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REVIEW ARTICLE

Effectiveness of Epiduroscopy for Patients with Failed Back Surgery Syndrome: A Systematic Review and Meta-analysis

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■ **Abstract**

Introduction: Low-back or leg pain in patients suffering from failed back surgery syndrome (FBSS) is often severe, having a major impact on functionality and quality of life. Despite conservative and surgical treatments, pain can be persistent. An alternative treatment option is epiduroscopy, a minimally invasive procedure based on mechanical adhesiolysis of epidural fibrosis. As epidural fibrosis is speculated to be a major contributor in the pathophysiologic process of FBSS, this review evaluates the effectiveness of epiduroscopy in FBSS patients.

Methods and materials: A systematic literature search was performed in PubMed, Embase, and Cochrane databases. Critical appraisal was performed using validated tools. Meta-analysis was performed using generic inverse variance analysis.

Results: From the 286 identified articles, nine studies were included. The visual analogue scale (VAS) average was 7.6 at baseline, 4.5 at 6, and 4.3 at 12 months. The Oswestry Disability Index (ODI) average was 61.7% at baseline, 42.8% at 6, and 46.9% at 12 months. An average of 49% of patients experienced significant pain relief at 6 and 37% at 12 months. Meta-analysis showed a pooled VAS mean difference of 3.4 (2.6 to 4.1; 95% confidence interval [CI]) and 2.8 (1.6 to 4.0; 95% CI) and pooled ODI mean difference of 19.4% (12.5 to 26.4%; 95% CI) and 19.8% (13.8 to 25.9%; 95% CI) at 6 and 12 months, respectively.

Conclusion: Current literature demonstrates a clinically relevant reduction in pain and disability scores at 6 to 12 months after mechanical adhesiolysis in FBSS patients. The quality of evidence is moderate, and the level of recommendation is weak. Practitioners should consider the benefits of epiduroscopy after weighing the risks for individual patients with FBSS. ■

Key Words: epiduroscopy, failed back surgery syndrome, endoscopic adhesiolysis, systematic review, recurrent low-back pain, leg pain

INTRODUCTION

Lower-back pain remains the major cause of disability in most western countries, with 70% of adults experiencing at least one episode of low-back pain or discomfort during their lifetime.[1] Spinal surgery is an increasingly utilized treatment option for both degenerative and nondegenerative diseases of the spine. Recent long-term cohort studies demonstrated a significant increase in spinal surgeries in the past 15 years with a fivefold increase among the elderly.[2–4] Unfortunately, 10% to 40% of patients experience recurrent or persistent low-back pain with or without leg pain after technically

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successful spinal surgery.[5,6] These symptoms are known as failed back surgery syndrome (FBSS).[7]

The etiology of FBSS is not clear. Recurrent pathology, surgical complications, inflammation, and the formation of epidural fibrosis are considered possible causes,[8] of which epidural fibrosis most frequently seems to be associated with FBSS.[8,9] The latter consists of dense fibrous scar tissue that can form within the epidural space after surgery. It may lead to adhesions to the dura mater and tether nerve roots.[8] It is hypothesized that nerve compression and accumulation of inflammatory mediators affect nerve nutrition, which may cause increased sensitivity and the development of chronic neuropathic(-like) pain and nociceptive pain.[10]

Treatment options for FBSS include physical therapy, pain medication, interventional procedures (eg, lumbar steroid injections and percutaneous/endoscopic adhesiolysis) neurostimulation, and reoperations. FBSS is often refractory to drug therapy.[11,12] Revisional surgery, to remove epidural fibrosis, is only effective in 5% to 30% of the cases.[13,14] Interventional procedures, such as percutaneous adhesiolysis, and physical therapy are supported by moderate to strong evidence.[11] While the strongest long-term evidence exists for the effectiveness of spinal cord stimulation (SCS), SCS is often reserved as last-resort treatment modality.[15,16]

A relatively unknown interventional treatment for FBSS is epiduroscopy, a minimally invasive endoscopic procedure. The therapeutic effectiveness is allegedly based on endoscopic adhesiolysis of epidural adhesions,[17,18] by mechanical movement of the catheter and saline injection(s) surrounding the affected nerve root.[10] Other forms of endoscopic adhesiolysis include laser,[19] radiofrequency,[20] and, chemically, administration of ozone.[21–24] After adhesiolysis, targeted drugs, such as corticosteroids, can be accurately delivered in the affected areas. Epidural adhesiolysis can especially benefit patients with FBSS given the hypothesized pathology of pain.

The reported effectiveness of epiduroscopy in studies is promising; however, previously published systematic reviews show moderate level of evidence (level II to III[25] and level 2B+[26]) with a weak recommendation.[7,10,27] The reviews included articles covering a heterogeneous group of patients with different spinal pathologies, elderly with lumbar stenosis and disc herniations without previous spinal surgery, and describing a wide range of endoscopic adhesiolysis techniques.[27] The most recent review was published in 2016.[27] However, since then several new studies, including one randomized controlled trial (RCT), have been published.

At present, the benefits of mechanical adhesiolysis with or without target drug placement in patients with FBSS remain unclear. Therefore, we attempt to gather all available evidence on the effect of epiduroscopy on pain and functionality at 6 and 12 months after mechanical adhesiolysis using epiduroscopy in patients suffering from FBSS.

METHODS AND MATERIALS

Systematic Search Strategy

A systematic search was conducted in three databases (PubMed, Embase, Cochrane Database for Systematic reviews, and Central Register of Controlled Trials) on November 20, 2019. Search terms included "failed back surgery syndrome" and "epiduroscopy" and their synonyms (Appendix S1).

Study Selection

All studies were imported into Rayyan QCRI, a systematic review application,[28] and duplicates were removed. Title and abstract screening was performed by two authors (M.G., A.K.) independently using the following inclusion criteria: original studies (both observational and interventional) written in English, Dutch, or German language including adult patients with low-back and/or leg pain following prior spinal surgery, who received epiduroscopy, reporting a clinical outcome with a minimum follow-up of 6 months. Any disagreements were settled by a third author (M.R.). In the next phase, the same authors performed full-text screening. Further selection criteria were a study population of at least 80% FBSS patients in the primary statistical analyses or in secondary analyses, the use of the sacral approach during epiduroscopy, and including only mechanical adhesiolysis with or without targeted drug treatment. Conference abstracts and articles with no full text available were excluded. Backward selection was performed on the included articles.

Quality Assessment

The PRISMA-protocol was used for this systematic review.[29] All included studies were assessed by two authors (A.K., M.G.). The applicability of all included studies to the research question was scored on a three-

point scale (poor, moderate, good applicability) for the domain, determinant, and outcome of the study. The quality of all studies was assessed using the Cochrane Risk of Bias (RoB)[30] tool for RCTs, the Newcastle Ottawa Scale (NOS)[31] for nonrandomized (observational cohort and case–control) studies, and the Quality Assessment Tool for Before–After Studies with No Control Group of the National Institute of Health (NIH).[32] Critical appraisal tools quantified the quality of studies on a three-point scale: poor, moderate, and good quality. To be able to compare results, poor-quality studies were excluded from the meta-analysis. The quality of evidence (rated as very low, low, moderate, or high) and associated recommendation (weak or strong) were assessed using the Cochrane GRADE tool.[33]

Data Extraction

For each study, single-arm data including the intervention mechanical adhesiolysis with or without targeted drug treatment were extracted. Outcome measures extracted were pre- and postprocedure visual analogue scale (VAS) or Numerical Rating Scale (NRS) for pain, Oswestry Disability Index (ODI),[34] percentage of patients with significant pain relief (> 50% pain relief) at 12-month follow-up, and adverse events.

The VAS on a scale from 0 to 10, where 0 represents no pain and 10 the worst imaginable pain, was extracted as a group average with standard deviation (SD). For this review, VAS and NRS scores were considered equivalent. ODI data were either presented as a score (0 to 50; 0 is minimal disability, 50 is maximal disability) or percentage (0% to 100%; 0% to 20% is minimal disability, 80% to 100% represents bed-bound). For the purpose of comparison, the ODI scores were converted into percentages. The percentage of patients with significant relief was collected as absolute numbers and percentages. For all studies, the definition of significant pain relief was extracted and compared.

Meta-analysis

All outcome measures registered before epiduroscopy are presented as baseline data. For the VAS and ODI scores, the mean difference was calculated with standard error (SE) at both 6 and 12 months post surgery. The single-arm data were displayed in a forest plot. The analysis was performed with RevMan 5.3[35] (The Cochrane Collaboration's software for preparing and maintaining Cochrane reviews) using the generic inverse variance (GIV) data type and a random effects analysis model with 95% confidence interval (CI). Using a P value equal to 0.05 as statistically significant.

RESULTS

Study Selection

The systematic search yielded 286 unique articles which were screened on title and abstract, of which 227 did not meet the in- and exclusion criteria. The remaining 59 articles were eligible for full-text screening. Nine articles were included in the final analysis, and seven articles with the highest quality were included in the meta-analysis (Figure 1).

Study Characteristics

Two articles were RCTs,[36,37] three were prospective-,[38–40] and four were retrospective[41–44] observational studies. Together, they included 392 patients. Results from one of the RCTs are reported per study arm because both study arms included mechanical adhesiolysis with different targeted drug treatment regimens.[37] For further study characteristics, see Table 1.

Quality Assessment

Risk of bias is shown in Appendix S2. One RCT was rated as good[37] quality and one as fair[36] (Table 2a). Fair quality was due to possible attrition bias. Follow-up data at 3 months were used as 6-month data, and at 6 months as 12-month data if no further data were available. Using the NOS for observational studies, four were rated as good,[39,41,43,44] one as moderate,[42] and two as poor[38,40] (Table 2b). Poor quality was rated because patients were excluded from follow-up based on outcome or due to incomplete reporting of data. The quality assessment using the NIH showed risk of bias in the enrolment of participants, unaccounted or high loss to follow-up, and small sample sizes with insufficient power. The overall applicability was good: three studies had good applicability[37,41,42] (Appendix S2, Table 2c), four had moderate applicability due to varying outcome and follow-up data,[37,39,40,44,45] and one study[36] had moderate applicability due to mixed population (Appendix S3). Results from Geurts et al.[38] were not included due to exclusion of patients from follow-up based on outcome.

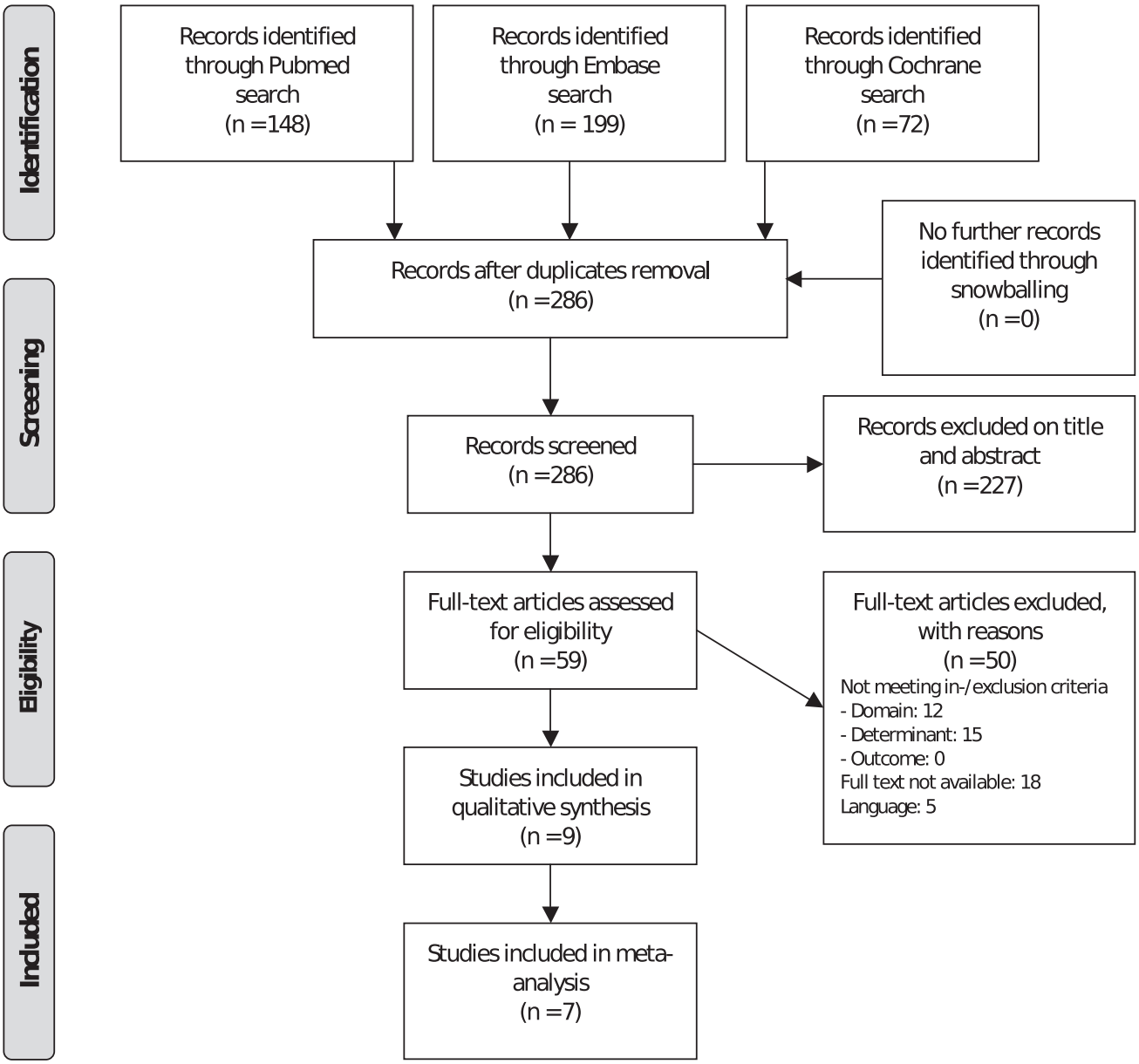

Figure 1. Flowchart of systematic search, performed on November 20, 2019.

The overall quality of evidence is categorized as "moderate" and the corresponding level of recommendation "weak." Since only single-arm data were extracted from the RCTs, the evidence presented in the review is based on primarily observational data. Therefore, the evidence has the level of evidence of observational studies and cannot be considered "high."

Results from Individual Studies

Full table of results is included in Appendix S4, Table 3a–c.

Visual Analogue Scale. Five studies, including six study arms, reported VAS as primary outcome at 6 months[36,37,41,42] and four studies (five study arms) at 12 months.[36,37,41,42] The average was 7.6 at baseline, 4.7 at 6 months, and 4.9 at 12 months (Figure 2A,B). This decline in VAS was significant in five out of six study arms.

The meta-analysis for VAS at 6 and 12 months included five study arms.[36,37,41,42] Two studies were excluded from analysis; one due to high loss of follow-up[38] and one because SE could not be calculated.[44] The pooled VAS mean difference was 3.42 (2.67 to 4.16;

Table 1. Study Characteristics

Study	Study Design	Study Arms	Epiduroscopy Adhesiolysis Technique	Number of FBSS Patients	Mean Age of Population	Reported Outcomes	Reported Follow-Up (Months)
Avellanal et al. 2014	Prospective	1. Epiduroscopy 2. Conventional* 3. Surgery*	Not stated	18	57.9	VAS	> 12
Ceylan et al. 2019	Retrospective	Previous spinal surgery 1. Stabilized 2. Nonstabilized	Mechanical + hyaluronidase	82	50.7	VAS ODI PSS	1,3,6,12
Geurts et al. 2002	Prospective	1. Epiduroscopy	Mechanical + methylprednisolone acetate, hyaluronidase, clonidine	14	47	VAS GSER	3,6,9,12
Hazer et al. 2018	Retrospective	1. FBSS patients 2. Non-FBSS patients	Mechanical	66	57.9	VAS ODI	6,12
Manchikanti et al. 2005	Randomized controlled, double-blinded	1. Epiduroscopy 2. Sacral steroid injection	Mechanical + corticosteroids	66	50	VAS ODI Opioid use, Employment, Psychology	6,12
Manchikanti et al. 1999	Retrospective	1. Epiduroscopy 2. Nonendoscopic*	Mechanical + xylocaine, celestone, soluspan	60	48.7	VAS pain relief	2,3,6,12
Rapcan et al. 2018	Randomized controlled, double blinded	1. Epiduroscopy 2. Epiduroscopy with target drug placement	Mechanical/corticosteroids and hyaluronidase	48	50.2	VAS back and leg ODI PSS PSCS	6, 12
Takeshima et al. 2009	Prospective	Sites of epiduroscopic adhesiolysis 1. Epidural space 2. Nerve root 3. Both	Mechanical + methylprednisolone	28	57.4	ADL RDQODI JOA	1, 3, 6
Tuijp et al. 2018	Retrospective	1. Epiduroscopy	Mechanical + methylprednisolone	35	49	GPE NRS	0.25, 6

ADL, activities of daily living; FBSS, failed back surgery syndrome; GPE, global perceived effect; GSER, global subjective efficacy rating; JOA, Japanese Orthopedic Association score; NRS, numeric rating scale; ODI, Oswestry Disability Index; PSCS, patient specific function scale; PSS, patients satisfactory scale; RDQ, Roland–Morris disability questionnaire; VAS, visual analogue scale.
*Study arms using nonepiduroscopic techniques or consisting of non-FBSS patients were not included in this review.

95% CI) and 2.81 (1.60 to 4.02; 95% CI) at 6 (Figure 3A) and 12 months (Figure 3B), respectively.

Oswestry Disability Index. The ODI was the primary outcome in one study with only 6 months follow-up.[39] The ODI was reported in six study arms and five study arms at 6[36,37,39,41,42] and 12 months,[36,37,41,42] respectively. The ODI average was 61.7% at baseline, 42.8% at 6 months, and 46.9% at 12 months (Figure 4A,B). At 6 months, the difference met the criteria of significance in five study arms, and at 12 months in three out of five study arms when compared with baseline.

The meta-analysis for ODI at 6 months included six study arms.[36,37,39,41,42] One study[39] failed to report an outcome at 12 months; hence, the analysis only included five study arms at 12 months. The pooled ODI mean difference was 19.42% (12.47% to 26.37%; 95% CI) and 19.84% (13.82% to 25.86%; 95% CI) at 6 (Figure 5A) and 12 (Figure 5B) months, respectively.

Pain Relief. Pain relief was defined as follows: patients with 50% pain reduction at follow-up in five studies,[36,38,40,41,43] 50% improvement in global perceived effect in one study,[44] and patient status score "good" and "very good" in one study.[42] Five study arms out of ten reported pain relief at 6 months with an average of 49.2%, ranging from 30% to 78%.[36,38,42–44] At 12 months, five study arms reported pain relief with an average of 36.6%, ranging from 22% to 48%[36,38,40,41,43] (Figure 6). Due to differences in definitions and high variability in follow-up data, no meta-analysis was performed on this outcome.

Adverse Events. No serious adverse events were reported in the studies. Most frequent adverse events

Table 2. Critical Appraisal of (A) the Cochrane Risk of Bias Tool for Randomized Controlled Trials and (B) the Newcastle Ottawa Scale (NOS) of Nonrandomized Observational Studies

	Random Sequence Generation (Selection Bias)	Allocation Concealment (Selection Bias)	Selective Reporting (Reporting Bias)	Other Bias	Blinding of Participant and Personnel (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Data Outcome (Attrition Bias)
Manchikanti et al. 2005							
Rapcan et al. 2018							

	Selection				Comparability	Outcome				
Study	Representativeness of the Exposed Cohort	Selection of the Nonexposed Cohort	Ascertainment of Exposure	Demonstration that Outcome of Interest was not Present at Start of Study	Comparability of Cohorts on the Basis of the Design or Analysis	Assessment of Outcome	Was Follow-up Long Enough for Outcomes to Occur	Adequacy of Follow-Up of Cohorts	Total Score	Power
Hazer et al. 2018	★	★	★	★	★,-	★	★	★	8/9	Good
Ceylan et al. 2019	★	★	★	★	-,-	★	★	★	7/9	Moderate
Avellanal et al. 2014	★	★	★	★	-,-	★	★	-	5/9	Poor
Geurts et al. 2002	★	★	★	-	★,-	★	-	-	4/9	Poor
Takeshima et al. 2009	★	★	★	-	★,-	★	-	★	6/9	Good
Tuijp et al. 2018	★	-	★	★	★,★	★	-	★	7/9	Good
Machikqnti et al. 1999.	★	★	★	★	★,-	★	★	★	7/9	Good

Explanation of the Risk of Bias (RoB) tool: White+, low risk of bias; dashed, unclear risk of bias; black, high risk of bias. Explanation of NOS power interpretation: a study can be awarded a maximum of two stars for compatibility and a maximum of one star for selection and outcome (yes: ★; no: -). The NOS uses a three-point power scale: good, moderate, and poor quality. Good quality = 3 or 4 stars in selection domain, 1 or 2 stars in comparability domain, and 2 or 3 stars in outcome domain. Moderate quality = has 2 stars in selection domain, 1 or 2 stars in comparability domain, and 2 or 3 stars in outcome domain. Poor quality = 0 or 1 star in selection domain, 0 star in comparability domain, or 0 or 1 star in outcome domain.

Table 3. Results of (A) Visual Analogue Scale (VAS) and (B) Oswestry Disability Index 2.0 (ODI) for each Study per Included Study Arm prior to surgery and at 6- and 12-Month Follow-up After Epiduroscopy. (C) Percentage of Patients with Significant Pain Relief as Defined per Study per Study Arm at 6- and 12-month Follow-up After Epiduroscopy

Study	Study Arm[§]	Intervention Code	Number of Patients per Study Arm (% FBSS)	VAS Baseline (SD)	VAS at 6 Months (SD; *P* value)	VAS at 12 Months (SD; *P* value)
(A)						
Avellanal et al. 2014	1.	M[¶]	18 (100%)	—	—	—
Ceylan et al. 2019	1. + 2.[‡]	M + C[†]	82 (100%)	7.67 (0.69)	3.28(0.50) ($P < 0.001$)*	3.02(0.57) ($P < 0.001$)*
Geurts et al. 2002.	1.	M + C[†]	12 (100%)	7.3(0.94)	3.2(2.98)	1.2(0.85)
Hazer et al. 2018	1.	M[¶]	66 (100%)	7.3 (1.1)	3.2 (1.5) ($P < 0.001$)*	3.7 (1.6) ($P < 0.001$)*
Manchikanti et al. 2005	1.	M + C[†]	50 (84%)	9.0(0.9)	5.3(2.5) ($P < 0.001$)*	5.7(2.5) ($P < 0.001$)*
Manchikanti et all. 1999	1.	M + C[†]	60 (100%)	—	—	—
Rapcan et al. 2018	1.	M[¶]	22 (100%)	6.50	5.09 ($P = 0.024$)*	6.45 ($P = 0.714$)
	2.	M + C[†]	23 (100%)	7.52	5.65 ($P = 0.037$)*	5.73 ($P = 0.011$)*
Takeshima et al. 2009	1.	M + C[†]	10 (100%)	—	—	—
	2.	M + C[†]	9 (100%)	—	—	—
	3.	M + C[†]	9 (100%)	—	—	—
Tuijp et al. 2018	1.	M + C[†]	35 (100%)	7.7	5.9 ($P < 0.01$)*	—

Study	Study Arm[§]	Intervention Code	Number of Patients per Study Arm (% FBSS)	ODI Baseline (%; SD)	ODI at 6 Months (%) (SD; *P* value)	ODI at 12 Months (%) (SD; *P* value)
(B)						
Avellanal et al. 2014	1.	M[¶]	18 (100%)	—	—	—
Ceylan et al. 2019	1. + 2.[‡]	M + C[†]	82 (100%)	64.94(5.42)	42.68(4.36) ($P < 0.001$)*	41.74(4.3) ($P < 0.001$)*
Geurts et al. 2002.	1.	M + C[†]	12 (100%)	—	—	—
Hazer et al. 2018	1.	M[¶]	66 (100%)	73 (16)	38 (17) ($P < 0.002$)*	44 (17) ($P < 0.002$)*
Manchikanti et al. 2005	1.	M + C[†]	50 (84%)	72(9)	50(23.4) ($P < 0.001$)*	50(25.4) ($P < 0.001$)*
Manchikanti et all. 1999	1.	M + C[†]	60 (100%)	—	—	—
Rapcan et al. 2018	1.	M[¶]	22 (100%)	59.41	49.18 ($P = 0.055$)	53.68 ($P = 0.40$)
	2.	M + C[†]	23 (100%)	54.22	40.26 ($P = 0.024$)*	45.09 ($P = 0.111$)
Takeshima et al. 2009	1.	M + C[†]	10 (100%)	47 (13)	42 (11) ($P = 0.6241$)	—
	2.	M + C[†]	9 (100%)	48 (7.8)	33.8(10.2) ($P = 0.0209$)*	—
	3.	M + C[†]	9 (100%)	43.8 (8.4)	34.4(14.8) ($P = 0.0117$)*	—
Tuijp et al. 2018	1.	M + C[†]	35 (100%)	—	—	—

Study	Study Arm[§]	Intervention Code	Number of Patients per Study Arm (% FBSS)	Definition of Pain Relief	% of Patients with Pain Relief at 6 Months	% of Patients with Pain Relief at 12 Months
(C)						
Avellanal et al. 2014	1	M[¶]	18 (100%)	> 50% reduction VAS	—	38.9%
Ceylan et al. 2019	1 + 2[‡]	M + C[†]	82 (100%)	PSS (good or very good)	78%	—
Geurts et al. 2002.	1	M + C[†]	12 (100%)	> 50% reduction VAS	42%	33%
Hazer et al. 2018	1	M[¶]	66 (100%)	> 50% reduction VAS	—	62% ($P = 0.011$)
Manchikanti et al. 2005	1	M + C[†]	50 (84%)	> 50% reduction VAS %	56%* ($P < 0.001$)	48%* ($P < 0.001$)
Manchikanti et all. 1999	1	M + C[†]	60 (100%)	> 50% reduction VAS %	40%	22%
Rapcan et al. 2018	1	M[¶]	22 (100%)	—	—	—
	2	M + C[†]	23 (100%)	—	—	—
Takeshima et al. 2009	1	M + C[†]	10 (100%)	—	—	—
	2	M + C[†]	9 (100%)	—	—	—
	3	M + C[†]	9 (100)	—	—	—
Tuijp et al. 2018	1	M + C[†]	35 (100%)	> 50% reduction GPE	30%	—

FBSS, failed back surgery syndrome; GPE, global perceived effect; PSS, patients satisfactory scale; SD, standard deviation.
*Significant difference ($P < 0.05$) when compared with baseline.
[†]M + C, mechanical adhesiolysis and targeted drug placement used during epiduroscopy. [‡]Combined data were reported in the original article. [§]Study arm numbers correspond with Table 2. [¶]M, only mechanical adhesiolysis used during epiduroscopy.

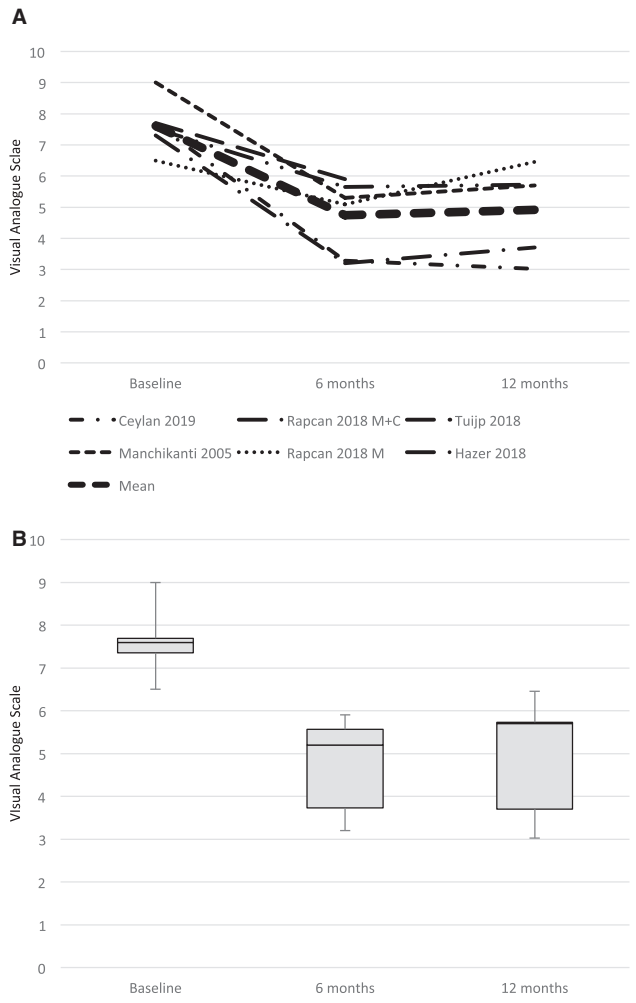

Figure 2. Visual analogue scale (A) for each study at baseline and 6 and 12 months after epiduroscopy and (B) box and whisker plot of combined data at baseline, 6, and 12 months after epiduroscopy. M + C, study arm with patients receiving mechanical adhesiolysis with target drug placement; M, study arm with patients receiving only mechanical adhesiolysis.

were dural and arachnoid puncture or rupture; with a combined 22 cases, leading to six cases of postdural puncture headache.

DISCUSSION

Current literature demonstrates an overall clinically relevant reduction in pain and disability scores 6 and 12 months after mechanical adhesiolysis using epiduroscopy, with a mean reduction in pain score by 2.8 points and a mean reduction in disability by approximately 20% 1 year after the procedure. This suggests that epiduroscopy can be an effective treatment for patients with FBSS.

The overall quality of evidence is categorized as "moderate" and the corresponding level of recommendation as "weak." Before we further discuss the clinical data, we first want to explain why the quality of evidence is categorized as moderate because there are two RCTs included in the review both showing a beneficial effect of epiduroscopy. In the RCT by Rapcan et al.,[37] both study arms included mechanical adhesiolysis. Data from both arms were extracted for the meta-analysis and are treated as observational data. In the RCT by Manchicanti,[36] the intervention mechanical adhesiolysis was compared with corticosteroid injection only. However, the study was rated as fair quality due to possible attrition bias. Using the Cochrane GRADE tool, the maximum quality was "high" with the inclusion of two RCTs. However, it was downgraded by one point to moderate based on the arguments described above. This can be interpreted as that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Focusing on the data presented by the different studies, the treatment effect does not benefit patients equally. At 6 months after epiduroscopy, 30% to 78% of patients report relief of pain, a highly variable proportion. One year after epiduroscopy, this decreases to 22% to 48% of patients. Hence, the overall reduction in VAS is caused by a select group of patients that benefits considerably from epiduroscopy. In order to identify patients with higher chance of success, it is of critical importance to investigate prognostic factors associated with the outcome of epiduroscopy in patients with epidural fibrosis.[45]

Several studies have demonstrated that the type of spinal surgery correlates with the epiduroscopic outcome. Ceylan et al.[42] showed that patients with stabilizing spine surgery have a poor outcome compared with nonstabilizing spinal surgery (like disc herniations and laminectomies). This finding is supported by a previous study, which demonstrated that patients after anterior or posterior lumbar interbody fusion have a worse clinical outcome after epiduroscopy when compared with discectomy and laminectomy.[46] This could explain the big decrease in VAS in Hazer et al., who only included patients following microdissection. Rapcan et al.[37] hypothesized that the number of open spinal surgeries and the extent of epidural fibrosis affect the success of epiduroscopy negatively and that patients with severely damaged nerve roots had a poor clinical outcome.

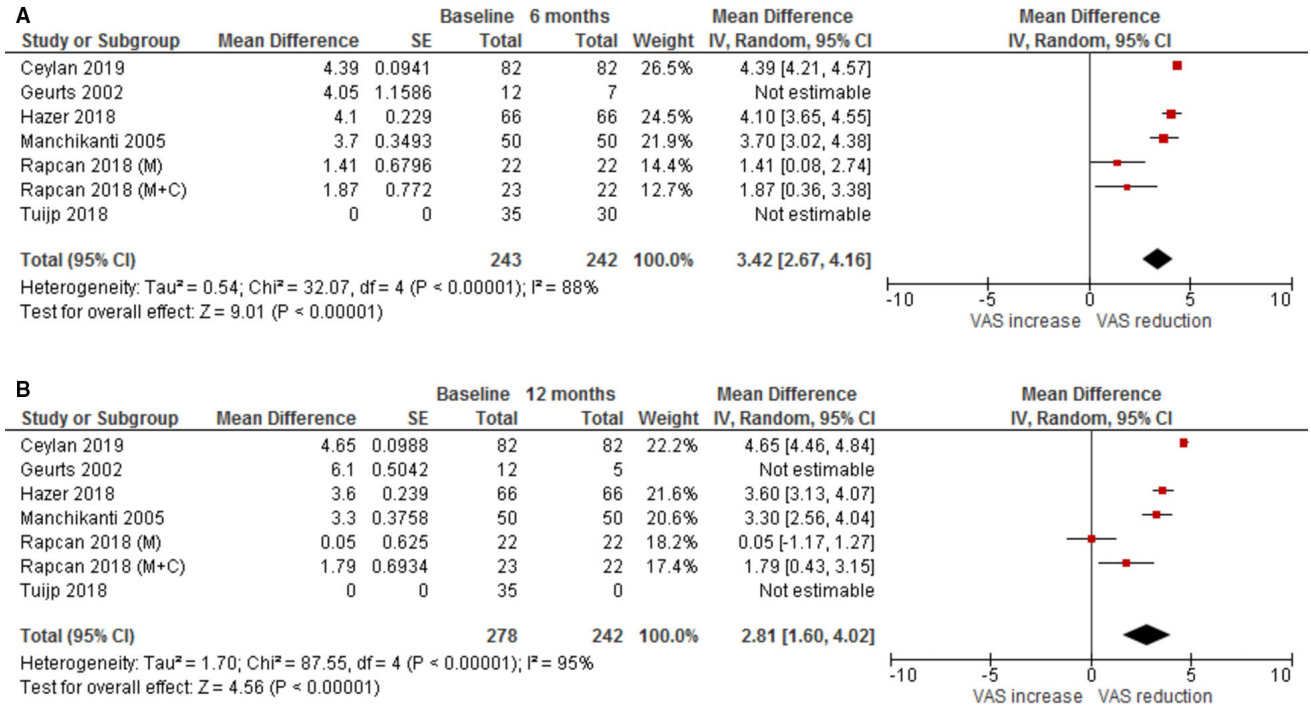

Figure 3. Forest plot of visual analogue scale mean difference (A) between baseline and 6 months after epiduroscopy, (B) between baseline and 12 months after epiduroscopy, both using the generic inverse variance and random effects analysis model. CI, confidence interval; IV, inverse variance; M, study arm with patients receiving only mechanical adhesiolysis; M + C, study arm with patients receiving mechanical adhesiolysis with target drug placement; SE, standard error.

Takeshima et al.[39] performed adhesiolysis based on fluoroscopic findings of the epidural space and specific sites around affected nerve roots. Readhesions appeared to occur faster after epiduroscopy in the central epidural space than around nerve roots. This correlated with the finding that patients with dominant nerve root adhesions had an increased long-term benefit from nerve root adhesiolysis. This suggests that the anatomical location of adhesions must correlate with the location of pain in order to have a positive outcome. Rapcan et al.[37] also attributed recurrent pain at 6 months to the formation of readhesions. There appears to be no correlation between rigidity of epidural fibrosis and the time interval between spinal surgery and epiduroscopy.[47]

Improved selection procedures that aid the identification of patients who will benefit from epiduroscopy are warranted. One promising technique for the identification of these patients is quantitative sensory testing (QST). Several studies have used QST to create presurgical somatosensory profiles, studying their relation to postsurgical clinical outcome.[48,49] QST can differentiate between cervical radicular pain and nonspecific neck pain.[49] As patients with predominant nerve root adhesions had an increased long-term benefit from nerve root adhesiolysis, objective measurement of radicular pain and sensory function may be predictive of postsurgery clinical pain outcome.[50,51]

In conclusion, careful selection of patients for epiduroscopy will affect the success rate of the procedure. Therefore, future studies need to include the assessment of prognostic factors for the epiduroscopy success rate and pain phenotyping using, for instance, QST measures.

The studies in our review did not report serious adverse events following epiduroscopy. There are, however, several case reports describing serious adverse events. Retinal hemorrhage with acute vision loss has been reported in two cases.[52,53] Another case report described encephalopathy and rhabdomyolysis following dural tear, most likely due to intrathecal neurotoxicity of contrast agents.[54] Other adverse events include epidural hematoma,[55] formation of intradural lumbosacral cyst,[56] and transient neurological deficits with seizures during the procedure.[57] Considering the potential risk for patients, it is advised that the epiduroscopy procedure should be performed in specialized centers.

So far, only "reasonable"[10] and "limited"[27] evidence has been described that supports the use of epiduroscopy

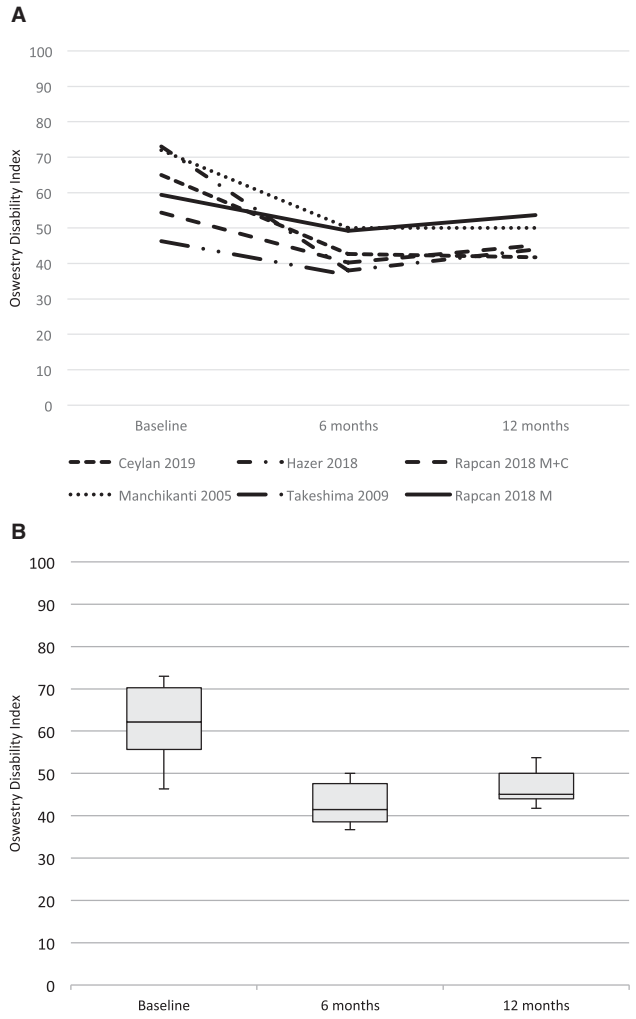

Figure 4. Oswestry Disability Index (A) for each individual study at baseline and 6 and 12 months after epiduroscopy and (B) combined in box and whisker plot of combined data at baseline and 6 and 12 months after epiduroscopy. M, study arm with patients receiving only mechanical adhesiolysis; M + C, study arm with patients receiving mechanical adhesiolysis with target drug placement.

in the treatment of FBSS. Although new studies have been published, extending the body of evidence, a high-quality RCT has not been published on the effectiveness of epiduroscopy compared with conventional therapy, sham procedures, or other interventions such as neurostimulation.

This systematic review has several limitations. Few studies are available that objectively compare epiduroscopy with other interventions. Therefore, this review investigated single-arm data prior to and post intervention with long-term follow-up. No control group was available; hence, the effect of time could not be accounted for. FBSS patients suffer from a number of heterogeneous symptoms, with varying duration, extent, and intensity of symptoms, which may impact clinical outcome. No clear definition of diagnostic criteria were mentioned in the studies. Most studies did not describe the specifics of the initial spinal surgery, which may further influence the outcome of epiduroscopy.[17] The extent and technical success rate of epiduroscopy were not always mentioned either. This might be of influence, considering that 40% of epiduroscopy procedures are not fully performed due to high-density fibrosis.[17] Studies did not specify treatment restrictions, such as increasing pain medication or crossover to surgery, during follow-up, possibly aiding the observed positive effect.

Another important observation that may influence the outcome of this review is the wide range in baseline VAS, with a maximum of 9 to a minimum of 6.5. This is either due to the heterogeneity of the patient population or other factors such as cultural differences in pain perception and/or presentation. The location which the VAS refers to is also inconsistent, including both lower-back and lower-extremity pain.

Finally, one study had a significant impact on the results even with a random effect model: Ceylan et al.[42] reported a significantly smaller SD than other studies (tenfold difference), without adequate explanation in the discussion.

CONCLUSION

When correctly indicated, epiduroscopy demonstrates to be a promising therapy for patients with FBSS. An average decrease of around three points in VAS and 20% in ODI is an impressive outcome considering the often refractory symptoms in patients with FBSS. Serious adverse events following epiduroscopy have been described in case reports but were not reported in the included studies. Taking into account that the overall quality of evidence is categorized as "moderate" and the corresponding level of recommendation as "weak," practitioners should weigh the risks and benefits of epiduroscopy for their individual patients with FBSS. Careful assessment of patients who more likely benefit from the procedure by pain phenotyping may aid this process. Also the option of neuromodulation should be considered while making the pain management plan.

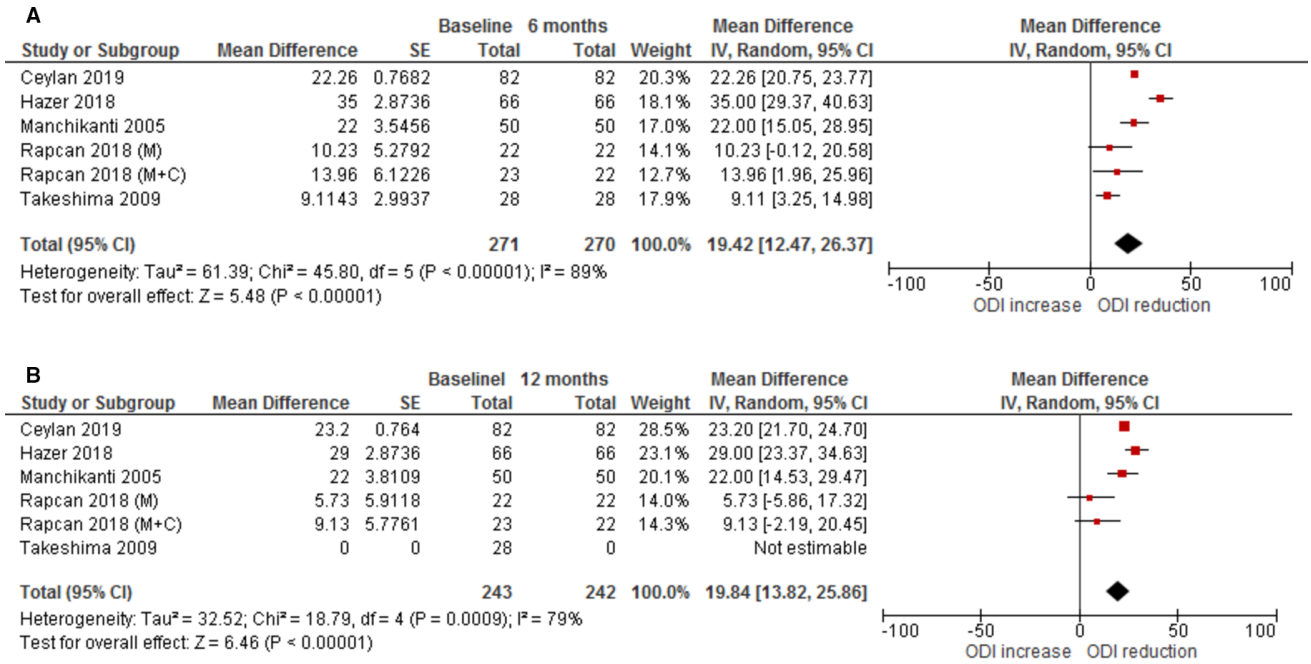

Figure 5. Forest plot of Oswestry Disability Index mean difference (A) between baseline and 6 months after epiduroscopy and (B) between baseline and 12 months after epiduroscopy, both using the generic inverse variance and random effects analysis model. CI, confidence interval; IV, inverse variance; M, study arm with patients receiving only mechanical adhesiolysis; M + C, study arm with patients receiving mechanical adhesiolysis with target drug placement; SE, standard error.

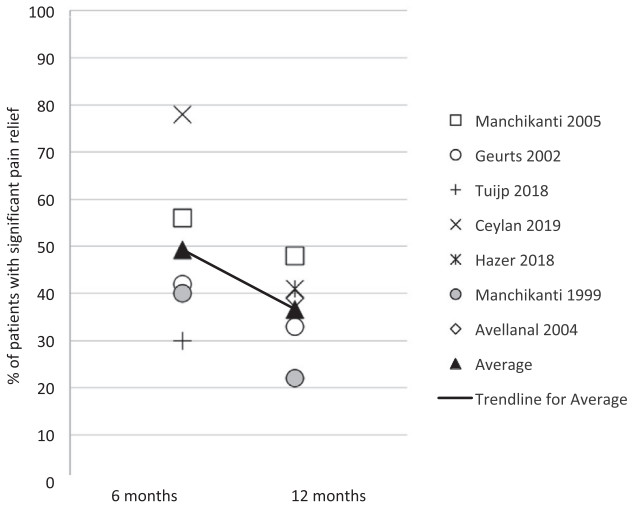

Figure 6. Scatterplot of percentage (%) of patients experiencing relief of pain according to respective definitions of individual studies at 6- and 12-month follow-up after epiduroscopy, including average (mean) with trendline.

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CONFLICT OF INTEREST

All authors have no conflict of interest to disclose concerning this topic.

AUTHOR CONTRIBUTIONS

Matthijs W. Geudeke: conducting systematic search; article screening and selection; critical appraisal; data extraction and analysis; preparation of first draft and preparation of revisional draft after review from coauthors. Annelot C. Krediet: article screening and selection; critical appraisal; critical revision of final draft. Suleyman Bilecen: critical revision of final draft. Frank J.P.M. Huygen: critical revision of final draft. Mienke Rijsdijk: initiator; supervision of data extraction and analysis and preparation of first draft; critical revision of final draft.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. Full syntax for search strategy.

Appendix S2. Full critical appraisal of Cochrane risk of bias and National Institute of Health tool.

Appendix S3. Full applicability.

Appendix S4. Full study results tables.

REFERENCES

1. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388:1545–1602.

2. Grotle M, Småstuen MC, Fjeld O, et al. Lumbar spine surgery across 15 years: trends, complications and reoperations in a longitudinal observational study from Norway. *BMJ Open*. 2019;9:e028743.

3. Steiger HJ, Krämer M, Reulen HJ. Development of neurosurgery in Germany: comparison of data collected by polls for 1997, 2003, and 2008 among providers of neurosurgical care. *World Neurosurg*. 2012;77:18–27.

4. Martin BI, Mirza SK, Spina N, Spiker WR, Lawrence B, Brodke DS. Trends in lumbar fusion procedure rates and associated hospital costs for degenerative spinal diseases in the United States, 2004 to 2015. *Spine (Phila Pa 1976)*. 2019;44:369–376.

5. Hsu E, Atanelov L, Plunkett AR, Chai N, Chen Y, Cohen SP. Epidural lysis of adhesions for failed back surgery and spinal stenosis: factors associated with treatment outcome. *Anesth Analg*. 2014;118:215–224.

6. North RB, Kidd D, Shipley J, Taylor RS. Spinal cord stimulation versus reoperation for failed back surgery syndrome: a cost effectiveness and cost utility analysis based on a randomized, controlled trial. *Neurosurgery*. 2007;61:361–369.

7. Hayek SM, Helm S, Benyamin RM, Singh V, Bryce DA, Smith HS. Effectiveness of spinal endoscopic adhesiolysis in post lumbar surgery syndrome: a systematic review. *Pain Physician*. 2009;12:419–435.

8. Pereira P, Avelino A, Monteiro P, Vaz R, Castro-Lopes JM. New insights from immunohistochemistry for the characterization of epidural scar tissue. *Pain Physician*. 2014;17:465–474.

9. Chan C, Peng P. Failed back surgery syndrome. *Pain Med*. 2011;12:577–606.

10. Kallewaard JW, Vanelderen P, Richardson J, Van Zundert J, Heavner J, Groen GJ. Epiduroscopy for patients with lumbosacral radicular pain. *Pain Pract*. 2014;14:365–377.

11. Amirdelfan K, Webster L, Poree L, Sukul V, McRoberts P. Treatment options for failed back surgery syndrome patients with refractory chronic pain: an evidence based approach. *Spine (Phila Pa 1976)*. 2017;42:S41–S52.

12. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*. 2007;132:179–188.

13. Nachemson AL. Evaluation of results in lumbar spine surgery. *Acta Orthop Scand*. 1993;64(sup251):130–133.

14. Hazard RG. Failed back surgery syndrome: surgical and nonsurgical approaches. *Clin Orthop Relat Res*. 2006;443:228–232.

15. Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. *Pain*. 2004;108:137–147.

16. Taylor RS, Van Buyten J-P, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine (Phila Pa 1976)*. 2005;30:152–160.

17. Dakheel R, De Vooght P, Puylaert M, et al. The extent of epidural adhesiolysis with epiduroscopy relates to outcome in failed back surgery syndrome patients. *Eur J Pain Suppl*. 2011;5:287.

18. Gruyters I, De Vooght P, Puylaert M, Mestrum R, Van Zundert J, Vanelderen P. Outcome and extent of epidural adhesiolysis attainable with epiduroscopy in failed back surgery syndrome relates to the type of previous lumbar surgery. *Eur J Anaesthesiol*. 2013;30:207–208.

19. Ruetten S, Meyer O, Godolias G. Application of holmium:YAG laser in epiduroscopy: extended practicabilities in the treatment of chronic back pain syndrome. *J Clin Laser Med Surg*. 2002;20:203–206.

20. Raffaeli W, Righetti D. Surgical radio-frequency epiduroscopy technique (R-ResAblator) and FBSS treatment: preliminary evaluations. *Acta Neurochir Suppl*. 2005;92:121–125.

21. Magalhães FNDO, Soares SC, Torres JM, et al. The effect of ozone therapy applied by spinal endoscopy in patients with failed back pain syndrome: pilot study. *Eur J Pain Suppl*. 2011;5:103.

22. Barbosa DC, Ângelos JSD, Macena GMJD, Magalhães FNDO, Fonoff ET. Effects of ozone on the pain and disability in patients with failed back surgery syndrome. *Rev Assoc Med Bras*. 2017;63:355–360.

23. de Nêuton F, Magalhães O, Soares SC, et al. Effects of ozone applied by spinal endoscopy in patients with chronic pain related to failed back surgery syndrome: a pilot study. *Neuropsychiatr Dis Treat*. 2013;9:1759–1766.

24. Donato AD, Fontana C, Pinto R, et al. The effectiveness of endoscopic epidurolysis in treatment of degenerative chronic low back pain: a prospective analysis and follow-up at 48 months. *Acta Neurochir Suppl*. 2011;108:67–73.

25. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med*. 2001;20(3 Suppl):21–35.

26. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians task force. *Chest*. 2006;129:174–181.

27. Helm S 2nd, Racz GB, Gerdesmeyer L, et al. Percutaneous and endoscopic adhesiolysis in managing low back and lower extremity pain: a systematic review and meta-analysis. *Pain Physician*. 2016;19:E245–E282.

28. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan – a web and mobile app for systematic reviews. *Syst Rev*. 2016;5:210.

29. Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:1–6.

30. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaborations tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343.

31. Wells G, Shea B, O'Connell D, et al.The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Non-Randomized Studies in Meta-Analysis [Internet]; 2000. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp (accessed May 5, 2020).

32. U.S. Department of Health & Human Services. Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. National Institute of Health. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (accessed May 5, 2020).

33. Higgins JPT, Thomas J, Chandler J, et al., *Cochrane Handbook for Systematic Reviews of Interventions*. 2nd ed. Chichester, UK: John Wiley & Sons; 2019. https://www.wiley.com/en-ae/Cochrane+Handbook+for+Systematic+Reviews+of+Interventions,+2nd+Edition-p-9781119536628

34. Fairbank JC, Pynsent PB. The Oswestry Disability Index. *Spine (Phila Pa 1976)*. 2000;25:2940–2952. discussion 2952.

35. The Nordic Cochrane Centre, The Cochrane Collaboration. *Review Manager (RevMan) [Computer Program]. Version 5.3*. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014.

36. Manchikanti L, Boswell MV, Rivera JJ, et al. [ISRCTN 16558617] A randomized, controlled trial of spinal endoscopic adhesiolysis in chronic refractory low back and lower extremity pain. *BMC Anesthesiol*. 2005;5:10.

37. Rapcan R, Kocan L, Mláka J, et al. Parallel pilot study assessing the effect of mechanical adhesiolysis vs adhesiolysis with corticosteroid and hyaluronidase administration into the epidural space during epiduroscopy. *Pain Med*. 2018;19:1436–1444.

38. Geurts JW, Kallewaard J-W, Richardson J, Groen GJ. Targeted methylprednisolone acetate/hyaluronidase/clonidine injection after diagnostic epiduroscopy for chronic sciatica: a prospective, 1-year follow-up study. *Reg Anesth Pain Med*. 2002;27:343–352.

39. Takeshima N, Miyakawa H, Okuda K, et al. Evaluation of the therapeutic results of epiduroscopic adhesiolysis for failed back surgery syndrome. *Br J Anaesth*. 2009;102:400–407.

40. Avellanal M, Diaz-Reganon G, Orts A, Soto S. One-year results of an algorithmic approach to managing failed back surgery syndrome. *Pain Res Manag*. 2014;19:313–316.

41. Hazer DB, Acarbaş A, Rosberg HE. The outcome of epiduroscopy treatment in patients with chronic low back pain and radicular pain, operated or non-operated for lumbar disc herniation: a retrospective study in 88 patients. *Korean J Pain*. 2018;31:109–115.

42. Ceylan A, Aşık İ, Özgencil GE, Erken B. Evaluation of the efficacy efficacy of epiduroscopic adhesiolysis in failed back surgery syndrome. *Turkish J Med Sci*. 2019;49:249–257.

43. Manchikanti L, Pampati V, Bakhit CE, Pakanati RR. Non-endoscopic and endoscopic adhesiolysis in post-lumbar laminectomy syndrome: a one-year outcome study and cost effectiveness analysis. *Pain Physician*. 1999;2:52–58.

44. Tuijp SJ, Van Zundert J, De Vooght P, et al. Does the use of epiduroscopic lysis of adhesions reduce the need for spinal cord stimulation in failed back surgery syndrome? A short-term pilot study. *Pain Pract*. 2018;18:839–844.

45. Bosscher HA, Heavner JE. Lumbosacral epiduroscopy findings predict treatment outcome. *Pain Pract*. 2014;14:506–514.

46. Gruyters I, De Vooght P, Puylaert M, Mestrum R, Van Zundert J, Vanelderen P. Outcome and extent of epidural adhesiolysis attainable with epiduroscopy in failed back surgery syndrome relates to the type of previous lumbar surgery: 14AP2-2. *Eur J Anaesthesiol*. 2013;30:207–208.

47. Lebrun C, van Zundert J, Puylaert M, et al. Does the rigidity of epidural fibrosis correlate with the time interval between surgery and epiduroscopy in failed back surgery syndrome? *Pain Pr*. 2012;12:155.

48. Lindbäck Y, Tropp H, Enthoven P, Gerdle B, Abbott A, Öberg B. Altered somatosensory profile according to quantitative sensory testing in patients with degenerative lumbar spine disorders scheduled for surgery. *BMC Musculoskelet Disord*. 2017;18:264.

49. Tampin B, Slater H, Hall T, Lee G, Briffa NK. Quantitative sensory testing somatosensory profiles in patients with cervical radiculopathy are distinct from those in patients with nonspecific neck-arm pain. *Pain*. 2012;153:2403–2414.

50. Tampin B, Slater H, Jacques A, Lind CRP. Association of quantitative sensory testing parameters with clinical outcome in patients with lumbar radiculopathy undergoing microdiscectomy. *Eur J Pain*. 2020;24:1377–1392.

51. Tschugg A, Löscher WN, Lener S, et al. The value of quantitative sensory testing in spine research. *Neurosurg Rev*. 2017;40:411–418.

52. Biersteker HA, Geurts JW, Kallewaard JW. Retinal hemorrhage after epiduroscopy in a patient using dexamethasone: a case report. *Interv Pain Manag Rep*. 2019;3:33–36.

53. Amirikia A, Scott IU, Murray TG, Halperin LS. Acute bilateral visual loss associated with retinal hemorrhages following epiduroscopy. *Arch Ophthalmol*. 2000;118:287–289.

54. Mizuno J, Gauss T, Suzuki M, Hayashida M, Arita H, Hanaoka K. Encephalopathy and rhabdomyolysis induced by iotrolan during epiduroscopy. *Can J Anaesth*. 2007;54:49–53.

55. Yu Y, Kim TH, Lee SH, Chang MC. . Epidural hematoma after trans-sacral epiduroscopic laser

decompression: a case report. *Photobiomodul Photomed Laser Surg*. 2020;38:112–114.

56. Ryu KS, Rathi NK, Kim G, Park CK. Iatrogenic intradural lumbosacral cyst following epiduroscopy. *J Korean Neurosurg Soc*. 2012;52:491–494.

57. Beyaz SG. Seizures and transient neurological deficits during epiduroscopy in a patient with failed back surgery syndrome. *Pain Med*. 2015;16:825–827.