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Review Article

Failed Back Surgery Syndrome

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Abstract

Background. Failed back surgery syndrome (FBSS) is a chronic pain condition that has considerable impact on the patient and health care system. Despite advances in surgical technology, the rates of failed back surgery have not declined. The factors contributing to the development of this entity may occur in the preoperative, intraoperative, and postoperative periods. Due to the severe pain and disability this syndrome may cause, more radical treatments have been utilized. Recent trials have been published that evaluate the efficacy and cost-effectiveness of therapeutic modalities such as spinal cord stimulation for the management of patients with failed back surgery.

Review Summary. This article will describe the epidemiology and etiology of FBSS. The importance of prevention will be emphasized. In those patients with established FBSS, a guide to interdisciplinary evaluation and management will be outlined. Special attention will focus on recent trials that have studied the efficacy of more invasive procedures such as spinal cord stimulation. Finally, a suggested management pathway is presented.

Conclusion. FBSS is a challenging clinical entity with significant impact on the individual and society. To better prevent and manage this condition, knowledge of the factors contributing to its development is necessary. While research on FBSS has increased in recent years, perhaps the best strategy to reduce incidence and morbidity is to focus on prevention. Patients diagnosed with FBSS should be managed in an interdisciplinary environment. More radical treatments for FBSS have now been extensively studied providing clinicians with much needed evidence on their efficacy. Incorporating these results into our current knowledge provides a basis on which to construct an evidence-based guide on how best to manage patients who suffer from FBSS.

Key Words. Failed Back Surgery Syndrome; Chronic Pain; Spinal Surgery; Interdisciplinary Management; Spinal Cord Stimulation

Failed Back Surgery Syndrome—Etiology, Evaluation, Prevention, and Management

Introduction

Failed back surgery syndrome (FBSS) is a term embracing a constellation of conditions that describes persistent or recurring low back pain, with or without sciatica following one or more spine surgeries [1]. A more functional definition proposes FBSS results when the outcome of lumbar spinal surgery does not meet the pre-surgical expectations of the patient and surgeon [2].

Literature on management guidelines for patients with FBSS is scant, in large part due to the complexity of this entity with diversity of the underlying etiology [3–5] and lack of high-quality clinical trials assessing response to treatment. Furthermore, it is likely that multiple factors (biological, psychological, and social) are involved with the development of the pain process, necessitating an interdisciplinary approach to management. However, the past 5 years has witnessed the conclusion of several trials designed to address the efficacy and appropriate patient selection for different management modalities. In addition, comparisons between different types of treatment have been the objectives of individual studies. The issue of cost-effectiveness has also been investigated. Despite the importance of recent evidence on FBSS management, an equally important but less studied aspect of FBSS is how to prevent the development of this disabling clinical entity.

This review of FBSS will summarize our current knowledge of the etiology and evaluation of FBSS. The importance of prevention and potential methods by which to achieve this will be discussed. Finally, a consolidation of the latest clinical findings with regard to the different treatments of FBSS are summarized in an attempt to try and identify a more logical evidence-based guide on how to manage this debilitating problem.

Epidemiology

Low back pain is common with a reported point prevalence in the general adult population of 37% [6] and a lifetime prevalence of between 60% and 85% [6,7]. In addition to the suffering and disability it may produce for

patients, the impact on society is considerable. The direct cost in the United States of low back pain has been estimated to be between 12.2 and 90.6 billion U.S. dollars annually [8]. Reasons for the large variation in cost estimates include differences in cost perspectives between studies, time delays between data collection and study publication, variable sources of data on which estimates were based, and variation in the number of categories of direct medical costs between the studies [8]. When compared with other chronic health conditions (e.g., angina pectoris, diabetes mellitus), mechanical low back pain was determined to be the fourth most expensive condition for employers in the United States [9]. Among other chronic pain conditions, the indirect costs of back pain were estimated to be 19.8 billion U.S. dollars, higher than arthritis and other pain conditions [10].

The number of spine surgeries has steadily increased in the past several decades [11–13]. In 1997, there were 317,000 lumbar surgeries performed in the United States, and the cost of surgery itself exceeded $4.8 billion per year [14]. Five years later in 2002, there were more than 1 million spinal procedures performed, of which 400,000 were instrumented [15–18]. Spinal fusion surgery alone generated costs of more than $16 billion in hospital charges in 2004 [19]. These trends have prompted concern among leading clinicians in the field of spine surgery [20–26]. One operation has garnered more attention than others and that is lumbar spinal fusion. Between 1990 and 2000, there was a 220% increase in spinal fusion surgery [13]. This was despite no clear indication and absence of demonstrated efficacy for spinal fusion [26].

Overall, several lines of evidence point to excessive rates of spine surgery in the United States. Comparing the international data, the rates of spine surgery in the United States are double that of other developed countries such as Australia, Canada, and Finland. Compared with the United Kingdom, the U.S. rates are five times greater [27]. Even within the United States, there is a large disparity between different regions [28]. A study performed within the U.S. state of Maine found that the best results from spine surgery (pain and function) occurred in areas with the lowest surgical rates, while the worst outcomes occurred in areas with the highest surgical rates [28]. Improvements in analgesia, function (Roland disability score), quality of life, and satisfaction were significantly greater in the regions with lower surgical rates [28]. While this study did not further investigate the reasons for the difference, the authors suggested that this observation was due to differences in selection criteria for surgical patients and physicians' recommendations for operations between the different areas [28].

The incidence of patients that will develop FBSS following lumbar spinal surgery is commonly quoted in the range of 10% to 40% [1,29–31]. These statistics come from studies that were published more than a decade ago on heterogeneous populations and different evaluation criteria for surgery among practitioners. Furthermore, success or satisfaction as measured by a surgeon or patient can differ significantly [32]. It is also known that the success rate falls if subsequent operations are performed. Nachemson's work revealed inferior results with each successive operation on the same patient. The initial success rate exceeded 50% but was reduced to 30% after a second surgery, 15% after the third, and to 5% after the fourth [33]. More recent trials commonly employed an independent and "unbiased observer" to measure surgical success [32]. With the increasing number of spine surgeries discussed earlier, an increase in the number of patients with FBSS is also observed [22,23,34]. Of the recent trials investigating lumbar fusion, results were reported as changes in pain scores and functional status post-surgery [35–38]. However, several of these trials did provide data identifying the proportion of patients who did not improve after lumbar fusion. In one trial, the number of patients still experiencing unchanged or worse pain post-surgery was 13 out of 28, giving a failure rate of 46% [38]. It is important to note that in this group, all the patients had previously undergone a discectomy procedure [38]. A second trial reported a success rate of 70% after surgery (independent observer), suggesting a failure rate of 30% [37]. In an earlier trial, 63% of patients rated themselves as "much better" or "better" post-surgery [36]. While one may argue about the different methods by which success was measured, the available data suggest the failure rate of lumbar fusion to lie between 30% and 46% based on the results of these trials. Microdiscectomy has generally been associated with success rates of 75% to 80% [39]. Several more recent randomized control trials (RCTs) demonstrated a success rate of 81% at 8 weeks, which extended to 2 years post-surgery [40,41]. The short-term outcome was superior to nonsurgical management, but the nonsurgical group reached the same level of success as the surgical group at 2 years [40,41]. Together, these results suggest the failure rate for microdiscectomy to be less than spinal fusion at between 19% and 25%. There is no evidence to suggest any difference in clinical outcome between microdiscectomy and open discectomy [42–45].

Several high-quality trials such as the Spine Patient Outcomes Research Trials looking at spinal decompression for symptomatic spinal stenosis with or without degenerative spondylolisthesis determined that decompressive surgery is moderately superior to nonsurgical therapy in terms of pain and function through 1 to 2 years [46–48]. However, it is difficult to determine the rate of FBSS from these trials because the main endpoints were changes in pain scores on average and functionality rather than in success rates. A retrospective study looking at patients who had undergone decompressive surgery for degenerative lumbar spinal stenosis found a 63.8% success rate as measured by the Zurich Claudication Questionnaire [49]. Consistently, 65% of patients reported a satisfactory result at long-term follow-up (4–12 years) in another study [50]. This would suggest a failure rate of 35% to 36.2% for lumbar decompressive surgery.

When compared with other surgical procedures performed for nonlife-threatening conditions, the success rates for spinal surgery (particularly, lumbar fusion) are poor. The

success rate for substantial improvements in pain and function for total knee replacement has been reported as 90% [51]. Similarly, in a trial comparing surgical with non-surgical management, clinical improvement following carpal tunnel release is quoted at 90%, which is significantly higher than conservative management [52].

Compared with other chronic pain models (e.g., rheumatoid arthritis), FBSS patients with severe neuropathic pain experience greater levels of pain, lower quality of life (as measured by the EuroQol measure of health outcome [EQ-5D] and Short Form (36) Health Survey [SF-36] scales), greater disability (as measured by the Oswestry Disability Index), and a higher rate of unemployment (78%) [53]. The annual cost for medical therapy for patients with FBSS, excluding further surgery or implantation of a spinal cord stimulator or intrathecal pump, is estimated to be $18,883 per patient in the United States [54]. Between 1997 and 2006, spinal cord implants had increased 159% in reports by Medicare [55]. In a study addressing the cost-effectiveness of intrathecal drug therapy in an FBSS population, the cumulative costs over a 5-year period were Canadian dollars (CAD) 29,410 for the intrathecal group compared with CAD 38,000 for conservative medical treatments [56]. For spinal cord stimulation (SCS) therapy, the cumulative health care costs over a 5-year period was CAD 29,123 per patient [57]. These costs only take into account direct costs and do not include costs related to lost productivity (indirect costs), which would make the final cost considerably higher.

In summary, chronic low back pain (CLBP) is a common and significant social and economic burden. The number of patients suffering from FBSS has increased with increasing rates of spine surgery. Despite advances in technology and surgical techniques, the rates of FBSS are similar to several decades ago [23]. However, failure rates differ between the different surgical procedures with procedures such as lumbar discectomy demonstrating high success rates. The impact of FBSS on an individual's quality of life and functional status are considerable and more disabling when compared with other common chronic pain conditions. These findings emphasize the importance of identifying strategies to prevent the development of FBSS and effective management guidelines for the management of established FBSS.

Etiology

A practical classification of the etiology of FBSS is based on preoperative, intraoperative, and postoperative factors (Table 1).

Table 1 Etiology of failed back surgery syndrome

Preoperative factors
- Patient
  - Psychological: anxiety, depression, poor coping strategies, hypochondriasis
  - Social: litigation, worker compensation
- Surgical
  - Revision surgery (50% increase in risk in spinal instability ≥4 revision)
  - Candidate selection (e.g., microdiscectomy for axial pain)
  - Surgery selection (e.g., inadequate decompression in multilevel pathology)

Intraoperative factors
- Poor technique (e.g., inadequate lateral recess decompression, misplaced screw)
- Incorrect level of surgery
- Inability to achieve the aim of surgery (e.g., far lateral discectomy)

Postoperative factors
- Progressive disease (e.g., recent disc herniation, spondylolisthesis)
- Epidural fibrosis (tethering effect, jeopardizing nutrition, and vascular supply to nerve root)
- Surgical complications (e.g., nerve injury, infection, and hematoma)
- New spinal instability (e.g., vertical stenosis)
- Myofascial pain development

Preoperative Factors

Patient Factors

Carragee et al. demonstrated that psychosocial risk factors were much more powerful in predicting low back pain disability than structural abnormalities [58]. Certain patients are at increased risk of developing FBSS [32]. A recent prospective trial demonstrated that both psychological factors or the presence of a personal injury claim were strong predictors of the surgical outcome [32]. The specific psychological factors that have been found to result in poor outcome for spinal surgery are significant levels of depression, anxiety, poor coping, somatization, and hypochondriasis [59–62], while poor surgical success in the presence of a worker's compensation claim has been a consistent finding throughout the spinal surgery literature [32,63–66].

However, it is important to point out that the presence of these factors should not exclude a patient for spinal surgery in the presence of significant pathology and a sound indication [32]. Rather, the presence of these risk factors will require attention and optimization before and after spinal surgery [32]. This may include pain education, psychological guidance, and a physiotherapy regimen focused on promoting active coping strategies [61]. Furthermore, in the case of lumbar disc surgery, these patients with poorer psychometric scores may benefit from surgery sooner [67]. Prolonged pain and distress in this population may exacerbate preexisting psychosocial stressors and reduce the benefits of lumbar disc surgery [67].

Surgical Factors

Repeated surgery is associated with reduced success rates [33]. Besides repetitive insult to soft tissues

structures, there is evidence that structural alteration in the spine and its contents has a role. Fritsch et al. found that spinal instability increased from 12% after the index operation to greater than 50% after four or more revisions [3].

Poor outcome after spinal surgery may also be due to the selection of inappropriate surgery or inappropriate candidate. The former is exemplified by performing discectomy on the basis of imaging findings in a patient presenting with axial pain. The latter is exemplified in a patient with severe spinal stenosis at multiple levels, and decompression at only one level is unlikely to achieve the desired effect of pain reduction and improvement in function [5].

Intraoperative Factors

Poor Technique

Inadequate decompression, most frequently in the lateral recess and neural foramens, is a potential cause of FBSS [68]. Overaggressive decompression, on the other hand, may lead to spinal instability and pain [5]. In addition, misplaced grafts and screws may also lead to impingement of neural structures and radicular pain [69].

Incorrect Level of Operation

The incidence of wrong level approach (discovered during operation and the correct level addressed) is approximately 2.1–2.7% [70,71]. The incidence of "unrecognized incorrect level of operation" at the time of operation is around 0.57–0.72% [72,73]. With the implementation of microscopic techniques, limited exposure may result in a greater occurrence of wrong level surgery [74]. Theoretically, operating at the wrong level would leave the pain generator untouched and thus, persistence of the pain post-surgery.

Inability to Achieve the Aim of Surgery

In certain cases, surgical correction of the pathology may be difficult. One well-acknowledged example is foraminal stenosis due to ligamentous hypertrophy or far lateral disc herniation. The reason why operating at this level is so difficult is because proper decompression of the neural foramen runs the risk of destabilizing the segment, making this technically challenging [75]. The pars interarticularis is often fractured during decompression [75]. The patient who undergoes a fusion for instability or degenerative changes may experience recurrence after the development of symptomatic pseudoarthrosis [5].

Postoperative Factors

Progressive Disease

Following discectomy, recurrent disc herniations are known to occur in up to 15% of patients, either at the site of operation or in the adjacent segment (due to alteration of load distribution) [76]. The original disease process, e.g., spondylolisthesis may cause worsening of pain at adjacent sites following both decompression and spinal stabilization [77]. The disease process may cause further spinal stenosis at sites separate from where the index operation takes place [77].

Epidural Fibrosis

Epidural fibrosis is probably inevitable after any surgery that involves manipulation of the epidural space. Based on preclinical and clinical research, this fibrosis may be the causative or contributing factor to persistent pain in 20–36% of FBSS patients [3,78–83]. Following spinal surgery, epidural scarring occurs, and as a consequence, nerve roots may become tethered [84,85]. This may cause pain on movement of the spine but may also reduce the ability of the spinal structures to cope with degenerative [86] changes and facet joint hypertrophy. Subsequent perineural fibrosis may interfere with cerebrospinal fluid mediated nutrition, resulting in hypersensitivity of nerve roots [87]. In addition, fibrosis may initiate vascular hypoxia due to compromise of the vascular supply to the nerve roots [85].

New Instability Secondary to Altered Biomechanics Following Surgery

Each form of spinal operation has the potential to alter the distribution of weight among the structures of the spine. The facet joints may become incompetent following laminectomy resulting in axial pain [88]. Spinal decompression invariably involves resection of the medial portion of the facet joint to relieve pressure on the nerve root. This resection may destabilize the joint, resulting in instability and pain [88]. Pain may also be a consequence after discectomy operations. Removal of herniated disc may result in partial collapse and reduction in the height of the interspace. The settling of the facet joints into a new position may compress the exiting nerve root between the superior pedicle above and the disc and pedicle below, an event known as "vertical stenosis" [88]. Discectomy may also create changes in the biomechanics of the spine, resulting in increased load distribution on adjacent segments accelerating preexisting disc degeneration [89]. This finding has been termed "transition syndrome" and has been reported to occur in up to 36% of patients following lumbar spinal fusion [89].

Complications of Surgery

Complications of surgery such as disc space infection, spinal or epidural hematoma, pseudomeningocele, and nerve root injury can contribute to persistent pain in the postoperative period [76]. Early identification and management of some of these complications is important as they can rapidly progress to permanent neurological deficits and death [90,91].

Postsurgical pseudomeningocele is a rare complication of spinal surgery [92]. They often result from inadvertent meningeal tear or inadequate closure during surgery [90,93]. The patient will often complain of wound swelling, headache, and focal neurologic symptoms including

radicular pain [90,93]. Another condition known as "battered root syndrome" may cause persistent radicular pain following lumbar spine surgery [94]. Risk factors for battered root syndrome include prolonged and aggressive root retraction, excessive bleeding and presence of a conjoined nerve root [94]. Surgery may produce arachnoiditis, which may result in persistent irritation of the nerve roots as the inflammation of the arachnoid persists [88]. This process may produce pain in both the spine and lower limbs [88].

Myofascial Pain Development

The paraspinal muscles are a potential source of back pain post-lumbar spine surgery. The events leading to muscular pain probably occur during and after the surgical procedure [88,95–98]. During surgery, dissection and prolonged retraction of the paraspinal musculature result in denervation and atrophy [95–97]. The intraoperative insults to the muscles may be compounded by postural changes in the postoperative period. With lumbar lordosis lost due to pedicle screw fixation, the paraspinal and hamstring muscles may spasm and then atrophy [88]. Typically, the patient may compensate with hyperextension of the thoracolumbar spine, which exacerbates poor posture and pain in the long-term period [88]. This myofascial pain is known as "fusion disease" [88,95–98].

Prevention of FBSS

On review of the literature, several findings relating to FBSS are of great concern. First, failure rates for spinal surgery have not changed in the past several decades [1,99]. Second, spinal surgery rates have increased in that time [11–13]. Third, limited epidemiologic studies demonstrate FBSS is of significant burden to affected patients and to the health care system [53,57]. While research on management of FBSS will help guide management decisions to improve pain and quality of life of FBSS sufferers, emphasis should now be placed squarely on methods by which to prevent the development of FBSS.

As "FBSS results when the outcome of lumbar spinal surgery does not meet the pre-surgical expectations of the patient and surgeon" [2], communication and education of the patient on probable success rate is obviously paramount. Presumably, patients' expectations are influenced largely by their discussion with the surgeon about the planned spinal surgery. Therefore, this discussion must be realistic for the patient and the objective and likely success of surgical intervention clearly defined. For example, if spinal surgery is indicated for preservation of limb function, this should be communicated clearly to the patient and that pain may persist following surgery.

While there is consensus that patients with major motor deficits and major spine trauma require surgery [19], the criteria for operating in cases of persistent pain are less clear. The need for guidelines for spinal surgery, in particular, fusion surgery, is apparent [21,22,24–26] and in recent years, high-quality reviews and trials have been published to try and form the basis for such guidelines to better direct when spinal surgery should be undertaken [35,37,38,40,41,47,99].

It has been demonstrated that sciatica improves within 3 months with conservative medical management in 75% of patients [100]. For those patients suffering from radicular pain longer than 3 months, current evidence shows surgery for herniated lumbar disc has a high success rate providing superior pain relief and improvement in physical function in the short term compared with medical management [101,102]. On the other hand, for nonradicular low back pain with degenerative spine, there is moderate evidence that spinal fusion is no better than an intensive rehabilitation program [35,37,38]. Continuing research will hopefully identify which cases of degenerative spine disease will respond favorably to fusion. Prevention of FBSS may also be achieved by performing more conservative surgery. In cases of spinal stenosis with evidence of degenerative spondylolisthesis, simple laminectomy alone has provided good to excellent outcomes in 82% of patients, with fusion only necessary for 2.7% of patients in long-term follow-up [103].

While prevention may be partly achieved by determining which surgical procedure is indicated, preoperative identification of psychological and social stressors is also strongly recommended [24]. These factors are not routinely evaluated in patients who are planned for surgery [24]. Furthermore, even when these factors are identified, there remains the question of what form of intervention should be applied for those patients at high risk. The effects of psychological intervention for those patients at high risk have not been investigated in high-quality trials [61]. However, given the strong influence of these factors on spinal surgical outcome [32], these patients should at the very least be offered psychological intervention.

Suggestions on how to establish guidelines for spinal surgery have been published [25,26]. Randomized controlled trials remain the best method by which to assess the efficacy of a certain procedure. However, these studies can be difficult to undertake in the practical sense and are associated with ethical concerns [104]. Alternatively, implementation of patient registries has been proposed as a method by which to gain valuable data on surgical rates and outcomes and consequently identify which spine surgical operations provide benefit and in which type of patients [25,26]. An example of the latter is the substantial improvement in outcomes post-spine fusion for spondylolisthesis but reduced improvement for patients with degenerative disc and axial back pain [105]. Limitations of registries are the hazards of making nonrandomized comparisons and problems with uncontrolled confounding factors [26]. Furthermore, for validity, the registry must obtain follow-up on every patient which is a huge undertaking [26].

In our current state of knowledge, spinal surgery for persistent pain should only be proposed after a period of

intensive rehabilitation including psychological intervention has failed. Likely outcomes from surgery should be clearly discussed with the patients and an informed decision by the patient should be achieved. Patients with psychological and social stressors should receive further psychological intervention to complement the proposed surgery. Obviously, if surgery proceeds, meticulous attention to surgical technique is needed to reduce complications.

Patient Evaluation

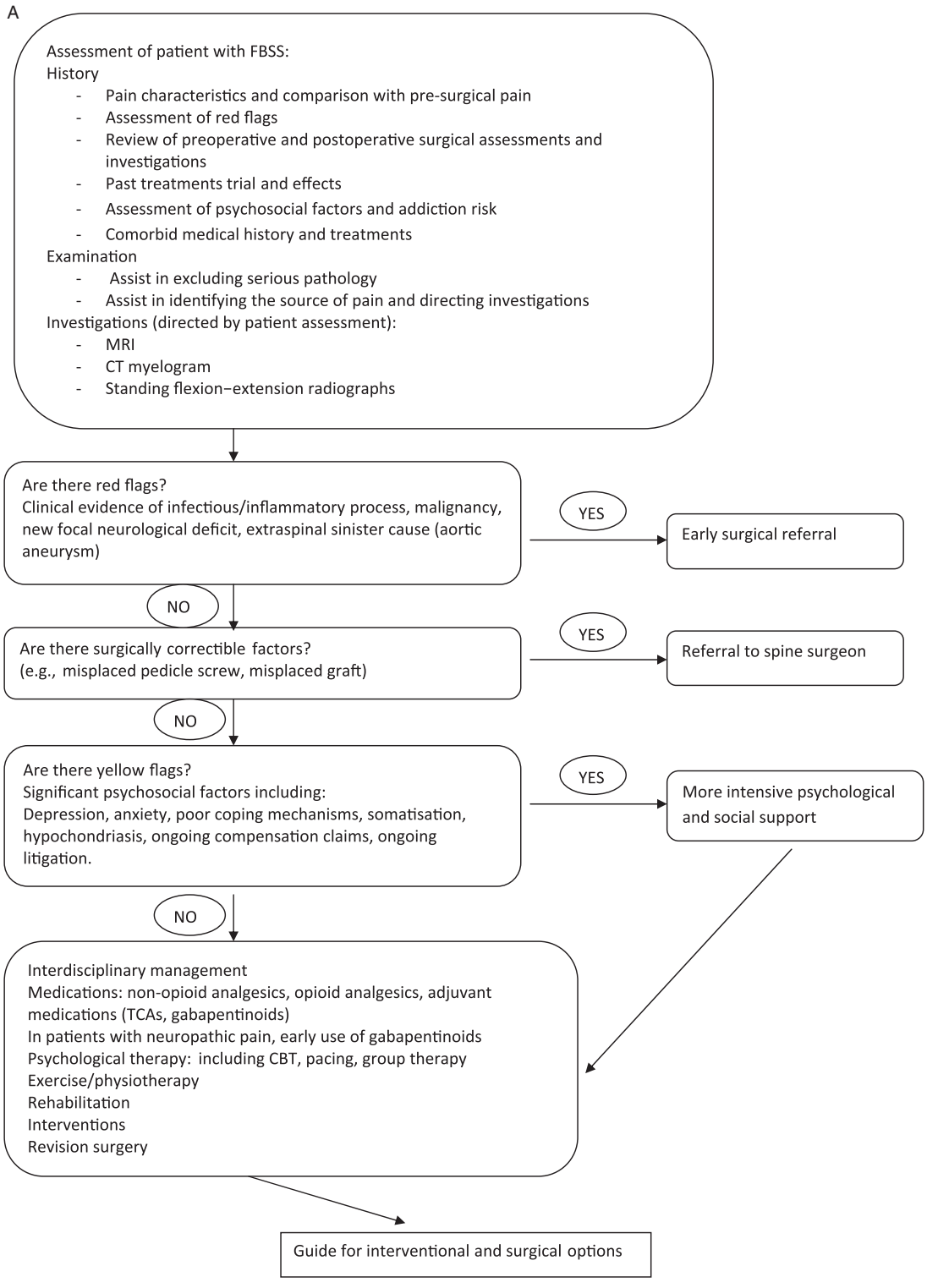
A detailed assessment of a patient with FBSS is important as it provides pertinent information in a few areas: the etiology of the persistent or recurring pain, the psychosocial aspects of the patient, the comorbidity (such as depression, anxiety, sleep disturbance), and previous management and investigations. A plan for assessment of the patient is suggested in Figure 1A: algorithm for assessment and management of established FBSS.

Based on the initial assessment, an individualized interdisciplinary management plan may be formulated.

History

A detailed description of the pain characteristics must be obtained (Figure 1A). Comparison with the preoperative symptomatology, both the exact location of the pain and the time course for the reappearance of pain, is important. Early onset of pain or persistence of pain is suggestive of those preoperative and intraoperative factors (Table 1). It is also useful to determine whether the pain is predominantly

Figure 1 Algorithms for the assessment and management of patients with failed back surgery syndrome (FBSS). (A) Management algorithm for FBSS. Patients with FBSS should be assessed by an interdisciplinary approach. While a comprehensive history and examination should be performed, special attention is given to the pain history and how this compares with pre-surgical pain. Red flags should be assessed, and if present, an early surgical opinion should be sought. If there is evidence of a surgical cause of pain that may be reversed, such as a misplaced pedicle screw compressing a nerve root, referral to a spine surgeon would be appropriate. The assessment should also focus on psychological and social factors that may contribute to both pain and impaired function. In patients who have identified yellow flags (significant psychosocial stressors), more intensive psychological and occupational therapy should be provided. Investigations will be directed by the findings on clinical assessment. If magnetic resonance imaging is contraindicated, computed tomography myelogram is a suitable alternative. Patients should be managed by an interdisciplinary team with medications, psychological therapy, exercise therapy, interventional procedures, and surgical procedures playing a role. A suggested guide on interventional procedures and surgical options are provided in Figure 1B. (B) Suggested guide for interventional procedures and surgical options for management of FBSS. When deciding on which procedures may be efficacious in FBSS patients, it is useful to determine if the pain is predominantly axial or radicular. For those patients with predominantly axial pain, diagnostic blockade may be performed to determine if the pain is arising from the zygapophysial joints or the sacroiliac joints. If there is positive response to lumbar medial branch blocks, radiofrequency rhizotomy may then be performed for longer lasting analgesia. For suspected discogenic pain, the clinician may consider lumbar provocation discography. However, the result cannot be interpreted alone and must be interpreted in the context of the interdisciplinary assessment. Furthermore, there is uncertainty regarding the best treatment for discogenic pain. For those patients with severe axial pain not responding to more conservative medical measures, intrathecal drug delivery systems may be considered (refer to text). Revision surgery should only be undertaken if a lesion amenable to surgical intervention is present, and in this case, review by an expert spine surgeon is recommended. For those patients with predominantly radicular pain, epidural injection of steroids under fluoroscopic guidance may be achieved via several routes. If there is a positive response, repeated injections may occur with an appropriate time interval. If epidural injection is unsuccessful, percutaneous epidural adhesiolysis may be considered. Percutaneous epidural adhesiolysis is considered before spinal cord stimulation due to the less invasive nature and therefore reduced risks associated with the former. A trial of spinal cord stimulation is to be strongly considered in all patients with radicular pain who have failed the more conservative measures. The demonstrated efficacy for spinal cord stimulation in randomized control trials makes this a better option than an intrathecal drug delivery system or revision surgery.



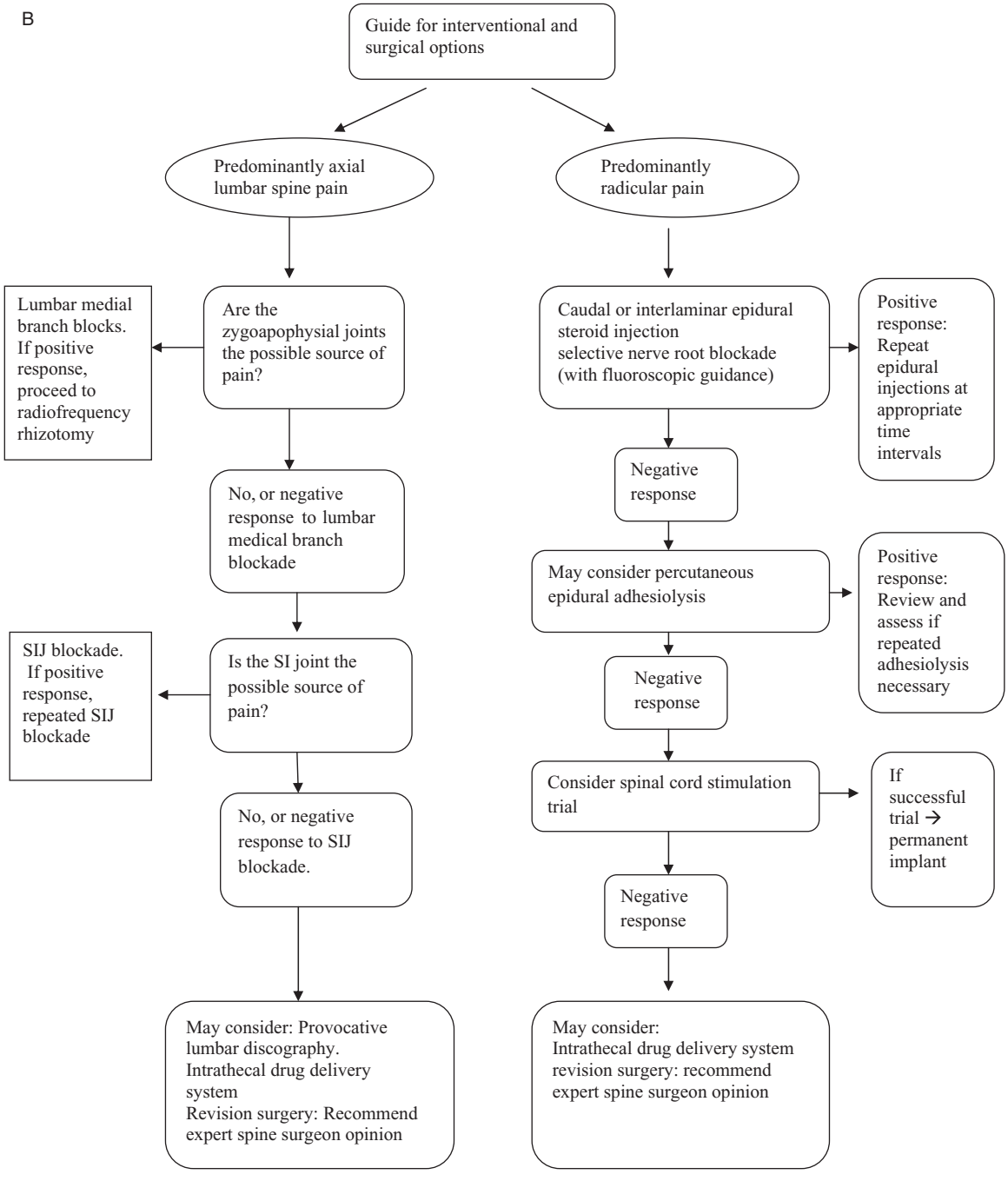


Figure 1 Continued

in the lower back (axial) or the leg (radicular) [5,106]. If the pain is mainly radicular, it is more likely to be due to inadequate decompression, foraminal stenosis, epidural fibrosis, or recurrent disc herniation or residual disk or fragments [5,106]. Leg pain, which is different in character and appears shortly after surgery, is more suggestive of an instrumentation issue, such as a pedicle screw compressing an exiting nerve root [5,106].

Pain that is predominantly in the lower back is more suggestive of facet joint, sacroiliac joint (SIJ) degeneration, myofascial, or discogenic causes [5]. If centralization is present, this is suggestive of discogenic pain [107,108]. This refers to pain moving centrally toward the lumbar spine or peripherally from the lumbar spine in response to repeated lumbar movements [109,110]. In postoperative cases of spinal fusion, pseudoarthrosis should be

considered. It is important to determine if the pain may be due to a cause other than spinal pathology.

Red flags should be identified if present (Figure 1A). The patient should be questioned to rule out possible abdominal or pelvic inflammatory disease, infectious of malignant lesions such as psoas abscess, pancreatic cancer [5]. Also, the clinician should be aware that rare but more life-threatening causes of back pain such as thoracic and abdominal aortic aneurysms may be the cause of pain [5]. Other red flags, such as bowel and bladder paralysis, should also be ruled out. Of course, if these symptoms are present, more urgent investigation (gadolinium-enhanced magnetic resonance imaging [MRI]) and definitive treatment (e.g., emergency surgery for drainage of epidural abscess) should be undertaken depending on clinical presentation. If red flags are present early, surgical referral should be sought (Figure 1A).

In addition to the patient's description of pain, past case notes should be reviewed. This includes preoperative and postoperative investigations and operative reports. This may be helpful in identifying incorrect diagnoses and surgery or if there is other pathology that was not addressed during the index surgery. The pain treatments the patient has tried thus far including pharmacological and non-pharmacological should be identified. An exploration of medication efficacy and adverse effects is mandatory. An assessment of addiction and drug abuse risk is also recommended [111] considering that opioids (e.g., sustained release morphine or oxycontin) are commonly prescribed [112].

Comorbid medical history and treatment should be obtained as this may influence choice of treatments.

As stated earlier, "yellow flags" (significant psychosocial stressors) also are now known to play an important role in chronic pain conditions with FBSS being no exception (refer to Figure 1A). Specific inquiry into the possibility of anxiety, depression, active or passive coping mechanisms, ongoing litigation, and worker's compensation must be carried out to plot a suitable course of management. This is more so if secondary surgery is planned as the failure rate for secondary surgery is higher [113].

Examination

The examination serves two purposes (Figure 1A). First, it assists in ruling out serious pathology. Examination of vital signs (e.g., temperature) is of importance and further examination of the abdominal, pelvic and vascular systems if any of the before mentioned red flags are suspected. The second purpose is to attempt to identify the source of pain. The examination is similar to any patient examination but will be largely directed by the findings on history.

General inspection should include assessment of posture, gait, and function such as undressing. Even at this point during the examination, note should be made of the ability of the patient to undress and of any associated pain behavior. During the examination period, much can be observed including pain behavior and the presence of yellow flags. The interpretation of Waddell's signs are controversial, but recent research suggested their presence as indicative of psychological distress [114]. However, they should be interpreted together with patient history and overall evaluation rather than in isolation [114].

The lumbar spine is inspected, and surgical scars and alignment of vertebrae are taken note of. Palpation of the lumbar spine should attempt to identify points that elicit pain, step-offs, and indentations suggestive of spondylolisthesis. Next, the range of movement should be assessed and whether individual movements elicit back or radicular pain. Pain associated with spinal stenosis typically increase with hyperextension of the spine and reduce on leaning forwards, although this observation remains more of an expert opinion and have not been substantiated in any controlled way [115]. Pain not conforming to an anatomical distribution is usually viewed as "non-organic" pain [66,116] but occurs in high prevalence especially in the context of litigation and compensation [117].

Muscle power is assessed by resistance testing of each muscle group with comparison with the corresponding group on the contralateral side. If a reduction in power is detected, the clinician should attempt to determine if whether the reduction is global or focal and whether it follows a nerve root distribution. This will assist in reducing the zones of interest, which will be of interest if further investigations are ordered. Similarly, sensation is tested in the lower limbs and an attempt to see whether any positive or negative phenomena follow a dermatomal or peripheral nerve territorial distribution.

Special tests are then used to assess if there is evidence of nerve tension. This may occur when a nerve root is stretched over a herniated disc or if a pedicle screw is actively impinging on an exiting nerve root. The femoral stretch test, straight leg raise (SLR), or Laseuge's sign are common tests used in this case.

Examination of the SIJ should also be performed to determine if this is the source of FBSS pain. Single SIJ provocation tests in isolation are not informative [108,118]. However, if a combination of SIJ pain provocation tests are positive, the probability of the SIJ as the pain generator is more likely [107,108,118]. One validity study demonstrated that the SIJ as the source is 28 times more likely when there are three or more positive provocation tests [107].

Validity of Clinical Assessment in Identifying the Source of Pain

While the aforementioned is a reflection of various clinical practice guidelines on the assessment of patients with persistent back pain [119], the ability of the clinical assessment to identify the source of pain is variable [108]. Sensitivity measures the proportion of actual positives that

are correctly identified as such [120]. Thus, in patients with pain, it refers to the ability of a test to detect the condition (source of pain) it is testing for. Specificity measures the proportion of negatives that are correctly identified [120]. In patients with pain, specificity refers to the ability of a test to exclude the possibility of the condition (source of pain) [120]. Ideally, an optimal test should have a sensitivity and specificity of 100%. However, as the sensitivity of a test increases, the specificity tends to decrease and vice versa [121]. Clinically, the sensitivity of a test is more important than specificity [121]. This is because lower sensitivity results in the condition being undiagnosed or undetected, which is a high false-negative rate [121]. This may be detrimental clinically as a treatment that can greatly reduce pain is not initiated due to the test not detecting the source of pain in the patient [121].

The disc, facet joint, and SIJ are potential sources of persistent low back pain. In a recent systematic review, no tests to identify the facet joints as the source of pain were useful [108]. However, evidence on the clinical assessment to identify the disc or the SIJ as the source of low back pain was demonstrated. For pain suspected to arise from the disc, centralization was found to be the only clinical feature correlating with identifying the disc as the source of pain [108]. One validity study demonstrated low sensitivity (0.47) but high specificity (1.00) [107]. Conversely, the absence of MRI degenerative changes was found to reduce the probability of the disc being the site of pain [108]. SIJ pain provocation tests in composite, not individually, demonstrated diagnostic validity [107,118,122,123].

The use of SLR to test for impingement that may signify disc herniation, epidural fibrosis, disc fragments, or a combination has been reviewed recently for its validity based on MRI findings [124]. On pooled data, the SLR showed high sensitivity (0.92), with widely varying specificity (0.1–1.00) [124]. The crossed SLR showed low sensitivity (0.28) but high specificity (0.9) [124]. Combining positive test results increased specificity [124].

While these physical tests have been studied in the native spine population, there has been little study performed in the postsurgical spine. The presence of instrumentation and epidural fibrosis may make interpretation even more difficult. Therefore, while some tests may change the probability of a certain structure being the source of pain, these changes are small at best [108] and the use of standard investigations (e.g., imaging studies) and more specialized diagnostic investigations are required.

Investigations

The choice of investigations is dictated to an extent by findings on history and examination. Imaging studies are commonly performed, but laboratory tests measuring markers of infection (white cell count, ESR, C reactive protein) are indicated in the presence of constitutional symptoms. Electrodiagnostic studies are rarely helpful in the diagnosis but may assist in distinguishing from other causes of neuropathic pain such as peripheral neuropathy [5].

Plain radiographs including flexion/extension view may show the presence of instability, pars defect, and deformity [125]. In addition, they can evaluate the surgical site, bone alignment, and degenerative changes [125]. Perhaps, the one advantage of plain radiographs over MRI is the ability to detect spondylolisthesis on flexion–extension views that may not be apparent on MRI examination [125]. Spondylolisthesis is the forward displacement of a lumbar vertebra relative to the adjacent vertebra and may be graded into four types [126]. Despite the potential for instability of the spine with spondylolisthesis, clinical symptoms do not necessarily correlate [127]. However, plain radiographs will miss spinal stenosis and will not give any information to the clinician on soft tissue conditions including neural impingement [128].

MRI provides very useful information in investigating the cause of symptoms. Gadolinium-enhanced MRI helps with the differentiation of scar tissue (postoperative epidural fibrosis) from recurrent or residual disc herniation [128]. Nerve root enhancement (NRE) on postoperative MRI correlates with recurrent or residual symptoms (positive predictive value [PPV] 83.7%) [129]. This correlation was stronger in the presence of both nerve root thickening and recurrent disc herniation [129]. When NRE was combined with nerve root thickening, the PPV increased to 87.7%, and when recurrent disc herniation was also identified, the PPV increased to 94.1% [129]. Other information that can be revealed by MRI includes stenosis in the lateral recess and neural foramens, diskitis, and pseudomeningocele [68,128]. Furthermore, presence of gadolinium enhancement in the intervertebral disc and vertebral bodies may indicate presence of postoperative infection.

The formation of fibrosis and adhesions within the epidural space is a normal response to spine surgery and will be observed on MRI in the majority of postoperative patients [130,131]. Despite this, studies have demonstrated that the severity of scar tissue correlates with recurrent radicular- and activity-related pain [78,131–134]. Ross et al. discovered that patients with extensive epidural fibrosis depicted on MRI scanning were 3.2 times more likely to experience recurrent radicular pain than patients with less scar [78]. This was also demonstrated on spinal endoscopy where manipulation of the scope in areas of fibrosis produced pain similar to their usual pain [131]. Due to the inevitable formation of epidural scar, studies have described grading systems for the evaluation of epidural fibrosis with intraobserver and interobserver agreement [135]. The probability of increasing pain correlated with increasing epidural scar score, with every 25% increase in scarring, the risk of recurrent radicular pain increased twofold [78].

In some patients, MRI is contraindicated such as those with pacemakers, cerebral aneurysm clips [136]. Furthermore, the presence of metal instrumentation or hardware from previous spinal surgery can produce significant

artifact on scanning [5]. In these cases, a computed tomography (CT) myelogram is recommended [5]. CT with myelography is useful in demonstrating compression of neural structures by bony elements [5].

Specialized Interventional Diagnostic Investigations

While features on clinical presentation and imaging are suggestive, more invasive diagnostic tests are often necessary to identify the source of pain.

Lumbar Medial Branch Blocks

Predominantly axial lumbar spine pain may arise from the lumbar zygoapophysial joints. The medial branches of the lumbar dorsal rami supply the articular branches of the zygoapophysial joints [137–140]. Lumbar medial branch blocks performed under fluoroscopic guidance are target-specific and valid for diagnosing zygoapophysial joint pain [141,142]. It is important for the physician to be aware that metal hardware or graft in the spine of FBSS patients may make imaging and identification of the target zones for the lumbar medial branches difficult. Furthermore, the presence of instrumentation may hinder accurate needle placement when attempting to block these nerves.

The facet joints have been identified as the source of pain in 15–45% of patients with CLBP [143,144] based on controlled diagnostic blocks according to International Association for the Study of Pain (IASP) criteria [145]. Using the same IASP criteria, a recent prospective nonrandomized study determined that the pain source in 16% of patients with recurrent pain after lumbar spine surgery originated from the facet joints [146]. It is important to note that this study did not control for patient age and type of surgery [146].

SIJ Blocks

The SIJ may be susceptible to altered biomechanics following lumbar spine operations producing persistent low back pain. In the FBSS population, older studies suggest the SIJ may be responsible in 2% of cases [2,4,147]. Diagnosing the SIJ as the pain source lacks accuracy with clinical history and examination [148–150]. While a combination of positive SIJ pain provocation maneuvers increases the probability of this joint as being the pain source, SIJ blockade is still required to make the diagnosis [108]. In contrast to the zygoapophysial joints, the supplying nerves cannot be anaesthetized accurately as they do not travel in a sufficiently fixed course to allow accurate blockade [151]. Thus, the diagnosis of SIJ pain (widely accepted at the present time) is made by performing controlled SIJ blockade [151].

Selective Nerve Root Block

For predominantly radicular pain, the transforaminal injection of local anesthetic and corticosteroids may greatly assist in diagnosing a certain spinal level as the source of pain and provides possibility of long-lasting analgesia [152]. Compared with the interlaminar or caudal routes, there is the added advantage of delivering the drug in maximal concentration closer to the suspected site of pathology [151]. These injections must be performed under imaging guidance (fluoroscopic and CT) to ensure accurate lumbosacral spine level and placement of medication and to avoid inadvertent intravascular or intrathecal injection [153]. The response to transforaminal epidural steroid injections may also help determine whether surgery might be beneficial for pain associated with a herniated disc [154].

Provocative Lumbar Discography

In FBSS, the disc is believed to be the pain generator in 17% and 21.5% of patients [2,4]. While imaging studies (CT, MRI) can demonstrate disc pathology, these changes are also found in asymptomatic individuals [155–158]. To improve the accuracy in diagnosing discogenic pain, provocative lumbar discography was introduced [155].

The utility of provocative lumbar discography has been questioned on several fronts. One concern is the demonstration that 40% of asymptomatic individuals may experience pain after disc injection, which is indistinguishable from symptomatic patients [159]. Furthermore, patients with psychological issues display a much higher rate of injection-induced pain than those without psychological problems, be they symptomatic or asymptomatic [159].

A recent systematic review concluded that lumbar provocation discography was useful in evaluating patients with lumbar discogenic back pain [160]. Variable and conflicting results from studies of lumbar provocation discography were due to use of outdated techniques, differing evaluation criteria for a positive discogram, and assessing the utility of discography based on the response to surgery (spinal fusion and artificial disc replacement) [160]. As mentioned earlier, the success rate of spinal fusion is relatively low [26,36,38]. Therefore, assessing construct validity based on a treatment that is only partially effective will intrinsically distort interpretation [160].

The International Spine Intervention Society (ISIS) guideline states a positive discogram occurs when there is greater than or equal to 7/10 concordant pain elicited at <50 psi above opening pressure, a grade III annular tear, and a painless control disc [161]. Pooled data on studies adhering to the ISIS guidelines demonstrate a false-positive rate of 9.3% per patient and 6.0% per disc [162]. Despite these findings, provocation discography cannot be said to be the gold standard for diagnosing discogenic pain [160]. At present, it remains a diagnostic aid where findings require correlation with clinical presentation. For example, discogenic pain is more likely if there are features of centralization and positive provocation discography.

Management

Management of Established FBSS

Patients with FBSS usually have a long-standing history of pain [1]. As pain persists, psychological influence and environmental factors assume more significant role in disability, perhaps exacerbating and maintaining pain. A stereotyped approach is unlikely to succeed and each patient deserves individual consideration for management. The general management plan in this group of patients should not focus solely on medical therapy. The objectives of management should be directed to restoration of functional ability, improvement of quality of life, coping strategies, and pain self-management [163]. To achieve these goals, various aspect of cognitive behavioral therapy (CBT) should be emphasized in addition to medical and surgical therapies to address the multiple etiologies (discussed earlier) that may be present (Figure 1A). An interdisciplinary management center is a valuable resource in providing an organized approach to help this patient population.

The treatment options for CLBP are considerable. A recent review article found evidence of over 60 pharmaceutical products, 32 different manual therapies, 20 different exercise programs, nine educational and psychological therapies, and 20 different injection therapies offered to patients [164]. Evidence-based guidelines on low back pain management have recently been published to aid treating clinicians [165]. The nature of therapies may be divided into conservative (pharmacological, physical, and cognitive–behavioral and rehabilitative), interventional, and surgical (Table 2).

Table 2 Management options in patients with failed back surgery syndrome

Conservative
- Pharmacological
  - Acetaminophen
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Cyclooxygenase-2 (COX-2) inhibitors
  - Tramadol
  - Muscle relaxants
  - Antidepressants
  - Gabapentinoids
  - Opioids
- Physical
  - Exercise therapy/physical therapy
  - Spinal manipulation (chiropractor)
  - Massage
  - Acupuncture
  - Transcutaneous electrical nerve stimulation (TENS)
  - Yoga
  - Inferential therapy
- Psychological therapy and educational
  - Cognitive behavioral/rehabilitative therapy
  - Educational
  - Back school

Interventional
- Facet medial branch blocks and rhizotomy
- Sacroiliac joint blockade
- Epidural Steroids
- Percutaneous epidural adhesiolysis

Surgical
- Spinal cord stimulation
- Intrathecal drug delivery systems
- Revision surgery

Trials specifically examining the response to therapies in FBSS are less prevalent than those for CLBP. Due to the difficulty in treating some patients with FBSS and their associated disability, physicians have looked to more radical modes of therapy to reduce pain and improve functional capacity and quality of life in these patients. Whereas in the past, there were very few trials looking at the efficacy of these modalities, the past 5 years has witnessed the completion of several trials and meta-analyses addressing the success of various interventions in treating FBSS.

Conservative Medical Management

The various conservative therapies discussed later have been well-studied in CLBP and various neuropathic pain models. However, studies addressing these therapies specifically in the management of FBSS are lacking.

Pharmacological

While prescribed to reduce pain, medications should facilitate exercise therapy and enable improvements in functional status. The choice of analgesics is similar to other pain syndromes with non-opioid and opioid analgesics being employed. The American Pain Society recently published clinical practice guidelines based on a review of trials studying the different pharmacological agents in CLBP [166]. These guidelines found good evidence demonstrating efficacy for antidepressants (e.g., amitriptyline) [166]. In addition, studies show fair evidence that acetaminophen, opioids, tramadol, benzodiazepines, and gabapentin (for radiculopathy) are effective for pain relief [166]. However, the authors of the guidelines could not find sufficient evidence to recommend one medication over another due to complex benefit to harm profiles for each medication [166]. A limitation of the literature is that the majority of studies have short follow-up times of less than 8 weeks [166].

Simple analgesics such as acetaminophen and anti-inflammatory drugs (nonsteroidal anti-inflammatory drugs [NSAIDS]) and COX-2 inhibitors are commonly prescribed. An updated Cochrane review has found that the anti-inflammatory medications are effective for symptomatic relief in CLBP [167]. However, there was also a statistically significant higher rate of side effects (gastrointestinal and renal) compared with placebo [167].

There was no discernible difference in efficacy or incidence of side effects between the various NSAIDS [167]. The COX-2 inhibitors were reported to have significantly fewer side effects than the conventional NSAIDs [167]. However, this Cochrane review did not include the recent trials demonstrating the significantly dangerous cardiovascular side effects from COX-2 inhibitors that have necessitated the withdrawal of some formulations [168–173]. While their efficacy is proven, the side effect profile of NSAIDS and COX-2 inhibitors make them a less attractive medication for long-term use in patients at risk of gastrointestinal, renal, and cardiovascular events.

Tramadol has been found to be moderately more effective than placebo for short-term pain and functional status after 4 weeks [174]. In the same study, the rate of withdrawal in the tramadol group due to adverse effects was similar to the placebo group [174]. It should be pointed out that the follow-up period for the antidepressant and tramadol trials was short, neither exceeding 8 weeks [174,175].

The benefit of antidepressant medication for analgesia in patients with chronic back pain has been well-documented, although there is no improvement in function [175]. In addition, antidepressants were associated with a significantly higher risk of adverse effects compared with placebo [175]. The most frequently reported of these were dry mouth, dizziness, and constipation [175].

While their effectiveness has not been formally assessed in FBSS, antineuropathic agents such as the gabapentinoids are frequently prescribed if there is a radicular or neuropathic component to chronic pain [176]. The European Federations of Neurological Societies recommends gabapentinoids and tricyclic antidepressants as first-line agents in the majority of neuropathic pain conditions except for trigeminal neuralgia [176]. There are promising data in the form of case reports describing the efficacy of gabapentin monotherapy in reducing pain but more importantly, improving function in FBSS [177]. With their improved side-effect profile and reduced need for monitoring via blood tests, this medication is an attractive option.

Pain societies recognize that opioid analgesics are safe and effective in the management of moderate to severe chronic noncancer pain [166,178,179]. Despite, this, considerable controversy exists because of the concern among health care providers over the efficacy, side effects, and particularly, the stigma of addiction [180]. Furthermore, physicians are concerned about the potential liability and censure by regulatory agencies [181]. In response to this, consensus statements have been published by the Canadian Pain society to indicate that the use of opioids for the relief of chronic noncancer pain is a legitimate medical practice [182]. In addition to analgesia, an important goal of opioid therapy should be an improvement in functional capacity [179].

There have been no published articles looking specifically at the use or efficacy of opioids in patients with FBSS. One researcher, in his role as an impartial examiner, has observed that many patients with FBSS have "intractable pain, depression, and addiction to narcotic pain medication" [22]. A recent Cochrane review looked at the safety and efficacy of opioids taken long term for chronic noncancer pain [183]. This included trials with patients on oral, transdermal, and intrathecal opioids. All trials reported clinically significant pain reduction for all three modes of delivery, but the degree of pain relief varied between studies [183]. Many participants discontinued opioid treatment due to adverse effects or inadequate analgesia [183]. Unfortunately, quality of life data and functional status were inconclusive. The authors concluded that there exists weak evidence that patients who are able to take long-term opioids experience clinically significant pain relief [183]. Due to heterogeneity of data, recommendations of one opioid preparation over another could not be made [183].

While there are no studies determining opioid efficacy in patients following their lumbar spine surgeries, concern was raised in a recent publication investigating mortality after lumbar fusion surgery [184]. In this study, the leading cause of mortality (accounting for 31% of all deaths) was analgesic-related [184]. The overwhelming majority of deaths were related to opioids (20/22 patients with analgesic related death). While the majority were accidental, three deaths were the result of suicide [184]. Of those patients who suffered from analgesic related mortality, all had undergone either an instrumented fusion or intervetebral cage procedure. No patients with receiving lumbar fusion from autograft or allograft suffered from analgesic-related death [184]. While more investigation is required to determine why patients with instrumentation may be more prone to serious complications of opioid analgesia, this finding should caution the physician to be careful when prescribing analgesics for FBSS and to undertake close monitoring of patients on chronic opioids for pain [179].

The efficacy of opioids in low back pain is controversial. A recent systematic review could not detect a reduction in pain with long-term opioids when compared either with placebo or with another non-opioid analgesic [185]. Furthermore, in the trials that assessed pain levels from baseline, opioid therapy demonstrated a nonsignificant reduction in pain from baseline [185]. The authors noted that there were limitations in the review including retrieval, publication biases, and in general, poor study quality [185]. Of concern is that no trial exceeded 16 weeks of follow-up.

Methadone is emerging as a popular analgesic medication used in the management of chronic noncancer pain [186]. It is because of its many advantages: affordable compared with other sustained release preparation [187]; lower affinity for the μ-receptor, which may result in fewer μ-receptor-related side effects such as constipation [188]; lower risk of opioid-induced tolerance and possibly effect on neuropathic pain that may be related to the N-methyl-D-aspartate (NMDA)-receptor antagonist activity of the d-isomer [189,190]; and lack of active metabolic and

insignificantly removed by dialysis making it ideal for patients with renal impairment [186]. In FBSS patients that present with both somatic and neuropathic pain and fail to respond to conventional opioid therapy, methadone may be the analgesic of choice.

In patients with a partial response to monotherapy of gabapentinoid, opioids, or tricyclic antidepressant, a combination therapy provides synergistic effects [191,192].

In summary, non-opioid analgesics and adjuvants have demonstrated efficacy but prescribing may be governed more by their unique adverse effect profiles in individual patients. Considering the conflicting results and the poor quality of opioid trials, the general guidelines for opioid prescribing in FBSS remain [179]. Patients should be individually assessed for suitability for opioid medication including risk assessment for aberrant drug behavior [111,193]. Patients with FBSS should have a trial period and goals (pain relief, function) clearly set out in a discussion between practitioner and patient. Long-acting opioids (e.g., oxycontin or sustained release morphine preparations) should be prescribed rather than short-acting ones (e.g., oxycodone or immediate release morphine syrup) if the trial is successful and long-term prescribing is undertaken by the clinician [179]. Failure to meet goals or evidence of aberrant behavior should prompt reconsideration and discontinuation of opioids. In patients with a partial response to monotherapy, a combined therapy may be considered.

Exercise Therapy/Physiotherapy

A number of patients with FBSS will become deconditioned, leading to weakness of the musculature (e.g., transverses abdominis, paraspinal muscles) responsible for maintaining spinal stability. Though different approaches exist, the general aim of exercise therapy is to decrease pain, improve posture, stabilize the hypermobile segments, improve fitness, and reduce mechanical stress on spinal structures [194]. An additional benefit is that patients are taught active coping mechanisms with pain, giving them a sense of control over their predicament [195].

For CLBP, a recent Cochrane review determined exercise therapy to be mildly to moderately superior to no treatment for pain relief at early follow-up [196,197]. This finding was supported by three separate systematic reviews [198–200]. A further review focusing on work outcomes discovered that exercise reduced sick leave in the first year and increased the proportion of patients who had returned to work at the 1-year mark [201]. There are many exercise therapy programs described in the literature but no evidence exists to support one form of exercise therapy over another in terms of outcomes [202].

The important components of an exercise program have been identified. The investigators who conducted the Cochrane review performed a meta-regression analysis and concluded that an exercise program composed of supervision, stretching, and strengthening and was individualized was associated with superior outcomes [197]. More recent evidence, which was not included in the systematic reviews, suggests benefits of core muscle strengthening to improve stability of the spine and reduce pain [203].

Psychological Therapy CBT

Considering the influence of psychological factors on CLBP, it is not surprising that psychological therapy is an accepted component of therapy. CBT is broadly defined as interventions that apply psychological principles to change the overt behavior, thoughts, or feelings of persons with chronic pain to help them experience less distress and enjoy more satisfying and productive daily lives [163]. The common components of CBT include the following: teaching and maintenance of relaxation skills; behavioral activation such as goal setting and pacing strategies; interventions to change perception such as visual imagery, desensitization, or hypnosis; and promotion of self-management perspective. The effectiveness of this therapy in CLBP and chronic pain in general has been supported by recent reviews [204–208].

In one meta-analysis of CBT trials for back pain, which included only four randomized controlled studies, the authors showed significant improvement in pain reports and subjectively reported pain behavior and disability but not observed pain behavior and mood [204]. The more recent, high-quality Cochrane review also found CBT to have positive effects on short-term pain and behavioral outcomes, but no significant change in functional status [208]. A subsequent systematic review by Hoffman et al. found positive effects of CBT on pain intensity, quality of life, and depression [207]. An important finding in this study was that interdisciplinary care with a psychological component was found to have positive effects on short-term pain interference and long-term effects on return to work [207].

To summarize these studies, psychological intervention is effective for CLBP, but no studies specifically addressed the patients with FBSS. The advantages of this treatment modality are cost-effectiveness [209], reversible nature in treatment, and absence of side effects. Its efficacy for not only pain but improved function is increased when it is incorporated with physical therapy and medical management as part of an interdisciplinary treatment program.

Interdisciplinary Management

Interdisciplinary assessment and care is now the cornerstone of the treatment of many chronic pain conditions [210–213]. A Cochrane review has found intensive interdisciplinary rehabilitation to be effective for CLBP [214,215]. There was strong evidence that function improved with intensive interdisciplinary rehabilitation with functional restoration [215]. There was moderate evidence that pain was improved [215]. However, there were contradictory vocational results with some trials reporting

improved work readiness, while others did not show an improvement in sick days [215]. An important finding of this review was that the interdisciplinary rehabilitation needed to be intensive (>100 hours) [214,215]. Non-intensive interdisciplinary care demonstrated no difference to non-interdisciplinary or usual care for pain and functional outcomes [214,215].

The value of interdisciplinary management has been assessed in FBSS. Miller et al. conducted a prospective study to compare treatment responses between non-FBSS and FBSS patients with CLBP [216]. Their study was designed to determine the responses to multidisciplinary care (including psychologist and physical therapist) [216]. The outcome measures of interest were pain scores, functional and emotional aspects of pain, quality of life, degree of functional impairment, and the helpfulness of the multidisciplinary care they had received [216]. They found that overall, both FBSS and non-FBSS patients improved with regard to pain and functional level. Interestingly, the non-FBSS group reported greater improvements in self-reported pain and disability, while the FBSS group demonstrated greater improvement on the physical therapy measures [216].

Other Therapies

Other therapies, many of them non-pharmacological, exist for the management of CLBP [164,217]. These therapies are listed in Table 2. Spinal manipulation, while moderately superior to sham manipulation, was no different to general practitioner care, exercise therapy, or back school [217]. A Cochrane review found inadequate evidence to suggest transcutaneous electrical nerve stimulation as effective for CLBP [218]. Limited evidence exists for the other therapies in CLBP [217]. None of these therapies have been studied individually in FBSS. However, in some studies, one or more of these modalities may have been incorporated into the conservative management programs [216,219].

Interdisciplinary programs differ between institutions. However, the basic objectives remain similar. Besides pain control and rationalization of medications, improved function, return to work, return to leisure activities, and reduction in health care utilization are other objectives [220]. The components of an interdisciplinary program include but are not limited to pain control, pacing, body mechanics, stress management, active coping skills teaching, behavioral modification, job planning, and follow-up care [220].

Unfortunately, many FBSS patients will not achieve adequate analgesia and functional improvement with conservative measures alone [219,221]. These patients will require more invasive interventions including injections, implantable therapies, and surgery.

Interventional Management Options

Procedural interventions should be employed in the context of an interdisciplinary management program. Their use should complement the therapies discussed earlier. The commonly used interventions for the management of FBSS may serve as both diagnostic and therapeutic (Figure 1B).

Medial Branch Blocks and Radiofrequency Neurolysis

In CLBP, pain may originate from the zygoapophysial joints. Reliable diagnosis may be drawn from the response to medial branch blocks with local anesthetic [153]. The criteria for positive response are at least 80% relief following two blocks with concordant response [222,223]. Based on these criteria, the facet joints may be responsible for persistent pain in up to 16% of patients with FBSS [146]. In those patients with a positive response, radiofrequency neurotomy may produce more sustained analgesia [222,223]. If the appropriate diagnostic criteria and technique are followed, at 12 months follow-up, 60% of patients will have at least 90% pain reduction, while 87% of patients will have greater than 60% pain relief [222,223].

Epidural Injections

The placement of steroids in the epidural space to relieve radicular pain of spinal origin has been a long used method in pain medicine [224]. The evidence for interlaminar epidural steroids in lumbar radicular pain is strong for short-term relief and limited for long-term benefit [224]. The evidence for caudal epidural steroid injections was strong for short-term relief and moderate for long-term relief in chronic lumbar radicular pain and radicular pain associated with FBSS [224]. The evidence for transforaminal epidural steroid injections for lumbar nerve root pain was strong for both short-term and long-term improvement [224]. The exact mechanism by which epidural corticosteroids exert their analgesic effect remained to be fully elucidated. The proposed mechanisms include an anti-inflammatory effect [225], reducing vascular permeability [226], and sodium channel blockade [86].

Epidural steroids are effective for epidural fibrosis, disc disruption, disc herniation, and spinal stenosis [227]. Therefore, epidural steroids may address several of the pathologies associated with the development of FBSS. Looking specifically at FBSS, two early studies demonstrated analgesic benefit with a 50% reduction in pain at 6-month follow-up [228,229]. These studies were performed without fluoroscopy. Even though loss of resistance is a reliable indicator in most cases of FBSS, surface anatomy has been shown to be unreliable [230]. Indeed, without fluoroscopic guidance, inaccurate needle placement may occur in 23% of cases [231]. A more recent randomized study compared the effects of caudal epidural with local anesthetic alone with local anesthetic combined with steroid [227]. Caudal epidural was performed fluoroscopically with epidural confirmation with nonionic contrast. The study found that the epidurals in both groups provided significant pain relief (>50%) in 60% of patients and functional improvement in 55–70% of patients, with no significant differences in the groups at 1-year follow-up [227]. This study did not include a placebo group, which

weakens the data, but interestingly, could not find a difference between local anesthetic alone and local anesthetic with corticosteroids.

There are important anatomical differences between patients with FBSS and those with CLBP who have not undergone surgery. The presence of epidural fibrosis, instrumentation, and anatomical alteration in the FBSS spine increases the difficulty of depositing corticosteroid accurately in the epidural space and the risk of dural puncture, with rates as high as 20% quoted [230,232]. Therefore, most authors recommend the use of fluoroscopic guidance and a caudal approach to overcome these factors [227,230–233]. Even with correct radiographic placement, studies have demonstrated that the injection of steroids via the caudal route may still not ensure that steroid will reach the desired site [231]. In a study involving interlaminar epidural at the site of interest and passage of a catheter, contrast injection demonstrated that the steroid solution may only reach the site of interest in 26% of cases [230].

An alternative approach to the epidural space is through the transforaminal route. While this approach is efficacious in patients who have not received prior lumbar spine surgery, the success rates in patients with FBSS were low [234]. Only 27% of the treated patients had >50% reduction in pain scores at 6 months follow-up [234].

Percutaneous Epidural Adhesiolysis

Epidural fibrosis is a common occurrence after spinal surgery. Some researchers state that epidural fibrosis may be the culprit in as many as 36% of cases of FBSS [3,82]. Furthermore, fibrosis may inhibit the passage of regional medication to areas of spinal pathology responsible for pain [227]. Percutaneous epidural adhesiolysis aims to reduce epidural fibrotic tissue and improve the delivery of epidurally administered drugs to their target tissue (e.g., nerve roots) [79,235,236].

To address the efficacy of percutaneous adhesiolysis for FBSS, a systematic review was recently published [237] that included three RCTs and four observational studies [237]. This review found that strong evidence exists for short- and long-term pain relief with the use of this intervention [237]. Long-term relief was defined as efficacy longer than 6 months. In total, there were 13 studies identified, with only three randomized trials and four observational studies meeting the necessary methodological quality for inclusion [237]. Interestingly, in the three randomized trials, two demonstrated that adhesiolysis, with or without hypertonic saline neurolysis, provided effective treatment for FBSS [235,238]. The third trial demonstrated a superior effect in analgesia for neuroplasty compared with conservative physiotherapy [239]. Patients in all three RCTs had failed conservative management including fluoroscopically directed epidural steroid injections before being randomized for adhesiolysis [235,238,239]. The superiority of adhesiolysis over epidural steroid injections is hypothesized to result from the placement of the catheter tip within the fibrosis and expanding the perineural space [237]. Once opened, the medication including steroids may then reach the appropriate lesion site and provide neural blockade and anti-inflammatory effect [237].

The patient populations studied in these trials suggest that percutaneous adhesiolysis is best reserved for FBSS patients experiencing radicular pain who have failed conservative measures including epidural steroid trials. However, future studies to determine if percutaneous adhesiolysis performed earlier is associated with improved outcome would be valuable.

Surgical Options for Management of FBSS

SCS

SCS involves the placement of electrodes in the epidural space and production of an electrical current by means of a pulse generator, which is buried subcutaneously [240]. The analgesia produced by SCS is believed to work by the gate control mechanism and modulation of excitatory and inhibitory neurotransmitter release in the dorsal horn [241]. Initially, SCS was seen as a therapy with some utility for patients with neuropathic/radicular pain who had failed all other therapies [242]. In 2004, a high-quality systematic review found only moderate evidence for use of SCS in FBSS [243]. At that time, the review noted that the majority of the studies were case studies [72] and there was only one published RCT at that time [243].

Since 2004, the argument for SCS efficacy has been strengthened with the completion of two RCTs comparing SCS with other treatments for FBSS [219,244]. North and colleagues randomized 60 patients and compared SCS (30 patients) vs repeated lumbosacral spine surgery (30 patients) with results reported at 6 months and a mean of 2.9 years [244]. The more recent prospective, randomized, controlled multicenter study of patients with FBSS (PROCESS) study recruited 100 patients with FBSS, comparing SCS in combination with conventional medical management (CMM) (52 patients) to CMM alone (48 patients) with follow-up at 6, 12, and 24 months [219]. The primary outcome measure in both studies was the proportion of patients who had 50% or greater pain relief. The results of both trials, including cost studies, are presented in Table 3. The studies indicate that there is strong evidence for the efficacy of SCS in appropriately selected patients with FBSS. The studies, so far, have only demonstrated analgesic and functional benefit in FBSS patients with pain that is predominantly radicular in nature (Figure 1B) [219,244]. There is no evidence that SCS is effective for FBSS where the back pain is predominantly axial with little radicular component.

The North et al. study [244] also assessed opioid analgesic use and patient preference for treatment in their RCT comparing SCS with repeated lumbosacral spine surgery [244]. The results were significantly in favor of SCS compared with repeat back surgery at both time intervals (6

Table 3 Summary of randomized control trials (RCTs) studying spinal cord simulation (SCS) for the management of failed back surgery syndrome (FBSS)

		No. of patients		
Study	Control group	SCS	Control	Results and Outcome Measures
Kumar et al. (2002) [57]	CMM	60	40	QoL in SCS vs CMM group improved by 27% vs 12%, respectively. After 2.5 years, SCS becomes cost effective
Kumar et al. (2007) [219]	CMM	52	40	Pain relief >50% in 48% of SCS vs 9% of CMM patients
Kumar et al. (2008) [245]	CMM	42	41	Pain relief >50% in 47% of SCS vs 7% of CMM patients in "per treatment analysis" 37% in SCS vs 2% CMM patients in "intention-to-treat analysis"
North et al. (2005) [244]	Reoperation	19	26	Significant pain relief in 39% of SCS vs 12% reoperation group; ↓ opioid consumption in 87% of SCS vs 58% in reoperation group
North et al. (2007) [246]	Reoperation	19	21	↓ cost in SCS (U.S. $48,357) vs reoperation group (U.S. $105,928)

CMM = conventional medical management; QoL = quality of life.

and 24 months) [246]. A significantly greater number of the SCS group achieved equal to or greater than 50% pain relief when compared with the surgical group ($P = 0.0149$) [244]. The opioid requirements in the SCS group were also reduced. Furthermore, at 6 months follow-up, 67% of the reoperation group opted for crossover to SCS therapy [244]. This compared with only 17% of the patients starting in the SCS group [244].

The more recent PROCESS trial assessed the outcome of SCS for FBSS as opposed to CMM [219]. This multicenter study included patients with predominantly neuropathic pain of radicular origin with a documented history of nerve injury [219]. CMM included oral medications (simple analgesics, opioid analgesics, and antineuropathic medications), nerve blocks, epidural corticosteroids, and physical and psychological therapy. The group that underwent SCS experienced improved back and leg pain relief (48% [SCS] vs 18% [CMM] at 12 months follow-up), quality of life, and functional capacity ($P < 0.05$) [219]. However, rates of return to work did not differ between the groups [219]. A notable finding was that at 6 months follow-up, 32% of the patients had experienced device-related complications [219].

An updated systematic review including both of these studies found level II-1 or level II-2 evidence for SCS in relieving chronic intractable pain of FBSS on a long-term basis [247].

A concern with SCS has been the high cost associated with the insertion and maintenance of these devices [248]. In an extension of the PROCESS trial, an assessment of resource consumption and cost in addition to changes in quality of life was performed [221]. The follow-up at 6 months demonstrated a significantly greater health care cost in the SCS group (CAD 19,486) vs the CMM group (CAD 3,994), the mean adjusted difference being CAD 15,395 [221]. However, the authors pointed out that the gain in health-related quality of life was considerably greater in the SCS group (EQ-5D score difference of 0.21 at 6 months [$P < 0.001$] [221]). Longer term data were generated from the earlier RCT comparing SCS with revision surgery [246]. All the cost analysis results were significantly in favor of SCS. The mean per patient costs, on intention to treat calculations, was U.S. $31,530 for SCS and U.S. $38,160 for reoperation [246]. The treated as intended calculations demonstrated U.S. $48,357 for SCS and U.S. $105,928 for reoperation [246]. As expected, patients who crossed over into the alternative treatment incurred higher costs. What was dramatic was that the mean cost of success for crossover to SCS was U.S. $117,901 while no crossover to surgery was met with success [246]. However, the latter incurred significantly higher costs of U.S. $260,584 [246].

A systematic review by Bala et al. 2008, including the aforementioned data, suggests that when measured long term, SCS is more effective and less costly, but there is an initial high cost with the implantation and maintenance of the device [249]. However, these cost-effectiveness studies have been criticized due to lack of calculation of cost-effectiveness ratios, confounding factors in cohort designs, small sample sizes, and lack of adequately designed trials [250].

Notwithstanding the difficulties in establishing accurate cost-effectiveness comparisons, the accumulation of recent data points to SCS as an effective treatment modality for FBSS. For FBSS, the evidence for SCS

efficacy is strongest for those patients with predominantly radicular pain [219,244,247]. Patient selection for this therapy should still conform to the guidelines as set out by the American Academy of Pain Medicine [251]. A patient should only receive a permanent SCS implant if he or she has a successful screening trial. A successful screening trial [251] is defined by the following:

- At least 50% patient reported pain relief.
- This pain relief persists in spite of appropriate provocative physical therapy.
- Analgesic consumption should remain stable or reduced during the trial period.
- The patient is satisfied both with the effects of SCS as well as the technical aspects of controlling and caring for the SCS implant.

Intrathecal Analgesic Delivery Implant Systems

While the majority of published trials have addressed cancer pain, the popularity of using intrathecal drug delivery for patients with chronic nonmalignant pain has increased in recent years [252–254]. Studies have documented the efficacy of intrathecal drug delivery systems for chronic nonmalignant pain [255,256]. However, concerns have been raised about the lack of long-term evidence for these devices [257]. Furthermore, side effects including urinary retention, constipation [258,259], equipment malfunction [260], and rare but devastating catheter tip granulomas have been reported [261–263]. Tolerance to opioids and the need for increasing medication dosage is also a problem with the long-term use of this therapy [264].

On review of the literature, there are no published RCTs on intrathecal infusion device systems for chronic noncancer pain. Several observational studies have been published [258,265–267]. While different pain conditions were studied in these populations, the majority of patients in three of these studies suffered from FBSS [258,265,266]. Analgesia was found to be effective, with 67.4% pain reduction at 6 months [258], and a mean pain reduction of 64% [265]. Roberts et al. reported that 74% of patients experienced increased activity levels after initiation of intrathecal therapy [265]. Within the studied populations, 88% to 92% of patients undergoing intrathecal therapy reported satisfaction or high satisfaction levels [258,265].

One study evaluated the differing responses of pain types (e.g., nociceptive or neuropathic) to intrathecal drug therapy, including opioids and adjuvant medications [258]. They observed that in the short term, the nociceptive group reported the greatest reduction in pain (77%), though this decreased at long-term follow-up [258]. On the other hand, deafferentation and neuropathic pain displayed the best long-term results with 68% and 62% pain reduction, respectively [258]. A separate study performed a retrospective analysis that determined that in patients on combination therapy (opioid and local anesthetic), the total dose of morphine was reduced by 23% and higher patient satisfaction was recorded compared with the opioid only group [266]. These patients also reported superior pain relief and a reduced number of family doctor's, pain clinic, and emergency room visits [266].

Despite these promising results, the lack of high-quality RCTs limits the evidence strength with two recent systematic reviews concluding that there is only level II-3 or level III evidence for the effectiveness of intrathecal drug therapy for chronic noncancer pain [253,268]. Overall, both reviews concluded that the use of the intrathecal infusion system resulted in improvements in pain (30–56% of patient with >50% pain relief) and function [253,268]. On review of the observational trials, drug side effects were common, with nausea/vomiting (mean rate weighted by sample size = 33%), urinary retention (24%), and pruritis (26%) as the most prevalent [253]. In addition, complications relating to hardware malfunction were also common [268].

In the current state of evidence, intrathecal infusion devices can only be recommended in patients where all other viable options have failed. Several authors agree that candidates for this mode of analgesia should have undergone all medically appropriate treatments, including oral opioid therapy with dose escalation [269,270]. If the patient experiences inadequate analgesia or intolerable side effects, they may be a candidate for a trial of intrathecal administration. It is important that the patient experiences an analgesic response to opioids as opioid resistant pain is unlikely to respond to intrathecal administration [269,270]. Patients should undergo psychological evaluation before implantation [252,269,270]. After these criteria are satisfied, then a trial may be initiated. If there is a positive response to the trial, then implantation of the intrathecal pump may then be performed [269,270].

Revision Surgery

The decision to perform revision surgery is difficult as studies have demonstrated the overall success rate in FBSS after reoperation is low and declines after each additional procedure [1,113,271]. On follow-up at 2 years, these studies demonstrate successful outcome being only between 22% and 40% [1,3,271]. One group attributed the poor trend after recurrent disc surgery to the development of epidural fibrosis and instability [3]. Due to the nature of these studies, the decision for reoperation was based on the treating surgeon's discretion. The only randomized study was conducted by North et al., comparing SCS vs reoperation [244]. Unfortunately, the term "failed back surgery syndrome" itself may discourage clinicians to perform further operations as the initial surgery was unsuccessful [272]. Probably the most important aspect of the decision for reoperation is for consultation with an expert spine surgeon with experience with FBSS.

In the absence of high-quality trials to guide us, the decision for further surgery is similar to indications for the index

surgery. As before, if there is any significant major neurologic deficit amenable to surgery, then surgery should proceed [19]. In the case of FBSS, if there is evidence that increased pain is due to problems with hardware, such as a pedicle screw impinging on a nerve root, corrective surgery would be indicated. The decision to reoperate in the remaining cases with ongoing pain is difficult. However, a small prospective study suggests that with proper patient selection, correct diagnosis, and indicated surgical procedure targeted at the pain generator, successful outcome as measured by >50% pain reduction and reduction in Oswestry Disability Questionnaire score is in the region of 90% [273]. However, this study only followed patients up to 1 year, whereas the other studies showed a trend to poor outcome at 2 years follow-up [1,3].

Summary and Conclusions

FBSS is a challenging clinical entity for both the patients who suffer from persistent pain and impaired function and the clinicians who try their best to manage them. Unfortunately, the failure rate for spinal surgery has not changed in the past several decades. With increasing rates of spine surgery, the number of patients with FBSS has increased. Fortunately, the medical community has recently initiated and completed high-quality trials to address whether surgery is the best treatment for patients with spinal problems where the main clinical symptom is persistent pain. While more data are required to provide consistent evidence-based guidelines for spinal surgery, these trials represent a step in the right direction. Better selection of patients, appropriate spinal surgical procedure, and psychological intervention for high-risk patients represent some measures important in preventing continuing high rates of FBSS.

For those patients with FBSS, the importance of an interdisciplinary care model for pain control but also to improve function cannot be overemphasized. Attention to psychological and social factors is important. The role of conservative medications and interventions should be within a model of care where the major aim is to facilitate an improvement in function and where possible, a return to the patient's premorbid social role. Unfortunately, some patients will not improve with these measures, and more interventional therapies will be required. The evidence base for these interventions has grown in recent times. The efficacy of epidural adhesiolysis and SCS in particular are now accepted. Other therapies such as intrathecal drug delivery systems still require further investigation. Due to the studied patient populations, equipment problems, and adverse effects, these therapies cannot be recommended as first line at this stage. Their roles in FBSS management are when all conservative measures fail and when the patient's pain patterns meet certain criteria (Figure 1). Our suggestions for the evaluation and management of FBSS patients based on the available evidence is outlined in an algorithm (Figure 1).

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