10.1016/j.spinee.2014.04.003
17. Foster NE, Anema JR, Cherkin D et al (2018) Prevention and treatment of low back pain: evidence, challenges, and promising directions. Lancet 391(10137):2368–2383. https://doi.org/10.1016/S0140-6736(18)30489-6
18. Page MJ, McKenzie JE, Bossuyt PM et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 372:n71. https://doi.org/10.1136/bmj.n71
19. Riley RD, Moons KGM, Snell KIE et al (2019) A guide to systematic review and meta-analysis of prognostic factor studies. BMJ 364:k4597. https://doi.org/10.1136/bmj.k4597
20. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C (2013) Assessing bias in studies of prognostic factors. Ann Intern Med 158(4):280–286. https://doi.org/10.7326/0003-4819-158-4-201302190-00009
21. Sauerbrei W, Taube SE, McShane LM, Cavenagh MM, Altman DG (2018) Reporting recommendations for tumor marker prognostic studies (REMARK): an abridged explanation and elaboration. J Natl Cancer Inst 110(8):803–811. https://doi.org/10.1093/jnci/djy088
22. Engle AM, Chen Y, Marascalchi B et al (2019) Lumbosacral radiculopathy: inciting events and their association with epidural steroid injection outcomes. Pain Med 20(12):2360–2370. https://doi.org/10.1093/pm/pnz097
23. Bahar-Ozdemir Y, Sencan S, Ercalik T, Kokar S, Gunduz OH (2020) The effect of pre-treatment depression, anxiety and somatization levels on transforaminal epidural steroid injection: a prospective observational study. Pain Physician 23(3):E273–E280
24. Rivest C, Katz JN, Ferrante FM, Jamison RN (1998) Effects of epidural steroid injection on pain due to lumbar spinal stenosis or herniated disks: a prospective study. Arthritis Care Res 11(4):291–297. https://doi.org/10.1002/art.1790110410
25. Schiff E, Eisenberg E (2003) Can quantitative sensory testing predict the outcome of epidural steroid injections in sciatica? A preliminary study. Anesth Analg 97(3):828–832. https://doi.org/10.1213/01.ANE.0000078583.47735.69
26. Shaikh H, Kumar A, Kishen TJ (2021) Temporal pattern of pain and disability following the administration of a selective nerve root block in lumbar disc herniation with radiculopathy. Int J Spine Surg 15(6):1090–1095. https://doi.org/10.14444/8195
27. Batistaki C, Angelopoulou A, Smyrnioti ME, Kitsou MC, Kostopanagiotou G (2017) Electromyographic findings after epidural steroid injections in patients with radicular low back pain: a prospective open-label study. Anesth Pain Med 7(6):e62556. https://doi.org/10.5812/aapm.62556
28. Tong HC, Williams JC, Haig AJ, Geisser ME, Chiodo A (2003) Predicting outcomes of transforaminal epidural injections for sciatica. Spine J 3(6):430–434. https://doi.org/10.1016/s1529-9430(03)00179-7
29. Şencan S, Çelenlioğlu AE, Asadov R, Gündüz OH (2020) Predictive factors for treatment success of transforaminal epidural steroid injection in lumbar disc herniation-induced sciatica. Turk J Med Sci 50(1):126–131. https://doi.org/10.3906/sag-1908-167
30. Ghahreman A, Bogduk N (2011) Predictors of a favorable response to transforaminal injection of steroids in patients with lumbar radicular pain due to disc herniation. Pain Med 12(6):871–879. https://doi.org/10.1111/j.1526-4637.2011.01116.x
31. Kanna RM, Shetty AP, Rajasekaran S (2019) Predictors of successful outcomes of selective nerve root blocks for acute lumbar disc herniation. Glob Spine J 9(5):473–479. https://doi.org/10.1177/2192568218800050
32. Choi SJ, Song JS, Kim C, Shin MJ, Ryu DS, Ahn JH, Jung SM, Park MS (2007) The use of magnetic resonance imaging to predict the clinical outcome of non-surgical treatment for lumbar intervertebral disc herniation. Korean J Radiol 8(2):156–163. https://doi.org/10.3348/kjr.2007.8.2.156
33. Cha SO, Jang CH, Hong JO, Park JS, Park JH (2014) Use of magnetic resonance imaging to identify outcome predictors of caudal epidural steroid injections for lower lumbar radicular pain caused by a herniated disc. Ann Rehabil Med 38(6):791–798. https://doi.org/10.5535/arm.2014.38.6.791
34. Paidin M, Hansen P, McFadden M, Kendall R (2011) Contrast dispersal patterns as a predictor of clinical outcome with transforaminal epidural steroid injection for lumbar radiculopathy. PMR 3(11):1022–1027. https://doi.org/10.1016/j.pmrj.2011.07.020
35. Elashmawy MA, Shaat RM, Abdelkhalek AM et al (2020) Caudal epidural steroid injection ultrasound-guided versus fluoroscopy-guided in treatment of refractory lumbar disc prolapse with radiculopathy. Egypt J Radiol Nucl Med 51:259. https://doi.org/10.1186/s43055-020-00388-8
36. Kwak S, Jang SH, Chang MC (2021) Long-term outcomes of transforaminal epidural steroid injection in patients with lumbosacral radicular pain according to the location, type, and size of herniated lumbar disc. Pain Pract 21(8):836–842. https://doi.org/10.1111/papr.13029
37. Pfirrmann C, Dora C, Schmid M, Zanelli M, Hodler J, Boos N (2004) MR image–based grading of lumbar nerve root compromise due to disk herniation: reliability study with surgical correlation. Radiology 230:583–588
38. Lee S, Lee J, Yeom J, Kim K-J, Kim H-J, Chung S, Kang H (2010) A practical MRI grading system for lumbar foraminal stenosis. Am J Roentgenology 194:1095–1098
39. Fardon D, Milette P (2001) Nomenclature and classification of lumbar disc pathology: recommendations of the combined task forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology. Spine 26:E93–113

40. Jungen MJ, ter Meulen BC, van Osch T et al (2019) Inflammatory biomarkers in patients with sciatica: a systematic review. BMC Musculoskelet Disord 20:156. https://doi.org/10.1186/s12891-019-2541-0
41. Rushton A, Zoulas K, Powell A, Staal JB (2018) Physical prognostic factors predicting outcome following lumbar discectomy surgery: systematic review and narrative synthesis. BMC Musculoskelet Disord 19(1):326. https://doi.org/10.1186/s12891-018-2240-2
42. Verwoerd AJ, Luijsterburg PA, Lin CW, Jacobs WC, Koes BW, Verhagen AP (2013) Systematic review of prognostic factors predicting outcome in non-surgically treated patients with sciatica. Eur J Pain 17(8):1126–1137. https://doi.org/10.1002/j.1532-2149.2013.00301.x
43. Ashworth J, Konstantinou K, Dunn KM (2011) Prognostic factors in non-surgically treated sciatica: a systematic review. BMC Musculoskelet Disord 12:208. https://doi.org/10.1186/1471-2474-12-208
44. Konstantinou K, Dunn KM, Ogollah R et al (2018) Prognosis of sciatica and back-related leg pain in primary care: the ATLAS cohort. Spine J 18(6):1030–1040. https://doi.org/10.1016/j.spinee.2017.10.071
45. Konstantinou K, Lewis M, Dunn KM, Ogollah R, Artus M, Hill JC, Hughes G, Robinson M, Saunders B, Bartlam B, Kigozi J, Jowett S, Mallen CD, Hay EM, van der Windt DA, Foster NE (2020) Stratified care versus usual care for management of patients presenting with sciatica in primary care (SCOPiC): a randomised controlled trial. Lancet Rheumatol 2(7):e401–e411. https://doi.org/10.1016/S2665-9913(20)30099-0
46. Moons KG, Royston P, Vergouwe Y, Grobbee DE, Altman DG (2009) Prognosis and prognostic research: what, why, and how? BMJ 338:b375. https://doi.org/10.1136/bmj.b375
47. Wertli MM, Rasmussen-Barr E, Weiser S, Bachmann LM, Brunner F (2014) The role of fear avoidance beliefs as a prognostic factor for outcome in patients with nonspecific low back pain: a systematic review [published correction appears in Spine J 14(8):a18]. Spine J 14(5):816–36.e4. https://doi.org/10.1016/j.spinee.2013.09.036