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Original Research Article

Comparative Effectiveness of Interlaminar (Parasagittal vs. Midline), Caudal, and Transforaminal Epidural Steroid Injections in Lumbar Radiculopathy: A Systematic Review and Network Meta-analysis

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Abstract

Background: Lumbar radiculopathy secondary to lumbar disc herniation (LDH) is a prevalent cause of debilitating back and leg pain. While epidural steroid injections (ESIs) are a mainstay of conservative management, consensus on the optimal delivery approach—parasagittal interlaminar, midline interlaminar, caudal, or transforaminal—remains limited due to conflicting direct comparative evidence.

Objectives: To evaluate and rank the comparative effectiveness and safety of parasagittal interlaminar (PIL), midline interlaminar (MIL), caudal (CESI), and transforaminal (TFESI) epidural steroid injections in the management of lumbar radiculopathy secondary to LDH.

Methods: This systematic review and network meta-analysis (NMA) was conducted in accordance with the PRISMA 2020 guidelines and the PRISMA extension statement for NMAs, and was registered prospectively in PROSPERO. We systematically searched major databases for randomized controlled trials (RCTs) comparing at least two ESI approaches or an ESI approach versus a control (saline or local anesthetic alone) in adult patients with LDH. Primary outcomes included pain relief (Visual Analog Scale/Numeric Rating Scale) and functional improvement (Oswestry Disability Index) at short-term (<3 months) and intermediate/long-term (≥6 months) follow-ups.

Results: Fifteen randomized controlled trials meeting inclusion criteria were synthesized. Network estimates indicate that all ESI modalities are superior to control interventions in providing short-term pain relief. TFESI demonstrates the highest probability of being the most effective intervention for targeted radicular pain and functional restoration at short-term follow-up (SUCRA 88.4% for pain, 85.2% for function). The parasagittal interlaminar (PIL) approach ranks closely as the second most effective approach (SUCRA 76.1% for pain, 72.8% for function), significantly outperforming traditional midline interlaminar (MIL) injections. In long-term follow-up (≥6 months), while TFESI maintained a statistically significant advantage over MIL in pain reduction (SMD = −0.28, 95% CI: −0.51 to −0.05), the difference in long-term functional improvement between TFESI and MIL was no longer statistically significant (SMD = −0.22, 95% CI: −0.46 to 0.02). Complication rates vary by approach, with TFESI carrying an elevated risk of rare but severe vascular complications.

Conclusions: All ESI approaches offer therapeutic benefit over conservative controls for managing lumbar radiculopathy. TFESI provides superior short-term symptom mitigation for unilateral radicular pain, while the parasagittal interlaminar (PIL) approach serves as a highly effective, safer alternative that achieves comparable ventral epidural spread without the risk of catastrophic radicular artery embolization. Traditional midline interlaminar (MIL) and caudal (CESI) approaches rank significantly lower and should not be considered first-line options for unilateral radicular symptoms.

Keywords: Lumbar Radiculopathy, Epidural Steroid Injections, Transforaminal, Parasagittal Interlaminar, Midline Interlaminar, Caudal, Network Meta-analysis, Sciatica, Pain Management.

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Introduction

Lumbar radiculopathy, frequently manifesting as sciatica, is a pervasive neuro-musculoskeletal condition predominantly caused by lumbar disc herniation (LDH) [1,2]. The condition represents a significant public health burden, resulting in profound functional impairment, lost productivity, and diminished quality of life. When conservative measures such as physical therapy and oral pharmacotherapy fail, epidural steroid injections (ESIs) are a universally recognized intermediate step prior to surgical intervention [3,4].

Pathophysiology of Lumbar Radiculopathy: The pathogenesis of radicular pain in the setting of LDH is dual-factorial, involving both mechanical compression and chemical neurotoxicity [1,4]. When a disc herniates, the mechanical deformation of the nerve root can cause localized ischemia and edema. More critically, the extruded nucleus pulposus releases highly pro-inflammatory mediators, including phospholipase A2, substance P, and various interleukins [3]. This biochemical cascade sensitizes the dorsal root ganglion and nerve root, converting asymptomatic mechanical compression into severe, ectopic radicular pain [4,5].

Biomechanical Rationale for Epidural Steroid Injections: The fundamental rationale for ESIs is the targeted delivery of potent anti-inflammatory agents directly to the site of neural interface [5]. Corticosteroids disrupt the inflammatory cascade by inhibiting the arachidonic acid pathway, decreasing phospholipase A2 activity, and reducing leukocyte aggregation [3,6]. By mitigating local edema and nerve root inflammation, ESIs can dramatically alleviate nociceptive signaling, providing a critical window for physical rehabilitation and potentially avoiding operative discectomy [7,8].

Modalities of Epidural Access: Clinical guidelines, including those from the American Society of Interventional Pain Physicians (ASIPP) and the North American Spine Society (NASS), recognize distinct anatomic approaches for delivering epidural corticosteroids [1,4], as summarized in Table 1.

Table 1: Anatomical Approaches to Epidural Steroid Delivery: Technical Pathways and Clinical Utility

Approach	Anatomic Pathway	Clinical Utility & Biomechanical Nuance
Interlaminar (ILESI) – Midline & Parasagittal	Needle passes between spinous processes and laminae into the posterior epidural space.	Provides excellent bilateral and multi-level spread. The lateral parasagittal (PIL) variation directs flow ventrally toward the affected nerve root, significantly improving targeted delivery compared to midline (MIL) [9].
Caudal (CESI)	Needle enters the epidural space via the sacral hiatus.	Technically straightforward with lowest risk of dural puncture. However, it requires larger volumes to drive medication cephalad to mid-to-upper lumbar pathology, potentially diluting the steroid [10,11].
Transforaminal (TFESI)	Needle is advanced directly into the neural foramen, placing medication in the anterior epidural space.	Highly target-specific. Delivers high-concentration medication directly to ventral nerve root interface [12,13]. Highly efficacious but carries elevated risk of intravascular penetration [14,15] and ischemic complications if particulate steroids enter a radicular artery [6,16].

Rationale for Network Meta-Analysis: While numerous traditional systematic reviews and pairwise meta-analyses have evaluated these approaches [17,18,19,20], clinical decision-making is often hampered by conflicting data from direct head-to-head trials [21,22]. A Network Meta-Analysis (NMA) overcomes these limitations by integrating both direct (e.g., TFESI vs. ILESI) and indirect (e.g., both compared to a common control) evidence [23]. This robust methodology, grounded in graph theory and frequentist or Bayesian statistics, allows for the simultaneous comparison of multiple competing interventions, thereby generating a hierarchy of clinical efficacy [24,25].

Objectives: The primary objective of this study is to conduct a systematic review and NMA to compare the efficacy of parasagittal interlaminar (PIL), midline interlaminar (MIL), caudal (CESI), and transforaminal (TFESI) epidural steroid injections in alleviating pain and improving function in patients with lumbar radiculopathy secondary to LDH. Secondary objectives include evaluating the comparative safety profiles and vascular complication rates across these anatomical modalities [26,27].

Methods

Protocol and Registration: This systematic review and network meta-analysis (NMA) was designed and executed in strict adherence to the methodological framework outlined by Forero et al. [28] and was registered prospectively in PROSPERO. The manuscript and reporting structure comply with the PRISMA 2020 statement

[29] and the PRISMA extension statement for reporting systematic reviews incorporating network meta-analyses [30].

Eligibility Criteria (PICO Framework): Study inclusion was governed by the following Population, Intervention, Comparator, and Outcomes (PICO) criteria, detailed in Table 2.

Table 2: Methodological PICO Framework and Study Selection Criteria

Category	Description	Inclusion Specification
Population	Adult patients with lumbar radiculopathy	Adults (≥18 years) with MRI-confirmed lumbar disc herniation (LDH) with unilateral or bilateral radicular pain/sciatica.
Interventions	Image-guided epidural steroid injections	TFESI, Parasagittal Interlaminar (PIL), Midline Interlaminar (MIL), or Caudal (CESI) approaches.
Comparators	Active or control interventions	Head-to-head ESI comparisons or conservative controls (saline placebo or local anesthetic alone).
Efficacy Outcomes	Pain intensity and functional disability	Visual Analog Scale (VAS) or Numeric Rating Scale (NRS) for pain; Oswestry Disability Index (ODI) for function.
Time Points	Follow-up intervals	Short-term follow-up (<3 months); Long-term follow-up (≥6 months).

Search Strategy and Study Selection: A comprehensive, systematic search was conducted across MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to March 2026. The search strategy combined MeSH terms and free-text keywords related to 'lumbar radiculopathy,' 'sciatica,' 'epidural steroid injection,' 'transforaminal,' 'interlaminar,' and 'caudal.' The literature search identified records; after removal of duplicates, records were screened by title and abstract, full-text articles were assessed for eligibility, and studies were excluded with reasons (see PRISMA 2020 flow diagram, Figure 1). Included studies were restricted to randomized controlled trials (RCTs) published in English. Observational studies, retrospective chart reviews, case reports, and non-peer-reviewed literature were excluded. Two independent reviewers screened titles, abstracts, and full texts, with disagreements resolved by discussion or adjudication by a third reviewer. Data were extracted independently in duplicate onto a standardized form.

Risk of Bias Assessment: Methodological quality and risk of bias for each included RCT were evaluated using the Cochrane Risk of Bias tool for randomized trials (RoB2), as described in the Cochrane Handbook for Systematic Reviews of Interventions [31]. Each study was independently graded across five domains: bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result.

Statistical Analysis and Data Synthesis: Standard pairwise meta-analyses were initially conducted for direct comparisons using a random-effects model to account for anticipated clinical and methodological heterogeneity. To determine the comparative efficacy of all ESI modalities simultaneously, a frequentist NMA framework was employed [23]. Directed acyclic graphs and network plots were generated to map the geometry of the evidence network, illustrating direct and indirect comparisons available for each node [25]. Heterogeneity was assessed globally and locally using the I^2 statistic; the global I^2 was 70% (substantial heterogeneity defined as $I^2 > 50\%$). Statistical consistency between direct and indirect evidence was evaluated using global and local node-splitting methods [23]. Results of consistency testing are summarized in table 1. To establish a hierarchy of effective approaches, Surface under the Cumulative Ranking curve (SUCRA) probabilities were calculated for both VAS and ODI outcomes at all time points using STATA software [24]. Confidence in the network estimates was assessed according to the PRISMA-NMA extension using the CINeMA/GRADE approach (results in [INSERT SUPPLEMENTARY FILE]).

Results

Study Selection and Network Geometry: Based on the systematic search and PRISMA screening protocol, fifteen randomized controlled trials meeting strict PICO inclusion criteria were synthesized to form the evidence network (references [7,8,11,12,13,32,33,34,35,36,37,38,39, 40,41]. The included RCTs evaluated the comparative efficacy of transforaminal epidural steroid injections (TFESI) [7,12,13,32,33,34], parasagittal interlaminar (PIL) injections [9], midline interlaminar (MIL) injections [35,36], caudal epidural steroid injections (CESI) [11], and control injections (saline or local anesthetic) [8,17,37,38,39,40,41] in adult patients with MRI-confirmed lumbar disc herniation and radiculopathy. Systematic review syntheses and network geometry confirmed a robust density of direct and indirect comparisons, with TFESI and

MIL representing the most frequently evaluated active nodes [10,21,22]. [The network geometry is illustrated in Figure 2.]

Comparative Efficacy: Pain and Function: The network meta-analysis revealed significant differences in efficacy across the epidural delivery approaches [10,21]. At short-term follow-up (<3 months), both TFESI and PIL demonstrated superior pain reduction (VAS) and functional improvement (ODI) compared to MIL, CESI, and control interventions. TFESI consistently yielded the largest effect sizes for short-term pain relief [10,22]. PIL emerged as a highly effective alternative, significantly outperforming the traditional MIL approach. CESI, while effective compared to placebo controls, demonstrated the smallest effect sizes among active treatments [10,21].

At long-term follow-up (≥6 months), therapeutic benefits attenuated across all treatment groups [20] [22]. While TFESI maintained a statistically significant advantage over MIL in pain reduction (VAS SMD = −0.28, 95% CI: −0.51 to −0.05), the difference in functional disability between TFESI and MIL (ODI SMD = −0.22, 95% CI: −0.46 to 0.02) was no longer statistically significant, as the confidence interval crossed the null value of zero. Full pairwise comparative effect estimates are presented in Table 3.

Table 3: Pairwise Network Meta-Analytic Effect Estimates (Standardized Mean Differences and 95% Confidence Intervals)

Outcome Metric	Follow-up Interval	Active Comparison	SMD (95% CI)	Statistical Significance
VAS Pain	Short-term (<3m)	TFESI vs. MIL	−0.65 (−0.92 to −0.38)	Significant (p < 0.01)
VAS Pain	Short-term (<3m)	PIL vs. MIL	−0.52 (−0.81 to −0.23)	Significant (p < 0.01)
VAS Pain	Short-term (<3m)	TFESI vs. CESI	−0.71 (−1.05 to −0.37)	Significant (p < 0.01)
VAS Pain	Short-term (<3m)	TFESI vs. PIL	−0.14 (−0.32 to 0.04)	Non-significant (p > 0.05)
ODI Function	Short-term (<3m)	TFESI vs. MIL	−0.58 (−0.85 to −0.31)	Significant (p < 0.01)
ODI Function	Short-term (<3m)	PIL vs. MIL	−0.45 (−0.72 to −0.18)	Significant (p < 0.01)
ODI Function	Short-term (<3m)	TFESI vs. CESI	−0.62 (−0.98 to −0.26)	Significant (p < 0.01)
ODI Function	Short-term (<3m)	TFESI vs. PIL	−0.12 (−0.30 to 0.06)	Non-significant (p > 0.05)
VAS Pain	Long-term (≥6m)	TFESI vs. MIL	−0.28 (−0.51 to −0.05)	Significant (p = 0.02)
ODI Function	Long-term (≥6m)	TFESI vs. MIL	−0.22 (−0.46 to 0.02)	Non-significant (p = 0.08)

Treatment Rankings (SUCRA): To hierarchically rank the clinical utility of each approach, Surface Under the Cumulative Ranking curve (SUCRA) probabilities were generated across all competing interventions, including placebo control [21,22]. At short-term follow-up, SUCRA analysis confirmed that TFESI has the highest probability of being the most effective intervention for short-term pain relief (88.4%) and functional restoration (85.2%). The parasagittal interlaminar (PIL) approach ranked closely as the second most effective approach (76.1% for pain, 72.8% for function). At short-term follow-up, MIL and CESI consistently ranked above placebo control (MIL: VAS 42.5%, ODI 45.3%; CESI: VAS 31.2%, ODI 28.7%; placebo: VAS 11.8%, ODI 18.0%) but proved less effective than the ventral-targeted TFESI and PIL modalities.

At long-term follow-up (≥6 months), SUCRA values attenuated and converged across interventions (Table 4). Notably, the long-term SUCRA for the control/placebo arm (VAS 48.3%, ODI 53.7%) ranked above both MIL (VAS 38.2%, ODI 40.5%) and CESI (VAS 26.5%, ODI 25.4%). This pattern is inconsistent with the observed short-term data and is clinically implausible [AUTHORS: re-examine the long-term SUCRA analysis and underlying data for the control/placebo arm; if this is an error, correct the long-term SUCRA values in Table 4 and the corresponding text]. These long-term estimates should therefore be interpreted with caution.

Table 4: Treatment Hierarchy Ranked by Surface under the Cumulative Ranking Curve (SUCRA) Probabilities

Intervention Modality	SUCRA: Short-term VAS	SUCRA: Short-term ODI	SUCRA: Long-term VAS	SUCRA: Long-term ODI
Transforaminal (TFESI)	88.4%	85.2%	71.6%	68.3%
Parasagittal Interlaminar (PIL)	76.1%	72.8%	65.4%	62.1%
Midline Interlaminar (MIL)	42.5%	45.3%	38.2%	40.5%
Caudal (CESI)	31.2%	28.7%	26.5%	25.4%
Control/Placebo (Saline)	11.8%	18.0%	48.3%	53.7%

Discussion

Interpretation of Findings: In accordance with the methodological principles for synthesizing and interpreting meta-analytic data outlined by Forero et al. [28], the findings of this network meta-analysis extend beyond simple statistical superiority to highlight critical clinical nuances. Our synthesis demonstrates that while all epidural steroid injection (ESI) modalities provide superior short-term symptom mitigation compared to conservative controls [17], transforaminal (TFESI) and parasagittal interlaminar (PIL) approaches consistently outperform midline interlaminar (MIL) and caudal (CESI) techniques in the treatment of lumbar radiculopathy secondary to LDH.

Anatomical and Biomechanical Nuance: Reaching the Ventral Space: The clinical superiority of TFESI and PIL over traditional MIL is fundamentally rooted in spinal anatomy and fluid biomechanics. The primary nociceptive generator in lumbar disc herniation (LDH) is the interface between the herniated disc material and the inflamed nerve root, located in the anterior (ventral) epidural space [4,5].

- Midline Interlaminar (MIL): The traditional MIL approach frequently results in preferential spread of the injectate within the dorsal epidural space, separated from the target pathology by the thecal sac. This limits the concentration of corticosteroid reaching the inflamed ventral nerve root [9].
- Parasagittal Interlaminar (PIL): By directing the needle slightly lateral to the midline towards the symptomatic side, the PIL approach bypasses the posterior epidural median plica. Candido et al. demonstrated that the PIL approach significantly enhances the rate of targeted ventral epidural spread compared to MIL, delivering medication closer to the exact site of neural compression [9].
- Transforaminal (TFESI): TFESI provides the most direct and target-specific access. By advancing the needle directly into the neuroforamen, the physician reliably deposits a high concentration of medication directly into the ventral epidural space [12,13]. Desai et al. confirmed that achieving this specific ventral epidural contrast flow pattern correlates directly with superior clinical outcomes [42].

Balancing Efficacy and Safety: The Risk Profile of TFESI: While TFESI boasts the highest SUCRA probability for short-term pain relief and functional improvement, its application must be meticulously weighed against its unique complication profile [26,43]. TFESI carries an inherently higher incidence of intravascular needle penetration [16,44]. More alarmingly, it is uniquely associated with rare but catastrophic neurologic complications, including spinal cord infarction and permanent paraplegia [16,44]. These devastating events occur when particulate corticosteroids (e.g., triamcinolone, methylprednisolone) are inadvertently injected into a radicular artery; the particles aggregate and act as emboli, causing profound spinal ischemia [5,6].

To maximize safety without fully sacrificing efficacy, consensus guidelines strongly advocate for rigorous safeguards. Rathmell et al. emphasize that non-particulate steroids (e.g., dexamethasone) should be utilized as the first-line agent for TFESIs [5], alongside the mandatory use of real-time fluoroscopy with contrast enhancement or digital subtraction angiography to rule out vascular uptake prior to injection [5,14]. For patients where TFESI is deemed too high-risk—such as those with altered vascular anatomy or previous spinal surgery—the PIL approach offers a highly effective, safer alternative that mitigates the risk of catastrophic arterial embolization while still achieving excellent ventral flow [9,45].

Limitations and Future Directions: Several limitations in the current evidence base and our network geometry must be acknowledged. First, included RCTs exhibit clinical heterogeneity regarding baseline symptom duration, herniation level, and specific corticosteroid formulations. Second, while direct evidence comparing TFESI and MIL is robust, head-to-head trials exclusively isolating PIL against TFESI remain limited, requiring reliance on indirect network estimates; the PIL node relies partly on non-RCT anatomic evidence (e.g., contrast-flow studies), which is a methodological limitation. Third, as demonstrated in the results, therapeutic efficacy across all ESI modalities attenuates beyond six months [20] [22].

Future high-quality RCTs should prioritize direct head-to-head comparisons of PIL versus TFESI utilizing standardized non-particulate steroids, and should extend primary endpoints to evaluate objective long-term outcomes, specifically the rate at which these interventions avoid operative discectomy over a multi-year horizon [7] [8].

Conclusion

Based on this comprehensive network meta-analysis, transforaminal (TFESI) and parasagittal interlaminar (PIL) approaches offer superior short-term pain relief and functional restoration for lumbar radiculopathy compared to traditional midline interlaminar (MIL) and caudal (CESI) injections. While TFESI consistently ranks highest in clinical efficacy due to precise ventral epidural drug delivery, it carries an elevated risk of severe vascular complications, necessitating strict adherence to safety guidelines, real-time fluoroscopy, and the use of non-particulate steroids. The PIL approach emerges as a highly viable and effective alternative, balancing excellent ventral epidural spread with a more favorable safety profile. Ultimately, clinicians should tailor the choice of epidural approach based on individual patient anatomy, herniation level, and a rigorous risk-benefit analysis, moving away from MIL and CESI as first-line options for targeted unilateral radicular pain.

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