Pain Medicine Advance Access published June 10, 2016

Pain Medicine 2016; 0: 1–18
doi: 10.1093/pm/pnw091

*Original Research Article*

# The Effectiveness and Risks of Non–Image-Guided Lumbar Interlaminar Epidural Steroid Injections: A Systematic Review with Comprehensive Analysis of the Published Data

**Yakov Vorobeychik, MD, PhD,* Anil Sharma, MD,† Clark C. Smith, MD, MPH,‡ David C. Miller, MD, MA,§ Milan P. Stojanovic, MD,¶ Steve M. Lobel, MD,‖ Marc A. Valley, MD, MPH, MS,‖‖ Belinda Duszynski, BS,** and David J. Kennedy, MD†† on behalf of the Standards Division of the Spine Intervention Society**

*Department of Anesthesiology, Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, Pennsylvania; †Spine and Pain Centers, New Jersey and New York; ‡Columbia University College of Physicians and Surgeons, New York, New York; §Indiana University Health, La Porte, Indiana; ¶Anesthesiology, Critical Care and Pain Medicine Service, VA Boston Healthcare System, Boston, Massachusetts; ‖Medical Associates of North Georgia, Canton, Georgia; ‖‖CIRCE Medical Services, Johnson City, Tennessee; **Spine Intervention Society, Crystal Lake, Illinois; ††Department of Orthopedics, Stanford University, Redwood City, California, USA

*Correspondence to:* Yakov Vorobeychik, MD, PhD, Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Department of Anesthesiology, HU32, 500 University Drive, P.O. Box 850, Hershey, PA 17033-0850, USA. Tel: 717-531-5680; Fax: 717-531-4143; E-mail: yvorobeychik@psu.edu.

Conflicts of interest: None.

**Abstract**

**Objective. To determine the effectiveness and risks of non–image-guided lumbar interlaminar epidural steroid injections.**

**Design. Systematic review.**

**Interventions. Three reviewers with formal training and certification in evidence-based medicine searched the literature on non–image-guided lumbar interlaminar epidural steroid injections. A larger team of seven reviewers independently assessed the methodology of studies found and appraised the quality of the evidence presented.**

**Outcome Measures. The primary outcome assessed was pain relief. Other outcomes such as functional improvement, reduction in surgery rate, decreased use of opioids, and complications were noted, if reported. The evidence was appraised in accordance with the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system of evaluating evidence.**

**Results. The searches yielded 92 primary publications addressing non–image-guided lumbar interlaminar epidural steroid injections. The evidence supporting the effectiveness of these injections for pain relief and functional improvement in patients with lumbar radicular pain due to disc herniation or neurogenic claudication secondary to lumbar spinal stenosis is limited. This procedure may**

**provide short-term benefit in the first 3–6 weeks. The small number of case reports on significant risks suggests these injections are relatively safe. In accordance with GRADE, the quality of evidence is very low.**

**Conclusions. In patients with lumbar radicular pain secondary to disc herniation or neurogenic claudication due to spinal stenosis, non–image-guided lumbar interlaminar epidural steroid injections appear to have clinical effectiveness limited to short-term pain relief. Therefore, in a contemporary medical practice, these procedures should be restricted to the rare settings where fluoroscopy is not available.**

**Key Words. Blind; Lumbar; Interlaminar; Steroid, Injection; Epidural; Pain; Radiculopathy; Low Back Pain; Spinal Stenosis**

## Introduction

Lumbar interlaminar epidural steroid injections (L-ILESIs) are one of the most commonly performed medical procedures in the United States, and by far the most frequently performed intervention in pain medicine clinics [1]. Their use is also increasing significantly [2].

Results of many studies investigating the various aspects of L-ILESIs have been published. Their assertions and conclusions about indications and effectiveness have been conflicting because of different interpretations of the available data. Among other reasons, the lack of consensus could be attributable to the fact that this procedure has been used for different indications, such as radicular pain due to disc herniation, spinal stenosis, and even isolated axial low back pain (without radicular component) and many studies have failed to report results for these different subgroups. Failure to separately analyze the data on different pathological processes creates a fertile ground for data misinterpretation.

Traditionally, L-ILESIs have been performed without radiographic guidance or verification. The foundation for contemporary techniques is based on literature published before image guidance became available and was adopted in practice. Despite the increased use of fluoroscopy over the past 20 years, many practitioners still use a non–image-guided technical approach for depositing steroids to the epidural space [3]. With evidence that calls into question the accuracy of this procedure when performed "blindly" [4–7], it is pertinent to know the effectiveness of non–image-guided L-ILESIs.

The goal of this systematic review is to assess the data on the effectiveness of non–image-guided L-ILESI with attention to the specific underlying pathology. Additionally, the relative risks of the procedure will be reviewed.

## Methods

Three investigators, who all have formal training and certification in evidence-based medicine and are members of the Standards Division of the Spine Intervention Society, searched the scientific literature independently for publications on the effectiveness and any adverse effects of non–image-guided L-ILESIs. The literature search was conducted in PubMed using the keywords lumbar, epidural, steroid, injection, radicular pain, radiculopathy, radiculitis, stenosis, and back pain. The searches encompassed all scientific articles published until December 2015. The only exclusions were non-English language articles, non-human studies, studies with a follow-up of less than 2 weeks, conference abstracts, and case reports, unless they were reports of complications. When suitable articles were retrieved, the references of each were perused for relevant citations that had not been identified by the database searches.

Similar to previous systematic reviews done by the Standards Division, studies were sorted based upon their contents, methodology, and study type [8–11]. Manuscripts were also appraised by each of the investigators independently and then as a group, using an instrument developed by the Standards Division to facilitate reliable assessment of studies of therapeutic effectiveness. Of special note—many researchers have designed their randomized controlled trials (RCTs) using local anesthetic as a placebo control. However, because there are some data to suggest that local anesthetic may have some therapeutic effect, those studies that compared non–image-guided L-ILESI to local anesthetic were considered pragmatic studies in this review [12,13].

The data produced from all of the studies were appraised and the resultant body of evidence was analyzed to determine whether it provided evidence regarding effectiveness of the procedure for a given pathology. This was imperative because these diseases have different natural histories requiring different follow-up periods, and they possibly may incur different responses to treatment. Additionally, studies were assessed for their use of validated outcome measures and presentation of categorical data. The failure to use validated outcome instruments was considered a deficiency that was incompatible with a study providing any constructive evidence.

Many studies addressing non–image-guided L-ILESIs were published several decades ago, at a time when it was considered acceptable to report only group mean outcome data. While group data suggest a procedure is effective, they are inconclusive as they assume normally distributed pain scores and do not inform us about how many patients are benefitting and to what extent. In this systematic review, group data were accepted only as a

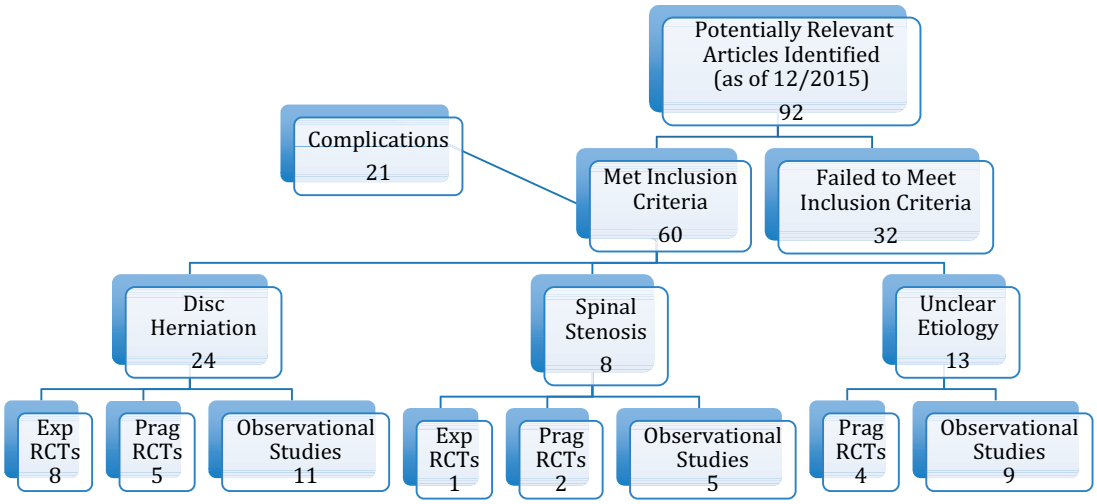


**Figure 1** Categorization of potentially relevant articles generated by the literature search. *(Note: Several studies addressed both lumbar disc herniation and lumbar spinal stenosis.)*

guide indicating the background trends, while for true assessment of effectiveness the categorical data from which success rates can be determined were used. The definition of success rates varied with pathology studied and was defined by the original authors.

That body of evidence was evaluated using the GRADE system of appraisal to determine the quality of the evidence of the effectiveness of non–image-guided L-ILESIs [14]. A similar process was undertaken for reviewing any potential risks associated with this procedure.

## Results

A literature search yielded 92 articles on non–image-guided L-ILESIs for treatment of low back and/or lower extremity pain of varying etiologies. Of the 92 articles, 32 were excluded for a variety of reasons (Table 1) [15–46]. These articles were assigned to the categories noted in Figure 1. Otherwise, accepted were 39 articles addressing the effectiveness of non–image-guided L-ILESI and 21 publications that discussed aspects of the safety of the procedure and its associated risks.

## Effectiveness

The 39 primary studies of effectiveness included 21 observational studies, nine pragmatic studies, and nine explanatory studies on a variety of spine pathologies. The methodological weaknesses of these studies are outlined in Tables 2a, 2b, and 2c.

### Radicular Pain Secondary to Lumbar Herniated Intervertebral Disc

The primary articles on non–image-guided L-ILESI for the treatment of lumbar radicular pain secondary to a disc herniation consisted of 11 observational studies, five pragmatic RCTs and eight explanatory RCTs. Overall, the literature was very diverse in both study design and quality.

#### *Observational Studies*

Of the 11 observational studies [47–57], only four [47,52,54,55] provided data on validated outcome measures. Among those that used validated outcome measures, only one study provided categorical data [47]. This recent prospective study of 62 patients reported a high success rate of 81% at 6-month follow-up following non–image-guided L-ILESI. Importantly, "success" was defined by the article's authors as a reduction of more than 10 points in Oswestry Disability Index (ODI) scores. The change of this magnitude is considered a minimal clinically important difference in chronic low back pain, but not in lumbar radicular pain [58], thus calling into question the clinical significance of the reported success rate.

#### *Pragmatic Studies*

Five pragmatic RCTs compared the effectiveness of "non–image-guided" L-ILESI with other treatments in patients with lumbar radicular pain due to an intervertebral disc displacement. All the studies exhibited significant shortcomings. Three studies failed to include any validated outcome measures (Table 2a). One study used a 75% subjective improvement as the only

**Table 1** Excluded studies

| Rationale | References |
|---|---|
| Technique description; no outcomes assessed | Barry and Kendall (1962) [16], Bartynski et al. (2005) [17] |
| Multiple independent interventions | Burn and Langdon (1970) [19], Nawani et al. (2010) [36], Thomas et al. (2003) [41], Warr et al. (1972) [44] |
| Lack of subgroup analysis (i.e., multiple techniques/ approaches, some use of imaging) | Arnhoff et al. (1977) [15], Butterman (2004) [21], Forrest (1980) [24], Friedly et al. (2008) [25], Heyse-Moore (1978) [28], Kraemer et al. (1997) [33], Mandel et al. (2013) [34], Radcliff et al. (2013) [38], Simotas et al. (2000) [39] |
| Poorly defined outcomes or outcomes unrelated to effectiveness of L-ILESI | Campbell et al. (2007) [22], Fanciullo et al. (2001) [23], Hopwood et al. (1993) [29], Jacobs et al. (1983) [31], Kang et al. (2012) [32], Wang et al. (1997) [42], Warfield and Crews (1987) [43], Yi et al. (2012) [45], Younes et al. (2007) [46] |
| Less than 2 weeks follow-up | Beliveau (1971) [18], Green et al. (1980) [26], Power et al. (1992) [37], Snoek et al. (1977) [40] |
| Pharmacokinetic only | Burn and Langdon (1974) [20] |
| Case reports (not related to complications) | Guten (1981) [26], Ice et al. (1995) [30] |
| Letter | Mangar and Thomas (1991) [35] |

outcome measure and observed no difference in this outcome between subjects treated with non–image-guided L-ILESI and those who received epidural local anesthetic [59]. Both patients with lumbar radicular pain due to disc herniation and those with neurogenic claudication were included in the study. The subgroup analysis did not demonstrate any dissimilarity in the outcome based on the diagnosis. Another RCT used a change in patients' conditions ("improved, no change, worse") as the outcome measure and reported that lumbar epidural injection of steroid together with local anesthetic produced significantly better results than lumbar epidural injection of local anesthetic alone when assessed at 1 month but not thereafter [60]. Finally, a small trial of 20 patients found equal effectiveness of epidural and intrathecal steroid injections in providing subjective pain relief, measured as "complete relief, improvement, or no benefit" in patients with clinically diagnosed lumbar radicular pain [61].

1Other RCTs used validated outcome instruments but did not provide any categorical data. Two studies investigated the effectiveness of non–image-guided L-ILESI versus conservative treatment. The first open label study randomly assigned patients to receive conservative care or conservative care plus non–image-guided L-ILESI and found no statistical significance in pain relief between these groups [62]. A double-blind pragmatic RCT compared the effectiveness of non–image-guided L-ILESI to lumbar intramuscular injection of the same steroid in the treatment of patients with heterogeneous pathology (including disc herniation, spinal stenosis, or combination of both) [63]. The authors concluded that regardless of the diagnosis, visual analog scale (VAS) scores were "better" in the non–image-guided L-ILESI group at 2 weeks and at 35 days but not at 2 years. No baseline or post procedure pain intensity scores were reported.

Due to the aforementioned major limitations, all the pragmatic studies failed to provide any meaningful evidence of effectiveness of non–image-guided L-ILESIs.

### *Explanatory Studies*

Eight explanatory RCTs met criteria for inclusion in this review.

#### Lower Quality Explanatory RCTs

All four studies in this category used a reasonable placebo in their control groups—administration of saline injection into interspinous ligament [64–67]. Two of these studies either did not present any data on validated outcome measures or presented the data only in a graph with no standard deviations so that neither exact pain intensity before and after the procedure could be determined, and 95% confidence intervals could not be calculated (Table 2a) [64,65].

In the first study, pain relief was approximated by calculation of the number of unspecified analgesic tablets consumed per day coupled with the patient's assessment of pain as "severe, not severe, or none" [64]. The authors reported a positive outcome favoring non–image-guided L-ILESI over the placebo injection based on pain relief and disability at 3 months. However, lack of validated outcome measurements, overlapping 95% confidence intervals, and a dropout rate of 20% significantly degraded the quality of these findings.

**Table 2a** Methodological weaknesses in lumbar disc herniation studies

| | Lack of categorical data | No data on validated outcome measures | Lack of double-blinding | Non-consecutive (or unclear if consecutive) patients | Inadequate duration or consistency of follow-up | Co-interventions not accounted for | Significant loss to follow-up | Unclear diagnosis or inclusion/ exclusion criteria |
|---|---|---|---|---|---|---|---|---|
| **Explanatory Studies** | | | | | | | | |
| Dilke et al. (1973) [64] | | • | | | | | • | |
| Klenerman et al. (1984) [65] | | • | | • | | | | |
| Ridley et al. (1988) [66] | • | | | | | • | | |
| Helliwell et al. (1985) [67] | | | • | | | • | | |
| Arden et al. (2005)/ Price et al. (2005) [68,69] | | | | | | | ⊙ | |
| Carette et al. (1997) [70] | | | | | | | | |
| Valat et al. (2003) [71] | | | | | | | | |
| **Pragmatic Studies** | | | | | | | | |
| Cuckler et al. (1985) [59] | • | • | | | • | • | | |
| Rogers et al. (1992) [60] | | • | | | | • | | |
| Winnie et al. (1972) [61] | | • | • | • | • | • | | |
| Buchner et al. (2000) [62] | • | | • | | | | | |
| Wilson-MacDonald (2005) [63] | • | | | | | • | | |
| **Observational Studies** | | | | | | | | |
| Baral (2011) [47] | | | | • | | | | |
| Berman et al. (1984) [48] | | • | | | | | | |
| Cho et al. (1970) [49] | • | • | | • | • | • | | |
| Ito et al. (1971) [50] | | • | | • | • | • | | |
| Mashari et al. (2012) [51] | | • | | | • | | • | |
| Mobaleghi (2011) [52] | • | | | • | | • | | |
| Papagelopoulos et al. (2001) [53] | | • | | | ■ | • | + | |
| Pirbudak et al. (2003) [54] | • | | | • | | | | |
| Rivest et al. (1998) [55] | • | | | • | • | • | • | |
| Schiff and Eisenberg (2003) [56] | | | | | • | • | | |
| Warfield and Crews (1987) [57] | • | • | | • | • | • | | |

⊙ less than 20% at 12 weeks; 23.7% at 52 weeks.
\+ unclear loss to follow-up.
■ although followed, data not presented prior to 1 year.

**Table 2b** Methodological weaknesses in lumbar spinal stenosis studies

| | Lack of categorical data | No data on validated outcome measures | Lack of double-blinding | Non-consecutive (or unclear if consecutive) patients | Inadequate duration or consistency of follow-up | Co-interventions not accounted for | Significant loss to follow-up | Unclear diagnosis or inclusion/ exclusion criteria |
|---|---|---|---|---|---|---|---|---|
| **Explanatory Studies** | | | | | | | | |
| Fukusaki et al. (1998) [73] | | | | | | | | |
| **Pragmatic Studies** | | | | | | | | |
| Cuckler et al. (1985) [59] | • | • | | | • | • | | |
| Wilson-MacDonald (2005) [63] | • | | | | | • | | |
| **Observational Studies** | | | | | | | | |
| Mashari et al. (2012) [51] | | • | | | • | | • | |
| Mobaleghi (2011) [52] | • | | | • | | • | | |
| Papagelopoulos et al. (2001) [53] | | • | | | ■ | • | + | |
| Rivest et al. (1998) [55] | • | | | • | • | • | • | |
| Swezey (1996) [72] | | • | | • | • | | | |

⊙ less than 20% at 12 weeks; 23.7% at 52 weeks.
+ unclear loss to follow-up.
■ although followed, data not presented prior to 1 year.

**Table 2c** Methodological weaknesses in studies with unclear or multiple etiologies

| | Lack of categorical data | No data on validated outcome measures | Lack of double-blinding | Non-consecutive (or unclear if consecutive) patients | Inadequate duration or consistency of follow-up | Co-interventions not accounted for | Significant loss to follow-up | Unclear diagnosis or inclusion/ exclusion criteria |
|---|---|---|---|---|---|---|---|---|
| **Pragmatic Studies** | | | | | | | | |
| Laiq et al. (2009) [83] | • | | • | | | | | • |
| McGregor et al. (2001) [84] | • | | • | | | | • | • |
| Owlia (2007) [85] | • | | • | | | | | • |
| Rocco et al. (1989) [86] | | | | • | • | • | • | • |
| **Observational Studies** | | | | | | | | |
| Bowman et al. (1993) [74] | • | | | • | | • | | • |
| Harley et al. (1967) [75] | | • | | | | | | • |
| Jamison et al. (1991) [76] | • | • | | • | • | • | • | • |
| Koning et al. (2002) [77] | | • | | | • | • | | • |
| Runu et al. (2005) [78] | | • | | • | | • | | • |
| Sayle-Creer and Swerdlow (1969) [79] | | • | | • | • | • | + | • |
| Andersen et al. (1987) [80] | | | | • | | • | | • |
| Hickey et al. (1987) [81] | | | | • | | • | | • |
| Rosen et al. (1988) [82] | | • | | • | • | • | | • |

⊙ less than 20% at 12 weeks; 23.7% at 52 weeks.
+ unclear loss to follow-up.
■ although followed, data not presented prior to 1 year.

The second study used two additional control groups: 20 mL of epidural bupivacaine and 20 mL of epidural saline [65]. The authors reported no difference in outcomes between the four groups and claimed that 75% of all the patients improved or were "cured" regardless of procedure performed. These results suggest that "success" is achieved for reasons other than agent injected. The small sample size and non-consecutive patients further diminished the quality of results.

A third study of 35 patients can be classified as an RCT for 2 weeks only; between 2 and 12 weeks, patients were unblinded to treatment and allowed to crossover to active treatment [66]. The authors claimed that non–image-guided L-ILESI provided better pain relief compared with placebo due to a 46% median decrease in VAS scores in the index group compared with no improvement in the control group at 2 weeks. Nonetheless, with no data on pain scores and no categorical data, the study cannot provide any compelling evidence of efficacy.

The fourth study was a small RCT with 39 patients and non-blinded investigators [67]. The data on the change in VAS and angle of straight leg raise were presented in graph formats only. The authors reported significant improvement in these outcomes in the index group compared with placebo at 1- and 3-month follow-up; however, this conclusion is difficult to accept given the lack of numerical data. The categorical outcome of a simple binary subjective patient response "definite improvement" or "no improvement" was more favorable in the treatment group, but no differences between the groups were found in the number of patients who were able to reduce their analgesic requirements by 50% or greater. In light of the aforementioned limitations, while these four lower quality explanatory RCTs are suggestive of a positive treatment effect, they provide nominal evidence of efficacy.

### Higher Quality Explanatory RCTs

Another four double-blind explanatory RCTs were more rigorous in presenting their outcomes and considered to be of higher quality (Table 3). Two of these presented similar empirical data on the same group of patients and were appraised as one study [68,69].

Each of the four RCTs recruited adequate numbers of consecutive patients with satisfactorily described inclusion/exclusion criteria, appropriately randomized patients to receive active/inactive well-described interventions, monitored outcomes with validated instruments at reasonably consistent follow-up intervals, blinded data acquisition, and performed suitable statistical analyses including presentation of categorical data, and attempted to control for concurrent co-interventions. By accounting for these variables, the precision and accuracy of their findings reduced errors related to both observer bias and chance, thereby providing more reliable information concerning the effects of non–image-guided L-ILESI for radicular pain and disability.

The first study of 158 patients compared one to three non–image-guided L-ILESIs with 80 mg of Depo-Medrol in 8 ml saline with epidural injection of 1 ml saline [70]. Mean VAS scores for leg pain improved more in the epidural steroid injection (ESI) group at 6 weeks, but the difference disappeared at 12 weeks. Categorical outcomes of patient-reported "marked" or "very marked" improvement and ODI of less than 20 found no statistically significant differences at any follow-up. None of the changes in several secondary outcome measures (Table 3) at 3-month follow-up differed significantly between the index and placebo groups.

In the second higher quality RCT, 85 subjects were randomized to receive either three epidural injections of 2 ml prednisolone or 2 ml of saline [71]. The primary categorical outcome measure was patients' perceived degree of overall improvement on a descriptive four-item scale ("recovery, marked improvement, slight improvement, or worse"). Patients rating their improvement as "recovery" or "marked improvement" were considered successfully treated. No significant difference in outcome between active treatment and placebo was demonstrated at the end of the study (day 35). The numerous secondary outcome measures [VAS, Schober test, straight leg raise test, Dallas pain questionnaire, Roland-Morris disability index] were reported only at 20-day follow-up, and none of them showed differences between the active treatment and the placebo groups.

The third study evaluated 228 participants and utilized an interspinous ligament injection of saline as a placebo [68,69]. The primary categorical outcome measure specified by the authors was ODI improvement of 75% or more. There were more patients who achieved success based on this outcome in the active treatment group compared with placebo at 3-week follow-up; however, because of overlapping 95% confidence intervals, statistically significant difference between the groups was not demonstrated (Table 3). The superiority of the active treatment compared with the placebo was also not present at 6 weeks or at 1-year follow-up. Additionally, other outcome measures including VAS pain scores, use of other health care resources, days off work, and return to work also showed no difference by 6-week follow-up.

## Neurogenic Claudication Secondary to Lumbar Spinal Stenosis

Despite the long history of performing non–image-guided L-ILESI for the treatment of patients with lumbar spinal stenosis, the literature on this subject was very scarce. The primary articles on this procedure for the treatment of neurogenic claudication consisted of five observational studies, two pragmatic RCTs, and one explanatory RCT (Table 2b).

**Table 3** Explanatory studies providing categorical data on validated outcome measures

| Reference | N | Diagnosis | Follow-up | Major outcome measures used | Definition of success | Success rate index vs placebo (confidence intervals) |
|---|---|---|---|---|---|---|
| **Carette et al. (1997)** [70] | 158 | Sciatica | 3,6,12 weeks | ODQ, Sickness Impact Profile, VAS, McGill Pain Questionnaire | ODQ $\leq$ 20 | 3 weeks: 19.5% (95% CI 10.65–28.35) vs 16.3% (95% CI 8.21–24.39)<br>3 months: 37.7% (95% CI 26.88–48.52) vs 41.8% (95% CI 30.99–52.61) |
| **Valat et al. (2003)** [71] | 85 | Sciatica | 20,35 days | VAS, Dallas Pain Questionnaire, Roland-Morris, use of analgesics | Patient-rated improvement as "recovery" or "marked improvement" + no need for pain medications | 20 days: 51% (95% CI 36.06–65.94) vs 36% (95% CI 21.48–50.52)<br>35 days: 49% (95% CI 34.06–63.94) vs 48% (95% CI 32.89–63.11) |
| **Arden et al. (2005)/ Price et al. (2005)** [68,69] | 228 | Unilateral Sciatica | 3,6,12,52 weeks | ODQ, Likert scale, VAS, SF-36 | 75% improvement in ODQ | 3 weeks: 12.5% (95% CI 6.58–18.42) vs 3.7% (95% CI 0.14–7.26)<br>6 weeks: N/A<br>12 weeks: N/A<br>52 weeks: 32.5% (95% CI 24.12–40.88) vs 29.6% (95% CI 20.99–38.21) |
| **Fukusaki et al. (1998)** [73] | 35* | Pseudo-claudication, spinal stenosis | 1 week, 1 month, 3 months | Walking distance | More than 20m of walking distance | 1 week: 63.2% (95% CI 41.52–48.87) vs 12.5% (95% CI 3.7–28.7)<br>1 month: 15.8% (95% CI −0.6–32.2) vs 6.3% (95% CI 5.6–18.2)<br>3 month: 5.3% (95% CI 4.77–15.37) vs 6.3% (95% CI 5.6–18.2) |

*In explanatory section of study.

**Table 4** Adverse effects and complications associated with non–image-guided L-ILESI

Adverse Effects and Complications

| Cause | Complication | Reference |
|---|---|---|
| Technique | Transient headaches—2 patients | Abram et al. (1979) [87] |
| | Subdural injection | Williamson (1990) [90] |
| | Subdural injection | Lehmann and Pallares (1995) [89] |
| | Horner's Syndrome and headache | Datta (2004) [95] |
| | Subarachnoid pneumocephalus | Hawley (2005) [88] |
| | Acute intracranial subdural hematoma | Ozdemir et al. (2007) [94] |
| | Paraplegia | Thefenne (2010) [91] |
| | Stroke; acute paraplegia | Oliver et al. (2012) [93] |
| Infection/Inflammation | Aseptic meningitis | Gutknecht (1987) [101] |
| | Epidural abscess | Chan (1989) [96] |
| | Extradural abscess | Goucke (1990) [98] |
| | Bacterial meningitis and cauda equina syndrome | Cooper (1996) [97] |
| | Aseptic lumbar epidural abscess | Sabel et al. (2000) [100] |
| | Epidural abscess and meningitis | Hooten (2004) [99] |
| Steroid | Cushing's Syndrome | Knight and Burnell (1980) [103] |
| | Transient hypercorticism | Stambough et al. (1984) [104] |
| | Suppression of adrenal function | Kay et al. (1994) [105] |
| | Cushing's Syndrome | Boonen (1995) [102] |
| | Epidural lipomatosis | McCullen et al. (1999) [106] |
| | Epidural lipomatosis | Sandberg and Lavyne (1999) [107] |
| Allergy | Allergic or pseudoallergic reaction | Simon et al. (1989) [108] |

*Observational Studies*

Four observational studies included subjects with both lumbar spinal stenosis and lumbar radicular pain due to disc herniation but provided separate data based on the patients' diagnoses. Among those, two studies [51,53] did not report any data on validated outcome measures and the other two [52,55] provided no categorical data. A retrospective study claimed improvement from non-image-guided L-ILESI in six out of 13 patients with neurogenic claudication due to lumbar spinal stenosis based only on the patient's decision to opt out of proposed surgery [72].

*Pragmatic Studies*

The two pragmatic RCTs presented the data separately based on the diagnosis. The first study used a 75% subjective improvement as the only outcome measure and observed no difference in this outcome between subjects treated with non–image-guided L-ILESI and those who received epidural local anesthetic [59]. The second study was a double-blind pragmatic RCT that compared the effectiveness of non–image-guided L-ILESI to lumbar intramuscular injection of the same steroid in the treatment of patients with heterogeneous pathology (including disc herniation, spinal stenosis or combination of both) [63]. The authors found that VAS scores were "better" in the non–image-guided L-ILESI group ($P < 0.004$) at 2 weeks and at 35 days, but not at 2 years. Unfortunately, acceptance of this data is hardly possible because no baseline or post procedure pain intensity scores were reported.

*Explanatory Studies*

The only explanatory RCT included 53 patients and used epidural saline and mepivacaine as the comparison treatment, whereas the index treatment consisted of epidural injection of a combination of this local anesthetic with methylprednisolone [73]. The study was well designed with a comparatively small number of subjects being the most noticeable of its very few drawbacks (Tables 2 and 3). All of the patients in the three groups had walking tolerance of less than 20 meters because of severe leg pain with this exercise. The primary outcome measure was walking distance with the criterion of success defined as the improved walking tolerance of more than 20 meters. A significant improvement at 1-week follow-up was demonstrated in patients who received either an epidural local anesthetic or its combination with steroid compared with epidural saline, but no difference between any of the groups was seen at 1 or 3 months post-intervention. The results led to the conclusion that non–image-guided L-ILESI had only a very short transitory effect on walking distance in patients with spinal stenosis and neurogenic claudication.

### Back and/or Leg Pain Secondary to Unclear or Multiple Etiologies

Many articles assessed the effectiveness of non–image-guided L-ILESI in groups of patients with disc herniation and stenosis and failed to present data for the different diagnoses: nine observational studies and four pragmatic RCTs (Table 2c).

*Observational Studies*

The majority of the observational studies did not provide categorical data on validated outcome measures [74–79]. Among three studies that did, one small study of 16 subjects with unclear inclusion criteria of "low back pain and sciatica," reported a positive outcome in only one patient 6 months after non–image-guided L-ILESI [80]. Hickey et al. published the results of a retrospective survey of 250 patients who had undergone one to three non–image-guided L-ILESIs and showed that about 85% of them reported VAS of 3/10 or less at 1-year follow-up [81]. Unfortunately, no pre-procedure scores were provided. An additional study claimed to use validated outcome instruments, but unfortunately did not provide any data [82].

*Pragmatic RCTs*

A single-blind trial demonstrated more pain relief in the non–image-guided L-ILESI group at 2 weeks and 1 month compared with the conservative care group, but this difference dissipated at 3-month follow-up [83]. Another open label RCT with poorly defined inclusion criteria allowing enrollment of patients with both axial low back and radicular pain compared the benefits of performing caudal ESI to non–image-guided L-ILESI [84]. Neither group demonstrated any benefits at 6 weeks or 6 months compared with baseline, and the loss to follow-up in this study reached 33% at 6 months. An open label trial compared two doses of epidural methylprednisolone in the treatment of patients with intervertebral disc herniation with or without spinal stenosis [85]. Subjects were randomized to receive either 80 mg or 40 mg of the steroid. No raw data on pain scores before and after treatment were reported and no separate analysis for the patients who had spinal stenosis was provided. The study demonstrated improvement in VAS scores in both groups, but did not find any difference in effectiveness between the groups at follow-ups from 2 weeks to 3 months.

One double-blind trial used both a validated outcome measure for pain intensity (VAS) and provided some rudimentary categorical data noting whether the patients got subjectively better or worse, or had no change after the treatment [86]. Enrolled patients with various somatic and lumbar radicular pain included under the umbrella of "post-laminectomy syndrome" were randomized into three groups: epidural steroid with local anesthetic, morphine and local anesthetic, or the combination of all three drugs. Only one patient in the steroid group experienced pain relief lasting longer than 1 month. The trial was discontinued early at an unspecified follow-up of more than 1 month because of life-threatening respiratory depression occurring in patients receiving epidural opioids. The dropout rate in this study reached a remarkable 58%.

### GRADE Evaluation of Evidence of Effectiveness

The effectiveness data were evaluated in accordance with the GRADE system of rating quality of evidence [14]. The data for the outcomes in patients with lumbar disc herniation (LDH) and lumbar spinal stenosis (LSS) were evaluated separately. Based on the findings provided by the high-quality explanatory studies, the evidence regarding effectiveness of non–image-guided L-ILESI in treating both LDH and LSS beyond 3–6 weeks post-injection was found to be lacking. The evidence of short-term pain relief from this procedure was conflicting because of inconsistent data among these trials. Therefore, it was deemed to be of low quality.

### Complications

Review of the literature on complications associated with non–image-guided L-ILESI was limited to case reports identifying complications and adverse effects attributable to technique, infection, and use of steroid. Table 4 provides a summary of the complications found in the literature.

The majority of technique-related adverse events and complications have been reported as a result of inadvertent injection of air into the subarachnoid space, resulting in transient headache and pneumocephalus [87,88], or subdural/subarachnoid injection of a local anesthetic, causing transient motor and sensory deficit [89,90]. More severe neurologic complications are rare, but have been reported. There was one case reported of irreversible paraplegia following the procedure in a patient with a previous spine surgery, with the magnetic resonance imaging (MRI) findings suggestive of medullary ischemia (possibly secondary to embolization of the artery during the injection) [91]. It must be noted, however, that this injection was performed with a sharp, 21-gauge needle at an unknown spinal level without using the loss of resistance technique. By no means was such an injection done in accordance with the set of criteria established to minimize the potential risk to a patient posed by the intervention [92]. One case report describes transient paraplegia after a lumbar epidural injection, resulting from a previously undiagnosed spinal dural arteriovenous fistula (SDAF) [93]. This patient exhibited normalization in neurological functions after the embolization procedure. Finally, acute intracranial subdural hematoma after accidental dural puncture during the injection was reported [94] and attributed to cerebrospinal fluid (CSF) leak causing low intracranial pressure and tearing of the bridging veins. The patient achieved complete recovery after a few days of conservative treatment. Incidental discovery of carotid artery

dissection 2 months after non–image-guided L-ILESI seems to be unrelated to the procedure, especially in light of a minor head trauma reported by the patient 1 week post-injection [95].

Infection has been reported six times based on cultures or MRI findings [96–100], with aseptic meningitis proposed in one report [101]. Symptoms were noted to develop from 2 days to 3 weeks following the procedure. The patients were treated surgically and/or with IV antibiotics in all of these cases, and complete recovery was noted in the majority of them.

Steroid-related complications usually occurred in patients who underwent multiple frequent non–image-guided L-ILESIs. Cushing's Syndrome [102–104], suppression of adrenal function [105], and epidural lipomatosis [106,107] have been reported following epidural steroid injections. Allergic reaction or pseudoallergic reaction to epidurally injected triamcinolone diacetate has also been reported [108].

### GRADE Assessment of Risks of Non–Image-Guided L-ILESI

When attempting to assess the quality of the evidence on the risks of non–image-guided L-ILESI in accordance with the GRADE system, it is noted that the published evidence consists only of case reports. Accordingly, the body of evidence is of very low quality: we have little confidence in the effect estimate and the true effect is likely to be substantially different from the estimate of effect. Readers must be careful not to confuse "evidence of very low quality" with "evidence of little significance" and perhaps go on to dismiss the risks of non–image-guided L-ILESI as too rare to be of concern. The evidence of risks is of very low quality because few cases of serious complications have been published. This may reflect publication bias. There is a tendency for serious complications not to be publicized in articles. Thus, the frequency of complications after non–image-guided L-ILESI is uncertain, but when they do occur they can be catastrophic.

## Discussion

This systematic review of literature evaluated the evidence on non–image-guided L-ILESIs for the treatment of lumbar radicular pain or neurogenic claudication by utilizing GRADE. Most systematic reviews focus only on RCTs. While RCTs may, in fact, deserve the most attention, it is equally important to consider the study methodology when performing systematic reviews. In that light, a poorly designed and conducted RCT may be less valuable than a well-designed observational study. Because the study samples from RCTs may not represent the patient population seen in a daily conventional practice, observational studies are very useful in providing data that reflect effectiveness of a procedure in the real-world setting. The GRADE system follows in the footsteps of recommendations made by Dr. Archie Cochrane, a pioneer of evidence-based medicine, who advised consideration of all published evidence, giving weight to the data based upon the types and methodologies of studies from which they are derived [109].

Many studies investigating "non–image-guided" L-ILESI were conducted decades ago when less rigorous scientific standards in medical research were acceptable, the procedural technique was not standardized, and the underlying diagnosis was unknown due to lack of imaging. Perhaps, reflecting the contemporary perception of the necessity of voluminous injection, an injected steroid was diluted in 8–20 ml of fluid in almost all of the studies regardless of their design. The overwhelming majority of investigators did not limit the treatment to one non–image-guided L-ILESI. One may postulate that they performed several non–image-guided procedures in a row because of concerns of inaccuracy. Even comparatively better-defined inclusion criteria that allowed only subjects with radicular pain to be enrolled in a study did not exclude patients with acute radicular pain of a very short duration. It has been shown that the natural course of such pain is benign with about 60% of subjects reporting a marked decrease in pain during the first 2 months [110]. Therefore, short-term assessments of the effectiveness of ESI in acute radicular pain is challenging due to favorable natural history. The presented data in such studies could lead to type 2 errors when the difference between the index and control groups is falsely blunted because both groups would be expected to improve within several weeks.

In this review, the vast majority of observational studies reported various degrees of pain relief in patients with low back and/or radicular pain. Generally, most observational studies yield a low or very low quality of evidence because of the inherent biases, resulting in overestimation of the investigated treatment's effect. However, in unusual circumstances, GRADE supports rating the evidence provided by such studies as of moderate or even high quality. To qualify for such an "upgrade," the observational evidence base must demonstrate certain features, such as large magnitude of effect or the presence of a dose-response gradient [14]. The observational evidence base investigating the effects of non–image-guided L-ILESI does not satisfy these criteria. Quite to the contrary, the observational evidence is plagued by inadequate statistical analyses, lack of validated outcome measures, absence of categorical data, short follow-up periods, and significant loss to follow-up.

Pragmatic studies compare the effectiveness of an index treatment to other treatments and provide the quality of evidence similar to that of observational studies if no superiority of an investigated intervention was found. However, if a pragmatic study demonstrates a greater success of the index treatment, the quality of evidence it yields is on par with that of an explanatory RCT. In this review, the evidence provided by pragmatic studies that compared non–image-guided L-ILESI with

other treatments (all pragmatic studies) were relegated to be of low quality because of the various combinations of serious methodological flaws as detailed earlier.

Explanatory trials compare an index treatment with a placebo and demonstrate if the former is more effective than the nonspecific effects of a sham intervention. Methodologically sound explanatory studies may provide the highest quality evidence. Several explanatory RCTs in our review were considered to be of a lesser quality for a variety of reasons: no validated outcome measures were used [59,64], categorical data were not provided [66], or appropriate blinding was not performed [67]. The other studies were found to be of higher quality [68–71,73]. These double-blind explanatory RCTs used validated outcome instruments for pain intensity and physical functioning, and reported on use of other health care resources. Every high-quality explanatory RCT provided categorical data. The study by Valat et al. did not demonstrate any statistically significant pain relief from non–image-guided L-ILESI in patients with radicular complaints [71], while the other trials in this category showed a short-lived improvement in pain and function lasting only 1 week in subjects with spinal stenosis [73] and 3–6 weeks in patients with radicular pain [68–70]. No significant improvement was demonstrated in patients suffering from spinal stenosis or radicular pain beyond a 6-week follow-up after the last injection. For these reasons, it would be reasonable to conclude that non–image-guided L-ILESI may have only a very limited role for the treatment of radicular pain. This would include short-term pain relief and utilization only in settings where fluoroscopy is not available for a more accurate approach to the epidural space.

This review also included studies reporting complications with non–image-guided L-ILESI. While most of the reported complications are reasonably common and known, the two reports of paraplegia stand out [91,93]. While paraplegia due to radicular artery embolization is a recognized potential complication of transforaminal epidural steroid injections with particulate steroids [111], the same complications were not typically linked to the interlaminar approach. However, two features make these case reports atypical. In the first case, the substandard technique was used while performing non–image-guided L-ILESI on the patient who had previous lumbar surgery that might contribute to an aberrant vascularization pattern [91]. In the second case, the patient suffered from previously undiagnosed SDAF with resolution of paraplegia after an embolization procedure [93]. As paraplegia has not been reported in patients without a history of back surgery and SDAF, it would seem that, in the absence of these conditions, there is no documented risk of paraplegia with non–image-guided L-ILESI.

## Conclusions

The evidence supporting effectiveness of non–image-guided L-ILESI for reduction of pain and improved function in patients with lumbar radicular pain and neurogenic claudication is very limited. There is an observed trend suggesting that these procedures may provide short-term benefit in the first 3–6 weeks after the procedure, but the trend was not consistent. The small number of case reports on significant risks with non–image-guided L-ILESI suggests that the procedure is relatively safe, with the exception of patients with a history of previous surgery and SDAF, likely due to aberrant vascularization pattern. The main limitation of this systematic review, however, is that it cannot explain whether the limited success of this intervention stems from its inherent ineffectiveness or from its lowered accuracy rate due to the inadequate technical aspects, including lack of fluoroscopic guidance and injection of highly diluted steroid medications that used to be a standard in the past. If technical aspects including the use of fluoroscopy do make a difference, non–image-guided L-ILESI may only have a very limited role only in settings where fluoroscopy is not available.

## Acknowledgments

The authors wish to thank the other members of the Spine Intervention Society's Standards Division, Dr. Andrew Engel, Dr. Wade King, Dr. D. Scott Kreiner, and Dr. Milton Landers, who read the final draft and offered comments on it. They also wish to acknowledge Professor Nikolai Bogduk, who although not involved in the preparation of this article provided the inspiration for it by advocating this style of systematic review, stratifying RCTs as pragmatic and explanatory studies.

## References

1 Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Epidural steroids: A comprehensive, evidence-based review. Reg Anesth Pain Med 2013;38(3):175–200.

2 Friedly J, Chan L, Deyo R. Increases in lumbosacral injections in the Medicare population: 1994 to 2001. Spine 2007;32(16):1754–60.

3 Cluff R, Mehio AK, Cohen SP, et al. The technical aspects of epidural steroid injections: A national survey. Anesth Analg 2002;95(2):403–8.

4 White AH, Derby R, Wynne G. Epidural injections for the diagnosis and treatment of low-back pain. Spine 1980;5(1):78–86.

5 Broadbent CR, Maxwell WB, Ferrie R, et al. Ability of anaesthetists to identify a marked lumbar interspace. Anaesthesia 2000;55(11):1122–6.

6 Fredman B, Nun MB, Zohar E, et al. Epidural steroids for treating "failed back surgery syndrome": Is

fluoroscopy really necessary? Anesth Analg 1999; 88(2):367–72.

7 Sharrock NE. Recordings of, and an anatomical explanation for, false positive loss of resistance during lumbar extradural analgesia. Br J Anaesth 1979; 51(3):253–8.

8 Engel A, King W, MacVicar J. The effectiveness and risks of fluoroscopically guided cervical transforaminal injections of steroids: A systematic review with comprehensive analysis of the published data. Pain Med 2014;15(3):386–402.

9 King W, Ahmed SU, Baisden J, et al. Diagnosis and treatment of posterior sacroiliac complex pain: A systematic review with comprehensive analysis of the published data. Pain Med 2015;16(2):257–65.

10 Kreiner DS, MacVicar J, Duszynski B, Nampiaparampil DE. The mild(R) procedure: A systematic review of the current literature. Pain Med 2014;15(2):196–205.

11 MacVicar J, King W, Landers MH, Bogduk N. The effectiveness of lumbar transforaminal injection of steroids: A comprehensive review with systematic analysis of the published data. Pain Med 2013; 14(1):14–28.

12 Bicket MC, Gupta A, Brown CH, IV, Cohen SP. Epidural injections for spinal pain: A systematic review and meta-analysis evaluating the "control" injections in randomized controlled trials. Anesthesiology 2013;119(4):907–31.

13 Tachihara H, Sekiguchi M, Kikuchi S, Konno S. Do corticosteroids produce additional benefit in nerve root infiltration for lumbar disc herniation? Spine 2008;33(7):743–7.

14 Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64(4):401–6.

15 Arnhoff FN, Triplett HB, Pokorney B. Follow-up status of patients treated with nerve blocks for low-back pain. Anesthesiology 1977;46(3):170–8.

16 Barry PJ, Kendall PH. Corticosteroid infiltration of the extradural space. Ann Phys Med 1962;6: 267–73.

17 Bartynski WS, Grahovac SZ, Rothfus WE. Incorrect needle position during lumbar epidural steroid administration: Inaccuracy of loss of air pressure resistance and requirement of fluoroscopy and epidurography during needle insertion. AJNR 2005; 26(3):502–5.

18 Beliveau P. A comparison between epidural anaesthesia with and without corticosteroid in the treatment of sciatica. Rheumatol Phys Med 1971;11(1):40–3.

19 Burn JM, Langdon L. Lumbar epidural injection for the treatment of chronic sciatica. Rheumatol Phys Med 1970;10(7):368–74.

20 Burn JM, Langdon L. Duration of action of epidural methyl prednisolone. A study in patients with the lumbosciatic syndrome. Am J Phys Med 1974; 53(1):29–34.

21 Buttermann GR. Treatment of lumbar disc herniation: Epidural steroid injection compared with discectomy. A prospective, randomized study. J Bone Joint Surg Am Vol 2004;86-a(4):670–9.

22 Campbell MJ, Carreon LY, Glassman SD, McGinnis MD, Elmlinger BS. Correlation of spinal canal dimensions to efficacy of epidural steroid injection in spinal stenosis. J Spinal Disord Tech 2007;20(2):168–71.

23 Fanciullo GJ, Hanscom B, Seville J, Ball PA, Rose RJ. An observational study of the frequency and pattern of use of epidural steroid injection in 25,479 patients with spinal and radicular pain. Reg Anesth Pain Med 2001;26(1):5–11.

24 Forrest JB. The response to epidural steroid injections in chronic dorsal root pain. Can Anaesth Soc J 1980;27(1):40–6.

25 Friedly J, Nishio I, Bishop MJ, Maynard C. The relationship between repeated epidural steroid injections and subsequent opioid use and lumbar surgery. Arch Phys Med Rehabil 2008;89(6):1011–5.

26 Green PW, Burke AJ, Weiss CA, Langan P. The role of epidural cortisone injection in the treatment of diskogenic low back pain. Clin Orthop Relat Res 1980;153:121–5.

27 Guten G. Herniated lumbar disk associated with running. A review of 10 cases. Am J Sports Med 1981;9(3):155–9.

28 Heyse-Moore GH. A rational approach to the use of epidural medication in the treatment of sciatic pain. Acta Orthop Scand 1978;49(4):366–70.

29 Hopwood MB, Abram SE. Factors associated with failure of lumbar epidural steroids. Reg Anesth 1993;18(4):238–43.

30 Ice DA, Dillingham TR, Belandres PV. Epidural corticosteroid injections for acute radiculopathy in a 95-year-old woman. South Med J 1995;88(2):222–4.

31 Jacobs S, Pullan PT, Potter JM, Shenfield GM. Adrenal suppression following extradural steroids. Anaesthesia 1983;38(10):953–6.

32 Kang SS, Hwang BM, Son H, et al. Changes in bone mineral density in postmenopausal women treated with epidural steroid injections for lower back pain. Pain Physician 2012;15(3):229–36.

33 Kraemer J, Ludwig J, Bickert U, Owczarek V, Traupe M. Lumbar epidural perineural injection: A new technique. Eur Spine J 1997;6(5):357–61.

34 Mandel S, Schilling J, Peterson E, Rao DS, Sanders W. A retrospective analysis of vertebral body fractures following epidural steroid injections. J Bone Joint Surg Am Vol 2013;95(11):961–4.

35 Mangar D, Thomas PS. Epidural steroid injections in the treatment of cervical and lumbar pain syndromes. Reg Anesth 1991;16(4):246.

36 Nawani DP, Agrawal S, Asthana V. Single shot epidural injection for cervical and lumbosaccral radiculopathies: A preliminary study. Korean J Pain 2010; 23(4):254–7.

37 Power RA, Taylor GJ, Fyfe IS. Lumbar epidural injection of steroid in acute prolapsed intervertebral discs. A prospective study. Spine 1992;17(4):453–5.

38 Radcliff K, Kepler C, Hilibrand A, et al. Epidural steroid injections are associated with less improvement in patients with lumbar spinal stenosis: A subgroup analysis of the Spine Patient Outcomes Research Trial. Spine 2013;38(4):279–91.

39 Simotas AC, Dorey FJ, Hansraj KK, Cammisa F, Jr. Nonoperative treatment for lumbar spinal stenosis. Clinical and outcome results and a 3-year survivorship analysis. Spine 2000;25(2):197–203. discussions -4.

40 Snoek W, Weber H, Jorgensen B. Double blind evaluation of extradural methyl prednisolone for herniated lumbar discs. Acta Orthop Scand 1977;48(6):635–41.

41 Thomas E, Cyteval C, Abiad L, et al. Efficacy of transforaminal versus interspinous corticosteroid injectionin discal radiculalgia—a prospective, randomised, double-blind study. Clin Rheumatol 2003;22(4-5):299–304.

42 Wang YL, Tan PP, Yang CH, Tsai SC, Chung HS. Epidural dexamethasone reduces the incidence of backache after lumbar epidural anesthesia. Anesth Analg 1997;84(2):376–8.

43 Warfield CA, Crews DA. Work status and response to epidural steroid injection. J Occup Med 1987;29(4):315–6.

44 Warr AC, Wilkinson JA, Burn JM, Langdon L. Chronic lumbosciatic syndrome treated by epidural injection and manipulation. The Practitioner 1972; 209(249):53–9.

45 Yi Y, Hwang B, Son H, Cheong I. Low bone mineral density, but not epidural steroid injection, is associated with fracture in postmenopausal women with low back pain. Pain Physician 2012;15(6):441–9.

46 Younes M, Neffati F, Touzi M, et al. Systemic effects of epidural and intra-articular glucocorticoid injections in diabetic and non-diabetic patients. Joint Bone Spine 2007;74(5):472–6.

47 Baral BK, Shrestha RR, Shrestha AB, Shrestha CK. Effectiveness of epidural steroid injection for the management of symptomatic herniated lumbar disc. Nepal Med Coll J 2011;13(4):303–7.

48 Berman AT, Garbarino JL, Jr., Fisher SM, Bosacco SJ. The effects of epidural injection of local anesthetics and corticosteroids on patients with lumbosciatic pain. Clin Orthop Relat Res 1984; (188): 144–51.

49 Cho KO. Therapeutic epidural block with a combination of a weak local anesthetic and steroids in management of complicated low back pain. Am Surg 1970;36(5):303–8.

50 Ito R. The treatment of low back pain and sciatica with epidural corticosteroids injection and its pathophysiological basis. Nihon Seikeigeka Gakkai Zasshi 1971;45(9):769–77.

51 Mashari A, Minty R, Minty L, Hopman WM, Kelly L. Epidural steroid injections for low back pain in rural practice: A 5-year retrospective study. Canad J Rural Med 2012;17(4):127–34.

52 Mobaleghi J, Allahdini F, Nasseri K, et al. Comparing the effects of epidural methylprednisolone acetate injected in patients with pain due to lumbar spinal stenosis or herniated disks: A prospective study. Int J General Med 2011;4:875–8.

53 Papagelopoulos PJ, Petrou HG, Triantafyllidis PG, et al. Treatment of lumbosacral radicular pain with epidural steroid injections. Orthopedics 2001;24(2): 145–9.

54 Pirbudak L, Karakurum G, Oner U, Gulec A, Karadasli H. Epidural corticosteroid injection and amitriptyline for the treatment of chronic low back

pain associated with radiculopathy. The Pain Clinic 2003;15(3):247–53.

55 Rivest C, Katz JN, Ferrante FM, Jamison RN. Effects of epidural steroid injection on pain due to lumbar spinal stenosis or herniated disks: A prospective study. Arthritis Care Res 1998;11(4):291–7.

56 Schiff E, Eisenberg E. Can quantitative sensory testing predict the outcome of epidural steroid injections in sciatica? A preliminary study. Anesth Analg 2003; 97(3):828–32.

57 Warfield CA, Crews DA. Epidural steroid injection as a predictor of surgical outcome. Surg Gynecol Obstet 1987;164(5):457–8.

58 Hagg O, Fritzell P, Nordwall A. The clinical importance of changes in outcome scores after treatment for chronic low back pain. Eur Spine J 2003; 12(1):12–20.

59 Cuckler JM, Bernini PA, Wiesel SW, et al. The use of epidural steroids in the treatment of lumbar radicular pain. A prospective, randomized, double-blind study. J Bone Joint Surg Am Vol 1985; 67(1):63–6.

60 Rogers P, Nash TP, Schiller D, Norman J. Epidural steroids for sciatica. Pain Clinic 1992;5(2):67–72.

61 Winnie AP, Hartman JT, Meyers HL, Jr., Ramamurthy S, Barangan V. Pain clinic. II. Intradural and extradural corticosteroids for sciatica. Anesth Analg 1972;51(6):990–1003.

62 Buchner M, Zeifang F, Brocai DR, Schiltenwolf M. Epidural corticosteroid injection in the conservative management of sciatica. Clin Orthop Relat Res 2000;375:149–56.

63 Wilson-MacDonald J, Burt G, Griffin D, Glynn C. Epidural steroid injection for nerve root compression. A randomised, controlled trial. J Bone Joint Surg Br Vol 2005;87(3):352–5.

64 Dilke TF, Burry HC, Grahame R. Extradural corticosteroid injection in management of lumbar nerve root compression. Br Med J 1973;2(5867):635–7.

65 Klenerman L, Greenwood R, Davenport HT, White DC, Peskett S. Lumbar epidural injections in the treatment of sciatica. Br J Rheumatol 1984;23(1):35–8.

66 Ridley MG, Kingsley GH, Gibson T, Grahame R. Outpatient lumbar epidural corticosteroid injection in the management of sciatica. Br J Rheumatol 1988; 27(4):295–9.

67 Helliwell M. Outpatient treatment of low back pain and sciatica by a single extradural corticosteroid injection. Br J Clin Pract 1985;39(6):228–31.

68 Arden NK, Price C, Reading I, et al. A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: The WEST study. Rheumatology 2005;44(11):1399–406.

69 Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. Health Technol Assess 2005;9(33):1–58.

70 Carette S, Leclaire R, Marcoux S, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. N Engl J Med 1997;336(23):1634–40.

71 Valat JP, Giraudeau B, Rozenberg S, et al. Epidural corticosteroid injections for sciatica: A randomised, double blind, controlled clinical trial. Ann Rheum Dis 2003;62(7):639–43.

72 Swezey RL. Outcomes for lumbar stenosis. J Clin Rheumatol 1996;2(3):129–34.

73 Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. Clin J Pain 1998;14(2):148–51.

74 Bowman SJ, Wedderburn L, Whaley A, Grahame R, Newman S. Outcome assessment after epidural corticosteroid injection for low back pain and sciatica. Spine 1993;18(10):1345–50.

75 Harley C. Extradural corticosteroid infiltration. A follow-up study of 50 cases. Ann Phys Med 1967; 9(1):22–8.

76 Jamison RN, VadeBoncouer T, Ferrante FM. Low back pain patients unresponsive to an epidural steroid injection: Identifying predictive factors. Clin J Pain 1991;7(4):311–7.

77 Koning HM, Koning AJ, Bruinen TCM, Koster HG, Heybroek E. The period of pain relief following a successful epidural steroid injection for low back pain. Pain Clinic 2002;13(4):331–8.

78 Runu R, Sinha NK, Pai R, Shankar PR, Vijayabhaskar P. Our experience with epidural steroid injections in management of low backpain and sciatica. Kathmandu Univ Med J (KUMJ) 2005; 3(4):349–54.

79 Sayle-Creer W, Swerdlow M. Epidural injections for the relief of lumbo-sciatic pain. Acta Orthop Belg 1969;35(3):728–34.

80 Andersen KH, Mosdal C. Epidural application of cortico-steroids in low-back pain and sciatica. Acta Neurochir 1987;87(1–2):52–3.

81 Hickey RF. Outpatient epidural steroid injections for low back pain and lumbosacral radiculopathy. N Z Med J 1987;100(832):594–6.

82 Rosen CD, Kahanovitz N, Bernstein R, Viola K. A retrospective analysis of the efficacy of epidural steroid injections. Clin Orthop Relat Res 1988;228: 270–2.

83 Laiq N, Khan MN, Iqbal MJ, Khan S. Comparison of Epidural Steroid Injections with conservative management in patients with lumbar radiculopathy. J Coll Phys Surg 2009;19(9):539–43.

84 McGregor AH, Anjarwalla NK, Stambach T. Does the method of injection alter the outcome of epidural injections? J Spinal Disord 2001; 14(6):507–10.

85 Owlia MB, Salimzadeh A, Alishiri G, Haghighi A. Comparison of two doses of corticosteroid in epidural steroid injection for lumbar radicular pain. Singapore Med J 2007;48(3):241–5.

86 Rocco AG, Frank E, Kaul AF, Lipson SJ, Gallo JP. Epidural steroids, epidural morphine and epidural steroids combined with morphine in the treatment of post-laminectomy syndrome. Pain 1989;36(3): 297–303.

87 Abram SF, Cherwenka RW. Transient headache immediately following epidural steroid injection. Anesthesiology 1979;50(5):461–2.

88 Hawley JS, Ney JP, Swanberg MM. Subarachnoid pneumocephalus from epidural steroid injection. Headache 2005;45(3):247–8.

89 Lehmann LJ, Pallares VS. Subdural injection of a local anesthetic with steroids: Complication of epidural anesthesia. South Med J 1995;88(4):467–9.

90 Williamson JA. Inadvertent spinal subdural injection during attempted spinal epidural steroid therapy. Anaesth Intensive Care 1990;18(3):406–8.

91 Thefenne L, Dubecq C, Zing E, et al. A rare case of paraplegia complicating a lumbar epidural infiltration. Ann Phys Rehabil Med 2010;53(9):575–83.

92 Jones RL, Landers MH. Has rare case of paraplegia complicating a lumbar epidural infiltration been reported? Ann Phys Rehabil Med 2011; 54(4):270.

93 Oliver TA, Sorensen M, Arthur AS. Endovascular treatment for acute paraplegia after epidural steroid injection in a patient with spinal dural arteriovenous malformation. J Neurosurg Spine 2012;17(3):251–5.

94 Ozdemir O, Calisaneller T, Yildirim E, Altinors N. Acute intracranial subdural hematoma after epidural steroid injection: A case report. J Manipulative Physiol Ther 2007;30(7):536–8.

95 Datta S, Candido KD. Incidental discovery of carotid artery dissection as a cause of horner's syndrome and headache in a patient presenting for follow-up of lumbar epidural steroid injection: A case report with a three year follow-up. Pain Physician 2004;7(4):483–5.

96 Chan ST, Leung S. Spinal epidural abscess following steroid injection for sciatica. Case report. Spine 1989;14(1):106–8.

97 Cooper AB, Sharpe MD. Bacterial meningitis and cauda equina syndrome after epidural steroid injections. Canad J Anaesth 1996;43(5 Pt 1): 471–4.

98 Goucke CR, Graziotti P. Extradural abscess following local anaesthetic and steroid injection for chronic low back pain. Br J Anaesth 1990; 65(3):427–9.

99 Hooten WM, Kinney MO, Huntoon MA. Epidural abscess and meningitis after epidural corticosteroid injection. Mayo Clin Proc 2004;79(5):682–6.

100 Sabel M, Felsberg J, Neuen-Jacob E, et al. Enlargement of a chronic aseptic lumbar epidural abscess by intraspinal injections–a rare cause of progressive paraparesis. Zentralbl Fur Neurochir 2000;61(2):111–4.

101 Gutknecht DR. Chemical meningitis following epidural injections of corticosteroids. Am J Med 1987; 82(3):570.

102 Boonen S, Van Distel G, Westhovens R, Dequeker J. Steroid myopathy induced by epidural triamcinolone injection. Br J Rheumatol 1995;34(4):385–6.

103 Knight CL, Burnell JC. Systemic side-effects of extradural steroids. Anaesthesia 1980;35(6): 593–4.

104 Stambough JL, Booth RE, Jr., Rothman RH. Transient hypercorticism after epidural steroid injection. A case report. J Bone Joint Surg Am Vol 1984;66(7):1115–6.

105 Kay J, Findling JW, Raff H. Epidural triamcinolone suppresses the pituitary-adrenal axis in human subjects. Anesth Analg 1994;79(3):501–5.

106 McCullen GM, Spurling GR, Webster JS. Epidural lipomatosis complicating lumbar steroid injections. J Spinal Disord 1999;12(6):526–9.

107 Sandberg DI, Lavyne MH. Symptomatic spinal epidural lipomatosis after local epidural corticosteroid injections: Case report. Neurosurgery 1999;45(1):162.

108 Simon DL, Kunz RD, German JD, Zivkovich V. Allergic or pseudoallergic reaction following epidural steroid deposition and skin testing. Reg Anesth 1989;14(5):253–5.

109 Cochrane A. Effectivness and Efficiency. Cambridge: Cambridge University Press; 1977.

110 Benoist M. The natural history of lumbar disc herniation and radiculopathy. Joint Bone Spine 2002; 69(2):155–60.

111 Kennedy DJ, Dreyfuss P, Aprill CN, Bogduk N. Paraplegia following image-guided transforaminal lumbar spine epidural steroid injection: Two case reports. Pain Med 2009;10(8):1389–94.