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Systematic Review

# Percutaneous and Endoscopic Adhesiolysis in Managing Low Back and Lower Extremity Pain: A Systematic Review and Meta-analysis

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**Background:** Chronic refractory low back and lower extremity pain is frustrating to treat. Percutaneous adhesiolysis and spinal endoscopy are techniques which can treat chronic refractory low back and lower extremity pain.Percutaneous adhesiolysis is performed by placing the catheter into the tissue plane at the ventrolateral aspect of the foramen so that medications can be injected. Adhesiolysis is used both for pain caused by scarring which is not resistant to catheter placement and other sources of pain, including inflammation in the absence of scarring.Mechanical lysis of scars with a catheter may or may not be necessary for percutaneous adhesiolysis to be effective. Spinal endoscopy allows direct visualization of the epidural space and has the possibility to use laser energy to treat pathology.

**Study Design:** A systematic review of the effectiveness of percutaneous adhesiolysis and spinal endoscopic adhesiolysis to treat chronic refractory low back and lower extremity pain

**Objective:** To evaluate and update the effectiveness of percutaneous adhesiolysis and spinal endoscopic adhesiolysis to treat chronic refractory low back and lower extremity pain

**Methods:** The available literature on percutaneous adhesiolysis and spinal endoscopic adhesiolysis in treating persistent low back and leg pain was reviewed. The quality of each article used in this analysis was assessed.

The level of evidence was classified on a 5-point scale from strong, based upon multiple randomized controlled trials to weak, based upon consensus, as developed by the U.S. Preventive Services Task Force (USPSTF) and modified by ASIPP.

Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 to September 2015, and manual searches of the bibliographies of known primary and review articles.

**Outcome Measures:** Pain relief of at least 50% and functional improvement of at least 40% were the primary outcome measures.

Short-term efficacy was defined as improvement of 6 months or less; whereas, long-term efficacy was defined more than 6 months.

**Results:** For this systematic review, 45 studies were identified. Of these, for percutaneous adhesiolysis there were 7 randomized controlled trials and 3 observational studies which met the inclusion criteria. For spinal endoscopy, there was one randomized controlled trial and 3 observational studies.

Based upon 7 randomized controlled trials showing efficacy, with no negative trials, there is Level I or strong evidence of the efficacy of percutaneous adhesiolysis in the treatment of chronic refractory low back and lower extremity pain.

Based upon one high-quality randomized controlled trial, there is Level II to III evidence supporting the use of spinal endoscopy in treating chronic refractory low back and lower extremity pain.

Conflicts of Interest
Dr. Helm is a clinical investigator for Myelotec. Dr. Racz is a consultant for Epimed. Epimed is owned by members of Dr Racz's family. He is a shareholder in Halozyme and Stemwave. Dr. Justiz is a consultant and research advisor for St. Jude Medical, Epimed International and Veriflex. Dr. Hayek is a consultant for Boston Scientific. Dr. Gerdesmeyer, Dr. Kaplan, Dr. El Terany, and Dr. Knezevic report no conflicts.

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**Conclusion:** The evidence is Level I or strong that percutaneous adhesiolysis is efficacious in the treatment of chronic refractory low back and lower extremity pain. Percutaneous adhesiolysis may be considered as a first-line treatment for chronic refractory low back and lower extremity pain.

The evidence is Level II to III that spinal endoscopy is effective in the treatment of chronic refractory low back and lower extremity pain.

**Key words:** Spinal pain, chronic low back pain, post lumbar surgery syndrome, epidural scarring, adhesiolysis, endoscopy, radicular pain**:**

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Chronic refractory low back pain with or without lower extremity pain which does not resolve after conservative therapy or even surgical treatment can present a vexing therapeutic problem (1-8).Low back and lower extremity pain is often treated with surgery, with the most common indications being disc protrusion with radiculitis, spinal stenosis and spondylolisthesis (9). While the evidence supporting surgery for disc protrusions is strong, outcomes for other conditions is less compelling (10-15). There is a need for therapies to help patients with chronic persistent low back and lower leg pain who either do not want surgery or who are not candidates for surgery. In addition, cost pressures, the introduction of alternate payments systems and the increasing importance of comparative effectiveness research all create an impetus for cost-effective therapies, such as interventional techniques, to treat these problems (16).

Two techniques which have been developed to treat persistent low back and radicular pain are percutaneous adhesiolysis and epiduroscopic adhesiolysis. Percutaneous adhesiolysis was first described by Racz as a three-day procedure (17-19).The protocol has been modified so that it can be done as a one day procedure (20).More recently, both Kim and Choi have separately described a transforaminal balloon treatment for foraminal stenosis, while Bosscher has described a transforaminal dilation technique (21-23).

Epiduroscopy is approved for visualization of the epidural space and the delivery of drugs approved for epidural injection (24,25). Epiduroscopy has been used as a therapeutic tool to perform adhesiolysis It offers the advantage over percutaneous adhesiolysis of directly visualizing pathology and potentially documenting the cause of pain.

More recently, laser epiduroscopy has been evaluated for both lysis of adhesions and for treatment of intradiscal disorders (26-30). This review specifically does not cover endoscopic laser treatments.

Both percutaneous adhesiolysis and epiduroscopy have been the subject of systematic reviews.

While there is some debate as to how often a systemic review should be updated, a consensus is forming that systematic reviews have a five-year life span (31-34). Preeminent among the reviews more than five years old is the 2007 American Pain Society (APS) evidence review for treating low back pain (35). The APS evidence review concluded that there was insufficient evidence to issue a recommendations (36). In like manner, a 2009 NICE review did not issue any recommendation regarding endoscopic adhesiolysis (37).

Van Boxem, in a 2010 review focusing on lumbosacral radicular pain, felt that adhesiolysis and epiduroscopy could be considered in refractory conditions, preferably in a study (38).

Tran, in a 2010 review of the treatment of lumbar spinal stenosis, examined one preliminary report of randomized controlled trial (RCT) of adhesiolysis (39,40). Tran concluded that percutaneous adhesiolysis was a promising therapeutic modality.

Helm published systematic reviews of percutaneous adhesiolysis and of epiduroscopy in 2012 and 2013 (41,42). Using a three-point scale, Helm found fair evidence supporting the use of percutaneous adhesiolysis in post lumbar surgery syndrome and in spinal stenosis. Helm also found fair evidence for the use of spinal endoscopy in post lumbar surgery syndrome. The current systematic review is an update of these reviews.

Hsu evaluated the factors associated with success outcomes from epidural lysis of adhesions for failed back surgery syndrome and for spinal stenosis in 2014 (43). Paradoxically, he found the improved outcomes were related to age >81 or patients on Workers' Compensation or seeking disability. A review out of the

same group looked at both percutaneous adhesiolysis and epiduroscopy (44). Lee assessed the evidence supporting the use of various injectates used in adhesiolysis. He found that the evidence for the use of hyaluronidase was conflicting, the evidence for the use of hypertonic saline was moderately strong, that the use of high volumes of injectate was strongly positive and that there was no evidence for the role of mechanical disruption. The study found that the evidence seemed to indicate that adhesiolysis was superior to epidural injections or conservative therapy, although there needed to be clarity as to what the target population was. Lee also concluded that there was insufficient evidence to determine the role of epiduroscopy.

Kallewaard published a systematic review of epiduroscopy in 2014, focusing on radicular pain (45). The reviewed focused on the role of epiduroscopy in identifying sources of pain and fibrosis, and in providing targeted drug delivery, particularly in failed back syndrome. This reviewed recommended epiduroscopy with adhesiolysis in refractory cases of failed back syndrome.

Jamison reviewed percutaneous epidural adhesiolysis in 2014 (46). He found percutaneous adhesiolysis to be useful for failed back surgery and spinal stenosis.

Avellanal performed a systematic review of epiduroscopy in 2014 (47) He concluded that epiduroscopy was a safe and effective procedure.

A 2015 review by Moon is excluded as it is written in Korean (48).

This systematic review is an update of previous systematic reviews on percutaneous adhesiolysis (41) and on epiduroscopy (42) in treating low back and radicular pain. In addition, complications of these procedures will be analyzed. Literature up until September 2015 was reviewed.

## 1.0 Methods

The methodology utilized in this review followed the formal processes developed for the systematic review and meta-analysis of randomized trials and observational studies (49-63).

### 1.1 Criteria for Considering Studies for This Review

#### *1.1.1 Types of Studies*

- Randomized controlled trials (RCT)
- Non-randomized observational studies
- Case reports and reviews were evaluated for adverse effects

#### *1.1.2 Types of Participants*

Patients with chronic refractory low back pain with or without lower extremity pain of at least 4 months' duration and not responsive to conservative care, including medications, physical or chiropractic therapy or epidural injections.

#### *1.1.3 Types of Interventions*

Caudal lumbar percutaneous adhesiolysis and endoscopic adhesiolysis.

#### *1.1.4 Types of Outcome Measures*

The primary outcome parameter was pain relief.

The secondary outcome measures were functional status improvement, change in psychological status, or a reduction in either opioid use or reliance on health care interventions.

### 1.2 Literature Search

Searches were performed from the following sources, limited to articles published in English:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. Cochrane Library
   www.thecochranelibrary.com/view/0/index.htmL
3. U.S. National Guideline Clearinghouse (NGC)
   www.guideline.gov/
4. Google Scholar
   scholar.google.com
5. Previous systematic reviews
6. Clinical Trials
   clinicaltrials.gov/
7. Communication with investigators active in the field.
8. Bibliographies of reviewed papers were also examined.

The search period was from 1966 through September 2015.

### 1.3 Search Strategy

The search terminology included epidural adhesiolysis, epidural fibrosis, epidural lysis of adhesions, epidural neurolysis, epidural neuroplasty, percutaneous adhesiolysis, percutaneous neuroplasty, Racz procedure, endoscopic adhesiolysis, epidural endoscopy, epiduroscopy, spinal endoscopy.

## 1.4 Data Collection and Analysis

Two review authors independently, in an unblinded standardized manner, developed search criteria, searched for relevant literature and selected the manuscripts.

### *1.4.1 Selection of Studies*

Two review authors screened the abstracts of all identified studies against the inclusion criteria. All articles with possible relevance were then retrieved in full text for comprehensive assessment of internal validity, quality and adherence to inclusion criteria.

### *1.4.2 Inclusion and Exclusion Criteria*

Only RCTs and observational studies with at least 6 months follow up, with statistical analysis and with at least 50 patients in the study or with 25 patients in a group were included. Reports without appropriate diagnoses, non-systematic reviews, book chapters, and case reports were excluded.

For any condition, if there were more than 5 randomized trials, nonrandomized or observational studies were not utilized.

### *1.4.3 Methodological Quality or Validity Assessment*

The quality of each individual article used in this analysis was assessed by Cochrane review criteria (Appendix Table 1) (60) and American Society of Interventional Pain Physicians (ASIPP) interventional Pain Management techniques -- Quality Appraisal of Reliability and Risk of Bias Assessment (IPM – QRB) for randomized trials (Appendix Table 2) (64) , and ASIPP interventional pain management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment for Nonrandomized Studies (IPM – QRBNR) for nonrandomized and observational studies (Appendix Table 3) (65).

Utilizing Cochrane review criteria, studies meeting the inclusion criteria with at least 8 of 12 criteria were considered high quality and 5-7 were considered moderate quality. Those meeting criteria of less than 5 were considered as low quality and were excluded.

Based on IPM-QRB criteria for randomized trials and nonrandomized studies, the studies meeting the inclusion criteria scoring of 32 to 48 were considered high quality trials; studies with scores between 20 to 31 were considered moderate quality; studies scoring less than 20 were considered low quality and were excluded.

### *1.4.4 Data Extraction and Management*

Methodologic quality assessment was performed by the authors with groups of 2 authors reviewing multiple manuscripts. The assessment was carried out independently in an unblinded standardized manner to assess the methodologic quality and internal validity of all the studies considered for inclusion. Any discrepancies in the methodologic quality assessment were evaluated by a third reviewer and settled by consensus.

If there was conflict of interest with a reviewed manuscript, the involved author(s) did not review the manuscript for methodologic quality assessment.

### *1.4.5 Meta-Analysis*

If the literature search provided at least 3 randomized trials meeting the inclusion criteria and they are clinically homogenous for each modality and condition evaluated, a meta-analysis was performed.

Qualitative (the direction of a treatment effect) and quantitative (the magnitude of a treatment effect) conclusions were evaluated. Random-effects meta-analysis to pool data was also used. For placebo controlled trials, the net effect between 2 treatments was utilized. However, for active-controlled trials, the differences between baseline and at the follow-up period were utilized.

## 1.5 Outcome Measurements

Previously, the consensus was that at least a 2-point change on a 0 to 10 point pain scale, such as the visual analog scale or numerical rating scale, was necessary to document a clinically meaningful change (53,54,57,60,66-72). The current consensus is that clinically meaningful change requires the more rigorous standard of 50% pain relief (40,73-85).

This study will define clinically meaningful pain relief as a 50% reduction from baseline. Clinically meaningful functional status improvement is 40% or more.

Short-term efficacy is defined as less than 6 months; long-term efficacy is defined as 6 months or longer.

## 1.6 Grading of Evidence

The grading of the evidence was performed using ASIPP's modification of the United States Preventive Services Task Force's (USPSTF) and other criteria. (86-93).

Table 1 shows the evidence rating, ranging from Level 1, consensus, at the bottom to Level 5, multiple randomized controlled trials, as the strongest level of evidence.

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

| | |
|---|---|
| Level I | Evidence obtained from multiple relevant high quality randomized controlled trials |
| Level II | Evidence obtained from at least one relevant high quality randomized controlled trial or multiple relevant moderate or low quality randomized controlled trials |
| Level III | Evidence obtained from at least one relevant moderate or low quality randomized controlled trial with multiple relevant observational studies<br>or<br>Evidence obtained from at least one relevant high quality nonrandomized trial or observational study with multiple moderate or low quality observational studies |
| Level IV | Evidence obtained from multiple moderate or low quality relevant observational studies |
| Level V | Opinion or consensus of large group of clinicians and/or scientists |

Source: Manchikanti L, Falco FJE, Benyamin RM, Kaye AD, Boswell MV, Hirsch JA. A modified approach to grading of evidence. Pain Physician 2014; 17:E319-E325 (???).

## 2.0 Results

Figure 1 shows a flow diagram of study selection as recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (58).

There were 45 trials considered for inclusion (20,21,26,28,40,43,85,94-131).

Meta-analysis was performed for percutaneous adhesiolysis. Studies with no control group or useable numeric data were excluded (20,125,126,132).

Appendix Table 4, List of Excluded Randomized and Non-randomized Studies, shows the reasons for exclusion.

Appendix Table 5 illustrates the characteristics of the trials considered for inclusion. There were 7 randomized controlled trials (40,85,120,122-124,132) and 3 observational trials evaluating percutaneous adhesiolysis (20,125,126). As there are more than 5 randomized controlled trials, the observational studies are not utilized to assess the quality of evidence.

There was one randomized trial evaluating endoscopic adhesiolysis (127) and 3 observational trials (128-130).

### 2.1 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials (RCTs) meeting inclusion criteria was carried out utilizing Cochrane review criteria and randomized trials and observational studies utilizing IPM-QRB and IPM-QRBNR criteria as shown in Tables 2-4..

### 2.2 Meta-Analysis

There was sufficient homogeneity of the percutaneous adhesiolysis to allow a meta-analysis. There was not a sufficient basis for a meta-analysis of spinal endoscopy.

The results of the meta-analysis are shown in:

- Table 5, Pain improvement; short term follow up 3 months (5a) and long term follow up 12 months (5b),
- Table 6. Functional improvement; short term follow up 3 months (6a) and long term follow up 12 months (6b).

Analysis showed statistical significantly better pain improvement, functional improvement and successful pain outcome (> 50% pain improvement) than in the control group for both time points of 3 months and 12 months (Table 7).

### 2.3 Study Characteristics

Appendix Tables 6 and 7 show the study characteristics of the included studies for randomized trials and observational studies evaluating percutaneous adhesiolysis and spinal endoscopic adhesiolysis

There are 7 randomized controlled trials dealing with percutaneous adhesiolysis. Gerdesmeyer (120) used a 3-day protocol with ventrolateral catheter placement to evaluate patients with radicular pain and no muscle weakness, with 28 of 31 patients having more than 50% improvement in ODI.

Chun-jing (122) looked at patients with radiculopathy after surgery, with a 3.24 mean decrease in VAS at 6 months.

Manchikanti, in 2 distinct studies, (40, 85) one looking at post lumbar surgery patients and another looking at spinal stenosis patients, found that over 70% of both groups had clinical significant improvements in pain and function.

Heavner (132) found in a heterogeneous population that adhesiolysis provided pain relief.

Manchikanti (123) found that both hypertonic saline and normal saline provided clinically significant relief.

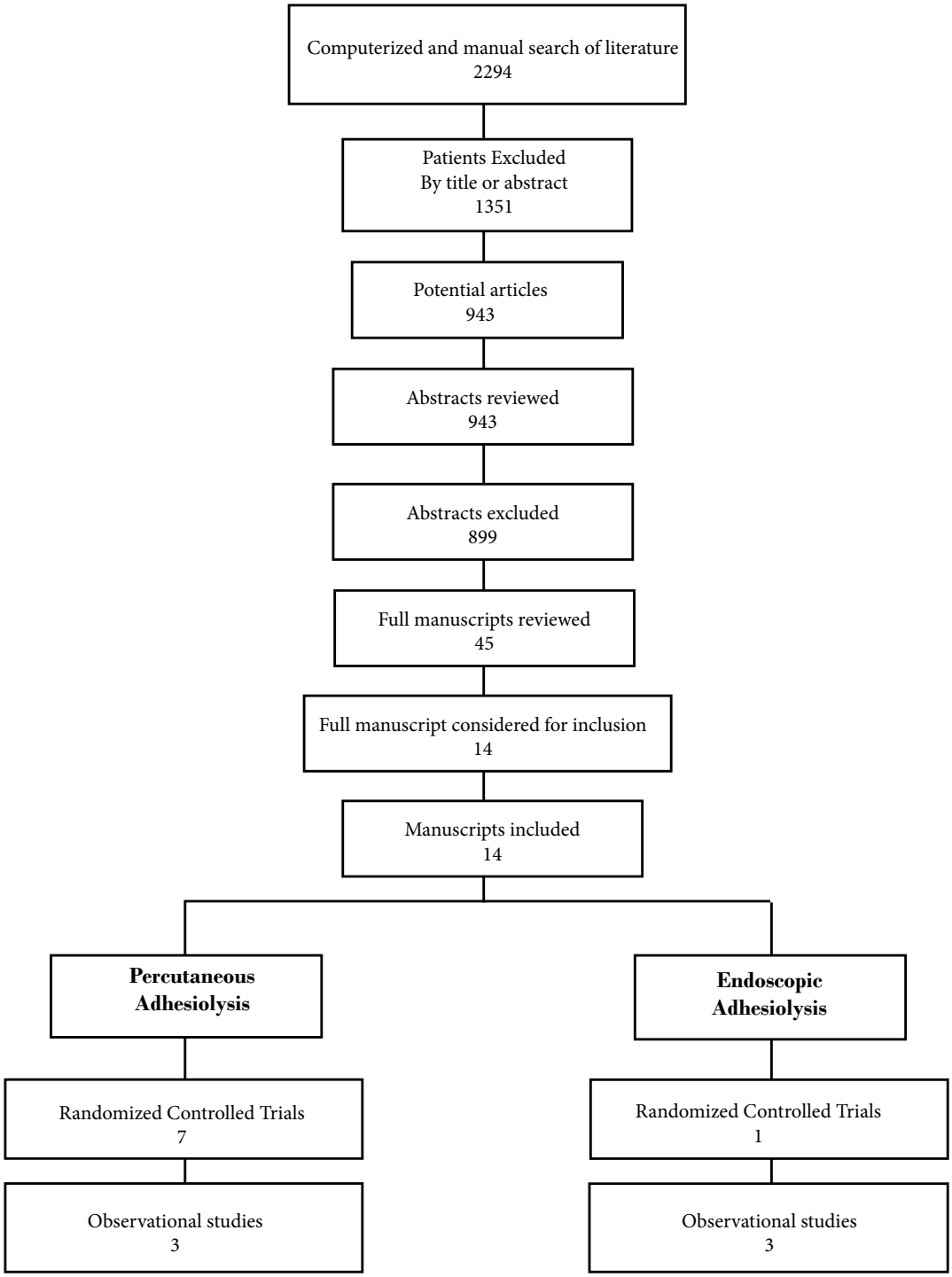



Fig. 1. *Schematic presentation of study selection.*

Table 2. *Methodological Quality Assessment of Randomized Trials of Percutaneous Adhesiolysis and Spinal Endoscopic Adhesiolysis Procedures Utilizing Cochrane Review Criteria*

| | Gerdesmeyer 2013 (120) | Chun-jing 2012 (122) | Manchikanti 2009 (85) | Heavner 1999 (132) |
|---|---|---|---|---|
| Randomization adequate | Y | Y | Y | U |
| Concealed treatment allocation | Y | Y | Y | U |
| Patient blinded | Y | Y | Y | Y |
| Care provider blinded | N | N | N | N |
| Outcomes assessor blinded | Y | Y | U | Y |
| Drop-out rate described | Y | Y | Y | Y |
| All randomized participants analyzed in the group | Y | Y | Y | Y |
| Reports of the study free of suggestion of selective outcome reporting | Y | Y | Y | Y |
| Groups similar at baseline regarding most important prognostic indicators | Y | Y | Y | Y |
| Co-intervention avoided or similar in all groups | Y | Y | Y | Y |
| Compliance acceptable in all groups | Y | Y | Y | Y |
| Time of outcome assessment in all groups similar | Y | Y | Y | Y |
| Score | 11/12 | 11/12 | 10/12 | 9/12 |

| | Manchikanti 2009 (40) | Manchikanti 2004 (123) | Veihelmann 2006 (124) | Manchikanti 2005 (127) |
|---|---|---|---|---|
| Randomization adequate | Y | Y | Y | Y |
| Concealed treatment allocation | Y | Y | Y | y |
| Patient blinded | Y | Y | N | y |
| Care provider blinded | N | N | N | n |
| Outcomes assessor blinded | Y | Y | N | y |
| Drop-out rate described | Y | Y | Y | y |
| All randomized participants analyzed in the group | Y | Y | Y | y |
| Reports of the study free of suggestion of selective outcome reporting | Y | Y | Y | y |
| Groups similar at baseline regarding most important prognostic indicators | Y | Y | Y | y |
| Co-intervention avoided or similar in all groups | Y | Y | N | y |
| Compliance acceptable in all groups | Y | Y | Y | y |
| Time of outcome assessment in all groups similar | Y | Y | Y | y |
| Score | 11/12 | 11/12 | 10/12 | 11/12 |

Furlan AD, Pennick V, Bombardier C, van Tulder M. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. Spine (Phila Pa 1976). 2009;34(18):1929-1941.(60)

Veihelmann (124) found clinically significant improvement in pain and function at up to 12 months.

## 2.4 Analysis of Evidence

The evidence was synthesized based on the modality of treatment. Tables 8 and 9 show the results of therapeutic studies.

### *2.4.1 Percutaneous Adhesiolysis*

There are 7 randomized controlled trials (40,85,120,122-124,132) and 3 observational trials evaluating percutaneous adhesiolysis (20,125,126) showing efficacy or effectiveness of percutaneous adhesiolysis. Since the publication of the 2012 systematic review of percutaneous adhesiolysis, there are two new

Table 3. *Methodologic quality assessment of randomized trials of percutaneous and endoscopic adhesiolysis interventions utilizing IPM – QRB criteria.*

| | | Gerdes Meyer 2013 (120) | Chun-Jing (122) | Manchikanti 2009 (85) | Heavner 1999 (132) | Manchikanti 2009 (40) | Manchikanti 2004 (123) | Veihelmann 2006 (124) | Manchikanti 2005 (127) |
|---|---|---|---|---|---|---|---|---|---|
| I. | Trial design and guidance reporting | | | | | | | | |
| 1. | Consort or Spirit | 3 | 0 | 3 | 0 | 3 | 3 | 1 | 2 |
| II. | Design Factors | | | | | | | | |
| 2. | Type and design of trial | 3 | 2 | 2 | 2 | 2 | 2 | 3 | 2 |
| 3. | Setting/physician | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 2 |
| 4. | Imaging | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 5. | Sample size | 2 | 2 | 3 | 0 | 3 | 2 | 2 | 2 |
| 6. | Statistical methodology | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| III. | Patient factors | | | | | | | | |
| 7. | Inclusiveness of population | 2 | 2 | 2 | 1 | 2 | 1 | 2 | 1 |
| 8. | Duration of pain | 2 | 1 | 2 | 2 | 2 | 2 | 0 | 2 |
| 9. | Previous treatments | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 10. | Duration of follow-up with appropriate interventions | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| IV. | Outcomes | | | | | | | | |
| 11. | Outcomes assessment criteria for significant improvement | 4 | 2 | 4 | 0 | 4 | 2 | 0 | 2 |
| 12. | Analysis of all randomized participants in the groups | 2 | 2 | 2 | 1 | 2 | 2 | 1 | 2 |
| 13. | Description of drop out rate | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 1 |
| 14. | Similarity of groups at baseline for important prognostic indicators | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 |
| 15. | Role of co-interventions | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| V. | Randomization | | | | | | | | |
| 16. | Method of randomization | 2 | 2 | 2 | 0 | 2 | 2 | 1 | 2 |
| VI. | Allocation concealment | | | | | | | | |
| 17. | Concealed treatment allocation | 2 | 2 | 2 | 1 | 2 | 1 | 1 | 2 |
| VII. | Blinding | | | | | | | | |
| 18. | Patient blinding | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 19. | Care provider blinding | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20. | Outcome assessor blinding | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 |
| VIII. | Conflicts of interest | | | | | | | | |
| 21. | Funding and sponsorship | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| 22. | Conflicts of interest | 3 | 3 | 3 | 0 | 3 | 3 | 1 | 3 |
| Total | | 41 | 34 | 42 | 23 | 40 | 37 | 25 | 38 |

Manchikanti L, Hirsch JA, Cohen SP, 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.(64)

high quality randomized controlled trials, one from Kiel, Germany and one from Beijing (120,122). There are now multiple indications for which adhesiolysis has shown be efficacious, including low back and radicular pain without radiculopathy (120,124), low back and radicular pain with radiculopathy (122), post lumbar surgery syndrome (85), spinal stenosis(40), low back and leg pain with unspecified radiculopathy or origin(123,132). All of these seven studies are randomized controlled trials.

Table 4. *IPM checklist for assessment of nonrandomized or observational studies of percutaneous and endoscopic adhesiolysis interventions utilizing IPM-QRBNR.*

| | | Manchikanti 1999[20] | Gerdesmeyer 2005[125] | Oh 2014[126] | Lee 2014[129] | Igarashi 2004[128] | Manchikanti 1999[130] |
|---|---|---|---|---|---|---|---|
| I. | Study design and guidance reporting | | | | | | |
| 1. | Strobe or trend guidance | 2 | 2 | 0 | 0 | 0 | 1 |
| II. | Design factors | | | | | | |
| 2. | Study design and type | 1 | 3 | 1 | 1 | 0 | 1 |
| 3. | Setting/physician | 2 | 1 | 1 | 1 | 1 | 3 |
| 4. | Imaging | 3 | 3 | 3 | 3 | 3 | 3 |
| 5. | Sample size | 1 | 0 | 1 | 1 | 0 | 1 |
| 6. | Statistical methodology | 2 | 2 | 2 | 2 | 2 | 2 |
| III. | Patient factors | | | | | | |
| 7. | Inclusiveness of population | 2 | 3 | 4 | 4 | 4 | 4 |
| 8. | Duration of pain | 2 | 0 | 2 | 2 | 1 | 2 |
| 9. | Previous treatments | 1 | 2 | 2 | 2 | 2 | 2 |
| 10. | Duration of follow-up with appropriate interventions | 3 | 2 | 2 | 2 | 3 | 3 |
| IV. | Outcomes | | | | | | |
| 11. | Outcomes assessment criteria for significant improvement | 2 | 2 | 2 | 4 | 0 | 2 |
| 12. | Description of drop out rate | 0 | 0 | 0 | 0 | 1 | 1 |
| 13. | Similarity of groups at baseline for important prognostic indication | 1 | 0 | 1 | 1 | 1 | 1 |
| 14. | Role of co-interventions | 1 | 1 | 2 | 2 | 2 | 2 |
| V. | Assignment | | | | | | |
| 15. | Method of assignment of participants | 3 | 2 | 3 | 3 | 2 | 3 |
| VI. | Conflicts of interest | | | | | | |
| 16. | Funding and sponsorship | 2 | 2 | 2 | 2 | 2 | 2 |
| Total | | 28/48 | 25/48 | 28/48 | 30/48 | 24/48 | 33/48 |

*Manchikanti L, Hirsch JA, Heavner J, 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-E317. (65)*

Based upon the grading of evidence of best evicence synthesis, as shown in Table 1, there is Level I or strong evidence of the efficacy of percutaneous adhesiolysis in the treatment of low back and radicular pain.

### *2.4.2 Endoscopic Adhesiolysis*

There is one randomized trial evaluating endoscopic adhesiolysis (127) and 3 observational trials (128-130). There have been no new studies published since 2012 systematic review. Based upon Table 1, grading of evidence, as the one study is high-quality, there is Level II or fair evidence supporting the use of spinal endoscopy in post lumbar surgery syndrome.

## 3.0 Complications

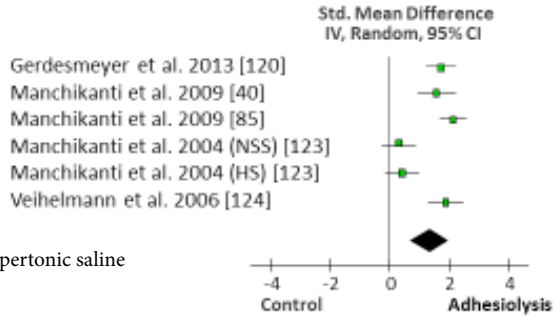
Complications of percutaneous epidural adhesiolysis and endoscopic adhesiolysis have been extensively reviewed (17,19,26,38,105,133-188).

The most commonly noted complication of percutaneous was dural puncture. Veihelmann et al (124) noted 2 instances of dural puncture out of 47 patients. The greatest concern with dural puncture is the risk of spread of hypertonic saline into the subarachnoid space (189). Generally, as long as hypertonic saline does not get into the subarachnoid space, dural puncture does not require treatment and is not of significant clinical concern. There is one report of decreased CSF pressure with a chronic subdural hematoma after dural puncture (190).

Table 5. Results of meta-analysis of pain status change

A. Short-term follow-up 3 months of pain status.

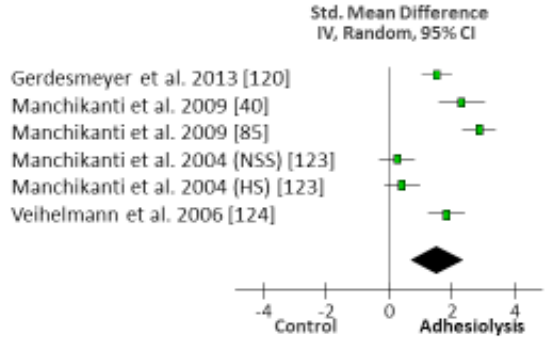
| Study or subgroup | Control | | | Adhesiolysis | | | Weight | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Total | Mean | SD | Total | | IV, random, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 1.9 | 1.1 | 44 | 3.8 | 1.1 | 46 | 17.1% | 1.71 [1.23, 2.20] |
| Manchikanti et al, 2009 [40] | 2.6 | 1.1 | 25 | 4.2 | 0.9 | 25 | 15.9% | 1.57 [0.93, 2.21] |
| Manchikanti et al, 2009 [85] | 3 | 0.8 | 60 | 4.7 | 0.8 | 60 | 17.4% | 2.11 [1.66, 2.56] |
| Manchikanti et al, 2004 (NS) [123] | 1.2 | 9.3 | 25 | 4 | 8.9 | 25 | 16.6% | 0.30 [-0.26, 0.86] |
| Manchikanti et al, 2004 (HS) [123] | 1.2 | 9.3 | 25 | 4.2 | 4 | 25 | 16.5% | 0.41 [-0.15, 0.97] |
| Veihelmann et al, 2006 [124] | 0.8 | 2 | 27 | 4.7 | 2.1 | 46 | 16.5% | 1.87 [1.30, 2.44] |
| | | | | | | | | |
| Total (95% CI) | | | 206 | | | 227 | 100.0% | 1.34 [0.71, 1.96] |
| Heterogeneity: $Tau^2$=0.54; $Chi^2$=40.88, df=5 (P< 0.00001); $I^2$=88% | | | | | | | | |
| Test for overall effect: Z= 4.18 (P< 0.0001) | | | | | | | | |




NS=Normal saline HS=Hypertonic saline

B . Long-term follow-up 12 month of pain status.

| Study or subgroup | Control | | | Adhesiolysis | | | Weight | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Total | Mean | SD | Total | | IV, Random, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 3.9 | 1.1 | 44 | 5.5 | 1 | 46 | 17.1% | 1.51 [1.04, 1.98] |
| Manchikanti et al, 2009 [40] | 1.8 | 0.9 | 25 | 3.9 | 0.9 | 25 | 15.9% | 2.30 [1.57, 3.02] |
| Manchikanti et al, 2009 [85] | 1.8 | 0.8 | 60 | 4.1 | 0.8 | 60 | 16.9% | 2.86 [2.34, 3.37] |
| Manchikanti et al, 2004 (NS) [123] | 1.2 | 9.3 | 25 | 3.6 | 8.9 | 25 | 16.7% | 0.26 [-0.30, 0.82] |
| Manchikanti et al, 2004 (HS) [123] | 1.2 | 9.3 | 25 | 4.2 | 4 | 25 | 16.7% | 0.41 [-0.15, 0.97] |
| Veihelmann et al, 2006 [124] | 0.5 | 2 | 27 | 4.3 | 2.1 | 46 | 16.7% | 1.82 [1.26, 2.39] |
| | | | | | | | | |
| Total (95% CI) | | | 206 | | | 227 | 100% | 1.52 [0.70, 2.35] |
| Heterogeneity: $Tau^2$= 0.98; $Chi^2$= 66.25, df=5 (p< 0.00001); $I^2$= 92% | | | | | | | | |
| Test for overall effect: Z= 3.62 (P= 0.0003) | | | | | | | | |

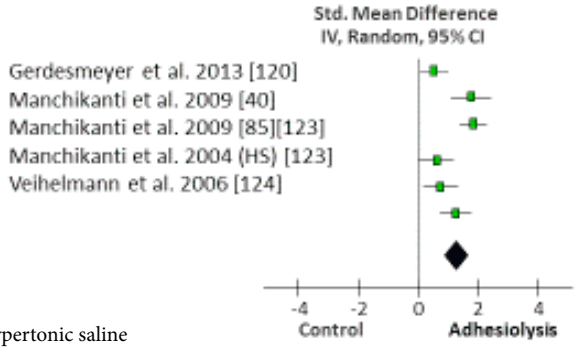



NS=Normal saline HS=Hypertonic saline

Table 6. *Results of meta-analysis of assessment of functional status.*

A. Functional improvement (short-term follow-up 3 months)

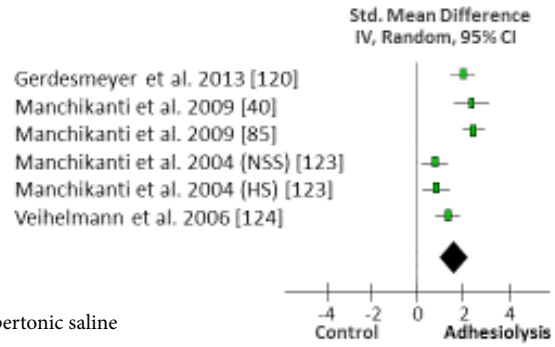
| Study or subgroup | Control | | | Adhesiolysis | | | Weight | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Total | Mean | SD | Total | | IV, random, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 13.6 | 11.5 | 44 | 28.9 | 10.8 | 46 | 18.1% | 1.36 [0.90, 1.82] |
| Manchikanti et al, 2009 [40] | 6.9 | 4.9 | 25 | 15 | 4.1 | 25 | 14.4% | 1.76 [1.10, 2.43] |
| Manchikanti et al, 2009 [85] | 8.4 | 4.1 | 60 | 16 | 4.1 | 60 | 18.6% | 1.84 [1.41, 2.27] |
| Manchikanti et al, 2004 (NS) [123] | 2 | 14.5 | 25 | 11 | 14.1 | 25 | 16.0% | 0.62 [0.05, 1.19] |
| Manchikanti et al, 2004 (HS) [123] | 2 | 14.5 | 25 | 12 | 11.9 | 25 | 15.9% | 0.74 [0.17, 1.32] |
| Veihelmann et al, 2006 [124] | 3.1 | 8.1 | 27 | 12.5 | 7.1 | 46 | 17.0% | 1.24 [0.72, 1.76] |
| | | | | | | | | |
| Total (95% CI) | | | 206 | | | 227 | 100% | 1.27 [0.87, 1.67] |
| Heterogeneity: $Tau^2$= 0.17; $Chi^2$= 17.24, df=5 (P= 0.004); $I^2$= 71% | | | | | | | | |
| Test for overall effect: Z= 6.24 (P< 0.00001) | | | | | | | | |




NS=Normal saline HS=Hypertonic saline

B. Functional improvement (long-term follow-up 12 months)

| Study or subgroup | Control | | | Adhesiolysis | | | Weight | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Total | Mean | SD | Total | | IV, Random, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 24.7 | 11.5 | 44 | 45.7 | 9.3 | 46 | 17.2% | 2.00 [1.49, 2.51] |
| Manchikanti et al, 2009 [40] | 4.8 | 4.4 | 25 | 15 | 4.1 | 25 | 15.1% | 2.36 [1.63, 3.10] |
| Manchikanti et al, 2009 [85] | 5.3 | 4.1 | 60 | 15.4 | 4.1 | 60 | 17.5% | 2.45 [1.97, 2.92] |
| Manchikanti et al, 2004 (NS) [123] | 2 | 14.1 | 25 | 13 | 14.1 | 25 | 16.6% | 0.77 [0.19, 1.34] |
| Manchikanti et al, 2004 (HS) [123] | 2 | 14.1 | 25 | 13 | 11.9 | 25 | 16.6% | 0.83 [0.25, 1.41] |
| Veihelmann et al, 2006 [124] | 0.2 | 8.1 | 27 | 11.6 | 8.7 | 46 | 17.1% | 1.33 [0.80, 1.85] |
| | | | | | | | | |
| Total (95% CI) | | | 206 | | | 227 | 100.0 % | 1.62 [1.02, 2.21] |
| Heterogeneity: $Tau^2$= 0.47; $Chi^2$= 34.25, df=5 (P< 0.00001); $I^2$=85% | | | | | | | | |
| Test for overall effect : Z= 5.33 (P< 0.00001) | | | | | | | | |

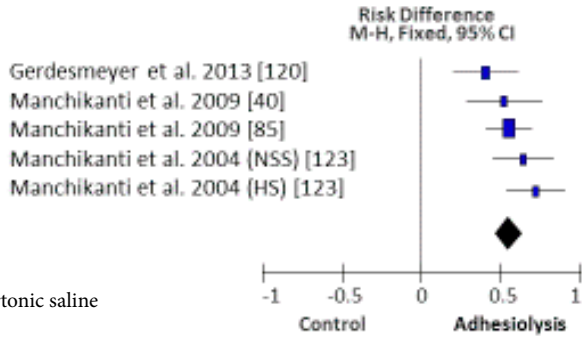



NS=Normal saline HS=Hypertonic saline

*Table 7. Results of meta-analysis of significant improvement ≥ 50% pain relief).*

A. Successful outcomes for pain (>50% pain improvement) (short term follow-up 3 months)

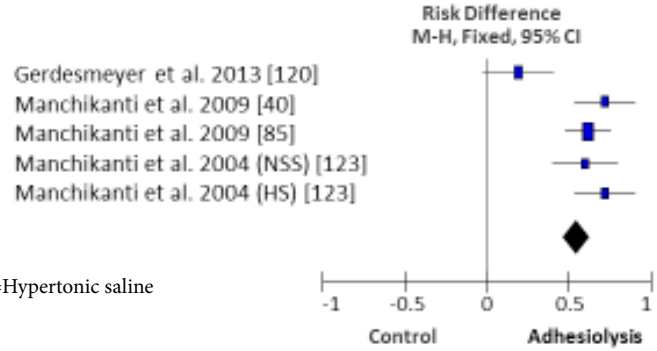
| Study or subgroup | Control | | Adhesiolysis | | Weight | Risk Difference |
|---|---|---|---|---|---|---|
| | Events | Total | Events | Total | | M-H, Fixed, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 12 | 36 | 31 | 42 | 22.3% | 0.40 [0.20, 0.61] |
| Manchikanti et al, 2009 [40] | 7 | 25 | 20 | 25 | 14.4% | 0.52 [0.28, 0.76] |
| Manchikanti et al, 2009 [85] | 21 | 60 | 54 | 60 | 34.5% | 0.55 [0.41, 0.69] |
| Manchikanti et al, 2004 (NSS) [123] | 0 | 25 | 16 | 25 | 14.4% | 0.64 [0.45, 0.83] |
| Manchikanti et al, 2004 (HS) [123] | 0 | 25 | 18 | 25 | 14.4% | 0.72 [0.54, 0.90] |
| | | | | | | |
| Total (95% CI) | | 171 | | 177 | 100.0% | 0.55 [0.47, 0.64] |
| Heterogeneity: $Chi^2$= 6.19,df=4 (P= 0.19); $I^2$=35% | | | | | | |
| Test for overall effect: Z= 12.72 (P< 0.00001) | | | | | | |




NS=Normal saline HS=Hypertonic saline

B. Successful

| Study or subgroup | Control | | Adhesiolysis | | Weight | Risk Difference |
|---|---|---|---|---|---|---|
| | Events | Total | Events | Total | | M-H, Fixed, 95% CI |
| Gerdesmeyer et al, 2013 [120] | 18 | 36 | 29 | 42 | 22.3% | 0.19[-0.02, 0.41] |
| Manchikanti et al, 2009 [40] | 1 | 25 | 19 | 25 | 14.4% | 0.72 [0.54, 0.90] |
| Manchikanti et al, 2009 [85] | 7 | 60 | 44 | 60 | 32.5% | 0.62 [0.40, 0.75] |
| Manchikanti et al, 2004 (NSS) [123] | 0 | 25 | 15 | 25 | 14.4% | 0.60 [0.40, 0.80] |
| Manchikanti et al, 2004 (HS) [123] | 0 | 25 | 18 | 25 | 14.4% | 0.72 [0.54, 0.90] |
| | | | | | | |
| Total (95% CI) | | 171 | | 177 | 100.0% | 0.55 [0.47, 0.63] |
| Heterogeneity: $Chi^2$= 18.57, df=4, (P=0.001); $I^2$=78% | | | | | | |
| Test for overall effect: Z= 12.97 (P< 0.00001) | | | | | | |




NS=Normal saline HS=Hypertonic saline

Table 8. Analysis of Effectivess of percutaneous adhesiolysis.

| Study<br><br>Study Characteristic<br><br>Methodological Quality Scoring | Patients | Interventions | Pain Relief and Function | | | Result | | Comments |
|---|---|---|---|---|---|---|---|---|
| | | | 3 mos. | 6 mos. | 12 mos. | Short-Term <6 mos | Long-Term ≥ 6 mos. | |
| Gerdesmeyer 2013 [120]<br><br>IPM-QRB 41/48 | 90 | Ventral adesiolysis, 3-day | 26/45 of treated group had >50% improvement in ODI | 31/42 of treated group had >50% improvement in ODI | 28/31 of treated group had >50% improvement in ODI | P | P | High quality placebo controlled study documenting efficacy |
| Chun-jing 2012 [122]<br>RA/AC<br>IPM-QRB 34/48 | 76 | Ventral adhesiolysis with high volume saline | NA | >3 points relief on VAS, with 46% relief | NA | P | NA | High quality study documenting efficacy with high volume saline. |
| Mahcnikanti 2009 [85] | 120 | One-day adhesiolysis v caudal ESI | 58% of adhesiolysis had >50% relief vs 38% of comparator | 54% of adhesiolysis had >50% relief vs 27% of comparator | 51% of adhesiolysis had >50% relief vs 23% of comparator | P | P | High quality study showing efficacy with repeated one-day adhesiolysis procedure in post lumbar surgery syndrome |
| Heavner[132] | Adhesiolysis with 0.9% or 10% saline and with or without hyaluronidase | 3-day adhesiolysis with either 0.9% or 10% saline and with or without hylauronidase | About 50% of subjects had more than 10/100 improvement in VAS | About 50% of subjects had more than 10/100 improvement in VAS | About 50% of subjects had more than 10/100 improvement in VAS | P | P | Moderate quality study showing equivalency between 0.9% and 10% saline and with and without saline |
| Manchikanti 2009[40] | 50 | One-day adhesiolysis v caudal ESI | 80% of adhesiolysis had >50% relief vs 26% for caudal | 80% of adhesiolysis had >50% relief vs 12% for caudal | 76% of adhesiolysis had >50% relief at 12 months after 3.5 average injections | P | P | High quality study showing efficacy with repeated one-day adhesiolysis procedure in spinal stenosis patients |
| Manchikant 2004[123] | 75 | One day adhesiolysis with 0.9% and 10% saline versus epidural injection | 72% of 10% saline group, 64% of 0/9% group and 0% of caudal had >50% relief. | 72% of 10% saline group, 60% of 0/9% group and 0% of caudal had >50% relief. | 72% of 10% saline group, 60% of 0/9% group and 0% of caudal had >50% relief. | P | P | High quality study showing equivalency between normal and hypertonic saline adhesiolysis. |
| Veihelmann 2006[124] | 99 | One-day adhesiolysis with 10% saline vs. physical therapy | Mean improvement of the treated group was >50% in VAS and >40% in ODI. Treatment group had ~10% relief. | Mean improvement of the treated group was >50% in VAS and >40% in ODI. Treatment group had ~10% relief. | Mean improvement of the treated group was >50% in VAS and >40% in ODI. Treatment group had ~10% relief. | P | P | Moderate quality study showing superiority of adhesiolysis over physical therapy in persistent radicular pain |
| Manchikanti 1999[20]<br><br>Retrospective | 150 | 1 vs 2 vs 3 day adhesiolysis. Three-day results from a different study | Average of 37% of 2-day adhesiolysis and 26% had >50% relief after 4 procedures | Average of 21% of 2-day adhesiolysis and 14% had >50% relief after 4 procedures. | Average of 4% of 2-day adhesiolysis and 4% had >50% relief | P | P | No differences between 1,2 and 3 day procedures |
| Gerdesmeyer 2005[125] | 61 | 3-day ventral adhesiolysis | >50% improvement in ODI | >50% improvement in ODI | NA | P | P | No control Heterogeneous population |
| Oh 2014[126] | 303 | One-day adhesiolysis comparing ventral with dorsal catheter placement4 | Statically significant improvement in leg pain in ventral vs. dorsal group. Ventral and dorsal groups both had >50% relief for back and leg pain. | Statically significant improvement in leg pain in ventral vs. dorsal group. Ventral and dorsal groups both had >50% relief for back and leg pain. | NA | P | P | No control Moderate quality retrospective study |

RA = randomized; DB = double-blind; AC = active control; SI = significant improvement; P = positive; N = negative; NA = not applicable

*Table 9 Efficacy of spinal endoscopic adhesiolysis*

| Study<br><br>Study Characteristic<br><br>Methodological Quality Scoring | Patients | Interventions | Pain Relief and Function | | | Result | | | Comments |
|---|---|---|---|---|---|---|---|---|---|
| | | | 3 mos. | 6 mos. | 12 mos. | Short-Term ≤ 6 mos | Long-Term > 6 mos. | ≥ 1 year | |
| Manchikanti 2005 [127]<br>RCT<br>IPM_QRB 38/48 | 83 patients with radicular pain, primarily post lumbar surgery syndrome | Endoscopic adhesiolysis vs caudal epidural injection | 80% of endoscopy patient had >50% relief vs 30% of caudal | 56% of endoscopy patient had >50% relief vs 0% of caudal | 48% of endoscopy patient had >50% relief vs 0% of caudal | P | P | P | High quality study showing efficacy of adhesiolysis in post lumbar surgery syndrome and in persistent leg pain |
| Lee 2014 [129]<br><br>Retrospective | 114<br>Failed back patients | Endoscopic adhesiolysis v transforaminal epidural steroid injection | NA | >50% of endoscopic group had >50% improvement in VAS and >40% improvement in ODI vs ~30% of transforaminal group.<br>Patients with discectomy did better than those with fusions. | NA | P | NA | NA | Epiduroscopy is more effective than transforaminal steroid injections at 6 months. Patients with discectomies did better than those with fusions. |
| Igarashi 2004 [128]<br>Prospective<br>IPM-QRBNR 24/48 | 58 lumbar stenosis patients with either radicular pain or multisegmental dysesthesia | Endoscopic lysis of adhesions | Mean VAS for low back pain went from 8/10 to ~2/10 | Mean VAS for low back pain went from 8/10 to ~2.5/10 | Mean VAS for low back pain went from 8/10 to ~2.5/10 | P | P | P | Epiduroscopy can relieve pain in degenerative lumbar stenosis |
| Manchikanti 1999[130]<br>Retrospecitive<br>IPM-QRBNR 33/48 | 120 post lumbar surgery syndrome patients | Percutaneous vs. endoscopic adhesiolysis | >50% pain relief | At 6 months, after a second procedure, 75% of the endoscopic group had > 50% relief, while only 22% of the percutaneous group did. However, looking at both groups regardless of the number of procedures done, 40% of endoscopic patients had > 50% relief, whereas 72% of percutaneous group did. | 25% of endoscopic and 10% of percutaneous adhesiolysis patients had >50% relief after 2 procedures. Endoscopic group had ~ 2 procedures/ year; the percutaneous group had ~4 procedures/ year | P | P | P | Both treatment s are effective. The percutaneous group has more procedures but is also more cost effective. |

RA = randomized; DB = double-blind; AC = active control; ST = steroid; LA = local anesthetic; SAL = saline; SI = significant improvement; *P* = positive; N = negative; NA = not applicable

Transient neurologic deficits have been reported. Generally, these deficits are resolve spontaneously (124,191,143). A case report of arachnoiditis has been presented, but the volumes injected were very high and injections were done despite patient complaints of unexpected pain (146).

Lee (192) reported a rare complication after the subarachnoid injection of hypertonic (10%) saline during lumbar adhesiolysis of reverse Takotsubo cardiomyopathy, a variant of stress induced cardiomyopathy, in which stress causes cardiomyopathy.

Birkenmaier (193) performed an in vitro evaluation

of the effects of the medications used in adhesiolysis on fibroblast proliferation. This study was prompted by a case of urinary incontinence after adhesiolysis, with no known subarachnoid injection. In culture, fibroblast proliferation was reduced. Hypertonic saline inhibits scar formation because of the effects of human fibrocytes. The relationship of fibroblast inhibition and urinary incontinence is not clear.

Catheter shearing has also been reported. (120) (138) (194) (145) (195) With the change in type of needle used to enter the vertebral foramen, away from the RK needle, the risk of shearing is essentially removed. Unless symptomatic, the catheter is left in situ.

As with any procedure, there is a risk of infection or hematoma (20, 125, 135, 137,196). A needle point in the buttock, away from the intertriginous region, is an important safety technique.

No cases of epidural hematoma have been reported.

There are no reported cases of serious neurologic deficits after adhesiolysis, other than the one case of urinary incontinence, described above. The incidence of complications from percutaneous adhesiolysis is low and the complications are generally minimal and self-limited.

Spinal endoscopic adhesiolysis is generally a well tolerated procedure, with minimal and transient complications, including localized pain and self-limited irritation of the nerve root (142) Heavner, Van Boxem and Avellanal et al have reviewed the complications of epiduroscopy, finding it to be safe procedure with no mortality and little morbidity (38,47,178).

The greatest risk with spinal endoscopy is blindness associated with excessive epidural hydrostatic pressure associated with the administration of high volumes of fluid or a bolus of fluid (185-187). Heavner et al (197) reviewed blindness after epiduroscopy, evaluating 12 cases. About 80% of these cases resolved. They recommended injecting the saline at less than 1 mL/second.

Other complications potentially associated with epiduroscopy include dural tear, epidural bleeding with potential hematoma formation, and infection. (116,198). In and of itself, entering the subarachnoid space is not a cause for concern. Case reports exist for neurogenic bladder, transient decreased hearing and seizures (199,110,200).

The upper limit of saline which can be safely injected during epiduroscopy is not known. One hundred cc is often used, although a range from 60 mL to 250 mL has been proposed (47).

Both percutaneous adhesiolysis and endoscopic adhesiolysis should be considered to be low risk for serious adverse events when performed by well-trained physicians.

## 4.0 Discussion

Refractory low back and lower extremity pain has been successfully treated with percutaneous adhesiolysis. Studied indications include low back and leg pain with radicular symptoms in the absence of motor weakness, spinal stenosis and post lumbar surgery syndrome. As its name implies, adhesiolysis is primarily focused on breaking up adhesions. However, the wide variety of conditions treated suggest that other mechanisms may be at play (201-205). One of these other mechanism might be the peridural membrane, which is innervated and can become inflamed, particularly in the infraradicular space, causing low back pain without scarring (22,206,207). The lack of correlation with the extent of central spinal stenosis and relief from adhesiolysis supports role of factors other than scarring being relieved by adhesiolysis, as does the fact that the catheter is not moved during the three-day adhesiolysis procedure (101).

Some question whether scarring can cause pain because of the presence of scarring after successful lumbar surgery (208-212). However, there is extensive literature suggesting that scarring can be painful (41,42,213-224).

Bosscher, using an epiduroscope, identified two levels of epidural fibrosis: non-resistant loose or continuous strings and sheets of fibrous material, and dense, resistant fibrous material which could be penetrated with difficulty or not at all (225). The level of fibrosis and vascular changes was associated with the outcome of epiduroscopic adhesiolysis (226).

Epidural fibrosis can cause pain via several mechanisms. One is tethering of the nerve root, so that the root is no longer able to move freely in the epidural space and foramen with movement of the body (227-229). A trapped nerve root is susceptible to tension and compression and lack of nutrition (21,230). Circulation can be impaired causing ischemic pain (231). Veins can become engorged, with either impaired circulation or direct compression of the nerve. Such congestion can be caused by outflow obstruction, arteriovenous anastomoses or inflammation with secondary congestion Improvement in filling defects after adhesiolysis is associated with pain relief (232). Kuslich identified scarring between the posterior longitudinal ligament and the ventral dura, but did not highlight that scarring

as a source of pain because he could not differentiate between pain from that scarring and pain from the annulus (233).

Epidural fibrosis is usually diagnosed with MRI or CAT scan, both having sensitivity and specificity of identifying dorsal and lateral epidural scarring of about 50%-70% (226,234-236).

Epiduroscopy is significantly more effective in identifying ventral epidural scarring than was MRI. Eighty percent of post lumbar surgery patients with persistent low back pain or radiculopathy who had no epidural scarring on MRI had severe scarring found on epiduroscopy. Based upon epiduroscopy findings, the incidence of severe scarring after lumbar surgery is at least 83% and of any scarring at least 95%. Only 40% of patients had scarring demonstrated on MRI (225). Given the need to place the catheter in the ventral epidural space (126), scarring responsive to adhesiolysis is under diagnosed by MRI or CAT scan. Further, dense, post-surgical scarring is found the dorsal, not ventral, epidural space.

Racz has developed a clinical test of epidural fibrosis, particularly ventral adhesions, the "dural tug," with the patient sitting with the legs extended, flexing at the waist until back pain first occurs and then rapidly flexing the neck (228). Patients are remarkably able to identify pain level accurately.

Birkenmaier has performed in vitro studies confirming that dense, post-surgical scarring, would not be mechanically lysed (237). This finding conforms with the clinical experience.

Adhesiolysis depends upon the placement of a spring-wound catheter in the correct tissue plane, in the ventrolateral aspect of the foramen, to allow injection of radiopaque dye, local anesthetic, steroids, saline and hyaluronidase (237). Both 0.9 (normal) saline and 10%, (hypertonic) saline, are effective (123). The procedure is clearly distinct from an epidural steroid injection.

Hyaluronidase increases the absorption and dispersion of infused fluids and drugs, allowing the injectate to find the path of least resistance (238).This ability of hyaluronidase to facilitate spreading is being evaluated for use with rapid acting insulin and cancer treatment (239,240). The explanation that has been accepted is the compartmental filling principle by Angelo Rocco (241).Hyaluronidase is well tolerated (193).

Recently, the space between the L5 dorsal root ganglion and S1 nerve root has been found to be an exceptionally scarred area that cannot be entered by the usual size spring guide wire catheter. The tissue plane between the dense scar and the dorsal root ganglion can be entered by a small caliber (21g) VERSA-KATH™ through the S1 foramen (229,242,243).

One aspect of adhesiolysis which is often over looked is post procedural exercises to stretch the nerve root, called "neural flossing." These add mechanical traction to the epidural hydrostatic lysis.

Percutaneous adhesiolysis has a high cost utility at about $2,650 for one year of quality-adjusted life for both central spinal stenosis and post lumbar surgery syndrome (244).

There are now 7 RCTs, with supportive observational studies documenting the efficacy of adhesiolysis. There are no RCTs which do not show efficacy. A meta-analysis confirms the efficacy of percutaneous adhesiolysis to decrease pain and improve function. The indications for which these RCTs have been done vary widely and include post lumbar surgery syndrome, spinal stenosis and radicular pain with a disc bulge and without motor weakness. The appropriate indication for percutaneous adhesiolysis is low back and leg pain refractory to conservative treatment, including the epidural steroid injections. Gerdesmeyer's recommendation that percutaneous adhesiolysis should be the first line treatment for patients with chronic lumbosacral radicular pain should be accepted (120).

Endoscopic adhesiolysis has limited evidence supporting it use. Epiduroscopy's utility, including blunt epiduroscopy, balloon endoscopic adhesiolysis and laser endoscopic procedures, is still being explored. One particularly interesting area of exploration is the laser application of heat to the disc to treat annular disruption. An interesting hypothesis is that the limited efficacy of previous efforts to treat the pain from annular tears is that these efforts failed to deal with the associated ventral scarring. An RCT to test this hypothesis is underway. A related RCT will look at the diagnostic value of epiduroscopy.

Laser endoscopy has been used to decompress nerve roots. This technique needs to be refined to ensure that untoward complications do not occur.

One interesting development regarding epiduroscopy is the understanding of the limitations which exist regarding what can be identified. The current understanding is that structures such as the facets, discs and nerve roots are often difficult to visualize; the focus is on identifying the extent of scarring and vascularity. This understanding has lowered the learning curve and made the procedure more accessible. With this accessibility, there is international renewal of interest in the procedure.

## 5.0 Conclusion

Percutaneous adhesiolysis of epidural adhesions to treat refractory low back and lower extremity pain is a technique whose efficacy has been documented by multiple RCTs. It is a safe and effective procedure, with minimal complications when performed by trained practitioners. A meta-analysis documents its efficacy for pain relief and improved function.

Endoscopic adhesiolysis is a technique which has limited evidence supporting its use. There is still a limited understanding of its role, including what the indications are, such as treating discogenic disease in the young or spinal stenosis in the elderly; whether to use laser; and technical issues, such as the maximum volume. Collection of high quality data to answer these questions is underway.

## Acknowledgments

We would like to thank the staff of Pain Physician for their assistance and the editorial board of Pain Physician for their review and criticism in improving the manuscript.

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

| | | |
|---|---|---|
| A | 1. Was the method of randomization adequate? | Yes/No/Unsure |
| B | 2. Was the treatment allocation concealed? | Yes/No/Unsure |
| C | Was knowledge of the allocated interventions adequately prevented during the study? | |
| | 3. Was the patient blinded to the intervention? | Yes/No/Unsure |
| | 4. Was the care provider blinded to the intervention? | Yes/No/Unsure |
| | 5. Was the outcome assessor blinded to the intervention? | Yes/No/Unsure |
| D | Were incomplete outcome data adequately addressed? | |
| | 6. Was the drop-out rate described and acceptable? | Yes/No/Unsure |
| | 7. Were all randomized participants analysed in the group to which they were allocated? | Yes/No/Unsure |
| E | 8. Are reports of the study free of suggestion of selective outcome reporting? | Yes/No/Unsure |
| F | Other sources of potential bias: | |
| | 9. Were the groups similar at baseline regarding the most important prognostic indicators? | Yes/No/Unsure |
| | 10. Were co-interventions avoided or similar? | Yes/No/Unsure |
| | 11. Was the compliance acceptable in all groups? | Yes/No/Unsure |
| | 12. Was the timing of the outcome assessment similar in all groups? | Yes/No/Unsure |

Source: Furlan AD, Pennick V, Bombardier C, van Tulder M; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; 34:1929-1941 (60)

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

| | | Scoring |
|---|---|---|
| **I.** | CONSORT OR SPIRIT | |
| **1.** | Trial Design Guidance and Reporting | |
| | 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 |

| | | Scoring |
|---|---|---|
| **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 |
| **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<br>OR<br>< 20% change in pain rating or functional status | 0 |
| | Pain rating with a decrease of 2 or more points or more than 20% reduction<br>OR<br>functional status improvement of more than 20% | 1 |
| | Pain rating with decrease of ≥ 2 points<br>AND<br>≥ 20% change or functional status improvement of ≥ 20% | 2 |
| | Pain rating with a decrease of 3 or more points or more than 50% reduction<br>OR<br>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 |
| **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 MAXIMUM** | | 48 |

Source: Manchikanti L, Hirsch JA, Cohen SP, et al. Assessment of methodologic quality of randomized trials of interventional techniques: development of an interventional pain management specific instrument. Pain Physician. 2013;17(3):E263-290.[64]

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

| | | |
|---|---|---|
| **I.** | STROBE OR TREND Guidance | Scoring |
| **1.** | Study Design Guidance and Reporting | |
| | 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 |
| | Fluoro | 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 |
| **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 1 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<br>OR<br>< 20% change in pain rating or functional status | 0 |
| | Pain rating with a decrease of 2 or more points or more than 20% reduction<br>OR<br>functional status improvement of more than 20% | 1 |
| | Pain rating with decrease of ≥ 2 points<br>AND<br>≥ 20% change or functional status improvement of ≥ 20% | 2 |
| | Pain rating with a decrease of 3 or more points or more than 50% reduction<br>OR<br>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 despite proper allocation | 0 |
| | Groups dissimilar without significant influence on outcomes despite proper allocation | 1 |
| | Groups similar with appropriate allocation | 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 |

Source: Manchikanti L, Hirsch JA, Heavner J, 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-E317.(65)

*Appendix Table 4. List of Excluded Randomized and Non-randomized Studies*

| Study | Number of Patients | Treated vs. Control | Reason for Exclusion | |
|---|---|---|---|---|
| | | | Follow-up Period | Other Reason(s) |
| **Randomized Controlled Trials** | | | | |
| Kim (21) | 62 | Transforaminal epidural injections with and without balloon treatment | 3 months | |
| Yousef (97) | 38 | Caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline, local anesthetic, and hyaluronidase. | 12 months | The authors studied caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline, local anesthetic, and hyaluronidase; however, there was no adhesiolysis performed with catheter or by other means except potentially with hypertonic saline and hyaluronidase. |
| **Non-Randomized Studies** | | | | |
| Hsu 2014 (43) | 115 | Adhesiolysis | 1 month | Included procedures without a catheter |
| Gerdesmeyer 2013 (98) | 25 | 3-day adhesiolysis | 3 months | Failure to meet requirement of at least 50 patients |
| Devulder 1995 (99) | 34 | Caudal epidural steroid injection with non-wire reinforced catheter No control | 12 months | Failure to meet requirement of at least 50 patients; procedure was done without wire reinforced catheter; catheter not placed at site of pathology |
| Manchikanti 2001 (100) | 45 | 1-day adhesiolysis v physical therapy | 12 months | 1-day adhesiolysis v physical therapy |
| Manchikanti 2001 (96) | 23 | 1-day adhesiolysis No control. Spinal stenosis | 2 years | Failure to meet requirement of at least 50 patients |
| Park (101) | 66 | One-day adhesiolysis with hypertonic saline | 6 months | Goal of study was to evaluate relationship between central stenosis and results of adhesiolysis, not effectiveness of procedure. |
| Lee & Lee (102) | 86 | Percutaneous adhesiolysis with Navicath | 12 months | The authors studied clinical effectiveness of percutaneous adhesiolysis using Navicath for the management of chronic pain due to lumbosacral disc herniation. This procedure is distinct from percutaneous adhesiolysis. |
| Dashfield 2005 (103) | 60 | Endoscopic steroid injection vs caudal epidural steroid injection | 6 months | Adhesiolysis was performed in only 3 of the patients. The study looked at targeted steroid injections. No imaging was performed. |
| Richardson 2008 (94) | 38 | Endoscopy to identify source of pain and to perform adhesiolysis | 12 months | Failure to have 50 patients |

| Study | Number of Patients | Treated vs. Control | Reason for Exclusion | |
|---|---|---|---|---|
| | | | Follow-up Period | Other Reason(s) |
| Warnke & Mourgela 2007 (104) | 23 | Subarachnoid endoscopy (thecaloscopy) | 24 months | Failure to have 50 patients.<br>Procedure was subarachnoid, |
| Richter 2011 (26) | 154 | Laser epiduroscopy | Not provided | Review focused on laser epiduroscpy |
| Richter and Rothstein 2011 (105) | 24<br>. | Laser epiduroscopy | 3 months to 6 months, mean 4months | Failure to have 50 patients.<br>Review focused on laser epiduroscopy |
| Ruetten 2003 (106) | 93 | Laser epiduroscopy | Not provided | Review evaluated laser epiduroscopy |
| Saberski 2000 (107) | 35 | Epiduroscopy vs laminectomy | 2 months | Failure to have 50 patients |
| Sakai 2008 (108) | 19 | Endoscopic adhesiolysis | 3 months | Failure to have 50 patients |
| Tobita 2003 (109) | 55 | Epiduroscopy and subarachnoid endoscopy in all patients | None | Procedure was done for diagnosis only, with no therapy provided. |
| Avellanal & Diaz-Reganon 2008 (110) | 19 | Interlaminar epiduroscopy | 6 months | Failure to have 50 patients |
| Geurts et al, 2002 (95) | 24 | Epiduroscopy | 12 months | Failure to have 50 patients |
| Takeshima et al, 2009 (111) | 28 | Epiduroscopy | 6 months | Failure to have 50 patients |
| Mavrocordatos & Cahana, 2011 (112) | 32 | Epiduroscopy with targeted O2/ O3 and steroid delivery | 2 years | Failure to have 50 patients |
| Jo 2012 (113) | 69 | Caudal epidural injections | None | No adhesiolysis performed. Study compared dye flow with pain |
| DiDonatao 2010 (114) | 350 | Epiduroscopy for chronic degenerative low back pain | Up to 60 months | Treatment included ozone and ciprofloxacin<br>All patients had a preprocedure<br>VAS of > 5. A successful outcome was a VAS of < 5. It is not possible to tell how many patients had a 50% reduction or a 3 point reduction in VAS. An ODI of < 40% was considered a success. 60% of patients had an ODI equal to or less than 40% at the start of the study, so it is not possible to assess functional improvement. |
| Manchikaniti 2000 (115) | 85 | Epiduroscopy | 12 months | Failure to define patient selection criteria. |
| Murai 2007 (116) | 183 | Epiduroscopy | 3 months | Failure to have at least 6 months follow up |
| 2Kim 2011 (28) | 109 | Endoscopic adhesiolysis with and without laser | 3 months and last visit | Failure to have at least 6 months follow up |
| Choy 1998 (117) | 752 | Endoscopic laser disc decompression | Need to get article xxzzyy | Study dealt with laser epiduroscopy |
| Jo 2013 (118) | 77 | epiduroscopic laser neural decompression | 2 months | Failure to have at least 6 months' follow-up<br>Study dealt with laser epiduroscopy |
| Jo 2014 (119) | 39 | epiduroscopic laser neural decompression in patient with back and leg pain, comparing those with and without a history of lumbar surgery | 4 weeks | Failure to have at least 50 patients.<br>Failure to have at least 6 months' follow-up<br>Study dealt with laser epiduroscopy |
| Magalhães 2013 (131) | 13 | Endoscopic application of ozone in post lumbar surgery patients | 6 months | Failure to have at least 50 patients.<br>Study dealt with ozone therapy |

Appendix Table 5. *Characteristics of inclusion criteria of randomized trials and observational studies.*

| Manuscript Authors | Type of Study | Number of patients | Treatment vs. Comparator | Length of Follow up | Outcome Parameters | Comments |
|---|---|---|---|---|---|---|
| **Percutaneous Adhesiolysis** | | | | | | |
| Gerdesmeyer 2013 (120) | RA/PC/P | 90 | Percutaneous neurolysis 3-day protocol vs subcutaneous injection | 12 months | ODI, VAS | High quality, true placebo study showing efficacy in patients with radicular pain with concordant MRI and no absolute stenosis or motor weakness |
| Chun-jing2012 (122) | RA/AC/P | 76 | Ventral epidural vascular catheter with 50-80 ml saline and 10 mg dexamethasone vs 10 mg dexamethasone | 6 months | VAS, opioid use | Presence of radiculopathy was an inclusion criterion |
| Heavner 1999 (132) | RA, AC | 59 Epidural fibrosis with radicular pain | 3 day adhesiolysis protocol 4 groups: Group I: hypertonic saline plus hyaluronidase Group II: hypertonic saline Group III: isotonic saline (0.9% NaCl) Group IV: isotonic saline plus hyaluronidase | 12 months | MPQ VAS for back, right leg, and left leg pain | Purpose of study was to determine if hyaluronidase or hypertonic saline improved the outcome. 29% drop out rate Low back rather than leg pain was the greatest problem. Hyaluronidase was effective with combination with hypertonic saline in reducing frequency of additional procedures. Hyaluronidase did not provide benefit. Hypertonic saline patients required fewer additional treatments than patients treated with normal saline. Maximum VAS scores were improved in between 25% and 60% of patients at 12 months. |
| Manchikanti 2009 (85) | RA/AC/P | 120 Post lumbar surgery syndrome | 60 patients receiving 1-day adhesiolysis 60 patients with caudal epidural. Repeat procedures allowed at 3 months based upon initial improvement then deterioration of pain relief to below 50%. | 12 months Crossover allowed at 3 months. Of caudal group, 10 were unblinded at 6 months and 33 at 12 months; of the adhesiolysis group, 2 were unblinded prematurely. | NRS ODI Opioid intake Employment/ work status | 90% of adhesiolysis group had >50% relief at 3 months and 73% did at 12 months. 35% of caudal group had >50 relief at 3 months and 12% did at 12 months. 77% of adhesiolysis group had >40% improvement in ODI at 12 months compared to 13% of caudal group. Average of 3.5 adhesiolysis procedures/year with an average relief/year of 4½ weeks. |
| Manchikanti 2009 (40) | RA/AC/P | 50 Spinal stenosis | 25 patients receiving 1-day adhesiolysis 25 patients with caudal epidural. Repeat procedures allowed at 3 months based upon initial improvement then deterioration of pain relief to below 50%. | 12 months Of caudal group, 18 were unblinded prematurely. None of the adhesiolysis group were unblinded prematurely. | NRS ODI Opioid intake Employment/ work status | 76% of adhesiolysis patients had significant relief at one year. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Manchikanti 2004 (123) | RA/AC | 75 Low back pain without response to epidural injection and no facet disease Between 64% and 72% patients had prior lumbar surgery; between 4% and 20% had spinal stenosis | 25 caudal epidural steroid injection 25 1-day adhesiolysis with normal saline 25 1-day adhesiolysis with hypertonic saline Patients averaged 2.1 to 2.7 procedures | 12 months Unblinding at 3 or 6 months | VAS ODI Work status Opioid intake Range of motion Psychological evaluation by P3 | 72% of hypertonic saline and 60% of normal saline patients had >50% relief at 12 months, versus 0% of caudal injections. 18 of the caudal group were unblinded by 6 months. |
| Veihelmann 2006 (124) | RA/AC | 99 | One day adhesiolysis with 10% saline versus physical therapy | 3, 6, 12 months | VAS, ODI, GHS | Mean improvement of the treated group was >50% in VAS and >40% in ODI at 3, 6 and 12 months. Treatment group had ~10% relief. |
| Manchikanti 1999 (20) | RE | 150 | One-day vs Two-day adhesiolysis 3-day adhesiolysis results were obtained from a different study (19) Up to four procedures in one year | 3, 6, 12 months | Pain relief | Study showing equivalency of one-day and three-day adhesiolysis. Does not have functional evaluation |
| Gerdesmeyer 2005 (125) | Prospective | 61 | Three day adhesiolysis | 6 months | ODI, McNabb Score | Preliminary study for subsequent randomized study |
| Oh 2014 (126) | Retrospective review | 303 Single level disc disease with or without radicular pain without prior surgery or spinal stenosis | One day adhesiolysis with the catheter positioned either ventrally or dorsally | 6 months | VAS back and leg; Odom's criteria | Study evaluated whether catheter positioning either ventrally or dorsally influenced outcomes |
| **Endoscopic Adhesiolysis** | | | | | | |
| Manchikanti 2005 (127) | RA, AC, P | 83 patients <65 years of age with chronic low back and leg pain ~75% had prior surgery | Endoscopic adhesiolysis vs. caudal epidural steroid injection | 12 months | VAS, P3 and ODI | 48% of endoscopy patients had >50% relief at 12 months; 0% of caudal patients did. |
| Lee 2014 (129) | RE | 114 patients with low back and extremity pain after either discectomy or fusion | Endoscopic Adhesiolysis vs transforaminal epidural | 6 months | NRS, ODI | Endoscopic adhesiolysis provided better relief at 6 months than did transforaminal epidural steroid injections. Patients who had discectomy did better than those who had fusion. |
| Igarashi 2004 (128) | P | 58 lumbar stenosis | Endoscopic lysis of adhesions in patients with either radicular pain or multisegmental dysesthesia. | 12 months | VAS, motor deficit, sensory deficit | >50% relief of low back pain at 12 months for both groups and >50% relief of leg pain at 12 months for radicular group |
| Manchikanti 1999 (130) | RE | 120 | Percutaneous adhesiolysis vs endoscopic adhesiolysis in post lumbar surgery patients | 12 months | >50% relief | Both adhesiolysis and endoscopy are effective providing pain relief. |

RA = randomized; PC = Placebo control; AC = Active-control; P = Prospective; RE =Retrospective; VAS = Visual analog scale; ODI = Oswestry Disability Index; RMDQ = Roland Morris Disability Questionnaire; P-3 = Pain Patient Profile; FBSS = Failed back surgery syndrome; ROM=Range of motion; ADLs – Activities of Daily Living; MPQ = McGill Pain Questionnaire; GHS=Gerbershagen score

*Appedix Table 6. Study characteristics of randomized controlled trials and observational studies assessing percutaneous adhesiolysis.*

| **Study**<br><br>**Study Characteristic Methodological Quality Scoring** | **Number of Patients & Selection Criteria** | **Interventions/ Control** | **Outcome measures** | **Time of Measurement** | **Results** | **Weaknesses** | **Strengths** | **Conclusions** |
|---|---|---|---|---|---|---|---|---|
| Gerdesmeyer 2013[120]<br><br>Randomized, Placebo controlled.<br><br>Cochrane 11/12<br>IPM-QRB 41/48 | 90<br>Patients with radicular pain, positive Leségue sign, concordant MRI and no muscle weakness | Adhesiolysis<br>3-day protocol with ventrolateral catheter placement | ODI/VAS | 3, 6 and 12 months | 28/31 of the treated group had a >50% improvement in ODI at 12 months, vs 9/26 of the control<br>29/31 of the treated group have >50% improvement in VAS at 12 months, vs 18/26 of control | Did not measure change in opioid consumption | Well designed prospective, high quality placebo controlled study with functionality as primary outcome | Documents efficacy versus placebo, with improvements in function and pain. |
| Chun-jing 2012 [122]<br><br>Randomized, active control<br>Cochrane 11/12<br>IPM-QRB 34/48 | 92 patients with pain and radiculopathy 6 months after surgery for disc herniation<br>76 patients were evaluated | Vascular catheter with guidewire was passed to ventral epidural space. 50-90 ml and 10 mg of dexamethasone were injected. Control got 10 mg dexamethasone only | VAS, Opioid use; MacNab criteria[245] | 1 week, one month,6 months | 3.24 mean decrease in VAS at 6 months in treated group, vs .82 in control.<br>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 2009[85]<br><br>Randomized Active Control<br>Cochrane 11/12<br>IPM-QRB 34/48 | 120<br><br>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.<br>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.<br>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 1999 [132]<br><br>Randomized active control<br><br>IPM-QRB 23/48 | 83 | Adhesiolysis in four groups,<br><br>0.9% saline,<br>10% saline,<br>with or without hyaluronidase | VAS,<br>Magill Pain Questionnaire | 3, 6, 12 months | No significant difference between the four groups.<br>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.<br>24 of 83 patients were removed from study Ventral | Showed only moderate additional benefit from either 10% saline or hyaluronidase | Moderate quality study comparing 4 treatment options<br>Reduced additional procedures. |
| Manchikanti[40]<br><br>Randomized Active Control<br>IPM-QRB 40/48 | 50 spinal stenosis with low back and leg pain | Adhesiolysis with 10% saline vs S3 caudal injection with 0.9% saline | NRS, ODI, Employment status, opioid use | 3, 6, 12 months | 76% of adhesiolysis procedures had >50% relief and also >40% ODI improvement at 12 months, vs 4% of caudal. | 8 of 25 in the control group were lost to follow up at 12 months, vs 0 in the adhesiolysis.<br>18 control were unblinded prematurely vs 0 in the control | High quality equivalency study. | Adhesiolysis, one day, repeated up to 3.5 times a year, is effective in providing decreased pain and increased function in the spinal stenosis population. |

| Study<br><br>Study Characteristic Methodological Quality Scoring | Number of Patients & Selection Criteria | Interventions/ Control | Outcome measures | Time of Measurement | Results | Weaknesses | Strengths | Conclusions |
|---|---|---|---|---|---|---|---|---|
| Manchikanti 2004 [123]<br><br>Randomized Active Control Cochrane 11/12<br>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.<br><br>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. |
| Veihelmann 2004[124]<br><br>Randomized prospective study with active control<br><br>Cochrane 11/12<br><br>IPM-QRB 25/48 | 99 patients with radicular pain with concordant imaging findings | One day adhesiolysis with 10% saline vs. physical therapy | VAS, ODI, GHS | 3, 6, 12 months | Mean improvement of the treated group was >50% in VAS and >40% in ODI at 3, 6 and 12 months. Treatment group had ~10% relief. | 25 patients in the control group were lost t follow up, 10 lost to follow up, 12 crossing over to adhesiolysis, 10 having surgery | Moderate quality comparative effectiveness study | Adhesiolysis is superior to physical therapy in treating persistent back and leg pain with concordant imaging findings. |
| Manchikanti 1999 [20]<br><br>Retrospective observational<br><br>IPM-QRBNR 28/48 | 150 patients selected from 532 who had had adhesiolysis. | One day vs 2 day adhesiolysis with hypertonic saline Compared to Racz 1999 for 3 day adhesiolysis | Pain relief of > 50% | 3, 6, 12 months | No difference between one-day, two-day or three-day adhesiolysis Repeat procedures showed significant (>50%) relief with longer duration. | Retrospective study, with one leg obtained from an unrelated study. | Large scale study with | Moderate quality study showing that one day adhesiolysis is as effective as three-day. |
| Gerdesmeyer 2006 [125] Prospective observational<br><br>IPM-QRBNR 25/48 | 61 patients with radiculopathy | Ventral three-day adhesiolysis | ODI, MacNab scale | 3, 6 months | ODI was reduced >50% at 3 and 6 months | Mixture of multiple etiologies No control group | Prospective, tightly controlled study | Moderate quality study documenting that replication of pain leads to functional improvement in adhesiolysis. |
| Oh 2014[126] Retrospective<br><br>IPM-QRBNR 28/48 | 303 patients with one-level disc disease with low back and or leg pain. No previous surgery or stenosis | One-day adhesiolysis with either ventral or dorsal catheter placement | VAS, Odom's criteria | 1, 3, 6 months | VAS for leg pain was significantly greater at 3 and 6 months for ventral group. Both ventral and dorsal placement showed >50% reduction of back and leg pain | Retrospective study with no control. | Large scale, single center study | Ventral placement appears to provide better oucomes. |

VAS= Visual Analog Scale; NRS=Numeric Rating Scale; ODI=Oswestry Disability Index

Appendix Table 7 *Study characteristics of randomized controlled trials and observational studies assessing spinal endoscopic adhesiolysis.*

| Study Characteristic Methodological Quality Scoring | Number of Patients & Selection Criteria | Interventions/ Control | Outcome measures | Time of Measurement | Results | Weaknesses | Strengths | Conclusions |
|---|---|---|---|---|---|---|---|---|
| Manchikanti 2005 [127] RCT IPM_QRB 38/48 | 83 patients with chronic low back and radicular pain. ~75% were post lumbar surgery | Endoscopic adhesiolysis v caudal epidural injection | >505 VAS improvement. ODI, opioid intake and work status | 12 months | 48% of endoscopy patients had >50% relief at 12 months; 0% of caudal patients did. | Co-mingled patient population. Not clear if repeat procedure were performed | Rigorously designed study | High quality study showing effectiveness of endoscopy in primarily post lumbar surgery syndrome patients |
| Lee 2014[129] Retrospective IPM-QRBNR 30/48 | 52 endoscopy and 62 transforaminal epidural steroid injections Persistent lower extremity pain after either discectomy or fusion | Endoscopic adhesiolysis vs. transforaminal epidural steroid injections. | >50% improvement in NRS and >40% improvement in ODI | 6 months | ~55% of endoscopic group had relief compared to ~30% of transforaminal Patients with discectomy did better than fusion | Retrospective study Volume in saline used in endoscopy not reported | Single center study | Epiduroscopy is more effective than transforaminal injection at providing significant pain relief and functional improvement in failed back surgery patients. |
| Igarashi 2004 [128] Prospective 24/48 IPM-QRBNR | 58 lumbar stenosis patients with either radicular pain or multisegmental dysesthesia | Endoscopic lysis of adhesions | VAS back and leg, motor deficit, sensory deficit | 3, 6 12 months | >50% relief of low back pain at 12 months for both groups and >50% relief of leg pain at 12 months for radiculargroup | Prospective, uncontrolled study. Lack of clear distinction between groups. No pre-specified definition of successful outcomes | Evaluates efficacy of epiduroscopy in adhesiolysis patient. | Moderate quality study showing effectiveness of adhesiolysis in spinal stenosis patients. |
| Manchitkanti 1999 [130] Retrospective IPM-QRBNR 33/288 | 120 post lumbar surgery patients | 60 patients with percutaneous adhesiolysis; 60 patients with endoscopic adhesiolysis | >50% relief of pain | 3, 6 12 months | At one month, 72% of percutaneous and 97% of endoscopic patients had > 50% relief. At 3 months, it was 10% and 52%. After the second procedure, 22% of the percutaneous group had > 50% relief, whereas 75% of the endoscopic group did. Percutaneous adhesiolysis is more cost-effective than endoscopic adhesiolysis. | Retrospective evaluation Limited outcome parameters | All patients were post lumbar surgery patients. Direct comparison between percutaneous and endoscopic adhesiolysis. | High quality study showing effectiveness of both percutaneous and endoscopic adhesiolysis in post lumbar surgery patientns |

VAS= Visual Analog Scale; NRS=Numeric Rating Scale; ODI=Oswestry Disability Index

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