Systematic Review

# Effectiveness of Transforaminal, Interlaminar, and Caudal Epidural Injections in Lumbosacral Disc Herniation: A Systematic Review and Network Meta-analysis

Sang Gyu Kwak, PhD[1], Yoo Jin Choo, MD[2], Soyoung Kwak, MD[2], and Min Cheol Chang, MD[2]

From: [1]Department of Medical Statistics, College of Medicine, Catholic University of Daegu, Daegu, Republic of Korea; [2]Department of Rehabilitation Medicine, College of Medicine, Yeungnam University, Daegu, Republic of Korea

Address Correspondence: Min Cheol Chang, MD Department of Physical Medicine and Rehabilitation, College of Medicine, Yeungnam University 317-1, Daemyungdong, Namku, Daegu, 705-717, Republic of Korea E-mail: wheel633@gmail.com

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**Background:** Epidural injection (EI) has been used to manage lower back and radicular leg pain caused by a herniated lumbar disc. There are 3 types of EI techniques currently being used: transforaminal (TFEI), interlaminar (ILEI), and caudal epidural injections (CEI).

**Objectives:** To evaluate the comparative effectiveness of TFEI, ILEI, and CEI in reducing pain and improving function in patients with HLD.

**Study Design:** Systematic review and meta-analysis.

**Methods:** The PubMed, Embase, Cochrane Library, and Scopus databases were searched from the earliest records up to August 2022 for randomized controlled trials (RCTs) and non-RCTs. The standard mean differences (SMDs) in the changes in the Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores were calculated from one week through one month posttreatment (short-term) and from 4 months through 6 months posttreatment (long-term).

**Results:** In total, 11 studies comprising 1,050 patients were included. Network meta-analysis showed that the improvement in the VAS scores was better with TFEI than with CEI (SMD = −1.16, 95% CI = −2.10 to −0.23). Ranking probability analysis showed that TFEI had the highest probability of being the best treatment for reducing pain and improving function in the short- and long-term evaluation periods.

**Limitations:** Only a small number of previous studies were included in our analysis. Also, subgroup analysis according to the injection volume, material type, or pain onset could not be conducted.

**Conclusions:** TFEI had the best potential of the 3 EI techniques to reduce pain and improve function in patients with a herniated lumbar disc. Further qualified trials comparing the effects of these 3 techniques are warranted to derive definitive conclusions.

**Key words:** Disc herniation, back pain, radicular pain, epidural injection, transforaminal injection, interlaminar injection, caudal injection, lumbar spine

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A herniated lumbar disc (HLD) is one of the most common musculoskeletal diseases causing lower back and lumbosacral radicular pain in the lower extremities (1). The primary mechanism underlying the pain associated with an HLD is chemical inflammation surrounding the sinuvertebral nerves in the ventral epidural space and nerve roots (2). In most HLD cases, the pain can be successfully managed with conservative treatment (3). Various oral medications and procedures are used to control inflammation caused by an HLD. Among these therapeutic methods, epidural injection (EI) is frequently used in clinical

practice (4-14). The injected drugs control the axial or radicular pain by reducing inflammation around the HLD. Several previous studies have reported the favorable HLD-induced pain-reducing effect of these injected drugs (4-14). Three types of EI techniques, including transforaminal EI (TFEI), interlaminar EI (ILEI), and caudal EI (CEI), have been utilized in clinical practice (4-14).

Because the HLD is usually located in the ventral epidural space, it is logical to consider that drugs should be administered into this space. While TFEI can deliver drugs directly into the ventral epidural space, ILEI delivers drugs into the posterior epidural spaces with the expectation that the injected drugs will eventually spread to the ventral epidural spaces ( 15,16). CEI is considered as an easy and safe procedure providing favorable clinical outcomes (17). However, because CEI is not administered specifically in the pathologic area, a significant portion of the injectate may not reach the target area even when a large drug volume is injected. Since TFEI can directly deliver the drugs into the ventral epidural space, we believe that it can achieve better clinical effects than the other EI methods. However, conflicting outcomes regarding the superiority of the techniques have been reported in previous studies (4-14).

To date, a few meta-analyses have compared the effects of the aforementioned 3 techniques on an HLD (18-22), and some have compared only 2 of the 3 procedures. Our study used a network meta-analysis to synthesize and compare the effects of TFEI, ILEI, and CEI on HLD pain. Ranking the effectiveness of each EI technique would be clinically useful and could help clinicians choose appropriate treatments for patients with an HLD.

## Methods

### Search Strategy

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The protocol of this meta-analysis was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (Registration number: INPLASY202280091). The relevant articles were systematically searched using PubMed, Embase, Cochrane Library, and Scopus databases up to August 2022.

The following "Population/Patient, Intervention, Comparison, and Outcome" question guided the search strategy: "In patients with lower back and radicular leg pain caused by HLD, which intervention among TFEI, ILEI, and CEI has a better effect on pain reduction and functional improvement when compared to the others?" The search was conducted using the established individual search terms in the search engine of each database (Supplemental File 1).

### Study Selection

The detailed inclusion criteria for the network meta-analysis were studies with 1) patients aged ≥ 18 years; 2) patients having lower back and radicular leg pain caused by an HLD; 3) a diagnosis of an HLD on radiological evaluation, such as magnetic resonance imaging or computed tomography; 4) randomized controlled trials (RCTs) and non-RCTs, including at least two therapeutic arms comprising TFEI, ILEI, or CEI; (5) using the Visual Analog Scale (VAS) or Oswestry Disability Index (ODI) for outcome measurements; and 6) written in English.

The exclusion criteria were 1) studies with patients with a previous history of lumbar and lumbosacral surgery, nonspecific lower back pain without a definite diagnosis of an HLD, severe disc degeneration, intradiscal derangement or a bulging disc, spinal stenosis, or prominent spinal instability; 2) reviews, case reports, commentaries, letters, and animal studies; and 3) studies with outcomes that were not reported or were insufficient.

Two independent reviewers excluded articles after reading the titles and abstracts (SGK and MCC); full-text assessments were conducted to exclude those that did not fulfill the inclusion criteria. The reviewers attempted to resolve any disagreements through consensus. If necessary, the opinion of a third reviewer (YJC) was considered to resolve the disagreement.

### Data Extraction

All data were extracted independently by 2 reviewers (SGK and MCC) using a standard data collection form. If the designated outcome variables were unavailable or incomplete in the published articles, the corresponding authors were contacted for the original data. The following data were recorded using a table for each eligible article: 1) name of the first author; 2) year of publication; 3) number of patients; 4) type and dose of injectate; 5) type of approach technique; 6) follow-up period; 7) clinical evaluation tools; and 8) comparative results extracted from the selected articles.

### Quality Assessment

To assess the methodological quality assessment and qualitative analysis utilizing best evidence synthesis principles, the Interventional Pain Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) (23) was used for RCTs (n = 9) (4,6-12,14) and Interventional Pain Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies (IPM-QRBNR) (24) was used for non-RCTs (n = 2) (5,13).

The IPM-QRB assesses the following 22 domains: trial design guidance and reporting, type and design of trial, setting/physician, imaging, sample size, statistical methodology, inclusiveness of the population, duration of pain, previous treatments, duration of follow-up with appropriate interventions, outcome assessment criteria for significant improvement, analysis of all randomized patients in the groups, description of dropout rate, similarity of groups at baseline for important prognostic indicators, role of co-interventions, method of randomization, concealed treatment allocation, patient blinding, care provider blinding, outcome assessor blinding, funding and sponsorship, and conflicts of interest.

The IPM-QRBNR assesses the following 16 domains: study design guidance and reporting, study design and type, setting/physician, imaging, sample size, statistical methodology, inclusiveness of population, duration of pain, previous treatments, duration of follow-up with appropriate interventions, outcome assessment criteria for significant improvement, description of drop-out rate, similarity of groups at baseline for important prognostic indicators, role of co-interventions, method of assignment of patients, and funding/ sponsorship.

The IPM-QRB and IPM-QRBNR were provided as checklists for scoring each item. Scores from 32 to 48 were considered to be high-quality studies. A score of 16–31 was considered a moderate-quality study. A score of less than 16 was considered a low-quality study (25). These evaluations were conducted by 2 independent reviewers (SGK and MCC), and all discrepancies were resolved through discussions between them.

### Data Synthesis and Analysis

Continuous variables were analyzed with the outcomes presented as standard mean differences (SMDs) and 95% confidence intervals (CI) for the changes in the VAS and ODI scores in the short- and long-term periods. The short- and long-term periods were defined as the period from one week through one month posttreatment and from 4 months through 6 months posttreatment, respectively. If there were several measurements within the same time frame (short-term or long-term), the outcome recorded during the last follow-up was used in the meta-analysis.

The $I^2$ statistic and Cochran's Q test were used to determine the heterogeneity of direct comparisons. Significant heterogeneity was assumed in the case of $I^2$ values > 50% and $P$ values < 0.05. Probability ranking metrics were used to reflect the clinically important relative differences in outcomes, which were shown on the ranking probability curves and surface under the cumulative ranking area (SUCRA). The SUCRA value ranged between 0 and 1; treatments with a higher SUCRA value suggest better effectiveness and superior ranking (26). It was presented as the percentage of the mean rank of each treatment in relation to the presumed best intervention (27). Publication bias was examined using Egger's regression test and by inspecting the distribution pattern of the effect size on the funnel plot. All analyses were performed using R 4.2.1 software (The R Foundation); $P$ values < 0.05 were considered statistically significant.

## Results

### Study Selection and Characteristics

In total, 3,588 articles were identified as potentially relevant in the primary literature search (Fig. 1). After reviewing the titles and abstracts and assessing their eligibility based on the full text, 11 studies were included in the meta-analysis (Table 1).

Of the 11 studies included, 8 studies compared TFEI with ILEI, 4 studies compared ILEI with CEI, and 2 studies compared TFEI with CEI. This meta-analysis included 1,050 patients, of which 401, 449, and 200 received ILEI, TFEI, and CEI, respectively.

### Results of the Meta-analysis

The values of $I^2$ and $P$ values in Cochran's Q test were > 50% and < 0.05, respectively, in all the meta-analyses. A random-effect model was used for all the meta-analyses and showed the following results: short-term VAS, $I^2$ = 89.2% and $P$ < 0.001; long-term VAS, $I^2$ = 79.5% and $P$ < 0.001; short-term ODI, $I^2$ = 93.4% and $P$ < 0.001; and long-term ODI, $I^2$ = 93.8% and $P$ < 0.001.

Regarding short-term VAS changes, the pairwise meta-analysis showed no significant differences in the comparisons between ILEI and TFEI (SMD = 0.33, 95% CI = –0.12 to 0.79), ILEI and CEI (SMD = 0.10, 95% CI =

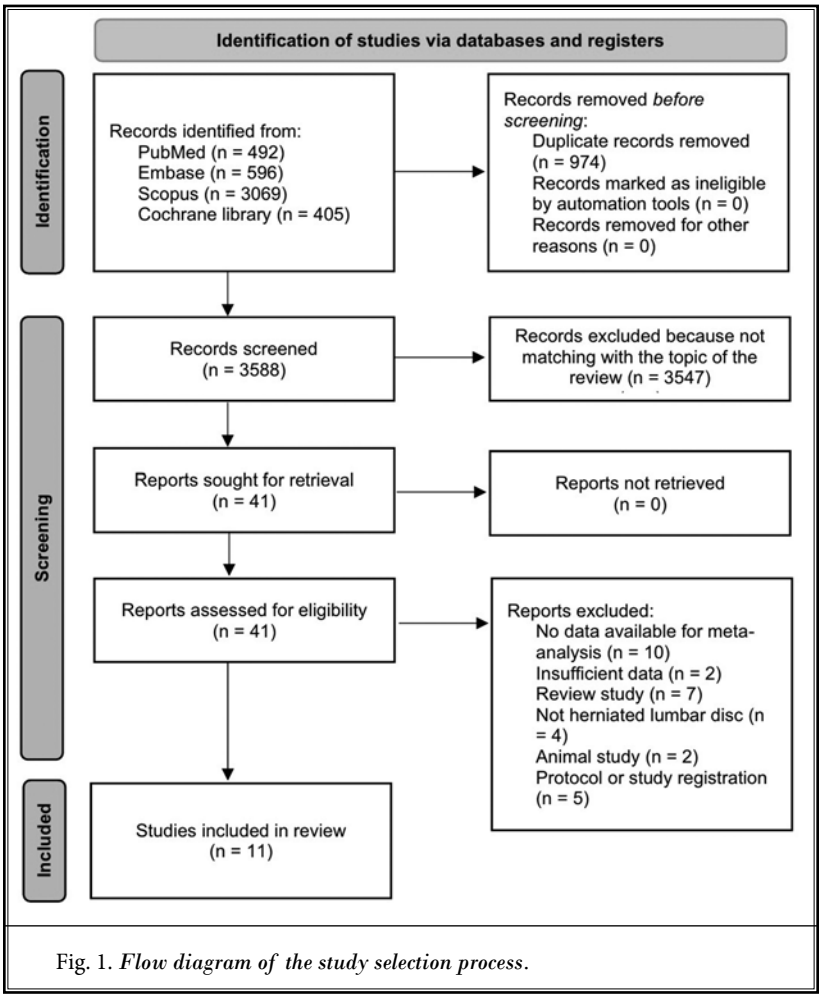


Fig. 1. *Flow diagram of the study selection process.*

–0.40 to 0.61), and TFEI and CEI (SMD = –1.18, 95% CI = –2.73 to 0.38) (Fig. 2A). Figure 3A shows the network graph closing the geometry of the treatment network. In the network meta-analysis, the improvement in the VAS score was better with TFEI than with CEI (SMD = –1.16, 95% CI = –2.10 to –0.23) (Fig. 4A). However, no significant differences were found in the comparisons between ILEI and CEI (SMD = 0.10, 95% CI = –1.48 to 1.68) and between ILEI and TFEI (SMD = 0.34, 95% CI = –0.26 to 0.95) (Fig. 4A). The rank probability results and SUCRA values are presented in Fig. 5A and Table 2, respectively. TFEI had the highest probability of being the most effective treatment (77.6%), CEI had the highest probability of ranking second (51.1%), and ILEI was most likely to be the least effective (21.3%).

Regarding the long-term VAS changes, the pairwise meta-analysis showed no significant differences in the comparisons between ILEI and TFEI (SMD = 0.31, 95% CI = –0.14 to 0.77), ILEI and CEI (SMD = –0.04, 95% CI = –0.27 to 0.18), and TFEI and CEI (SMD = –0.11, 95% CI = –0.73 to 0.51) (Fig. 2B). Figure 3B shows the network graph closing the geometry of the treatment network. In the network meta-analysis, no EI method was found to be superior to the other methods (ILEI vs. CEI: SMD = 0.00, 95% CI = –0.69 to 0.69; TFEI vs. CEI: SMD = –0.11, 95% CI = –0.69 to 0.48; ILEI vs. TFEI: SMD = – 0.31, 95% CI = –0.11 to 0.73) (Fig. 4B). The rank probability results and SUCRA values are presented in Fig. 5B and Table 2, respectively. TFEI had the highest probability of being the most effective treatment (59.9%), CEI had the highest probability of ranking second (39.4%), and ILEI was most likely to be the least effective (66.6%).

Regarding the short-term ODI changes, the pairwise meta-analysis did not reveal any significant differences in the comparisons between ILEI and TFEI (SMD = 0.43, 95% CI = –0.89 to 1.74), ILEI and CEI (SMD = 0.35, 95% CI = –0.16 to 0.86), and TFEI and CEI (SMD = –0.29, 95% CI = –2.46 to 1.89) (Fig. 2C). Figure 3C shows the network graph closing the geometry of the treatment network. In the network meta-analysis, no EI method was found to be superior to the other methods (ILEI vs. CEI: SMD = 0.35, 95% CI = –1.86 to 2.57; CEI vs. TFEI: SMD = –0.29, 95% CI = –1.87 to 1.29; ILEI vs. TFEI: SMD = 0.43, 95% CI = –0.86 to 1.71) (Fig. 4C). The rank probability results and SUCRA values are presented in Fig. 5C and Table 2, respectively. TFEI had the highest probability of being the most effective treatment (59.3%), CEI had the highest probability of ranking second (55.0%), and ILEI was most likely to be the least effective (35.7%).

Regarding long-term ODI changes, the pairwise meta-analysis revealed no significant differences in the comparisons between ILEI and TFEI (SMD = 0.51, 95% CI = –0.60 to 1.62), ILEI and CEI (SMD = 0.07, 95% CI = –0.55 to 0.70), and TFEI and CEI (SMD = 0.04, 95% CI = –1.27 to 1.36) (Fig. 2D). Figure 3D shows the network graph closing the geometry of the treatment network.

Table 1. *Characteristics of the included studies*.

| First author, year | Study design | Comparison (subject number) | Medication | Evaluation | Follow up | Outcome | Major adverse effect |
|---|---|---|---|---|---|---|---|
| Ackermann, 2007 (4) | RCT | TFEI (30) vs. ILEI (30) vs. CEI (30) | TFEI & ILEI: 40 mg of triamcinolone + one mL of normal saline<br>CEI: 40 mg of triamcinolone + 19 mL of normal saline | VAS, BDI, NPIS, OLBPS | 6 months | TFEI > ILEI or CEI | - |
| Bensler, 2020 (5) | Retrospective | TFEI (99) vs. ILEI (99) | TFEI and ILEI: 40 mg of triamcinolone + one mL of 0.2% ropivacaine | NRS, PGIC | one day – one month | No significant difference | - |
| Candido, 2008 (6) | RCT | TFESI (28) vs. ILEI (29) | TFEI & ILEI: 80 mg of methylprednisolone + one mL of normal saline + one mL of 1% lidocaine | VAS | 2 weeks – 4 months | No significant difference | - |
| Ghai, 2014 (7) | RCT | TFEI (30) vs. ILEI (32) | 2 mL of methylprednisolone acetate + 2 mL sterile normal saline | VAS, MODQ | 3, 6, 9, 12 months | No significant difference | - |
| Gharibo, 2011 (8) | RCT | TFESI (20) vs. ILEI (18) | TFEI: 40 mg of triamcinolone + one mL of 0.25% bupivacaine<br>ILEI: 80 mg of triamcinolone + 2 mL of 0.25% bupivacaine | NRS, ODI | 2-3 weeks | No significant difference | - |
| Kamble, 2016 (9) | RCT | TFEI (30) vs. ILEI (30) vs. CEI (30) | TFEI: 40 mg of triamcinolone + one mL of bupivacaine + 2 mL of lignocaine<br>ILEI and CEI: 40 mg of triamcinolone + one mL of bupivacaine + one mL of lignocaine + 10 mL of normal saline | VAS, ODI | one, 6 months | TFEI > ILEI or CEI | - |
| Makkar, 2019 (10) | RCT | TFESI (20) vs. ILEI (21) | TFEI & ILEI: 80 mg of methylprednisolone + 2 mL of 1% lidocaine | VAS, MODQ | 2 weeks – 6 months | TFESI > ILEI | - |
| Manchikanti, 2015 (11) | RCT | TFESI (120) vs. ILEI (120) vs. CEI (120) | TFEI: 1.5 mL of 1% lidocaine with 0.5 mL of sodium chloride solution or 3 mg of betamethasone<br>ILEI: 6 mL of 0.5% lidocaine or 5 mL of lidocaine with one mL of steroid<br>CEI: 10 mL of 0.5% lidocaine or 9 mL of lidocaine with one mL of steroid | NRS, ODI | 3 – 24 months | No significant difference | - |
| Rados, 2011 (12) | RCT | TFESI (32) vs. ILEI (32) | TFEI: 40 mg of methylprednisolone + 3 mL of 0.5% lidocaine<br>ILEI: 80 mg of methylprednisolone + 8 mL of 0.5% lidocaine | VAS, ODI | 6 months | No significant difference | - |
| Schaufele, 2006 (13) | Case-control study | TFESI (20) vs. ILEI (21) | TFEI: 80 mg of methylprednisolone + 2-3 mL of 2% lidocaine<br>ILEI: 80 mg of methylprednisolone + 2-3 mL of 2% lidocaine | NRS | one hour - 3 weeks | TFEI > ILEI | - |
| Singh, 2016 (14) | RCT | TFEI (20) vs. CEI (20) | TFEI: 80 mg of methylprednisolone + 5 mL of lignocaine<br>CEI: 80 mg of methylprednisolone + 10 mL of lignocaine + 20 mL of normal saline | VAS, ODI | one, 3, 6 months, one year | Caudal > TFEI | - |

RCT: randomized controlled trial, TFEI: transforaminal epidural injection, ILEI: interlaminar epidural injection, CEI: caudal epidural injection, VAS: Visual Analog Scale, BDI: Back depression index, NPIS: numeric pain intensity score, OLBPS: Oswestry low back pain scale, PGIC: Patient Global Impression of Change, ODI: Oswestry Disability Index, MODQ: Modified Oswestry Disability Questionnaire

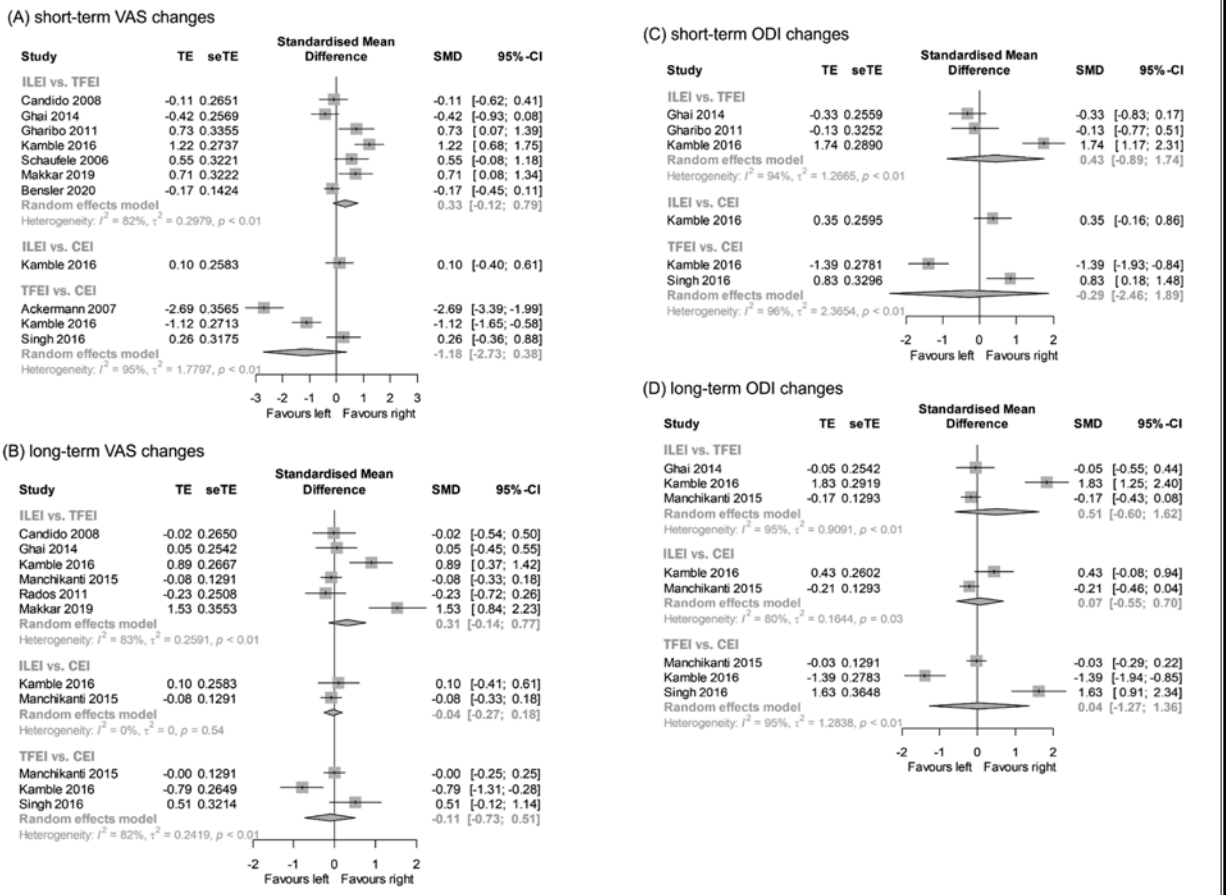


Fig. 2. *Forest plots of pairwise comparison of the changes in the Visual Analog Scale and Oswestry Disability Index scores. (A) Short-term VAS changes; (B) Long-term VAS changes; (C) Short-term ODI changes; (D) Long-term ODI changes.* (VAS, Visual Analog Scale; ODI, Oswestry Disability Index; TFEI, transforaminal epidural injection; ILEI, interlaminar epidural injection; CEI, caudal epidural injection; SMD, standard mean difference; CI, confidence interval)

In the network meta-analysis, no EI method was found to be superior to the other methods (ILEI vs. CEI: SMD = 0.10, 95% CI = –1.16 to 1.37; TFEI vs. CEI: SMD = 0.03, 95% CI = –1.02 to 1.08; ILEI vs. TFEI: SMD = 0.51, 95% CI = –0.53 to 1.55) (Fig. 4D). The rank probability results and SUCRA values are presented in Fig. 5D and Table 2, respectively. CEI had the highest probability of being the most effective treatment (65.2%), TFEI had the highest probability of ranking second (56.6%), and ILEI was most likely to be the least effective (28.2%).

## Assessment of the Study Quality

The results of the methodological quality assessment of RCTs and non-RCTs performed using IPM-QRB and IPM-QRBNR are detailed in Supplemental Files 2 and 3, respectively. Items that could not be evaluated because of ambiguous information were assigned zero points. Based on the IPM-QRB criteria for randomized trials, 6 studies (7,8,10-12,14) were considered high-quality studies and 3 studies (4,6,9) were considered to have moderate quality (Supplemental Table 1). As a result of the evaluation according to the IPM-QRBNR criteria for nonrandomized trials, one high-quality study (13), and one moderate-quality study (5) were classified (Supplemental Table 2).

## Publication Bias

The funnel plots do not show significant asymmetry in the intergroup comparisons of the SMDs of the short-term and long-term VAS and ODI changes (Fig. 6). Furthermore, the *P* values of Egger's test were > 0.05 (short-term VAS changes, $P = 0.192$; long-term VAS changes, $P = 0.365$; short-term and long-term ODI changes data were not available for calculating *P* values).

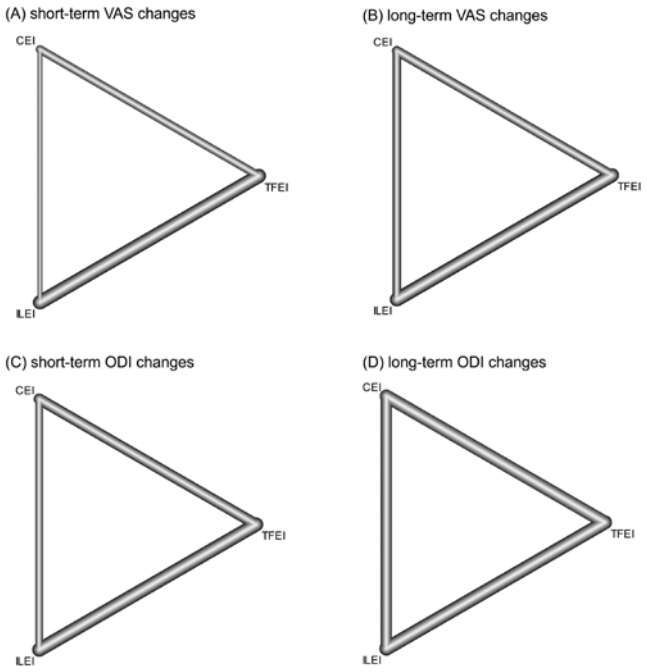


Fig. 3. *Network plots of transforaminal epidural injection, interlaminar epidural injection, and caudal epidural injection.*
*(A) Short-term VAS changes; (B) Long-term VAS changes; (C) Short-term ODI changes; (D) Long-term ODI changes.*
(VAS, Visual Analog Scale; ODI, Oswestry Disability Index; TFEI, transforaminal epidural injection; ILEI, interlaminar epidural injection; CEI, caudal epidural injection)

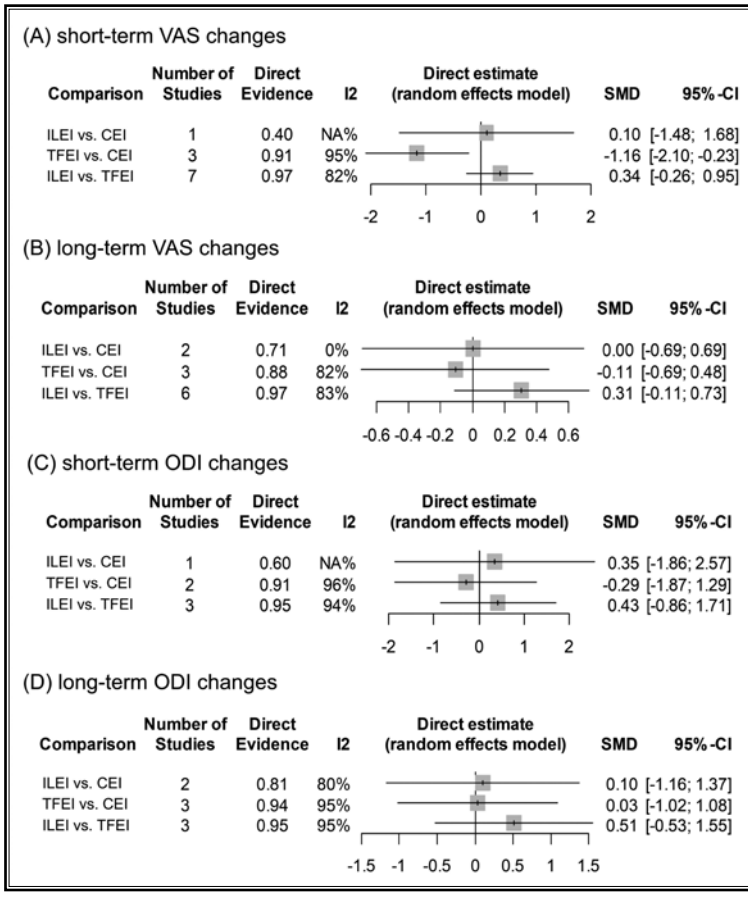


Fig. 4. *Forest plots of network comparisons.*
*(A) Short-term VAS changes; (B) Long-term VAS changes; (C) Short-term ODI changes; (D) Long-term ODI changes.*
(VAS, visual analog scale; ODI, Oswestry Disability Index; TFEI, transforaminal epidural injection; ILEI, interlaminar epidural injection; CEI, caudal epidural injection; SMD, standard mean difference; CI, confidence interval; NA, not applicable)

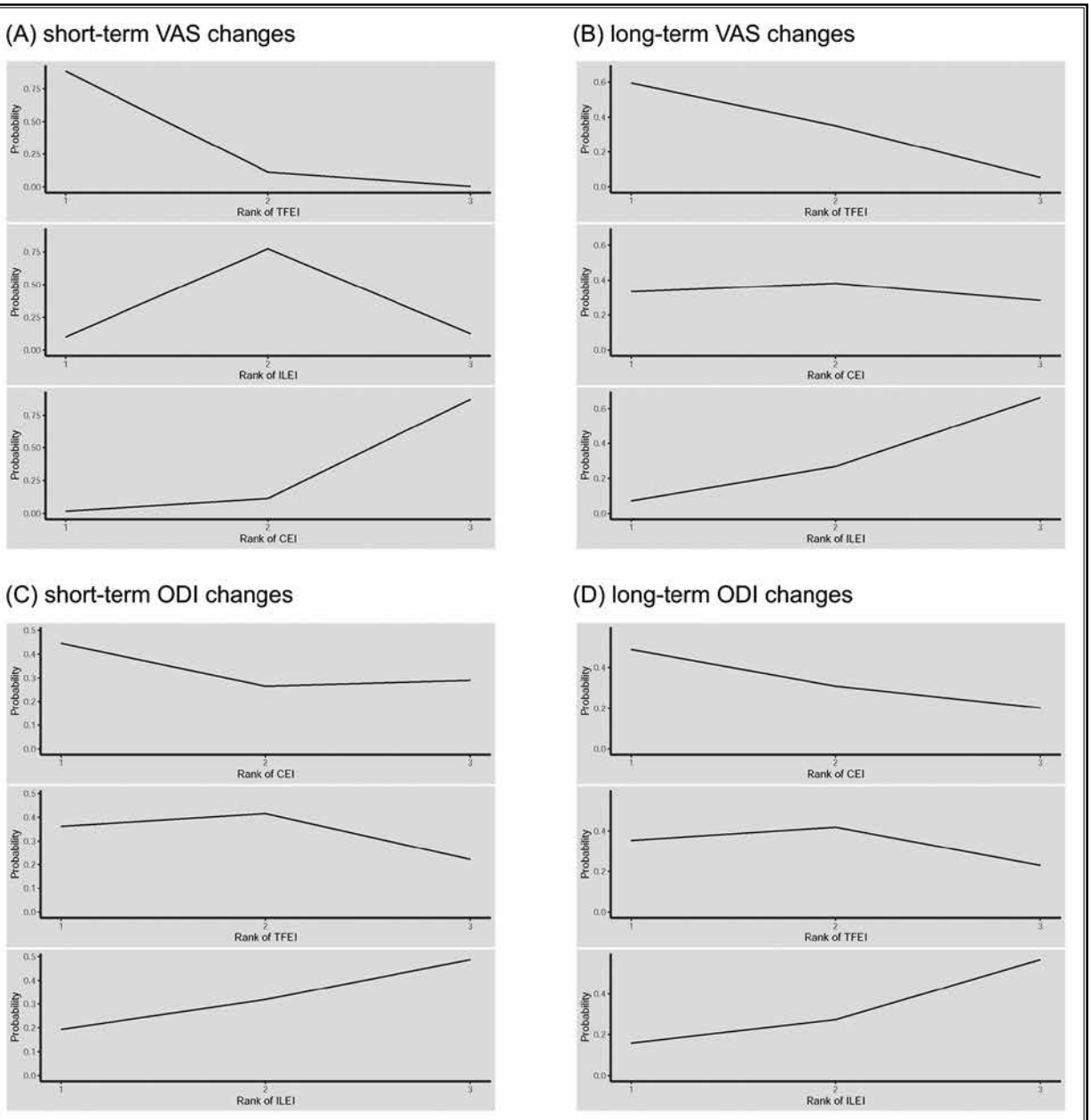


Fig. 5. *Ranking probabilities for transforaminal epidural injection, interlaminar epidural injection, and caudal epidural injection.*
*(A) Short-term VAS changes; (B) Long-term VAS changes; (C) Short-term ODI changes; (D) Long-term ODI changes.*
(VAS, Visual Analog Scale; ODI, Oswestry Disability Index; TFEI, transforaminal epidural injection; ILEI, interlaminar epidural injection; CEI, caudal epidural injection)

## Discussion

This meta-analysis evaluated the comparative effectiveness of TFEI, ILEI, and CEI in the treatment of lower back and radicular leg pain in patients with an HLD using evidence from previous studies. In the network meta-analysis, the improvement in the VAS score was more significant with TFEI than with CEI during the short-term follow-up period (from one week through one month post-TFEI). Furthermore, in the test deter-

mining the ranking of treatment effects among TFEI, ILEI, and CEI, TFEI showed the highest probability of being the best procedure for long- and short-term pain reduction and functional improvement.

TFEI has the advantage of targeting the nerve root that is affected in an HLD, which causes radicular pain. Moreover, TFEI delivers the injected medications into the ventral epidural space (28). Because the herniated disc is located within the ventral epidural space, TFEI facilitates the injection of the medication closer to the pathological site (28). Therefore, we believe that TFEI is more effective than the other EI methods in controlling pain associated with an HLD. ILEI logically targets the dorsal epidural space. Additionally, because it does not target a specific nerve root, a relatively small volume of the injected medication is delivered to the radicular pain-causing nerve root.

To deliver medications at the herniated disc site using CEI, a large volume of the drug should be injected (17). Because the injectate spreads diffusely in a non-specific pattern after CEI, the amount of medication delivered at the pathological site could be less than that delivered by the other methods. Furthermore, during CEI, intravascular injection may occur frequently because the sacral canal contains a dense epidural venous plexus (17). Furthermore, degenerative changes in the lumbosacral spine hinder the appropriate delivery of the injectate at the target pathologic site.

The tests for treatment effectiveness showed that TFEI has the highest probability of being the best procedure. However, the network meta-analysis revealed a significant difference among the 3 procedures only in the VAS score during the short-term follow-up comparison between TFEI and CEI. Usually, the effect of the steroids contained in the injectate for EI is sustained for approximately 3 months (29). Therefore, we believe that the long-term effect of EI would not differ largely from that of the short-term effect.

Patients experience discomfort due to needle puncture more frequently during TFEI than during ILEI or CEI (30). Additionally, spinal cord infarction after TFEI has been reported in previous studies (31,32). However, serious side effects can be avoided if particulate steroids are not used (33). For better treatment outcomes, TFEI is recommended for patients with lower back pain and radicular leg pain caused by an HLD.

Table 2. *Surface Under the Cumulative Ranking (SUCRA) of the reduction of Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) at short- and long-term follow-up.*

| | VAS reduction (short-term) | | VAS reduction (long-term) | |
|---|---|---|---|---|
| **Rank** | **Treatment** | **SUCRA** | **Treatment** | **SUCRA** |
| 1 | TFEI | 92.9 | TFEI | 77.3 |
| 2 | ILEI | 50.2 | CEI | 50.5 |
| 3 | CEI | 7.0 | ILEI | 22.2 |
| | ODI reduction (short-term) | | ODI reduction (long-term) | |
| | Treatment | SUCRA | Treatment | SUCRA |
| 1 | TFEI | 58.9 | CEI | 65.7 |
| 2 | CEI | 55.7 | TFEI | 56.7 |
| 3 | ILEI | 32.5 | ILEI | 27.6 |

TFEI: transforaminal epidural injection, ILEI: interlaminar epidural injection, CEI: caudal epidural injection

## Conclusion

Our study found that among the 3 EI techniques, TFEI has the potential to be the best procedure to reduce pain and improve function in patients with an HLD. However, the evidence level was considered low because no significant difference was observed in the network meta-analysis of the long-term VAS and short- and long-term ODI changes. Our study is the first network-meta analysis to compare the therapeutic effects of TFEI, ILEI, and CEI in patients with an HLD. However, our study has some limitations. First, only a small number of previous studies were included in our analysis. Second, subgroup analysis according to the injection volume, material type, or pain onset could not be conducted. To strengthen this evidence, future network meta-analysis comprising a larger number of studies is warranted.

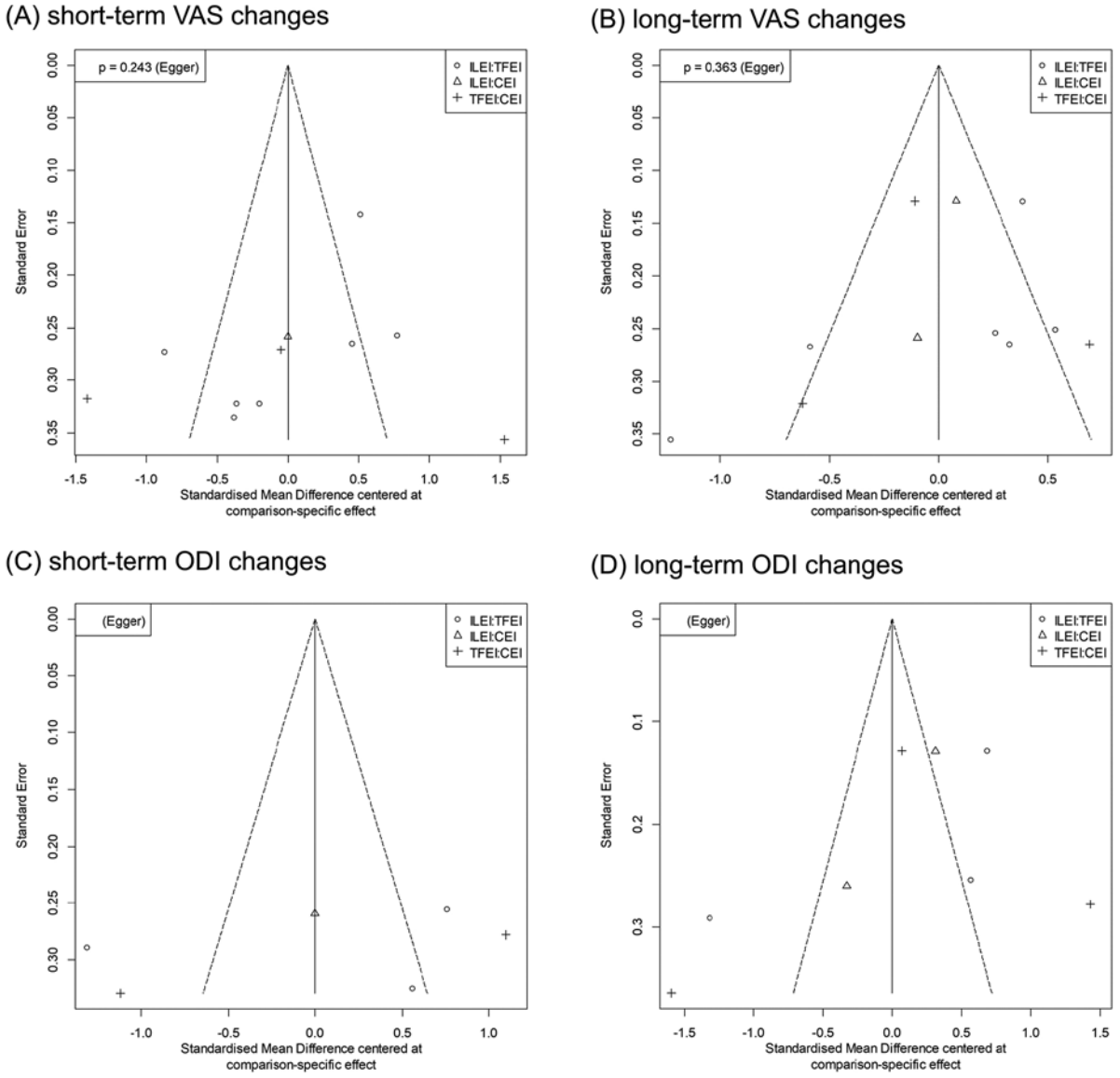


Fig. 6. *Graphical funnel plots of the included studies.*
*(A) Short-term VAS changes; (B) Long-term VAS changes; (C) Short-term ODI changes; (D) Long-term ODI changes.*
(VAS, Visual Analog Scale; ODI, Oswestry Disability Index; TFEI, transforaminal epidural injection; ILEI, interlaminar epidural injection; CEI, caudal epidural injection)

**Supplemental material available at www.painphysicianjournal.com**

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## Supplementary File 1

### *Search strategy*

A search strategy was developed to identify studies comparing the effects of transforaminal (TFEI), interlaminar (ILEI), and caudal epidural injections (CEI) for managing lower back or radicular leg pain from herniation of lumbar disc (HLD).

The search keywords were combined as follows:

"Lumbosacral disc," "Lumbar disc," "Radiculopathies," "Radiculopathy," "radiculitis," "nerve root," "back pain," "sciatica," "sciaticas," "sciatic"

AND

"epidural injection," "sympathetic block," "epidural block"

The search keywords were devised using a combination of subject indexing terms in the titles and abstracts. For the index related to HLD, TFEI, ILEI, and CEI, [Lee JH, Shin KH, Bahk SJ, Lee GJ, Kim DH, Lee CH, Kim DH, Yang HS, Lee SH. Comparison of clinical efficacy of transforaminal and caudal epidural steroid injection in lumbar and lumbosacral disc herniation: A systematic review and meta-analysis. Spine J. 2018 Dec;18(12):2343-2353. Appendix E. Search terms.] was referenced.

Search strategy for: Lee JH, Shin KH, Bahk SJ, Lee GJ, Kim DH, Lee CH, Kim DH, Yang HS, Lee SH. Comparison of clinical efficacy of transforaminal and caudal epidural steroid injection in lumbar and lumbosacral disc herniation: A systematic review and meta-analysis. Spine J. 2018 Dec;18(12):2343-2353. Appendix E. Search terms.

### *MEDLINE (Pubmed)*

(((((“Intervertebral Disc Displacement”[Mesh]) OR (Disc[tiab] OR Discs[tiab] OR Disk[tiab] OR Disks[tiab] OR Radiculopathies[tiab] OR Radiculopathy[tiab] OR “Nerve Root”[tiab] OR Radiculitis[tiab] OR Radiculitides [tiab] OR Radiating[tiab] OR Radicular[tiab]))) AND (((Lumbosacral[tiab] OR Lumbar[tiab] OR intervertebral [tiab])) OR ((((“Back”[Mesh:noexp]) OR “Lumbosacral Region”[Mesh]) OR “Lumbar Vertebrae”[Mesh])))) OR ((((“Sciatica”[Mesh]) OR “Back Pain”[Mesh])) OR (Sciat- ica[tiab] OR Sciaticas[tiab] OR Sciatic[tiab] OR “Back Pain”[tiab])) AND ((((“Adrenal Cortex Hormones”[Mesh: NoExp] OR “Glucocorticoids”[Mesh] OR “Triamcinolone”[Mesh] OR “Dexamethasone”[Mesh] OR Triamcino- lone[TIAB] OR Glucocorticoids[TIAB] OR betamethasone [TIAB] OR dexamethasone[TIAB] OR Glucocorticoid [TIAB] OR “Steroids, Fluorinated”[Mesh:NoExp] OR Ste- roids[TIAB] OR Steroid[TIAB] OR “Lidocaine”[Mesh] OR “Lidocaine”[TIAB] OR “Hyaluronoglucosaminidase” [Mesh] OR Hyaluronidase[TIAB] OR “Anesthetics, Local”[Mesh] OR “Local Anesthetics”[TIAB] OR “Local Anesthetic”[TIAB] OR “Anti-Inflammatory Agents”[Mesh: NoExp] OR “Bupivacaine”[Mesh] OR “Bupivacaine” [TIAB]) AND ((Block[tiab] OR injection[tiab] OR injec- tions[tiab]) AND (Autonomic[tiab] OR Sympathetic[tiab] OR epidural[tiab] OR interlaminar[tiab] OR transforaminal [tiab] OR caudal[tiab] OR ((spinal[tiab] OR dorsal [tiab]) AND (“root”[tiab] OR “nerve”[tiab] OR ganglia[tiab])) OR (“Ganglia, Spinal”[Mesh] OR “Ganglia, Spinal” [Mesh])))) OR (“Injections, Epidural”[Mesh:NoExp] OR “Autonomic Nerve Block”[Mesh:NoExp] OR (Block [tiab] OR injection[tiab] OR injections[tiab]) AND (Auto- nomic[tiab] OR Sympathetic[tiab] OR epidural[tiab] OR interlaminar[tiab] OR transforaminal[tiab] OR caudal [tiab] OR ((spinal[tiab] OR dorsal [tiab]) AND (“root” [tiab] OR “nerve”[tiab] OR ganglia[tiab])) OR (“Ganglia, Spinal”[Mesh] OR “Ganglia, Spinal”[Mesh])))))

### *EMBASE*

((’intervertebral disk hernia’/exp OR disc:ab,ti OR discs: ab,ti OR disk:ab,ti OR disks:ab,ti OR radiculopathies:ab,ti OR radiculopathy:ab,ti OR ’nerve root’:ab,ti OR radiculi- tis:ab,ti OR radiculitides:ab,ti OR radiating:ab,ti OR radicular:ab,ti AND (lumbosacral:ab,ti OR lumbar:ab,ti OR intervertebral:ab,ti OR ’back’/de OR ’intervertebral disk’/ exp OR ’lumbar disk’/exp OR ’lumbar spine’/exp OR ’lum- bar vertebra’/exp OR ’lumbosacral spine’/exp) OR ’low back pain’/exp OR ’sciatica’/exp OR sciatica:ab,ti OR scia- ticas:ab,ti OR sciatic:ab,ti OR ’back pain’:ab,ti) AND ((“Injections, Epidural”/exp OR “Autonomic Nerve Block”[Mesh:NoExp] OR ((Block:ab,ti OR injection:ab,ti OR injections:ab,ti) AND ((Autonomic:ab,ti OR Sympa- thetic:ab,ti)OR (epidural:ab,ti OR interlaminar:ab,ti OR transforaminal:ab,ti OR caudal:ab,ti) OR ((spinal:ab,ti OR dorsal:ab,ti) AND (“root”:ab,ti OR “nerve”:ab,ti OR gan- glia:ab,ti)) OR (’spinal

ganglion'/8928bdd/_Lib_Prox- y_Url/www.embase.com/exp)))) OR (((Block:ab,ti OR injection:ab,ti OR injections:ab,ti) AND ((Autonomic:ab,ti OR Sympathetic:ab,ti)OR (epidural:ab,ti OR interlaminar: ab,ti OR transforaminal:ab,ti OR caudal:ab,ti) OR ((spinal: ab,ti OR dorsal:ab,ti) AND ("root":ab,ti OR "nerve":ab,ti OR ganglia:ab,ti)) OR ('spinal ganglion'/8928bdd/_Lib_- Proxy_Url/www.embase.com/exp)))AND(("AdrenalCortex Hormones"[Mesh:NoExp] OR "Glucocorticoids"[Mesh] OR "Triamcinolone"[Mesh] OR "Dexamethasone"[Mesh]) OR (Triamcinolone:ab,tiO RGlucocorticoids:ab,tiORbetamethasone:ab,ti OR dexamethasone:ab,ti OR Glucocorticoid:ab,ti) OR ("Steroids, Fluorinated"[Mesh:NoExp] OR Steroids:ab,ti ORSteroid:ab,ti)OR("Lidocaine"[Mesh]OR"Lidocaine":ab, ti) OR ("Hyaluronoglucosaminidase"[Mesh] OR Hyaluroni- dase:ab,ti) OR ("Anesthetics, Local"[Mesh] OR "Local Anesthetics":ab,ti OR "Local Anesthetic":ab,ti) OR "Anti- Inflammatory Agents"[Mesh:NoExp] OR ("Bupivacaine"[-Mesh]OR"Bupivacaine":ab,ti))))

***COCHRANE***

("Intervertebral Disc Displacement"[Mesh:NoExp] OR (Disc[tiab] OR Discs[tiab] OR Disk[tiab] OR Disks [tiab] OR Radiculopathies[tiab] OR Radiculopathy[tiab] OR "Nerve Root" [tiab] OR Radiculitis[tiab] OR Radi- culitides[tiab] OR Radiating[tiab] OR Radicular[tiab])) AND (Lumbosacral[tiab] OR Lumbar OR[tiab] OR Back[Mesh:NoExp] OR "Lumbosacral Region" [Mesh: NoExp] OR "Lumbar Vertebrae" "[Mesh:NoExp]) OR (Sciatica[Mesh:NoExp] OR "Back Pain" [Mesh:NoExp] OR Sciatica[tiab] OR Sciaticas [tiab] OR Sciatic[tiab] OR "Back Pain" [tiab]) AND (("Injections, Epidural"[-Mesh:NoExp] OR "Autonomic Nerve Block"[Mesh: NoExp] OR ((Block[tiab] OR injection[tiab] OR injec- tions[tiab]) AND ((Autonomic[tiab] OR Sympathetic [tiab]) OR (epidural[tiab] OR interlaminar[tiab] OR transforaminal[tiab] OR caudal[tiab]) OR ((spinal[tiab] OR dorsal [tiab]) AND ("root"[tiab] OR "nerve"[tiab] OR ganglia[tiab])) OR (("Ganglia, Spinal"[Mesh] OR "Ganglia, Spinal"[Mesh])))))) OR (((Block[tiab] OR injection[tiab] OR injections[tiab]) AND ((Autonomic [tiab] OR Sympathetic[tiab]) OR (epidural[tiab] OR interlaminar[tiab] OR transforaminal[tiab] OR caudal [tiab]) OR ((spinal[tiab] OR dorsal [tiab]) AND ("root" [tiab] OR "nerve"[tiab] OR ganglia[tiab])) OR (("Gan- glia, Spinal"[Mesh] OR "Ganglia, Spinal"[Mesh]))))) AND (("Adrenal Cortex Hormones"[Mesh:NoExp] OR "Glucocorticoids"[Mesh] OR "Triamcinolone"[Mesh] OR "Dexamethasone"[Mesh]) OR (Triamcinolone [TIAB] OR Glucocorticoids[TIAB] OR betamethasone [TIAB] OR dexamethasone[TIAB] OR Glucocorticoid [TIAB]) OR ("Steroids, Fluorinated"[Mesh:NoExp] OR Steroids[TIAB] OR Steroid[TIAB]) OR ("Lidocaine"[- Mesh] OR "Lidocaine"[TIAB]) OR ("Hyaluronoglucosa- minidase"[Mesh] OR Hyaluronidase[TIAB]) OR ("Anesthetics, Local"[Mesh] OR "Local Anesthetics" [TIAB] OR "Local Anesthetic"[TIAB]) OR "Anti- Inflammatory Agents"[Mesh:NoExp] OR "Bupivacaine"[Mesh] OR "Bupivacaine"[TIAB])))

***KOREAMED***

(Lumbosacral disc OR Lumbar disc OR Radiculopathies OR Radiculopathy OR radiculitis OR nerve root OR back pain OR sciatica OR sciaticas OR sciatic AND epidural injection) OR (Lumbosacral disc OR Lumbar disc OR Radiculopathies OR Radiculopathy OR radiculitis OR nerve root OR back pain OR sciatica OR sciaticas OR sciatic AND sympathetic block) OR (Lumbosacral disc OR Lum- bar disc OR Radiculopathies OR Radiculopathy OR radicu- litis OR nerve root OR back pain OR sciatica OR sciaticas OR sciatic AND epidural block)

***Selection of eligible studies***

We searched trial registers using the "Lumbosacral disc," "Lumbar disc," "Radiculopathies," "Radiculopathy," "radiculitis," "nerve root," "back pain," "sciatica," "sciaticas," "sciatic," "epidural injection," "sympathetic block," and "epidural block" index, and databases including PubMed, Embase, Scopus, and the Cochrane library for studies published up to August 22, 2022. The results of the database searches were entered into an EndNote X9 library. Duplicates were deleted using the deduplication function in EndNote X9. Two reviewers preferentially removed irrelevant records for selection based on the titles and abstracts. Thereafter, the reviewers checked the full texts to finally select the papers that meet the selection criteria.

Each database was searched under the following conditions:

1. PubMed (492)
   - Language: English
2. Embase (596)

- Publication type: article

3. Scopus (3069)
   - Document type: article
   - Publication stage: final
   - Keyword: human, humans
   - Source type: journal
   - Language: English
4. Cochrane library (405)
   - trials

### *Eligibility criteria*

| | |
|---|---|
| Population | Patients with low back pain and radicular leg pain due to HLD were included. |
| Intervention | A paper evaluating the effects of TFEI, ILEI, and CEI was included. We investigated the results of visual analog scale and Oswestry disability index. |
| Comparison | The studies including at least two therapeutic arms comprising TFEI, ILEI, or CEI were selected. |
| Outcome | Studies were considered eligible for inclusion in this review if they reported on visual analog scale scores or Oswestry disability index scores. |
| Study design | The design of the studies to be included in this study was not specific and a full range of designs was considered. Consequently, 7 randomized controlled trial and 3 retrospective studies were included. Studies published as case reports, reviews, letters, or other undistinctive forms were excluded. |
| Limitation | Publications in a language other than English were excluded. |

Supplemental Table 1. *A checklist and assessment results to evaluate the risk of bias in randomized controlled trials using interventional pain management techniques.*

| Evaluation items | | Study | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **scoring** | **criteria** | **Ackerman, 2007 (4)** | **Candido, 2008 (6)** | **Ghai, 2014 (7)** | **Gharibo, 2011 (8)** | **Kamble, 2015 (9)** | **Makkar, 2019 (10)** | **Manchikanti, 2015 (11)** | **Rados, 2011 (12)** | **Singh, 2017 (14)** |
| I. CONSORT OR SPIRIT | | | | | | | | | | |
| 1. Trial Design Guidance and Reporting | | | | | | | | | | |
| 0 | Trial designed and reported without any guidance | | | | | | | | | |
| 1 | Trial designed and reported utilizing minimum criteria other than CONSORT or SPIRIT criteria or trial was conducted prior to 2005 | ✓ | ✓ | | ✓ | ✓ | | ✓ | ✓ | ✓ |
| 2 | Trial implies it was based on CONSORT or SPIRIT without clear description with moderately significant criteria for randomized trials or the trial was conducted before 2005 | | | | | | | | | |
| 3 | Explicit use of CONSORT or SPIRIT with identification of criteria or trial conducted with high level reporting and criteria or conducted before 2005 | | | ✓ | | | | | | |
| II. DESIGN FACTORS | | | | | | | | | | |
| 2. Type and Design of Trial | | | | | | | | | | |
| 0 | Poorly designed control group (quasi selection, convenient sampling) | | | | | | | | | |
| 2 | Proper active-control or sham procedure with injection of active agent | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| 3 | Proper placebo control (no active solutions into active structures) | | | | | | | | | |
| 3. Setting/Physician | | | | | | | | | | |
| 0 | General setting with no specialty affiliation and general physician | ✓ | | | | ✓ | | ✓ | | |
| 1 | Specialty of anesthesia/PMR/neurology/ radiology/ortho, etc. | | ✓ | ✓ | | | ✓ | | | ✓ |
| 2 | Interventional pain management with interventional pain management physician | | | | ✓ | | | | ✓ | |
| 4. Imaging | | | | | | | | | | |
| 0 | Blind procedures | | | | | | | | | |
| 1 | Ultrasound | | | | | | | | | |
| 2 | CT | | | | | | | | | |
| 3 | Fluoro | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

Supplemental Table 1 con't. *A checklist and assessment results to evaluate the risk of bias in randomized controlled trials using interventional pain management techniques.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 5. Sample Size | | | | | | | | | | |
| 0 | Less than 50 participants in the study without appropriate sample size determination | | | | | ✓ | | | | |
| 1 | Sample size calculation with less than 25 patients in each group | | | | ✓ | | | | | |
| 2 | Appropriate sample size calculation with at least 25 patients in each group | | ✓ | ✓ | | | ✓ | | ✓ | ✓ |
| 3 | Appropriate sample size calculation with 50 patients in each group | ✓ | | | | | | ✓ | | |
| 6. Statistical Methodology | | | | | | | | | | |
| 0 | None or inappropriate | | ✓ | | | | | | | |
| 1 | Appropriate | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| III. PATIENT FACTORS | | | | | | | | | | |
| 7. Inclusiveness of Population | | | | | | | | | | |
| 7a. For epidural procedures: | | | | | | | | | | |
| 0 | Poorly identified mixed population | | | | | | | | | |
| 1 | Clearly identified mixed population | | | | | | | | | |
| 2 | Disorders specific trials (i.e. well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post surgery syndrome) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| 7b. For facet or sacroiliac joint interventions: | | | | | | | | | | |
| 0 | No diagnostic blocks | | | | | | | | | |
| 1 | Selection with single diagnostic blocks | | | | | | | | | |
| 2 | Selection with placebo or dual diagnostic blocks | | | | | | | | | |
| 8. Duration of Pain | | | | | | | | | | |
| 0 | Less than 3 months | ✓ | | | | ✓ | | | | |
| 1 | 3 to 6 months | | | | | | ✓ | | | |
| 2 | > 6 months | | ✓ | ✓ | ✓ | | | ✓ | | ✓ |
| 9. Previous Treatments | | | | | | | | | | |
| Conservative management including drug therapy, exercise therapy, physical therapy, etc. | | | | | | | | | | |
| 0 | Were not utilized | | ✓ | | | | | | | |
| 1 | Were utilized sporadically in some patients | ✓ | | | | | | | | |
| 2 | Were utilized in all patients | | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

Supplemental Table 1 con't.. *A checklist and assessment results to evaluate the risk of bias in randomized controlled trials using interventional pain management techniques.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 10. Duration of Follow-up with Appropriate Interventions | | | | | | | | | | |
| 0 | Less than 3 months or 12 weeks for epidural or facet joint procedures, etc. and 6 months for intradiscal procedures and implantables | | | | ✓ | | | | | |
| 1 | 3 to 6 months for epidural or facet joint procedures, etc., or 1 year for intradiscal procedures or implantables | ✓ | ✓ | | | ✓ | ✓ | | ✓ | |
| 2 | 6 months to 17 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables | | | ✓ | | | | | | ✓ |
| 3 | 18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables | | | | | | | ✓ | | |
| IV. OUTCOMES | | | | | | | | | | |
| 11. Outcomes Assessment Criteria for Significant Improvement | | | | | | | | | | |
| 0 | No descriptions of outcomes<br>OR < 20% change in pain rating or functional status | | | | | | | | | |
| 1 | Pain rating with a decrease of 2 or more points or more than 20% reduction<br>OR functional status improvement of more than 20% | | ✓ | | | | | | | |
| 2 | Pain rating with decrease of ≥ 2 points<br>AND ≥ 20% change or functional status improvement of ≥ 20% | | | | | | | | | |
| 2 | Pain rating with a decrease of 3 or more points or more than 50% reduction<br>OR functional status improvement with a 50% or 40% reduction in disability score | | | | ✓ | | | | ✓ | |
| 4 | Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores | | | ✓ | | ✓ | ✓ | ✓ | | ✓ |
| 12. Analysis of all Randomized Participants in the Groups | | | | | | | | | | |
| 0 | Not performed | | | | | | | | | |
| 1 | Performed without intent-to-treat analysis without inclusion of all randomized participants | | | | | | | | | |
| 2 | All participants included with or without intent-to-treat analysis | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

Supplemental Table 1 con't.. *A checklist and assessment results to evaluate the risk of bias in randomized controlled trials using interventional pain management techniques.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 13. Description of Drop Out Rate | | | | | | | | | | |
| 0 | No description of dropouts, despite reporting of incomplete data or ≥ 20% withdrawal | | | | | | | ✓ | | |
| 1 | Less than 20% withdrawal in one year in any group | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ |
| 2 | Less than 30% withdrawal at 2 years in any group | | | | | | | | | |
| 14. Similarity of Groups at Baseline for Important Prognostic Indicators | | | | | | | | | | |
| 0 | Groups dissimilar with significant influence on outcomes with or without appropriate randomization and allocation | | | | | ✓ | | | | |
| 1 | Groups dissimilar without influence on outcomes despite appropriate randomization and allocation | | ✓ | | ✓ | | | ✓ | | ✓ |
| 2 | Groups similar with appropriate randomization and allocation | ✓ | | ✓ | | | ✓ | | ✓ | |
| 15. Role of Co-Interventions | | | | | | | | | | |
| 0 | Co-interventions were provided but were not similar in the majority of participants | | ✓ | ✓ | ✓ | ✓ | | ✓ | | |
| 1 | No co-interventions or similar co-interventions were provided in the majority of the participants | ✓ | | | | | ✓ | | ✓ | ✓ |
| V. RANDOMIZATION | | | | | | | | | | |
| 16. Method of Randomization | | | | | | | | | | |
| 0 | Quasi randomized or poorly randomized or not described | | | | | | | | | |
| 1 | Adequate randomization (coin toss, drawing of balls of different colors, drawing of ballots) | | | | | | | | | |
| 2 | High quality randomization (computer generated random sequence, pre-ordered sealed envelopes, sequentially ordered vials, telephone call, pre-ordered list of treatment assignments, etc.) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| VI. ALLOCATION CONCEALMENT | | | | | | | | | | |
| 17. Concealed Treatment Allocation | | | | | | | | | | |
| 0 | Poor concealment of allocation (open enrollment) or inadequate description of concealment | | | | | | | | | |
| 1 | Concealment of allocation with borderline or good description of the process with probability of failure of concealment | | | | | | | | | |
| 2 | High quality concealment with strict controls (independent assignment without influence on the assignment sequence) | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |

Supplemental Table 1 con't.. *A checklist and assessment results to evaluate the risk of bias in randomized controlled trials using interventional pain management techniques.*

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| VII. BLINDING | | | | | | | | | | |
| 18. Patient Blinding | | | | | | | | | | |
| 0 | Patients not blinded | ✓ | ✓ | | ✓ | | | | | |
| 1 | Patients blinded adequately | | | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ |
| 19. Care Provider Blinding | | | | | | | | | | |
| 0 | Care provider not blinded | | ✓ | | | ✓ | | | ✓ | ✓ |
| 1 | Care provider blinded adequately | ✓ | | ✓ | ✓ | | ✓ | ✓ | | |
| 20. Outcome Assessor Blinding | | | | | | | | | | |
| 0 | Outcome assessor not blinded or was able to identify the groups | | | | | | | ✓ | ✓ | ✓ |
| 1 | Performed by a blinded independent assessor with inability to identify the assignment-based provider intervention (i.e., subcutaneous injection, intramuscular distant injection, difference in preparation or equipment use, numbness and weakness, etc.) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | | | |
| VIII. CONFLICTS OF INTEREST | | | | | | | | | | |
| 21. Funding and Sponsorship | | | | | | | | | | |
| -3 | Trial included industry employees | | | | | | | | | |
| -3 | Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts | | | | | | | | | |
| 0 | Industry or organizational funding with reimbursement of expenses with some involvement | ✓ | ✓ | | | | | ✓ | | ✓ |
| 1 | Industry or organization funding of expenses without involvement | | | | | | | | | |
| 2 | Funding by internal resources only with supporting entity unrelated to industry | | | ✓ | ✓ | ✓ | ✓ | | ✓ | |
| 3 | Governmental funding without conflict such as NIH, NHS, AHRQ | | | | | | | | | |
| 22. Conflicts of Interest | | | | | | | | | | |
| 0 | None disclosed with potential implied conflict | ✓ | ✓ | | | | | ✓ | | |
| 1 | Marginally disclosed with potential conflict | | | | | | | | | |
| 2 | Well disclosed with minor conflicts | | | | | | | | | |
| 3 | Well disclosed with no conflicts | | | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ |
| -1 | Hidden conflicts with poor disclosure | | | | | | | | | |
| -2 | Misleading disclosure with conflicts | | | | | | | | | |
| -3 | Major impact related to conflicts | | | | | | | | | |
| TOTAL MAXIMUM SCORE = 48 | | | | | | | | | | |
| TOTAL SCORE | | 30 | 24 | 41 | 33 | 30 | 40 | 32 | 34 | 35 |

Supplemental Table 2 . *A checklist and assessment results to evaluate the risk of bias in non-randomized controlled trials using interventional pain management techniques.*

| Evaluation items | | Study | |
|---|---|---|---|
| **scoring** | **criteria** | **Bensler et al. 2020 (5)** | **Schaufele et al. 2006 (13)** |
| I. STROBE OR TREND Guidance | | | |
| 1. Study Design Guidance and Reporting | | | |
| 0 | Case Report/Case Series | | |
| 1 | Study designed without any guidance | | |
| 2 | Study designed with minimal criteria and reporting with or without guidance | ✓ | ✓ |
| 3 | Study designed with moderately significant criteria or implies it was based on STROBE or TREND without clear description or the study was conducted before 2011 or similar criteria utilized with study conducted before 2011 | | |
| 4 | Designed with high level criteria or explicitly uses STROBE or TREND with identification of criteria or conducted prior to 2011 | | |
| II. DESIGN FACTORS | | | |
| 2. Study Design and Type | | | |
| 0 | Case report or series (uncontrolled – longitudinal) | | |
| 1 | Retrospective cohort or cross-sectional study | ✓ | |
| 2 | Prospective cohort case-control study | | ✓ |
| 3 | Prospective case control study | | |
| 4 | Prospective, controlled, nonrandomized | | |
| 3. Setting/Physician | | | |
| 0 | General setting with no specialty affiliation and general physician | | |
| 1 | Specialty of anesthesia/PMR/neurology, etc. | ✓ | |
| 2 | Interventional pain management with interventional pain management physician | | ✓ |
| 4. Imaging | | | |
| 0 | Blind procedures | | |
| 1 | Ultrasound | | |
| 2 | CT | | |
| 3 | Fluoro | ✓ | ✓ |
| 5. Sample Size | | | |
| 0 | Less than 100 participants without appropriate sample size determination | | ✓ |
| 1 | At least 100 participants in the study without appropriate sample size determination | ✓ | |
| 2 | Sample size calculation with less than 50 patients in each group | | |
| 3 | Appropriate sample size calculation with at least 50 patients in each group | | |
| 4 | Appropriate sample size calculation with 100 patients in each group | | |

Supplemental Table 2 con't. *A checklist and assessment results to evaluate the risk of bias in non-randomized controlled trials using interventional pain management techniques.*

| | | | |
|---|---|---|---|
| 6. Statistical Methodology | | | |
| 0 | None | | |
| 1 | Some statistics | | |
| 2 | Appropriate | ✓ | ✓ |
| III. PATIENT FACTORS | | | |
| 7. Inclusiveness of Population | | | |
| 7a. For epidural procedures: | | | |
| 1 | Poorly identified mixed population | | |
| 2 | Poorly identified mixed population with large sample (≥ 200) | | |
| 3 | Clearly identified mixed population | | |
| 4 | Disorders specific trials (i.e. well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post surgery syndrome) | | ✓ |
| 7b. For facet or sacroiliac joint interventions: | | | |
| 1 | No specific selection criteria | | |
| 2 | No diagnostic blocks based on clinical symptomatology | | |
| 3 | Selection with single diagnostic blocks | | |
| 4 | Selection with placebo or dual diagnostic blocks | | |
| 8. Duration of Pain | | | |
| 0 | Less than 3 months | ✓ | ✓ |
| 1 | 3 to 6 months | | |
| 2 | > 6 months | | |
| 9. Previous Treatments | | | |
| 1 | Conservative management including drug therapy, exercise therapy, physical therapy, etc. | | |
| 2 | Were not utilized | | |
| 3 | Were utilized sporadically in some patients | | |
| 4 | Were utilized in all patients | ✓ | ✓ |
| 10. Duration of Follow-up with Appropriate Interventions | | | |
| 1 | Less than 3 months or less for epidural or facet joint procedures, etc., and 6 months for intradiscal procedures and implantables | | ✓ |
| 2 | 3-6 months for epidural or facet joint procedures, etc., or one year for intradiscal procedures or implantables | ✓ | |
| 3 | 6-12 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables | | |
| 4 | 18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables | | |
| IV. OUTCOMES | | | |
| 11. Outcomes Assessment Criteria for Significant Improvement | | | |
| 0 | No descriptions of outcomes<br>OR < 20% change in pain rating or functional status | | |

Supplemental Table 2 con't. *A checklist and assessment results to evaluate the risk of bias in non-randomized controlled trials using interventional pain management techniques.*

| | | | |
|---|---|---|---|
| 1 | Pain rating with a decrease of 2 or more points or more than 20% reduction<br>OR functional status improvement of more than 20% | | |
| 2 | Pain rating with decrease of ≥ 2 points<br>AND ≥ 20% change or functional status improvement of ≥ 20% | | ✓ |
| 3 | Pain rating with a decrease of 3 or more points or more than 50% reduction<br>OR functional status improvement with a 50% or 40% reduction in disability score | | |
| 4 | Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores | | |
| 12. Description of Drop Out Rate | | | |
| 0 | No groups or groups dissimilar with significant influence on outcomes | | |
| 1 | Groups dissimilar without significant influence on outcomes | ✓ | ✓ |
| 2 | Groups similar | | |
| 13. Similarity of Groups at Baseline for Important Prognostic Indicators | | | |
| 0 | No description of dropouts, despite reporting of incomplete data or ≥ 20% withdrawal | | |
| 1 | Less than 20% withdrawal in one year in any group | ✓ | |
| 2 | Less than 30% withdrawal at 2 years in any group | | ✓ |
| 14. Role of Co-Interventions | | | |
| 1 | Dissimilar co-interventions or similar co-interventions in some of the participants | | |
| 2 | No co-interventions or similar co-interventions in majority of the participants | ✓ | ✓ |
| V. ASSIGNMENT | | | |
| 15. Method of Assignment of Participants | | | |
| 1 | Case report/case series or selective assignment based on outcomes or retrospective evaluation based on clinical criteria | ✓ | |
| 2 | Prospective study with inclusion without specific criteria | | |
| 3 | Retrospective method with inclusion of all participants or random selection of retrospective data | | |
| 4 | Prospective, well-defined assignment of methodology and inclusion criteria (quasi randomization, matching, stratification, etc.) | | ✓ |
| VI. CONFLICTS OF INTEREST | | | |
| 16. Funding and Sponsorship | | | |
| -3 | Trial included industry employees with or without proper disclosure | | |
| -3 | Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts | | |
| 0 | Industry or organizational funding with reimbursement of expenses with some involvement or no information available | | |
| 1 | Industry or organization funding of expenses without involvement | | |
| 2 | Funding by internal resources only | ✓ | ✓ |
| 3 | Governmental funding without conflict such as NIH, NHS, AHRQ | | |
| TOTAL MAXIMUM SCORE = 48 | | | |
| TOTAL SCORE | | 29 | 33 |