Systematic Review

Effectiveness of Percutaneous Adhesiolysis in Post Lumbar Surgery Syndrome: A Systematic Analysis of Findings of Systematic Reviews

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Background: Post lumbar surgery syndrome is common and often results in chronic, persistent pain and disability, which can lead to multiple interventions. After failure of conservative treatment, either surgical treatment or a nonsurgical modality of treatment such as epidural injections, percutaneous adhesiolysis are often contemplated in managing post lumbar surgery syndrome. Multiple previous systematic reviews have reached discordant conclusions about the level of evidence for the effectiveness of percutaneous adhesiolysis in managing post lumbar surgery syndrome and other conditions.

Study Design: A systematic review of previously published systematic reviews assessing efficacy of percutaneous adhesiolysis in managing post lumbar surgery syndrome.

Objective: To evaluate the value and validity of previous systematic reviews performed after 2015 on effectiveness of percutaneous adhesiolysis in managing chronic refractory low back and lower extremity pain secondary to post lumbar surgery syndrome.

Methods: Previous systematic reviews on percutaneous adhesiolysis were evaluated. The quality of each systematic review was assessed by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and A Measurement Tool to Assess Systematic Reviews (AMSTAR).

The randomized trials included in the available systematic reviews were assessed by Cochrane review criteria and Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) for methodologic quality.

Data sources included relevant systematic reviews and the randomized trials included in those systematic reviews published since 2015 with searches of PubMed, Cochrane reviews, and Google Scholar through February 2019.

Outcome Measures: Outcome measures were significant improvement defined as 50% pain relief and improvement in functional status. Short-term efficacy was defined as improvement of 6 months or less, whereas long-term efficacy was defined as more than 6 months.

Results: Three systematic reviews and 4 randomized controlled trials (RCTs) of post lumbar surgery syndrome with chronic refractory low back and lower extremity pain showed notable evidence of significant pain relief. Only one systematic review, which was of low quality with inappropriate analysis, showed lack of evidence.

Conclusion: Overall, the present analysis shows Level I evidence for percutaneous adhesiolysis based on significant evidence from published RCTs and 3 of the 4 systematic reviews.

Key words: Post lumbar surgery syndrome, epidural fibrosis, percutaneous adhesiolysis, systematic reviews, randomized controlled trials

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Manchikanti et al (1) described that progress and innovations in health care are measured by evidence-based medicine (EBM), systematic reviews, and meta-analysis. A systematic review is defined as, "the application of scientific strategies that limit bias by the systematic assembly, critical appraisal, and synthesis of all relevant studies on a specific topic." Thus, systematic reviews are aimed at acquiring all evidence involving a reproducible and thorough search of the literature and critical evaluation of eligible studies. A systematic review can be either qualitative, in which all eligible studies are summarized, or quantitative, known as meta-analysis with data from all individual studies are statistically combined (2). Consequently, not all systematic reviews may result in meta-analysis. However, while it is ideal to perform a qualitative review of the evidence prior to quantitative review, some meta-analysis may not have been preceded by a systematic review. Further, qualitative analysis is essential to ensure that findings are not affected by selection bias (2). Conducting a thorough systematic review, specifically with meta-analysis, is a cumbersome and multistep process that involves carefully designing a rigorous protocol in accordance with established guidelines for conducting systematic reviews, such as Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and performing robust statistical analysis (3,4).

In recent years, there have been large volumes of research conducted and published, often with conflicting results, specifically in interventional pain management (5-39). The literature suggests that differences in conclusions are based on physician preference, lack of understanding of the basis of procedural aspects, lack of clinical experience, overenthusiasm to publish, publication of negative studies more frequently than positive studies, conflicts, and confluence of interest (38-46). Indeed, with the mass production of redundant, misleading, and conflicted systematic reviews and meta-analysis (16), the value and sustainability of EBM has been questioned (47-58). The study of methodological and reporting quality of systematic reviews published in the highest-ranking journals in the field of pain by Riado Minguez et al (53) showed there was no improvement in the methodological and reporting quality of systematic reviews before or after the publication of A Measurement Tool to Assess Systematic Reviews (AMSTAR) (59) and PRISMA checklists (3). This review included multiple journals from Anesthesiology and Pain across the globe, but has not found any systematic reviews to be included from the journal Pain Medicine. Pain Physician published a large number of systematic reviews of moderate to high quality. Further, Ross et al (54) in assessing methodologic quality of systematic reviews referenced in clinical practice guidelines for the treatment of opioid use disorder concluded that underperforming areas in AMSTAR included conflicts of interest, funding, and publication bias, whereas in PRISMA, they found protocol registration and risk of bias as issues of concern.

Consequently, systematic reviews may vary, and a systematic review does not guarantee high methodological and reporting rigor as shown by Riado Minguez et al (53), Ross et al (54), and others (16,55-58). Multiple systematic reviews have been published assessing percutaneous adhesiolysis, an interventional procedure utilized for recalcitrant, resistant conditions involving spinal pain, specifically in spinal stenosis, post lumbar surgery syndrome, and recalcitrant degenerative disc disease including disc herniation (17,33,60-62). These systematic reviews (17,30,60-62) have been performed with inclusion of randomized controlled trials (RCTs) (63-69), specifically in failed back surgery, spinal stenosis, and disc herniation with discordant results. Cho et al (33) also evaluated the quality of systematic reviews performed in adhesiolysis for post lumbar surgery syndrome, with inclusion of other systematic reviews (33) and comparison of the evidence with RCTs (63,64,70,71) and systematic reviews of spinal cord stimulation (11,72). Since publication of these systematic reviews, 3 additional RCTs have been published (73-75) with 2 of them in post lumbar surgery syndrome (74,75). Of the 4 systematic reviews performed since 2015, 3 of them (17,33,60,61) concentrated on post lumbar surgery syndrome, whereas one (17) assessed all conditions with inclusion of observational studies. However, meta-analysis was performed in only one systematic review by Helm et al (17), which showed significant improvement qualitatively and quantitatively in post lumbar surgery syndrome and spinal stenosis. In contrast, Cho et al (33) showed higher level of evidence for adhesiolysis, than spinal cord stimulation. The reasons for discordant results may relate to a lack of understanding of the procedure, lack of understanding of principles of EBM with importance of utilization of clinical expertise, and finally confluence of interest (16,45-50).

Therefore, this assessment was undertaken to systematically review the evidence derived from systematic reviews of percutaneous adhesiolysis and determine the appropriateness in post lumbar surgery syndrome.

Methods

This systematic review analyzed the data from systematic reviews and published primary studies. Thus, no patient data were included. Consequently, no approval from Institutional Review Board (IRB) was required.

Inclusion Criteria

We analyzed adhesiolysis-related systematic reviews with or without meta-analysis. The included manuscripts were limited to study of post lumbar surgery syndrome with or without inclusion of other conditions.

Exclusion Criteria

Duplicate systematic reviews, narrative reviews, guidelines, and the RCTs not included in the systematic reviews were excluded. The RCTs which failed to include at least 75% of the patients with post lumbar surgery syndrome were excluded.

Literature Search

The MEDLINE database from 2015 to 2018 was searched using an advanced search for systematic reviews with or without meta-analysis, assessing post lumbar surgery syndrome.

Data Extraction and Management

In a standardized, unblinded manner, 2 review authors independently developed search criteria, searched for the literature, and selected the manuscripts. They also extracted the included studies in the appropriate systematic reviews. Two review authors also assessed risk of bias and methodologic quality assessment, scoring of AMSTAR, PRISMA, and Scottish Intercollegiate Guidelines Network (SIGN), and synthesized the evidence. Any disagreement among 2 review authors assigned for a task were resolved by discussion between the 2 reviewers; however, if consensus was not reached, a third author was called in for further discussion. In addition, any conflicts of interest with a reviewed manuscript concerning authorship were resolved by eliminating those authors and involvement of the review of the manuscripts.

Outcome Measures

The primary outcome was pain relief of 50% or more at various points in time.

The secondary outcomes included improvement of functional status, return to work, and reduction in opioid use.

Methodological and Reporting Quality Assessment

Risk of bias and methodological and reporting quality assessment was performed utilizing 3 tools: AMSTAR, PRISMA, and SIGN. In addition, risk of bias and quality assessment of RCTs was performed utilizing Cochrane review criteria (76), Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria (77), and SIGN (78).

Correlations between the total scores of AMSTAR, PRISMA, and SIGN for systematic reviews and Cochrane review, IPM-QRB, were assessed for RCTs.

Scoring AMSTAR

Based on the previous publication (53) studying pain related articles, each AMSTAR item was rated as one point if the criterion is met or 0 points if the criterion is not met, unclear, or not applicable. Possible range for AMSTAR score for each systematic review was 0 to 11. Systematic reviews were then classified as high 8 to 11 points, medium 4 to 7 points, or low methodologic quality 0 to 3 points as reported by multiple authors (53,54). For compliance with individual AMSTAR items, cut-offs of 90% to 100% was utilized as high compliance, 70% to 89% as medium compliance, 30% to 69% as low compliance, and 0% to 29% as very low compliance.

Scoring PRISMA

The degree of compliance with PRISMA was assessed by scoring every item rated as yes for total compliance, unclear for partial compliance, or no for noncompliance, corresponding to the score values of 1, 0.5, or 0 respectively (53,54). Possible range for PRISMA scores for each systematic review was 0 to 27. To assess the compliance with individual PRISMA items, high compliance was utilized as 90% to 100%, medium compliance as 70% to 89%, low compliance as 30% to 69%, and 0% to 29% as very low compliance.

Scoring SIGN

Methodologic quality assessment of systematic reviews was also conducted utilizing SIGN (78). Cho et al (33) utilizing SIGN in assessing treatment outcomes for patients with post lumbar surgery syndrome, which also included percutaneous adhesiolysis along with comparative analysis of spinal cord stimulation. The quality assessment was based on 3 options, i.e., those which were designated as ++ (indicated all or most of

all standards are met), + (indicated some of the stand are met), and – (indicated all or most of all standards are not met).

Scoring Cochrane Review Criteria

Utilizing Cochrane review criteria, studies meeting the inclusion criteria with at least 9 of 13 criteria were considered high quality; 5 to 8 were considered moderate quality. Those meeting criteria of less than 5 were considered as low quality and were excluded.

Scoring IPM-QRB Criteria

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

Analysis of Evidence

The analysis of evidence was based on best evidence synthesis for qualitative evidence (79) and the Systems to Rate the Strength of Scientific Evidence of the Agency for Healthcare and Quality (AHRQ) (80), as shown in Table 1 and 2.

In addition, recommendation grade was also utilized with classification from A to D based on the results of the evidence as shown in Table 3 (78).

Results

Fig. 1 shows a flow diagram of the literature search and selection of 4 systematic reviews (17,33,60,61) and 4 RCTs utilized in the systematic reviews (63,64,66,68).

Methodologic Quality of Systematic Reviews

Methodologic quality of systematic reviews was

Table 1. *Qualitative modified approach to grading of evidence.*

Level I	Strong	Evidence obtained from multiple relevant high quality randomized controlled trials for effectiveness
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
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
Level IV	Limited	Evidence obtained from multiple moderate or low quality relevant observational studies
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, effectiveness of other measures.

Modified from: Manchikanti et al. A modified approach to grading of evidence. Pain Physician 2014; 17:E319-E325 (79).

Table 2. *Degree of evidence as described by SIGN.*

1++	- High quality meta-analysis and systematic review conducted by randomized clinical trials - Randomized controlled trials with a very low risk of bias
1+	- Well-designed meta-analysis and systematic review conducted by randomized or non-randomized clinical trials - Randomized or non-randomized clinical trials with a low risk of bias
1-	- Meta analysis and systematic review conducted by randomized or non-randomized clinical trials - Randomized or non-randomized clinical trials with a high risk of bias
2++	- High-quality systematic review conducted by a patient control study, cohort study, or diagnosis analytic study - High-quality patient control study, cohort study, or diagnosis analytic study of very low risk of confounding, bias or contingency, or a high possibility of cause and effect relationship
2+	- High-quality patient control study, cohort study, or diagnosis analytic study of the low risk of a confounding, bias or contingency, or the normal possibility of a cause and effect relationship
2-	- Patient control study, cohort study, or diagnosis analytic study of the high risk of a confounding bias or contingency, or the low possibility of a cause and effect relationship
3	- Non-analytic studies, e.g., before-and-after study, case series, case report
4	- Expert opinion

Source: Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001; 323:334-336 (78).

Table 3. *Recommendation grade.*

A	- At least one metaanalysis, systematic review, or RCT rated as 1 + + and directly applicable to the target population or - A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1 + directly applicable to the target population and demonstrating overall consistency of results
B	- A body of evidence including studies rated as 2 + + directly applicable to the target population and demonstrating overall consistency of results or - Extrapolated evidence from studies rated as 1 + + or 1 +
C	- A body of evidence including studies rated as 2 + directly applicable to the target population and demonstrating overall consistency of results or - Extrapolated evidence from studies rated as 2 + +
D	- Evidence level 3 or 4 or - Extrapolated evidence from studies rated as 2 +

Source: Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001; 323:334-336 (78).

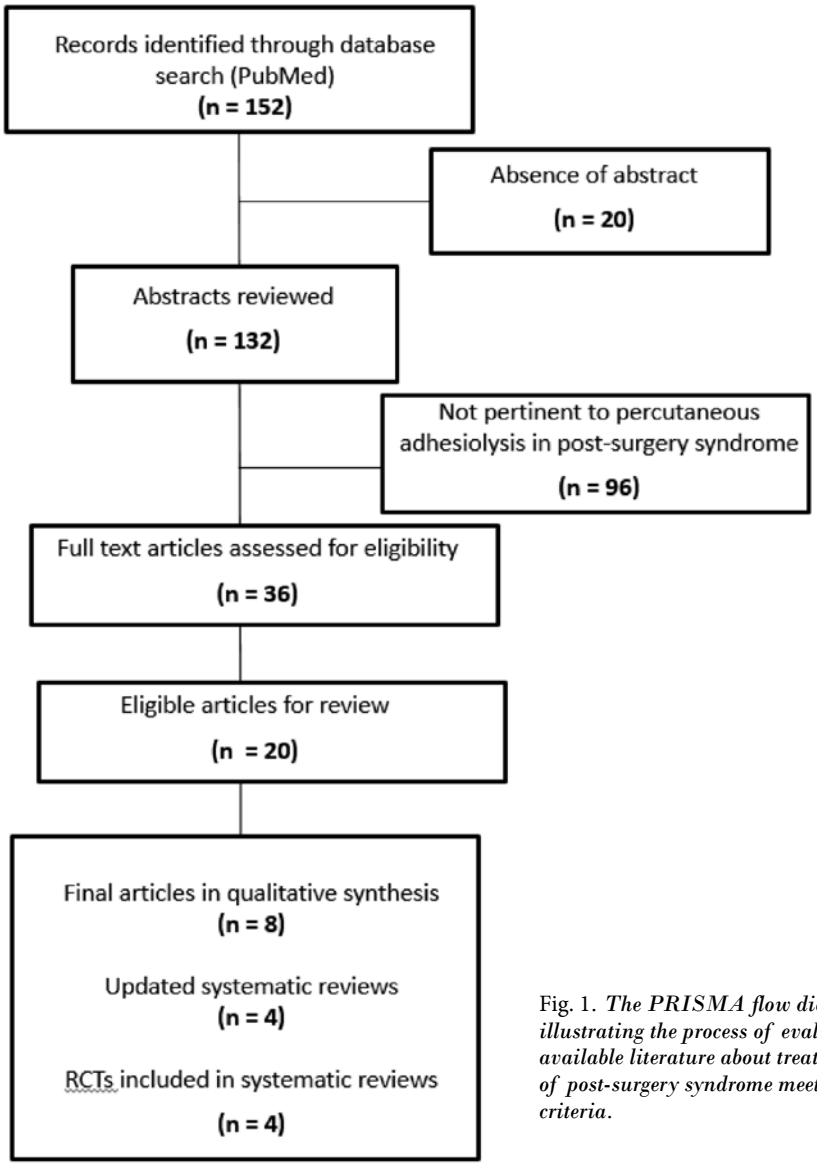

Fig. 1. *The PRISMA flow diagram illustrating the process of evaluating available literature about treatment outcomes of post-surgery syndrome meeting inclusion criteria.*

conducted utilizing PRISMA, AMSTAR, and SIGN checklists.

Compliance with PRISMA checklist is shown in Table 4. Based on the scoring principles, only one systematic review (17) met high compliance criteria with a score of 25 of 27, 2 of the systematic reviews (33,60) met medium compliance with scores of 22 and 23, whereas one systematic review (61) was of low compliance rate with compliance of 16.

AMSTAR scoring is shown in Table 5. Based on this

Table 4. *Compliance with PRISMA checklist.*

PRISMA Item	Helm et al (17)	Manchikanti et al (60)	Cho et al (33)	Brito-García et al (61)
TITLE				
1. Systematic review, meta-analysis, or both in the title?	1	1	1	1
ABSTRACT				
2. Structured summary in the abstract?	1	1	1	1
INTRODUCTION				
3. Rationale for review in the introduction?	1	1	1	0
4. Objectives statement in the introduction?	1	1	1	1
METHODS				
5. Protocol registration information provided?	0	0	0	1
6. Methods for eligibility criteria included?	1	1	1	1
7. Information sources in the methods?	1	1	1	0
8. Full search strategy provided?	1	1	1	1
9. Process of study selection provided?	1	1	1	0
10. Process of data extraction provided?	1	1	1	0
11. List and define all variables for which data were sought?	1	1	1	0
12. Methods for risk of bias in individual studies provided?	1	1	1	1
13. Methods for principal study measures provided?	1	1	1	1
14. Methods for synthesis of results provided?	1	1	1	0
15. Methods for risk of bias across studies provided (publication bias)?	1	1	1	0
16. Methods of additional analyses provided?	1	0	1	0
RESULTS				
17. Description of studies included/excluded?	1	1	1	1
18. Study characteristics for the included studies provided?	1	1	1	1
19. Risk of bias in individual studies assessed?	1	1	1	1
20. Results of the individual studies presented ideally in a forest plot?	1	1	1	1
21. Clear synthesis of the results with proper measurements in consistency?	1	0	0	0
22. Risk of bias across individual studies assessed (publication bias)?	0	0	0	0
23. Results of any additional analyses provided?	1	0	0	0
DISCUSSION				
24. Summary of evidence in the discussion?	1	1	1	1
25. Discussion of limitations of the study?	1	1	1	1
26. Discussion of the implications and future research?	1	1	1	1
FUNDING				
27. Funding source and roles of the authors provided?	1	1	1	1
TOTAL	25	22	23	16

Source: Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009; 151:264–269, W64 (3).

Table 5. *Compliance with individual AMSTAR checklist items of systematic reviews.*

	Helm et al (17)	Manchikanti et al (60)	Cho et al (33)	Brito-García et al (61)
1. Was a priori design provided (protocol established before the conduct of review)?	1	1	1	1
2. Was there duplicate study selection and data extraction?	1	1	1	1
3. Was a comprehensive literature search performed?	1	1	1	0
4. Was the status of publication (ie, gray literature) used as an inclusion criterion?	0	0	0	0
5. Was a list of studies (included and excluded) provided?	1	1	1	0
6. Were the characteristics of the included studies provided?	1	1	1	1
7. Was the scientific quality of the included studies assessed and documented?	1	1	1	1
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	1	1	1	0
9. Were the methods used to combine the findings of studies appropriate?	1	1	1	0
10. Was the likelihood of publication bias assessed?	1	1	1	0
11. Was the conflict of interest included, both for the systematic review authors and included studies' authors?	1	1	1	0
TOTAL	10	10	10	4

Y=Yes; N=No; NA=Not applicable
Source: A Measurement Tool to Assess Systematic Reviews (AMSTAR). https://amstar.ca/ (59)

scoring, 3 systematic reviews (17,33,60) were shown to be of high quality with 90% compliance, whereas one systematic review (61) was shown to be of low compliance.

SIGN scoring is shown in Table 6. This showed high quality review for 3 of the 4 systematic reviews (17,33,60), whereas one systematic review (61) was of low quality or unacceptable. Finally, it was utilized as low quality rather than rejected, based on the consensus.

Table 7 summarizes the compliance with AMSTAR, PRISMA, and SIGN checklists for systematic reviews. Only one systematic review was rated with high compliance with all 3 checklists (17). Two systematic reviews (33,60) rated high with AMSTAR and SIGN; however, medium with PRISMA. The final systematic review (61) rated low quality with AMSTAR, PRISMA, and SIGN checklists.

Methodologic Quality Assessment of RCTs

Risk of bias and methodologic quality assessment of RCTs in 4 published systematic reviews is shown in Table 8. Three of the 4 studies consistently were rated as high quality (63,64,69), whereas, one study was rated as moderate quality (66).

Two systematic reviews (33,61) included 2 RCTs (63,64), one of them (60) included 3 RCTs (63,64,66) and one included 4 RCTs (63,64,66,69). Table 8 shows methodologic quality assessment utilizing Cochrane Review criteria, SIGN checklist, or IPM-QRB checklist. Methodologic quality was rated as high for Chun-Jing et al (63) in 2 of the 4 reviews; whereas in one systematic review (33), a trial was not included and in another systematic review it was rated as moderate quality with Cochrane Review criteria by Brito-García et al (61). Manchikanti et al's RCT (64) utilized in all 4 systematic reviews was shown to be of high quality in 3 systematic reviews (17,33,60) and low quality in one systematic review. Two other RCTs (66,69) were analyzed only in 2 systematic reviews (17,33) showing high quality with Cochrane Review criteria, as well as IPM-QRB.

Study Characteristics

Study characteristics of 4 RCTs are shown in Table 9.

Synthesis and Analysis of Evidence

As shown in Table 10, the evidence is Level I based on best evidence synthesis and Grade A, based on grading recommendations (78).

Discussion

The results of the present research demonstrate that of the 4 current systematic reviews, 3 were performed appropriately and one was performed inappropriately providing low methodologic quality assessment and inappropriate conclusions. Based on the analysis from the 4 systematic reviews and 4 RCTs included in the system-

Table 6. *SIGN checklist for systematic reviews.*

Section 1: INTERNAL VALIDITY In a well conducted systematic review		Does this study do it?		Helm et al (17)	Manchikanti et al (60)	Cho et al (33)	Brito-García et al (61)
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper. If no, reject	Yes ☐	No ☐	Y	Y	Y	N
1.2	A comprehensive literature search is carried out. If no, reject	Yes ☐	No ☐	Y	Y	Y	N
		Not applicable ☐					
1.3	At least two people should have selected studies.	Yes ☐	No ☐	Y	Y	Y	Y
			Can't say ☐				
1.4	At least two people should have extracted data.	Yes ☐	No ☐	Y	Y	Y	Y
			Can't say ☐				
1.5	The status of publication was not used as an inclusion criterion.	Yes ☐	No ☐	Y	Y	Y	Y
1.6	The excluded studies are listed.	Yes ☐	No ☐	Y	Y	N	N
1.7	The relevant characteristics of the included studies are provided.	Yes ☐	No ☐	Y	Y	Y	Y
1.8	The scientific quality of the included studies was assessed and reported.	Yes ☐	No ☐	Y	Y	Y	Y
1.9	Was the scientific quality of the included studies used appropriately?	Yes ☐	No ☐	Y	Y	Y	N
1.10	Appropriate methods are used to combine the individual study findings.	Yes ☐	No ☐	NA	NA	NA	NA
			Not applicable ☐				
1.11	The likelihood of publication bias was assessed appropriately.	Yes ☐	No ☐	Y	Y	Y	N
		Not applicable ☐					
1.12	Conflicts of interest are declared.	Yes ☐	No ☐	Y	Y	Y	Y
Section 2: OVERALL ASSESSMENT OF THE STUDY							
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐		++	++	++	-
		Acceptable (+) ☐					
		Low quality (-) ☐					
		Unacceptable – reject 0 ☐					
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐		Y	Y	Y	N

Table 7. *Compliance with AMSTAR, PRISMA, and SIGN checklists for systematic reviews.*

Systematic Reviews	AMSTAR (0-11)	PRISMA (0-27)	SIGN
Helm et al (17)	High - 10	High - 25	++
Manchikanti et al (60)	High - 10	Medium - 22	++
Cho et al (33)	High - 10	Medium - 23	++
Brito-García et al (61)	Low - 4	Low - 16	-

Table 8. *Methodologic quality assessment utilizing Cochrane Review criteria or SIGN checklist or IPM-QRB.*

	Helm et al (17)		Cho et al (33)	Manchikanti et al (60)		Brito-García et al (61)
	Cochrane	IPM-QRB	SIGN	Cochrane	IPM-QRB	Cochrane
Chun-Jing et al (63)	12/13	34/48	1++	N/A	N/A	6/11
Manchikanti et al (64)	12/13	42/48	1++	9/12	41/42	4/11
Heavner et al (66)	10/13	23/48	N/A	9/12	37/42	N/A
Manchikanti et al (69)	12/13	37/48	N/A	9/12	40/42	N/A

atic reviews, the present study showed Level I evidence for percutaneous adhesiolysis in managing post lumbar surgery syndrome patients with recalcitrant pain and disability after failure of fluoroscopically directed epidural injections. Post spinal surgery syndrome or post lumbar surgery syndrome is often conflated with failed back surgery syndrome, which is considered as a misnomer and derogatory for surgical specialties (33,81). Post lumbar surgery syndrome nonresponsive to epidural injections or other treatments correcting available pathology are commonly treated with percutaneous adhesiolysis or spinal cord stimulation. Cho et al (33) in a systematic review described and showed significant evidence for both percutaneous adhesiolysis and spinal cord stimulation with a recommendation of Level A for epidural adhesiolysis for 6 to 24 months of pain relief and functional improvement and Level B for spinal cord stimulation.

Among these systematic reviews, Helm et al (17) performed an appropriate methodologic quality assessment of RCTs utilizing Cochrane review criteria (76) and IPM-QRB criteria (77). They found Level I or strong evidence for the efficacy of percutaneous adhesiolysis in the treatment of chronic refractory low back and lower extremity pain of various origins. Level I was defined as evidence obtained from multiple relevant, high quality RCTs based on qualitative modified approach on grading of evidence (79). In reference to RCTs, utilizing Cochrane review criteria, all the manuscripts were rated as high quality, and IPM-QRB criteria, one manuscript was rated as moderate quality, while all 3 manuscripts (63,64,69) referring to post laminectomy syndrome were rated as high quality. Helm et al (17) also performed meta-analysis showing significant improvement related to percutaneous adhesiolysis contributing to Level I results.

Manchikanti et al (60) evaluated the effectiveness of percutaneous adhesiolysis in the treatment of post lumbar surgery syndrome with inclusion of 4 RCTs, of which 3 of the 4 were rated as high quality based on Cochrane review criteria as well as IPM-QRB (76,77). Utilizing grading and synthesis of best evidence by qualitative analysis, they concluded that evidence was Level II based on best evidence synthesis. The authors have not performed meta-analysis due to variability among the studies.

Cho et al (33) in 2017 published the results of treatment outcomes for patients with failed back surgery in a systematic review. In this assessment, they have analyzed spinal cord stimulation, percutaneous adhesiolysis, and caudal epidural injections. With identification of 6 RCTs to include all techniques and 4 systematic reviews, they utilized various types of criteria for judgement of quality assessment, degree of evidence, and recommendation grading. They utilized ++ as highest for criteria for judgement of quality assessment, 1++ for degree of evidence, and A for recommendation grade. They also utilized SIGN checklist for RCTs and for systematic reviews for methodologic quality assessment (78). These authors have provided a high level of methodologic quality for RCTs (63,64). Internal validity of percutaneous adhesiolysis was similar or even superior to the RCTs and systematic reviews of spinal cord stimulation (11,70-72). Based on this analysis, they showed that epidural adhesiolysis showed Grade A evidence for 6-24 months.

In contrast to these 3 systematic reviews published since 2015, a 2018 publication by a nonphysician primary author and none of the authors practicing in this procedure assessed efficacy, effectiveness, safety, and cost effectiveness of epidural adhesiolysis for treating failed back surgery syndrome in a systematic review without meta-analysis (61). They provided erroneous methodologic quality assessment rating the trials with downgrading to low quality, which have been rated as of high quality by Cochrane review (76), IPM-QRB (77), and SIGN (78). They considered them as high risk of bias utilizing only 2 studies for efficacy or effectiveness by Manchikanti et al (64) and Chun-Jing et al (63).

In recent years, significant controversy has been

Table 9. Study characteristics of randomized controlled trials assessing percutaneous adhesiolysis included in systematic reviews.

Study **Study Characteristic** **Methodological Quality Scoring**	**Number of Patients & Selection Criteria**	**Interventions/ Control**	**Outcome measures**	**Time of Measurement**	**Results**	**Weaknesses**	**Strengths**	**Conclusions**
Chun-jing et al 2012 (63) Randomized, active control Cochrane 12/13 IPM-QRB 34/48	92 patients with pain and radiculopathy 6 months after surgery for disc herniation 76 patients were evaluated	Catheter with guidewire was passed to ventral epidural space. 50-90 mL and 10 mg of dexamethasone were injected in the treatment group. Control group received 10 mg dexamethasone only	VAS, Opioid use; MacNab criteria	1 week, one month,6 months	3.24 mean decrease in VAS at 6 months in treated group, vs .82 in control. Patients in treated group who did not have improvement in dye flow did not have clinical improvement	Lateral views only were obtained; no measure of function	High quality study	Adhesiolysis is effective using the vascular catheter with ventral placement of the catheter. Improvements in dye flow are necessary for good clinical outcomes.
Manchikanti et al 2009 (64) Randomized Active Control Cochrane 12/13 IPM-QRB 42/48	120 Post lumbar surgery syndrome	Adhesiolysis with 10% saline vs S3 caudal injection with 0.9% saline	NRS, ODI, employment status, opioid use	3, 6 and 12 months	~70% of adhesiolysis procedures had >50% relief and also >40% ODI improvement at 12 months, vs ~12% of caudal. Average of 3.5 adhesiolysis procedures vs. 2.2 caudal injection	33 of 60 in the control group were lost to follow up at 12 months, vs 2 in the adhesiolysis. 43 control were unblinded prematurely vs 2 in the control	High quality equivalency study.	Adhesiolysis, one day, repeated up to 4 times a year, is effective in providing decreased pain and increased function in the post lumbar surgery population.
Heavner et al 1999 (66) Randomized active control Cochrane 10/13 IPM-QRB 23/48	83	Adhesiolysis in four groups, 0.9% saline, 10% saline, with or without hyaluronidase	VAS, McGill Pain Questionnaire	3, 6, 12 months	No significant difference between the four groups. Adhesiolysis did provide pain relief in about 50% of subjects. Most subjects require more than one procedure	Successful pain relief was 10/100 reduction in VAS. 24 of 83 patients were removed from study	Showed only moderate additional benefit from either 10% saline or hyaluronidase	Moderate quality study comparing 4 treatment options. Reduced additional procedures
Manchikanti et al 2004 (69) Randomized active control Cochrane 12/13 IPM-QRB 37/48	75	One-day adhesiolysis with either 0.9% or 10% saline vs epidural steroid injection.	VAS, ODI, work status, opioid intake, range of motion measurement, and P-3	3, 6, 12 months	72% of adhesiolysis and hypertonic neurolysis and 60% of 0.9% saline adhesiolysis compared to 0% of epidural group had >50% relief at12-months	18 of the ESI group were unblinded by 6 months. Repeat procedures allowed based upon response to previous procedures, rather than examining one injection only.	Comparison of hypertonic and normal saline vs epidural steroid injection	High quality RCT showing that adhesiolysis provides significant relief regardless of whether normal saline or hypertonic saline is used.

Table 10. *Articles for synthetic analysis showing the effectiveness of epidural adhesiolysis for FBSS.*

Authors	Type	Intervention and control	F/U period (mos.)	Conclusion	Methodologic Quality
Chun-Jing et al (63)	RCT	EA (N = 46) ESI (N = 46)	6	Patients on epidural lysis reported that the clinical effectiveness rate was 50%. For control patients it was 5.26%, and there was a statistical difference between the 2 groups.	Cochrane 11/12 IPM-QRB 34/48
Manchikanti et al (64)	RCT	EA (N = 60) ESI (N = 60)	24	Significant pain relief and functional improvement were recorded in 73% and 82% of the patients in the EA group versus 12% and 5% in the ESI group at the 1- and 2-year follow-up (P < 0.001).	Cochrane 11/12 IPM-QRB 34/48
Heavner et al (66)	RCT	83 patients in 4 groups	3, 6, 12 months	Moderate quality study comparing 4 treatment options. Reduced additional procedures	IPM-QRB 23/48
Manchikanti et al (69)	RCT	75	3, 6, 12 months	High quality RCT showing that adhesiolysis provides significant relief regardless of whether normal saline or hypertonic saline is used.	Cochrane 11/12 IPM-QRB 37/48
Helm et al (17)	SR	NA	NA	Applying the USPSTF criteria, there is reasonable evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by FBSS.	AMSTAR 10/11 PRISMA 25/27 SIGN ++
Manchikanti et al (60)	SR	NA	NA	Applying the USPSTF criteria, there is reasonable evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by FBSS.	AMSTAR 10/11 PRISMA 22/27 SIGN 1++
Cho et al (33)	SR	NA	NA	Applying AHRQ criteria. Authors have presented percutaneous adhesiolysis 1++ evidence, whereas spinal cord stimulation was 1++ with Grade A recommendation, compared to spinal cord stimulation of Grade B recommendation.	AMSTAR 10/11 PRISMA 23/25 SIGN 1++
Brito-García et al (61)	SR	NA	NA	Applying deeply flawed methodology with lack of understanding of the procedure, misrepresentation of the evidence leading to erroneous conclusions. Authors have concluded that the evidence of the efficacy and cost effectiveness of adhesiolysis for treating FBSS was nonexistent.	AMSTAR 4/11 PRISMA 16/27 SIGN -

developed in performing RCTs, as well as synthesizing the evidence with systematic reviews and meta-analysis. Clark et al (20) filed a complaint with the chief editor of Cochrane reviews and published articles regarding inaccurate reporting, misreporting, inability to identify all the available studies, and undisclosed conflicts of interest. Similar reports have been found for interventional pain management over the years with biased assessment, not only for percutaneous adhesiolysis and vertebroplasty, but for epidural injections, facet joint interventions, and other treatments and cost effective utility analysis (82-86).

While 3 systematic reviews performed were of high quality and one was of low quality by Brito-García et al (61), this systematic review failed to follow principles of EBM and lacked clinical experience and understanding of the procedure. Authors of this systematic review (61) raised a multitude of questions in reference to the RCT by Manchikanti et al (64), in reference to allocation concealment and blinding, in addition to other

misconceptions. However, the manuscript described the allocation concealment clearly along with blinding for the intervention. Of course, double-blinding is difficult for the performing physician; however, blinding was maintained by multiple means by separating the physician performing the procedure and the one assessing the results, and also mixing the study patients with other patients receiving routine treatment. Even then, the authors (64) have provided information that blinding was considered inadequate in patients in Group I as the physician performing the procedure was informed of Group I as it was necessary to position the catheter at S3, which was not a usual practice. However, the drugs injected during the usual procedure were not injected in the operating room, and the group assignment was not revealed to other staff members or the outcome assessor.

Brito-Garcia et al (61) have described that the dropout rate was not acceptable. Dropout rate was described and acceptability is a subjective matter. The dropout rate in the treatment group was only 3% at the end of one year and 10% at the end of 2 years. The authors (61) also criticized similarity in groups at baseline as the most important prognostic indicator. However, there were no differences between the groups for any of the indicators, specifically the most important indicators which are pain distribution, pain ratio, and surgical history. They (61) were also unclear about co-interventions, if they were avoided or comparable. Co-interventions were clearly described in the manuscript, which were similar in both groups (64). All of them also continued previously directed therapeutic exercise programs, as well as their work, if they were working, which is succinctly described as other parameters (64).

In reference to the compliance and its acceptability in all groups, the compliance was overwhelmingly acceptable in Group II, whereas in Group I, patients withdrew because of the continued pain (64), even though Brito-Garcia et al (61) appears to misunderstand several basic elements of the study.

Further criticism also included that criteria for repeating epidural injections were not disclosed (61), which is disappointing. The succinct description shows that adhesiolysis was repeated after 3 or more months if the degree of improvement in disability or pain relief experienced after the first procedure deteriorated to ≥ 50% as described in the manuscript itself. Further, they also described losses of 87% in the caudal epidural group, which was the control group after they have failed the epidural injections at 2 years rather than one year (64). At one year, it was more reasonable with 62% dropout in the control group, whereas it was less than 20% at 6 months.

Brito-Garcia et al (61) also criticized that patients could have undergone epidural injections before entering the trial, so it is unclear whether they were blinded to the treatment they received. A more robust review of the inclusion criteria would have demonstrated that all patients had previously failed epidural injections; however, without catheterization (64). The authors (61) also stated patients could be informed of the treatment they had been assigned to if they asked about it. This is not described anywhere in the manuscript. Patients were informed of the treatment only at the time of unblinding. They stated that groups were not similar at baseline in important variables, e.g., opioid use; however, they have not described any other aspects and it is unclear where these thoughts came from as they were not discussed in the analysis or the manuscript.

Brito-Garcia et al (61) also missed the fact that cost effectiveness studies have already been published (82). Further, they attempted to evaluate safety from RCTs and small observational studies, which is problematic for the reasons described above.

Similar criticism was provided about Chun-Jing et al's (63) manuscript.

They (61) also excluded 2 manuscripts by Heavner et al (66) and Manchikanti et al (69), which included an overwhelming proportion of post lumbar laminectomy patients. The present systematic review of systematic reviews and analysis of RCTs included in these systematic reviews succinctly demonstrates the value of EBM and at the same time shows the consequences of inappropriate analysis.

Conclusion

This systematic review of 4 systematic reviews which included 4 RCTs, succinctly demonstrates the value of performing appropriate risk of bias and quality assessment of RCTs and subsequent analysis of systematic reviews. Moreover, the present study demonstrates significant evidence when the systematic review is performed appropriately, without bias, knowledge of methodology, and with an understanding of clinical activity. Overall, the present analysis shows Level I evidence for percutaneous adhesiolysis, based on evidence from 4 published RCTs and 3 of the 4 systematic reviews.

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