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The role of percutaneous neurolysis in lumbar disc herniation: systematic review and meta-analysis

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Background: Recalcitrant disc herniation may result in chronic lumbar radiculopathy or sciatica. Fluoroscopically directed epidural injections and other conservative modalities may provide inadequate improvement in some patients. In these cases, percutaneous neurolysis with targeted delivery of medications is often the next step in pain management.
Methods: An evidence-based system of methodologic assessment, namely, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used. Multiple databases were searched from 1966 to January 2021. Principles of the best evidence synthesis were incorporated into qualitative evidence synthesis. The primary outcome measure was the proportion of patients with significant pain relief and functional improvement (≥ 50%). Duration of relief was categorized as short-term (< 6 months) and long-term (≥ 6 months).
Results: This assessment identified one high-quality randomized controlled trial (RCT) and 5 moderate-quality non-randomized studies with an application of percutaneous neurolysis in disc herniation. Overall, the results were positive, with level II evidence.
Conclusions: Based on the present systematic review, with one RCT and 5 non-randomized studies, the evidence level is II for percutaneous neurolysis in managing lumbar disc herniation.

Key Words: Catheterization; Epidural Space; Evidence-Based Medicine; Intervertebral Disc Displacement; Low Back Pain; Meta-Analysis; Observational Study; Pain Management; Radiculopathy; Randomized Controlled Trial; Saline Solution, Hypertonic; Systematic Review.

INTRODUCTION

Chronic lumbar radicular pain or sciatica may be due to a multitude of reasons including disc herniation, spinal stenosis, and post-lumbar surgery syndrome [1]. There has been extensive literature since the initial description of disc herniation by Mixter and Barr in 1934 [2]. Symptomatic herniated lumbar disc was shown to be present in 1% to 3% [3], whereas the highest prevalence was among people aged 30 to 50 years [4]. Further, herniated discs occurred

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most commonly at the lower lumbar spine (L4/5 and L5/S1 levels) and also among those aged 25 to 55 years [5,6].

The mechanism of radicular pain in disc herniation may relate to mechanical compression or inflammation [1,7-10]. While surgical interventions are considered the mainstay of treatment for lumbar disc herniation or radiculopathy [11], multiple studies have shown epidural injections to be effective [1,10].

Epidurals with local anesthetics, with or without steroids, performed under fluoroscopic guidance, have been shown to be effective in managing disc herniation and radiculitis in multiple studies with level I evidence [1,10]. However, the failure of epidural injections may range from 30% to 50% of patients on a long-term basis. In such cases, percutaneous neurolysis may be employed in the nonsurgical management of chronic lumbar radicular pain [1,12].

Percutaneous neurolysis has been described to treat post-lumbar surgery syndrome and central spinal stenosis; however, systematic evaluations of effectiveness are lacking with disc herniation and chronic radicular pain [1,12-17]. Percutaneous neurolysis, epidural lysis, or lysis of epidural adhesions has been utilized for the past 30 years [1,12-17]. Epidural neurolysis is based on several premises, including that epidural fibrosis may present with low back pain and/or radicular pain, not only in post-surgical syndromes and spinal stenosis, but also disc displacements with leakage of disc materials. These adhesions can cause pain by immobilizing the nerve roots and also prevent injected materials from reaching the intended targets in the epidural space. As a result, pain relief can be achieved by removing these adhesions with the adhesiolysis (neurolysis) procedure that facilitates therapeutic medications reaching the target site and restores the normal movement of the nerve roots [1,12-16,18-25]. McCarron [20] showed that the nucleus pulposus produces local inflammation and scarring in the epidural space in dogs. Further, in humans, microstructural defects accumulate over time with age, and the nucleus pulposus protrudes deeper into the annulus, resulting in tears of the annulus and disc material leaking into the epidural space [21]. This may result in epidural adhesion formation and pain related to it, based on rich innervation of the posterior longitudinal ligament, which is an important source of back pain associated with epidural adhesions [22].

Thus, in the present investigation, we have sought to evaluate the effectiveness of percutaneous neurolysis in managing chronic lumbar disc herniation and lumbar radicular pain with a systematic review and meta-analysis.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [26] was used for methodological and reporting quality of the systematic review and meta-analysis. The objective was to assess the effectiveness of percutaneous neurolysis in managing chronic lumbar disc herniation and radiculopathy.

1. Inclusion criteria

All randomized controlled trials (RCTs) and observational studies with inclusion of patients with chronic disc herniation, undergoing percutaneous neurolysis with caudal, lumbar interlaminar, or lumbar transforaminal approaches were considered.

2. Outcome measures

The proportion of patients with significant (≥ 50%) pain relief and improvement in function was the primary outcome.

3. Data sources

All available studies in the English language, or with available translation, with appropriate reporting of outcomes data for 6 months were included. Searches were performed using multiple databases, including PubMed (www.ncbi.nlm.nih.gov/pubmed); the Cochrane Library (www.thecochranelibrary.com); the US National Guideline Clearinghouse (www.guideline.gov/); clinical trials (www.clinicaltrials.gov/); and Google Scholar (https://scholar.google.com) from 1966 to January 2021.

4. Search strategy

The search terminology was as follows:
((((((((((((((((chronic low back pain) OR nerve root compression) OR lumbosciatic pain) OR radicular pain) OR radiculitis) OR sciatica) OR disc herniation) AND ((((((((((epidural injection) OR epidural adhesiolysis OR neurolysis) OR epidural neuroplasty) OR epidural lysis of adhesions) OR percutaneous adhesiolysis OR neurolysis `OR transforaminal injection) OR corticosteroid) OR methylprednisolone) OR bupivacaine OR lidocaine))) AND ((meta-analysis [pt] OR randomized controlled trial [pt] OR controlled clinical trial [pt] OR systematic review OR randomized controlled trials [mh] OR nonrandomized studies OR observational studies OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw]

OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp])))).

5. Data collection and analysis

This review focused on percutaneous adhesiolysis/neurolysis for disc herniation with multiple approaches. All studies that provided appropriate outcome data and analysis for 6 months were reviewed. Book chapters, case reports, and reports without an appropriate diagnosis were not considered.

6. Inclusion criteria

Studies of interest included patients suffering from chronic lumbar radiculopathy due to disc herniation and treated with percutaneous epidural neurolysis or adhesiolysis. Studies of patients with fractures, malignancies, acute trauma, and inflammatory diseases were excluded. All RCTs and non-randomized studies with inclusion of at least 50 participants were included.

7. Data collection process

Identification of the relevant literature, the manuscript selection, and extraction of the data from the included studies was conducted independently by 2 of the review authors. Any disagreement between them was resolved by the third author. Any and all conflicts of interest of the reviewers with authorship of the manuscripts was resolved by assigning them to other reviewers.

8. Data synthesis and analysis

Two authors completed the quality assessment of each individual manuscript. Three authors completed evidence synthesis. All conflicts were resolved as stated above by a fourth author.

9. Risk of bias of individual studies

The quality of each RCT was assessed using the Cochrane review rating system (**Appendix Table 1**) [27] and Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment Tool (IPM-QRB) for RCTs (**Appendix Table 2**) [28]. Non-randomized or observational studies were assessed by Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for nonrandomized or observational studies (IPM-QRBNR) (**Appendix Table 3**) [29].

Randomized trials meeting at least 9 of the 13 inclusion criteria of the Cochrane review were considered high-quality. The trials meeting 5 to 8 criteria were considered moderate-quality, and those meeting fewer than 5 criteria were considered low-quality, and were excluded.

Based on the IPM-QRB and IPM-QRBNR criteria, randomized trials and observational studies meeting scores from 32 to 48 were considered high-quality, studies scoring from 16 to 31 were considered moderate quality; and studies scoring less than 16 were considered low quality, and were excluded.

Table 1. Qualitative modified approach to grading of evidence

Level I	Strong	Evidence obtained from multiple relevant high-quality randomized controlled trials for effectiveness or Evidence obtained from multiple relevant high quality observational studies or large case series for assessment of preventive measures, adverse consequences, and effectiveness of other measures.
Level II	Moderate	Evidence obtained from at least one relevant high-quality randomized controlled trial or multiple relevant moderate or low-quality randomized controlled trials or Evidence obtained from at least 2 high-quality relevant observational studies or large case series for assessment of preventive measures, adverse consequences, and effectiveness of other measures.
Level III	Fair	Evidence obtained from at least one relevant high-quality nonrandomized trial or observational study with multiple moderate or low-quality observational studies or At least one high-quality relevant observational studies or large case series for assessment of preventive measures, adverse consequences, and effectiveness of other measures.
Level IV	Limited	Evidence obtained from multiple moderate or low-quality relevant observational studies or Evidence obtained from moderate quality observational studies or large case series for assessment of preventive measures, adverse consequences, and effectiveness of other measures.
Level V	Consensus based	Opinion or consensus of large group of clinicians and/or scientists for effectiveness as well as to assess preventive measures, adverse consequences, and effectiveness of other measures.

Adapted from the article of Manchikanti et al. (Pain Physician 2014; 17: E319-25) [30].

10. Outcome of the studies

Clinically important outcome measures of 50% significant improvement from the baseline pain score, or a change of at least 3 points on an 11-point pain scale of 0 to 10 and a change of 30% or more on disability scores.

Based on the relevance and effectiveness of the neurolysis in disc herniation, either compared to a control group or from baseline to follow-up, a study was categorized as positive or negative/neutral. Reference point measurements were considered at 3 months, 6 months, and one year.

11. Analysis of evidence

The best-evidence synthesis developed by the American Society of Interventional Pain Physicians, modified and collated using multiple criteria, was used for qualitative analysis (**Table 1**) [30]. The evidence synthesis varied from strong to opinion- or consensus-based using 5 levels of evidence.

12. Meta-analysis

Software Review Manager (Rev Man 5.3) was used (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2008) for conventional or dual-arm meta-analysis. Software Comprehensive Meta-analysis version 3.0 was used (Biostat Inc., Englewood, NJ) for single-arm meta-analysis. The standardized mean differences with 95% confidence intervals were reported for pain and improvement of function data. Data were plotted by using forest plots to evaluate treatment effects. Heterogeneity was interpreted through I^2 statistics.

RESULTS

1. Study selection

Fig. 1 shows a flow diagram of the study selection using the PRISMA study selection process [26].

Based on the search criteria, 13 manuscripts were identified and considered for inclusion [18,25,31-41]. A total of 6 studies met the inclusion criteria [25,31,33,37,38,40]. Of the 6 studies included, 2 of them [18,41] studied disc prolapse, along with post-lumbar surgery syndrome, and subgroup data analysis was not available. One study had a small sample size of 20 patients [34].

Four studies were excluded due to short-term follow-up of 6 months since less than a 3-month follow-up would not provide any long-term clinical relevance [32,35,36,39]. Of these, there was only one placebo-controlled RCT [25].

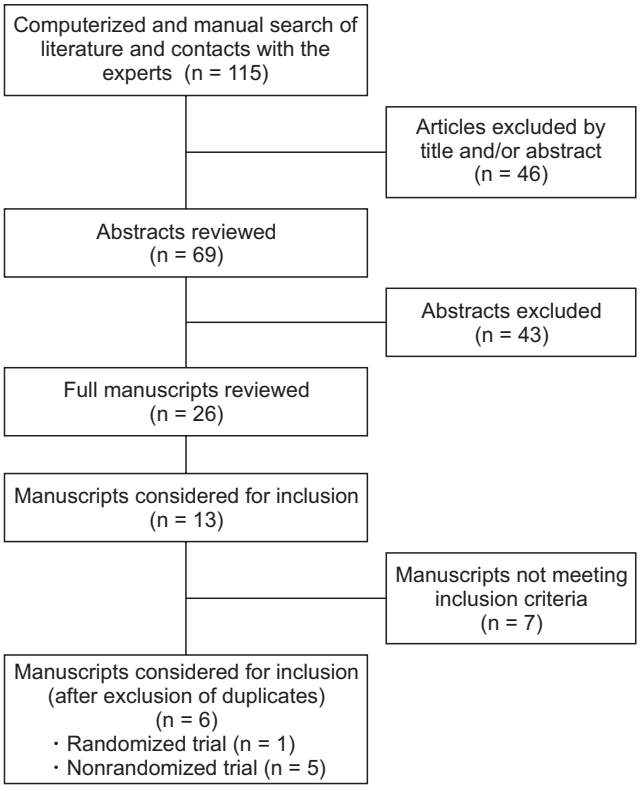

Fig. 1. Flow diagram illustrating published literature evaluating percutaneous adhesiolysis/neurolysis in lumbar disc herniation.

2. Methodologic quality and risk of bias assessment

Of the 6 manuscripts meeting inclusion criteria [25,31,33,37,38,40], there was only one placebo-controlled RCT [25]. **Appendix Tables 4 and 5** show the methodologic quality assessment and risk of bias of the one RCT utilizing the Cochrane review criteria and the IPM-QRB criteria respectively [27,28]. Assessment by the Cochrane review criteria and IPM-QRB of this RCT showed high quality [25].

Appendix Table 6 shows the assessment of the included nonrandomized or observational studies, utilizing IPM-QRBNR criteria. Five studies [31,33,37,38,40] were included. Assessment by IPM-QRBNR showed all studies to be of moderate quality.

3. Study characteristics

Table 2 shows the characteristics and outcomes of the studies meeting the inclusion criteria which involved receiving percutaneous adhesiolysis/neurolysis for lumbar disc herniation.

4. Qualitative analysis

Qualitative analysis was performed utilizing a modified

Table 2. Characteristics of included studies of percutaneous adhesiolysis/neurolysis in lumbar disc herniation

Study	Study characteristics	Methodological quality scoring	Participants and interventions	Outcome measures	Pain relief and function			Results			Comment(s)
					3 mo	6 mo	12 mo	Short-term	Long-term		
								≤ 3 mo	> 6 mo	≥ 12 mo	
Gerdesmeyer et al., 2013 [25]	RA, PC, DB Chronic lumbar radicular pain lasting longer than 4 months	Quality scores: Cochrane: 13/13 IPM-QRB 41/48	The authors screened 90 patients from 381 patients with chronic radicular pain lasting longer than 4 months over a period of 4 years. Randomization: Placebo control group = 44 • In the placebo group, a needle and catheter was inserted through caudal approach and the needle was intentionally inserted without entering the spinal canal and the catheter was inserted into the subcutaneous tissue overlying the afflicted level. • 10 mL of preservative-free sodium chloride solution was injected for 3 days and the catheter was removed. Neurolysis group = 46 • The catheter was placed through sacral canal with injection of 10 mL of contrast with identification of filling defects. Subsequently a Tun-L catheter was inserted through the epidural needle and advanced to the anterolateral area of the filling defect. • Local anesthetic, 10 mL, 0.25% bupivacaine was injected through the catheter, followed by 10 mL of preservative free sodium chloride solution containing 150 units per mL of hyaluronidase. • Sodium chloride solution, 10 mL, 10%, containing 40 mg of triamcinolone was then injected slowly, along with 2 mL of 0.25% bupivacaine. • On the 2nd and 3rd days, 10 mL of 0.25% bupivacaine was injected through the catheter, followed by slow injection of 10 mL of 10% sodium chloride solution and 2 mL, 0.25% bupivacaine. The catheter was removed on the third day in both groups.	Primary outcome measure: ODI at 3, 6, and 12 months VAS: At least 50% reduction in ODI scores and VAS scores at 3, 6, and 12 months after treatment	Placebo group = 17% (7/42) Lysis group = 58% (26/45)	Placebo group = 11% (4/37) Lysis group = 74% (31/42)	Placebo group = 35% (9/26) Lysis group = 90% (28/31)	P	P	P	This is the first true placebo controlled trial, injecting and inert substance into an inert structure, yet it showed positive response in some patients. Overall, there were significant differences in the active treatment group and lysis group compared to placebo group. Ten-year follow-up also showed significant improvement and surgery was avoided in majority of the patients. Surgery was avoided in 85% of the patients.

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Table 2. Continued

Study	Study characteristics	Methodological quality scoring	Participants and interventions	Outcome measures	Pain relief and function			Results			Comment(s)
					3 mo	6 mo	12 mo	Short-term	Long-term		
								≤ 3 mo	> 6 mo	≥ 12 mo	
Ji et al., 2015 [40]	Retrospective Lumbar disc herniation	Quality Scores: IPM-QRB-NR 30/48	Authors studied correlation of dural sac cross sectional area with a single-level disc disease and effectiveness of percutaneous epiduroplasty. Number of patients = 363 Categorization to spinal canal compromise Category 1 – less or more than 50% Category 2 – lesser than one-third, between a third and two-thirds, and more than two-thirds with subcategories • Catheterization was performed with a caudal approach. After final positioning of the Racz catheter, 6 mL of 0.2% preservative free ropivacaine containing 1,500 units of hyaluronidase and 4 mL of 40% triamcinolone acetate was injected. • One-hour after the procedure, 6 mL of 8% sodium chloride solution was infused over 30 minutes in the recovery room under monitoring. • Epidural catheter was removed.	VAS for back pain and leg pain, Odom's criteria Assessment intervals: 3, 6, 12, and 24 months	SI in VAS	SI in VAS	SI in VAS	SI in VAS	SI in VAS	SI in VAS	This study looking at dural cross sectional area in single level disc disease showed no significant difference based on dural sac cross sectional area. The results show that percutaneous epidural neuroplasty is an effective procedure in treating single-level lumbar disc herniation without affecting dural sac cross sectional area.
Moon et al., 2017 [33]	Retrospective Lumbar disc herniation	Quality Scores: IPM-QRB-NR 30/48	• 407 patients were evaluated retrospectively to predict the outcome of percutaneous epidural adhesiolysis in patients with lumbar disc herniation. • All patients underwent percutaneous adhesiolysis with an RK needle and Racz catheter through caudal approach. After final positioning of the catheter in the anterior epidural space of the target site, 3-5 mL of 1% lidocaine was administered as a test dose. This was followed by 10 mL of 0.9% sodium chloride solution, followed by injection of 0.125% bupivacaine mixed with 5 mg of dexamethasone. • After 5 minutes, 10 mL of 10% sodium chloride solution was slowly injected under real-time fluoroscopic guidance. • Catheter was removed and insertion site was sutured.	The primary outcome measure was substantial response of 4 or more points or 50% of pain relief in the numerical rate scaling pain score, 12 months after treatment. Repeat procedure was performed if needed at 3 months. Six-months not available.	NA	NA	SI in 72.2% of patients	NA	NA	P	This is a positive study with long-term follow-up assessing factors predicting favorable outcome of percutaneous epidural adhesiolysis. The presence of high intensity zone on magnetic resonance imaging was a predictor of substantial response to percutaneous epidural adhesiolysis for 12 months.

Table 2. Continued

Study	Study characteristics	Methodological quality scoring	Participants and interventions	Outcome measures	Pain relief and function			Results			Comment(s)
					3 mo	6 mo	12 mo	Short-term	Long-term		
								≤ 3 mo	> 6 mo	≥ 12 mo	
Cho et al., 2019 [31]	Retrospective Lumbar disc herniation	Quality Scores: IPM-QRB-NR 30/48	• This study included 430 consecutive patients with a single-level disc herniation undergoing percutaneous epidural neuroplasty. Authors categories LDH type as bulging, protrusion, extrusion, and sequestration. LDH type inclusion: bulging 124, protrusion 240, extrusion 56, sequestration 10, total 430. • All patients were treated with percutaneous adhesiolysis or neuroplasty through a caudal approach with placement of the catheter ventrally and laterally. Following the satisfactory positioning of the catheter and injection of contrast, 6 mL of 0.2% preservative free ropivacaine containing 1,500 units of hyaluronidase and 4 mL of betamethasone sodium phosphate was injected. • One hour after the procedure, 6 mL of 8% sodium chloride solution was infused over a period of 30 minutes under monitoring in the recovery room. Epidural catheter was removed.	VAS for back pain and leg pain, Odom's criteria with classification of outcomes as excellent, good, fair or poor. Outcomes were recorded at 1, 3, 6, and 12 months	Significant decrease in VAS scores for back and leg pain	Significant decrease in VAS scores for back and leg pain	Significant decrease in VAS scores for back and leg pain	Good or excellent outcome = 73.1	Good or excellent outcome = 74.8	Good or excellent outcome = 71.7	Overall, this is a positive study with positive results with a single treatment of one-day percutaneous adhesiolysis providing improvement in VAS of back and leg pain lasting for one-year. Surgery was avoided in more than 70% of the patients with extrusion or sequestration. Patients with Pfirrmann's Grades 1 to 3, shows a significantly higher rate of subsequent surgery than with Pfirrmann Grade 0.

Table 2. Continued

Study	Study characteristics	Methodological quality scoring	Participants and interventions	Outcome measures	Pain relief and function			Results			Comment(s)
					3 mo	6 mo	12 mo	Short-term	Long-term		
								≤ 3 mo	> 6 mo	≥ 12 mo	
Park et al., 2018 [37]	Retrospective Lumbar disc herniation and/or spinal stenosis	Quality Scores: IPM-QRB-NR 29/48	Authors sought to evaluate clinical significance of epidurography contrast patterns after adhesiolysis. Number of patients = 78 • Both spinal stenosis and disc herniation patients were included without separating the data. • Procedure was performed with caudal entry. After appropriate positioning of the catheter, a mixture of 10 mL of 0.9% sodium chloride solution and 300 units of hyaluronidase was injected. Following this, another epidurogram was carried out. After epidurogram a mixture of 0.2% ropivacaine 8 mL and 40 mg of triamcinolone was slowly injected. • Significant improvement in VAS scores, back pain and leg pain • Significant improvement in ODI scores • Extraforaminal leakage of the contrast was associated with a tendency for decreased pain and significant better quality of life.	VAS, ODI, 12-item short-form health survey (SF-32) Outcomes assessed at 1, 3, 6, and 12 months	SI	SI	SI	P	P	P	In this study assessing clinical significance of epidurography contrast patterns, authors reported positive results and authors also showed that when there is extraforaminal contrast spread, outcomes were superior.

Table 2. Continued

Study	Study characteristics	Methodological quality scoring	Participants and interventions	Outcome measures	Pain relief and function			Results			Comment(s)
					3 mo	6 mo	12 mo	Short-term	Long-term		
								≤ 3 mo	> 6 mo	≥ 12 mo	
Choi et al., 2017 [38]	Retrospective Lumbar disc herniation and/or spinal stenosis	Quality Scores: IPM-QRB-NR 30/48	• This study included 543 patients assessing 5% or 10% hypertonic sodium chloride solution injection. • 5% group = 333 • 10% group = 210 • Procedure was performed with a caudal entry and catheterization after final catheter position was achieved. 5 mL of 0.25% ropivacaine containing 1,500 units of hyaluronidase was injected. After confirming the absence of any complications, 6 mL of 10% or 5% sodium chloride solution was injected at a rate of 1 mL every 15 minutes for 1.5 hours. This was followed by injection of 2 mL of 0.9% sodium chloride solution containing 40 mg of triamcinolone. • Epidural catheter was removed before discharging the patients	NRS	No significant differences between the groups. Both groups showed significant improvement in pain rating.	No significant differences between the groups. Both groups showed significant improvement in pain rating.	NA	P	P	NA	Short-term follow-up with positive outcomes showing no significant difference between 5% or 10% sodium chloride solution.

RA: randomized, PC: placebo control, DB: double-blind, ODI: Oswestry Disability Index, VAS: visual analog scale, SI: significant improvement, NA: not applicable, P: positive, IPM-QRB: Interventional Pain Management techniques – Quality Appraisal of Reliability and Risk of Bias Assessment, IPM-QRBNR: Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Non-randomized Studies, NRS: numeric rating scale, LDH: lumbar disc herniation.

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approach for the grading of evidence [28] with moderate (level II) evidence from one relevant high-quality RCT and 5 relevant moderate-quality observational studies. All of the studies consistently showed improvement in patients undergoing neurolysis at 6 months and one-year follow-up periods.

5. Quantitative analysis

1) Single-arm meta-analysis

Conventional dual-arm analysis was not feasible due to only one RCT being available. Consequently, single-arm meta-analysis was performed in observational studies for pain relief and functional status improvement, utilizing data from 5 studies [31,33,37,38,40].

2) 6-month follow-up

Fig. 2 shows results of the 6-month follow-up. As shown in **Fig. 2A**, there were 5 studies [25,31,37,38,40] included in this single-arm meta-analysis, and the results showed an improvement in the numeric rating scale (NRS) pain scores at 6 months after adhesiolysis/neurolysis, with an average of 2.678 ($P < 0.001$).

As shown in **Fig. 2B**, there were 2 studies [25,37] included in this single-arm meta-analysis, and the results showed an improvement in the functionality scores at 6 months after adhesiolysis/neurolysis, with an average of 9.977 (on 0-50 scale) ($P < 0.001$).

3) One-year follow-up

Fig. 3 shows results of the one-year follow-up. As shown in **Fig. 3A**, there were 5 studies [25,31,33,37,40] included in this single-arm meta-analysis, and the results showed an improvement in the NRS pain scores at 12 months after adhesiolysis/neurolysis, with an average of 2.013, which was statistically significant ($P < 0.001$).

As shown in **Fig. 3B**, there were 2 studies [25,37] included in this single-arm meta-analysis, and the results showed an improvement in the Oswestry Disability Index (ODI) functionality scores after adhesiolysis/neurolysis at 12 months, with an average of 10.268 (on 0-50 scale) ($P < 0.001$).

DISCUSSION

Analysis of the effectiveness of percutaneous adhesiolysis/

A

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	P value
Choi et al., 2017 [38]	−2.640	0.084	0.007	−2.805	−2.475	−31.429	0.000
Gerdesmeyer et al., 2013 [25]	−2.400	0.184	0.034	−2.761	−2.039	−13.043	0.000
Cho et al., 2019 [31]	−2.700	0.082	0.007	−2.861	−2.539	−32.935	0.000
Park et al., 2018 [37]	−2.900	0.277	0.077	−3.443	−2.357	−10.469	0.000
Ji et al., 2015 [40]	−2.760	0.106	0.011	−2.967	−2.553	−26.161	0.000
	−2.678	0.049	0.002	−2.773	−2.583	−55.071	0.000

Statistics for each study

Difference in means and 95% CI

−4.00 −2.00 0.00 2.00 4.00

Heterogeneity				Tau-squared			
Q-value	df (Q)	P value	I-sauared	Tau squared	Standard error	Variance	Tau
3.906	4	0.433	0.000	0.000	0.009	0.000	0.000

B

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	P value
Gerdesmeyer et al., 2013 [25]	−14.500	1.438	2.068	−17.318	−11.682	−10.083	0.000
Park et al., 2018 [37]	−8.400	0.849	0.721	−10.064	−6.736	−9.894	0.000
	−9.977	0.731	0.534	−11.410	−8.544	−13.646	0.000

Statistics for each study

Difference in means and 95% CI

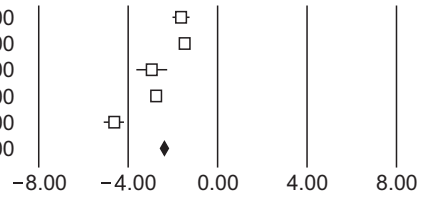
−20.00 −10.00 0.00 10.00 20.00

Heterogeneity				Tau-squared			
Q-value	df (Q)	P value	I-sauared	Tau squared	Standard error	Variance	Tau
13.343	1	0.000	92.506	17.211	26.311	692.292	4.149

Fig. 2. Changes in pain and functional status from baseline at 6 months. (A) Change in pain levels using the numeric rating scale from baseline at 6 months in patients treated with adhesiolysis/neurolysis. (B) Change in functionality status scores using the Oswestry Disability Index from baseline at 6 months in patients treated with adhesiolysis/neurolysis. CI: confidence interval, df: degrees of freedom.

A

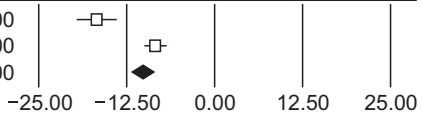
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P* value
Gerdesmeyer et al., 2013 [25]	−1.600	0.184	0.034	−1.961	−1.239	−8.696	0.000
Cho et al., 2019 [31]	−1.400	0.072	0.005	−1.542	−1.258	−19.384	0.000
Park et al., 2018 [37]	−2.900	0.328	0.108	−3.543	−2.257	−8.841	0.000
Ji et al., 2015 [40]	−2.690	0.110	0.012	−2.906	−2.474	−24.455	0.000
Moon et al., 2017 [33]	−4.600	0.199	0.040	−4.990	−4.210	−23.116	0.000
	−2.013	0.054	0.003	−2.120	−1.907	−37.013	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	*P* value	I-sauared	Tau squared	Standard error	Variance	Tau
291.116	4	0.000	98.626	1.402	1.300	1.690	1.184

B

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-value	*P* value
Gerdesmeyer et al., 2013 [25]	−16.800	1.482	2.196	−19.705	−13.895	−11.336	0.000
Park et al., 2018 [37]	−8.400	0.793	0.628	−9.953	−6.847	−10.598	0.000
	−10.268	0.699	0.488	−11.638	−8.898	−14.692	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	*P* value	I-sauared	Tau squared	Standard error	Variance	Tau
24.981	1	0.000	95.997	33.868	49.893	2489.357	5.820

Fig. 3. Changes in pain and functional status from baseline at 12 months. (A) Change in pain levels using the numeric rating scale from baseline at 12 months in patients treated with adhesiolysis/neurolysis. (B) Change in functionality scores using the Oswestry Disability Index from baseline at 12 months in patients treated with adhesiolysis/neurolysis. CI: confidence interval, df: degrees of freedom.

neurolysis in managing lumbar disc herniation showed Level II or moderate evidence in the present systematic review and meta-analysis, which included one RCT and 5 observational studies with at least 6 months of follow-up in one study and 12 months of follow-up in all the others.

The single RCT by Gerdesmeyer et al. [25], in a well-designed, relevant, high-quality RCT, studied 90 patients with 44 patients in the placebo group and 46 patients in the neurolysis group. In the placebo design, a needle and catheter were inserted through a caudal approach. The needle was intentionally inserted without entering the spinal canal and the catheter was inserted into the subcutaneous tissue overlying the afflicted level. In the neurolysis group, the catheter was placed over the lumbar spine with adhesiolysis, followed by an injection of local anesthetic, hyaluronidase, and a steroid. In both groups, the catheters were left for 3 days and additional injections were performed.

The results showed, at one year, greater than 50% improvement in the ODI was seen in 90% of the patients in the lysis group, whereas it was seen in 35% of the patients in the placebo group. In reference to the observational studies, all 5 studies [31,33,37,38,40] were of moderate quality with inclusion of a large number of patients. Of the 5 studies meeting inclusion criteria, only one study by Park et al. [37] had less than 100 patients, with an inclusion of 78 patients. However, the other 4 studies included a large patient population ranging from 363 to 543 [31,33,38,40]. Total number of patients included in the observational studies were 1,821, assessing the role of percutaneous neurolysis in managing lumbar disc herniation or chronic lumbar radiculopathy. Consequently, the results of this study provide robust evidence from one high-quality RCT [25] and 5 observational studies [31,33,37,38,40] with a large proportion of patients with at least one-year follow-up in 4 studies [31,33,37,40] and 6-month follow-up in one study [38]. Overall, the number of patients included in long-term follow-up, including the RCT, were 1,268.

The present investigation is the first systematic review and meta-analysis focused on determining the role of neurolysis in managing chronic recalcitrant disc herniation or chronic lumbar radicular pain. The results of this systematic review and meta-analysis are similar to the results of systematic reviews and meta-analyses performed in post-lumbar surgery syndrome and central spinal stenosis [12-16]. Caudal epidural injections have been used since 1901, with a description of entering the epidural space from the sacral hiatus [1,42,43]. Epidural injections are also performed with an interlaminar or transforaminal approach [1]. However, the caudal approach, even though it requires

higher volumes, has been considered the safest and earliest technique. The most common approach for percutaneous neurolysis is through the sacral hiatus [1]. The majority of the studies were related to entry through the sacral hiatus. Administration of steroids in the epidural injections was described by Robecchi and Capra [44] and Lievre et al. [45] in 1952 and 1953. Effectiveness, safety, cost utility, and utilization patterns of epidural interventions have been extensively described [1,10,46-50].

Epidural injections have been shown to be with level I evidence in managing disc herniation or chronic lumbar radiculopathy with all 3 approaches, namely caudal, interlaminar, and transforaminal [1]. However, there also have been negative studies in the literature as well [51]. There have been significant discussions on this subject, including various types of bias in studies in interventional pain management [1,10]. In fact, Manchikanti et al. [10] performed a comparative systematic review and meta-analysis of the study by Chou et al. [51], which showed significantly different results when the analysis was performed utilizing methodology that did not convert active-controlled trials to placebo-controlled trials. Similar issues were also raised with findings of systematic reviews in assessing multiple interventional techniques, including the effectiveness of percutaneous adhesiolysis in post-lumbar surgery syndrome [13,15,16,52].

Limitations of this systematic review include lack of multiple RCTs, and the large scale observational studies are of only moderate quality.

In conclusion, the present systematic review and meta-analysis of epidural neurolysis in management of chronic recalcitrant disc herniation or lumbar radiculopathy shows level II evidence, based on one relevant, high-quality RCT [25] and 5 relevant moderate-quality observational studies [31,33,37,38,40]. The present analysis has not shown any significant side effects or complications derived from these studies.

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CONFLICT OF INTEREST

Dr. Hirsch is a consultant for Medtronic and Senior Affiliate Research Fellow at the Neiman Policy Institute.

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Appendices

Appendix Table 1. Sources of risk of bias and Cochrane review rating system

Bias domain		Source of bias	Possible answers
Selection	(1) Was the method of randomization adequate?	A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a dice (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, preordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and preordered list of treatment assignments. Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number.	Yes/No/Unsure
Selection	(2) Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/Unsure
Performance	(3) Was the patient blinded to the intervention?	Index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.	Yes/No/Unsure
Performance	(4) Was the care provider blinded to the intervention?	Index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.	Yes/No/Unsure
Detection	(5) Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for each primary outcome separately. This item should be scored ''yes'' if the success of blinding was tested among the outcome assessors and it was successful or: • for patient-reported outcomes in which the patient is the outcome assessor (*e.g.*, pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored ''yes'' • for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (*e.g.*, clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination • for outcome criteria that do not suppose a contact with participants (*e.g.*, radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome • for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (*e.g.*, cointerventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item ''4'' (caregivers) is scored ''yes'' • for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data	Yes/No/Unsure
Attrition	(6) Was the drop-out rate described and acceptable?	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a ''yes'' is scored. (N.B. these percentages are arbitrary, not supported by literature).	Yes/No/Unsure
Attrition	(7) Were all randomized participants analyzed in the group to which they were allocated?	All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of noncompliance and cointerventions.	Yes/No/Unsure
Reporting	(8) Are reports of the study free of suggestion of selective outcome reporting?	All the results from all prespecified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.	Yes/No/Unsure

Appendix Table 1. Continued

Bias domain		Source of bias	Possible answers
Selection	(9) Were the groups similar at baseline regarding the most important prognostic indicators?	Groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).	Yes/No/Unsure
Performance	(10) Were cointerventions avoided or similar?	If there were no cointerventions or they were similar between the index and control groups.	Yes/No/Unsure
Performance	(11) Was the compliance acceptable in all groups?	The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered for several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (*e.g.*, surgery), this item is irrelevant.	Yes/No/Unsure
Detection	(12) Was the timing of the outcome assessment similar in all groups?	Timing of outcome assessment should be identical for all intervention groups and for all primary outcome measures.	Yes/No/Unsure
Other	(13) Are other sources of potential bias unlikely?	Other types of biases. For example: • When the outcome measures were not valid. There should be evidence from a previous or present scientific study that the primary outcome can be considered valid in the context of the present. • Industry-sponsored trials. The conflict of interest (COI) statement should explicitly state that the researchers have had full possession of the trial process from planning to reporting without funders with potential COI having any possibility to interfere in the process. If, for example, the statistical analyses have been done by a funder with a potential COI, usually ''unsure'' is scored.	Yes/No/Unsure

Source: Furlan et al.; Editorial Board of the Cochrane Back, Neck Group. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. Spine (Phila Pa 1976) 2015; 40: 1660-73 [27].

Appendix Table 2. Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM-QRB

		Scoring
I.	TRIAL DESIGN AND GUIDANCE REPORTING	
1.	CONSORT or SPIRIT	
	Trial designed and reported without any guidance	0
	Trial designed and reported utilizing minimum criteria other than CONSORT or SPIRIT criteria or trial was conducted prior to 2005	1
	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	2
	Explicit use of CONSORT or SPIRIT with identification of criteria or trial conducted with high level reporting and criteria or conducted before 2005	3
II.	DESIGN FACTORS	
2.	Type and Design of Trial	
	Poorly designed control group (quasi selection, convenient sampling)	0
	Proper active-control or sham procedure with injection of active agent	2
	Proper placebo control (no active solutions into active structures)	3
3.	Setting/Physician	
	General setting with no specialty affiliation and general physician	0
	Specialty of anesthesia/PMR/neurology/radiology/ortho, etc.	1
	Interventional pain management with interventional pain management physician	2
4.	Imaging	
	Blind procedures	0
	Ultrasound	1
	CT	2
	Fluoro	3
5.	Sample Size	
	Less than 50 participants in the study without appropriate sample size determination	0
	Sample size calculation with less than 25 patients in each group	1
	Appropriate sample size calculation with at least 25 patients in each group	2
	Appropriate sample size calculation with 50 patients in each group	3
6.	Statistical Methodology	
	None or inappropriate	0
	Appropriate	1
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	
7a.	For epidural procedures:	
	Poorly identified mixed population	0
	Clearly identified mixed population	1
	Disorders specific trials (*i.e.*, well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post-surgery syndrome)	2
7b.	For facet or sacroiliac joint interventions:	
	No diagnostic blocks	0
	Selection with single diagnostic blocks	1
	Selection with placebo or dual diagnostic blocks	2
8.	Duration of Pain	
	Less than 3 months	0
	3 to 6 months	1
	> 6 months	2
9.	Previous Treatments	
	Conservative management including drug therapy, exercise therapy, physical therapy, etc.	
	Were not utilized	0
	Were utilized sporadically in some patients	1
	Were utilized in all patients	2

Appendix Table 2. Continued

		Scoring
10.	Duration of Follow-up with Appropriate Interventions	
	Less than 3 months or 12 weeks for epidural or facet joint procedures, etc. and 6 months for intradiscal procedures and implantables	0
	3 to 6 months for epidural or facet joint procedures, etc., or 1 year for intradiscal procedures or implantables	1
	6 months to 17 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables	2
	18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables	3
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	
	No descriptions of outcomes OR < 20% change in pain rating or functional status	0
	Pain rating with a decrease of 2 or more points or more than 20% reduction OR functional status improvement of more than 20%	1
	Pain rating with decrease of ≥ 2 points 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 OR functional status improvement with a 50% or 40% reduction in disability score	2
	Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores	4
12.	Analysis of all Randomized Participants in the Groups	
	Not performed	0
	Performed without intent-to-treat analysis without inclusion of all randomized participants	1
	All participants included with or without intent-to-treat analysis	2
13.	Description of Drop Out Rate	
	No description of dropouts, despite reporting of incomplete data or ≥ 20% withdrawal	0
	Less than 20% withdrawal in one year in any group	1
	Less than 30% withdrawal at 2 years in any group	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	
	Groups dissimilar with significant influence on outcomes with or without appropriate randomization and allocation	0
	Groups dissimilar without influence on outcomes despite appropriate randomization and allocation	1
	Groups similar with appropriate randomization and allocation	2
15.	Role of Co-Interventions	
	Co-interventions were provided but were not similar in the majority of participants	0
	No co-interventions or similar co-interventions were provided in the majority of the participants	1
V.	RANDOMIZATION	
16.	Method of Randomization	
	Quasi randomized or poorly randomized or not described	0
	Adequate randomization (coin toss, drawing of balls of different colors, drawing of ballots)	1
	High quality randomization (Computer generated random sequence, pre-ordered sealed envelopes, sequentially ordered vials, telephone call, pre-ordered list of treatment assignments, etc.)	2
VI.	ALLOCATION CONCEALMENT	
17.	Concealed Treatment Allocation	
	Poor concealment of allocation (open enrollment) or inadequate description of concealment	0
	Concealment of allocation with borderline or good description of the process with probability of failure of concealment	1
	High quality concealment with strict controls (independent assignment without influence on the assignment sequence)	2
VII.	BLINDING	
18.	Patient Blinding	
	Patients not blinded	0
	Patients blinded adequately	1
19.	Care Provider Blinding	
	Care provider not blinded	0
	Care provider blinded adequately	1

Appendix Table 2. Continued

		Scoring
20.	Outcome Assessor Blinding	
	Outcome assessor not blinded or was able to identify the groups	0
	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.)	1
VIII.	CONFLICTS OF INTEREST	
21.	Funding and Sponsorship	
	Trial included industry employees	-3
	Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts	-3
	Industry or organizational funding with reimbursement of expenses with some involvement	0
	Industry or organization funding of expenses without involvement	1
	Funding by internal resources only with supporting entity unrelated to industry	2
	Governmental funding without conflict such as NIH, NHS, AHRQ	3
22.	Conflicts of Interest	
	None disclosed with potential implied conflict	0
	Marginally disclosed with potential conflict	1
	Well disclosed with minor conflicts	2
	Well disclosed with no conflicts	3
	Hidden conflicts with poor disclosure	–1
	Misleading disclosure with conflicts	–2
	Major impact related to conflicts	–3
TOTAL		48

IPM-QRB: Interventional Pain Management techniques – Quality Appraisal of Reliability and Risk of Bias Assessment.
Source: Manchikanti et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. Pain Physician 2014; 17: E263-E290 [28].

Appendix Table 3. IPM checklist for assessment of nonrandomized or observational studies of IPM techniques utilizing IPM-QRBNR

		Scoring
I.	STUDY DESIGN AND GUIDANCE REPORTING	
1.	STROBE or TREND Guidance	
	Case Report/Case Series	0
	Study designed without any guidance	1
	Study designed with minimal criteria and reporting with or without guidance	2
	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	3
	Designed with high level criteria or explicitly uses STROBE or TREND with identification of criteria or conducted prior to 2011	4
II.	DESIGN FACTORS	
2.	Study Design and Type	
	Case report or series (uncontrolled – longitudinal)	0
	Retrospective cohort or cross-sectional study	1
	Prospective cohort case-control study	2
	Prospective case control study	3
	Prospective, controlled, nonrandomized	4
3.	Setting/Physician	
	General setting with no specialty affiliation and general physician	0
	Specialty of anesthesia/PMR/neurology, etc.	1
	Interventional pain management with interventional pain management physician	2
4.	Imaging	
	Blind procedures	0
	Ultrasound	1
	CT	2
	Fluoroscopy	3
5.	Sample Size	
	Less than 100 participants without appropriate sample size determination	0
	At least 100 participants in the study without appropriate sample size determination	1
	Sample size calculation with less than 50 patients in each group	2
	Appropriate sample size calculation with at least 50 patients in each group	3
	Appropriate sample size calculation with 100 patients in each group	4
6.	Statistical Methodology	
	None	0
	Some statistics	1
	Appropriate	2
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	
7a.	For epidural procedures:	
	Poorly identified mixed population	1
	Poorly identified mixed population with large sample (≥ 200)	2
	Clearly identified mixed population	3
	Disorders specific trials (*i.e.*, well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post-surgery syndrome)	4
7b.	For facet or sacroiliac joint interventions:	
	No specific selection criteria	1
	No diagnostic blocks based on clinical symptomatology	2
	Selection with single diagnostic blocks	3
	Selection with placebo or dual diagnostic blocks	4
8.	Duration of Pain	
	Less than 3 months	0
	3 to 6 months	1
	> 6 months	2
9.	Previous Treatments	
	Conservative management including drug therapy, exercise therapy, physical therapy, etc.	
	Were not utilized	0
	Were utilized sporadically in some patients	1
	Were utilized in all patients	2

Appendix Table 3. Continued

		Scoring
10.	Duration of Follow-up with Appropriate Interventions	
	Less than 3 months or less for epidural or facet joint procedures, etc., and 6 months for intradiscal procedures and implantables	1
	3-6 months for epidural or facet joint procedures, etc., or one year for intradiscal procedures or implantables	2
	6-12 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	4
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	
	No descriptions of outcomes OR < 20% change in pain rating or functional status	0
	Pain rating with a decrease of 2 or more points or more than 20% reduction OR functional status improvement of more than 20%	1
	Pain rating with decrease of ≥ 2 points 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 OR functional status improvement with a 50% or 40% reduction in disability score	2
	Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores	4
12.	Description of Drop Out Rate	
	No description despite reporting of incomplete data or more than 30% withdrawal	0
	Less than 30% withdrawal in one year in any group	1
	Less than 40% withdrawal at 2 years in any group	2
13.	Similarity of Groups at Baseline for Important Prognostic Indicators	
	No groups or groups dissimilar with significant influence on outcomes	0
	Groups dissimilar without significant influence on outcomes	1
	Groups similar	2
14.	Role of Co-Interventions	
	Dissimilar co-interventions or similar co-interventions in some of the participants	1
	No co-interventions or similar co-interventions in majority of the participants	2
V.	ASSIGNMENT	
15.	Method of Assignment of Participants	
	Case report/case series or selective assignment based on outcomes or retrospective evaluation based on clinical criteria	1
	Prospective study with inclusion without specific criteria	2
	Retrospective method with inclusion of all participants or random selection of retrospective data	3
	Prospective, well-defined assignment of methodology and inclusion criteria (quasi randomization, matching, stratification, etc.)	4
VI.	CONFLICTS OF INTEREST	
16.	Funding and Sponsorship	
	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	-3
	Industry or organizational funding with reimbursement of expenses with some involvement or no information available	0
	Industry or organization funding of expenses without involvement	1
	Funding by internal resources only	2
	Governmental funding without conflict such as NIH, NHS, AHRQ	3
TOTAL MAXIMUM		48

IPM-QRBNR: Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies.
Source: Manchikanti et al. Development of an interventional pain management specific instrument for methodologic quality assessment of nonrandomized studies of interventional techniques. Pain Physician 2014; 17: E291-317 [29].

Appendix Table 4. Methodological quality assessment of randomized trials of percutaneous adhesiolysis/neurolysis in lumbar disc herniation utilizing Cochrane review criteria

	Gerdesmeyer et al. [25]
Randomization adequate	+
Concealed treatment allocation	+
Patient blinded	+
Care provider blinded	+
Outcome assessor blinded	+
Drop-out rate described	+
All randomized participants analyzed in the group	+
Reports of the study free of suggestion of selective outcome reporting	+
Groups similar at baseline regarding most important prognostic indicators	+
Co-interventions avoided or similar	+
Compliance acceptable in all group	+
Time of outcome assessment in all groups similar	+
Are other sources of potential bias likely	+
Score	13/13

Source: Furlan et al.; Editorial Board of the Cochrane Back, Neck Group. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. Spine (Phila Pa 1976) 2015; 40: 1660-73 [27].

Appendix Table 5. Methodologic quality assessment of randomized trials of percutaneous adhesiolysis/neurolysis in lumbar disc herniation utilizing IPM-QRB

		Gerdesmeyer et al. [25]
I.	TRIAL DESIGN AND GUIDANCE REPORTING	
1.	CONSORT or SPIRIT	3
II.	DESIGN FACTORS	
2.	Type and Design of Trial	3
3.	Setting/Physician	2
4.	Imaging	3
5.	Sample Size	2
6.	Statistical Methodology	1
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	2
8.	Duration of Pain	2
9.	Previous Treatments	2
10.	Duration of Follow-up with Appropriate Interventions	2
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	4
12.	Analysis of all Randomized Participants in the Groups	2
13.	Description of Drop Out Rate	1
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	2
15.	Role of Co-Interventions	1
V.	RANDOMIZATION	
16.	Method of Randomization	2
VI.	ALLOCATION CONCEALMENT	
17.	Concealed Treatment Allocation	2
VII.	BLINDING	
18.	Patient Blinding	1
19.	Care Provider Blinding	1
20.	Outcome Assessor Blinding	1
VIII.	CONFLICTS OF INTEREST	
21.	Funding and Sponsorship	2
22.	Conflicts of Interest	3
TOTAL		44

IPM-QRB: Interventional Pain Management techniques – Quality Appraisal of Reliability and Risk of Bias Assessment.
Source: Manchikanti et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. Pain Physician 2014; 17: E263-90 [28].

Appendix Table 6. Assessment of nonrandomized or observational studies of percutaneous adhesiolysis/neurolysis in lumbar disc herniation meeting inclusion criteria utilizing IPM-QRBNR

		Ji et al. [40]	Moon et al. [33]	Cho et al. [31]	Park et al. [37]	Choi et al. [38]
I.	STUDY DESIGN AND GUIDANCE REPORTING					
1.	STROBE or TREND GUIDANCE	1	1	1	1	1
II.	DESIGN FACTORS					
2.	Study Design and Type	1	1	1	1	1
3.	Setting/Physician	2	2	2	2	2
4.	Imaging	3	3	3	3	3
5.	Sample Size	4	4	4	3	4
6.	Statistical Methodology	2	2	2	2	2
III.	PATIENT FACTORS					
7.	Inclusiveness of Population	2	2	2	2	2
8.	Duration of Pain	2	2	2	2	2
9.	Previous Treatments	2	2	2	2	2
10.	Duration of Follow-up with Appropriate Interventions	2	2	2	2	2
IV.	OUTCOMES					
11.	Outcomes Assessment Criteria for Significant Improvement	1	1	1	1	1
12.	Description of Drop Out Rate	1	1	1	1	1
13.	Similarity of Groups at Baseline for Important Prognostic Indicators	1	1	1	1	1
14.	Role of Co-Interventions	2	2	2	2	2
V.	ASSIGNMENT					
15.	Method of Assignment of Participants	1	1	1	1	1
VI.	CONFLICTS OF INTEREST					
16.	Funding and Sponsorship	3	3	3	3	3
TOTAL		30	30	30	29	30

IPM-QRBNR: Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies.
Source: Manchikanti et al. Development of an interventional pain management specific instrument for methodologic quality assessment of nonrandomized studies of interventional techniques. Pain Physician 2014; 17: E291-317 [29].