

REVIEW

Current Trends in Failed Back Surgery Syndrome. A Brief Literature Review, Management Guide and the Romanian Perspective

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Abstract

Failed back surgery syndrome (FBSS), as described by Follett and Dirks¹ is the least desirable situation for any patient dealing with pain in the lumbar region. Not a syndrome in itself, but rather a syntagm, the term FBSS is generally coined to describe unsuccessful surgical results despite correct surgery. Failed Back Surgery Syndrome is an emerging public health problem throughout the World, which has the unfortunate end-results of generating liability, disability and last but not least, heavy psychological and economical tolls. This paper acts as a brief literature review and tries to summarize available data regarding FBSS epidemiology, prevention and treatment. At the same time, the authors wish to offer neurosurgeons and spine surgeons a relevant starting point on how to handle this emerging public healthcare problem and how to help minimize its impact.

Keywords: Failed Back Surgery Syndrome, spine surgery, literature review, management.

Rezumat

Termenul de Failed Back Surgery Syndrome (FBSS), cunoscut mai nou în literatura de specialitate din România sub sintagma de „Sindrom Spinal Post-chirurgical”, a fost descris inițial de Follet și Dirks¹ în 1993 și reprezintă cea mai neplăcută situație cu care se pot confrunta atât pacienții cât și neurochirurgii sau chirurgii spinali în încercarea lor de a trata durerea lombară. Termenul de sindrom spinal postchirurgical descrie în linii mari contradicția generată de lipsa unei evoluții favorabile a pacientului în pofida unei intervenții chirurgicale corecte. Sindromul spinal post-chirurgical reprezintă o problemă acută de sănătate publică pe întreg Mapamondul generând disabilități și litigii și exercitând o foarte mare presiune psihologică și financiară asupra pacienților. În lucrarea de față autorii efectuează o recenzie a literaturii de specialitate și încearcă să furnizeze date relevante cu privire la epidemiologia sindromului spinal post-chirurgical, a prevenției și nu în ultimul rând a tratării acestuia. În același timp, autorii doresc să ofere neurochirurgilor și chirurgilor spinali un punct de plecare solid pentru managementul acestei situații și minimizarea impactului acesteia.

Cuvinte cheie: Failed Back Surgery Syndrome, sindrom spinal post-chirurgical, chirurgie spinală, management, recenzie a literaturii.

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INTRODUCTION

The International Association for the Study of pain, defines Failed Back Surgery Syndrome as a “lumbar pain of unknown origin, either persisting despite surgical intervention or appearing after surgical intervention for spinal pain, originally in the same topographical location”². Briefly summarized, the origins of Failed Back Surgery Syndrome reside in any combination of the following:

- Improper history taking and patient assessment
- Improper differential diagnosis of symptoms
- Improper diagnosis of associated pathologic entities
- Improper non-operative treatment plan
- Improper patient selection for surgery
- Improper surgical technique used
- Improper complication management
- Patient lack of compliance to treatment or recommendations.

As constant progress throughout the various fields of medicine can be translated (from a broad point of view) into the ever growing average age of the general population, the number of patients suffering from degenerative processes of the spine is continuously increasing. In the European Union alone, 19.7% of the population have an age greater than 65 (an increase of +2.8% since 2008). This percentage is expected to rise over the next decades³. Furthermore, available data illustrates that elderly patients meet spine fusion criteria more often while at the same time, suboptimal bone quality is becoming more frequent^{4,5}.

The authors feel obligated to note that low back pain is currently the second most frequent reason for which patients seek medical aid⁶ and while data from western countries illustrates a general increase in the numbers of surgeries performed for low back pain, reported surgical failures and complications have a tendency to remain constant^{7,8}. The direct repercussion of these issues is the ever growing number of patients reporting surgical complications, needing reinterventions or even ending up dealing with Failed Back Surgery Syndrome.

MATERIALS AND METHODS

Epidemiology and statistics

Spine Surgery has constantly evolved since the early interventions described by Elsberg, Putti or Mixter and Barr^{9,10,11,12} to such an extent that in 1997, physicians

from the U.S. reported 317.000 lumbar interventions. By the year 2002 the number rose to over 1.000.000 interventions^{13,14,15,16}. A few years later, in 2005, Deyo et al. reported that spine surgery rates had increased by 220% since 1990 (even though no clear indication had been observed and efficacy of spinal fusion hadn't yet been fully demonstrated for degenerative disease^{17,18}). Under these circumstances, literature data has clearly noted a constant increase in patients with Failed Back Surgery Syndrome^{18,19,20}.

In 2018, Martin et al., published a paper regarding lumbar fusion rates in the United States between 2004 and 2015. They reported a 62.3% increase in the volume of elective lumbar fusions performed - from 122.679 cases reported in 2004 to 199.140 cases reported in 2015. Increases were greatest in people aged 65 or older, with cases of disc degeneration, herniation and lumbar stenosis representing 42.3% of all elective lumbar fusions. Hospital costs for the year 2015 exceeded \$10.000.000.000 averaging at more than \$50.000 per admission²¹.

Most papers dealing with the incidence of FBSS state that the syndrome is likely to occur in about 8 to 35% of all patients undergoing lumbar surgery, however these papers date back at least to the early 1990's and should be regarded with a critical eye, as reports vary greatly from author to author and no standard terminology or definition is used^{22,23,24,25}. More recent studies estimate the incidence of FBSS to lie between 30-46% off all patients operated on the lumbar spine. A more detailed analysis shows that patients with lumbar fusions have a higher risk of developing FBSS while patients submitted to microdiscectomy have a smaller risk^{22,23,24,25,26}. In the latter category, incidence of FBSS is estimated to be between 19 and 25%²⁶.

Despite multiple studies being available, no clear statements regarding the epidemiology of failed back surgery syndrome can be made as large standardized series of cases are difficult to obtain and examine.

Chronic pain is an extremely important aspect of FBSS. By comparison with other chronic pain patterns (such as rheumatoid arthritis for example), patients with FBSS show significantly higher levels of pain and an impaired quality of life on the EQ-5D and SF-36 questionnaires^{26,27}. These patients score higher on the Oswestry Disability Index (ODI Scale) (Figure 1) and have a higher unemployment rate. For patients with chronic pain alone, treatment costs (excluding reintervention, intrathecal pumps or spinal cord stimulation) can go as high as \$19.000 per year²⁸.

LOW BACK PAIN AND DISABILITY INDEX (REVISED OSWESTRY)

Patient Name: _____

Date: ____/____/____

Please read instructions carefully.

This questionnaire has been designed to give the doctor information as to how your low back pain has affected your ability to manage everyday life. Please read all statements in each section and mark the box which most closely describes your problem.

SECTION 1 - PAIN INTENSITY

- The pain comes and goes and is very mild.
- The pain is mild and does not vary much.
- The pain comes and goes and is moderate.
- The pain is moderate and does not vary much.
- The pain comes and goes and is very severe.
- The pain is severe and does not vary much.

SECTION 2 - PERSONAL CARE

- I do not have to change my way of washing or dressing to avoid pain.
- I do not normally change my way of washing or dressing even though it causes some pain.
- Washing and dressing increases the pain but I manage not to change my way of doing it.
- Washing and dressing increases the pain and I find it necessary to change my way of doing it.
- Because of the pain, I am unable to do some washing and dressing without help.
- Because of the pain, I am unable to do any washing or dressing without help.

SECTION 3 - LIFTING

- I can lift heavy objects without any extra pain.
- I can lift heavy objects, but it gives extra pain.
- Pain prevents me from lifting heavy objects off the floor.
- Pain prevents me from lifting heavy objects off the floor but I can manage if they are conveniently positioned on a table.
- Pain prevents me from lifting heavy objects but I can manage light to medium objects.
- I can only lift very light objects at the most.

SECTION 4 - WALKING

- I have no pain on walking.
- I have some pain but it does not increase with distance.
- I cannot walk more than one mile without increasing pain.
- I cannot walk more than 1/2 mile without increasing pain.
- I cannot walk more than 1/4 mile without increasing pain.
- I cannot walk at all without increasing pain.

SECTION 5 - SITTING

- I can sit in any chair as long as I like.
- I can only sit in my favorite chair as long as I like.
- Pain prevents me from sitting more than one hour.
- Pain prevents me from sitting more than half an hour.
- Pain prevents me from sitting more than 10 minutes.
- I avoid sitting because it increases pain.

SECTION 6 - STANDING

- I can stand as long as I want without pain.
- I have some pain on standing but it does not increase with time.
- I cannot stand for longer than one hour without increasing pain.
- I cannot stand for longer than 1/2 hour without increasing pain.
- I cannot stand longer than 10 minutes without increasing pain.
- I avoid standing because it increases the pain.

SECTION 7 - SLEEPING

- I get no pain in bed.
- I get pain in bed but it does not prevent me from sleeping well.
- Pain reduces my normal sleep by 1/4 each night.
- Pain reduces my normal sleep by 1/2 each night.
- Pain reduces my normal sleep by 3/4 each night.
- Pain prevents me from sleeping at all.

SECTION 8 - SOCIAL LIFE

- My social life is normal and gives me no pain.
- My social life is normal but increases the degree of pain.
- My social life is unaffected by pain apart from limiting more energetic interests.
- Pain has restricted my social life and I do not go out very often.
- Pain has restricted my social life to my home.
- I have hardly any social life because of the pain.

SECTION 9 - DRIVING / RIDING IN CAR, ETC.

- I get no pain while traveling.
- I get some pain while traveling but none of my usual forms of travel make it any worse.
- I get extra pain while traveling but it does not compel me to seek alternate forms of travel.
- I get extra pain while traveling which compels me to seek alternate forms of travel.
- Pain restricts all forms of travel.
- Pain prevents all forms of travel except that done lying down.

SECTION 10 - CHANGING DEGREE OF PAIN

- My pain is rapidly getting better.
- My pain fluctuates but overall is definitely getting better.
- My pain seems to be getting better but improvement is slow at present.
- My pain is neither getting better or worse.
- My pain is gradually worsening.
- My pain is rapidly worsening.

LOW BACK PAIN SCALE

Rate the severity of your **Low Back Pain** by indicating on the following scale.

Absence I-----I **Extreme**

Figure 1. The Oswestry Disability Index questionnaire²⁹

The Etiology and pathophysiology of FBSS (although still unclear) can be described in relationship with: preoperative factors, intraoperative factors and postoperative factors.

Note: *It is the authors' opinion that a global consensus is required to perform terminology standardization and development of future guidelines for studies related to FBSS.*

In the preoperative moment of any spine intervention, surgeons should always carefully assess their patients and note their findings as patient-related factors are extremely important for the follow up: Psychosocial factors (rather than physical aspects) are important predictive factors for treatment failure. Pre-existing depression, anxiety related to own status, lacking or inadequate coping mechanisms and last but not least corticalization of chronic pain, as well as already existing personal injury claims are constant findings in patients with FBSS³⁰⁻³⁸. Decreasing values recorded by patients on standardized questionnaires or reports regarding failure to improve psychologic status should always be considered a red flag by attending physicians. Nevertheless, pre-existing psychologic issues should never deprive a patient from treatment if the anatomical basis for pain exists and if surgical indication is certain.

When identified, the above mentioned risk factors should guide the surgeon to carefully tailor treatment and adequately plan for surgery (but only if it's needed) while at the same time prompting him / her to focus on educating the patient, communicating and recommending appropriate psychologic / psychiatric care and counselling. In the authors' opinion, it is vital to develop a progressive treatment algorithm reserving surgery SOLELY for situations when every other treatment fails.

Intraoperative factors generally refer to gestures performed in the operating theatre by the attending surgeon. Note however that these factors also include prior surgeries. Multiple interventions for lumbar pain in one patient are always associated with higher surgical failure rates. As demonstrated by Nachemson since 1993 if initial success rate is accepted to be greater than 50%, a reintervention lowers success rates to 30%, a third surgery lowers success rates to 15%, while a fourth surgery lowers success rates to around 5%³⁸. Segment instability is a constant risk in repeat surgery.

Improper patient selection for surgery is always an incriminated factor in patients developing FBSS. A typical situation is that in which a spine surgeon or neurosurgeon performs a discectomy based on imaging

alone, without considering the neurologic examination. E.G.: a visible disc protrusion in a patient without radiating pain. Note that electrophysiological diagnosis can be used to consolidate neurologic findings and establish surgical indication.

Surgical planning, used techniques and gestures are tremendously important aspects and should be constantly scrutinized: a single level decompression (rather than an extensive cross-over approach) in a patient with multiple level lumbar stenosis may prove to be unsatisfactory. Aggressive muscle disinsertion, thermal injuries, careless decompression or prolonged traction may lead to residual pain. Over instrumentation (unnecessary fusion) will lead to an increase in axial pain, it may cause segment instability, adjacent segment disease or even radicular lesions. In some cases, surgical correction of the pathology may be difficult to achieve. Far-lateral herniations pose a risk of pars-interarticularis³⁹ fractures during decompression. If unnoticed, a fractured pars interarticularis may develop a symptomatic pseudarthrosis and subsequent pain.

When discussing with patients regarding the risks and benefits of surgery, most surgeons should describe that progressive disc disease is an important postoperative complication which is frequently met. New or recurrent disc herniations do occur following discectomy as lumbar biomechanics become altered. Adjacent level disease may lead to a worsening of pain while unnoticed pars interarticularis fractures superimposed with discectomy may lead to microinstability. Epidural fibrosis following spine surgery contributes to postoperative chronic pain either through root tethering or compression, which causes mechanical pain and at the same time alters the vascular supply to the nerve root via the vasa nervorum, thus making the nerve root more sensitive to stimuli^{26,40,41,42,43}.

It is well-known that an extensive bone removal during the posterior approach of the lumbar spine (for example during a laminectomy) may generate local instability and subsequent pain. Removal of more than 1/3 of the medial portion of the articular processes is a well-known instability generator and therefore any surgical interactions in this area should be carefully weighed⁴⁴. Besides the obvious vascular risks, extensive discectomy will generate an otherwise inexistent space between two adjacent vertebrae leading to biomechanical modifications in the lumbar spine. Such a potential height reduction may generate stenosis in the nerve root foramina and translate to radicular pain⁴⁴ via the so called „transition syndrome” in which axial load

is distributed to the adjacent levels, thus accelerating lumbar degeneration⁴⁵.

Disc prosthetics have been used for a few years in the past two decades. Even though their development has helped us better understand the processes taking place in the spine, the authors consider them to be less relevant nowadays. Their use could be regarded as an additional risk factor towards FBSS, with regard to adjacent segment disease, segment instability, over instrumentation, possible infections and so on.

Postoperative factors usually refer to complications of surgery or originating from patient noncompliance. They include but are not limited to: spondylodiscitis, hematomas, pseudomeningoceles, nerve root injuries, instability and so on. Pseudomeningoceles often result following reckless gestures or sharp dissection in the surgical field generating overlooked dural tears. This is the reason we advocate for the use of surgical microscopes and not loupes, careful inspection of the surgical field and last but not least a flexible OR timetable allowing the surgeon all the time he needs for the surgery. Inappropriate wound suturing is another possible cause for pseudomeningoceles.

Arachnoiditis is another possible complication which may inflict significant pain to the patient. Prolonged nerve root manipulation or retraction will cause chronic radicular pain. Surgeons must avoid as much as possible manipulation of the nerve root, localized bleeding and should pay close attention to conjoined nerve roots.^[46]

Paraspinal muscles are potential pain generators if surgery is not conducted appropriately. A midline fascial incision may damage the interspinous ligaments; extensive monopolar dissection and prolonged retraction with bone disinsertion usually lead to muscle denervation and atrophy, to which careless motion behavior (patient posturing) contributes. With fusion, paraspinal muscles may spasm and atrophy. The patient may compensate to some extent by hyperextending the thoraco-lumbar spine, however, this exaggerates spino-pelvic parameters and generates pain in the long term generating „fusion disease”^{47,48}. Surgeons should always be aware whether a complete orthopedic exam with spine parameters assessment is needed.

The successful management of FBSS is one of the most difficult challenges for practicing neurosurgeons and spine surgeons. Failed Back Surgery Syndrome is a reemerging concept which needs debate and review. As we speak, there are still no clear guidelines regarding the prevention and treatment of FBSS. Given its

multifactorial pathophysiology, FBSS should be approached in a multimodal fashion. Patients with failed back surgery syndrome constantly describe long lasting pain, which, over time, predisposes them to a number of significant psychological complications. As this is the case, each patient requires an individualized approach.

The first line of treatment should always be conservative in nature, however, in most cases it fails. In all cases there is a lack of agreement between the preoperative expectations of the patient and the surgeon versus the postoperative results. As this is the case, proper patient preparing and clear discussions are mandatory. For example, if the patient expects a complete remission of axial pain following surgery, remind him that most of the times, surgery is performed to decompress the nerves and to preserve limb function and that pain may persist beyond the point of surgery. The main obstacle in front of a guideline-based approach for FBSS is the lack of consensus between physicians and specialties.

Note: From our point of view, the criteria for surgery (both for emergencies and elective procedures) need to be reviewed and redefined, keeping in mind the patient's desire to control pain. For example, a patient with intermittent lumbar pain, with intermittent pain radiation in the leg, without neurologic deficit, without instability, should never be operated, yet alone have pedicular screws set in place.

Literature data suggests that 70% of all patients suffering from radiating pain will improve in 3 months' time with conservative treatment. Chronic radiating pain (lasting for more than 3 months) generally has a better chance of improvement with surgery, which yields higher success rates than standalone medical treatment. Axial pain however lacks a proper response to spine fusion and the patients would be better by simply undergoing physical therapy. As this is the case, we advocate for a more cautious approach to axial pain when surgery is not clearly mandated. Only after the patient is subjected to conservative treatment and physical therapy with failure to improve should surgery be considered. Even so, surgery should be performed only after careful scrutiny of the patient and discussions about their expectations, possible outcomes, complications etc.

Another important aspect for the successful management of FBSS is constant outpatient assessment. Always take note on the possible source of the pain, the patient's age and gender, psychosocial aspects (education, financial status, their need for financial gains or pensioning, work environment etc.), existing comor-

bidities such as smoking, alcoholism, depression, anxiety, pain medication, sleep pattern, prior surgeries or management strategy, prior investigations etc.

The patient's psychologic and psychiatric status should be periodically assessed by a psychologist or psychiatrist and in most situations the management strategy should be tailored according to the patient's needs. Quality of life should also be investigated using the ODI and EQ-5D questionnaires as psychosocial stress factors have tremendous impact on patients with chronic pain: Anxiety, depression, ongoing litigations and any demanded material compensation should be noted. Do take into consideration that surgery is likely to fail if certain psychosocial criteria are met.

History taking for these patients should be meticulous, with emphasis on pain appearance, location, evolution, timespan, remission, improving and worsening factors etc. Radicular vs. axial pain should be clearly defined. If radicular pain is identified the surgeon should weigh in on whether decompression would be helpful or not. If a patient is operated on for axial pain and the character of the pain becomes altered with onset of radicular symptoms, chances are high for a postoperative complication to occur. Location of axial pain is also important. Non-irradiating low back pain is often met in patients with facet or sacro-iliac joint degeneration. Local inflammation, suffering of the muscular system or aponeurosis should also not be excluded. Pseudarthrosis should be considered in patients developing low back pain subsequent to lumbar spine fusion.

Inspection is relevant as it offers data regarding posture, walking and underscores dysfunctions with basic functions. The sagittal vertebral axis and the hip-line offer much data regarding the basic functions of the patient's spine. Flexion and extension should highlight any potential segmental instability. The full range of movement is to be assessed as pain associated with spinal stenosis is higher in spine hyperextension and is improved when the patient leans forward. Motor function should always be assessed during a neurological exam. This stresses any neurologic deficit which should accurately pinpoint any nerve root involved by the ongoing pathologic processes. Key sensory points should always be tested. Examination of the sacro-ileal joint should be performed to determine whether it represents the source of the pain.

Radiographs of the spine in orthostatism, flexion and extension may outline segment instability, fractures, defects of the pars interarticularis or modified

spinopelvic parameters. They can evaluate surgical sites, bone alignment and degenerative changes. Unlike magnetic resonance imaging, plain radiographs may illustrate dynamic spondylolisthesis visible only during the shift between flexion and extension. Plain X-rays on the other hand lack most of the features of magnetic resonance and will most likely miss disease such as lumbar stenosis, ligament status or nerve-root compression. Further information regarding the bony elements of the spine can be obtained using computed tomography with 3D reconstruction.

Magnetic resonance imaging enables the surgeon to observe scar tissue, recurrent or residual disc herniations, epidural fibrosis, nerve root thickening, stenosis of the lateral recess and neural foramina, spondylodiscitis and pseudomeningoceles. Epidural fibrosis is normal in patients with prior spine surgery, however, studies have demonstrated that the severity of scar tissue formation correlates with recurrent radicular and activity related pain⁴⁹. Due to the inevitable formation of epidural fibrosis, researchers have begun describing grading systems for the evaluation of epidural fibrosis as a direct link this process and increasing pain was noticed⁵⁰.

Electromyographs and electrodiagnosis are an extremely useful means to objectively illustrate a compressed or damaged nerve root and to identify the site of a potential lesion. They are cheap and easy to perform, however they require good communication between surgeon and examining neurologist. The examining neurologist must be well versed in performing this investigation and interpreting its findings.

Over the years, a number of **inverventional diagnostic investigations** have emerged with the purpose of helping clinicians distinguish the origin of pain in FBSS. As lumbar axial pain may originate in the lumbar zygapophysial joints, medial lumbar branch blocks may be useful in diagnosing zygapophysial joint pain. Take note however that since these studies have been published since the early 1980s' and up to the year 2008 the results are somewhat open to interpretation as more extensive studies are needed⁵¹⁻⁵⁷.

Sacroiliac joint blockade is another possibly useful maneuver according to some authors. Following lumbar spine surgery, the sacroiliac joints may be subjected to altered biomechanics. Literature data suggests that the nerves supplying the sacroiliac joints cannot be accurately blocked in a less invasive manner and therefore, in our opinion this maneuver still needs to demonstrate utility in controlled trials.

Selective nerve root blocks are routinely used by neurointerventionists and have demonstrated great usefulness in diagnosing the source of radicular pain and alleviating symptoms. The use of these techniques may help determine the usefulness of surgery for pain management associated with a herniated disc.

Pharmacotherapy employs various classes of opioid and non-opioid analgesics or antidepressants. Antineuropathic agents, myorelaxants and anti-inflammatory medication are also constantly used. Antidepressant medication for pain associated with FBSS has well documented results in the literature, however it doesn't improve the patient's quality of life as motility is not improved. Antineuropathic agents, on the other hand, such as gabapentin are frequently prescribed as the European Federation of Neurological Societies recommends gabapentinoids and tricyclic antidepressants as first-line agents for neuropathic pain. Literature data suggests they are effective in reducing pain to some extent and their main advantage is they improve patient function. This aspect makes them a viable option for treatment^{58,59,60}.

Opioid analgesics are effective solutions for pain management, however they should be used carefully due to their potential addictive character. Nevertheless, oral, transdermal or intrathecal opioids show a valuable clinical response in patients with FBSS. Quality of life and functional status in patients with FBSS treated using opioids are unknown due to the lack of data in the literature. Another key item regarding the use of opioids is the fact that the leading cause of mortality in patients after lumbar fusion was related to opioid use. An article in *Spine*, since 2009, debating the mortality in patients who underwent lumbar fusion raised a serious red flag stating that 31% of all deaths were analgesic related⁶⁰.

Methadone, by contrast, is an emerging potential analgesic due to many advantages: it has an affordable price, it has a lower affinity for the μ receptor resulting in fewer use-related complications, it poses a lower risk of addiction and has a possible effect on neuropathic pain related to the N-methyl-D-aspartate receptor⁶¹. Last but not least, methadone is easy to clear through dialysis (making it ideal for patients with renal impairment)⁶²⁻⁶⁶.

Physiotherapy for patients with FBSS aims to improve status following muscle deconditioning. The general aim of physiotherapy is to decrease pain, improve posturing and patient motility and if possible to

stabilize segments with abnormal mobility thus reducing stress on the spine.

As stated by Chan et al.²⁶ exercise therapy is superior to no treatment for pain relief at early follow-up. Physiotherapy reduces sick leave and improves patient psychologic status (offering a possible coping mechanism). Research conducted by Lindback et al., as well as Fors et al., has illustrated that physiotherapy generates better scores on the ODI with decrease in depression and better behavior with relation to anxiety and fear avoidance beliefs^{[67][68]}. It is the authors' opinion that physiotherapy – when correctly performed – provides valuable improvement in the status of patients diagnosed with FBSS. Unfortunately, for Romania, rehabilitation medicine is a neglected specialty and centers with appropriate staff and logistics are limited.

Psychological therapy aims to reduce the influence of patient psychologic factors regarding the objective medical outcome. The common components of psychological therapy include: teaching and maintenance of relaxation skills, behavioral activation such as goal setting and pacing strategies, interventions to change perception. The effectiveness of this therapy in chronic low back pain patients and chronic pain patients in general has been supported by recent reviews⁶⁹⁻⁷².

According to Manchikanti et al. (2007), **Medial branch blocks and radiofrequency neurolysis** have good results in about 16% of all patients with chronic low back pain within FBSS^{73,74}. In these patients, according to the same authors, radiofrequency neurotomy may produce a more sustained analgesia with drastic improvement in quality of life^{75,76}.

Epidural injection of corticoids is a widely accepted and relatively cheap method to achieve short term pain relief with relative safety. In patients with FBSS, epidural steroids maintain their short term usefulness, however, chronic use will induce a lower response with time^{77,78}. Given their wide therapeutic potential, in our opinion, epidural steroids may help surgeons avoid an unnecessary intervention on the spine and should be always considered for wide use. According to Chan et al., epidural steroids are useful in patients with FBSS however, fluoroscopy should always be used due to the unreliability of surface anatomy and possible inadequate needle placement^{26,79}. Furthermore, prior surgery, with or without spinal fusion may predispose the patient to potential complications such as dual penetration or fistulas or lack of response following wrong location steroid depositing.

Percutaneous adhesiolysis is a technique developed in the early 2000s whose efficiency was tested in multiple studies. Results obtained so far suggest that percutaneous adhesiolysis is superior to epidural steroid injection in what regards pain management and quality of life of patients following the procedure. Available data suggests that this procedure has an improved rate of success in patients with FBSS mediated by radicular pain. In these patients, once the percutaneous catheter is inserted in the arachnoid adhesions the perineural space is expanded and medication has a better local penetration^{26,80-83}. Even though it was frequently overlooked in the past, this technique appears to gain popularity with surgeons.

Intrathecal infusion devices were initially developed for cancer patients dealing with excruciating pain. Over the last two decades intrathecal infusion devices made a reappearance as the obtained analgesia is satisfactory and patient quality of life becomes better given both neuropathic and nociceptive pain respond to such therapeutic gestures. The pump delivers ideally a mixture of a local anesthetic and opioid which in time reduces the number of hospital days for pain management. Even so, due to a lack of objective recent studies, intrathecal pumps should be discussed only when there is no other possible means of therapy.

Other pharmacologically active agents (orphan drugs) are continuously being tested for potential use. Among these, Ziconotide, a synthetic analogue of the venom from the *Conus magnus* sea slug, has been approved for use in the European Union under the name Prialt. The drug is administered via intrathecal injection and acts by blocking presynaptic calcium channels. By comparison with morphine, most of the adverse reactions of ziconotide are limited^{84,85,86}.

Spinal Cord Stimulation, as its name suggests, is a technique employed by neurosurgeons to place electrodes in the epidural space and, through electric impulse generation, modulate neurotransmitter release and pain sensation. Despite initial disappointing results, more recent studies illustrated strong arguments that carefully selected FBSS patients will benefit from this technique. Authors show that patients with an important radicular component to their chronic pain will have functional improvement, pain decrease and reduced opioid use when compared to their baseline condition⁸⁷⁻⁹⁰. The disadvantage of the technique is the increased price of equipment and long learning curve for the surgeon.

Surgery for patients with FBSS should be, such as intrathecal infusion devices, last on the list of gestures to be performed. Unfortunately, available data shows that only 2-4 of every 10 patients are likely to benefit from revision surgery and with every additional surgery performed, failure is more likely to occur thus degrading the patient's condition even more. Surgery should be performed cautiously and only when clear indication (E.G. progressive neurologic deficit) is encountered.

DISCUSSIONS

I. As stated before, in our opinion, the true epidemiology of FBSS is still unknown. For Romania, which is a small-average sized country (238.397 km²; 19.4 million inhabitants), the years spent under the communist regime (until 1989) represented a constant decline for the national healthcare system regarding policies, investments and mentalities. Currently, in Romania, surgeons still have no national database for patients with interventions on the spine. Such a registry would be an invaluable tool for medical research regarding diseases of the spine including FBSS. No rates for Failed Back Surgery Syndrome have been reported in Romania so far to the extent of the authors' knowledge.

II. The tremendous financial pressure that patients with diseases of the spine exert on the healthcare system does mandate the need to develop a registry such as the one described above. A clear evidence regarding investigations, means of treatment and medication is needed. Furthermore the occupational status of such patients needs to come under more strict scrutiny as most of these patients will end up with a disability pension. It is our opinion that clear criteria for pensioning need to be developed and that professional reorientation and reconversion could be a method to keep patients with FBSS active in the economy.

III. A national strategy for patients with degenerative spine disease and FBSS needs to be developed and unanimously approved as this represents the first step towards offering our patients the best standardized healthcare. Furthermore, a national prevention strategy for degenerative diseases of the spine needs to be implemented.

IV. International consensus regarding terminology used and surgical indications is another mandatory step in developing standardized treatment for patients with FBSS and degenerative diseases of the spine. For

example: If a patient is successfully operated (elective surgery) for a disc herniation (with clear clinical improvement for 7 days postoperative) and the patient develops radicular pain (same symptoms as before surgery) on the 8th day – is the situation considered to be a FBSS? What if the radicular pain occurs 1 month after discharge? What if the patient develops radicular pain after a year? Is it a recurrence, is it a new herniation, is it a FBSS Situation?

V. From the author's point of view, lumbar spine surgery needs to be performed only when there is no other alternative for treatment. Spine surgeons and neurosurgeons unfortunately rush to operate patients that could benefit from an attempted conservative strategy. Therefore, we urge spine surgeons and neurosurgeons to reconsider the ease with which they recommend surgery.

CONCLUSIONS

1. Available demographic data indicates that the general population is constantly aging. This means that in the future, surgeons will see an increase in the number of patients dealing with degenerative diseases of the spine. As the rate of complications is constant following lumbar spine surgery, a constant increase in the number of patients suffering from FBSS is to be expected.
2. FBSS is an emergent public health concern given its high treatment costs and tremendous pressure it exerts on public health systems. Despite existing studies, no clear cause or pathophysiologic mechanisms for FBSS can be identified, only predisposing or potentially generating factors can be highlighted. National standardized records are mandatory for understanding FBSS and its impact on the population.
3. Patient selection and choice of techniques are vital in preventing unwanted complications for lumbar

degenerative disease. Furthermore, clearer guidelines regarding the indication for surgery of the degenerated spine should help us deliver the best treatment for our patients and thus reduce the number of patients with FBSS.

4. When identified, FBSS should be approached in a multimodal manner, reserving surgery only for otherwise untreatable cases. The therapeutic approach should be performed in an incremental fashion, starting with basic gestures and saving surgery for otherwise untreatable cases.
5. A new severity score for patients suffering from FBSS is to be designed if we are to provide the best standard of care for our patients. Such a score should help, first of all, to standardize care for patients
6. Psychosocial aspects are important prognostic factors in the treatment of FBSS.
7. From the authors' point of view, a general review of degenerative spine disorders needs to be performed Worldwide and new standards of care have to be imposed as surgery for degenerative spine disease is offered as therapeutic means way too much ease.
8. From a financial point of view, patients with FBSS should be carefully assessed and any disability pension should be scrutinized by authorities. Only after all attempts of professional reorientation and re-conversion fail should pensioning occur.
9. A national revised strategy for patients with degenerative disease of the spine is needed urgently.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

- Follett, K. A., & Dirks, B. A. (1993). Etiology and evaluation of the failed back surgery syndrome. *Neurosurgery quarterly*, 3(1), 40.
- Fairbank, J. C., & Pynsent, P. B. (2000). The Oswestry disability index. *Spine*, 25(22), 2940-2953.
- Eurostat (Web Page) Population structure and ageing. Updated July 2019. Available online at: https://ec.europa.eu/eurostat/statisticsexplained/index.php/Population_structure_and_ageing#The_share_of_elderly_people_continues_to_increase. Accessed: August 1, 2019.
- Salzmann, S. N., Derman, P. B., Lampe, L. P., Kueper, J., Pan, T. J., Yang, J., ... & Hughes, A. P. (2018). Cervical spinal fusion: 16-year trends in epidemiology, indications, and in-hospital outcomes by surgical approach. *World neurosurgery*, 113, e280-e295.
- Reitman, C. A., Nguyen, L., & Fogel, G. R. (2004). Biomechanical evaluation of relationship of screw pullout strength, insertional torque, and bone mineral density in the cervical spine. *Clinical Spine Surgery*, 17(4), 306-311.
- Hoy, D., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., ... & Buchbinder, R. (2014). The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Annals of the rheumatic diseases*, 73(6), 968-974.
- Daniell, J. R., & Osti, O. L. (2018). Failed back surgery syndrome: a review article. *Asian spine journal*, 12(2), 372.
- Arseni C. Aldea H. Obreja Th. Hernia de disc lombara inferioara. Ed. Didactica si Pedagogica, Bucuresti, 1985. p.7
- Eisberg, C. A., & Beer, E. (1911). The operability of intramedullary tumors of the spinal cord. *Am J Med Sci*, 142, 636-647.
- Eisberg, C. A. (1931). The extradural ventral chondromas (ecchon-droses), their favorite sites, the lumbar spinal cord and root symptoms they produce, and their surgical treatment. *Bull Neurol Inst (New York)*, 1, 350-388.
- Putti, V. (1927). New conceptions in the pathogenesis of sciatic pain. *Lancet*, 2(July 9), 53-60.
- Mixter, W. J., & Barr, J. S. (1934). Rupture of the intervertebral disc with involvement of the spinal canal. *New England Journal of Medicine*, 211(5), 210-215.
- Weinstein, J. N., Lurie, J. D., Olson, P., Bronner, K. K., Fisher, E. S., & Morgan, M. T. S. (2006). United States trends and regional variations in lumbar spine surgery: 1992-2003. *Spine*, 31(23), 2707.
- Lieberman, I. H. (2004). Disc bulge bubble: Spine economics 101. *The Spine Journal*, 4(6), 609-613.
- Wenger, D. R. (2007). Spine surgery at a crossroads: does economic growth threaten our professionalism?. *Spine*, 32(20), 2158-2165.
- Deyo, R. A., & Mirza, S. K. (2006). Trends and variations in the use of spine surgery. *Clinical Orthopaedics and Related Research (1976-2007)*, 443, 139-146.
- Deyo, R. A., Gray, D. T., Kreuter, W., Mirza, S., & Martin, B. I. (2005). United States trends in lumbar fusion surgery for degenerative conditions. *Spine*, 30(12), 1441-1445.
- Burton, C. V. (2006). Failed back surgery patients: the alarm bells are ringing. *Surgical neurology*, 65(1), 5.
- Mark, V. H. (2004). Instrumented fusions: a need for guidelines and research. *Surgical neurology*, 61(4), 318-319.
- Pawl, R. (2008). Lumbar spinal surgery, where have we gone?. *Surgical neurology*, 6(69), 558-560.
- Martin, B. I., Mirza, S. K., Spina, N., Spiker, W. R., Lawrence, B., & Brodke, D. S. (2019). Trends in lumbar fusion procedure rates and associated hospital costs for degenerative spinal diseases in the United States, 2004 to 2015. *Spine*, 44(5), 369-376.
- North, R. B., Campbell, J. N., James, C. S., Conover-Walker, M. K., Wang, H., Piantadosi, S., ... & Long, D. M. (1991). Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. *Neurosurgery*, 28(5), 685-691.
- Wilkinson, H. A. (2012). *The failed back syndrome: etiology and therapy*. Springer Science & Business Media.
- Law, J. D., Lehman, R. A., & Kirsch, W. M. (1978). Reoperation after lumbar intervertebral disc surgery. *Journal of neurosurgery*, 48(2), 259-263.
- Lehmann, T. R., & LaROCCA, H. S. (1981). Repeat lumbar surgery. A review of patients with failure from previous lumbar surgery treated by spinal canal exploration and lumbar spinal fusion. *Spine*, 6(6), 615-619.
- Chan C. Peng P. (2011) Failed Back Surgery Syndrome. *Pain medicine* 12:577-606
- Thomson, S., & Jacques, L. (2009). Demographic characteristics of patients with severe neuropathic pain secondary to failed back surgery syndrome. *Pain Practice*, 9(3), 206-215.
- De Lissovoy, G., Brown, R. E., Halpern, M., Hassenbusch, S. J., & Ross, E. (1997). Cost-effectiveness of long-term intrathecal morphine therapy for pain associated with failed back surgery syndrome. *Clinical Therapeutics*, 19(1), 96-112.
- Fairbank, J. C., & Pynsent, P. B. (2000). The Oswestry disability index. *Spine*, 25(22), 2940-2953
- Voorhies, R. M., Jiang, X., & Thomas, N. (2007). Predicting outcome in the surgical treatment of lumbar radiculopathy using the Pain Drawing Score, McGill Short Form Pain Questionnaire, and risk factors including psychosocial issues and axial joint pain. *The Spine Journal*, 7(5), 516-524.
- Spengler, D. M., Freeman, C., Westbrook, R., & Miller, J. W. (1980). Low-back pain following multiple lumbar spine procedures: failure of initial selection?. *Spine*, 5(4), 356-360.
- Block, A. R., Gatchel, R. J., Dearthoff, W. W., & Guyer, R. D. (2003). The psychology of spine surgery. American Psychological Association.
- Celestin, J., Edwards, R. R., & Jamison, R. N. (2009). Pretreatment psychosocial variables as predictors of outcomes following lumbar surgery and spinal cord stimulation: a systematic review and literature synthesis. *Pain Medicine*, 10(4), 639-653.
- Mannion, A. F., & Elfering, A. (2006). Predictors of surgical outcome and their assessment. *European Spine Journal*, 15(1), S93.
- Bosacco, S. J., Berman, A. T., Bosacco, D. N., & Levenberg, R. J. (1995). Results of lumbar disk surgery in a city compensation population. *Orthopedics*, 18(4), 351-355.
- Klekamp, J., McCarty, E., & Spengler, D. M. (1998). Results of elective lumbar discectomy for patients involved in the workers' compensation system. *Clinical Spine Surgery*, 11(4), 277-282.
- Taylor, V. M., Deyo, R. A., Ciol, M., Farrar, E. L., Lawrence, M. S., Shonnard, N. H., ... & Goldberg, H. I. (2000). Patient-oriented outcomes from low back surgery: a community-based study. *Spine*, 25(19), 2445-2452.
- Waddell, G., Main, C. J., Morris, E. W., Di, M. P., & Gray, I. C. (1984). Chronic low-back pain, psychologic distress, and illness behavior. *Spine*, 9(2), 209-213.
- Nachemson, A. L. (1993). Evaluation of results in lumbar spine surgery. *Acta Orthopaedica Scandinavica*, 64(sup251), 130-133.
- Ross, J. S., Robertson, J. T., Frederickson, R. C., Petrie, J. L., Obuchowski, N., Modic, M. T., & deTribolet, N. (1996). Association between peridural scar and recurrent radicular pain after lumbar discectomy: magnetic resonance evaluation. *Neurosurgery*, 38(4), 855-863.
- Trescot, A. M., Chopra, P., Abdi, S., Datta, S., & Schultz, D. M. (2007). Systematic review of effectiveness and complications of adhesiolysis in the management of chronic spinal pain: An update. In *Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]*. Centre for Reviews and Dissemination (UK).
- Kayaoglu, C. R., Calikoğlu, C., & Binler, S. E. D. A. T. (2003). Re-operation after lumbar disc surgery: results in 85 cases. *Journal of international medical research*, 31(4), 318-323.

42. Jayson, M. I. (1992). The role of vascular damage and fibrosis in the pathogenesis of nerve root damage. *Clinical orthopaedics and related research*, (279), 40-48.
43. Onesti, S. T. (2004). Failed back syndrome. *The neurologist*, 10(5), 259-264.
44. Kumar, M., Baklanov, A., & Chopin, D. (2001). Correlation between sagittal plane changes and adjacent segment degeneration following lumbar spine fusion. *European spine journal*, 10(4), 314-319.
45. Scott Meyer, R., & Garfin, S. R. (2001). Recurrent lumbar disc herniation. *Mastercases: Spine Surgery. New York: Thieme*, 143-7.
46. Gejo, R., Matsui, H., Kawaguchi, Y., Ishihara, H., & Tsuji, H. (1999). Serial changes in trunk muscle performance after posterior lumbar surgery. *Spine*, 24(10), 1023-1028.
47. Kawaguchi, Y., Matsui, H., Gejo, R., & Tsuji, H. (1998). Preventive measures of back muscle injury after posterior lumbar spine surgery in rats. *Spine*, 23(21), 2282-2287.
48. Bosscher, H. A., & Heavner, J. E. (2010). Incidence and severity of epidural fibrosis after back surgery: an endoscopic study. *Pain Practice*, 10(1), 18-24.
49. Ross, J., Obuchowski, N., & Modic, M. (1999). MR evaluation of epidural fibrosis: proposed grading system with intra-and inter-observer variability. *Neurological research*, 21(sup1), S23-S26.
50. Bogduk, N. (1983). The innervation of the lumbar spine. *Spine*, 8(3), 286-293.
51. Dreyfuss, P., Schwarzer, A. C., Lau, P., & Bogduk, N. (1997). Specificity of lumbar medial branch and L5 dorsal ramus blocks: a computed tomography study. *Spine*, 22(8), 895-902.
52. Kaplan, M., Dreyfuss, P., Halbrook, B., & Bogduk, N. (1998). The ability of lumbar medial branch blocks to anesthetize the zygapophysial joint: a physiologic challenge. *Spine*, 23(17), 1847-1852.
53. Schwarzer, A. C. (1994). *The role of the zygapophysial joint in chronic low back pain*. University of Sydney.
54. Manchikanti, L., Boswell, M. V., Singh, V., Pampati, V., Damron, K. S., & Beyer, C. D. (2004). Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. *BMC Musculoskeletal Disorders*, 5(1), 15.
55. Merskey, N. (1994). Classification of chronic pain; Description of chronic pain syndromes and definitions of pain Terms. *Task force on taxonomy of the International Association for the study of pain*, 41-43.
56. Manchikanti, L., Manchukonda, R., Pampati, V., Damron, K. S., & McManus, C. D. (2007). Prevalence of facet joint pain in chronic low back pain in postsurgical patients by controlled comparative local anesthetic blocks. *Archives of physical medicine and rehabilitation*, 88(4), 449-455.
57. Attal, N., Cruccu, G., Haanpää, M., Hansson, P., Jensen, T. S., Nurmikko, T., ... & Wiffen, P. (2006). EFNS guidelines on pharmacological treatment of neuropathic pain. *European journal of neurology*, 13(11), 1153-1169.
58. Braverman, D. L., Slipman, C. W., & Lenrow, D. A. (2001). Using gabapentin to treat failed back surgery syndrome caused by epidural fibrosis: A report of 2 cases. *Archives of physical medicine and rehabilitation*, 82(5), 691-693.
59. Salerno, S. M., Browning, R., & Jackson, J. L. (2002). The effect of antidepressant treatment on chronic back pain: a meta-analysis. *Archives of Internal Medicine*, 162(1), 19-24.
60. Juratli, S. M., Mirza, S. K., Fulton-Kehoe, D., Wickizer, T. M., & Franklin, G. M. (2009). Mortality after lumbar fusion surgery. *Spine*, 34(7), 740-747.
61. Fishman, S. M., Wilsey, B., Mahajan, G., & Molina, P. (2002). Methadone reincarnated: novel clinical applications with related concerns. *Pain medicine*, 3(4), 339-348.
62. Dickerson, E. D. (2001). Methadone: the question or the answer for US opioid therapy and pharmaco-economics?. *Supportive Care in Cancer*, 9(8), 646-647.
63. Daeninck, P. J., & Bruera, E. (1999). Reduction in constipation and laxative requirements following opioid rotation to methadone: a report of four cases. *Journal of pain and symptom management*, 18(4), 303-309.
64. Parsons, C. G. (2001). NMDA receptors as targets for drug action in neuropathic pain. *European journal of pharmacology*, 429(1-3), 71-78.
65. Davis, A. M., & Inturrisi, C. E. (1999). d-Methadone blocks morphine tolerance and N-methyl-D-aspartate-induced hyperalgesia. *Journal of Pharmacology and Experimental Therapeutics*, 289(2), 1048-1053.
66. Turner, J. A. (1996). Educational and behavioral interventions for back pain in primary care. *Spine*, 21(24), 2851-2857.
67. Fors, M., Öberg, B., Lindbäck, Y., Enthoven, P., & Abbott, A. (2020). What Mediates Treatment Effects in a Pre-surgery Physiotherapy Treatment in Surgical Candidates with Degenerative Lumbar Spine Disorders? A Mediation and Conditional Process Analysis of the PREPARE Randomized Controlled Trial. *The Clinical Journal of Pain*.
68. Harvey, A. M. (1995). Classification of chronic pain—descriptions of chronic pain syndromes and definitions of pain terms. *The Clinical Journal of Pain*, 11(2), 163.
69. Van Tulder, M. W., Koes, B. W., & Bouter, L. M. (1997). Conservative treatment of acute and chronic nonspecific low back pain: a systematic review of randomized controlled trials of the most common interventions. *Spine*, 22(18), 2128-2156.
70. Hoffman, B. M., Pappas, R. K., Chatkoff, D. K., & Kerns, R. D. (2007). Meta-analysis of psychological interventions for chronic low back pain. *Health psychology*, 26(1), 1.
71. Hayden, J., Van Tulder, M. W., Malmivaara, A., & Koes, B. W. (2005). Exercise therapy for treatment of non-specific low back pain. *Cochrane database of systematic reviews*, (3).
72. Manchikanti, L., Manchukonda, R., Pampati, V., Damron, K. S., & McManus, C. D. (2007). Prevalence of facet joint pain in chronic low back pain in postsurgical patients by controlled comparative local anesthetic blocks. *Archives of physical medicine and rehabilitation*, 88(4), 449-455.
73. Manchikanti, L., Pampati, V., Fellows, B., & Bakhit, C. E. (1999). Prevalence of lumbar facet joint pain in chronic low back pain. *Pain physician*, 2(3), 59-64.
74. Manchikanti, L., Pampati, S., & Cash, K. A. (2010). Making sense of the accuracy of diagnostic lumbar facet joint nerve blocks: an assessment of the implications of 50% relief, 80% relief, single block, or controlled diagnostic blocks. *Pain Physician*, 13(2), 133-143.
75. Manchikanti, L. (2009). Accuracy of diagnostic lumbar facet joint nerve blocks: A 2-year follow-up of 152 patients diagnosed with controlled diagnostic blocks. *Pain Physician*, 12, 855-866.
76. Abdi, S., Datta, S., Trescot, A. M., Schultz, D. M., Adlaka, R., Atluri, S. L., ... & Manchikanti, L. (2007). Epidural steroids in the management of chronic spinal pain: a systematic review. In *Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]*. Centre for Reviews and Dissemination (UK).
77. Boswell, M. V., Hansen, H. C., Trescot, A. M., & Hirsch, J. A. (2003). Epidural steroids in the management of chronic spinal pain and radiculopathy. *Pain Physician*, 6(3), 319-334.
78. Manchikanti, L., Cash, K. A., Pampati, V., McManus, C. D., & Damron, K. S. (2004). Evaluation of fluoroscopically guided caudal epidural injections. *Pain Physician*, 7(1), 81.
79. Racz, G. B., Heavner, J. E., & Raj, P. P. (1999). Percutaneous epidural neurolysis: Prospective one-year follow-up. *Pain Digest*, 9, 97-102.
80. Epter, R. S., Helm, S., Hayek, S. M., Benyamin, R. M., Smith, H. S., & Abdi, S. I. (2009). Systematic review of percutaneous adhesiolysis and management of chronic low back pain in post lumbar surgery syndrome. *Pain physician*, 12(2), 361-78.
81. Manchikanti, L., Rivera, J. J., Pampati, V., Damron, K. S., McManus, C. D., Brandon, D. E., & Wilson, S. R. (2004). One day lumbar epidural adhesiolysis and hypertonic saline neurolysis in treatment of chronic low back pain: a randomized, double-blind trial. *Pain Physician*, 7(2), 177-186.

82. Veihelmann, A., Devens, C., Trouillier, H., Birkenmaier, C., Gerdemeyer, L., & Refior, H. J. (2006). Epidural neuroplasty versus physiotherapy to relieve pain in patients with sciatica: a prospective randomized blinded clinical trial. *Journal of Orthopaedic Science*, *11*(4), 365-369.
83. Kumar, K., Taylor, R. S., Jacques, L., Eldabe, S., Meglio, M., Molet, J., ... & Buchser, E. (2007). Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain*, *132*(1-2), 179-188.
84. McGivern, J. G. (2007). Ziconotide: a review of its pharmacology and use in the treatment of pain. *Neuropsychiatric disease and treatment*, *3*(1), 69.
85. Sanford, M. (2013). Intrathecal ziconotide: a review of its use in patients with chronic pain refractory to other systemic or intrathecal analgesics. *CNS drugs*, *27*(11), 989-1002.
86. Lindbäck, Y., Tropp, H., Enthoven, P., Abbott, A., & Öberg, B. (2018). PREPARE: presurgery physiotherapy for patients with degenerative lumbar spine disorder: a randomized controlled trial. *The Spine Journal*, *18*(8), 1347-1355.
87. Kumar, K., North, R., Taylor, R., Sculpher, M., Van den Abeele, C., Gehring, M., ... & Jacobs, M. (2005). Spinal cord stimulation vs. conventional medical management: a prospective, randomized, controlled, multicenter study of patients with failed back surgery syndrome (PROCESS study). *Neuromodulation: Technology at the Neural Interface*, *8*(4), 213-218.
88. Swanson, K. I., Smith, K. A., Mirzadeh, Z., Ponce, F. A., Heck, C. N., King-Stephens, D., ... & Piantadosi, S. A. (2019). Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Operative Neurosurgery*, *17*(Supplement_1), S209-S228.
89. Cho, J. H., Lee, J. H., Song, K. S., Hong, J. Y., Joo, Y. S., Lee, D. H., ... & Lee, C. S. (2017). Treatment outcomes for patients with failed back surgery. *Pain physician*, *20*(1), E29-E43.
90. Winkelmüller, M., & Winkelmüller, W. (1996). Long-term effects of continuous intrathecal opioid treatment in chronic pain of nonmalignant etiology. *Journal of neurosurgery*, *85*(3), 458-467.