Systematic Review

Treatment Outcomes for Patients with Failed Back Surgery

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Background: Failed back surgery syndrome (FBSS) is a frequently encountered disease entity following lumbar spinal surgery. Although many plausible reasons have been investigated, the exact pathophysiology remains unknown. Various medications, reoperations, interventions such as spinal cord stimulation, epidural adhesiolysis or epidural injection, exercise therapy, and psychotherapy have been suggested treatment options. However, the evidence of the clinical outcome for each treatment has not been clearly determined.

Objectives: To evaluate the outcomes of each treatment modality and to present treatment guidelines for patients with FBSS.

Study Design: A systematic review of each treatment regimen in patients with FBSS.

Methods: The available literature regarding each modality for the treatment of refractory back pain or radiating pain for FBSS was reviewed. The quality assessment and the level of evidence were analyzed using the "Methodology Checklist" of SIGN (Scottish Intercollegiate Guidelines Network). Data sources included relevant English language literature identified through searches of Pubmed, EMBASE, and Cochrane library from 1980 to Feb 2016. The primary outcome measure was pain relief of back pain or radiating pain for at least 3 months. Secondary outcome measures were improvement of the patient's functional status, health-related quality of life, return to work, and reduction of opioid use.

Results: Twenty-three articles were finally identified and reviewed. Based on our analysis, epidural adhesiolysis showed a short-term (6 to 24 months) effect (grade A) and spinal cord stimulation showed a mid-term (2 or 3 years) effect (grade B). Epidural injections showed a short-term (up to 2 years) effect (grade C). However, other treatments were recommended as grade D or inconclusive.

Limitations: The limitations of this systematic review included the rarity of relevant literature.

Conclusions: Epidural adhesiolysis or spinal cord stimulation can be effective in order to control chronic back pain or leg pain due to FBSS, and its recommendation grades are A and B, respectively. Other treatments showed poor or inconclusive evidence.

Key words: Failed back surgery syndrome, post spinal surgery syndrome, chronic low back pain, post lumbar surgery syndrome, epidural adhesiolysis, spinal cord stimulation, epidural injection, revision

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Failed back surgery syndrome (FBSS) is a frequently encountered disease entity following lumbar spinal surgery. It has also been named "post lumbar surgery syndrome" and has been widely researched to date. If patients show chronic back pain or leg pain after successfully performed lumbar surgery, and there are no specific reasons for the pain, such as compressive lesions, infection, or others, then the diagnosis could be made. Although many plausible reasons have been investigated, the exact pathophysiology remains unknown. Residual lateral recess stenosis or foraminal stenosis, epidural fibrosis, recurrence of herniated nucleus pulposus, disc degeneration, adhesive arachnoiditis, or neuropathic pain have been suggested as etiologies of FBSS (1-4). In addition, many psychological risk factors, such as depression or worker's compensation, have also been suggested as possible etiologies of FBSS (5,6). However, as many patients who have persistent symptoms following successfully performed spinal surgery, there was a problem using the term, "failed back surgery." Because the term, "failed back surgery syndrome" has been suggested to be an inappropriate and illogical term, some authors have proposed using other terms, such as "postoperative persistent syndrome" (7) or "post lumbar surgery syndrome" (8-10).

Although successful clinical results can be expected with appropriate treatment for providing the correctable factor, it is difficult to determine which therapeutic approach will be effective as no specific reasons for FBSS are found in many patients. With this background, many clinical trials intended to relieve pain in patients with FBSS have been conducted. Various medications (11-14), re-operation (15-18), exercise therapy (19,20), spinal cord stimulation (SCS) (21-30), epidural adhesiolysis (9,31-34), epidural injection (35-37), intrathecal infusion (38-41) or psychotherapy (42) have been suggested as treatment options for FBSS. However, their clinical effects have not been clearly determined. Only a few systematic reviews have proposed direct evidence of specific treatments. However, to our knowledge, no study has systematically analyzed the clinical outcome of the overall therapeutic trials. The purpose of this systematic review is to reveal the evidence supporting each therapeutic modality for patients with FBSS.

Methods

Literature Search

A comprehensive literature search was conducted using PubMed, EMBASE, and Cochrane library from 1980 to February 2016. The references of previous systematic reviews were also searched. Keywords focused on the terms related to FBSS, including its diagnosis, symptoms, and treatment protocols. Search terminology was (((((failed back surgery syndrome (FBSS) OR) post lumbar surgery syndrome) OR post spinal surgery syndrome) OR chronic low back pain / chronic spinal pain after surgery) OR postoperative neuropathic pain) AND (each treatment modality such as medical treatment, exercise, chiropractic, spinal manipulation, massage, TENS, yoga, inferential therapy, cognitive behavioral therapy (CBT), rehabilitation, educational therapy, back school, intervention, facet block, facet joint block, medial branch block (MBB), rhizotomy, SI joint block; epidural block; epidural adhesiolysis, spinal cord stimulation, intrathecal drug delivery, and revision surgery).

Inclusion Criteria

The articles regarding the treatment outcomes of each treatment modality in patients with FBSS were included. All randomized controlled trials (RCTs), systematic reviews (SRs), and observational studies which contained more than 25 patients in each group or 60 patients in total were eligible for the review.

Exclusion Criteria

The exclusion criteria were as follows: 1) the topic is not focused on the treatment of FBSS, such as an economic study or narrative review; 2) it contained a mixed disease population such as patients with diabetic neuropathy; 3) a case report (the number of patients < 10); 4) observational studies which contained less than 25 patients in each group or 60 patients in total; 5) duplication, e.g., the same study population with a longer follow-up; 6) written in a language other than English; and 7) a too short-term follow-up (< 3months) or if the follow-up period was not discussed.

Outcome Measures

The primary outcome of this study was pain relief (e.g., the percentage of at least 50% or more pain reduction) at various points in time. The degree of pain

relief was assessed using a visual analogue scale (VAS) of the lower back and leg or according to subjective changes of patient symptoms. The secondary outcomes included improvement of functional status, health-related quality of life, return to work, and reduction in opioid use.

Quality Assessment

The quality assessment of each article was conducted according to the Methodology Checklist (2004.3.) of SIGN (Scottish Intercollegiate Guidelines Network) (43). The Methodology Checklist can be applied to 6 types of literature reports, including SRs, RCTs, observational studies, diagnostic studies, economic studies, and patient issues. Therefore, we used the first 3 types of checklists to assess the quality of each article (supplementary material 1, 2, and 3). After assessment of the internal validity, the overall assessment was checked using 3 options, i.e., those which were designated as ++, +, or – (Table 1). The quality assessment was conducted by 2, independent raters (J.H.C and H.Y.L). If there was disagreement, the 2 raters then came to an agreement.

Analysis of Evidence and Recommendations

The analysis of evidence and recommendations was referenced by the Systems to Rate the Strength of Scientific Evidence (2002) of the Agency for Healthcare Research and Quality (AHRQ) (44). The evidence in each article was classified from 1++ (most highly qualified) to 4 (most poorly qualified) (Table 2). The recommendations were classified to A, B, C, and D based on the results of the evidence (Table 3). The final decision regarding the recommendation grade using each method was obtained according to the agreement of the 4 raters (J.H.C, J.H.L, K.S.S, and J.Y.H).

Results

The literature search was conducted as shown in Fig. 1. Of the 492 searched literature reports, 469 abstracts of those articles were reviewed. Three hundred and eighty-three articles were excluded after review of the abstract. The remaining 86 articles were reviewed in their entirety. During this process, 27 articles were also excluded. The reasons for exclusion were also described in Fig. 1. Eight studies did not focus on our main topic, 7 articles did not mention the length of the exact follow-up period, 5 articles were excluded because we could not access the entire manuscript, and 2 RCTs showed duplication with the PROCESS trial.

Of the 59 remaining literature reports, 37 articles were not included in qualitative synthesis because they did not fulfill the sufficient number of patients (at least 25 patients in each group or 60 patients in total) or paucity of the relevant topic. Finally, 22 articles were

Table 1. *Criteria for judgement of quality assessment.*

++	All or most of all standards are met. It is certain that the results of the study will not be changed by the unmet standards.
+	Some of the standards are met. It is thought that the results of the study will not be changed by the unmet standards.
-	All or most of all standards are not met. It is thought that the results of the study may be changed by the unmet standards.

Table 2. *Degree of evidence.*

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

Table 3. *Recommendation grade.*

A	- One or more meta-analysis or systematic review or 1++ randomized, controlled trials and if it is applicable to target the population directly - Mainly 1+ studies are included, it is directly applicable to the target population, and the result shows overall consistency
B	- Mainly 2++ studies are included, it is directly applicable to the target population, and the result shows overall consistency - If the evidence is presumed by 1++ or 1+ studies
C	- Mainly 2+ studies are included, it is directly applicable to the target population, and the result shows overall consistency - If the evidence is presumed by 2++ studies
D	- Evidence 3 or 4 - If the evidence is presumed by 2+ studies

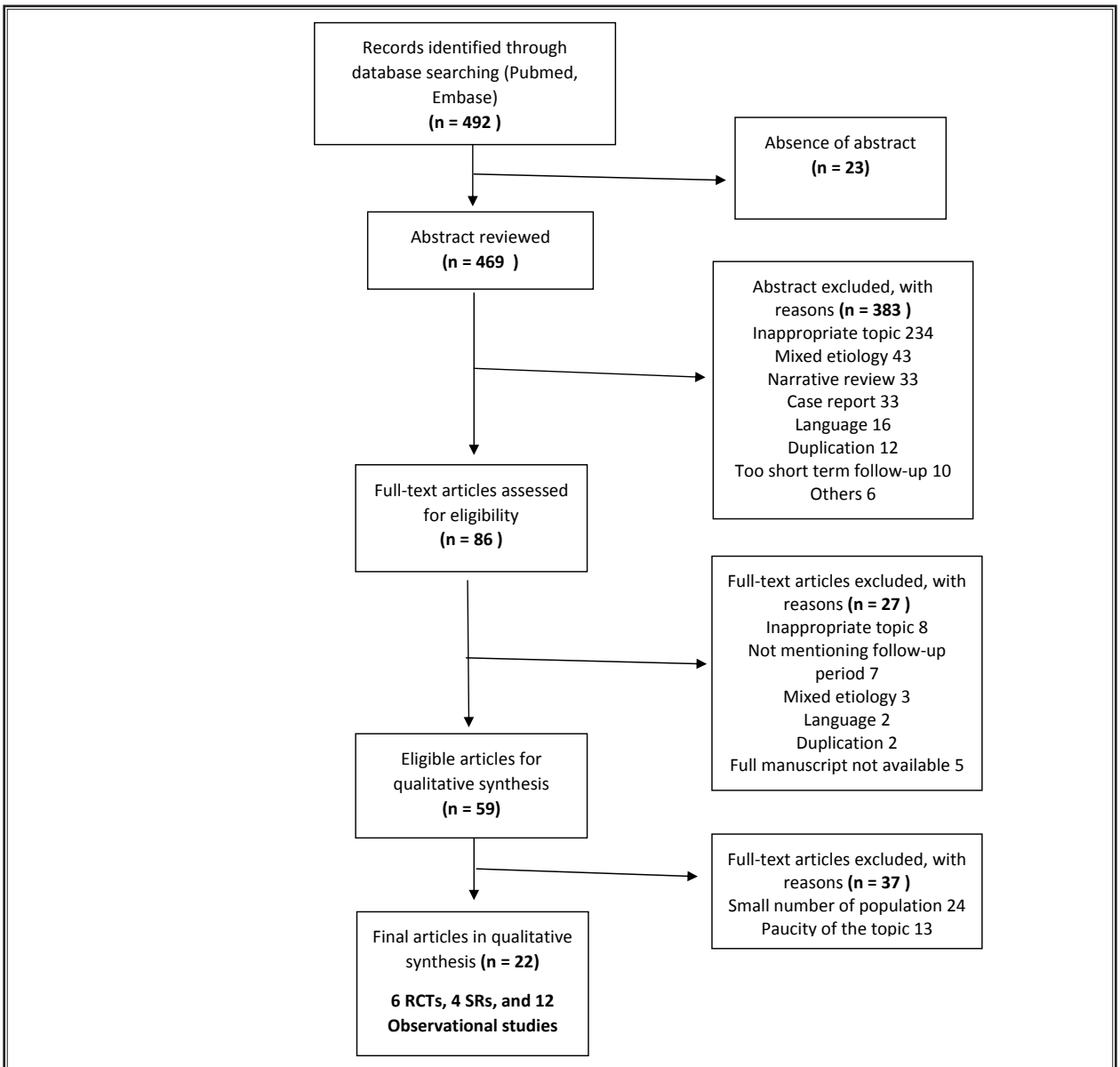

Fig. 1. *The PRISMA flow diagram illustrating the process of evaluating available literature about treatment outcomes of failed back surgery syndrome (FBSS).*

fully reviewed and assessed. They were classified according to the following procedures: 10 SCS, 5 epidural adhesiolysis, 2 epidural injections, and 5 revision surgeries. Other procedures including medication, exercise therapy, or psychotherapy were not enough to be included in synthetic analysis.

Spinal Cord Stimulation

Among eligible 27 studies that focused to the outcomes of SCS (21,26,27,45-68), only 10 studies were finally selected for synthetic qualitative analysis (27,45-49,52,65,67,68). These included 2 RCTs, 2 SRs, and 6 observational studies. The SIGN checklist was summarized in Table 4 (for RCTs) and Table 5 (for SRs). Of these, 2, RCTs revealed improved back pain and leg pain, functional status, and patient satisfaction compared to medical treatment and surgical treatment, respectively (45,46). The follow-up periods of those articles were 2 and 3 years, relatively long-term follow-ups. The evidence for SCS proposed II-1 or II-2 for long-term relief by one SR (47) and I or II evidence by the other SR (48). However, the SR by Grider et al (48) included a few articles about chronic spinal pain without history of previous surgery, which made the evidence weakened in our study. These 4 RCTs and SRs are summarized in Table 6. The other 6 observational studies are also summarized in Table 7. Because the control group differed in both RCTs, and one SR included the articles about

Table 4. *SIGN checklist for randomized controlled trials (RCTs).*

Section 1: INTERNAL VALIDITY						
	In a well conducted RCT study…		**Kumar K et al (45)**	**Manchikanti L et al (70)**	**Chun-jing H et al (69)**	**North RB et al (46)**
1.1	The study addresses an appropriate and clearly focused question.		Y	Y	Y	Y
1.2	The assignment of subjects to treatment groups is randomised.		Y	Y	Y	Y
1.3	An adequate concealment method is used.		Y	Y	Y	N
1.4	Subjects and investigators are kept 'blind' about treatment allocation.		Y	Y	Y	Not applicable
1.5	The treatment and control groups are similar at the start of the trial.		Y	Y	Y	Y
1.6	The only difference between groups is the treatment under investigation.		Y	N	Y	Y
1.7	All relevant outcomes are measured in a standard, valid and reliable way.		Y	Y	Y	Y
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?		13% (13 out of 100)	(33%) 60 out of 180	17% (16 out of 92)	10% (5 out of 50)
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).		Can't say	Y	Y	N
1.1	Where the study is carried out at more than one site, results are comparable for all sites.		Can't say	Not applicable	Not applicable	Not applicable
Section 2: OVERALL ASSESSMENT OF THE STUDY						
2.1	How well was the study done to minimise bias?	High quality (++)	1++	1++	1++	
		Acceptable (+)				1+
		Unacceptable – reject 0				
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?			The results of this study are limited by potentially inadequate double blinding, by the lack of a placebo group		
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?		Y	Y	Y	Y

Table 5. *SIGN checklist for systematic reviews (SRs).*

Section 1: INTERNAL VALIDITY				Epter RS et al (72)	Frey ME et al (47)	Helm S et al (9)	Grider JS et al (48)
In a well conducted systematic review:		Does this study do it?					
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper. If no, reject	Yes ☐	No ☐	Y	Y	Y	Y
1.2	A comprehensive literature search is carried out. If no, reject	Yes ☐	No ☐	Y	Y	Y	Y
		Not applicable ☐					
1.3	At least two people should have selected studies.	Yes ☐	No ☐	Y	Y	can't say	Y
			Can't say ☐				
1.4	At least two people should have extracted data.	Yes ☐	No ☐	can't say	can't say	Y	Y
			Can't say ☐				
1.5	The status of publication was not used as an inclusion criterion.	Yes ☐	No☐	maybe N	maybe N	maybe N	Y
1.6	The excluded studies are listed.	Yes ☐	No ☐	Y	Y	Y	Y
1.7	The relevant characteristics of the included studies are provided.	Yes ☐	No ☐	Y	Y	Y	Y
1.8	The scientific quality of the included studies was assessed and reported.	Yes ☐	No ☐	Y	Y	Y	Y
1.9	Was the scientific quality of the included studies used appropriately?	Yes ☐	No ☐	Y	Y	Y	Y
1.10	Appropriate methods are used to combine the individual study findings.	Yes ☐	No ☐	NA	NA	NA	NA
		Can't say ☐	Not applicable ☐				
1.11	The likelihood of publication bias was assessed appropriately.	Yes ☐	No ☐	maybe Y	maybe Y	maybe Y	maybe Y
		Not applicable ☐					
1.12	Conflicts of interest are declared.	Yes ☐	No ☐	Y	Y	Y	Y
Section 2: OVERALL ASSESSMENT OF THE STUDY							
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐		++	++	++	++
		Acceptable (+) ☐					
		Low quality (-) ☐					
		Unacceptable – reject 0 ☐					
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐		Y	Y	Y	Y

chronic spinal pain without surgery, the evidence of SCS for FBSS was downgraded. Finally, it was suggested that the SCS was effective for controlling back pain and leg pain caused by FBSS during the mid-term period (2 or 3 years) and its recommendation grade was B.

Epidural Adhesiolysis

Nine studies were evaluated in order to reveal the effectiveness of epidural adhesiolysis for FBSS (9,31,69-76). Among these, only 5 studies were included in synthetic qualitative analysis (9,69-72,75). These included 2 RCTs, 2 SRs, and one observational study. Two RCTs demonstrated the superiority of epidural adhesiolysis to that of epidural steroid injection alone (69,70,71). However, the follow-up periods were relatively short (6 and 24 months, respectively). However, the quality of both studies was excellent and was assessed as '1++'. Two SRs showed at least a 6-month effect of epidural adhesiolysis with level I or II-1, and demonstrated fair evidence according to the US Preventive Services Task Force (USPSTF) criteria, respectively (9,72). One other observational study also showed a higher proportion

Table 6. *Randomized studies and systematic reviews for synthetic analysis showing the effectiveness of spinal cord stimulation for FBSS.*

Authors	Type	Intervention and control	Primary outcome	Secondary outcome	Follow-up period (Mo)	Conclusion	SIGN
Kumar et al (45)	RCT	SCS (N = 48) Medical (N = 52)	VAS (50% or more pain relief in the legs)	EQ-5D, ODI	24	The SCS group experienced improved leg and back pain, QOL, function, as well as satisfaction ($P < 0.05$). In the intention-to-treat analysis at 6 months, 48% of the SCS patients and 9% of the medication patients achieved the primary outcome ($P < 0.001$).	1++
North et al (46)	RCT	SCS (N = 30) Reoperation (N = 30)	Pain relief at least ≥ 50%	Cost-effectiveness, overall pain, quality of life, crossover rate	36	SCS was more successful than repeat surgery [9/19 (47%) vs 3/26 (12%), $P < 0.01$]. However, in a worst case analysis, the success rate of SCS would become 9 of 23 (39%). Patients initially randomized to SCS were significantly less likely to cross over than were those randomized to repeat surgery [5/24 (21%) vs 14/26 (54%), $P = 0.02$]. Patients randomized to reoperation required increased opioid analgesics ($P < 0.025$). Activity of daily living or work status did not differ.	1+
Frey et al (47)	SR	Not applicable	Pain relief (short-term < 1y, long-term > 1y)	Functional status, Psychological status, return to work, opioid intake	Not applicable	The evidence for spinal cord stimulation is level II-1 or II-2 (developed the by U.S. Preventive Services Task Force) for long-term relief in managing patients with failed back surgery syndrome.	1++
Grider et al (48)	SR	Not applicable	Pain relief	Functional improvement	Not applicable	The evidence of efficacy for SCS in lumbar FBSS is level I to II. The evidence for high frequency stimulation is level II to III (USPSTF criteria).	1++

Table 7 *Observational studies for synthetic analysis showing the effectiveness of spinal cord stimulation for FBSS.*

Authors	Number of patients	Treatment protocol	F/U period (year)	Conclusions	SIGN
De La Porte et al (49)	78	SCS with unipolar wire-type electrode	4	The 64 patients were successful during trial period. The 35 patients (55%) continued to experience at least 50% pain relief at the latest follow-up.	3
Devulder et al (52)	69	SCS with a RF-coupled or battery system	13	Forty-three patients continued with the therapy and experienced good pain relief.	3
Kumar and Toth (68)	182	SCS with transverse tripolar electrode	8.8	165 patients (91%) experienced a satisfactory initial outcome. 48% of the patients experienced 50% or greater long-term pain relief with SCS	3
Rigoard et al (27)	76	Multicolumn SCS	0.5	At 6 months, 75.4% and 42.1% of the patients obtained at least 30% and 50% improvement of their back pain VAS score, respectively.	3
Gatzinsky et al (65)	71	SCS with octopolar lead	1.0	Responders (pain reduction ≥ 50%) at 12 months were 66% (44/67) for leg pain and 36% (24/67) for back pain.	3
Al-Kaisy et al (67)	67	HF-SCS	1.0	70% of the patients had ≥ 50% back pain relief at 12 months compared to baseline. The ODI decreased from 54 to 39 at 12 months ($P < 0.001$).	3

Table 8. *Articles for synthetic analysis showing the effectiveness of epidural adhesiolysis for FBSS.*

Authors	Type	Intervention and control	Primary outcome	Secondary outcome	F/U period (Mo)	Conclusion	SIGN
Chun-Jing et al (69)	RCT	EA (N = 46) ESI (N = 46)	Excellent or good case by modified MacNab evaluation	VAS	6	Patients on epidural lysis reported that the clinical effectiveness rate was 50%. For control patients it was 5.26%, and there was a statistical difference between the 2 groups.	1++
Machikanti et al (70,71)	RCT	EA (N = 60) ESI (N = 60)	50% or more reduction of NRS, 40% or more improvement of ODI	employment status, opioid intake	24	Significant pain relief and functional improvement were recorded in 73% and 82% of the patients in the EA group versus 12% and 5% in the ESI group at the 1- and 2-year follow-up ($P < 0.001$).	1++
Epter et al (72)	SR	NA	Pain relief (short-term < 6 m, long-term > 6 m)	Functional status, psychological status. Return to work, opioid intake	NA	The indicated level of evidence for percutaneous adhesiolysis is level I or II-1 based on the US Preventive Services Task Force (USPSTF) criteria.	1++
Helm et al (9)	SR	NA	Pain relief of at least 6 months	Functional status, change in psychological status, return to work, opioid use	NA	Applying the USPSTF criteria, there is reasonable evidence that percutaneous adhesiolysis is effective in relieving low back and/or leg pain caused by FBSS.	1++
Lee and Lee (75)	Observational study	PA vs TFESI (N = 114)	Pain relief (Numeric rating scale)	ODI	6	The proportion of successful results was higher for the PA group than for the TFESI group regarding the NRS and ODI scores at 6 months.	3

NA: not applicable; EA: epidural adhesiolysis; ESI: epidural steroid injection; PA: percutaneous adhesiolysis; TFESI: transforaminal epidural steroid injection

of successful results for the percutaneous adhesiolysis group than the epidural injection group (75). The SIGN checklist is summarized in Tables 4 and 5 , and the quality assessment is also summarized in Table 8. Based on these results, it was suggested that epidural adhesiolysis was effective for controlling pain caused by FBSS for a short-term period of 6 to 24 months), and its recommendation grade was A.

Epidural Injection

Two RCTs compared the effect of epidural injection according to the injection materials (77,78). However, no studies have been found which compare the outcome of epidural injection with that of other procedures, such as medication alone or surgical treatment. In one study, the analgesic effect was reduced at 3-month and 6-month follow-up after transforaminal injections (77). However, analgesic effect continued to 2-year follow-up after caudal injections by Manchikanti et al (78). The evidences of both studies were 2- and 2++, respectively. The above 2 studies are summarized in Table 9. Based on these results, short-term effect (up to 24 months) could be expected with epidural injection, and its recommendation grade was C.

Surgical Treatment

Among the eligible 8 articles (16,79-85), only 5 articles were selected for qualitative analysis (79,81-83,85). All of these articles were case series without any control group (Table 10). However, the outcomes of revision surgery were controversial. A successful outcome was reported at the final follow-up in only about 30% of the patient population in a few of these studies (79,83). However, it was reported that approximately 80% of the patients showed a good outcome in other studies (81,82,84), although its maintenance for a long-term period was denied (81). Based on these results, the outcomes following revision surgery showed a partial

Table 9. *Articles for synthetic analysis showing the effectiveness of epidural injection for PSSS.*

Authors	Intervention and control	Primary outcome	Secondary outcome	F/U period (Mo)	Conclusion	SIGN
Devulder et al (77)	Epidural inj. (transforaminal approach) (N = 60), Divided by 3 group according to injection materials	Not clearly defined	Verbal pain rating scale	6	Although injections induced analgesia at 1 month, these effects were reduced at 3- and 6-month follow-ups. No statistical difference were found between the three treatment groups.	2-
Manchikanti et al (78)	Epidural inj. (caudal approach) Nonparticulate betamethasone with lidocaine (N = 70) Lidocaine (N = 70)	At least 50% improvement of NRS and ODI	Employment status, opioid intake	24	Overall, 47% of lidocaine injection group and 58% of steroid injection group showed improvement at 24 months. There was no statistically significant differences between 2 groups.	2++

Table 10. *Articles for synthetic analysis showing the effectiveness of repeated operation for FBSS.*

Authors	Number of patients	Treatment protocol	F/U period (year)	Conclusions	SIGN
Arts et al (79)	100	Instrumented spinal fusion	1.3	Of 82 patients, 35% reported a good outcome, whereas 65% had unsatisfactory outcomes. This study showed a disappointing outcome.	3
Fritsch et al (81)	136	Reintervention after lumbar discectomy	2~27	In 80% of the patients the results were satisfactory in the short-term evaluation, and decreasing to 22% in the long-term follow up.	3
Markwalder et al (82)	171	Stabilization after diagnostic procedures to confirm instability	23.8 month	Excellent, good, satisfactory, moderate, and poor results in 87 (53%), 42 (26%), 23 (14%), nine (6%), and two (1%) patients, respectively.	3
North et al (83)	102	Repeated operation for lumbosacral decompression and/or stabilization	5.0	A successful outcome was recorded in 34% of the patients. Twenty-one patients who were disabled preoperatively returned to work postoperatively.	3
Delamarter et al (85)	674	Total disc replacement (TDR)	2.0	There were no differences in the outcomes between the prior surgery group and the non-prior surgery group. In properly selected patients with previously failed lumbar surgery, TDR can provide significant clinical improvement while maintaining normal range of motion.	3

effect for a limited patient population, and its recommendation grade was D.

Other Treatment Modalities

No articles were included in synthetic analysis. Gabapentin is the only drug to be researched so far (11,14). It was reported that the gabapentin patient group (1800 mg/day) showed more pain reduction than the naproxen group in a 6-month RCT (11) (Evidence 1+). In another study, adding on oral gabapentin to the standard epidural steroid injection was more effective at an early stage (14) (Evidence 1-). However, the recommendation grade could not be drawn because of the paucity of published literature reports.

Dorsal root rhizotomy or ganglionectomy was reported as a new approach for patients with FBSS, however, its effect was limited and the number of cases too small in order to arrive at any conclusions (86,87). Surgical radiofrequency epiduroscopy was also reported to be effective despite the small patient population (88). Subcutaneous stimulation combined with SCS was investigated in 2 articles. Although both studies showed decreased back pain with additional subcutaneous stimulation, they were not reliable due to the small sample size (89,90). Intrathecal infusion of opioids was also investigated and the effectiveness and safety were suggested in 2 case series (40,41). Interestingly, the usefulness of a capsaicin 8% patch was proposed (91). In that study, the mean VAS decreased from 7.4 preoperatively to 2.8 at postoperative 12 weeks.

Two articles have researched the role of patient exercise (19,20). One was a RCT comparing the effectiveness of intensive dynamic back exercises according to the inclusion of hyperextension exercise (19). However, the evidence regarding the exercise was assessed as level 3 as there were no other kinds of control groups, such as medication or epidural injection. The other article was a case series which revealed significant improvement in pain with a specific rehabilitation program (20). Psychotherapy could also be effective as patients with depression showed a tendency to experience more severe pain. However, only one RCT demonstrated the superiority of mindfulness-based stress reduction therapy for a patient control group during a 3-month, follow-up period (42) (Evidence 1-).

Discussion

Post-spinal surgery syndrome is a worrisome disease for patients and surgeons as it is chronic and resistant to conventional treatment. It also places a burden on the national economy (92,93).

Problems regarding the treatment of FBSS are its inexact nature and uncertain etiology. In fact, its exact identification has not been clearly defined. This was well described in one article (94) in which the author indicated that the term, "failed back surgery syndrome" was misused in terms of its uncertain pain mechanism. In fact, various authors differently assessed its definition. For example, in the PROCESS trial, it was defined as chronic, radicular pain that has recurred or persisted in the same amount and anatomical area, despite successfully satisfactory, previous spinal surgery (45). However, recurrent herniation or remaining foraminal stenosis were treated as the causes of FBSS in many literature reports (2,3). If the cause of FBSS is correctable, then revision surgery may be effective. The reason for the variable results of revision surgery in our study are based on the different study population. Regardless of the vague definition of FBSS, all of the pertinent articles about post spinal/lumbar surgery syndrome were initially searched and reviewed.

SCS has been the most frequently investigated method used to treat FBSS (approximately 40% in the current study). Although the treatment regimen was heterogeneous in the relevant studies, there were relatively good outcomes shown in most studies. However, as the control groups of finally selected 2 RCTs differed, i.e., medication and reoperation, respectively, the authors concluded that the SCS was not directly applicable to the entire target population (45,46). In addition, one systematic review also estimated its evidence as II-1 or II-2 according to the USPSTF, which supported our conclusion (47). However, the positive effect of SCS is not guaranteed for all patients with FBSS. Although the study population was different, the article by Turner et al (95) showed skeptical outcomes of SCS for chronic spinal pain by back injuries. They found little evidence for superiority of SCS over alternative treatments (95). In addition, the effect of SCS was minimal at 6-months follow-up, and disappeared by later follow-ups (95). Moreover, it is also not likely to last for a long time. The follow-up period of most literature studies which reported the positive response of SCS was approximately one or 2 years at most (51,55,57,59,61). Although long-term effects were proposed in several articles (49,53,56,68,96,97), the effect had been lowered according to the progression of time. Some authors proposed that it would be prudent to determine the use of SCS in terms of its cost-effectiveness (52). However, we did not focus on the cost-effectiveness of each treatment modality.

Meanwhile, the advanced technology of SCS by increasing number of leads showed effectiveness (56,58-61,63-65,68). However, direct comparison by the number of leads were not frequently studied. High frequency stimulation was studied by many authors (67,98), and superior results (level II or III evidence) were suggested by a recent systematic review (48). Paresthesia-free stimulation, so called burst stimulation, was researched by several authors (50,99). Although these articles showed the effectiveness of burst stimulation, inconclusive evidence (level IV) was suggested (48). Position-adaptive stimulation for chronic pain was also researched by a few authors (100). They showed this technology was safe and effective to alleviate the negative effect by positional changes.

The only level A evidence concerned epidural adhesiolysis, although its duration was relatively short (6 to 24 months). Two RCTs showed the effectiveness of epidural adhesiolysis compared to epidural steroid injection (69,70,71). Both studies also revealed the statistical difference in pain relief and functional outcome between the 2 groups. Therefore, we concluded that epidural adhesiolysis was effective for at least 6 to 24 months and could be directly applicable to the target population. Two SRs regarding epidural adhesiolysis also supported that conclusion with the evidence of I or II-1, and fair, respectively (9,72). In addition, Heavner et al (101) reported that percutaneous epidural neuroplasty reduced pain in 25% or more patients although

it was excluded because it did not state a previous operation. Although the population of the recent systematic review by Helm et al (102) was not limited to postoperative patients, epidural adhesiolysis showed level I or strong evidence for chronic refractory back pain or leg pain. This article also supports the result of our study. Nevertheless, there remain a few concerns: 1) whether or not perineural adhesion is the actual etiology of FBSS; 2) the adhesiolysis, itself, without any injection of materials can or cannot relieve symptoms; 3) the effect can or cannot last for a long-term period of time; and 4) the interlaminar approach requires caution because of possible nerve damage, postential subarachnoid injection and arachnoiditis by perineural adhesion from previous surgery. Thus, the interlaminar approach is thought to be relatively contraindicated in patients with FBSS. The above-mentioned problems should be investigated by further research.

In cases of epidural injection, no study has been found to compare the intervention to the use of other treatment modalities. Both RCTs showed the effectiveness of epidural injection using different injection materials (77,78). In addition, the method by Devulder et al (77) was only 2 transforaminal injections, which was relatively insufficient to assess. Furthermore, the duration of analgesic effect following injections was different between the 2 studies. It could result from different modalities of treatment: a transforaminal approach in one study (77) and a caudal approach in the other study (78). The analgesic effect might be lasting with a caudal approach. For this reason, we could not grant A or B to the use of the epidural injection.

Other than SCS, epidural adhesiolysis, and epidural injections, the evidence of other treatment modalities was not fully supported in the studies we investigated. Articles about repeated surgery for FBSS included heterogeneous populations, different surgical methods, and various follow-up periods. Although successful outcomes were reported in several literature reports (16,82,84), disappointing outcomes were also reported in other literature reports (79,83). Even if the outcome was successful, it had a tendency to diminish over time (81). Furthermore, the accuracy of surgical interventions could not be detected because they had heterogenous surgical methods and disease entities. Therefore, it was difficult to reach a conclusion regarding those heterogeneous literature reports. It was also difficult to conduct a randomized study in order to compare surgery with other types of treatment as surgical treatment was usually attempted when other interventions failed. This was one of the obstacles to reaching a conclusion. The studies regarding medication included only 2 RCTs, which revealed the analgesic efficacy of oral gabapentin (11,14). Although we did not reach a conclusion at this time, our study is expected to provide evidence regarding the need for further, relevant, randomized studies. Other types of interventions, such as dorsal rhizotomy, intrathecal infusion, radiofrequency ablation, or subcutaneous stimulation, were all probationary. Literature reports regarding exercise therapy or psycho-therapy were also very rare and did not support any conclusion.

This study has limitations as follows. First, possible candidate articles could have been missed because only Pubmed and EMBASE were used as a searching tool. Second, specific topics, such as cost-effectiveness analysis or simple review articles other than SRs, were excluded as we intended to reveal the pure clinical efficacy of each treatment modality. Third, relatively low quality articles were included considering the small number, and which might hinder making pure results. Fourth, only SIGN criteria were adopted as a methodological checklist. Although SIGN criteria are reliable, there are other well developed and widely used criteria such as Cochrane review criteria (103) or Interventional Pain Management Techniques – Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria, which was specific for interventional techniques (104).

Despite these limitations, this study was the first attempt to systematically approach the clinical outcomes of each therapeutic modality and this was the strongest feature of our study. Once more, as relevant RCTs and SRs were proposed in the future, the evidence of each modality will be fortified more than it currently is.

Conclusion

Overall results of synthetic analysis were summarized in Table 11. Among many treatment options, only epidural adhesiolysis was considered to have short-term (6 to 24 months) pain relief and functional improvement in patients with FBSS with recommendation grade A. SCS was considered to have a mid-term (up to 2 or 3 years) effect with recommendation grade B. Epidural injection showed a short effect (up to 2 years) with a recommendation grade C. Revision surgery could be considered with particular indications, although variable outcomes have been suggested (recommendation grade D). However, it requires caution to interpret the result about epidural adhesiolysis and epidural injections due to short-term follow-up of the articles. The

Table 11. *Recommendation grade of each treatment for FBSS.*

Treatment	Outcome	Recommendation
Epidural adhesiolysis	Short-term (6 to 24 months) pain relief and functional improvement	A
Spinal cord stimulation	Mid-term (up to 2 or 3 years) pain relief and functional improvement	B
Epidural injection	Short-term (up to 2 years) pain relief	C
Revision surgery	Variable	D

evidence regarding the success of other therapies, including medication, exercise, psychotherapy, and other types of intervention, were inconclusive.

This study might suggest the priority of the treatment for FBSS with synthetic evidences. That is, epidural adhesiolysis or SCS could be applicable for patients with FBSS preferentially. However, cost effectiveness should be considered although this study did not cover economic analysis. In the future, more RCTs comparing each treatment options will be required to support previous evidence or make new evidence for the treatment of FBSS.

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