COMPARATIVE ANALYSIS OF METHODS TO PREVENT CICATRICIAL ADHESIVE EPIDURITIS AFTER MICRODISCECTOMY IN THE LUMBOSACRAL SPINE

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Objective. To analyze the effectiveness of methods for the prevention of cicatricial adhesive epiduritis (CAE) after lumbar microdiscectomy.
Material and Methods. The results of treatment of 108 patients with herniated intervertebral discs at the lumbosacral level were analyzed. Cicatricial adhesive epiduritis was prevented using 4 % sodium carboxymethylcellulose gel in Group I (n = 36), by placing autograft from the internal leaf of the lumbar fascia into the space between the vertebral arches in Group II (n = 32), and prevention of CAE was not carried out in Group III (n = 40).
Results. Complete examination of patients after microsurgical removal of the herniated lumbar intervertebral disc revealed cicatricial adhesive changes in the epidural space in all studied groups, though the degree of their expression was different: in Groups I and II, cicatricial adhesive epiduritis was insignificant without clinical manifestations, in Group III, clinical manifestations were observed.
Conclusion. The proposed methods for prevention of cicatricial adhesive epiduritis after microsurgical treatment of herniated lumbar intervertebral disc protect the epidural space and perform a barrier function.
Key Words: cicatricial adhesive epiduritis, epidural fibrosis, microdiscectomy, herniated intervertebral disc, degenerative disease of the spine.

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Despite the effectiveness of surgeries for intervertebral disc herniation, there is still a significantly high percentage of poor postoperative outcomes caused by intractable radicular pain. According to [1], this percentage is as high as 5–20 %.

The estimated frequency of failed back surgery syndrome (FBSS) varies from 5 to 50 % [15]. This syndrome results from structural and biomechanical changes caused by surgical trauma and further progression of the degenerative disc disease [8].

The cicatricial adhesive process in the epidural space (epidural fibrosis) is one of the most common reasons for FBSS developing after surgeries to excise intervertebral disc herniation. The frequency of epidural fibrosis among the causes of FBSS can be as high as 24–60 % [3, 5–8, 13–15, 19].

The mechanisms of formation of excess connective tissue in the epidural space after surgical trauma have not yet been completely elucidated. It is still unclear why a severe cicatricial adhesive process develops postoperatively in some cases, while being less marked under the same conditions in other cases. The question regarding the possible association between the severity of the cicatricial adhesive process and the discectomy method used is disputable. It was reported in a number of studies that severity of epidural fibrosis in the postoperative period decreases when using barrier gel materials, isolation membranes, various procedures for preservation of the ligamentum flavum, and intraoperative irrigation of the neural structures with steroidal and non-steroidal anti-inflammatory drugs [4, 5, 11, 16–17]. However, there are also alternative opinions regarding the insufficient clinical effectiveness of the methods used to prevent cicatricial adhesive epiduritis [10, 12].

The medical and social importance of the problem under study is quite high, since postoperative radicular pain recurrence makes patients feel desperate, thus worsening their social adaptation. The development of effective methods for primary intraoperative prevention of cicatricial adhesive epiduritis makes this problem quite relevant.

This study was aimed at comparing the effectiveness of the techniques used to prevent cicatricial adhesive epiduritis during lumbar microdiscectomy.

Material and Methods

The outcomes of treatment of 108 patients with herniated intervertebral discs at the lumbosacral level who had been operated on at the Neurosurgery Department of the Naval Clinical Hospital No. 1469 in 2014–2016 were analyzed. The sex distribution of patients was as follows: 94 (87 %) males and 14 (13 %) females. The patients' mean age was 41.6 years (95 % DI: 39.6–43.6). The indications for surgery included cauda equina syndrome with progressive dysfunction of the pelvic organs and symptoms of radicular ischemia; radicular pain or low back pain persisted for at least 4 weeks; herniated disc of any localization but only at one level; verified MRI with axial sections; and conservative treatment proved ineffective. The exclusion criteria were as follows: combination of disc herniation and degenerative spinal stenosis; spondylolisthesis of any grade; disc herniation at two and more levels; previously operated segments and non-degenerative lesions of the lumbar spine.

The patients were divided into three groups. Group I consisted of 36 patients who had undergone excision of disc herniation through the intralaminar approach and subsequent prevention of cicatricial adhesive epiduritis using 4 % sodium carboxymethyl cellulose gel (Na-CMC). Group II comprised 32 patients who had undergone excision of disc herniation through the intralaminar approach and subsequent prevention of cicatricial adhesive epiduritis by placing an autograft from the internal leaf of the lumbar fascia into the space between the vertebral arches; and Group III consisted of 40 patients who had undergone the conventional microdiscectomy through the intralaminar approach, without primary prevention of cicatricial adhesive epiduritis.

In all study groups, the patients were subjected to preoperative neurological examination and multimodal instrumental examination, including radiography and provocative tests. MRI is the «gold standard» in differential diagnosis of the level of disc herniation. All the patients underwent electroneuromyography (ENMG) preoperatively and 12 months after the surgery.

The baseline clinical parameters were analyzed by assessing pain intensity using the Visual Analogue Scale (VAS) [2] and measuring the patient's functional disability using the Oswestry Disability Index (ODI). The sex distribution of patients was as follows: in Group I, 83.3 % males and 16.7 % females; in Group II, 87.5 % males and 12.5 % females; and in Group III, 90.0 % males and 10.0 % females, respectively (Fig. 1).

The age structure in the study group was as follows: the mean age in Group I was 46.3 years; in Group II, 46.6 years; and in Group III, 47.3 years (Fig. 2). No intergroup differences in age were revealed (ANOVA; $F = 2.043$; $p = 0.135$).

An analysis of clinical signs in the study group is shown in Table 1.

The studies focusing on prevention of epidural fibrosis and minimizing its negative sequelae are still ongoing. The materials used in these studies typically provide a tangible interlayer between the neural structures and the surrounding tissues. The range of materials is rather broad (e.g., ADCON-L gel, Gelfoam (gelatin sponge), ElastoPOB membrane, DuraSealXact and Oxiplex gel materials) and the findings are quite different [5, 7, 10].

In this study, we used 4 % Na-CMC gel, a component of many modern barrier gel implants (Mesogel, Oxiplex, etc.). The gel has neither general toxic nor local irritative effect; it is not an allergen. Acting as a temporary barrier between the neural structures and the adjacent tissues, it separates these surfaces until healing. The gel is subsequently completely resorbed. This material is used in neurosurgery of the peripheral nervous system [10].

All the patients underwent microdiscectomy through the intralaminar approach using the procedure proposed by Caspar [9]. The surgery was performed to patients under general anesthesia lying on the side of his/her body contralateral to disc herniation. The level of surgical intervention was specified by intraoperative ultrasound topometric evaluation using an OpmiPico microscope (Zeiss).

In Group I, Na-CMC gel (2–3 ml) applied with a micro-irrigator (Fig. 3) was used to prevent cicatricial adhesive epiduritis in the surgical site after decompression of the neural structures. The gel covered the anterior epidural space, the dural sac, and the nerve roots, thus isolating them from the surrounding tissues.

In Group II, after the main surgery stage, an autograft from the internal leaf of the lumbar fascia was placed into the space between the vertebral arches on the arches of adjacent vertebrae (Fig. 4). The autograft had been harvested earlier when performing the surgical approach.

In Group III, the patient underwent the conventional microdiscectomy not accompanied by prevention of cicatricial adhesive epiduritis.

Statistical data analysis was conducted using Microsoft Excel spreadsheet and Statistica for Windows software. Descriptive statistics were used; the normal distribution of quantitative variables was checked using the Shapiro–Wilk test, plotting histograms and quantile plots. Analysis of differences was conducted using the nonparametric statistical methods. The intergroup differences for the parameters of interest were determined using the Kruskal – Wallis test or one-way ANOVA depending on normality of data distribution. If significant difference was revealed, *a posteriori* multiple comparison tests were performed, with correction of the confidence interval with allowance to the number of comparisons. The hypotheses were accepted for the confidence interval no less than 95 % ($p < 0.05$); the Bonferroni correction was used for pairwise comparison of several groups. The Wilcoxon signed-rank test was used to compare the differences between the related groups.

Results and Discussion

The short- and long-term treatment outcomes were assessed after 24 h, 10 days, 6, 9, and 12 months. The conclusions whether the eliminated compression of the neural structures accompanied by prevention of cicatricial adhesive epiduritis was effective or not were based on thorough analysis of the dynamics of clinical symptoms, MRI data, CT data, the VAS score, and ODI. The modified Nurick scale (Table 2) and MacNab criteria were used to assess the treatment outcomes [2].

Twenty-four hours post-surgery, a significant improvement in condition and complete regression of neurological symptoms were observed in 30 (83.3 %) Group I patients (corresponding to level 1 of functional ability according to the modified Nurick scale). In Group II and III patients, level 1 of functional abili-

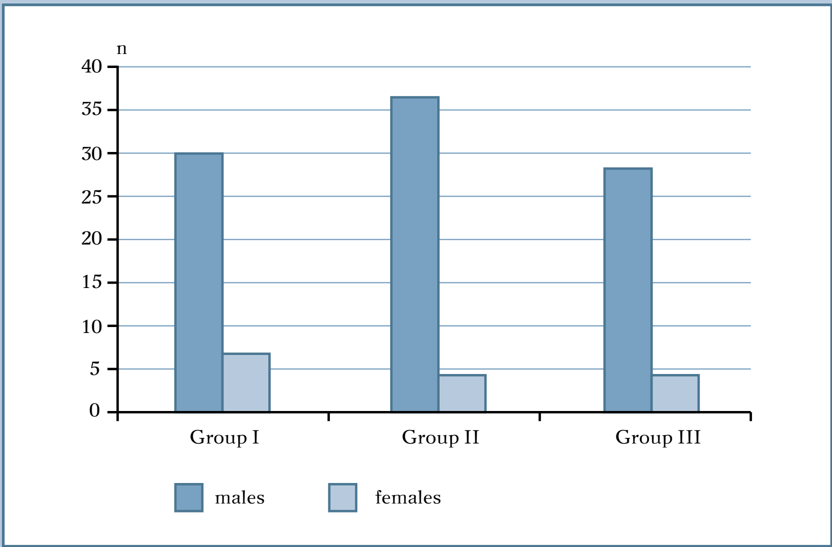

Fig. 1
Sex distribution in the study groups

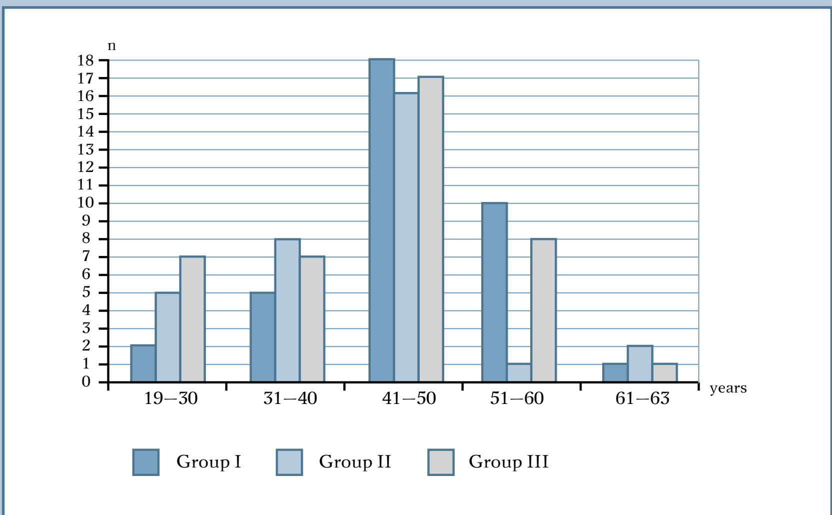

Fig. 2
Age structure of the study groups

ty was observed in 28 (87.5 %) and 33 (82.5 %) cases, respectively. Improvement in patients' condition (mainly due to regression of the radicular pain syndrome) corresponding to level 2 of functional ability was observed in 5 (13.9 %) patients in Group I, in 4 (12.5 %) patients in Group II, and in 4 (10.0 %) patients in Group III. No improvement in condition was observed in one (2.8 %) Group I patient and in 3 (7.5 %) Group III patients, while being observed in none of Group II patients. None of the patients showed deterioration of their condition after the surgery (Table 3).

The follow-up examination one year after the surgery demonstrated that the negative dynamics were prevailing in Group III: the percentage of good outcomes decreased from 92.5 % (n = 37) 24 h after the surgery to 70.0 % (n = 28) after one year. In Group I, these parameters were 97.2 % (n = 35) and 91.6 % (n = 33) and in Group II, 100 % (n = 32) and 90.6 % (n = 29), respectively (Table 4).

The overall outcomes of surgical treatment assessed using the MacNab criteria are consistent with the similar data obtained using the modified Nurick scale. However, the MacNab criteria take into account the subjective evaluation of patient's condition. Hence, having compared the subjective and objective criteria 24 h after the surgery, the outcomes in 31 (86.1 %) patients in Group I, 29 (90.6 %) patients in Group II, and 33 (82.5 %) patients in Group III were regarded as good. Fair outcomes were observed in 5 (13.9 %) patients in Group I, 3 (9.4 %) patients in Group II, and 7 (17.5 %) patients in Group III. In all three groups, patients had neither poor nor excellent outcomes (Table 5).

Table 1
Distribution of patients in the study groups according to clinical signs, n (%)

Clinical group	L4–L5 level	L5–S1 level	Low back pain	Radiating pain to the lower extremities	Lasegue's sign	Impaired sensitivity
I	13 (36.1)	23 (63.9)	36 (100.0)	35 (97.2)	32 (88.9)	27 (75.0)
II	11 (34.4)	21 (65.6)	32 (100.0)	29 (90.6)	28 (87.5)	23 (71.9)
III	16 (40.0)	24 (60.0)	40 (100.0)	38 (95.0)	33 (82.5)	31 (77.5)

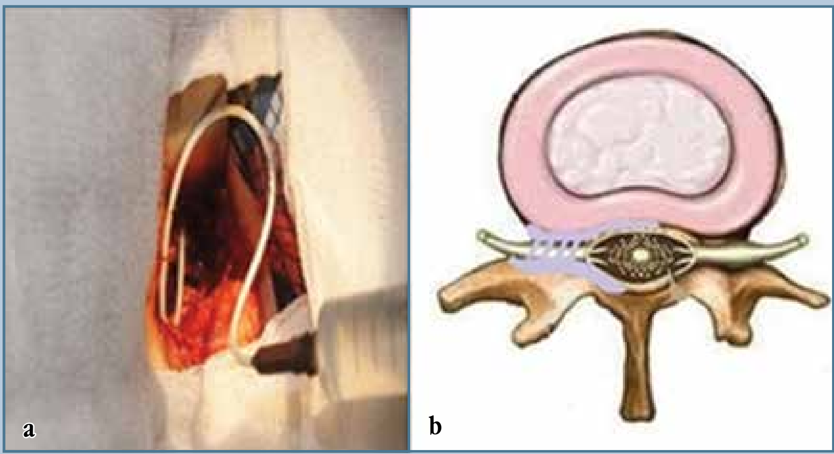

Fig. 3
Application of Na-CMC gel: **a** – an intraoperative image; **b** – the scheme of application

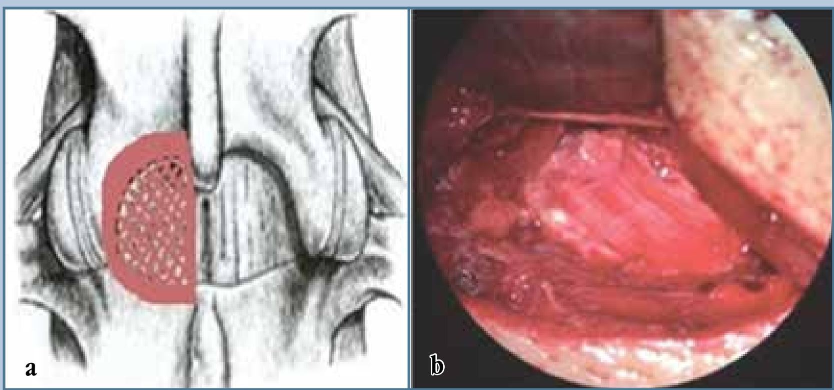

Fig. 4
Reconstruction of the space between the vertebral arches with the internal leaf of lumbar fascia: **a** – scheme of autograft placement; **b** – the autograft placed into the space between the vertebral arches

The VAS score for subjective pain was assessed; the results indicated that the pain syndrome was significantly alleviated in early postoperative period (Fig. 5).

We would like to mention that no differences in the VAS score for pain intensity were observed between the patients in three groups: $\chi^2_{(2)} = 0.720$; $p = 0.698$. The median VAS score for pain intensity was 4 (Me = 4; Q1 = 3.25 and Q3 = 4) in Group I and 4 (Me = 4; Q1 = 3 and Q3 = 4) in Groups II and III.

On postoperative day 10, patients in all three groups showed a significant reduction in pain intensity (Wilcoxon test, $p < 0.0001$): the median VAS score for pain intensity on day 10 was 0 (Me = 0; Q1 = 0 and Q3 = 1) in all groups. As compared to pain intensity by the time of surgery, this improvement was still observed in all groups 6 and 12 months after surgery.

No intergroup differences in pain intensity ($\chi^2_{(2)} = 0.019$; $p = 0.990$) were revealed in the short-term postoperative period (on day 10 after surgery) or 6 months after surgery ($\chi^2_{(2)} = 2.234$; $p = 0.327$). Meanwhile, significant intergroup differences in pain intensity were revealed in the long-term postoperative period: $\chi^2_{(2)} = 6.226$; $p = 0.044$. These differences were observed only between Groups I and III: the Mann–Whitney U-test = 557.5; Z = -1.253; p = 0.15. Such difference was revealed neither between Groups I and II nor between Groups II and III: the Mann–Whitney U-test = 516.0; Z = -2.435; p = 0.204 (at p = 0.17, with allowance for correction of the confidence interval for the number of comparisons).

Intergroup differences in the ODI were observed neither in the preoperative period ($\chi^2_{(2)} = 1.871$; $p = 0.392$) nor 10 days after the surgery ($\chi^2_{(2)} = 0.068$; $p = 0.966$). Meanwhile, long-term follow-up of the ODI showed a significance intergroup difference: $\chi^2_{(2)} = 48.797$; $p < 0.0001$. This difference was observed only between Group I and the other two groups: for the difference in the Oswestry Disability Index between Groups I and II, the Mann – Whitney U-test = 161.0; Z = –5.207; p < 0.001 and between Groups I and III, the Mann – Whitney U-test = 115.5; Z = –6.365; p < 0.001. No differences in ODI between Groups II and III were revealed: the Mann – Whitney U-test = 446.5; Z = -2.251; p = 0.024 (at p-value = 0.17).

The dynamics of ODI at the moment of surgery and 6 and 12 months after it were as follows: in Group I, 54.0 (Me = 54.0; Q1 = 52.0 and Q3 = 56.0), 3.3 (Me = 3.3; Q1 = 3.3 and Q3 = 6.6) and 12.0 (Me = 12.0; Q1 = 12.0 and Q3 = 14.0); in Group II, 54.0 (Me = 54.0; Q1 = 54.0 and Q3 = 57.0), 3.3 (Me = 3.3; Q1 = 3.3 and Q3 = 6.6) and 15.0 (Me = 15.0; Q1 = 14.0 and Q3 = 16.0); in Group III, 54.0 (Me = 54.0; Q1 = 52.0 and Q3 = 58.0), 3.3 (Me = 3.3; Q1 = 3.3 and Q3 = 6.6) and 15.0 (Me = 16.0; Q1 = 15.0 and Q3 = 17.0; Fig. 6).

The surgical outcomes in all the study groups in the short- and long-term periods were measured by analyzing the MRI data of the lumbosacral spine. MRI examination was performed on a PHILIP-SINTERA 1.5 T 6 CH MRI scanner. T1- and T2-weighted sequences were recorded, with the STIR sequence used to suppress signal from fat in the sagittal and axial views.

On postoperative day 10, the patients presented with swelling of soft tissues and their saturation with blood. The mass effect observed during this period

Table 2

The modified Nurick scale

Level 1	Complete regression of neurological symptoms
Level 2	Improvement in neurological symptoms
Level 3	Unchanged neurological symptoms
Level 4	Aggravation of the neurological status

Table 3

Evaluation of patients' clinical status 24 h after surgery using the modified Nurick scale

Level	Patients, n (%)		
	Group I	Group II	Group III
1	30 (83.3)	28 (87.5)	33 (82.5)
2	5 (13.9)	4 (12.5)	4 (10.0)
3	1 (2.8)	0 (0.0)	3 (7.5)
4	0 (0.0)	0 (0.0)	0 (0.0)
Total	36 (100.0)	32 (100.0)	40 (100.0)

Table 4

Evaluation of patients' clinical status one year after surgery using the modified Nurick scale

Level	Patients, n (%)		
	Group I	Group II	Group III
1	30 (83.3)	27 (84.3)	24 (60.0)
2	3 (8.3)	2 (6.3)	4 (10.0)
3	1 (2.8)	1 (3.1)	2 (5.0)
4	2 (5.6)	2 (6.3)	10 (25.0)
Total	36 (100.0)	32 (100.0)	40 (100.0)

Table 5

Evaluation of the outcomes using the MacNab scale 24 h after surgery

Outcomes	Patients, n (%)		
	Group I	Group II	Group III
Excellent	0 (0.0)	0 (0.0)	0 (0.0)
Good	31 (86.1)	29 (90.6)	33 (82.5)
Fair	5 (13.9)	3 (9.4)	7 (17.5)
Poor	0 (0.0)	0 (0.0)	0 (0.0)
Total	36 (100.0)	60 (100.0)	40 (100.0)

can suggest that there is recurrent disc herniation; the edema resolves approximately one month after the surgery. MRI of the lumbosacral spine 3 months after surgery shows increased signal intensity from the bone marrow, vertebral endplates, and the nucleus pulposuson T2-weighted images. Signs of reactive epiduritis can still be observed 6 months after surgery; the edema in the posterior epidural space is superseded by fibrosis. Differential diagnosis between fibrosis and recurrent disc herniation is the key aspect for selecting the treatment approach.

Contrast-enhanced MRI is one of the methods to diagnose the cicatricial adhesive epiduritis: it allows one to reliably discriminate between postoperative epiduritis and recurrent disc herniation using the following criteria. It takes 6–10 min for the cicatricial tissue to be contrast-enhanced, while for the recurrent disc herniation, it takes 30–45 min and signal intensity is much lower than that of the cicatricial tissue [16]. Signal intensities on non-contrast-enhanced MR images of the spine are identical for both the cicatricial tissue and the recurrent disc herniation. Herniation is the continuation of the disc and is usually separated by the hypointense posterior longitudinal ligament. However, this association is lost upon sequestration and the sequestrum, similar to fibrosis, can lie aside from the disc. Dural sac retraction towards this structure is an indirect sign of fibrosis; dural sac compression is more typical of disc herniation. These signs have a very low degree of specificity. Both the disc and disc herniation are avascular structures. Contrariwise, the granulation and fibrotic tissues contain blood vessels. Hence, they get contrast-enhanced upon MRI, which makes it possible to discriminate between the cicatrix and the recurrent herniation. Contrast enhancement is associated with vascularization. The accuracy of MRI is >90% (Fig. 7). The problem is that the recurrent herniation and the cicatricial adhesive process are not mutually exclusive but often coexist.

When the treatment outcomes in Group I patients who received Na-CMC gel were evaluated at discharge, all 36 (100.0 %) patients had pain regression. Among 27 patients who had impaired sensitivity before surgery, these disorders either completely regressed in 24 (66.7 %) patients or partly regressed in 2 (5.6 %) patients. Follow-up evaluation one year after surgery showed that impaired sensitivity persisted in one (2.8 %) patient. The motor impairment

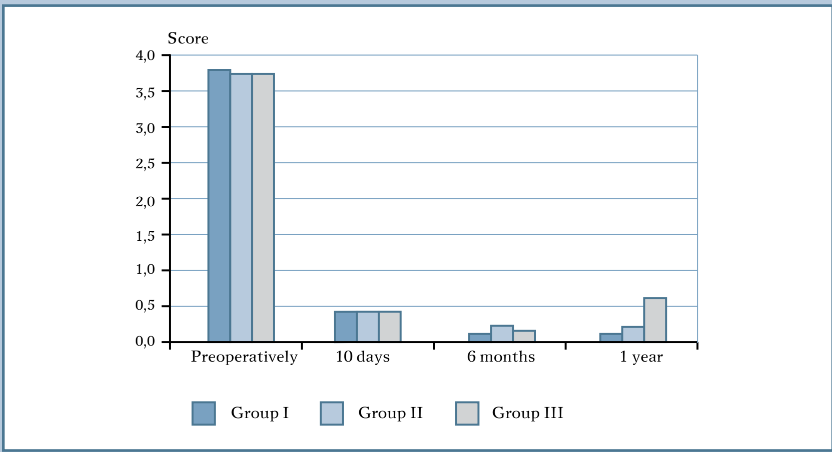

Fig. 5
Pain intensity (VAS score) in patient groups

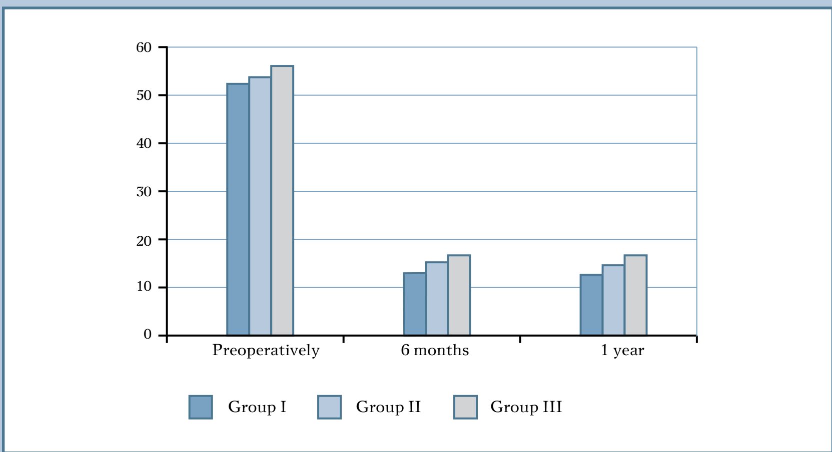

Fig. 6
Dynamics of the Oswestry Disability Index

that had existed in 4 (11.1 %) patients completely regressed. No postoperative complications were reported.

In Group II patients managed by placing an autograft of the internal leaf of the lumbar fascia, regression of radicular pain was observed in 32 (100.0 %) cases. Among 23 patients who had impaired sensitivity before surgery, 21 (65.6 %) patients showed complete regression of impaired sensitivity; the impairment was alleviated in 1 (3.1 %) patient. In one (3.1 %) patient, follow-up evaluation showed that impairment still persisted 3 months after surgery and partially regressed 6 months after surgery. The motor impairment observed in 6 (18.75 %) patients completely regressed by the time of analyzing the long-term outcomes. One case of worsened condition was related to instability of the spinal motion segment. The patient underwent surgery involving stabilization; the surgeons noted that the nerve root could be easily mobilized and was not intergrown with cicatricial tissue.

In Group III patients who received no prevention of the cicatricial adhesive epiduritis, radicular pain regression was observed in 40 (100.0 %) cases. Among 31 patients who had impaired sensitivity before surgery, this condition completely regressed in 22 (71.0 %) patients and partially improved in 4 (12.9 %) patients. A follow-up examination 6 months after the surgery showed that impaired sensitivity remained at the same level in 5 (16.1 %) patients. Seven (31.8 %) patients who had complete regression of motor impairment after surgery, showed the negative dynamics manifesting itself as aggravating sensitivity impairment. Regression of motor impairments was observed in 9 (22.5 %) patients having these impairments before surgery. Two cases of the negative dynamics were associated with recurrent disc herniation. The patients were reoperated. During the reoperation, attention was paid to autograft density; scarring was moderate; the cicatricial tissue did not form coarse adhesions to the dural sac and the nerve root.

The main reason for the poor outcomes in Group III achieved 3 months after surgery is related to the development and progression of MRI-verified postoperative compressive cicatricial adhesive epiduritis (Fig. 8). Two patients underwent reoperation for this reason; significant changes in the dural sac region and dense coarse adhesions with the adjacent tissues were visualized intraoperatively (Fig. 9).

The treatment outcomes 1 year after the surgery are listed in Table 6.

Conclusions

1. The results of multimodal examination of the patients after microsurgical excision of herniated disc at the lumbar level showed cicatricial adhesive changes in the epidural space in all the groups but their severity varied. Mild epiduritis without clinical manifestations was observed in the group where gel was applied and the procedure for isolating the epidural space with the fascia was performed, while clinical manifestations of cicatricial adhesive epiduritis were detected in the group where no gel had been applied.

2. Contrast-enhanced MRI is the most informative method for differential diag-

nosis of cicatricial adhesive epiduritis in the long-term period.

3. The proposed methods for preventing cicatricial adhesive epiduritis after microsurgical excision of lumbar disc herniation have similar effectiveness.

The study received no funding from sponsors. The authors declare no conflict of interest.

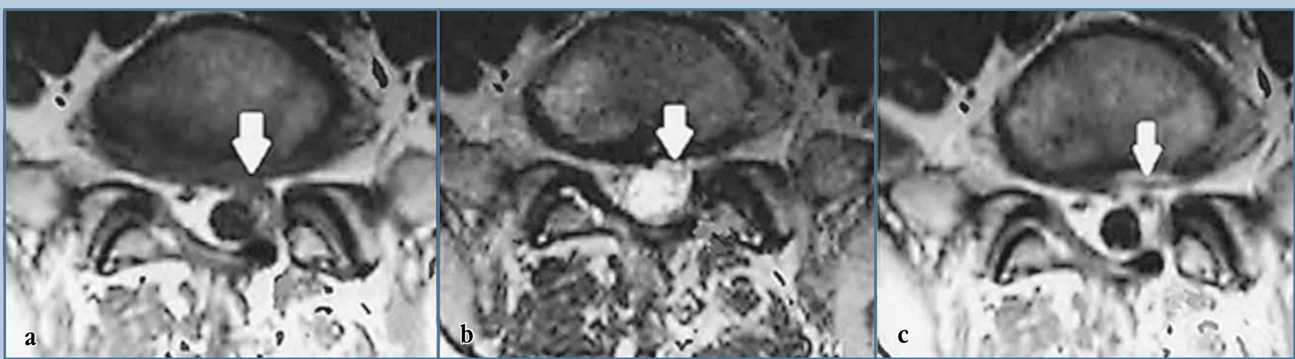

Fig. 7
Axial MRI of the lumbosacral spine and MRI 6 months after the surgery: **a** – T1-weighted image; an arrow shows the soft-tissue component without a mass effect; **b** – T2-weighted image: the intensity of MR signal from the epidural fibrosis zone surrounding the left S1 nerve root (shown with an arrow) is slightly increased with respect to the tissue of the adjacent disc portions; **c** –T1-weighted post-contrast image: diffuse accumulation of the contrast agent in a small region of epidural fibrosis surrounding the left S1 nerve root and in projection of the postoperative defect along the posterior disc surface (shown with an arrow) is visualized

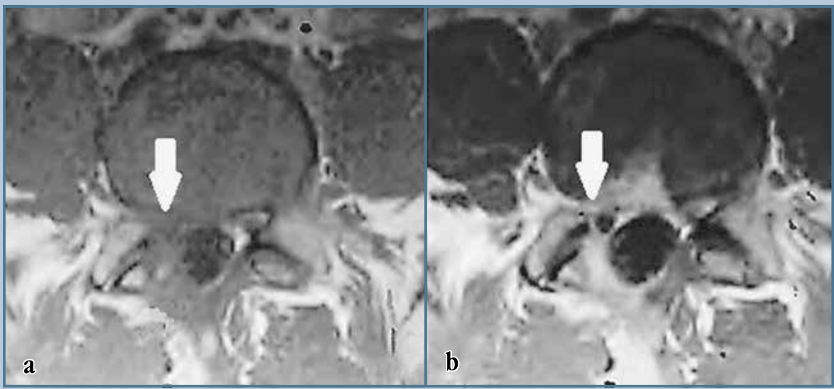

Fig. 8
MRI of the lumbosacral spine 6 months after surgery: **a** –axial T1-weighted image; a well-defined region of epidural fibrosis (shown with an arrow); **b** – axial T1-weighted post-contrast image; the arrow shows the diffuse accumulation of contrast agent in the region of epidural fibrosis

Fig. 9
Cicatricial adhesive process in the spinal canal: **a** – intraoperative view; **b** – macrospecimen; **c** – microspecimen of fibrous tissue stained with hematoxylin and eosin, 40 magnification

Table 6
Distribution of patients in study groups with respect to clinical signs one year after treatment, n (%)

Group	Low back pain	Radiating pain to the lower extremities	Lasegue's sign	Impaired sensitivity
I	1 (3.6)	1 (3.6)	0	1 (2.8)
II	1 (3.2)	1 (3.2)	1 (3.2)	1 (3.2)
III	2 (5)	3 (7.5)	7 (17.5)	13 (32.5)

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