

## Systematic Review

## Systematic Review of Percutaneous Adhesiolysis and Management of Chronic Low Back Pain in Post Lumbar Surgery Syndrome

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**Background:** Post lumbar surgery syndrome or failed back surgery syndrome with persistent pain continues to increase over the years. The speculated causes of post lumbar laminectomy syndrome include acquired stenosis, epidural fibrosis, arachnoiditis, radiculopathy, and recurrent disc herniation. Epidural fibrosis may account for as much as 20% to 36% of all cases of failed back surgery syndrome. Percutaneous epidural adhesiolysis has been employed in interventional pain management in the treatment of chronic, refractory low back and lower extremity pain after back surgery.

**Study Design:** A systematic review of randomized trials and observational studies.

**Objective:** To evaluate the effectiveness of percutaneous adhesiolysis in managing chronic low back and lower extremity pain due to post lumbar surgery syndrome.

**Methods:** A comprehensive literature search was conducted utilizing electronic databases, as well as systematic reviews and cross references from 1966 through December 2008.

The quality of individual articles used in this analysis was assessed by modified Cochrane review criteria for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) criteria for assessment of observational studies.

Clinical relevance was evaluated using 5 questions according to the criteria recommended by the Cochrane Review Back Group.

Analysis was conducted using 5 levels of evidence, ranging from Level I to III, with 3 subcategories in Level II.

**Outcome Parameters:** The primary outcome measure was pain relief (short-term relief of at least 6 months and long-term relief of more than 6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and change in opioid intake.

**Results:** Of the 13 studies considered for inclusion, 3 randomized trials and 4 observational studies met the inclusion criteria for methodologic quality assessment and evidence synthesis based on methodologic quality scores of 50 or more. Evidence of percutaneous adhesiolysis in the management of chronic low back pain in post-lumbar surgery syndrome is Level I to Level II-1, with evidence derived from 3 randomized trials.

**Limitations:** There is a paucity of efficacy and pragmatic trials. No trials have been published after 2006.

**Conclusion:** The indicated level of evidence for percutaneous adhesiolysis is Level I or II-1 based on the US Preventative Services Task Force (USPSTF) criteria.

**Key words:** Chronic low back pain, post lumbar surgery syndrome, post surgery syndrome, failed back surgery syndrome, spinal stenosis, epidural fibrosis, interventional techniques, percutaneous adhesiolysis, hypertonic saline neurolysis

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Intervertebral disc herniation, spinal stenosis, and degenerative spondylolisthesis with stenosis are the 3 most common diagnoses of low back and leg symptoms for which surgery is performed (1,2). Post surgery syndrome and other synonyms such as post lumbar laminectomy syndrome or failed back surgery syndrome represent a cluster of syndromes following spine surgery wherein the expectations of the patient and spine surgeon are not met. Persistent pain following lumbar surgery is common (3-14). Since discectomies and spinal fusions have been increasing exponentially, it appears that the prevalence of persistent pain following lumbar spine surgery continues to increase (15-21). Further, the prevalence of chronic persistent pain along with seeking care for that pain have been reported to be increasing (22,23).

Hypothesized causes of post laminectomy syndrome include acquired stenosis, adjacent segment degeneration, internal disc disruption, recurrent disc herniation, retained disc fragment, spondylolisthesis, epidural or intraneural fibrosis, degenerative disc disease, radiculopathy, facet joint pain, sacroiliac joint pain, discitis, arachnoiditis, pseudoarthritis, segmental instability, and others (3-5,9-11,24-31). However, among multiple etiologies, epidural fibrosis, discogenic pain, recurrent disc herniation, and spinal stenosis can be treated with either caudal epidural injections or percutaneous adhesiolysis in patients nonresponsive to caudal epidural injections (24-28,32-40). However, facet joint and sacroiliac joint pain may be treated with other interventional techniques (41-46). Epidural fibrosis may account for as much as 20% to 36% of all cases of failed back surgery syndrome (9,10,24-28,47,48). A correlation between peridural scarring and radicular pain (9,49-51) and poor clinical outcomes (52) has been reported by some authors, while others (53-55) have contradicted the role of epidural fibrosis as a causative factor.

Animal models of post lumbar laminectomy syndrome demonstrate paraspinal muscle spasms, tail contractures, spontaneous pain behaviors, tactile allodynia, epidural and perineural scarring, and nerve root adherence to the underlying disc and pedicle (53-58). While, a 2005 Cochrane Review found that paucity and heterogeneity of evidence limited the conclusions regarding surgical efficacy for spinal stenosis (59). Weinstein et al (6) as part of the Spine Patient Outcomes Research Trial (SPORT) reported on 2-year outcomes of patients with spinal stenosis

without degenerative spondylosis with the conclusion that in the combined as treated analysis, patients who underwent surgery showed significantly more improvement in all primary outcomes than did patients who were treated non-surgically. However, a comparison of results by Huntoon and Buizgher (60) showed similar outcomes with caudal epidural injections.

Epidural injection for managing chronic low back pain is one of the most commonly performed interventions in the United States with exponential growth and geographic variations (26,32-38,60-66). However, in the case of postsurgery syndrome and spinal stenosis only a moderate proportion of patients showed improvement in pain and functional level with epidural injections (26,38,67,68). Two recent studies evaluating the effectiveness of caudal epidural injections secondary to post surgery syndrome and spinal stenosis showed encouraging results (32,33) even though injections were inferior when used to treat chronic low back pain secondary to disc herniation or discogenic pain without disc herniation (34,35). However, the evidence derived from percutaneous adhesiolysis procedures has been moderate to strong in managing pain of post surgery syndrome (24,26,27). Percutaneous epidural adhesiolysis has been employed in interventional pain management in the management of chronic, refractory low back and lower extremity pain (24-28,39,69-77) with the purpose of eliminating scar tissue and assuring the delivery of high concentrations of injected drugs to targeted areas.

The latest systematic review evaluating the effectiveness of epidural adhesiolysis was published in January 2007 (24) and it must also be noted that a significant proportion of systematic reviews are outdated within a 2-4 year period, specifically in assessment of emerging specialties (78). This systematic review was undertaken to provide a current evaluation of the effectiveness of percutaneous adhesiolysis in postsurgery syndrome.

## **METHODS**

### **Literature Search**

A comprehensive literature search was conducted using multiple databases including PubMed and EMBASE from 1966 through December 2008, Cochrane database, Clinical Trial Registry, systematic reviews, narrative reviews, and cross-references to the reviews published in the English language.

The search strategy emphasized chronic low back pain secondary to post surgery syndrome with a focus on percutaneous adhesiolysis. The search terminology included post lumbar surgery syndrome, failed back surgery syndrome, epidural fibrosis, chronic low back pain, adhesiolysis, epidural neuroplasty, epidural neurolysis, lysis of adhesions, percutaneous adhesiolysis, hypertonic and saline neurolysis.

### **Selection Criteria**

The review focused on randomized trials, observational studies, and reports of complications. The population of interest was patients suffering with chronic intractable low back pain with or without radicular findings for at least 6 months. Only percutaneous adhesiolysis procedures were evaluated. All the studies providing appropriate management with outcome evaluations of 6 months or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

### **Outcome Parameters**

The primary outcome measure was pain relief (short-term relief  $\leq$  6 months and long-term  $>$  6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and change in opioid intake.

### **Review Criteria**

Each study was evaluated by 2 physicians for stated criteria and any disagreements were resolved by a third physician.

If there was any conflict of interest with the reviewed manuscripts, the involved authors did not review the manuscripts for quality assessment, clinical relevance, evidence synthesis, or grading of evidence.

### **Methodologic Quality Assessment**

The quality of each individual article used in this analysis was assessed by modified Cochrane review criteria with weighted scores (79) for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) quality criteria for assessment of observational studies (80). Consensus-based weighted scoring developed by Koes et al (79) and Nelemans et al (81) was used for randomized trials and was adapted by the guidelines committee of the American Society of Interventional Pain Physicians (ASIPP) for use with ob-

servational studies and has been utilized in multiple; previous evaluations (36,40,42,43,82-90).

Only the studies scoring at least 50 of 100 on weighted scoring criteria were utilized for analysis.

Observational studies were only included in the evidence synthesis if there were less than 4 randomized trials meeting the inclusion criteria.

### **Clinical Relevance**

The clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (91,92). Each question was scored positive (+) if the clinical relevance item was met, negative (-) if the item was not met, and unclear (?) if data were not available to answer the question.

In the recent Cochrane review of "Injection Therapy for Subacute and Chronic Low Back Pain" (91) the authors considered a 20% improvement in pain scores (93) and a 10% improvement in functioning outcomes (94) to be clinically important. The current study utilized stricter criteria than general systematic reviews and previous systematic reviews. Any relief of 6 months or less was considered as short-term, whereas Cochrane reviews (91) and others have considered 6 weeks as short-term and longer than 6 weeks as long-term. We also utilized methodologic quality assessment criteria (91) for minimum inclusion, thus this systematic review is expected to provide robust results with stricter criteria. Further, in contrast to many other systematic reviews, in this systematic review, observational studies with scores of 50 or more on a scale of 0 - 100 based on AHRQ criteria were included. This improves the generalizability of the systematic review as well as the intervention (95-99).

### **Prior Treatment Criteria**

Patients must have undergone non-interventional treatment (physical therapy, oral medications) or prior fluoroscopically guided epidural steroid injections.

### **Analysis of Evidence**

Analysis was conducted using 5 levels of evidence, ranging from Level I to III with 3 subcategories in Level II, as illustrated in Table 1 (100).

### **Recommendations**

Grading recommendations were based on Guyatt et al's criteria as illustrated in Table 2 (101).

Table 1. *Modified quality of evidence developed by USPSTF.*

I:	Evidence obtained from at least one properly randomized controlled trial
II-1:	Evidence obtained from well-designed controlled trials without randomization
II-2:	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group
II-3:	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III:	Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees

Adapted and modified from the U.S. Preventive Services Task Force (USPSTF) (100).

Table 2. *Grading recommendations.*

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181 (101).

### Outcomes of the Studies

A study was judged to be positive if the percutaneous adhesiolysis was clinically relevant and effective, either with a placebo control or active control in randomized trials. This indicates that the difference in the effect for the primary outcome measure was statistically significant on the conventional 5% level. In a negative study, no difference between the study treatment or no improvement from baseline was reported. Further, the outcomes were judged at the reference point with positive or negative results reported at 3 months, 6 months, and one year.

For observational studies, a study was judged to be positive if the percutaneous adhesiolysis was ef-

fective, with outcomes reported at the reference point with positive or negative results at 3 months, 6 months, and one year.

### RESULTS

A literature search was carried out for percutaneous adhesiolysis as shown in Fig. 1.

Our search strategy yielded multiple studies evaluating the effectiveness of percutaneous adhesiolysis. These included 3 systematic reviews (24,27,102), one technology assessment (103), and 13 studies (69-77,104-107). Of these, there were 5 randomized trials (69,72-75), and 8 observational studies (70,71,76,77,104-107).

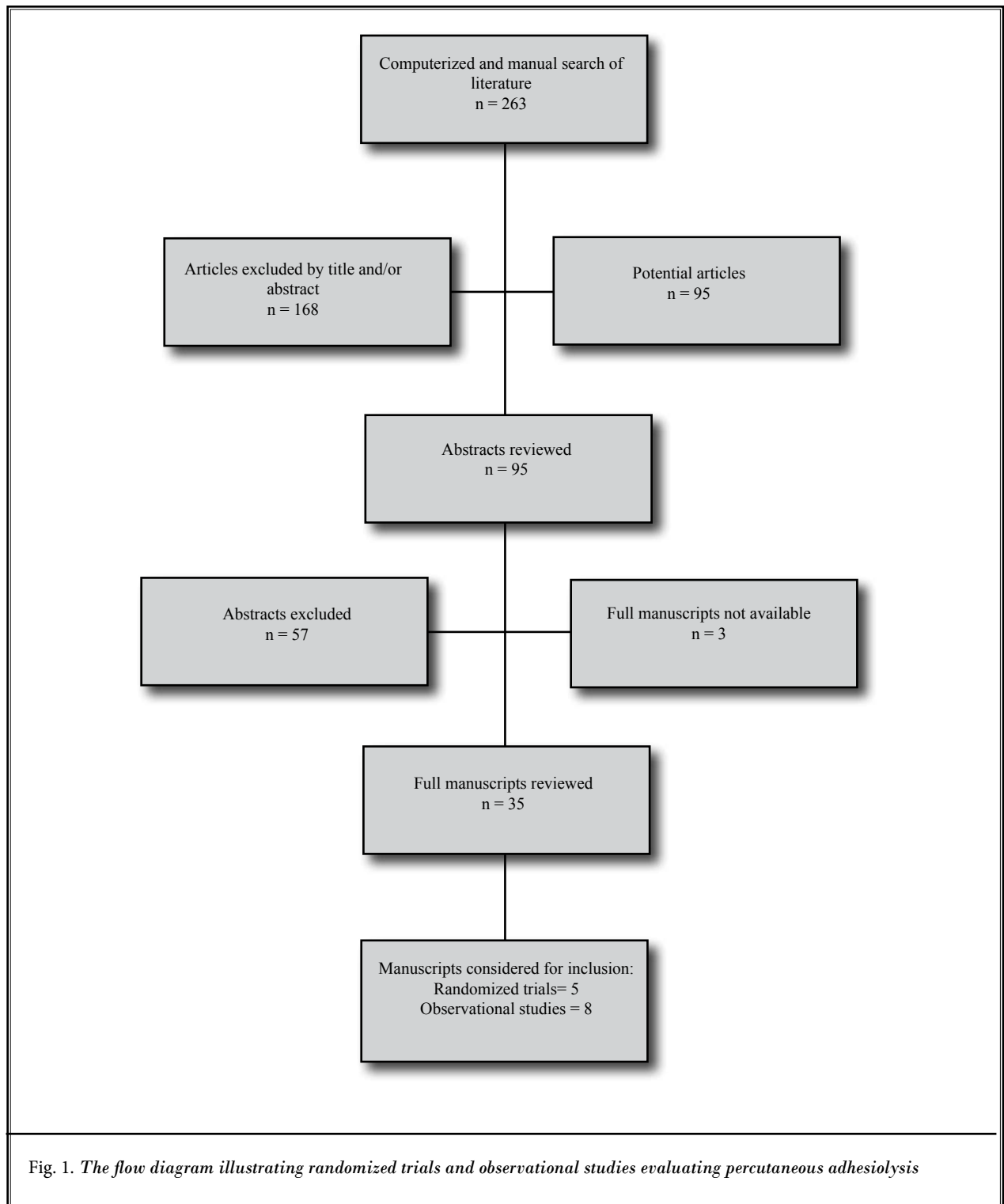


Fig. 1. The flow diagram illustrating randomized trials and observational studies evaluating percutaneous adhesiolysis

## Randomized Trials

### Methodologic Quality Assessment:

Of the 5 randomized trials (69,72-75), 3 of them met criteria (69,72,74), one was a duplication (73), and another one was a quasi randomized study (75), considered to be an observational study.

All 3 trials included heterogenous population.

Methodologic quality assessment criteria are illustrated in Table 3 showing all the randomized clinical trials evaluating the effectiveness of percutaneous adhesiolysis. The quality assessment criteria ranged from 55 to 74 with all 3 trials meeting inclusion criteria for evidence synthesis.

Table 4 illustrates the clinical relevance of the randomized trials.

### Clinical Relevance Assessment

All 3 studies met clinical relevance criteria (69,72,74).

### Study Characteristics

Study characteristics of published randomized trials of percutaneous adhesiolysis are illustrated in Table 5.

## Observational Studies

### Methodologic Quality Assessment

There were 8 observational studies considered for inclusion (70,71,76,77,105-108) with the addition of one study (75) which failed to meet design criteria of a randomized trial, and thus was considered obser-

Table 3. Methodological assessment of randomized clinical trials evaluating effectiveness of adhesiolysis.

Criterion		Weighted Score (points)	Manchikanti et al (74)	Heavner et al (72)	Veihelmann et al (69)
Study Population					
A	Homogeneity	2	2	2	2
B	Comparability of relevant baseline characteristics	5	5	5	5
C	Randomization procedure adequate	4	4	4	2
D	Drop-outs described for each study group separately	3	3	3	3
E	≤ 20% loss for follow-up	2	—	—	—
	≤ 10% loss for follow-up	2	—	—	—
F	> 50 subject in the smallest group	8	—	—	—
	> 100 subjects in the smallest group	9	—	—	—
Interventions					
G	Interventions included in protocol and described	10	10	10	10
H	Pragmatic study	5	5	5	5
I	Co-interventions avoided or similar	5	5	5	5
J	Placebo-controlled	5	—	—	—
Effect					
K	Patients blinded	5	5	5	—
L	Outcome measures relevant	10	10	10	10
M	Blinded outcome assessments	10	10	10	3
N	Follow-up period adequate	5	5	5	5
Data presentation and analysis					
O	Intention-to-treat analysis	5	5	—	—
P	Frequencies of most important outcomes presented for each treatment group	5	5	5	5
TOTAL SCORE		100	74	69	55

Methodological criteria and scoring adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288 (79).

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Table 4. Clinical relevance of randomized clinical trials evaluating the effectiveness of percutaneous adhesiolysis.

	Manchikanti et al (74)	Heavner et al (72)	Veihelmann et al (69)
A) Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?	+	+	+
B) Are the interventions and treatment settings described well enough so that you can provide the same for your patients?	+	+	+
C) Were all clinically relevant outcomes measured and reported?	+	+	+
D) Is the size of the effect clinically important?	+	?	+
E) Are the likely treatment benefits worth the potential harms?	+	+	+
<b>TOTAL CRITERIA MET</b>	5/5	4/5	5/5

+ = positive; - = negative; ? = unclear

Scoring adapted from Staal JB et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (91).

Table 5. Results of randomized trials of percutaneous adhesiolysis.

Study	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 mos Long-term relief > 6 mos
Veihelmann et al 2006 (69)	99 patients with chronic low back pain and sciatica (13 with prior back surgery). Nerve root compromise confirmed by MRI and CT. 52 patients treated with physiotherapy (PT) (control) • (5 prior surgery) 47 underwent epidural neuroplasty (percutaneous adhesiolysis) • 8 prior surgery PT patients could cross over after 3 months (12 patients crossed over).	Group I underwent physical therapy (no description of specific exercises), Group II underwent percutaneous adhesiolysis -Catheter placed through sacral hiatus to level of pathology after epidurogram to confirm position. 9 mL ropivacaine and 40mg triamcinolone catheter secured, 30 minutes later, 10 mL of 10% saline instilled, Unclear whether this was a 1 day or 3 day protocol.	Timing: 3 months, 6 months, 12 months. Outcome measures: VAS back, VAS leg, Oswestry disability score, Gerbershagen score, analgesic score.	Intention to treat analysis was performed. Among the adhesiolysis patients, there was a significant decrease in VAS and Oswestry scores at 1, 3, 6, and 12 months. 28 adhesiolysis patients were able to decrease 1° Gerbershagen grade compared to 2 PT patients.	Positive short- and long-term relief.
Manchikanti et al 2004 (74)	75 patients were evaluated. 25 patients in Group I served as controls and were treated with catheterization but no adhesiolysis. 25 patients in Group II were treated with catheterization, and adhesiolysis, followed by injection of local anesthetic, normal saline, and steroid. 25 patients in Group III, treatment consisted of adhesiolysis followed by injection of local anesthetic, hypertonic saline, and steroid.	Experimental groups: Adhesiolysis, hypertonic saline neurolysis, steroid and local anesthetic, and adhesiolysis, normal saline, steroid. Control group: Catheterization and no adhesiolysis.	Timing: 3 months, 6 months, and 12 months. Outcome measures: VAS pain scale, Oswestry Disability Index 2.0, work status, opioid intake, range of motion measurements, and psychological evaluation by P-3.	72% of patients in Group III (adhesiolysis and hypertonic neurolysis), 60% of patients in Group II (adhesiolysis only), compared to 0% in Group I (control) showed significant improvement at 12-month follow-up.	Positive short- and long-term relief.
Heavner et al 1999 (72)	59 patients with chronic intractable low back pain. All the patients failed conservative management, along with fluoroscopically directed epidural steroid injections.	Group I: hypertonic saline plus hyaluronidase. Group II: hypertonic saline Group III: isotonic saline (0.9% NaCl). Group IV: isotonic saline plus hyaluronidase.	Timing: 4 weeks, 3 months, 6 months, and 12 months. Outcome measure: Pain relief.	Initially 83% of the patients showed significant improvement compared to 49% of the patients at 3 months, 43% of the patients at 6 months, and 49% of the patients at 12 months.	Positive short- and long-term relief.

ational. Of the 9 studies, 4 met criteria for inclusion for methodologic quality assessment (71,75-77). Methodologic quality assessment criteria are illustrated in Table 6. Methodologic quality assessment showed

Table 6. Illustration of methodologic assessment of observational studies of percutaneous adhesiolysis.

CRITERION	Weighted Score (points)	Manchikanti et al (75)	Manchikanti et al (77)	Manchikanti et al (76)	Gerdesmeyer et al (71)
1. Study Question	2	2	2	2	2
• Clearly focused and appropriate question					
2. Study Population	8	5	5	5	5
• Description of study population	5	5	5	5	5
• Sample size justification	3	-	-	-	-
3. Comparability of Subjects	22	19	14	14	8
• Specific inclusion/exclusion criteria for all groups	5	5	5	5	5
• Criteria applied equally to all groups	3	3	3	3	-
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	3	3	3	-
• Study groups comparable to non-participants with regard to confounding factors	3	-	-	-	-
• Use of concurrent controls	5	5	-	-	-
• Comparability of follow-up among groups at each assessment	3	3	3	3	3
4. Exposure or Intervention	11	11	11	11	11
• Clear definition of exposure	5	5	5	5	5
• Measurement method standard, valid and reliable	3	3	3	3	3
• Exposure measured equally in all study groups	3	3	3	3	3
5. Outcome measures	20	15	15	15	10
• Primary/secondary outcomes clearly defined	5	5	5	5	5
• Outcomes assessed blind to exposure or intervention	5	-	-	-	-
• Method of outcome assessment standard, valid and reliable	5	5	5	5	5
• Length of follow-up adequate for question	5	5	5	5	-
6. Statistical Analysis	19	10	10	5	8
• Statistical tests appropriate	5	5	5	5	5
• Multiple comparisons taken into consideration	3	3	3	-	3
• Modeling and multivariate techniques appropriate	2	2	2	-	-
• Power calculation provided	2	-	-	-	-
• Assessment of confounding	5	-	-	-	-
• Dose-response assessment if appropriate	2	-	-	-	-
7. Results	8	8	8	6	3
• Measure of effect for outcomes and appropriate measure of precision	5	5	5	3	3
• Adequacy of follow-up for each study group	3	3	3	3	-
8. Discussion	5	5	5	5	5
• Conclusions supported by results with possible biases and limitations taken into consideration					
9. Funding or Sponsorship	5	5	5	5	2
• Type and sources of support for study					
TOTAL SCORE	100	80	75	68	54

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (80).



scores of 54 to 80. Five studies failed to meet the inclusion criteria: one study (105) evaluated the role of adhesiolysis in refractory spinal stenosis; the second study (106) evaluated the effectiveness of transforaminal ventral epidural adhesiolysis; the third study (107) described the relevance of epidurography and epidural adhesiolysis with a flimsy catheter, which was considered as adhesiolysis; the fourth study (108) was a case report utilizing a craniocaudal lateral intralaminar approach; and the fifth study (70) was a short-term follow-up.

Among the observational studies meeting the inclusion criteria for evidence synthesis, one study (77) included only post laminectomy patients, and 3 studies included heterogeneous populations, which also included post laminectomy syndrome patients (71,75,76).

### **Study Characteristics**

Study characteristics of all observational studies are illustrated in Table 7.

Gerdesmeyer et al (71), evaluated 98 patients initially and of these, 61 patients met inclusion criteria. Based on the review, even though specifically not mentioned, it appears that patients with disc herniation, as well as post lumbar laminectomy syndrome were included.

Among the 2 observational reports included (76,77), patient demographics were described in both studies. In one of the studies, the proportion of patients in Group II was 37% compared to 65% in Group I (76). In addition, work-related injury was lower in Group II (30%) than Group I (50%). Duration of pain was also longer in Group II compared to Group I. Patients in Group I received adhesiolysis and hypertonic saline neurolysis on 2 consecutive days with the catheter in place for the second day. In contrast, Group II patients received a single day procedure with percutaneous adhesiolysis, as well as hypertonic saline neurolysis. In one study (77), only patients with post lumbar laminectomy were included.

Manchikanti et al (75) studied 45 patients with 30 patients in the treatment group and 15 patients in the conservative management group with one-day adhesiolysis showing improvement with pain relief in 93% of the patients at 6 months and 47% of the patients at 1 year. However, procedures were repeated 1 to 3 times. Patients in the treatment group also showed significant improvement in functional and psychological status. The results of this study have not been

considered significant, as it was neither blinded, nor did it include a control group undergoing placebo injections.

### **Descriptive Characteristics**

All the studies included in the evidence synthesis described patient baseline characteristics (69,72,74). Of the 3 randomized trials, 2 studies (72,74) had similar patient characteristics. Manchikanti et al (74) also reported the proportion of patients included with a history of previous surgery, which ranged from 64% to 72% in all intervention groups. Patients in all 3 studies failed multiple conservative modalities of treatments including fluoroscopically directed epidural steroid injections. The study by Veihelmann et al (69) evaluated patients with a history of chronic low back pain and sciatica. Inclusion criteria were radicular pain with a corresponding nerve root with compressing substrate found on magnetic resonance imaging or computed tomography scans. Prior to randomization, all patients received physiotherapy, local injections, and analgesics. Local injections were not defined. All patients were evaluated for radicular pain by an independent neurologist. Exclusion factors were paralysis, spinal canal stenosis, rheumatologic disease, and malignancy. They did not identify which of these patients had post laminectomy syndrome. However, post laminectomy syndrome or epidural fibrosis were not exclusion criteria, and thus, it is believed that some of the patients probably included post laminectomy syndrome or epidural fibrosis patients.

Heavner et al (72) compared various types of solutions used after mechanical adhesiolysis; Group A received a combination of hyaluronidase and hypertonic saline; Group B, hypertonic saline solution; Group C, isotonic saline solution; and Group D, hyaluronidase and isotonic saline solution.

Manchikanti et al (74) divided 75 patients randomly into 3 groups, with Group I consisting of a control group without adhesiolysis, with injection of local anesthetic, steroid, and normal saline; Group II consisting of patients undergoing adhesiolysis, with injection of local anesthetic, steroid, and normal saline; and Group III consisting of patients undergoing adhesiolysis, with an injection of 10% sodium chloride solution, in addition to local anesthetic and steroid.

Heavner et al (72) evaluated a 3-day procedure where the catheter was inserted on the first day and the drugs were injected on the second and third day, whereas Manchikanti et al (74,75) evaluated one-day

Table 7. Results of observational studies of percutaneous adhesiolysis and hypertonic saline neurolysis.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 mos Long-term relief > 6 mos
Manchikanti et al (75)	45 patients were evaluated. 15 patients in Group I were treated conservatively. 30 patients in Group II were treated with percutaneous epidural adhesiolysis and hypertonic saline neurolysis.	Experimental group: adhesiolysis, hypertonic saline neurolysis, and epidural steroid injection, one or more occasions. Control group: physical therapy exercise program and medication.	Timing: 1 month, 3 months, 6 months, 1 year. Outcome measures: Pain relief, functional status, psychological status, employment status.	Experimental group showed improvement with pain relief in 97% at 3 months, 93% at 6 months, and 47% of the patients at 1 year. Generalized anxiety disorder, somatization disorder, average pain, and functional status improved significantly in Group II.	Positive short- and long-term relief.
Manchikanti et al (77)	60 post lumbar laminectomy patients were included after failure of conservative management.	Adhesiolysis, hypertonic saline neurolysis, and injection of steroid.	Timing: 3 months, 6 months, 12 months. Outcome measures: Pain relief.	With multiple injections, initial relief was seen in 100% of the patients, however it declined to 90% at 3 months, 72% at 6 months, and 52% at 1 year.	Positive short- and long-term relief.
Manchikanti et al (76)	A retrospective randomized evaluation of the effectiveness of one-day adhesiolysis and hypertonic saline neurolysis in 129 patients.	Adhesiolysis, hypertonic saline neurolysis, and injection of steroid.	Timing: 4 weeks, 3 months, 6 months, 12 months. Outcome measures: pain relief.	Initial relief was reported in 79% of the patients with 68% of the patients reporting relief at 3 months, 36% at 6 months, and 13% at 12 months with one injection.	Positive short-term and negative long-term relief.
Gerdesmeyer et al (71)	61 patients with lumbar radiculopathy treated with percutaneous adhesiolysis.	All patients underwent percutaneous adhesiolysis "according to Racz's technique"; unclear whether one day or 3 day protocol.	Evaluation at 3 and 6 months. Outcome measures: subjective pain scores (McNab score).	"Subjective pain perception clearly improved after 3 as well as 6 months."	Positive short-term and long-term relief.

adhesiolysis. Veihelmann et al (69) and Gerdesmeyer et al (70,71) used a 3-day protocol in all 3 studies. They also used hyaluronidase as part of the treatment protocol.

The outcome parameters by Heavner et al (72) included the short-form McGill Pain Questionnaire and Visual Analog Scale for back pain and leg pain. Manchikanti et al (74) utilized VAS pain scale, Oswestry Disability Index 2.0, work status, opioid intake, range of motion measurement, and psychological evaluation by Pain Patient Profile (P-3).

Outcome measures included in the third randomized clinical trial (76) were significant pain relief (> 50%), cumulative pain relief, physical health, mental health, functional status, narcotic intake, psychologi-

cal status, and return to employment. Veihelmann et al (69) used Visual Analogue Scale scores for back pain and leg pain, Oswestry Disability Score, Gerbershagen Score, and a quantified score for the use of analgesics. They also used a blinded observer.

### Effectiveness

Of the 3 randomized trials evaluating percutaneous adhesiolysis, all showed positive results for short- and long-term relief (69,72,74). Of the 4 observational studies, 3 studies showed positive results for both short- and long-term improvement (71,75,77), whereas one study (76) was positive for short-term and negative for long-term relief.

Table 8. Results of published studies effectiveness of percutaneous lysis of lumbar epidural adhesions.

Study	Study Characteristics	Participants	Pain Relief				Results	
			≤ 3 mos.	3 mos.	6 mos.	12 mos.	Short-term ≤ 6 mos.	Long-term >6 mos.
Manchikanti et al 2004 (74)	RA, DB	G1 = 25 G2 = 25 G3 = 25	G1 = 33% G2 = 64% G2 = 72%	G1 = 0% G2 = 64% G3 = 72%	G1 = 0% G2 = 60% G3 = 72%	G1 = 0% G2 = 60% G3 = 72%	P	P
Heavner et al 1999 (72)	RA, DB	59	83%	49%	43%	49%	P	P
Veihelmann et al 2006 (69)	RA	99	SI	SI	SI	SI	P	P
Manchikanti et al 2001(75)	O	G1 = 15 G2 = 30		97%	93%	47%	P	P
Manchikanti et al 1999(77)	O	60	100%	90%	72%	52%	P	P
Manchikanti et al 1999(76)	O	129	79%	68%	36%	13%	P	N
Gerdesmeyer et al 2005 (71)	O	61	SI	SI	SI	SI	P	P

RA = randomized; DB = double blind; O = observational; G = group; SI = significant improvement; P = positive; N = negative

Table 8 illustrates results of effectiveness of percutaneous adhesiolysis.

**Level of Evidence**

The indicated level of evidence is I or II-1 for short- and long-term relief for percutaneous adhesiolysis in post lumbar laminectomy syndrome.

**Recommendations**

Based on Guyatt et al (101), grading strength of recommendations and quality of evidence in clinical guidelines, the recommendation is strong, with 1B or 1C for percutaneous adhesiolysis in post lumbar laminectomy syndrome.

**Complications**

The most commonly reported complications of percutaneous adhesiolysis were dural puncture, catheter shearing, and infection (24-28,69-77,108-114). Other potential complications include intravascular injection; vascular injury; cerebral vascular or pulmonary embolus; reaction to the steroids; hypertonic saline, or hyaluronidase, and administration of high volumes of fluids potentially resulting in excessive epidural hydrostatic pressures; death; and brain damage (24-28,113).

Other side effects are related to the administration of steroids and are generally attributed to the chemistry or pharmacology of the steroids (115-118). However, therapeutic doses of epidural steroids in appropriate dosing did not result in complications (119).

**DISCUSSION**

This systematic review of the effectiveness of percutaneous adhesiolysis in post lumbar surgery syndrome indicated Level I or II-1 evidence for short- and long-term relief based on USPSTF criteria and strong/ 1B or 1C recommendation based on Guyatt et al's (101) criteria. The evidence was derived from randomized control trials and observational studies. The results of this systematic review are similar to previous systematic reviews and guidelines (24,26,27,102). However, in this evaluation we focused on post laminectomy syndrome only as there is a paucity of evidence for other conditions. Further, we have also expanded the definition of short-term relief to 6 months or less, whereas long-term relief is defined as longer than 6 months — a robust measure. Even then, evidence for percutaneous adhesiolysis for both and short- and long-term continues to be Level I or II-1, yielding a strong recommendation.

In this systematic review, we utilized 3 randomized trials (69,72,74) and 4 (71,75-77) observational studies meeting the inclusion criteria. This systematic review has shown that percutaneous adhesiolysis is an effective treatment, it is superior to epidural steroid injections, the addition of hypertonic sodium chloride solution and hyaluronidase may or may not improve the outcomes, and it is a safe procedure when performed appropriately. Of all the 3 randomized trials (69,72,74) and 4 observational studies (71,75-77) evaluated, the effectiveness of percutaneous adhesiolysis was demonstrated both with one-day and 3-day procedures. Two randomized trials (69,72) evaluated adhesiolysis with a 3-day protocol, whereas one randomized trial (74), and 3 observational studies evaluated percutaneous adhesiolysis on one-day basis (75-77). The study by Veihelmann et al (69) was not double blind, whereas Heavner et al (72) and Manchikanti et al (74) used a non-inferiority or equivalence control design (95,96, 120-122).

This review showed percutaneous adhesiolysis is clearly superior to fluoroscopically directed epidural steroid injections. Further, this review also demonstrated modalities of an effective management of chronic, refractory low back and lower extremity pain, specifically secondary to post lumbar laminectomy syndrome. This systematic review with stringent inclusion and exclusion as well as methodological quality criteria, demonstrated that the technique of adhesiolysis overcomes the obstacle of being able to get various medications to a lesion specific site by placing the tip of a soft spring catheter within the scar, and thereby opening the perineural space. Thus, the steroid and other solutions reach the appropriate site and provide anti-inflammatory effect and neural blockade.

Despite multiple publications, discussions continue with regards to long-term effectiveness of percutaneous adhesiolysis. This systematic review failed to show any significant evidence for hyaluronidase. Hyaluronidase is an enzyme additive used for adhesiolysis. Only a limited number of studies described the influence of drugs on hyaluronidase activity. In an experimental evaluation of hyaluronidase activity in combination with specific drugs applied in clinical techniques of interventional pain management, Schulze et al (123) showed that drugs affecting the activity of hyaluronidase with decreased effectiveness for iodinated contrast media and 10% sodium chloride solution; whereas, corticosteroids and isotonic sodium chloride solution, 0.9%, increased the activity

with no effect with combination of local anesthetics. Thus, it would be extremely difficult to evaluate the effect of hyaluronidase since multiple drugs are utilized in adhesiolysis.

The methodological quality and number of patients included in the studies may be criticized in the randomized trials of percutaneous adhesiolysis. Heavner et al (72) evaluated 59 patients with chronic intractable low back pain. All the patients failed conservative management, along with fluoroscopically directed epidural steroid injections. Consequently these authors studied the effect of isotonic saline, hypertonic saline plus hyaluronidase, and finally isotonic saline plus hyaluronidase. The patients functioned as their own controls for the purposes of adhesiolysis. The authors measured various outcomes at 4 weeks, 3 months, 6 months, and 12 months. Their outcome measures included pain relief by visual analog scale. From a total of 83 patients recruited, 24 patients were removed from the study before the injection series was completed, leaving 59 patients that completed the study. The authors did not perform an intention-to-treat analysis. The results showed 49% of the patients with significant improvement at 3 months, 43% at 6 months, and 49% at 12 months. However the study has been misinterpreted in the past due to a lack of differences between various groups (103). In this study (72), all the patients prior to being enrolled in the randomized, double-blind study failed to respond to many types of conservative modalities of treatment including fluoroscopically directed epidural steroid injections. Thus, this study provided evidence for the effectiveness of adhesiolysis, but not for injection of hypertonic saline or hyaluronidase.

The second randomized trial of percutaneous adhesiolysis by Manchikanti et al (74) evaluated one-day lumbar epidural adhesiolysis and hypertonic saline neurolysis in the treatment of chronic low back pain with a randomized, double-blind design. These authors studied a total of 75 patients with 25 patients in each group using 3 types of interventions. Group I served as controls undergoing catheterization without adhesiolysis, followed by injection of local anesthetic, normal saline, and steroid. Group II consisted of catheterization and adhesiolysis followed by injection of local anesthetic, normal saline, and steroid. Group III consisted of adhesiolysis followed by injection of local anesthetic, hypertonic saline, and steroid. These authors also incorporated statistical analysis which included intent-to-treat analysis. They included exten-

sive outcome measures with visual analog pain scores, Oswestry Disability Index, work status, opioid intake, range of motion measurement, and psychological status. They defined significant pain relief as average relief of 50% or greater. Their results showed that significant improvement was seen in patients in Group II and Group III at 3 months, 6 months, and 12 months, compared to baseline measurements, as well as compared to Group I without adhesiolysis. In this study, 72% of the patients in Group III with adhesiolysis and hypertonic saline neurolysis improved, compared to 60% of the patients in Group II with adhesiolysis only showed significant improvement at 12-month follow-up compared to 0% in Group I, which was without adhesiolysis, but did have a steroid injection. These authors also showed that the average number of treatments for one year were 2.76 in Group II and 2.16 in Group III. Duration of significant relief with the first procedure was  $2.8 \pm 1.9$  months in Group II and  $3.8 \pm 3.37$  months in Group III. Consequently, the authors of this review concur with the authors of the study which concluded that percutaneous adhesiolysis, with or without hypertonic saline neurolysis, is an effective treatment for chronic low back pain.

The third study also used by the American College of Occupational and Environmental Medicine (ACOEM) assessment was of Veihelmann et al (69). The study is described as a moderate quality randomized controlled trial looked at 99 patients with chronic low back pain and sciatica based on disc protrusion/prolapse or failed back surgery, with 52 patients receiving physiotherapy compared to 47 patients undergoing epidural neuroplasty on a short-term basis as well as at 12 months of follow-up. The diagnosis of sciatica was based on radicular pain and a positive MRI, with VAS scores suggesting slightly worse leg pain than low back pain (124). The authors of this manuscript (69) concluded that taking into account that the results of discectomy are not necessarily superior to conservative treatment, the data shows, for the first time, that for patients with radicular pain due to disc protrusion and herniation or epidural fibrosis, epidural neuroplasty seems to be an effective safe alternative treatment (124). The authors (69) also concluded that at least 3

months after neuroplasty, it is superior in comparison to conservative treatment with physiotherapy. Nevertheless, they suggested that further prospective randomized double-blinded studies should be performed to prove the effectiveness of epidural neuroplasty in comparison to placebo and in comparison to open discectomy procedures (69). Consequently, due to a poor evaluation process of ACOEM guidelines, reassessment of these guidelines was carried out (82). The quality of the guidelines was assessed (125) and the potential implications were described (126). In addition, multiple studies have been performed utilizing equivalence or non-inferiority design (32-35,72,74). Thus in appropriate evidence synthesis, all types of evidence must be utilized (130-134).

The limitations of this systematic review include the lack of new evidence since the previous systematic reviews. However, this systematic review continued to show significant evidence with studies meeting methodologic quality assessment. This systematic review is different from others in that short-term relief was defined as at least 6 months and long-term relief was defined as longer than 6 months. Combining assessment of clinical relevance and methodologic quality assessment, this review provides significant evidence of modest relief from percutaneous adhesiolysis in appropriately selected patients with post lumbar surgery syndrome with persistent pain.

## **CONCLUSION**

This systematic review of the effectiveness of percutaneous adhesiolysis in the management of chronic low back pain in post lumbar surgery syndrome indicated Level I to II-1 evidence, based on 3 randomized trials, with a strong recommendation.

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