Prospective Trial

The Correlation of Epidural Fibrosis with Epiduroscopic and Radiologic Imaging for Chronic Pain after Back Surgery

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Background: Chronic low back pain is observed frequently after lumbar spinal surgery. Epidural fibrosis has been implicated in the etiology of persistent pain after back surgery. The incidence of epidural fibrosis increases as the number and extent of spinal surgery increases. Epidural fibrosis can be detected by conventional radiologic methods [eg, lumbosacral magnetic resonance imaging (MRI) with gadolinium], but these methods are insufficient to reveal the presence of epidural adhesions. Imaging of the epidural cavity using an epiduroscope is one of the best methods for visualizing the spinal cavity without damaging anatomic structures.

Objectives: To evaluate the correlation between the type and number of surgery and the degree of epidural fibrosis and to compare epidural fibrosis in epiduroscopic and MRI findings in patients with failed back surgery syndrome (FBSS).

Study Design: A prospective trial.

Setting: A university hospital.

Methods: This study included 61 patients with persistent low back pain and/or radicular pain for at least 6 months, despite lumbar surgery and conservative treatment, and who accepted epiduroscopic imaging. All patients were evaluated in a physical examination using a visual analog scale (VAS) per the elapsed time after surgery. The patients were divided into 3 groups according to the number and type of surgeries. Epidural fibrosis was rated using MRI with gadolinium and epiduroscopy.

Results: When the relationship between admission symptoms and epidural fibrosis was evaluated, MRI findings of fibrosis were found to be significantly higher in all patients with both lumbar and radicular pain symptoms at the confidence level of 95% ($P = 0.001$). The degree of fibrosis detected using epiduroscopy was grade 1 and 2 in almost all patients who presented with low back pain only, only radicular pain, or only distal paresthesia ($P = 0.001$). In the correlation analysis between the duration of the postoperative period (4.13 ± 2.97 years) and the degree of fibrosis detected using MRI and epiduroscopy, a statistically significant relationship was found at the confidence level of 95% ($P < 0.05$). As the number and extent of spinal surgeries increased, the incidence of MRI fibrosis increased, which is compatible with the literature ($P = 0.001$) There was a statistically significant relationship between the degree of fibrosis as detected using MRI and epiduroscopy at the confidence level of 95% ($P < 0.05$). Differently, we observed that 6 patients had grade 1 fibrosis as diagnosed using epiduroscopy, whereas none had fibrosis on MRI.

Limitations: We did not have a control group. Further studies are required to demonstrate the relevance of these 2 imaging techniques (epiduroscopy and MRI) in terms of detecting epidural fibrosis in patients with FBSS.

Conclusions: Epiduroscopic imaging seems to be more sensitive than MRI in detecting grade I epidural fibrosis in patients with FBSS. Thus, the possibility of low-grade epidural fibrosis as a source of pain after back surgery, should be kept in mind in normally reported MRIs. Treatment should be planned accordingly.

Key words: Back surgery, epidural fibrosis, epiduroscopy, failed back surgery syndrome, low back pain

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Back pain is a common clinical problem that affects 80% of the population (1). There are several treatment modalities, including surgery offered for the treatment of low back pain with variable success rates. Postoperative complications tend to increase with and increase in surgical invasiveness and rates of spinal surgery (2,3). Scar tissue formation is part of the normal healing process after spinal surgery (4). Although scar tissue may be a cause of back pain or leg pain, it is rarely painful unless there is the involvement of nerve roots with the fibrotic tissue. Epidural fibrosis (EF) is a type of scar tissue, primarily produced by excessive fibroblast proliferation around the nerve root. Increased EF around the nerve roots can be defined as a postoperative complication (5-7).

Failed back surgery syndrome (FBSS) is a clinical condition, in which long-term relief of symptoms is unsatisfactory and low back and/or radicular pain is persistent or recurrent in patients undergoing 1 or more surgical procedures for lumbosacral disease. There are many causes of FBSS. The most common causes include lateral and central spinal stenosis, arachnoiditis, recurrent disc herniation, and EF (8-10). One possible postoperative complication is EF that leads to the replacement of normal epidural fat by scar tissue, but it may also occur in patients who respond well to back surgery. However, EF is considered to play a major role in the etiology of persistent pain after back surgery (11,12). Conventional radiologic methods [eg, lumbosacral magnetic resonance imaging (MRI) with gadolinium] can be used to detect EF. These methods, however, are insufficient to reveal the presence of epidural adhesions. Imaging of the epidural cavity with an epiduroscope is one of the best methods to visualize the spinal cavity without causing any damage to the anatomic structures (11,13-15).

Objectives

The aim of this study was to evaluate the correlation between the type and number of surgeries and the degree of EF, as well as to compare EF in epiduroscopy and MRI in patients with FBSS.

Study Design

A total of 61 patients with persistent low back and/or radicular pain after back surgery who accepted epiduroscopic imaging were included in the study. At the first visit, we evaluated activity-related pain, low back and radicular pain, range of motion, and straight leg raising (SLR) examinations of all patients, and noted all their symptoms on admission. Pain intensity was evaluated postoperatively using a visual analog scale (VAS). We also evaluated how long after lumbar surgery until the back pain started. The mean age of the patients was 58.9 years and their mean weight was 79.2 kg.

The inclusion criteria were VAS > 4, aged over 18 years, with persistent low back pain and/or radicular pain for at least 6 months, despite lumbar surgery and conservative treatment. Patients with predisposing risk factors (metabolic disorders, such as diabetes, vascular problems, viral infection, previous trauma, bleeding-clotting disorders, and tumors) were excluded.

Setting

A total of 61 patients with persistent low back and/or radicular pain after back surgery, who accepted epiduroscopic imaging, were evaluated at a university hospital pain clinic by a pain physician.

Methods

First, the patients were divided into 3 groups according to the number and type of surgeries they underwent: non-extensive surgery (1 surgery without instrumentation), moderate surgery (> 1 surgery, but no instrumentation), extensive surgery (> 1 surgery with instrumentation) (16).

EF was rated using an epiduroscope with a 4-level grading system according to the appearance and resistance to epiduroscope advancement. A double-ended flexible epiduroscope (RS-01-R flexible epidural video guide catheter, AMS / Italy) was inserted into the epidural space from the sacral hiatus with C-guided fluoroscopic A-P and lateral views under sedoanalgesia. For sedoanalgesia, we administered a combination intravenous midazolam (1-5 mg) and fentanyl (50-400 mcg) during epiduroscopy. A saline infusion was started through the working canal of the epiduroscope, visual inspection was performed, and areas of pathologic change were identified.

The grading classification was as follows: grade 1, loose strings and sheets of fibrosis; grade 2, more organized, continuous strings and sheets of fibrous material, not resistant to the scope; grade 3, dense continuous fibrous material, the scope can only be advanced with difficulty, and grade 4, dense continuous fibrous material, the scope cannot be advanced (16). MRI with gadolinium was used to detect epidural fibrosis in the epidural cavity after spinal surgery and EF was graded by a radiologist according to the modified Ross method (11,12). Ross et al (11), divided

the lumbar spinal canal into 4 quadrants by drawing perpendicular lines from the center of the dural sac. Quadrants A and B represent the right and left anterior epidural space, respectively, and encompass lateral recesses and spinal nerve roots. Quadrants C and D represent the right and left posterior epidural space, respectively. In the works of Ross et al (11), the method of estimation of EF in a single slice of MRI was described. This method is, however, based on planar quantification and lacks comprehensive volume information on the extent of the pathological process (11,12). Zvanimir et al (12) developed the modified Ross method. The proposed model allows estimation of the total amount of EF in the spinal canal after surgery. It is simple to use and does not require any additional software or hardware (12). In our study, we used the modified Ross method to determine the EF of patients using MRI. The grading made 5 categories: no fibrosis, mild, moderate, high, and serious EF. Then, the patients were compared according to the fibrosis detected in epiduroscopic imaging and the degree of fibrosis detected on MRI.

Statistical Analyses

Descriptive statistics are shown as mean ± standard deviation for variables with normal distribution, median (minimum-maximum) for nondistributed variables, and the number of cases (%) for nominal variables. When the number of groups was 2, the significance of the difference between the groups in terms of averages was investigated with the t-test and the significance of the difference in terms of median levels was investigated using the Mann-Whitney test. Nominal variables were compared using Pearson's Chi-square (χ^2) test. Correlation tests were used to evaluate the strength of linear relationships between 2 variables measured in a single group. All statistical analyses were performed using the SPSS statistical package (version 24.0, SPSS Inc., Chicago, IL, USA). A *P*-value of less than 0.05 was considered statistically significant.

Results

A total of 61 patients (41 women, 67.21%, 20 men, 32.79%) with persistent low back and/or radicular pain after back surgery who accepted epiduroscopic imaging were included in the study. The mean age of the patients was 58.95 ± 12.54 years and their mean weight was 79.23 ± 11.58 kg. The interval after surgery of our patients ranged between 1 and 11 years. Table 2 shows the average interval after surgery in years. The mean intervals after surgery of women and men were 4.53 ± 3.00 years and 3.30 ± 2.79 years, respectively; the mean interval after surgery of the entire cohort was 4.13 ± 2.97 years. There was no significant difference between the groups (Mann-Whitney U; $P = 0.074$). The relationship between the interval after surgery of our patients and their MR and epiduroscopic fibrosis grades were tested using a correlation test (Table 3), and a statistically significant relationship was found with 95% confidence ($P < 0.05$). When the correlation values were examined, a positive-oriented but weak relationship was seen between variables.

There was a positive correlation between the time elapsed after low back surgery and the incidence of fibrosis in our patients. This may be due to aging, disruption in the regeneration phase, spreading of granulomatous tissue around the surgical site, and degeneration of the spine structure over time. This may explain why pain develops in some patients after a long pain-free period. This condition might be interpreted as the incidence of fibrosis increases as time elapses after surgery. The relationship between the patients' presentation symptoms and MRI findings of fibrosis are summarized in Table 4. MRI findings of fibrosis were found to be minimal in almost all patients who presented with only low back pain, only radicular pain, or only distal paresthesia. MRI findings of fibrosis were found to be significantly higher in all patients with both lumbar and radicular pain symptoms at the confidence level of 95% ($P = 0.001$). The degree of fibrosis detected using epiduroscopy was grade 1 and 2 in almost all patients who presented with low back pain only, radicular pain only, or distal paresthesia only; however, it was found to be significantly higher (≥ grade 2) in all patients who had both lumbar and radicular pain at the confidence level of 95% ($P = 0.001$) (Table 5).

Table 1. *Age distribution of patients by gender.*

Gender	Mean ± Standard Deviation	*P*-value
Women	61.00 ± 10.89	0.067
Men	54.75 ± 14.79	
Total	58.95 ± 12.54	

Table 2. *Distribution of interval after surgery according to the gender of our patients.*

Gender	Mean ± Standard Deviation	*P*-value
Women	4.53 ± 3.00	0.074
Men	3.30 ± 2.79	
Total	4.13 ± 2.97	

The correlation between the age and the weight of our patients and the degree of fibrosis detected using MRI and epiduroscopy was analyzed using the correlation test (Table 6), and no statistically significant relationship was found. Table 7 shows the relationship between the type of surgery that our patients underwent and the degree of fibrosis on MRI. A statistically significant relationship was found between the type of surgery and the degree of fibrosis on MRI at the confidence level of 95% ($P = 0.001$).

As the number and extent of spinal surgeries increased, the incidence of MRI fibrosis increased, compatible with the literature. Table 8 shows the relationship between the type of surgery and the degree of fibrosis detected using epiduroscopy. A statistically significant relationship was found at the confidence level of 95% ($P = 0.001$). As the number and extent of spinal surgery increased, the incidence of epiduroscopic fibrosis increased, compatible with the literature ($P = 0.001$).

An analysis of the degree of fibrosis detected using MRI and epiduroscopy revealed that the degree of fibrosis detected with epiduroscopy was lower when that detected by MRI was also low (Table 9). Moreover, when the degree of fibrosis detected by MRI was high, that detected by epiduroscopy was also high. Furthermore, it was found that there was a relationship between 2 variables according to the Chi-square test (χ^2: 75.313, $P < 0.001$). In other words, there was a statistically significant relationship between the degree of fibrosis detected using MRI and epiduroscopy at the confidence level of 95% ($P < 0.05$). Contrastingly, we observed that 6 patients had grade 1 fibrosis as diag-

Table 3. *The relationship between the interval after surgery and the degree of fibrosis detected using MRI and epiduroscopy.*

	Interval after surgery (Years)	
	Correlation Value	***P*-value**
MRI finding of Fibrosis	0.261	0.042*
Epiduroscopic finding of Fibrosis	0.293	0.022*

Table 4. *The relationship between patients' symptoms and MRI findings of fibrosis.*

Symptoms on Admission	**MR Fibrosis Degrees**					***P*-value**
	No fibrosis	**Mild**	**Moderate**	**High**	**Serious**	
Low back pain	1	5	4	0	0	0.001
Radicular pain	1	8	1	0	0	
Distal Paresthesia	4	1	0	0	0	
Low Back Pain+ Radicular pain	0	0	13	18	5	
TOTAL	6	14	18	18	5	

* *P*-value indicates the total comparison.

Table 5. *The relationship between patients' symptoms and degree of fibrosis detected in epiduroscopy.*

Symptoms on Admission	**Epiduroscopic Fibrosis Degrees**				***P*-value**
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	
Low back pain	3	7	0	0	0.001
Radicular pain	3	7	0	0	
Distal Paresthesia	5	0	0	0	
Low Back Pain+ Radicular pain	0	5	18	13	
TOTAL	11	19	18	13	

**P*-value indicates the total comparison.

Table 6. *The relationship between the age and weight of the patients with the degree of fibrosis detected by MRI and epiduroscopy.*

	Age		**Weight**	
	Correlation value	***P*-value**	**Correlation Value**	***P*-value**
MRI finding of Fibrosis	0.144	0.267	-0.019	0.883
Epiduroscopic findings of Fibrosis	0.095	0.465	-0.019	0.887

Table 7. *The relationship between the type of surgery and degree of fibrosis on MRI.*

Surgery Type	Degree of Fibrosis on MRI						*P*-value
	No Fibrosis	Mild	Moderate	High	Serious	Total	
Non-extensive	6	11	8	0	0	25	0.001
Moderate	0	3	4	2	0	9	
Extensive	0	0	6	16	5	27	
TOTAL	6	14	18	18	5	61	

**P*-value indicates the total comparison.

Table 8. *The relationship between the type of surgery and the degree of fibrosis in epiduroscopy.*

Epiduroscopic Fibrosis Degrees						*P*-value
Surgery Type	Grade 1	Grade 2	Grade 3	Grade 4	Total	
Non-extensive	11	13	1	0	25	0.001
Moderate	0	6	2	1	9	
Extensive	0	0	15	12	27	
TOTAL	11	19	18	13	61	

**P*-value indicates the total comparison.

Table 9. *Comparison of degree of fibrosis detected by MRI and epiduroscopy.*

Fibrosis detected by MRI	Fibrosis detected by Epiduroscopy				Total
	Grade 1	Grade 2	Grade 3	Grade 4	
No fibrosis	6	0	0	0	6
Mild	5	9	0	0	14
Moderate	0	9	8	1	18
High	0	1	9	8	18
Serious	0	0	1	4	5
Total	11	19	18	13	61
Pearson Chi-square value: 75.313			*P*-value: 0.001		

nosed with epiduroscopic imaging, whereas none had fibrosis on MRI. Accordingly, epiduroscopic imaging seems to be more sensitive than MRI in detecting grade I epidural fibrosis in patients with FBSS.

Discussion

Chronic low back pain is observed frequently after lumbar spinal surgery. FBSS is one of the most common causes of postoperative persistent pain and EF is the most commonly blamed factor in its etiology. EF is known to develop at varying degrees in almost all patients after lumbar spinal surgery. The incidence of EF increases as the number and extent of spinal surgeries increase (16,17). McCarron et al (18), hypothesized that an annulus fibrosus tear might permit leakage of material from the nucleus pulposus, which in turn irritates the dural sac and its nerve root sleeves. Some failures of the surgical treatment of herniated discs may also be explained by continued leakage of this material from the same disc or adjacent discs. Accordingly, it should be kept in mind that there may be dural sac and nerve root irritation due to annulus fibrosus injury, which is thought to be caused by FBSS (18).

The function and significance of posterior epidural adipose tissue (PAT) have not been thoroughly studied. A few clinical articles stated that PAT removal might be associated with postoperative epidural fibrosis, chronic low back pain, recurrent radiating pain of the lower extremities, and deterioration of functional status- which has been termed post lumbar surgery syndrome (PLSS). The semi-fluid structure of the epidural adipose tissue allows the standing dura and nerve roots to move smoothly with the spine, without tension and compression. Therefore, loss or decrease of epidural adipose tissue after lumbar spinal surgery and EF causes compression and stretching in the nerve root and dura. Due to the fibrotic tissues covering the nerve roots, arterial blood flow and venous return in the nerves are reduced. Lee et

al (19), thought that PAT might have unknown functions beyond those described above. Human adipose tissue has been a focus because of its regenerative properties, such as adipose-derived mesenchymal stem cells (ADSCs). Based on the knowledge that adipose tissue has an impact on the regeneration of neighboring damaged tissues, PAT may aid in regenerating neighboring damaged dura, nerve root, and peridural connective tissue in the lumbar spine. The potential role of PAT in regeneration may relate to improving postoperative outcomes and prevent postoperative EF and PLSS, but no studies have addressed these possibilities. Thus, preserving epidural fat may be more favorable in postoperative outcomes of posterior decompression surgery for lumbar spinal stenosis (LSS) than removing epidural fat (19,20).

Several conservative methods can be used for the treatment of low back pain, including medical analgesic drugs, physical therapy and rehabilitation, lumbar epidural and transforaminal epidural steroid injections, facet denervation, and dorsal root ganglion (DRG) radiofrequency ablation. Advanced interventional methods (such as epiduroscopic adhesiolysis, spinal cord stimulation) can be tried for patients who do not respond to conservative therapies (21,22). Conventional MRI with gadolinium is widely used to evaluate the presence of EF in patients with low back pain after lumbar surgery, but is it the most reliable method for detecting EF? We think that it may not be sufficient to detect low-grade EF.

Imaging using epiduroscopy is the best minimally invasive method to visualize the epidural cavity without causing any damage to anatomic structures (11, 30). With epiduroscopic imaging, both fibrosis detection and adhesiolysis and drug administration can be performed on the existing fibrotic bands. In our study, there was a total of 61 patients, with persistent low back and/or radicular pain after back surgery, who accepted epiduroscopic imaging. The mean weight of our patients was 79.23 ± 11.58 kg. Lumbar pain is more common in overweight patients and becomes more frequent as the spine grows (24). In our study, however, no significant relationship was found between the patient's weight or age and EF.

Regarding EF and clinical recovery, Jinkins et al (23), suggested that fibrosis in the epidural space might be less important, whereas Coskun et al (24), found no relation between EF and pain scores; however, in our study, a correlation was found between pain scores and EF in all our patients. Ross et al (25), reported that there was a significant correlation between the presence of extensive peridural scar and the occurrence of recurrent radicular pain. In our study, we found that the incidence of EF as detected in both epiduroscopy and MRI was higher in patients who had both lumbar and radicular pain.

The amount of scar tissue has been shown to increase with the amount of surgical exposure. The formation of scar tissue takes 6 weeks to 6 months postoperatively (21). In the literature, several studies analyzed the relationship between the type of surgery and EF (9-17). Our study and other studies show that the rate of EF increases as the number and type of surgery increase (9-17), but no studies suggest a relationship between EF and the interval after surgery. In our study, the relation between the postoperative period and the degree of fibrosis detected using MRI and epiduroscopy was analyzed with a correlation test, revealing a positive relationship between the 2 variables.

There are insufficient data about the maximal amount of scarring and expected time of scarring, which may cause the etiology of pain. Variations in scarring and the relationship of number and type of surgeries and interval after surgery were evaluated in this study. We found the number and type of surgeries and the interval after surgery were directly correlated with the occurrence of EF; however, we cannot make any comment about the amount and expected time of scarring after low back surgery.

We also had the opportunity to review the difference between epiduroscopic and MRI fibrosis imaging in our study. The comparison between the degrees of fibrosis detected using MRI and epiduroscopy demonstrated that the degree of fibrosis detected in epiduroscopy was at the minimum level (grade 1 or 2) when the degree of fibrosis detected by MRI was also at the minimum level (no fibrosis/mild/moderate). On the other hand, when the degree of fibrosis detected using MRI was at the maximum level (high and serious), it also detected maximum levels (grade 3 or 4) in epiduroscopy. There was a statistically significant relationship between the degree of fibrosis detected using MRI and that detected by epiduroscopy at the confidence level of 95%.

On epiduroscopic imaging, grade 1 and 2 fibrosis were around the nerve root and not ventrally. The scar tissue was particularly prominent at the foramen entrance around the L4-5 or L5-S1 nerve root, especially on the surgical side. The dural tug test was performed on all patients. We observed adhesions in the posterolateral epidural area and around the nerve root for grade 1 and 2 fibrosis. We did not detect different

types of scar images. Interestingly, we found that 6 patients had grade 1 fibrosis as diagnosed using epiduroscopic imaging, whereas none had fibrosis on MRI. If we look at the characteristics of these six patients, all of these patients were those who did not respond to conservative treatment and were not considered for re-surgery. There was radicular pain in the calf as a physical examination finding. Also, in epiduroscopic imaging, fibrosis was observed in the nerve root, not at the posterior longitudinal ligament or dura. With all these findings, we wanted to emphasize that neuroplasty should be considered as a treatment option in patients who do not respond to conservative treatment, even though MR is reported as normal. Contrary to our study, Bosscher et al (16), reported that there was an approximately ten-fold difference between the incidence of posterior epidural fibrosis after back surgery, as diagnosed with MRI versus epiduroscopy. This difference might be because they did not use a grading system for MRI findings.

Conclusion

Compatible with the literature, we found that the incidence of MRI, epiduroscopic epidural fibrosis, and back pain increased as the number and extent of spinal surgeries increased. Therefore, the number and types of surgery that patients undergo should be carefully questioned and patients should be approached with this in mind. Epiduroscopic imaging seems to be more sensitive than MRI in detecting grade I epidural fibrosis in patients with FBSS. Accordingly, the possibility of low-grade epidural fibrosis should be kept in mind in normally reported MRI. In conclusion, epidural fibrosis should be suspected as a source of pain after back surgery in patients who are not found to have fibrosis on MRI or reported to be normal and treatment should be planned accordingly.

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