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Vucemilovic, Filip Bartolomeo

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**UNIVERSITY OF SPLIT
SCHOOL OF MEDICINE**

Filip Bartolomeo Vucemilovic

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FROM 2013-2018 AT THE DEPARTMENT OF NEUROSURGERY AT UNIVERSITY
HOSPITAL OF SPLIT, CROATIA**

Diploma Thesis

Academic year:

2018/2019

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Assist. Prof. Željko Bušić, MD, PhD

Split, September 2019

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1. Introduction

1.1. Defintion

Failed back surgery syndrome (FBSS) is a clinical pathological condition characterized by lumbar spinal pain of unknown origin. This pain either persists despite surgical intervention or appears after the original surgical intervention for spinal pain of the same topographical location. FBSS is becoming increasingly frequent, whose etiology is most likely attributed to the modern 21st century lifestyle. However, it still remains a poorly researched disease (1). In literature, the rate of failed back surgeries is said to be prevalent from 10% to up to 40% (2). In order to establish an accurate diagnosis, three key clinical investigations should be performed; history, physical examination, and imaging. A thorough patient history and physical examination is essential not only to accurately establish a differential diagnosis, but also to determine the location and exact cause of pain. This also gives the physician an idea of the patient's socio-economic background, a factor which is later discussed as an important predisposing factor (3). The MRI is the gold standard imaging study for the final diagnosis (4). Computed Tomography (CT) can also be used in situations where there are contraindications for the MRI, such as implants, i.e. pacemakers (5).

1.2. Anatomy

The spine consists of 33 vertebrae. There are 7 cervical vertebrae, 12 thoracic, 5 lumbar, 5 vertebrae that are fused that form the sacrum, and 5 fused vertebrae that form the coccyx. Each vertebra has certain architecture which has specific and multiple roles. From providing insertion points for muscles, attaching and supporting the torso, to providing cushion from compressive forces via the intervertebral discs, these roles are key to a functioning spine (6). However, arguably one of the most important roles is to protect the spinal cord, which is the extension of the central nervous system. Each vertebra is made out of three main parts. The largest component is the body, which lays in contact with the gelatinous intervertebral disc. The second part is the arches which surround the spinal cord. Lastly, the arches are the processes which protrude outwards, allowing for muscle and ligament attachment. Altogether, this is one body, one spinous process, two superior facets, two inferior facets and two transverse processes (6).

The cervical vertebra's main function is to support the head which weighs approximately ten pounds (5 kg). The cervical vertebrae have the greatest range of motion due to the first two vertebra which connects to the skull. The atlas (C1) and axis (C2) allow the head to move upwards and downwards along the horizontal axis in a nodding motion and left to right along the vertical axis in a "no" motion.

The thoracic vertebrae's main function is to be the anchoring point for the ribs. Together the thoracic vertebrae and the ribs work synergetically to protect the vital organs found in the thorax, such as the heart and lungs. The overall range of motion is limited in the thoracic vertebrae: they permit decent rotation along the vertical axis and even slighter rotation around the horizontal axis.

The main purpose of the lumbar spine is to bear most of the body's weight and to accommodate for daily activities, such as carrying heavy objects. Additionally, it is known to absorb stress. Due to this role, the lumbar vertebrae are larger in size when compared to the cervical or even thoracic vertebrae.

The role of the sacrum is quite unique. Since the sacrum is a structure made out of the fusion of 5 vertebrae, it has absolutely no mobility. Its task is to connect the spine to the hip bones and to protect the contents of the pelvis (6).

The Coccyx, even though small in size, plays an important role as a stabilizer for the pelvic floor. The 5 fused vertebrae provide a place for the pelvic ligaments and muscles to attach to (7).

Each mobile vertebra is cushioned and separated by individual disks. These intervertebral disks have a tough outer exterior called the annulus, and a soft internal gel-filled compartment called the nucleus (6). The annulus has intersecting fibrous bands which may resemble a tire tread. They play two major roles; one is to keep the nucleus from leaking out, and the other is to provide part of the cushioning. The nucleus similarly provides cushioning, but it does this in a special way. The gel-like structure allows the nucleus to evenly distribute the compression to prevent the disc from unevenly deforming, risking herniation. Throughout the day it is compressed by the gravitational forces acting on the body, and during the night it expands as the body lies in the horizontal position (6).

The spinal cord, which passes through the spinal canal, is approximately 18 inches in length and 15 to 27 mm in diameter (7). Just as the spinal cord thins as it extends caudally, so too do the cervical to lumbar spinal canals also change in diameter to accommodate. The spinal cord is an extension of the brain as the brain stem and extends all the way to the first

lumbar vertebrae. Therefore, it is also known as a part of the central nervous system. After L1, the spinal cord ends as the conus medullaris, and only the nerve roots continue to extend as the cauda equina. Therefore, the cauda equina, since it comprises of dorsal and ventral nerve roots, is part of the peripheral nervous system. It branches off through the sacrum and extends into the legs and feet.

There are thirty-one pairs of spinal nerves branch off the spinal cord. Each spinal nerve is derived from a pair of spinal roots after they have come together and passed the foramina, carrying impulses to or from the brain for motor or sensory stimuli. It is the posterior, dorsal roots, that carry the sensory information from the body back up to the brain, while the ventral roots carry motor stimuli to muscles (7).

Just as is the brain, the spinal cord, too, is covered by protective layers called the meninges. Looking from interior to exterior, they are known as the pia, arachnoid, and dura mater. The inner layer, the pia mater, is intimately attached to the spinal cord. As mentioned, the following layer is the arachnoid mater, with a gap between the pia and the arachnoid, known as the arachnoid space. Within this space flows cerebral spinal fluid, therefore this space is commonly accessed for diagnostic procedures, such as a lumbar puncture. Also, during myelograms, a contrast dye is injected into the arachnoid space. The final covering is the tough external layer called the dura mater (Figure 1). Between the dura and the vertebral body is the epidural space. This space contains fat and blood vessels, and anesthesia and steroid injections are delivered here when indicated (7).

Meninges of the Spinal Cord

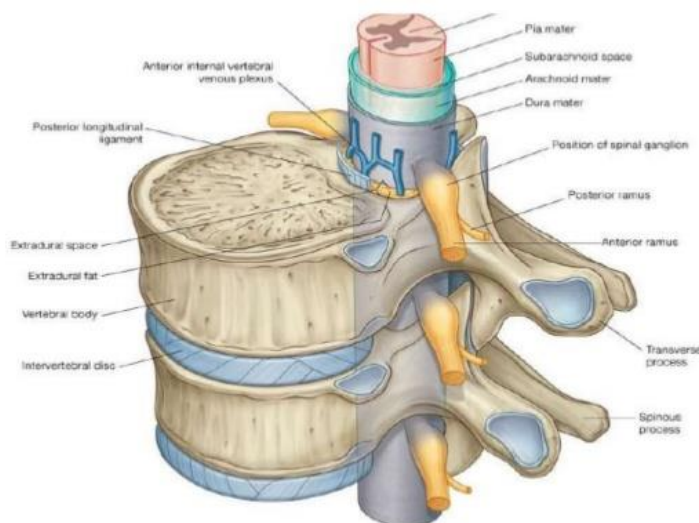


Figure 1: Anatomy of the vertebrae and spinal cord

Source: <https://www.slideshare.net/mrinaljoshi3/spinal-cord-and-applied-aspects-of-spine>

The movement, stability, and protection that is provided to the spine come from the ligaments, tendons, and muscles which are connected to the vertebrae (8). The ligaments play a vital role in controlling the extent of motion the vertebrae can exert by preventing hyperextension or hyperflexion. The major ligaments which provide support and protection to the vertebrae are the anterior and posterior longitudinal ligaments (located on the anterior and posterior of the vertebral body), supraspinous ligament (spinous processes), ligamentum flavum (runs from the base of the skull to the pelvis going in-between and anterior of the lamina), and the interspinous ligament (in-between the spinous processes and connecting to the ligamentum flavum) (8).

The two main subgroups which make up the spinal muscles are the extensors and flexors. Properly toned muscles are extremely important to have a healthy spine. A large abdomen or a poorly developed musculature can result in improper positioning of the spine, such as kyphosis or lordosis (abnormal amount of thoracic and lumbar spinal curvature), along with a lateral curvature of the spine known as scoliosis. The major extensor muscles are longissimus thoracic, iliocostalis thoracis, and spinalis thoracis. Their roles are in rotation and extension of the torso. The flexor muscles which are connected to the spine consist of the

psoas major, quadratus lumborum and multifidus muscle. Other examples of flexors are the rectus abdominis muscles, however, they do not directly connect to the spinal vertebrae (8).

1.3. Epidemiology

Lower back pain has become synonyms to daily life for most people around the world. In fact, it is prevalent up to 80% of the global population. Of this 80%, only 10% have chronic pain, meaning lasting for more than three months (3). Therefore, it is no surprise that over the past few decades, there has been a drastic increase in spinal surgeries. In 1997, in the United States, were 317,000 reported cases of lumbar surgeries whose costs exceeded the total of \$4.8 billion.

A few years later, in 2002, there were a total of 1 million spinal procedures of which 400,000 were instrumental (9-12). In 2004, spinal fusion by itself generated costs of \$16 billion (12). These statistics show a rapid increase in the rate of spinal surgeries. This is concerning due to the fact that there is an absence of concise demographics that could indicate the cause of such a rapid rise (13). A paper published in 2012 discussing the impact of failed back surgery syndrome concluded that “our understanding of the epidemiology of FBSS remains poor, and is, therefore, an important area for further research” (14).

The prevalence of FBSS in society is found in similar rates as is rheumatoid arthritis. It is 10 times more common than complex regional pain syndrome, 10 times less common than fibromyalgia, and 100 times less common than osteoarthritis (15). In the UK, neuropathic leg and back pain is found in 5,800 of every 100,000 people (16). Therefore, in England and Wales combined, there are 405,115 people suffering from neuropathic pain of which many could be classified under the broad definition of FBSS (15).

1.4. Leading factors of etiology

There is a variety of factors which could be attributed to causing FBSS. They can be divided into pre-operative, surgical, and post-operative factors.

1.4.1. Pre-operative factors

There exist many pre-operative factors which can affect FBSS. Such factors include the accuracy of diagnoses, socioeconomic, behavioral, and psychological factors. These pre-operative, or better dubbed, patient factors, have shown to have a particularly strong impact on the outcome of spinal operations. An important factor is lifestyle habits. An example of this is asserted by a prospective cohort study conducted by Michaëlsson, Försth, Sandén *et al* in 2011, which compared smokers and non-smokers after surgery for spinal stenosis. The study used a significant number of 4,555 patients, making the study a reliable source. Their study showed that those who smoked (17%) had a significantly weaker ability to walk, increased use of analgesics, and overall poorer quality of life after two years (17). Smoking itself has shown to also influence even post-surgical variables, including the rate of wound healing and infection. It has also shown a greater increase in the rate of non-union after spine fusion (81,82). Smoking is not the only factor that influences both pre and post-operative states. The addition of comorbidities such as obesity and emotional and psychological instability are also known factors (18,19).

Prior to the patient being cleared for surgery, an assessment should be performed for their psychological, behavioral, and socioeconomic state. This assessment is implemented due to the fact that individuals from lower socioeconomic backgrounds have shown to have an increased risk of having FBSS compared to their counterparts (20,21). Multiple studies have identified a positive correlation between patients who are clinically depressed and those with FBSS. In fact, depression is one of the most influential indicators for an unfavorable outcome following spinal surgery. Generally, clinically depressed patients have been found to be weaker, feel more pain, and require a longer recovery time before returning to work. This makes it vital for surgeons to assess their patients beforehand for signs of anxiety, depression, and other social and psychological factors (22,23).

1.4.2. Surgical factors

Recurrent surgeries, in general, have shown to have a lowered rate of success (24). According to a review article by Daniell JR and Osti OL, 50% of the first spinal surgeries are

considered performed successfully. However, after repeating surgeries two or more times, the percentage of successful operations drop to 30% after the second surgery, 15% after the third surgery, and 5% after the fourth attempt. This indeed shows us that as more invasive treatments are attempted the less optimistic both the patient and the surgeon can be on its outcome (3). One might conclude that the greater the number of spinal surgeries, the more frequently incurred risks for failure (25). Another study which supported the findings mentioned above suggested that the results were due to the differences in selection criteria for surgical patients and those not yet candidates for surgical intervention (25). Meaning that those patients who were in better condition were not surgical candidates and thus had more potential to heal because they condition originally was not as critical.

In addition to this, a number of other surgical factors further increase the risk for an unsuccessful outcome. Examples of these include a poor technique or even performing surgery on the incorrect location (5). Unfortunately, it is quite often that the surgical decompression was undertaken at the incorrect level (26). With each new surgery, there is a potential to create more instability and to cause or even accentuate pain due to incorrect spinal fusion (26). One study followed 105 patients who had lumbar fusion with a pedicle screw. Its results showed that there was a 6.5% to 12.0% incidence of error in screw placement, leading to implant breakage. This error can risk life-altering neurological complications (27).

1.4.3. Post-operative factors

Just like in the pre-operative and surgical factors of etiology, there are be many complications occurring in the post-operative period that may lead to FBSS. These can be separated into early and late complications.

Early complications comprise of hematoma formation, infection, and nerve injury. Hematomas form due to mechanical damage caused by the operation and can be found in the epidural or subdural spaces. They are quite commonly found, however, in most cases they show no major problems (28). Infections, on the other hand, continue to be a common cause of morbidity. The Scoliosis Research Society made a review of the morbidity and mortality rates of spinal surgery from 2004 to 2007. They managed to collect a total of 108,419 cases and found that the overall infection rate was 2.1%. Of this 2.1%, superficial wounds consisted of 0.8%, and the rest 1.3% comprised of deep wound infections. In conclusion, they

concluded that wound infections are an inherent risk which cannot be always avoided, even amongst the very skilled of spinal surgeons (29). Nerve injuries are one of the most significant complications which accompany FBSS. They have causative multiple factors, from epidural fibrosis and residual stenosis to synovial cysts, instability, and internal disk disruption. The main origin for nerve injury can be difficult to pinpoint even if using magnetic resonance imaging or neurophysiological studies (30).

The late complications of failed back surgery syndrome could also be comprised of multiple factors. The continuation of the pain may be caused by further spinal column degeneration or by biomechanical changes which undergo within the region of the operation, leading to compensatory loading by the adjacent muscles. The transfigured biomechanics are caused by the increase in tension of the paravertebral and post vertebral muscles (31). This elicits spasms, stiffness, inflammation and fatigue, causing symptoms of muscle pain. This change in weight-bearing is generally caused by damage to the muscles during surgery from incorrect dissection and retraction. This problem can be avoided by taking an anterior approach (32). Other characteristics of biomechanical changes can be seen as a fusion of the lumbar spine to the sacrum, increased rate of degeneration superiorly and inferiorly to the fusion, as well as sacroiliac joint disease caused by the fusion of multiple segments (33,34). Also, pathologies such as facet arthropathy can be seen, for as it degenerates it causes foraminal stenosis. Due to the changes in weight-bearing, there could also be central or foraminal stenosis caused by disc herniation or disc degeneration (31). Of course, just as in most other surgeries, post-surgical adhesions, more specifically epidural adhesions, must also be considered (10).

1.5. Differential diagnosis

In patients who have never undergone back surgery, the most common cause of back pain is associated with discogenic pain syndrome, a condition in which one or multiple intervertebral discs is the source of pain. This is followed by facet and sacroiliac joints as the cause of pain (36). In the majority of patients, the etiology can be easily confirmed after careful testing. However, when the matter at hand is FBSS pain, there is a number of differential diagnoses to consider. The most common differential is epidural fibrosis, which leads to neuropathic back pain. Moreover, the diagnosis of FBSS in its-self relies heavily on the patient's history. The immediate examination should rule out more serious conditions such

as infection, malignancy, or cauda equina syndrome. The goal must be to exact the cause of failure in order to efficiently treat the pain. Fortunately, around 95% of FBSS patients are usually provided with a definitive diagnosis for their back pain (3,37,38).

Even before the original surgery, the correct diagnosis needs to be established to ensure the possibility of success. A number of studies have found that up to 58% of diagnosed FBSS cases were found to be a misdiagnosed lateral stenosis of the spinal cord. These misdiagnoses expose the patient to health risks due to wrong or unnecessary procedures (39). Several other conditions have been commonly misdiagnosed as FBSS, one of which includes foraminal stenosis. This is a condition which is often misdiagnosed as back pain from the entrapment of the superior cluneal nerve (39,40).

1.6. Prognosis

FBSS in itself is a difficult diagnosis, for both the patient and the clinician. Throughout the years, the failure rate for spinal surgery has not decreased sufficiently. In fact, it has increased due to the increase in the number of procedures undertaken within the last decade. Due to this dilemma, the medical community proceeded to do high-quality trials to address the issue. They aimed to clarify whether surgery is the most appropriate treatment for those suffering from persistent pain from a spinal origin. Additional factors considered were patient selection criteria, the efficiency of psychological interventions for higher-risk patients, and which are the appropriate spinal surgical procedures if ultimately undertaken. Once these factors and criteria were well studied, the assumption is that the rate of FBSS would dramatically decrease.

It is important for the patient with FBSS to be approached with the interdisciplinary care model for pain control and function improvement. It is vital for the patient's psychological wellbeing in order for them to recover and get back on their feet and into their original social roles. Unfortunately, even with interdisciplinary care and a careful approach, some patients will not improve and will need possible interventional therapies such as spinal cord stimulation (SCS) and adhesiolysis. These two interventional approaches are being considered more often in the treatment of FBSS. More research is still required for other forms of therapy such as intrathecal drug delivery systems (5).

In conclusion, interventional therapies cannot be considered first-line treatments. They hold a multitude of risks such as equipment problems or adverse effects. They are good approaches to consider when all conservative measures have failed or in situations where the patient was contraindicated for a conservative approach. Figure 2. depicts a flow chart explaining the algorithm for assessing patients for surgical or conservative approaches. As mentioned earlier, careful attention must be placed on patient history and examination. The patient should be asked to describe the pain, and whether it is different from the pre-surgical pain. Additionally, effort should be placed to assess the patient's psycho-social status, and whether an approach with psychological or occupational therapy should be attempted (5).

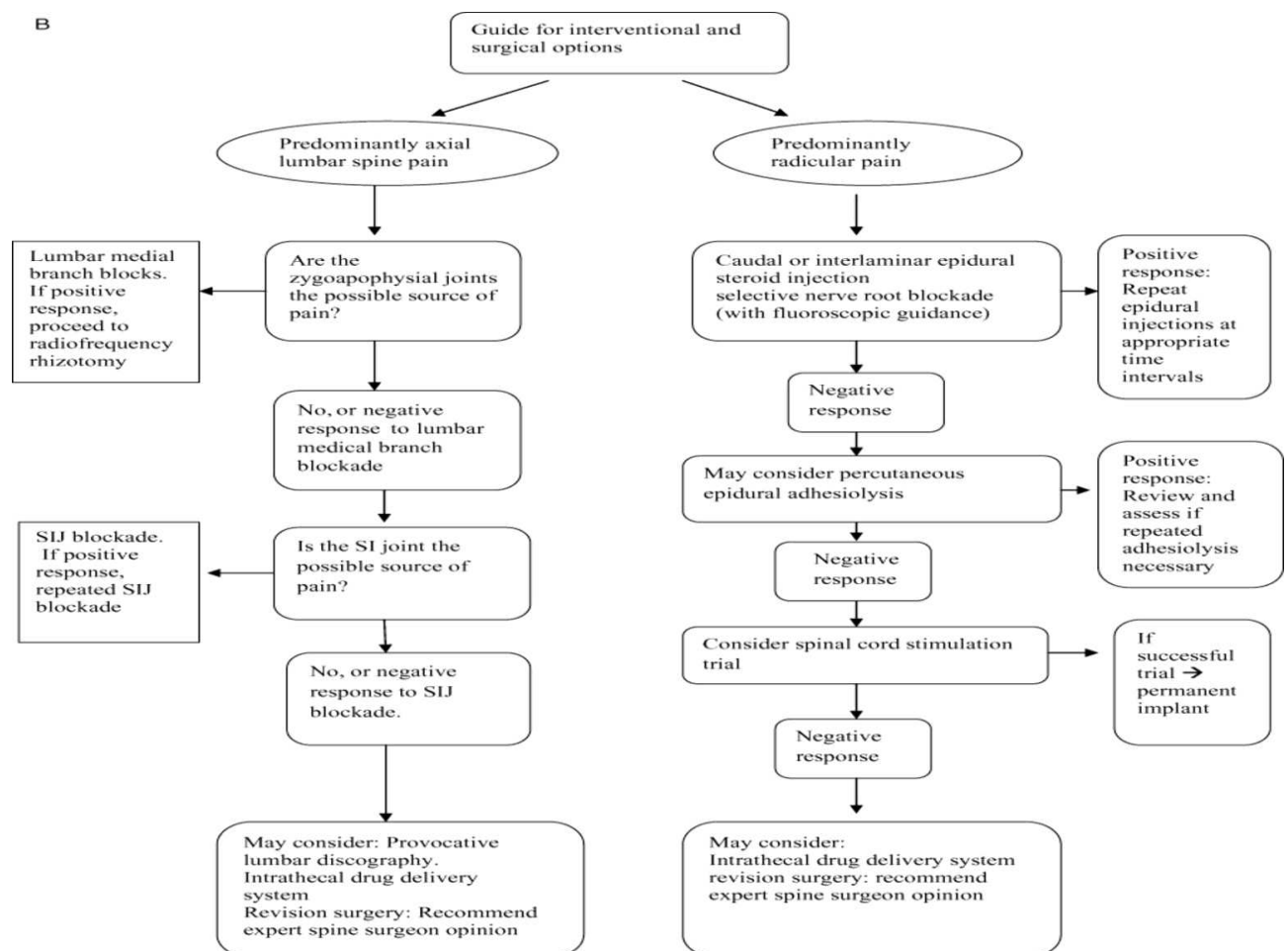


Figure 2. Algorithm to show the approach for the assessment of patients to determine whether they require a surgical or conservative approach.

Source: <https://academic.oup.com/painmedicine/article/12/4/577/1868602>

1.7. Methods of treatment

1.7.1. Surgical

There are various approaches when resolving lower back pain, however, this study will focus mainly on laminectomies, hemilaminectomies and microdiscectomies.

1.7.1.1. Laminectomy

A laminectomy is a surgical approach to decompression and used to be the primary treatment for nerve impingement. Currently, the approach to nerve impingement are microdiscectomies which will be talked about later on. Common ailments that may require a laminectomy for treatment are a prolapsed disc, a tumor, or age-related vertebral changes. The number of laminectomies is rapidly increasing over the years. From 1988 to 2008 they increased by 11.3%; from 92,390 to 107,790 (41). They can be performed under general anesthesia, using spinal block, or even with local anesthesia. The latter is becoming frequent as new techniques are being developed (42). By removing the lamina (arches) of the vertebra, it allows for the release of the pressure which was placed on the nerve. It must not be forgotten that inflammation could have been the cause of the pressure buildup

Just as in any procedure, there are certain risk factors associated with the operation itself. These may range from bleeding, infection, blood clots in the lungs and legs, to spinal cord injury and problems brought on by the anesthesia. Furthermore, the damaged nerves and vessels may cause weakness and numbing (43). After a laminectomy, in order to increase the stability of the vertebrae, spinal fusions are often performed. This involves taking a bone graft from another location in the body and making a “bridge” which connects the separated parts of the vertebrae. This is a so-called “living” bone graft which additionally helps instability by encouraging new bone growth. Similar methods may use rods, wires, hooks, plates or screws, in order to mechanically provide support (44).

There is another set of possible complications that may occur even after being discharged, and the patient is recovering at home. Firstly, it is quite important to keep the surgical site dry and clean (42). The patients must be vigilant for signs of infections or complications, such as fever, redness, bleeding, swelling, increased pain around the surgical

site, numbness, trouble urinating, or loss of bladder control (42). It is also important for practitioners to prescribe the proper pain medications. It must be kept in mind that the muscles which might have been affected in surgery must be allowed to relax, or it may risk bleeding in the local region.

The surgery has a multitude of possible complications, and there is no guarantee of success. This may put the patient in a situation where he/she is immobile for a longer period of time, or even in a worse state than originally. This is why any invasive method should not be the primary intervention for these patients. The patients must first attempt other methods of treatments. These include physiotherapy, activity changes, muscle relaxants, anti-inflammatory drugs, pain relievers, spinal injections, occupational therapy, weight loss (if necessary), smoking cessation, or mechanical back support (42).

After the patient has attempted a number of these conservative therapies and still has problems/pain, he/she may be a candidate for invasive treatment. There are serious conditions, however, in which the patient is not recommended to continue pursuing conservative treatments, but is immediately indicated for surgery. These conditions are an increase in severity, restrictions to normal daily activities, worsening of bladder control, and a sudden change inability to walk (unsteady or clumsy). It is important to note that even if imaging studies show an increase in pressure on the spinal cord or nerves, the results should not be an indication for surgery alone. The patient as a whole should be looked at (43).

1.7.1.2. Microdiscectomy

Traditionally, discectomies were performed by largely invasive surgeries in which the surgeons would make large incisions. By affect of these incisions, muscles of the back would be cut to approach the spine. Not only did these invasive surgeries cause severe muscle damage, but also were associated with slow and painful recoveries (83).

In attempt to cause lesser damage, less invasive procedures have been created. Compared to the discectomies, microdiscectomies require smaller incisions, and with special instrumentations can operate on the spine. In microdiscectomies, small parts of the lamina and

portions of the intervertebral disc can be removed. This less invasive procedure reduces the overall injury, leading to a quicker and less painful recovery.

The procedure is normally performed under general anaesthesia while the patients are in the prone position. Surgeons aim to remove the section of the disc which is pressing on the spinal cord or nerve. This means that only part of the disc is removed, and rarely do the surgeons remove majority or all of the disc. Most microdiscectomies last an hour long, and patients tend to fully recover within two weeks. Overall, a microdiscectomy should accomplish the same as a tradition open discectomy, but with less damage, pain, and with a faster recovery (83).

1.7.1.3. Hemilaminectomy

Hemilaminectomies differ from laminectomies from the that fact that when preformed, the surgeon only removes one of the two laminae of a vertebrae. This is done to alleviate excess pressure which is on the spinal nerve resulting from either a physical impingement or inflammation in the lower back. Hemilaminectomies tend to be preformed to alleviate either back pain or radiating leg pain.

1.7.1.4. Transforaminal lumbar interbody fusion

Transforaminal lumbar interbody fusion also known as TLIF is a modern techqniue used in spinal surgery (84). It is primarily indicated for degenerative disc disease, spondylolisthesis of low grade, and re-operation for disc herniation, particularly when an interbody fusion and posterior decompression is needed. A large advantage of TLIF is that it allows for a complete removal of the intervertebral disc trough a posterior transforminal approach when performing the decompression of the vertebral foramen and spinal canal. Additionally, through an access point lateral to the nerve root, it has a minimum risk of a neural lesion (84).

1.7.2. Conservative management

The initial approach to FBSS should normally be conservative. Only when all of the measures have been exhausted should the patient be advised to consider more aggressive and invasive procedures. There is one exception for the patients who may have any emergent symptoms. Physical therapy and pharmacological management are the cornerstones of first-line management of FBSS. Physical therapy can help the patient optimize gait and posture, and can improve muscle strength and physical function (8,42). Other conservative measures that may help postoperative back pain involve psychotherapy measures including stress reduction and cognitive behavioral therapy (43). Finally, noninvasive procedures including acupuncture and scrambler therapy can be used to minimize the pain associated with FBSS (44,45). These conservative measures should be done in conjunction with pharmacological management to optimize pain relief.

1.7.2.1. Pharmacological management

The main goal of medication treatment is to give the patient an opportunity to exercise and progress with their physical therapy without the debilitating effects of pain (44).

Generally, the choice for analgesics is similar to other pain-related syndromes. The patients are either prescribed a non-opioid or an opioid-based therapy. Considering there exist major side effects to each category of drugs, there exists a debate which is to be implemented. The American Pain Society published a study comparing multiple drugs and assessing their benefits and harm (44). The group studied included acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, benzodiazepines, antiepileptic drugs, skeletal muscle relaxants, opioid analgesics, tramadol, and systemic corticosteroids for acute or chronic low back pain (with or without leg pain) (44).

In most situations' acetaminophen, NSAIDs and COX-2 inhibitors are the common forms of therapy (45). A Cochrane review found that anti-inflammatory medications are effective for the short-term relief of symptoms in patients with chronic or acute lower back pain with sciatica. It is important to keep in mind that there is a statistically higher rate of

gastrointestinal and renal adverse effects associated with these medications when comparing to the placebo. Due to these side effects, these medications are not favorable in the long run (46,47,48,49,50).

Tramadol, an opioid pain reliever, showed to be moderately more effective than its placebo counterpart when considering short term pain and functional status after 4 weeks (51). However, there are no long-term studies that have followed the effects of Tramadol for more than 8 weeks (51,52).

The function and benefits of anti-depressants for chronic lower back pain has been well documented, but show no major improvement in function. In addition, antidepressants show a significant increase in side effects when compared to its placebo. The most common associated side effects were dry mouth, constipation and dizziness (52). Although the effectiveness has not been officially tested for the use in FBSS, they are still commonly prescribed for the radicular or neuropathic chronic pain (53). Common examples of these are gabapentin and tricyclic antidepressants. The European Federation of Neurological Society recommends them as first line therapy in the most of neuropathic pain conditions, but excluding trigeminal neuralgia (53). Case reports have shown quite promising data on the efficacy of gabapentin monotherapy in its ability to reduce pain and more importantly the function of patients with FBSS. All together with the decreased need for monitoring and number of side effects, gabapentin has become a favorable option (54).

Recognized by various pain societies, opioid analgesics are considered safe and effective in the management of moderate to severe chronic non-cancer related pain (44,45,48,49,50). Opioids are can be for their direct effect of reducing pain, so as to provide the patient with a pain-free environment especially when working on their physical therapy (36). Yet, there is an existing controversy over its efficacy vs the risks of side effects and potential for addiction (55). The Canadian Pain Society published a consensus statement making it a legitimate medical practice to prescribe opioids for the purpose of chronic noncancerous pain relief (56).

A Cochrane systematic review on “Long-term opioid management for chronic non-cancer pain,” stated results on efficiency with opioids applied orally, transdermally and intrathecally (57). Each trial showed a statistically significant reduction of pain with all three modes of application. However, the amount of pain relief could not be considered because it varied from study to study (57). Many of the patients stopped opioid therapy, either because

of adverse side effects or from inadequate analgesia. Therefore, the systematic review had inconclusive results concerning the quality of life data and functional status. Ultimately, it was concluded that there is only a weak association with long-term opioid treatment and pain relief. No recommendation on a specific opioid was mentioned (57).

1.7.2.2. Exercise therapy/physiotherapy

The weak musculature which might have caused FBSS is further compromised following surgery (e.g., paraspinal muscles, transverse abdominal muscles). A longer period of bed rest in the hospital may cause those muscle to further atrophy. Though there are multiple different techniques, the general goal is to ensure stability, reduce mechanical stress on spinal structures, improve fitness, improve posture, and decrease pain (58). This may drastically improve the psychological state of the patient by giving them a sense of control over their pain.

In the case of chronic low back pain (CLBP), multiple studies have confirmed that physiotherapy had a mild to moderate positive effect on pain reduction compared to no treatment. One study in 2004 found that patients after exercise therapy had a considerable increase in return to work after the 1-year mark, along with a decrease in sick leave (59).

No study has been able to confirm a specific program which would be better compared to other exercise programs. However, certain elements seem to be frequently mentioned as efficient (60). These elements include stretching and strength training. But still, it should remain a personalized approach. One study did conclude, however, that aerobic exercises, in particular, had better results compared to other forms of exercise (5,58).

1.7.2.3. Psychological therapy/ cognitive behavioral therapy

As mentioned earlier, there are many psychological factors encompassed within FBSS and chronic lower back pain. Depression and anxiety that normally follow a life of chronic pain, must be dealt with in psychological therapy. This in return will give the patient more

motivation to continue with their therapy for physical recuperation, promoting faster recovery (61).

Other than prescribing anti-depressants, there are other non-pharmacological approaches to psychological therapy. By setting proper goals and well defining the strategy, they can practice relaxation skills, perform visual imaging, and attempt desensitization (62). Hoffman *et al.* discussed in a systemic review of psychological interventions for CLBP. It was concluded that cognitive-behavioral and self-behavioral therapy treatments were found to be particularly efficient. It was highlighted in the review that interdisciplinary care is necessary and it proves to efficiently benefit the patient both in short term and longer-term results (5,63).

1.7.3. Interventional management

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

1.7.3.1. Medial branch blocks and radiofrequency neurolysis

In cases of CLBP, the origin may sometimes be found at the zygapophysial joints. This may be diagnosed by performing a medial branch block using local anesthesia. A successful outcome may be considered if 80% of the pain has regressed after administering the treatment twice (62,65). 16% of pain in patients with FBSS meet these criteria, thus the origin of pain originated in the facet joints (66). In this subset of patients, radiofrequency neurotomy may be particularly effective in producing sustained analgesia. There is shown a 90% pain reduction in 60% of patients, and a 60% pain relief in 87% of patients after a 12-month follow-up (5,64,65).

1.7.3.2. Epidural injections

One of the oldest forms of therapy for radicular pain of the spine is steroid epidural injections (66). The pharmacological mechanism behinds epidural corticosteroids are still not fully understood, however, the proposed mechanism of action is via a sodium channel blockade (67), an anti-inflammatory effect, and a reduction of vascular permeability. Epidural steroids may be implemented for a variety of uses such as epidural fibrosis, disc herniation, spinal stenosis, and disc disruption. This makes it a key method when treated the many pathologies associated with FBSS (68).

There exists strong evidence to support interlaminar epidural steroid injections for short term relief of lumbar radicular pain. However, limited information exists to support this therapy for long-term benefits. Caudal epidural steroid injections, on the other hand, have both a strong short-term relief and a moderate long term relief for both chronic lumbar radicular pain and radicular pain associated with FBSS. Transforaminal epidural steroid injections, too, have shown to have a short- and long-term results for lumbar root pain, but only in patients with CLBP but less in patients with FBSS (66). One study using the transforaminal route for steroid injections had over 50% pain reduction, but in only 27% of the patients after a 6-month follow up

Patients with FBSS compared to those with CLBP not surgically treated, have certain anatomical differences which must be taken into consideration before performing epidural injections. Damage or anatomical alterations caused by instrumentation, or epidural fibrosis can cause the surgeon difficulty when performing the injections. There is an additional risk of dural puncture which occurs at a rate of 20%. For these reasons, most authors recommend fluoroscopic guidance along with the caudal approach to better perform under these conditions. However, even with the proper radiological equipment, a risk remains that the medication did not arrive at the intended location. One study performing interlaminar epidural injections under catheter guidance had only a success rate of only 26% (5,69).

1.7.3.3. Percutaneous epidural adhesiolysis

As mentioned above, a common occurrence after spinal surgery is epidural fibrosis. Some studies have claimed that this may cause up to 36% of cases of FBSS (70). As mentioned earlier, epidural adhesion may hinder the ease of application of epidural injections. In response, percutaneous epidural adhesiolysis is a technique which decreases the amount of epidural fibrotic tissue and thus improves local medication administration (71). A systematic review found strong evidence for both short-term and long-term benefits, meaning for over to a 6-month period. It is hypothesized that adhesiolysis is a superior treatment to epidural injections, because the catheter tip is placed within the fibrosis, and therefore expands the epineural space. This expansion allows for the medication to reach the targeted lesion site. The review recommends that percutaneous epidural adhesiolysis should be implemented in cases of FBSS in which the patient has failed conservative measures such as epidural injections (5,72).

1.7.3.4. Spinal cord stimulation

Spinal cord stimulation (SCS) is a procedure where electrodes are placed within the epidural space. These electrodes give off an electrical current made by a pulse generator placed subcutaneously (73). The analgesic effect produced by SCS is thought to work by a gate control mechanism which modulates the dorsal root, controlling inhibitory and excitatory neurotransmitter release (74). At first, this therapy was reserved for patients who have failed other means of treatment (75). Today, it is shown to be well suited for cases of FBSS from radicular pain. SCS has shown little use for axial or nonradicular pain. If a patient successfully meets inclusion criteria, he or she may have a permanent SCS implanted. The inclusion requirements established by the American Academy of Pain Medicine are (86):

- The patient reports 50% or more pain relief after SCS.
- The pain relief provided by SCS continues even after being exposed to challenging physical therapy.
- The patient has maintained or decreased in use pain medications during the testing period.

- The patient is both satisfied with the analgesic effect of the SCS and is familiar and comfortable with the technical aspects of device management (ex: cleaning and controlling).

One study observed patients' outcomes of depression and anxiety after SCS treatment. Its results showed that after a 1 year follow up, there was a statistically significant decrease in depression and anxiety symptoms. Furthermore, pain intensity scores also decreased by more than 50%, and opioid analgesia was discontinued by 90% of the patients (5,77).

1.7.3.5. Revision surgery

It remains a difficult decision whether to perform a revision surgery or not. As mentioned in an earlier section (Surgical Factors), the rate of success for patients with FBSS decreases after every surgical attempt (78,79). By the fourth attempt, the success rate drops to a disheartening 5%. Ultimately, the decision to perform a revision surgery is based upon the surgeon's judgment rather than strict systematic indications (80). Therefore, it is important to consult a surgeon with expertise in FBSS. Conventionally, if there is evidence of pain originating from technical issues, for example from a pedicle screw pinching a nerve root, revision surgery is performed. In most other cases of FBSS, the revision surgery should be omitted and alternative treatments should be explored, focusing on both physical and psychological elements (5).

1.7.3.6. Fusion and stabilisation procedures

Another option to consider when performing revision surgeries is fusion and stabilisation procedures. These procedures should be considered if:

- The surgery performed removes the normal anatomical stabilisers of the vertebral column
- The patient has pain during disc movement
- Congenital or acquired defects cause the spine to be unstable (ex: spondylolysis)

Spinal instability can cause excessive movement which could lead to pinching of the nerves adjacent to the spinal column, leading to weakness, numbness, and leg pain. Spinal stabilisation and fusion, in attempt to relieve this source of pain, thus aims to limit the local movement of the spine. The two main approaches are lumbar fusion and dynamic stabilisation (85).

Traditionally, lumbar fusion was performed. This method was based on stimulating adjacent bone to grow between two or more of the spinal segments. During the growth process, metal instrumentation would be used to keep the spine in place while the bones fused together. The outcome would dramatically decrease the range of movement and prevent from further irritation. However, problems have arisen years after such operations. Massive stress would be placed onto the intervertebral discs above and below the fused vertebra. This would lead to their wearing down more quickly, often causing the need for future surgeries to resolve the new pathology . This has especially been found to be the case in younger, more active individuals.

Dynamic stabilisation has become an alternative to lumbar fusion. Dynamic stabilisation allows a better balance between movement and stabilisation. In this procedure, the surgeon inserts a dynamic stabilising device, which limits the movement at the chosen disc level. The device is then anchored to the two adjacent spinal levels with screws which are connected to ropes and plastic tubes. The ropes are used to prevent excessive tension, and the plastic tubes are inserted to prevent excessive compression. Through this well developed technique, dynamic stabilisation has better accomplished the control of movement while maintaining sufficient stability (85).

2. Objectives

The main objective of this study is to discover the incidence rate of failed back surgery syndrome in the University Hospital of Split, Croatia from 2013 to 2018. We are also interested in seeing the gender difference, age range, days of recovery, and what percent had neurological defects.

Hypothesis:

Prevalence of FBSS in Split, Croatia from years 2013-2018 will be lower compared to other studies.

3. Subjects and methods

3.1. Patients

Inclusion Criteria

- Two previous surgeries which have not been successful, leading the patient to need a third operation in its current year. (> 2 surgeries)
- Surgeries performed on the Lumbar spine
- Surgeries took place in Firule Operating room from 2013-2018
- The current surgery needed to be performed on the same level as the previous surgery.

Exclusion Criteria

1. Patients who did not meet the minimum of three surgeries were not included in this study.
2. Invasive procedures that were in the nature of pain medication application were not considered as existed no age limitation to the inclusion of this study, thus males and females of all ages were used surgical treatments and was thus not used to count as one of the minimum three operations.
3. Surgeries which were not laminectomies, hemilaminectomies and microdisectomies.

3.2 Organization of the study

This retrospective study was performed in association with the Neurosurgery department of the KBC University Hospital of Split, Croatia.

3.3. Place of the study

This study took place at the Department of Neurosurgery, University Hospital of Split, Croatia.

3.4. Methods of data collecting and processing

The study took place from January 2019 to September 2019. This study included patients who were considered to be suffering from failed back surgery syndrome. Under these criteria, a total of 170 patients were selected (93 males and 77 females; average age 54; with the youngest being 21 and oldest 83). Patient data were gathered from the hospital's patient records. The years 2013 to 2018 were studied. The data were analyzed using the Microsoft Excel 2010 for Windows version 10.0 and MedCalc (MedCalc Software Ostend, Belgium). Also in this study, descriptive statistics methods were used.

3.5. Description of research

Patients who require a regional surgery were admitted. Their personal data was collected along with the type of operation required. After the patient underwent the operation and was discharged from the hospital, further information was documented such as the length of stay in the hospital and if they suffered from any neurological deficits.

3.4.1. Primary outcome measurements

The primary outcome was number of patients that have undertaken three or more spinal operations performed at the same vertebral level. The data was collected by searching through the patient medical history at the Neurosurgery Department in Split, Croatia from the years 2013-2018. This data was compared with the overall number of revised back surgeries performed on the lumbar spine.

3.4.2. Secondary outcome measurements

The secondary outcomes were postoperative neurological defects, days spent in the hospital, age, and gender.

4. Results

A total of 170 patients were collected from the years 2013 to 2018. After collecting and analyzing the raw data from the patients' charts, it was evident that there were some difference and similarities in the patients. There showed to be a fairly wide age range with ages recorded from 21 to 83 years old. Therefore, even though the average age was calculated to be 53 years old, the standard deviation was 13 years. The hospital length of stay on the other hand had a smaller range, including from only 1 day to a maximum of 36 days of hospital stay. The calculated average showed that the hospital stays were around 10 days with a smaller standard deviation of 5 days. Therefore, the 36 days was more considered to be an outlier. This information is viewed in Figure 3, which shows two separate graphs portraying the frequencies of different ages and days of recovery. Table 1 shows more information, by listing the mean, standard deviation, and ranges of these two factors. In addition, when observing the rates of FBSS between males and females, there too was not shown to be a significant difference. It was recorded that 54.71% of the cases were males, and 45.29% of cases were female. Finally, it was noted that the cases with FBSS associated with neurological deficits was only 28.24%. This information is represented in Table 2.

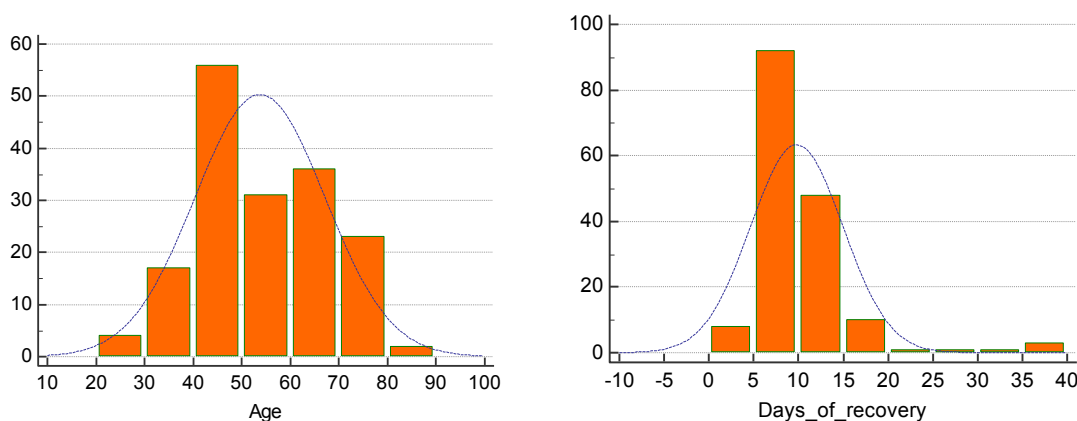


Figure 3. The frequency of age (Left) and days of recovery (right)

Table 1. Distribution of age and days of recovery

	Mean	Standard deviation	Range
Age (years)	54	13	21-83
Days of recovery	10	5	1-36

Data is presented as mean with standard deviation and range

Table 2. Frequency of gender and neurological deficit

	Frequency as n/N	Frequency in %
	N=170	
Male	93/170	54.71%
Female	77/170	45.29%
Neurological deficit	48/170	28.24%

Data is presented as n/N and in %

Figure 4 depicts the total number of interlaminectomies (microdisectomies) performed within each year. Although the number of operations within each years were not drastically different to the next year, there is an observable positive trend, implying that spinal issues are incurring at increased rate. Figures 5 and 6 portray the trends, in absolute number, over the years of laminectomies and hemilectomies, accordingly.

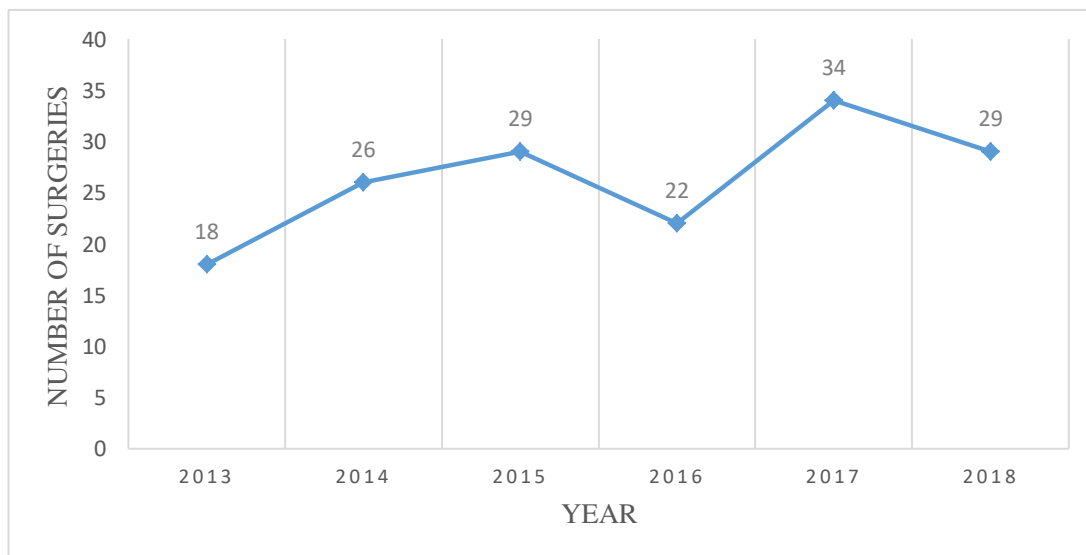


Figure 4. Interlaminectomy and microdisectomy surgeries performed between 2013 -2018.

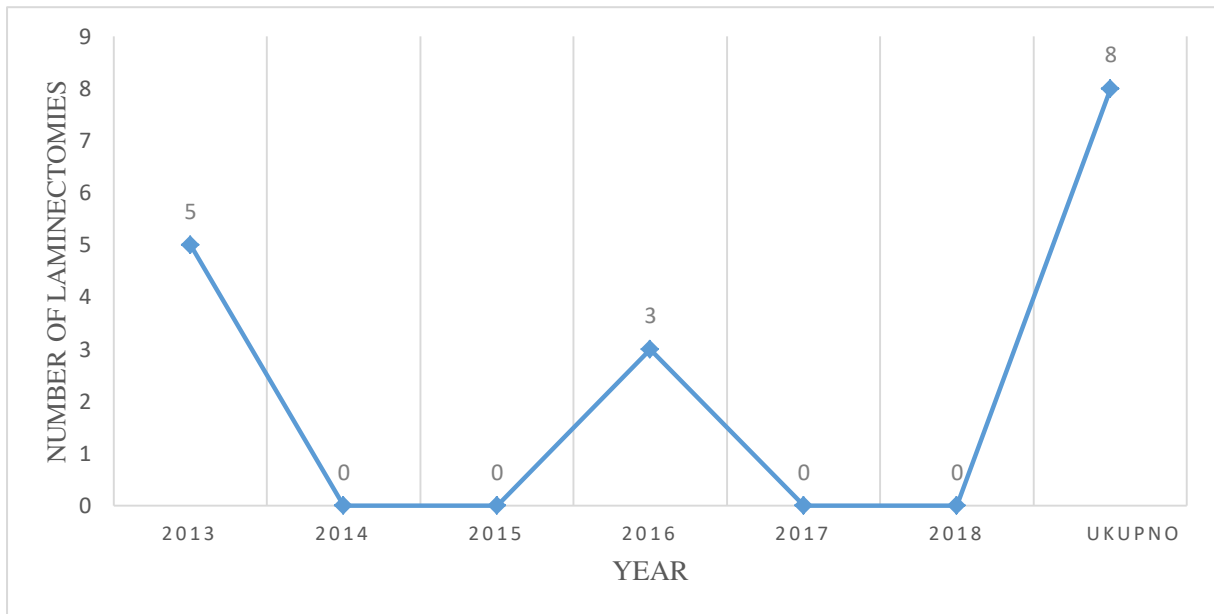


Figure 5. A line graph showing the number of laminectomy surgeries performed each year between 2013 and 2018.

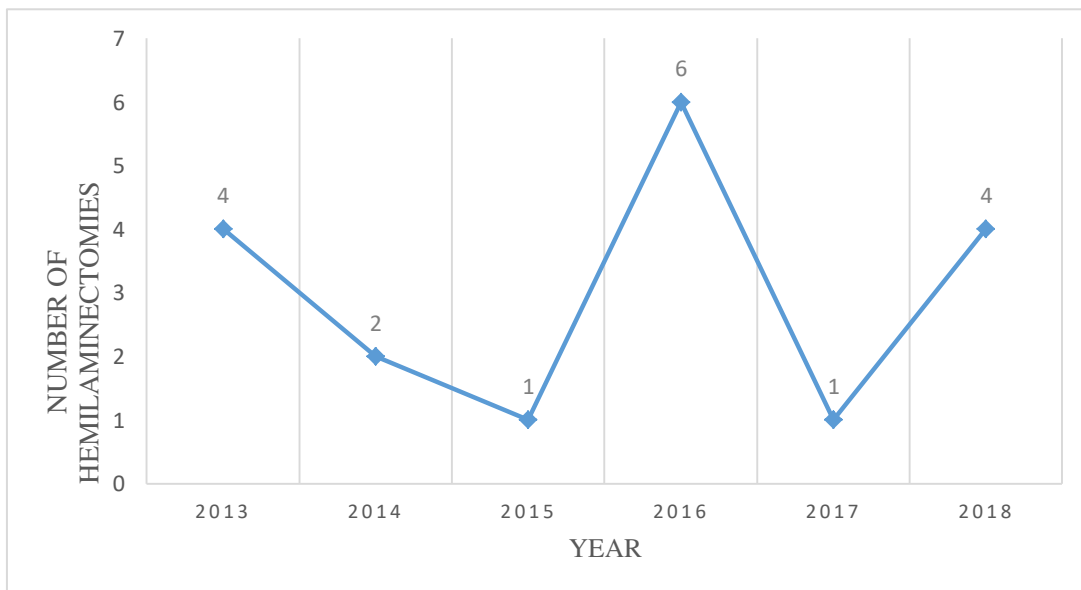


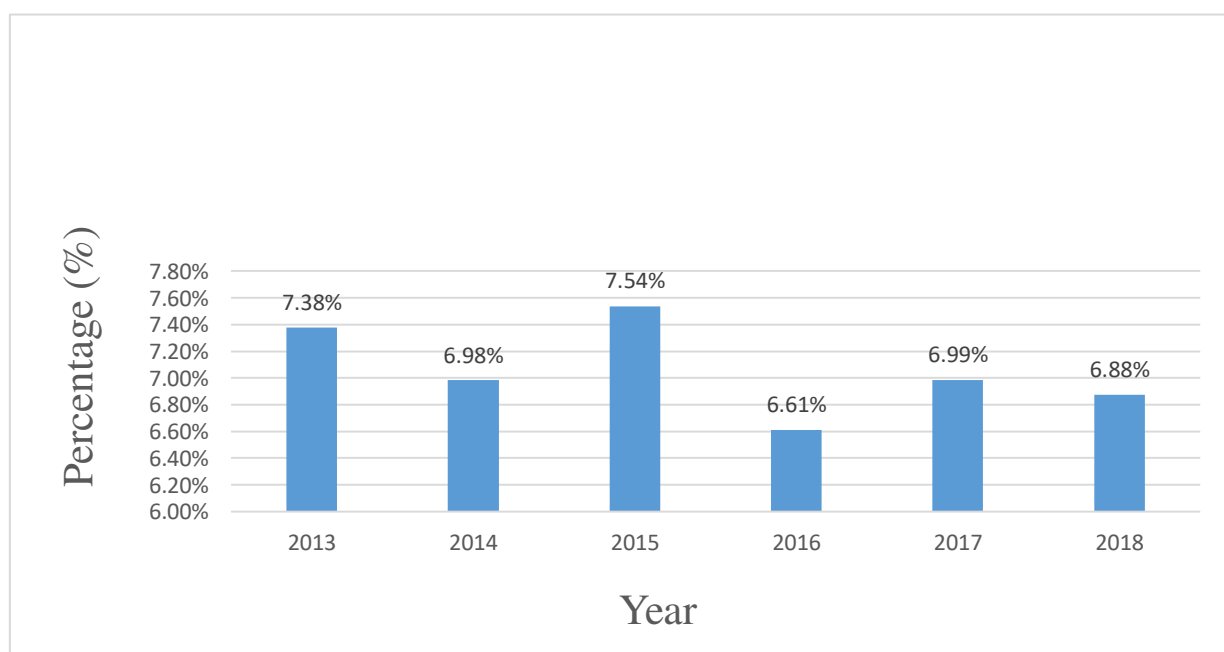
Figure 6. A line graph showing the number of hemilaminectomy surgeries performed each year between 2013 and 2018.

In table 3, we analyse further total number of spinal surgeries that were included under the diagnosis of FBSS. We see here the absolute number of performed spinal surgeries within each year and compare the value to the number of surgeries that were correlated with FBSS. Figure 7 focuses on the percentages of surgeries associated with FBSS in each year. When after the final data analysis, it was calculated that there was an average prevalence of 7% FBSS from the past 6 years at the the University Hospital of Split, Croatia.

Table 3. Analysis of total number of surgeries and surgeries for FBSS

Procedure	2013	2014	2015	2016	2017	2018	Total
Interlaminectomy/Microdisc.	18	26	29	22	34	29	158
Hemilaminectomy	4	2	1	6	1	4	18
Laminectomy	5	0	0	3	0	0	8
Total	27	28	30	31	35	33	184
Total number of back surgeries	366	401	398	469	501	480	2615
% of total back surgeries associated with FBSS	7.38	6.98	7.54	6.61	6.99	6.88	7.04%

Figure 7. Percentages of surgeries associated with FBSS in each year



5. Discussion

This study was conducted for FBSS cases over the last 6 years and had a result of 7% prevalence rate. With this information it would be useful for future research to focus more in depth to lifestyle factors and comorbidities. Since the diagnosis and aetiology of FBSS has remained puzzling future research could focus on the aetiology in search of comorbidities. With any new information found, it would help in the diagnosis, treatment, and even the prevention of FBSS. Multiple surgeries are too risky, costly, and found to be too inefficient to be continued as the main alternative for back pain. Further research into the mere topic of chronic back pain to additionally help in the future treatments of FBSS, for the definitions are intertwined.

Failed back surgery syndrome or FBSS in itself is a fairly new and not fully understood diagnosis yet. Due to this fact; therefore, prevalence around the world is still not yet truly elucidated. With this being said, there exists a small number of studies conducted on this very topic with which we could compare our results. There was a study published in 2017, which conducted a cross-sectional internet based survey with the goal of gaining a representative sample of the prevalence and the characteristic of FBSS in adult Japanese patients. The study included a sample size of 1,842 patients who had undergone lumbar surgery. According to their results, the prevalence of FBSS was 20.6% (95% CI), meaning that 1 in every 5 surveyed had continuous pain and problems. This percentage is a significant difference compared to our recorded 7% found in this study. It is important to note that the differences between FBSS statistics may lay in the very nature of the different cultures. It is acknowledged that the Japanese have culture that is rooted in hard work and efficiency, while, Americans, although are no stranger to strenuous labor may not feel the same pressures to prioritize work over health. This means that the Japanese cultural pressures to a work based life may be a cause to their significant findings.

Additionally, the Japanese study noted that order to decrease the rate of FBSS, it was important to establish an effective patient–provider relationship. Although this fact was not researched in this study, it is an important fact to remember, and could a factor that could be researched more in depth in future studies (86).

Another review article titled “Optimizing the Management and Outcomes of Failed Back Surgery Syndrome: A Consensus Statement on Definition and Outlines for Patient Assessment,” written in 2019. It described FBSS as a subgroup to chronic back and leg pain. It also cited FBSS to occur at about a 20% rate as the most recent statistic on this topic. Once again, this statistic was a significant difference to our results.

We must keep in mind that since FBSS is not a diagnosis with a standardized definition. This implies that the two studies mentioned above had different criteria of inclusion for FBSS. The review article from 2019 performed a systematic review of literature, searching studies with key words such as “Failed back surgery syndrome,” “Back pain,” “Chronic leg pain” with “Multidisciplinary” OR “Team,” “Clinical pathway” OR “Practice guideline” OR “Algorithm” OR “Guideline” OR “Protocol.” Any of the searched literature, each could have had different inclusion criteria as to what would pertain to FBSS. It would be beneficial for future researchers and future clinicians to have set criteria for the diagnosis of FBSS (87). The lack of formal criteria is the crucial step in setting a standardized definition for FBSS before it can become a useful diagnosis within the medical society.

The limitations of this study are first and foremost the lack of a standardized definition for failed back surgery syndrome. This allowed us to decide for ourselves which patients to include, but this does not necessarily imply that our inclusion criteria would be similar to other studies on the same topic. This together affects our collected data and the final statistic for the prevalence. All this makes it difficult to compare results with other studies. Another limitation was the fact that multiple primary surgery techniques were assessed, this made it difficult to analyse the original cause for revisional surgery. In addition to this note, comorbidities and risk factors were not taken into consideration, making it also difficult to assess the true cause of the required revisional surgeries.

6. Conclusion

- The prevalence of failed back surgery syndrome at the University Hospital of Split over the past six years was 7%.
- The analysis between males and females showed no significant difference, nor did the age of the patient, for the age range was so large.
- The prevalence of neurological deficit was 28.24%.
- It is concluded that it remains a diagnosis which still requires further research in hope for a general criteria to be set, which is a necessity for FBSS to become a standardized diagnosis.

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8. Summary

Objective:

The objective of this study is to find the prevalence of failed back surgery syndrome (FBSS) in the University Hospital of Split over the past 6 years (2013-2018). Additionally, the objective was to find average age, days spent in the hospital, whether there was a difference in prevalence between males and females, and finally the prevalence of neurological deficits amongst the patients.

Subjects and Methods:

The data was taken from the hospital records from the years 2013 to 2018. The inclusion criteria for FBSS was a patient to have 3 or more spinal surgeries, including laminectomies, hemilaminectomies and microdiscectomy. The patients had 2 previous unsuccessful operations and together with the current operation (done at the same anatomical level) totaled to 3 operations.

Results:

A total of 170 patients were collected over the six years studied (from 2013- 2018). The results showed that a 7% prevalence of FBSS in the University Hospital of Split. Along with this the average age was 54, but the range was from 21 to 83 years old making the average not a reliable reference. Additionally, results showed similarities between males and females, with 54.71% males and 45.29% female. There was a 28.24% prevalence of neurological deficits found.

Conclusion:

There is a prevalence of 7% of FBSS at the University Hospital of Split. In the assessment of gender, age, length of hospital stay, and neurological deficits there were no proven significant distinguishing features. This implies that there remains more to be studied about FBSS and its cofactors to aid a standardized diagnosis and approach to this disease.

9. Croatian summary

Prevalencija sindroma neuspjele operacije leđa (FBSS) u razdoblju od 2013. do 2018. u KBC-u Split, Hrvatska

Ciljevi:

Cilj je ovog istraživanja ispitati učestalost FBSS-a u KBC-u Split, u razdoblju od 2013. do 2018. godine. Također, cilj je rada ispitati prosječnu dob bolesnika, broj dana provedenih u bolnici, spol bolesnika, kao i pojavljivanje neuroloških ispada.

Materijali i metode:

Podatci su uzeti iz bolničke arhive od 2013. do 2018. godine. Kriteriji za FBSS bili su bolesnici koji su prošli minimalno tri ili više operacija kralježnice, uključujući laminektomije, hemilaminektomije i mikrodisektomije. Bolesnici su imali dvije prethodne neuspješne operacije na istom anatomskom nivou u rasponu godina koje smo naveli.

Rezultati:

U vremenskom periodu koje smo proučavali, nađeno je 170 bolesnika koji su zadovoljili kriterije uključenosti. Rezultati pokazuju prevalenciju od 7% FBSS-a u KBC-u Split. Također, prosjek godina bio je 54 godine (raspon od 21 do 83 godine), što nam pokazuje da je prosjek godina nepouzdan podatak. Učestalost je kod muškaraca i žena slična, s 54,71% muškaraca i 45,29% žena. Prevalencija neuroloških ispada je 28,24% .

Zaključak:

Nađeno je 7% slučajeva FBSS-a u KBC-u Split. Rezultati ovog istraživanja pokazali su kako dob, spol, broj dana hospitalizacije te neurološki ispadi nisu dokazani kao pokazatelji za dijagnozu FBSS-a. Rezultati studije impliciraju da postoji još neistraženih faktora koji bi pomogli pri stvaranju dijagnoze i pristupu bolesti.

10. Curriculum vitae

Name: Filip Bartolomeo Vucemilovic

Address: Getaldićeva 42, Split Croatia 21000

Date of Birth: December. 26.1994

Place of Birth: Poughkeepsie, New York

Email: filip.vucemilovic@gmail.com

Education:

2008-2013: St. Petersburg Catholic Highschool

2013-2019: University of Medicine Split, Croatia

Extracurricular activity:

- Student mass organizer in Split (2016-2019)
- School basketball and Volleyball team

Congresses:

- 25th FIAMC Congress – Zagreb, Croatia 2018
- Forum Plus International Congress – EU parliament, Brussels (Role: Moderator) 2018
- Global Leadership Summit- Zagreb, Croatia 2018
- Forum Plus International Summer School- Split, Croatia (Role: Moderator) 2019