Steroid for epidural injection in spinal stenosis: a systematic review and meta-analysis

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Purpose: To investigate the effectiveness and safety of epidural steroid injections in patients with lumbar spinal stenosis (LSS).

Methods: We performed a search on the CENTRAL, Pubmed, Embase and Cochrane databases up to September 2014. We recovered 17 original articles, of which only 10 were in full compliance with the randomized controlled trial (RCT) criteria. These articles were reviewed in an independent and blinded way by two reviewers who were previously trained to extract data and score their quality by the criteria of the Cochrane Handbook (5.1.0).

Results: We accepted ten studies with 1,010 participants. There is minimal evidence that shows that epidural steroid injections are better than lidocaine alone, regardless of the mode of epidural injection. There is a fair short-term and long-term benefit for treating spinal stenosis with local anesthetic and steroids.

Conclusions: This meta-analysis suggests that epidural steroid injections provide limited improvement in short-term and long-term benefits in LSS patients.

Keywords: lumbar spinal stenosis, epidural injection, steroid, local anesthetic, chronic pain

Introduction

Lumbar spinal stenosis (LSS) is a degenerative disease that affects the lumbar spine. LSS can cause back and leg pain due to the compression of neuronal structures and intraspinal vasculature due to the narrowing of the spinal canal. LSS is quite common in people older than 65 years, and its most significant clinical symptom is intermittent neurogenic claudication. Neurogenic claudication is characterized by pain, paresthesia, and cramping in one or both legs. It is caused suddenly by walking and prolonged standing and can be relieved through sitting and bending forward.

Neurogenic claudication is a main reason leading to disability and lost independence in the elderly population. The patients with symptomatic LSS not only suffer from back and leg pain, but are also at high risk for developing serious complications. Disability and lost independence may lead to physical deterioration and obesity, which may eventually lead to serious health problems. Those afflicted have more serious walking limitations than individuals with knee or hip osteoarthritis.

Consequently, their restricted ability to walk and stand lead to a significant decrease in quality of life. The rate of surgery for LSS has risen dramatically, especially in the USA. Some good outcomes from surgery have been demonstrated, but the literature has also suggested limited long-term benefits when compared to nonsurgical management. Some conservative treatment is recommended prior to surgical intervention. Researchers have focused on the use of epidural steroid injections to treat pain due to LSS.
Because pain and limited walking are the main impaired functions in patients with LSS, decreasing pain and improving walking ability are the primary goals for treatment. Two systematic reviews on epidural steroid injections for LSS are available. However, whether epidural steroid injections can relieve pain and improve walking ability in patients with LSS in short-term and long-term follow-ups is unclear. It is important to evaluate the role of epidural steroid injection treatments to manage patients with LSS. Therefore, we undertook a systematic review and meta-analysis of all the published literature to evaluate the effectiveness and safety of epidural steroid injection interventions for the treatment of LSS.

Materials and methods
We conducted this systematic review and meta-analysis according to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0; Oxford, UK).

Search strategy
The Cochrane library, Google Scholar, CENTRAL, Pubmed and Embase databases were searched independently by two investigators (KL and PCL), and relevant studies published before September 2014 were retrieved. The search strategy was based on a combination of the following medical subject headings (MeSH) and keywords: "steroid", "spinal stenosis", "pain", "epidural injection", and "local anesthetic". No restriction to specific languages or years of publication were included. The "related articles" function was used to broaden the search. The reference lists of the selected studies were also examined manually to identify relevant studies that were not discovered during the database searches. The corresponding authors were contacted when additional information was needed.

Study selection
We included randomized controlled trials (RCTs) that evaluated the efficacy and safety of epidural injections of steroids plus local anesthetic versus local anesthetic alone for the treatment of LSS patients. The inclusion criteria for the systematic review and meta-analysis were as follows: (1) randomized controlled trials in adults with LSS with epidural injection treatment; (2) clinical or radiological diagnosis of LSS; (3) describe neurogenic claudication with back (leg) pain and gait assessment; (4) provide the dosage and route of epidural steroid injection administration; and (5) outcomes measured, such as walking ability, pain intensity, quality of life, and global improvement. Studies evaluating radiculopathy caused by disc lesions were excluded. Studies with mixed populations were only included if the data for neurogenic claudication due to lumbar spinal stenosis were provided.

Outcome measures
All of the eligible studies were reviewed for baseline data (such as age and sex), intervention (such as epidural injection administration method, dose and duration) and outcome measures. Both subjective and objective functional outcome measurements were used to evaluate the data. However, the primary key polled outcomes were the pain scale (such as visual analog scale [VAS]) and walking ability. Adverse effects of epidural steroid injections were also examined. The quality of eligible studies was also assessed according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.

Quality assessment
The titles and abstracts of the publications were reviewed using the previously mentioned selection criteria by two readers (KL and PCL). The data extraction of all of the variables and outcomes of interest and assessment of the methodological quality were performed independently by two investigators. Any disagreement was resolved by discussion and consensus. The methodological quality of the trials was assessed using the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.

Statistical methods
Statistical analysis was performed by Review Manager 5.3.3 (Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark). For dichotomous variables, the relative risks (RRs) were measured with 95% confidence intervals (CIs), while the weighted mean difference (WMD) was measured with the 95% CIs for continuous variables. P-values <0.05 were considered statistically significant, and the 95% CIs are reported. Statistical heterogeneity among studies was evaluated by Q-statistic and quantified by the I² statistic. Both a fixed-effects model and a random-effects model were used to obtain summary RRs or WMDs. If the Q or I² statistic was significant, a random-effects model was used. Otherwise, a fixed-effects model was used. Funnel plots and the Egger test (with P<0.05 considered statistically significant) were created to visually evaluate the presence of publication bias. A sensitivity analysis was also conducted, in which the RCTs were excluded to determine the stability of the combined RRs or WMDs.
Results

Literature search

The initial literature search retrieved 101 relevant articles, and duplicates were discarded. After a careful screen of the titles, 84 articles were excluded as they did not cover the topic of interest. After reviewing the abstracts, seven more articles were excluded (one editorial and six reviews), leaving ten studies for further full publication review. Therefore, ten studies matched the selection criteria and were suitable for meta-analysis, and all of them were prospective randomized control trials (Figure 1). A total of 1,010 patients (498 who received epidural steroid injection and 512 who received epidural local anesthetic injection) were enrolled in the studies. The key characteristics of the included studies are summarized in Table 1. All the studies involved patients with LSS and a follow-up of at least 6 weeks. Ten level I–II studies from 1985 to 2014 that compared epidural steroid injection with epidural local anesthetic injection for the treatment of LSS prospectively and randomly were identified. On review of the data extraction, there was 100% agreement between the two investigators.

Figure 2 summarizes the methodological quality of the studies. All of the studies were RCTs with a high level of methodological quality. Thus, the methodological bias of this study was low.

Main analysis

Table 2 summarizes the outcomes of this meta-analysis. Minimal or no significant difference was found between the epidural steroid injection group and the epidural local anesthetic injection group for the short-term benefit, specifically, changes in the Roland–Morris Disability Questionnaire (RMDQ) Score (WMD, −1.80, 95% CI, −2.82 to −0.78; *P*=0.0005) for 3 weeks, changes in the leg pain VAS score (WMD, −7.00, 95% CI, −12.73 to −1.27; *P*=0.02) for 3 weeks, changes in the back pain...
Table 1 Transforaminal epidural steroid injections either with placebo or active control

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Number of patients/selection criteria</th>
<th>Control</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Times of measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cuckler et al1985</td>
<td>71 subjects in total, 37 with spinal stenosis, 36 with acute herniated nucleus pulposus, 37 males, 36 female, average age of 48.5 years in the experimental group and 49.5 years in the placebo group, Experimental group average 36.6 months in symptom duration, placebo group averaged 29.4 months</td>
<td>2 mL of saline combined with 5 mL of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=31, 17 with stenosis)</td>
<td>2 mL of sterile water containing 80 mg of methylprednisolone acetate combined with 5 mL of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=42, 20 with stenosis)</td>
<td>1) Subjective percentage of improvement with 75% required to be considered a treatment improvement, if less than 50% after 24 hours, was considered a treatment failure</td>
<td>24 hours, every 3 months up to 1 year</td>
</tr>
<tr>
<td>Zahaar et al1991</td>
<td>30 subjects, 37 male and 26 female. Steroid group averaged 46.5 years of age and 36.6 months of symptoms. 6 months of symptoms, control group averaged 49 years of age and 29.4 months of symptoms Setting: Medical facility in Egypt</td>
<td>2 x 2 mL of carboxaine, 4% injected into epidural space. Volume completed with sterile saline to 30 mL (n=12)</td>
<td>5 mL of hydrocortisone acetate suspension, 2 x 2 mL carboxaine, 4% volume completed with sterile saline to 30 mL (n=18)</td>
<td>2) Re-injection rates</td>
<td>24 hours, then every 3 months up to 1 year</td>
</tr>
<tr>
<td>Fukusaki et al1998</td>
<td>53 subjects, 38 males and 15 female. Group 1 averaged 70 years of age and 79 days of symptoms on average, group 2 averaged 69 years of age and an average of 82 days of symptoms, group 3 averaged 72 years of age and 94 days of symptoms on average Setting: Anesthesia department in Japan</td>
<td>Epidurial injection with 8 mL of 1% mepivacaine, repeated twice in the first week (n=18)</td>
<td>Epidurial injection with a mixture of 8 mL of 1% mepivacaine and 40 mg of methylprednisolone, repeated twice in the first week (n=19)</td>
<td>3) Surgery rates</td>
<td>24 hours, then every 3 months up to 1 year</td>
</tr>
<tr>
<td>Ng et al2005</td>
<td>86 patients; chronic unilateral radicular pain that failed conservative treatment Setting: Anesthesia department in Japan</td>
<td>A single transforaminal epidural injection with bupivacaine only (n=43)</td>
<td>A single TFESI with bupivacaine and methylprednisolone (n=43). Number of injections = 1</td>
<td>3) Nottingham Health Profile</td>
<td>6 and 12 weeks postinjection</td>
</tr>
<tr>
<td>Koc et al2009</td>
<td>29 subjects, 21 male, 8 female, average ages of 62.6, 61.1, and 53.1 years in the three groups respectively, average pain duration of 5.7 years, 5.0 years, and 5.7 years in the three groups Setting: Medical school department of physical medicine and rehabilitation in Turkey</td>
<td>Control group (n=10)</td>
<td>Lumbar epidural steroid injections, 10 mL of solution containing 60 mg of triamcinolone acetonide (1.5 mL), 15 mg of 0.5% bupivacaine hydrochloride (3 mL), and 5.5 mL of physiologic saline (0.9% NaCl) was injected in 3.5 minutes (n=10)</td>
<td>1) VAS</td>
<td>2 weeks, 1, 3, and 6 months</td>
</tr>
<tr>
<td>Tafazal et al2009</td>
<td>150 patients with radicular pain due to lumbar radiculitis either secondary to lumbar disc herniation or foraminal stenosis</td>
<td>Active controlled trial either with bupivacaine alone or bupivacaine with 40 mg of methylprednisolone</td>
<td>All patients received 2 mL of 0.25% bupivacaine alone or 2 mL of 0.25% bupivacaine and 40 mg of methylprednisolone. Number of injections = 1</td>
<td>4) RMID</td>
<td>6 weeks, 12 weeks, 1 year</td>
</tr>
<tr>
<td>Study</td>
<td>Description</td>
<td>Details</td>
<td></td>
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<tr>
<td>Manchikanti et al. 2012</td>
<td>60 patients over 30 years old with a history of chronic function-limiting low back pain and lower extremity pain of at least 6 on a scale of 0–10; pain for at least 6 months; a diagnosis of central spinal stenosis with radicular pain; patients who were competent to understand the study protocol and provide voluntary, written informed consent, and participate in outcome measurements; patients diagnosed with central spinal stenosis. And failed conservative management but not limited to, physical therapy, chiropractic manipulation, exercises, drug therapy, and bed rest.</td>
<td>Received lumbar interlaminar injections containing a local anesthetic (lidocaine 0.5%, 6 mL)</td>
<td>Mean pain relief of NRS, ODI, employment characteristics, procedure relief, opioid intake, changes in weight</td>
<td>3 months, 6 months, 12 months</td>
<td></td>
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<tr>
<td>Manchikanti et al. 2012</td>
<td>100 patients with central spinal stenosis with radicular pain of at least 6 months duration and that pain must have been function-limiting, 30 years or older, and the ability to understand the study protocol and provide voluntary, written informed consent and participate in outcome measurement and failed conservative management.</td>
<td>Epidural injections of local anesthetic (lidocaine 0.5%)</td>
<td>Received caudal epidural injections with 0.5% lidocaine 9 mL mixed with 1 mL of steroid, 6 mg (non-particulate betamethasone)</td>
<td>NRS, ODI, employment status, opioid intake, weight monitoring</td>
<td>3 months, 6 months, 12 months, 18 months, 24 months</td>
</tr>
<tr>
<td>Radcliffe et al. 2013</td>
<td>276 patients who had neurogenic claudication or radicular leg pain with associated neurological signs, spinal stenosis as seen on cross-sectional imaging, symptoms that had persisted for at least 12 weeks</td>
<td>no-ESI</td>
<td>ESI (epidural steroid injection)</td>
<td>SF-36, ODI, Pain, SBI, LBPBS, LPBS</td>
<td>4 years</td>
</tr>
<tr>
<td>Friedly et al. 2014</td>
<td>400 patients who had lumbar central spinal stenosis and moderate-to-severe leg pain and disability to receive epidural injections of glucocorticoids plus lidocaine or lidocaine alone.</td>
<td>Receive epidural injections of lidocaine alone. The patients received one or two injections before the primary outcome evaluation, performed 6 weeks after randomization and the first injection.</td>
<td>Receive epidural injections of glucocorticoids plus lidocaine. The glucocorticoid injectable solution consisted of 1 to 3 mL of 0.25% to 1% lidocaine followed by 1 to 3 mL of triamcinolone (60 to 120 mg), betamethasone (6 to 12 mg), dexamethasone (8 to 10 mg), or methylprednisolone (60 to 120 mg).</td>
<td>RMDQ, VAS, BPI, SSSQ, EQ–5D, PHQ-8, GAD-7</td>
<td>3 weeks, 6 weeks</td>
</tr>
</tbody>
</table>

**Abbreviations:** RMDQ, Roland–Morris Disability Questionnaire; VAS, visual analog scale; BPI, Brief Pain Inventory; SSSQ, Swiss Spinal Stenosis Questionnaire; SF-36, 36-Item Short Form Health Survey; EQ–5D, European Quality of Life–5 Dimensions; PHQ-8, Eight-question version of the Patient Health Questionnaire; ESI, epidural steroid injection; GAD-7, Generalized Anxiety Disorder 7 scale; LBPBS, Low Back Pain Bothersomeness Scale; ODI, Oswestry Disability Index; NRS, Numeric Rating Score; LBOS, Low back outcome score; SBI, Sciatica Bothersomeness Index; LPBS, Leg Pain Bothersomeness Scale; TFESI, transforaminal epidural steroid injections; RMDI, Roland Morris Disability.
VAS score (WMD, 0.60, 95% CI, 0.07 to 1.13; \( P = 0.03 \)) for 3 weeks, Swiss Spinal Stenosis Questionnaire (SSSQ) subscales for symptoms (WMD, −0.20, 95% CI, −0.34 to −0.06; \( P = 0.05 \)) for 3 weeks, and European Quality of Life-5 Dimensions (EQ-5D) (WMD, 0.04, 95% CI, 0.00 to 0.08; \( P = 0.03 \)) for 3 weeks. Because no significant heterogeneity was observed for the above comparisons, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

In terms of long-term benefit, there was significant difference between the epidural steroid injection group and the epidural local anesthetic injection group in terms of changes in bodily pain (BP) and physical function (PF) subscale scores, specifically, changes in the BP subscale scores (WMD, −11.90, 95% CI, −22.72 to −1.08; \( P = 0.03 \)) for 3 years and (WMD, −12.90, 95% CI, −23.88 to −1.92; \( P = 0.02 \)) for 4 years and changes in the PF subscale scores (WMD, −14.30, 95% CI, −25.28 to −3.32; \( P = 0.01 \)) for 4 years. Because no significant heterogeneity was observed for the change from the BP and PF subscale scores, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

With respect to the epidural local anesthetic injection group, there was no significant difference for most outcome measures, such as the Brief Pain Inventory (BPI) Interference Scale (3 weeks, 6 weeks); SSSQ Physical-Function Subscales (3 weeks, 6 weeks); Eight-question version of the Patient Health Questionnaire (PHQ-8) (3 weeks, 6 weeks); Generalized Anxiety Disorder 7 (GAD-7) scale (3 weeks, 6 weeks); Oswestry Disability Index (ODI) score (6 weeks, 3 months,
### Table 2 Meta-analysis of the outcomes of interest

<table>
<thead>
<tr>
<th>Outcomes of interest</th>
<th>Times of measurement</th>
<th>Number of studies</th>
<th>Participants</th>
<th>Overall effect</th>
<th>Statistical method</th>
<th>Effect estimate</th>
<th>P-value</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from RMDQ Score (0–24)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>-1.80 [-2.82, -0.78]</td>
<td>0.0005 NA NA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-1.10 [-2.21, 0.01]</td>
<td>0.05 NA NA</td>
<td></td>
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<tr>
<td>Change from leg pain VAS (0–100 mm)</td>
<td>3 weeks</td>
<td>1</td>
<td>381</td>
<td>MD (fixed, 95% CI)</td>
<td>-7.00 [-12.73, -1.27]</td>
<td>0.02 NA NA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>3</td>
<td>596</td>
<td>MD (fixed, 95% CI)</td>
<td>-3.21 [-7.86, 1.44]</td>
<td>0.18 0 0.57</td>
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<td></td>
<td>3 months</td>
<td>2</td>
<td>210</td>
<td>MD (fixed, 95% CI)</td>
<td>-1.50 [-10.03, 7.03]</td>
<td>0.73 0 0.9</td>
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<tr>
<td>Change from back pain VAS (0–100 mm)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>0.60 [0.07, 1.13]</td>
<td>0.03 NA NA</td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>3</td>
<td>596</td>
<td>MD (random, 95% CI)</td>
<td>-1.76 [-5.06, 1.55]</td>
<td>0.30 84 0.002</td>
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<tr>
<td></td>
<td>3 months</td>
<td>4</td>
<td>370</td>
<td>MD (random, 95% CI)</td>
<td>0.42 [-0.75, 1.59]</td>
<td>0.48 66 0.03</td>
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<td></td>
<td>6 months</td>
<td>2</td>
<td>160</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.23 [-0.76, 0.31]</td>
<td>0.40 0 0.59</td>
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<td></td>
<td>1 year</td>
<td>2</td>
<td>160</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.02 [-0.60, 0.56]</td>
<td>0.95 0 0.62</td>
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<tr>
<td></td>
<td>18 months</td>
<td>1</td>
<td>100</td>
<td>MD (fixed, 95% CI)</td>
<td>0.10 [-0.65, 0.85]</td>
<td>0.79 NA NA</td>
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<tr>
<td></td>
<td>2 years</td>
<td>1</td>
<td>100</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.10 [-0.89, 0.69]</td>
<td>0.80 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.30 [-0.90, 0.30]</td>
<td>0.33 NA NA</td>
<td></td>
<td></td>
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<tr>
<td>BPI Interference Scale (0–10)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.20 [-0.34, -0.06]</td>
<td>0.005 NA NA</td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.10 [-0.25, 0.05]</td>
<td>0.19 NA NA</td>
<td></td>
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<tr>
<td>SSSQ subscales for symptoms (1–5)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>0.00 [-0.12, 0.12]</td>
<td>1.00 NA NA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>0.10 [-0.03, 0.23]</td>
<td>0.13 NA NA</td>
<td></td>
<td></td>
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<tr>
<td>SSSQ Physical-Function Subscales (1–4)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>0.04 [0.00, 0.08]</td>
<td>0.03 NA NA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>0.02 [-0.02, 0.06]</td>
<td>0.31 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-SD (0–1)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>0.60 [-0.40, 1.60]</td>
<td>0.24 NA NA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.40 [-1.34, 0.54]</td>
<td>0.40 NA NA</td>
<td></td>
<td></td>
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<tr>
<td>PHQ-8 (0–24)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>0.20 [-0.71, 1.11]</td>
<td>0.67 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-0.30 [-1.17, 0.57]</td>
<td>0.50 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAD-7 scale (0–21)</td>
<td>3 weeks</td>
<td>1</td>
<td>384</td>
<td>MD (fixed, 95% CI)</td>
<td>-5.80 [-15.32, 3.72]</td>
<td>0.23 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks</td>
<td>1</td>
<td>386</td>
<td>MD (fixed, 95% CI)</td>
<td>-7.30 [-17.19, 2.59]</td>
<td>0.15 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from BP subscale scores (0–100)</td>
<td>1 year</td>
<td>1</td>
<td>93</td>
<td>MD (fixed, 95% CI)</td>
<td>-11.90 [-22.72, -1.08]</td>
<td>0.03 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 years</td>
<td>1</td>
<td>93</td>
<td>MD (fixed, 95% CI)</td>
<td>-12.90 [-23.88, -1.92]</td>
<td>0.02 NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 years</td>
<td>1</td>
<td>93</td>
<td>MD (fixed, 95% CI)</td>
<td>-7.40 [-16.92, 2.12]</td>
<td>0.13 NA NA</td>
<td></td>
<td></td>
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<td>4 years</td>
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<td>93</td>
<td>MD (fixed, 95% CI)</td>
<td>-9.60 [-19.39, 0.19]</td>
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<td>1</td>
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<td>MD (fixed, 95% CI)</td>
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<td>4 years</td>
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<td>MD (fixed, 95% CI)</td>
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<tr>
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<td>6 months</td>
<td>2</td>
<td>160</td>
<td>MD (fixed, 95% CI)</td>
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<td>0.06 0.94 0.94</td>
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<td></td>
<td>1 year</td>
<td>3</td>
<td>253</td>
<td>MD (fixed, 95% CI)</td>
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<td>0.09 0.44 0.44</td>
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<td>0.90 [−1.66, 3.46]</td>
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<td>1.00 [−1.72, 3.72]</td>
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<td>0.00 [−0.71, 0.71]</td>
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<td>−0.10 [−0.81, 0.61]</td>
<td>0.78</td>
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<td>−0.20 [−1.08, 0.68]</td>
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<td>−0.30 [−1.01, 0.41]</td>
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<td>Changes from weight (lbs)</td>
<td>1 year</td>
<td>2</td>
<td>160</td>
<td>0.28 [−2.49, 3.04]</td>
<td>0.84</td>
<td>0.74</td>
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<td>100</td>
<td>2.00 [−1.59, 5.59]</td>
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<td>Change in Opioid Intake (Morphine Equivalence mg)</td>
<td>3 months</td>
<td>2</td>
<td>160</td>
<td>−5.57 [−17.60, 6.45]</td>
<td>0.36</td>
<td>0.75</td>
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<td>6 months</td>
<td>2</td>
<td>160</td>
<td>−9.08 [−21.54, 3.39]</td>
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<td>1 year</td>
<td>2</td>
<td>160</td>
<td>−9.70 [−22.19, 2.78]</td>
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<td>18 months</td>
<td>1</td>
<td>100</td>
<td>−6.14 [−23.46, 11.18]</td>
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<td>2 years</td>
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<td>100</td>
<td>−5.84 [−23.18, 11.50]</td>
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<td>Change from LBOS</td>
<td>6 weeks</td>
<td>1</td>
<td>124</td>
<td>−1.00 [−5.85, 3.85]</td>
<td>0.69</td>
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<tr>
<td></td>
<td>3 months</td>
<td>1</td>
<td>124</td>
<td>−0.30 [−6.27, 5.67]</td>
<td>0.92</td>
<td>NA</td>
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<tr>
<td>Further surgery</td>
<td>1 year</td>
<td>1</td>
<td>129</td>
<td>0.65 [0.30, 1.40]</td>
<td>0.27</td>
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<td></td>
<td>3 months</td>
<td>1</td>
<td>129</td>
<td>−0.03 [−6.27, 5.67]</td>
<td>0.92</td>
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<td>Further root blocks</td>
<td>1 year</td>
<td>1</td>
<td>129</td>
<td>0.81 [0.34, 1.93]</td>
<td>0.64</td>
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<tr>
<td>Change from walking distance (yards)</td>
<td>6 weeks</td>
<td>1</td>
<td>86</td>
<td>−130.60 [−293.65, 32.45]</td>
<td>0.12</td>
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<td>3 months</td>
<td>1</td>
<td>86</td>
<td>−40.00 [−252.59, 172.59]</td>
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<td>Discharged</td>
<td>3 months</td>
<td>1</td>
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<td>0.85 [0.59, 1.22]</td>
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<tr>
<td>Results of treatment (Excellent and Good rate)</td>
<td>1 week</td>
<td>1</td>
<td>37</td>
<td>1.14 [0.66, 1.95]</td>
<td>0.64</td>
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<td></td>
<td>1 month</td>
<td>1</td>
<td>37</td>
<td>0.95 [0.22, 4.10]</td>
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<td></td>
<td>3 months</td>
<td>1</td>
<td>37</td>
<td>0.95 [0.06, 1.04]</td>
<td>0.97</td>
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<tr>
<td>Success rate &gt;75 percent improvement</td>
<td>1 day</td>
<td>1</td>
<td>37</td>
<td>1.42 [0.40, 5.08]</td>
<td>0.59</td>
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<td>&gt;20 months</td>
<td>1</td>
<td>37</td>
<td>1.52 [0.34, 6.81]</td>
<td>0.58</td>
<td>NA</td>
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<tr>
<td>Overall average percentage of subjective improvement</td>
<td>1 day</td>
<td>1</td>
<td>37</td>
<td>0.30 [−22.86, 23.46]</td>
<td>0.98</td>
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</table>

Note: The bold numbers mean that the effect estimate values for the contrast models are significant.

Abbreviations: CI, confidence interval; MD, Weighted Mean Difference; RR, Risk Ratio; NA, not applicable; RMDQ, Roland–Morris Disability Questionnaire; VAS, visual analog scale; BPI, Brief Pain Inventory; SSQ, Swiss Spinal Stenosis Questionnaire; EQ-5D, European Quality of Life-5 Dimensions; PHQ-9, Eight-question version of the Patient Health Questionnaire; GAD-7, Generalized Anxiety Disorder 7 scale; ODI, Oswestry Disability Index; BP, Bodily Pain; PF, Physical Function; LBOS, Low back outcome score.
6 months, 1 year, 18 months, 2 years, 3 years, 4 years; Sciatica Brothersoness Index (1 year, 2 years, 3 years, 4 years); Low Back Pain Brothersoness Scale (1 year, 2 years, 3 years, 4 years); weight change (lbs) (1 year, 2 years); Opioid Intake changes (Morpheine Equivalence mg) (3 months, 6 months, 1 year, 18 months, 2 years); low back outcome score (LBOS) (6 weeks, 3 months); further surgery rate (1 year); further root blocks rate (1 year); walking distance changes (yards) (6 weeks, 3 months); discharged rate (3 months); treatment results (Excellent and Good rate) (1 week, 1 month, 3 months); success rate (>75 percent improvement) (1 week, 1 month, 3 months); and overall average percentage of subjective improvement (1 day). Because no significant heterogeneity was observed for the change from the BP and PF subscale scores, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

Publication bias
We did not draw funnel plots because the trials for each comparison were less than ten.

Discussion
LSS is a significant problem that affects many elderly adults annually. Walking limitation due to neurogenic claudication of LSS is thought to be the hallmark of disability. Walking ability is essential for most daily living activities and has been identified as a relatively important outcome in LSS. Despite the rising prevalence of LSS, only a few studies have investigated nonsurgical treatment modalities. This systematic review and meta-analysis of RCTs summarizes all of the available studies on the use of epidural steroid injection for LSS patients. We were only able to identify ten randomized, double-blind, controlled trials involving a total of 1,010 patients. Overall, the evidence described that epidural steroid injections offered minimal or no effective analgesic and do not significantly improve walking ability in LSS patients, regardless of the method of epidural injection.

Overall, epidural steroid injection treatment seems to be quite safe. While there were very few adverse effects reported in these RCTs, the safety of epidural steroid injections needs to be further evaluated. Due to the lack of significant adverse effects, epidural steroid injections are thought to be a safe treatment for future clinical research.

Now it was hard to address through meta-analysis due to the heterogeneity and diversity of the criteria in patient selection, different epidural injection approaches, doses, follow-up lengths, and differences in sample sizes. Another weakness was the different outcome measurements, such as pain and walking ability assessments, which were measured in different ways.

In 2013, North America Spine Society’s (NASS) Evidence-Based Clinical Guideline Development Committee developed an evidence-based clinical guideline for the diagnosis and treatment of degenerative LSS. They found evidence supporting the recommendation of epidural steroid injection therapy, elaborating a B recommendation in favor of it use. However, this systematic review was based on only four14,16,19,31 trials.

The limitations of this meta-analysis were as follows. First, the epidural injection approaches, doses, frequencies, and duration in each trial were not exactly the same, which may have influenced the outcomes of interest. Second, some parameters of interest demonstrated a large degree of heterogeneity. The heterogeneity of change from back pain VAS score may be the result of bias from the different assessment methods used in the various trials. Last but not least, meta-analyses require greater patient numbers, and insufficient patients were included in this study. As such, larger high level studies are required to show the superiority of epidural steroid injection therapy for treating neurogenic claudication due to LSS.

Conclusion
On the basis of the reviewed trials, when compared with local anesthetic, we found no evidence that epidural steroid injection therapy provides a statistically significant improvement in pain symptoms or walking ability in LSS patients. Moreover, local anesthetic appears to play an unusual role in its efficacy for pain control. Additional better and rigorous studies with long-term observation are required to elucidate the effectiveness of epidural steroid injection treatment for LSS.

Acknowledgments
We would like to thank Run Liu for his assistance in developing the search strategy and retrieving relevant articles.

Disclosure
The authors report no conflicts of interest in this work.

References


