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EDITORIAL

Dear Colleagues,

I feel very privileged to be the person responsible for publishing this, the 1st issue, of our professional journal this year. It includes six clinical research studies, one basic science study, one case report, and one letter to the editor. I hope that each of you will take the time to review this issue very carefully and add the information and insights contained herein, to your already very well informed knowledge bases.

We are very happy to announce that JTSS is currently indexed in ten indices; Scopus, Ulakbim, Türkiye Atıf Dizini, Embase, J-Gate, Europub, Proquest, Gale Cengage learning, Ebsco Host and China Knowledge Resource Integrated.

The first study is a retrospective clinical study giving the results on "Dural Fibrosis in Spinal Surgery: Comparison of Ligamentum Flavum Sparing and Anti-Adhesion Gel Use Technique". The second is about "Minimally Invasive Unilateral Hemilaminectomy Approach for the Removal of Spinal Schwannomas. Impact on Pain and Neurological Results". In the third, one can read about a basic science study entitled "The Effect of Anti-inflammatory, Anti-oxidative, and Neuroprotective Characteristics of Aloperine on Experimental Acute Spinal Cord Injury in a Rat Model". The fourth article is about "Decompression with Instrumentation in the Treatment of Upper-level Disc Herniations". The authors of the fifth study examined "The Effect of Interferential Currents and TENS on Pain and Functionality in Patients with Chronic Mechanical Low Back Pain". The sixth study discusses "Low-energy Vertebral Compression Fractures: Differential Diagnosis Between Osteoporotic and Malignant Fractures by Inflammatory Biomarkers" while, in the seventh, the authors wrote about "Osteoporotic Vertebral Fractures; Comparative Analysis of Unilateral and Bilateral Vertebroplasty Results". The eighth article is a case report about "Coexistence of Spinal Dysraphism and Extrarenal Wilms Tumour: A Case Report and Review of the Literature". The ninth article is a letter to the editor about "Epidural Anesthesia for Postoperative Analgesia Following Video Assisted Thoracoscopic Surgery Anterior Vertebral Body Tethering".

I hope you found this issue stimulating and informative. It's my goal to provide you with the latest, and most up-to-date information in our field. I do this in an effort to keep all of us on the cutting edge of the latest research and developments.

I wish all our Turkish spinal surgeons and their families a healthy, peaceful, and prosperous year.

With kindest regards,

Editor in Chief
Metin Özalay, M.D., Prof.

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ORIGINAL ARTICLE

DURAL FIBROSIS IN SPINAL SURGERY: COMPARISON OF LIGAMENTUM FLAVUM SPARING AND ANTI-ADHESION GEL USE TECHNIQUE

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ABSTRACT

Objective: Fibrosis around the dura is a concern in spinal surgery, affecting outcomes. Ligamentum flavum (LF) sparing and anti-adhesion barrier gel are potential strategies. This study aimed to compare LF-sparing and anti-adhesion barrier gels in reducing dural fibrosis in spinal surgery patients.

Materials and Methods: Fifty patients underwent surgery at the thoracic/lumbar levels (T1 to S1). Twenty five received LF sparing and 25 received anti-adhesion barrier gels. Postoperative magnetic resonance imaging was performed 6 months post-surgery, using Ross classification for fibrosis assessment. Median fibrosis degree was computed, and surgical levels' impact on fibrosis was analyzed.

Results: The anti-adhesion barrier gel group had a higher mean age (53.68±7.54) than the LF-sparing group (48.36±8.03) (p<0.05, t-test). Gender distribution showed no significant difference (p=0.777, Chi-square test). The LF-sparing group had a lower mean degree of fibrosis (1.091.09±0.16) than the anti-adhesion barrier gel group (2.28±0.53) (p<0.001, Mann-Whitney U test). The LF sparing group's mean fibrosis had no significant variance among spinal levels (p>0.05), while the anti-adhesion barrier gel group showed significant differences (p=0.004, p<0.01) with the highest fibrosis at L4-S1, followed by T12-L1 and L2-L3, and the lowest at T1-T11.

Conclusion: LF sparing is more effective in reducing dural fibrosis than anti-adhesion barrier gel. Surgical level influence fibrosis, with LF sparing advantageous in the lower lumbar and thoracolumbar transitional zones.

Keywords: Ligamentum flavum sparing, anti-adhesion gels, postoperative fibrosis, hypermobility

INTRODUCTION

Spinal surgery is a common procedure for treating a variety of spinal disorders, including herniated discs, spinal stenosis, and spinal fractures. While the benefits of spinal surgery are well-established, the procedure also carries a risk of complications, including fibrosis around the dura. Fibrosis around the dura refers to the formation of scar tissue around the dura mater, which is the protective layer surrounding the spinal cord. This scar tissue can lead to nerve root compression, chronic pain, and other complications that can negatively impact patient outcomes.

To mitigate the risk of fibrosis around the dura, several techniques have been proposed, including ligamentum flavum (LF) sparing and the use of anti-adhesion barrier gels. The LF is a ligament located in the posterior spinal canal that is intimately associated with the dura mater. During spinal surgery, the LF can be thinned or completely removed to reduce the risk of fibrosis around the dura. Anti-adhesion barrier gels, on the other hand, are used to create a physical barrier between the dura mater and surrounding tissue, preventing the formation of scar tissue.

While both techniques have been shown to be effective in reducing the incidence of fibrosis around the dura, it is unclear which technique is more effective. Previous studies have reported conflicting results, with some studies suggesting that LF sparing is more effective than anti-adhesion barrier gel use, while others have found the opposite to be true[1-4].

The purpose of this study is to compare the degree of fibrosis around the dura in patients undergoing spinal surgery with LF-sparing and anti-adhesion barrier gel use. By comparing the degree of fibrosis in these two groups, we can gain insight into the effectiveness of these techniques and potentially identify the best approach for reducing the incidence of fibrosis around the dura in spinal surgery patients.

MATERIALS AND METHODS

The study was conducted between 2019 and 2022. A total of 50 patients were included in the study, with 25 patients undergoing LF sparing and 25 patients receiving anti-adhesion

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barrier gels during surgery. All patients underwent spinal surgery in the thoracic and lumbar region between T1 and S1 levels. Informed consent was obtained from our patients for our study. Institutional review board approval was obtained from the Ordu University Ethics Committee (approval number: 2023/167, date: 09.06.2023). In the ligament flavum sparing group, the ligament flavum was thinned and spared during surgery, while in the anti-adhesion barrier gel group, LF was totally removed and an anti-adhesion barrier gel was used to prevent adhesion formation. To provide detailed information on the degree of fibrosis in each patient, we evaluated the T1 and T2-weighted contrast-enhanced magnetic resonance imaging (MRI) assessments in relation to the extent of epidural fibrosis across five consecutive axial sections centered on the operated level. These sections were divided into four quadrants, with perpendicular lines drawn from the central aspect of the thecal sac as a reference. We graded the extent of fibrosis in each quadrant on a scale of 0 to 4, following Ross et al.'s[5] system. Grade 0 indicated no or minimal fibrosis, while Grade 4 indicated extensive fibrosis filling the quadrant. Fibrosis grades were recorded for each patient, considering four quadrants per section across the five sections. The median grade observed was used to determine the patient's scarring grade. The patient characteristics, including age, sex, and surgical levels, were also recorded for each patient. To investigate whether the degree of fibrosis is influenced by the surgical level in addition to the applied surgical technique, we divided the patients into four groups based on the level of surgery: upper thoracic (T1-T11), transitional zone (T12-L1), upper lumbar (L2-L3), and lower lumbar (L4-S1). The statistics for each level were calculated separately.

Statistical Analysis

The data were analyzed using SPSS version 27.0. Descriptive data were expressed in mean ± standard deviation (SD), median (minimum-maximum) or number and frequency. The Shapiro-Wilk test was used to check normality of distribution of quantitative variables. The independent samples t-test was used to compare normally distributed quantitative variables, while the Mann-Whitney U test was used to compare non-normally distributed quantitative variables between the groups. Kruskal-Wallis test was used for the between group comparisons of parameters without normal distribution. Chi-square test was used to compare qualitative variables. A p-value less than 0.05 were considered statistically significant.

RESULTS

In a total of 50 cases; including 50% (n=25) female and 50% (n=25) male, the ages of the cases ranged from 35 to 68, with a median age of 50.0 and a mean age of 51.02±8.16 years. The mean degree of fibrosis ranged from 0.8 to 3.2, with a median value of 1.4 and a mean value of 1.69±0.71 (Table 1). In addition, the mean age was significantly higher in the anti-adhesion barrier gel group (mean=53.68, SD=7.54) compared to the LF sparing group (mean=48.36, SD=8.03) ($p<0.05$, t-test). There was no statistically significant difference in sex ($p=0.777$, chi-square test) between the two groups (Table 2).

The degree of fibrosis was significantly lower in the LF-sparing group (mean=1.09, SD=0.16) compared to the anti-adhesion barrier gel group (mean=2.28, SD=0.53) ($p<0.001$, Mann-Whitney U test). The difference in mean fibrosis between the two groups was statistically significant (Table 2) (Figure 1).

There was no statistically significant difference observed in the mean degree of fibrosis measurements among the spinal levels in the Ligament Flavum Sparing group ($p>0.05$), and in all levels, the degree of fibrosis was lower (Table 3). However, in the Anti-Adhesion Barrier Gel Use group, a statistically significant difference was found in the mean degree of fibrosis measurements among the spinal levels ($p=0.004$; $p<0.01$). The highest mean degree of fibrosis was observed in the L4-S1 (Lower Lumbar) level, followed by the T12-L1 (Transitional Zone) and L2-L3 (Upper Lumbar) levels. The lowest mean degree of fibrosis was found in the T1-T11 (Upper Thoracic) level (Table 4) (Figure 2).

DISCUSSION

The LF is a thin, fibrous band that helps to maintain spinal stability and runs between adjacent vertebrae. LF serves as an important barrier against connective tissue formation on the dura after surgery[3,6]. During spinal surgery, the LF is often removed to access the spinal cord and other structures. However, recent studies have shown that preserving the LF during surgery can reduce the extent of fibrosis and improve surgical outcomes[7,8].

The present study investigated the degree of fibrosis around the dura in patients undergoing spinal surgery with ligament flavum sparing and anti-adhesion barrier gel use. Our results showed that the degree of fibrosis was significantly lower in the ligament flavum sparing group compared to the anti-adhesion barrier gel group, indicating that the use of ligament flavum sparing technique during spinal surgery may better reduce the degree of fibrosis around the dura.

These findings are in line with previous studies that have shown the benefits of LF sparing in reducing postoperative fibrosis and improving surgical outcomes[9,10]. Some studies have demonstrated that patients who underwent surgery

Table 1. Distribution of descriptive characteristics

		Min.-max. (Median)	Mean ± SD
Age (year)		35-68 (50.0)	51.02±8.16
Mean degree of fibrosis		0.8-3.2 (1.4)	1.69±0.71
		n	%
Gender	**Female**	25	50.0
	Male	25	50.0

SD: Standard deviation, Min.-max.: Minimum-maximum with LF preservation had a significantly lower incidence of postoperative fibrosis and lower back pain compared to those who underwent surgery without LF preservation[11,12].

On the other hand, there have been some conflicting findings in the literature regarding the effectiveness of anti-adhesion barrier gel in reducing fibrosis[13,14]. The use of anti-adhesion barrier gel significantly showed that can reduce the incidence of postoperative fibrosis compared to the control group, suggesting that it can also be effective in reducing the degree of fibrosis around the dura[15].

Several techniques have been described for reducing postoperative fibrosis. A systematic review and meta-analysis by Hosseini et al.[16] found that the use of anti-adhesion barrier gel was effective in reducing epidural fibrosis. Another study also recommended one-day adhesiolysis to reduce the extent of epidural fibrosis with a significant success rate[17].

Wang et al.[18] evaluated the use of cross-linked hyaluronic acid gel in reducing epidural fibrosis after lumbar discectomy. Cross-linked hyaluronic acid gel was found to prevent epidural adhesion by inhibiting inflammatory factors and downregulating the expression of TGFβ1 and COL1A1 mRNA, as demonstrated through *in vivo* and *in vitro* studies. This suggests that the use of an anti-adhesion barrier gel may have additional benefits beyond reducing fibrosis[18,19].

Various views have been proposed as to why connective tissue forms. Connective tissue formation may be a result of instability with age, sex, comorbidities, and axial predicates[20-22]. Removal of the developing connective tissue may cause new adhesions, and its removal with a second operation poses a major problem, especially because of nerve damage and dural opening[23,24]. Various suggestions on how to prevent connective tissue development have been reported. Among them are good control of wound bleeding, use of adhesion barriers agents, and recently, use of antifibrotic drugs[4,20,25,26]. However, the most effective method is LF preservation. This structure has an important role in the biomechanics of the spinal region. It is helps stabilizes of the spinal column and prevents hypermobility by protecting the range of motion. It also supports elasticity and stability by being among the spinal posterior column elements. Recent studies have shown that preserving the LF during spinal surgery can help maintain the biomechanical stability of the spine and reduce the risk of complications such as hypermobility and adjacent segment degeneration. While preserving the LF may help maintain spinal stability, there is limited evidence to suggest that it can reduce the risk of hypermobility specifically. However, preserving the LF can help maintain the integrity of the posterior spinal ligaments and reduce the risk of iatrogenic injury to these structures, which can lead to instability and hypermobility. Additionally, preserving the LF may help maintain the biomechanical function of the spinal column, which can contribute to overall spinal stability[8,27,28].

Also, we identified a significant relationship between the type of surgical technique used, the level of spinal surgery, and the degree of fibrosis. In the case of using the anti-adhesion barrier gel, higher degrees of fibrosis were observed in the hypermobile spine regions, specifically the lower lumbar region and thoracolumbar transitional zone. This suggests that better control of fibrosis development, especially in hypermobile regions, can be achieved through the preservation of the LF. These findings are consistent with previous studies reporting higher degrees of fibrosis in the hypermobile region or in the presence of instability. Thoracic and lumbar and lumbosacral regions of the spine are subject to different biomechanical stresses compared to other spinal levels, which might influence the healing process and the development of fibrosis. Additionally, hypermobility itself can contribute to the formation of fibrosis. Excessive movement in the spinal

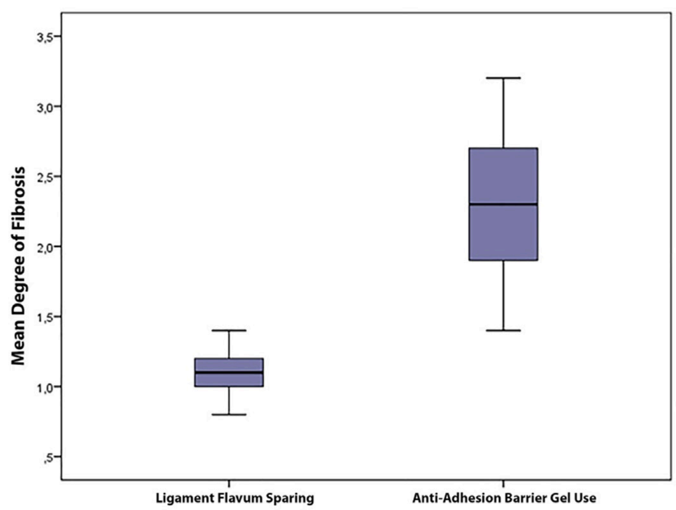

Figure 1. Distribution of mean degree of fibrosis levels by groups

Table 2. Evaluation of variables by groups

		Ligament flavum sparing	Anti-adhesion barrier gel use	p-value
Age (year)	Mean ± SD	48.36±8.03	53.68±7.54	[a]0.020*
	Median (Min.-max.)	48 (35-63)	54 (41-68)	
Sex; n (%)	Female	12 (48.0)	13 (52.0)	[b]0.777
	Male	13 (52.0)	12 (48.0)	
Mean degree of fibrosis	Mean ± SD	1.09±0.16	2.28±0.53	[c]0.001**
	Median (Min.-max.)	1.1 (0.8-1.4)	2.3 (1.4-3.2)	

[a]Student's t-test, [b]Chi-square test, [c]Mann-Whitney U test, *p<0.05, **p<0.01, SD: Standard deviation, Min.-max.: Minimum-maximum

segment can disrupt the delicate balance of tissue healing and increase the deposition of scar tissue. This can result in the formation of fibrotic adhesions around the spinal structures, including the epidural space[29,30].

The present study has some limitations, including a relatively small sample size and a lack of long-term follow-up data.

Table 3. Evaluation of mean degree of fibrosis among the spinal levels in the ligament flavum sparing group, (n=25)

Spinal level	Mean degree of fibrosis		p-value
	Mean ± SD	Median (Min.-max.)	
L2-L3 (Upper lumbar)	1.10±1.73	1.2 (0.9-1.2)	0.660
L4-S1 (Lower lumbar)	1.16±0.11	1.2 (1-1.3)	
T1-T11 (Upper thoracic)	1.04±0.18	1 (0.8-1.3)	
T12-L1 (Transitional zone)	1.11±0.18	1.1 (0.9-1.4)	

Kruskal-Wallis test, Bold value is not significant at the mentioned level of spine, SD: Standard deviation, Min.-max.: Minimum-maximum

Table 4. Evaluation of mean degree of fibrosis among the spinal levels in the anti-adhesion barrier gel use group (n=25)

Spinal level	Mean degree of fibrosis		p-value
	Mean ± SD	Median (Min.-max.)	
L2-L3 (Upper lumbar)	1.94±0.11	1.9 (1.8-2.1)	0.004**
L4-S1 (Lower lumbar)	2.72±0.31	2.65 (2.3-3.2)	
T1-T11 (Upper thoracic)	1.76±0.36	1.6 (1.4-3.2)	
T12-L1 (Transitional zone)	2.28±0.58	2.60 (1.6-2.8)	

Kruskal-Wallis test, **p<0.01, SD: Standard deviation, Min.-max.: Minimum-maximum

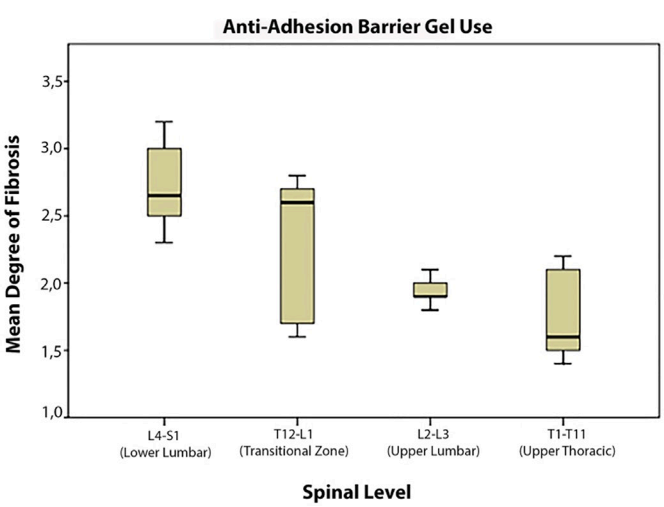

Figure 2. Distribution of mean degree of fibrosis levels in the anti-adhesion barrier gel use group by spinal level

However, further studies are required to identify the most effective strategies for preventing fibrosis, to determine the long-term effects of different surgical techniques on fibrosis and clinical outcomes in larger patient populations

In breaf, minimizing fibrosis formation is crucial in achieving successful spinal surgery outcomes, and recent literature suggests that the preservation of the LF and the use of minimally invasive surgical techniques may help reduce the extent of fibrosis and adhesion formation. Our study highlights the importance of using LF preserving technique that can reduce the degree of fibrosis around the dura during spinal surgery, particularly in the lower lumbar and thoracolumbar transitional region.

CONCLUSION

The use of the LF sparing technique can significantly reduce the degree of fibrosis around the dura compared to the use of anti-adhesion barrier gel. This reduction in fibrosis may result in improved patient outcomes and a decreased incidence of nerve root compression and chronic pain. Additionally, the level of surgery plays a crucial role in the development of fibrosis around the dura. To select the most effective surgical techniques for minimizing postoperative fibrosis, it is better to utilize the LF sparing technique rather than anti-adhesion barrier gels, particularly in the lower lumbar region and thoracolumbar transitional zone.

Ethics

Ethics Committee Approval: Institutional review board approval was obtained from the Ordu University Ethics Committee (approval number: 2023/167, date: 09.06.2023).

Informed Consent: Informed consent was obtained from our patients for our study.

Authorship Contributions

Surgical and Medical Practices: M.H., H.Ö., Concept: M.H., Design: M.H., Data Collection or Processing: M.H., H.Ö., Analysis or Interpretation: M.H., Literature Search: M.H., Writing: M.H., H.Ö.

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REFERENCES

1. Geisler FH. Prevention of peridural fibrosis: current methodologies. Neurol Res. 1999;21(Suppl 1):S9-22.
2. Subach BR, Copay AG. The use of a dehydrated amnion/chorion membrane allograft in patients who subsequently undergo reexploration after posterior lumbar instrumentation. Adv Orthop. 2015;2015:501202.
3. Petrie JL, Ross JS. Use of ADCON-L to inhibit postoperative peridural fibrosis and related symptoms following lumbar disc surgery: a preliminary report. Eur Spine J. 1996;5(Suppl 1):S10-7.

4. Wu L, Xu L, Chen Y, Xu G, Guo Q, Meng D, et al. Rolipram plays an anti-fibrotic effect in ligamentum flavum fibroblasts by inhibiting the activation of ERK1/2. BMC Musculoskelet Disord. 2021;22:818.
5. Ross JS, Robertson JT, Frederickson RC, Petrie JL, Obuchowski N, Modic MT, et al. Association between peridural scar and recurrent radicular pain after lumbar discectomy: magnetic resonance evaluation. ADCON-L European Study Group. Neurosurgery. 1996;38:855-61; discussion 861-3.
6. Çokluk C, Aydın K, Tümkaya L. Grading of epidural fibrosis in a new rabbit experimental model for epidural adhesive scar tissue formation. Journal of Experimental and Clinical Medicine (Turkey). 2009;26:107-11.
7. Olszewski AD, Yaszemski MJ, White AA 3rd. The anatomy of the human lumbar ligamentum flavum. New observations and their surgical importance. Spine (Phila Pa 1976). 1996;21:2307-12.
8. Wu CC, Jin HM, Yan YZ, Chen J, Wang K, Wang JL, et al. Biomechanical Role of the Thoracolumbar Ligaments of the Posterior Ligamentous Complex: A Finite Element Study. World Neurosurg. 2018;112:e125-33.
9. Song J, Park Y. Ligament-sparing lumbar microdiscectomy: technical note. Surg Neurol. 2000;53:592-6; discussion 596-7.
10. Ozer AF, Oktenoglu T, Sasani M, Bozkus H, Canbulat N, Karaarslan E, et al. Preserving the ligamentum flavum in lumbar discectomy: a new technique that prevents scar tissue formation in the first 6 months postsurgery. Neurosurgery. 2006;59:ONS126-33; discussion ONS126-33.
11. Li S, Xia H, Han C. Retrospective analysis on correlation factors of preserving the ligamentum flavum in microendoscopic discectomy. Clin Neurol Neurosurg. 2015;139:46-50.
12. Özay R, Ogur T, Durmaz HA, Turkoglu E, Caglar YS, Sekerci Z, et al. Revisiting Ligament-Sparing Lumbar Microdiscectomy: When to Preserve Ligamentum Flavum and How to Evaluate Radiological Results for Epidural Fibrosis. World Neurosurg. 2018;114:e378-87.
13. LeHuec JC, Sadikki R, Cogniet A, Rigal J, Demezon H, Aunoble S. Role of a collagen membrane in adhesion prevention strategy for complex spinal surgeries. Int Orthop. 2015;39:1383-90.
14. Chaturvedi AA, Lomme RM, Hendriks T, van Goor H. Prevention of postsurgical adhesions using an ultrapure alginate-based gel. Br J Surg. 2013;100:904-10.
15. de Tribolet N, Porchet F, Lutz TW, Gratzl O, Brotchi J, van Alphen HA, et al. Clinical assessment of a novel antiadhesion barrier gel: prospective, randomized, multicenter, clinical trial of ADCON-L to inhibit postoperative peridural fibrosis and related symptoms after lumbar discectomy. Am J Orthop (Belle Mead NJ). 1998;27:111-20.
16. Hosseini S, Niakan A, Dehghankhalili M, Dehdab R, Shahjouei S, Rekabdar Y, et al. Effects of adhesion barrier gel on functional outcomes of patients with lumbar disc herniation surgery; A systematic review and meta-analysis of clinical trials. Heliyon. 2021;7:e07286.
17. Masopust V, Holubová J, Skalický P, Rokyta R, Fricová J, Lacman J, et al. Neuromodulation in the treatment of postoperative epidural fibrosis: comparison of the extent of epidural fibrosis and the effect of stimulation. Physiol Res. 2021;70:461-8.
18. Wang K, Li XL, Liu J, Sun X, Yang H, Gao X. Using cross-linked hyaluronic acid gel to prevent postoperative lumbar epidural space adhesion: in vitro and in vivo studies. Eur Spine J 2020;29:129-40.
19. Turkoglu E, Dinc C, Tuncer C, Oktay M, Serbes G, Sekerci Z. Use of decorin to prevent epidural fibrosis in a post-laminectomy rat model. Eur J Pharmacol. 2014;724:86-91.
20. Sun C, Zhang H, Wang X, Liu X. Ligamentum flavum fibrosis and hypertrophy: Molecular pathways, cellular mechanisms, and future directions. FASEB J. 2020;34:9854-68.
21. Li S, Xia H, Han C. Retrospective analysis on correlation factors of preserving the ligamentum flavum in microendoscopic discectomy. Clin Neurol Neurosurg. 2015;139:46-50.
22. Yasargil MG. Microsurgical operation of herniated lumbar disc. Lumbar Disc Adult Hydrocephalus. Berlin, Heidelberg: Springer Berlin Heidelberg. 1977;81.
23. Askar Z, Wardlaw D, Choudhary S, Rege A. A ligamentum flavum-preserving approach to the lumbar spinal canal. Spine (Phila Pa 1976). 2003;28:E385-90.
24. Tatsui CE, Martinez G, Li X, Pattany P, Levi AD. Evaluation of DuraGen in preventing peridural fibrosis in rabbits. Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2005. J Neurosurg Spine. 2006;4:51-9.
25. Aydin Y, Ziyal IM, Duman H, Türkmen CS, Başak M, Sahin Y. Clinical and radiological results of lumbar microdiskectomy technique with preserving of ligamentum flavum comparing to the standard microdiskectomy technique. Surg Neurol. 2002;57:5-13; discussion 13-4.
26. Mastronardi L, Pappagallo M, Tatta C, Roperto R, Elsawaf A, Ferrante L. Prevention of postoperative pain and of epidural fibrosis after lumbar microdiscectomy: pilot study in a series of forty cases treated with epidural vaseline-sterile-oil-morphine compound. Spine (Phila Pa 1976). 2008;33:1562-6.
27. Widmer J, Cornaz F, Scheibler G, Spirig JM, Snedeker JG, Farshad M. Biomechanical contribution of spinal structures to stability of the lumbar spine-novel biomechanical insights. Spine J. 2020;20:1705-16.
28. Damm N, Rockenfeller R, Gruber K. Lumbar spinal ligament characteristics extracted from stepwise reduction experiments allow for preciser modeling than literature data. Biomech Model Mechanobiol. 2020;19:893-910.
29. Bezer M, Gokkus K, Kocaoglu B, Guven O. The influence of vertebral instability on peridural circulation and concomitant peridural fibrosis formation. Eur Spine J. 2006;15:959-64.
30. Izzo R, Guarnieri G, Guglielmi G, Muto M. Biomechanics of the spine. Part II: spinal instability. Eur J Radiol. 2013;82:127-38.

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MINIMALLY INVASIVE UNILATERAL HEMILAMINECTOMY APPROACH FOR THE REMOVAL OF SPINAL SCHWANNOMAS IMPACT ON PAIN AND NEUROLOGICAL RESULTS

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ABSTRACT

Objective: Spinal intradural tumors are commonly removed using laminectomy or laminotomy; however, these approaches can lead to postoperative pain, discomfort, kyphosis, and instability. Unilateral hemilaminectomy (UHL) is a minimally invasive alternative that may minimize these issues by using a smaller incision and less disruption to spinal structures.

Materials and Methods: From 2010 to 2021, 79 patients with schwannoma underwent UHL surgery. Surgery was generally limited to three levels, and the tumor was removed en bloc or piecemeal after ultrasonic debulking. Paramedial opening of the dura was performed, and neurophysiological monitoring was performed. Baseline medical data on demographic and clinical variables were analyzed, including patients' sex, age, tumor location and volume, overall operative time, length of postoperative immobilization, duration of hospitalization, preoperative (1-month/3-month postoperative Denis Pain Scale value), comorbidities, and modified McCormick Scale.

Results: Of these patients, 35 were female and 44 were male, with ages ranging from 19 to 72 years (mean 48.9±14.6). Pain and radiculopathy were the first symptoms in 56 (70.8%) and 36 (45.5%) patients, respectively. No spinal instability was observed postoperatively, and the mean estimated blood loss was 285 mL, ranging from 245-420 mL. The maximal sagittal diameter of the tumor was measured on contrast-enhanced T1-weighted images, with a mean of 26.0±12.4 mm (range, 8.2-36.2 mm).

Conclusion: Unilateral microsurgery for spinal intradural tumor removal has resulted in good neurologic and oncologic outcomes and reduced postoperative pain and discomfort. In addition, this approach has preserved spinal stability, eliminating the need for bracing, and enabling earlier rehabilitation.

Keywords: Spinal surgery, spinal schwannoma, pain, hemilaminectomy, minimally invasive neurosurgery

INTRODUCTION

Schwannomas of the spine are generally non-cancerous growths that develop gradually, originating from Schwann cells. These cells envelop and provide insulation to nerve fibers found in the peripheral nervous system[1]. They are most commonly found in the intradural extramedullary (IDEM) region of the spine[1]. Although these tumors are usually benign, they can cause symptoms by compressing nearby nerves or the spinal cord itself. Treatment options for spinal schwannomas typically involve surgical removal of the tumor[2]. In the field of neurosurgery, the technique of total laminectomy or laminotomy at single or multiple levels is frequently employed for the removal of intradural or extramedullary tumors within the spinal region, such as spinal schwannomas[3]. The selection of the surgical technique hinges on factors like the tumor's size and location, as well as the surgeon's personal preferences and level of expertise[4]. Both laminectomy and laminotomy techniques can effectively remove spinal tumors while minimizing damage to the spinal cord and nerves. However, the choice of surgical approach may differ based on factors such as tumor size, location, the patient's specific condition, and various other considerations. It's important to note that total laminectomy or laminotomy procedures can result in the removal of posterior bony structures, detachment of the paraspinal muscles, and disruption of the interspinous ligament, potentially leading to postoperative pain, the need for external bracing, and an increased risk of delayed spine instability or kyphosis. The detachment of the paraspinal muscles can also lead to persistent back pain. For tumors located anteriorly, the spinal cord may need to be manipulated or rotated after sectioning the dentate ligament, which can increase the risk of neural damage[5]. To minimize the potential complications associated with total laminectomy/laminotomy, some surgeons may opt for more conservative surgical approaches, such as

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hemilaminectomy or laminoplasty[4,5]. These techniques can preserve more of the spinal structures and may result in fewer postoperative complications.

In minimally invasive procedures, there is a greater emphasis on reducing the amount of bone and tissue removal compared to traditional open surgery[5]. This is done in order to reduce postoperative pain, minimize blood loss, shorten hospital stays, and eliminate the potential risk of instability[6]. Although minimally invasive methods and microsurgery have advanced in the field of spinal tumor removal, the unilateral hemilaminectomy (UHL) approach is not commonly employed and lacks widespread acceptance. There are limited recent publications on this technique, and it is typically referenced in neurosurgical textbooks only for addressing small tumors situated in lateral positions[5,7,8]. However, recent studies have suggested that the unilateral approach may be a valuable surgical option for certain spinal tumors, particularly those located in the thoracic spine[9,10]. The objective of this study appears to be to investigate whether a less invasive surgical strategy, consisting of UHL, tumor removal, and duraplasty, can achieve comparable surgical and clinical results to traditional open surgery for spinal tumors. The study aimed to determine whether this less invasive approach resulted in an increased risk of tumor recurrence, as has been reported in some studies in the literature[4,6].

MATERIALS AND METHODS

The study involved 79 adult patients who underwent minimally invasive UHL for IDEM spinal schwannoma which was confirmed by histopathological examination between 2010 and 2021, in the University of Health Sciences Turkey, Ankara Bilkent City Hospital, Clinic of Neurosurgery. Ethical approval for this study was obtained from the Ankara City Hospital No. 2 Clinical Research Ethics Committee (decision no: E2-23-5066, date: 27/09/2023). This retrospective study received approval from the Institutional Review Board, and written informed consent was obtained from each patient.

A total of twenty-two patients were excluded from the study. This exclusion comprised six patients with extradural paravertebral schwannoma, five patients with spinal schwannoma associated with neurofibromatosis, and eleven patients with extradural sacral schwannoma, whether or not they had retroperitoneal elongation. Patients with extradural paravertebral schwannoma may require a different surgical approach or have a different prognosis compared to patients with IDEM spinal schwannoma, so these patients were excluded from the study. Similarly, patients with spinal schwannoma due to neurofibromatosis may have a different clinical presentation or require a different management approach compared to patients with sporadic spinal schwannoma. In addition, patients diagnosed with non-schwannoma in histopathological examination were not included in the study.

We analyzed baseline medical data encompassing a variety of demographic and clinical variables, such as patients' gender, age, tumor location, and size, total surgical duration, duration of postoperative immobilization, length of hospital stay, preoperative, 1-month, and 3-month postoperative Denis Pain Scale values (DPS), comorbidities, and the modified McCormick Scale (mMcS)[11,12]. The DPS is a validated tool for measuring pain intensity and quality and can provide important information about the effectiveness of pain management strategies[12] (Table 1). In addition to pain evaluation, the study also included assessments of neurological function and quality of life at admission and 12 months after surgery. The modified mMcS, as applied by Klekamp for intramedullary tumors, was used to evaluate neurological function[11]. The mMcS is a widely used tool for assessing neurological function in patients with spinal cord injury or disease and can help determine the extent of any motor or sensory deficits[11] (Table 2).

To manage postoperative pain, intravenously infused analgesics were used for the first 24 hours after surgery. After this initial period, oral analgesics may be used to manage any remaining pain. For patients experiencing postoperative radicular and meningeal pain, methylprednisolone can be considered for reducing inflammation caused by cerebrospinal fluid (CSF) blood contamination. The choice of analgesic will depend on the severity of pain and individual patient factors. Prolonged analgesic therapy may be considered if pain persists beyond the initial postoperative period, and should be carefully managed to minimize the risk of adverse effects.

The tumor size was measured using the widest diameter in three planes and the volume was calculated using the ellipsoid method (D1xD2xD3/2). This is a common method for calculating tumor volume, and it allows for a more accurate assessment of the size and complexity of the tumors. Skilled neurosurgeons conducted all procedures.

Table 1. Denis' Pain Scale[12]

Grade	Description
P1	No pain
P2	Occasional minimal pain; no need for medication
P3	Moderate pain, occasionally medications and no interruption of work or activity of daily living
P4	Moderate pain, occasionally absent from work; significant changes in activities of daily living
P5	Constant, severe pain; chronic pain medications

Table 2. Modified McCormick Scale (Klekamp)[11]

Grade	Description
I	Neurologically intact, minimal dysesthesia
II	Mild motor and/or sensory deficit, independent
III	Moderate deficit, functionally impaired, external aid
IV	Severe deficit, limited function, dependent
V	Paraplegia or quadriplegia

Statistical Analysis

Data analysis was carried out using two statistical software programs: IBM SPSS 25.0 (IBM Corp., Armonk, NY) and MedCalc 15.8 (MedCalc Software bvba, Ostend, Belgium). The analysis included various descriptive statistical methods such as frequency, percentage, mean, standard deviation, median, minimum, and maximum values. To compare qualitative data, chi-square tests were employed, including Pearson's chi-square tests, Yates' Corrected chi-square tests, and Fisher's exact test. Relationships between variables were assessed using Spearman's rho correlation test. The statistical significance level was set at α=0.05.

Operative Technique

The patient was positioned in a prone orientation under general anesthesia. A midline skin incision, aligned with the radiograph marker located over the tumor's spinous process, was employed. Intraoperative neurophysiologic monitoring, a critical safety measure during surgery, was applied to all patients. Retaining the paravertebral muscles of the tumor side is a key feature of the UHL technique, as this helps to minimize damage to the muscles and surrounding tissue. The surgical procedure involved using a high-speed drill to remove the hemilaminae, exposing the dural sac. In cases where patients had lateral tumor extensions, a partial facetectomy was performed to access the tumor. A surgical procedure was performed involving a single-level hemilaminectomy using bone forceps and/or a high-speed drill. If necessary, the hemilaminectomy was extended to the adjacent cranial or caudal interlaminar spaces and, in some cases, to an additional lamina. To create more space, a section of the interspinous ligament, usually the most deep portion, was removed with Kerrison bone forceps, typically 2-3 millimeters. In cases where the mass could not be initially identified, the surgical team would begin their search by extending the surgical opening in a cranial direction. Before opening the protective layer known as the meninges, intraoperative ultrasonography with specialized probes was employed to assist in locating the mass. Following this, the dura, the outermost protective layer of the spinal cord, was carefully opened in a paramedial fashion, ensuring a sufficient medial flap remained to facilitate easy suturing. Subsequently, the spinal cord and/or nerve roots were visualized through a tangential corridor. If better visibility was needed, the operating table could be rotated to optimize exposure of the ventral aspect of the spinal cord. For enhanced visualization, an operating microscope was utilized, and a cavitron ultrasonic aspirator helped decompress the tumor internally. Subsequently, the next step was to meticulously dissect the capsule from the surrounding tissues. Occasionally, particularly in the thoracic region, it was necessary to sacrifice the sensory nerve root when capsule dissection wasn't feasible. In situations where the tumor was located in the cervical and lumbar regions, a small residue of tumor tissue might intentionally be left behind to prevent nerve damage. Following the removal or decompression of the tumor, the dura mater was securely sutured with an appropriate thickness of non-absorbable surgical suture, ensuring a watertight closure. Typically, fibrin glue and fat were applied epidurally to reinforce the closure and support the healing process.

RESULTS

Of these patients, 35 were female and 44 were male, and their ages ranged from 19 to 72 years (mean 48.9±14.6). Pain and radiculopathy were the first symptoms to occur in 56 (70.8%) and 36 (45.5%) patients, respectively. Regional pain and radiculopathy were seen together in 20 (25.3%) patients (Table 3).

According to the DPS, when preoperative pain evaluated, 16 patients were graded P5 (constant pain), 34 patients were P4 and 16 patients were P3. 13 patients had no pain. At first month's follow-up, the grading improved to P1 in 23 patients, P2 in 20 patients, and P3 in 36 patients. At third months follow-up grading improved to P1 in 33 patients and P2 in 39 patients. 7 of patients were graded P3. The overall results on pain were also evaluated: preoperative versus 3rd month's follow-up pain decreasement was significant ($p<0.05$) (Table 4).

Out of the 79 patients, 31 experienced varying degrees of paraparesis/monoparesis: 5 had moderate paraparesis (mMcS: III), while 6 had severe paraparesis (mMcS: IV). Sphincter

Table 3. Baseline characteristics of patients and tumors

Patient characteristics	Value (Range)
Patient numbers	79
Male	44
Female	35
Age (years)	48.9±14.6 (19-72)
Symptom duration (months)	20.8±27.8 (0.5-120)
Tumors' details	
Number of tumors (total)	79
Maximal sagittal diameter (mm)	26.0±12.4 mm (range, 8.2-36.2 mm)
Maximal axial diameter (mm)	14.2±6.1 mm (range, 8.0-33.1 mm)
Tumor volume (cm)	0.52 cm (range, 0.35-0.70)
Location of tumors	
Cervical	20
Cervicothoracic	5
Thoracic	21
Thoracolumbar	5
Lumbar	24
Lumbosacral	4
Histopathology	
Grade 1	77
Malignant transformation	2

Values are numbers or mean ± Standard deviation

Table 4. Details of the symptom "pain", classified according to Denis Pain Scale

Denis grade	Preoperative	1st month	3rd month
P1	13	23	33
P2	None	20	39
P3	16	36	7
P4	34	None	None
P5	16	None	None

dysfunction and plegia (mMcS: V) were observed in 10 patients. Remarkably, 13 patients achieved complete neurological recovery (mMcS: I), while 7 exhibited residual spasticity and minor hypoesthesia (mMcS: II). Four patients regained the ability to walk independently, albeit with moderate spasticity and occasional assistance (mMcS: IV). However, complete recovery from sphincter dysfunction and paraplegia was notably challenging, with only three patients achieving it. In the overall analysis of neurological recovery, no statistically significant differences were observed (p>0.05) (Table 5).

It seems that the duration of surgery for the cases ranged from 100 to 220 minutes with an average of 160 minutes. It's important to note that the duration of surgery can be affected by various factors such as the complexity of the procedure, the patient's medical condition, and the surgeon's experience and skill level. In this study, the mean estimated blood loss of 285 mL, ranges between 245-420 mL.

When the location of tumors are evaluated; there were lumbosacral tumors in 4 patients, lumbar tumors in 24 patients, thoracolumbar tumors in 5 patients, thoracic tumors in 21 patients, cervicothoracic tumors in 5 patients, and cervical tumors in 20 patients (Table 3, Figure 1).

The tumor maximal sagittal diameter was measured on contrast-enhanced T1-weighted images: 26.0±12.4 mm (range, 8.2-36.2 mm). In addition, maximal axial diameter was measured 14.2±6.1 mm (range, 8.0-33.1 mm). Tumor volume was calculated by the ellipsoid method, with a mean of 0.52 cm (range, 0.35-0.70). A foraminal tumor extension was identified in 19 (24.05%) patients.

All tumors in this study were successfully dissected and excised, even in the foraminal extended portion. The achievement of GTR in all tumors was accomplished. There is no need for posterior fixation in any patient. The histopathological confirmation of all tumors were done as schwannomas (Figure 2).

Three patient developed CSF leakage on postoperative, and revision surgery for dural repair was performed for 1 patient. Lumbar drain were inserted to other 2 patients. Otherwise, no serious postoperative complications developed. The patients' mean hospital stay were 5.8 days (range, 2-19 days). Recurrence was seen in 4 patients. Three patients were reoperated, and one patient was treated with stereotactic radiosurgery.

The mean follow-up time was 41.2±35.3 months. We considered that a 12-month follow-up period is a common and reasonable time frame for evaluating the outcomes of surgical treatment.

Table 5. Outcome of patients, modified McCormick Scale

Grade	Preoperative	Postoperative 12th month
I	48	61
II	10	7
III	5	None
IV	6	4
V	10	7

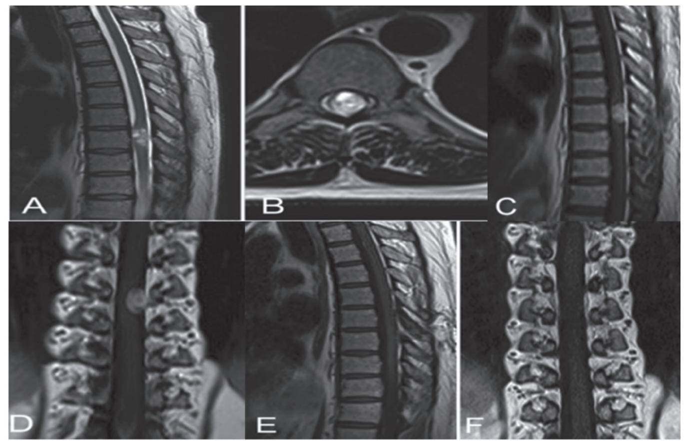

Figure 1. A 50-year-old male patient who presented with low back pain and numbness in both lower regions. Pre-op T2 sagittal **(A)** and axial **(B)** MR images, sagittal (**C)** and axial **(D)** contrast MR images. T1-weighted sagittal **(E)** and axial **(F)** images with contrast 3rd month postop, postop axial CT image

MR: Magnetic resonance, CT: Computed tomography

It allows sufficient time for patients to recover from surgery and for any potential complications or recurrence of symptoms to become apparent. Additionally, it provides a meaningful assessment of the effectiveness of the surgical intervention and any associated therapies.

DISCUSSION

The size of the transosseous, transligamentous corridor required for safe and effective intraspinal benign tumor resection depends on various factors such as the location, size, and extent of the tumor, as well as the surgeon's experience and skill. Generally, the corridor should be wide enough to provide adequate exposure of the tumor margins while minimizing the risk of damaging the spinal cord and nerve roots[13,14]. A thorough preoperative evaluation and planning, including imaging studies and neurological assessment, can help guide the surgeon in determining the appropriate size of the corridor needed for safe and effective removing the tumor completely; and avoid spinal deformity and/or instability[13].

The study utilized the DPS to assess preoperative pain levels and observed significant improvements in pain levels at one-month and three-month follow-up assessments, highlighting the surgical intervention's effectiveness in relieving pain, a primary treatment goal for spinal cord schwannomas. A

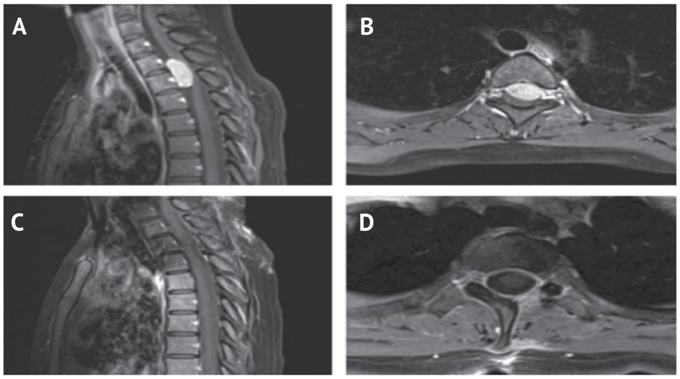

Figure 2. A 44-year-old female patient. **A, B)** A ventral intradural extramedullary tumor was detected at T2-T3 level on sagittal and axial preoperative T1-weighted contrast-enhanced MR images. **C, D)** Sagittal and axial postoperative T1-weighted contrast-enhanced MR images showed no residual tumor

MR: Magnetic resonance

significant proportion of patients had preoperative paraparesis or monoparesis. While many achieved full neurological recovery, overcoming sphincter dysfunction and paraplegia proved more challenging. Nevertheless, surgery led to substantial neurological improvements, offering promise for spinal cord schwannoma patients.

The average surgery duration (160 minutes) and estimated blood loss were within safe ranges, underscoring the procedure's feasibility and safety, particularly in the hands of experienced surgeons. Complication rates related to surgery duration and blood loss were low, supporting the procedure's safety. Tumor locations varied, with cervical and lumbar regions being the most common. GTR was achieved in all tumors, even those with foraminal extension, affirming the surgical approach's effectiveness. Despite a generally low postoperative complication rate, a few cases of CSF leakage required revision surgery. Notably, no posterior fixation was needed, demonstrating surgical stability. Tumor recurrence rates were relatively low, with successful reoperation or stereotactic radiosurgery for recurrent cases. The lengthy average follow-up period of 41.2 months provides a comprehensive evaluation of short and long-term outcomes, shedding light on surgical outcome durability and potential late complications or recurrences.

Certain authors have documented that hemilaminectomy is a surgical approach that has the potential to alleviate pain and maintain spinal stability in cases involving schwannomas. Additionally, they suggest that this restricted surgical corridor may be suitable for addressing ventral and lateral meningiomas[15].

While laminotomy may preserve more of the spinal stability than laminectomy, it still involves the sectioning of the interspinous ligament, bilateral stripping and retraction of muscles, and bilateral disruption of the ligamentum flavum, which may result in spinal instability in some cases[16]. Furthermore, laminotomy may not provide sufficient exposure for complete tumor removal in all cases, particularly for larger or more complex tumors[7,16]. In these cases, a more extensive laminectomy or other surgical approach may be necessary to achieve adequate exposure and safe tumor removal. Postoperative spinal instability, deformity, and epidural fibrosis are potential complications of laminectomy, laminotomy, and other spinal surgeries. External bracing may be necessary to help support the spinal column during the healing process and reduce the risk of postoperative complications[17].

Yaşargil et al.[14] indeed advocated for the unilateral approach as the primary choice when it comes to removing intraspinal tumors, especially when these tumors are situated in the ventral and lateral regions of the spinal canal. This recommendation was grounded in the concept that a UHL offers sufficient tumor exposure while reducing the potential for spinal instability and deformity when contrasted with more extensive laminectomy techniques[5,14]. By removing only, a portion of the affected lamina, the unilateral approach preserves spinal stability and avoids the need for external bracing, while also reducing the risk of postoperative spinal deformity and epidural fibrosis. The approach also allows for better preservation of the paraspinal muscles and soft tissues, which may contribute to better postoperative pain control and faster recovery[17].

It's truly reassuring to note that all patients in our series experienced an improvement in their preoperative pain, with the majority able to discontinue analgesic medications shortly after surgery. Prolonged and intense pain stemming from muscular or spinal sources can have substantial adverse effects on patients, including extended hospital stays, reduced comfort, an increased risk of depression, prolonged recovery at home, elevated social and healthcare expenditures, and potential legal issues. Beyond the impact on the patient's physical and emotional well-being, unmanaged pain can also influence the quality of care delivered by healthcare providers and, consequently, the broader healthcare system[18,19]. It is important to acknowledge that our paper does not provide a detailed analysis of chronic pain treatment, but rather focuses on the surgical approach for the removal of benign intradural tumors. However, the results of our study suggest that the unilateral approach may be superior to the bilateral approach in terms of improving pain as a main symptom in these patients. Exploring the potential advantages of the unilateral approach in pain management for patients with benign intradural tumors, such as meningiomas and schwannomas, certainly merits further investigation. Subsequent studies could delve deeper into the analysis of medication regimens, usage patterns, treatment durations, and an evaluation of the comprehensive costs linked to the care of these patients.

It is reassuring to hear that none of the cases in our study experienced early or late spinal deformity or instability, and that external bracing was not necessary. Low complication rate, with only one case of transient new neurological deficit and negligible postural headache and meningeal inflammation, is also noteworthy in this study. However, the three cases of CSF leakage/pseudo meningocele requiring reoperation or lumbar drain insertion are a potential concern. While these complications are not uncommon following intradural spinal surgery, they can lead to significant morbidity and may require further intervention.

It is important to continue to monitor and assess the potential risks and benefits of surgical approaches for the removal of benign intradural tumors, and to develop strategies to minimize the risk of complications such as CSF leakage and pseudo meningocele. This may include optimizing surgical techniques, implementing strict postoperative protocols for monitoring and management, and providing appropriate patient education and follow-up care.

Study Limitations

The study suggests that identifying anatomical structures through a narrow surgical corridor can be difficult for beginners and that dural closure is particularly challenging in microsurgical techniques. The study also notes that the choice of surgical approach is subjective and based on the preferences and experience of the individual surgeons. This suggests that there may be variability in the techniques used by different surgeons and highlights the importance of individualized patient care. It is worth noting that this study represents the experience of a single surgeon and may not be generalizable to other surgical contexts or practitioners. Further research is needed to fully understand the challenges and benefits of UHL approaches for intradural schwannoma removal and to develop standardized guidelines for surgical management.

CONCLUSION

When employed accurately and following a reasonable learning curve, the UHL approach offers an efficient and sufficient path to access the dural sac. As a result, it ensures the secure removal of nearly all schwannomas encountered in neurosurgical practice. This technique presents numerous advantages in the management of intraspinal tumors. These benefits encompass its capacity to avert instability, facilitate early mobilization and rehabilitation, limit manipulation of the spinal cord, mitigate blood loss, and diminish postoperative discomfort. These advantages can profoundly influence the patient's recuperation and overall quality of life.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Ankara City Hospital No. 2 Clinical Research Ethics Committee (decision no: E2-23-5066, date: 27/09/2023).

Informed Consent: Written informed consent was obtained from each patient.

Authorship Contributions

Surgical and Medical Practices: A.E.S., Ö.Ö., A.D., Concept: A.E.S., E.Ç., A.D., Design: E.Ç., A.D., Data Collection or Processing: A.E.S., D.D., Analysis or Interpretation: D.D., Literature Search: E.Ç., Ö.Ö., Writing: A.E.S., E.Ç.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Conti P, Pansini G, Mouchaty H, Capuano C, Conti R. Spinal neurinomas: retrospective analysis and long-term outcome of 179 consecutively operated cases and review of the literature. Surg Neurol. 2004;61:34-43; discussion 44.
2. Ghani AR, Ariff AR, Romzi AR, Sayuthi S, Hasnan J, Kaur G, et al. Giant nerve sheath tumour: report of six cases. Clin Neurol Neurosurg. 2005;107:318-24.
3. Seppälä MT, Haltia MJ, Sankila RJ, Jääskeläinen JE, Heiskanen O. Long-term outcome after removal of spinal schwannoma: a clinicopathological study of 187 cases. J Neurosurg. 1995;83:621-6.
4. Walha S, Fairbanks SL. Spinal Cord Tumor Surgery. Anesthesiol Clin. 2021;39:139-49.
5. Helal A, Yolcu YU, Kamath A, Wahood W, Bydon M. Minimally invasive versus open surgery for patients undergoing intradural extramedullary spinal cord tumor resection: A systematic review and meta-analysis. Clin Neurol Neurosurg. 2022;214:107176.
6. Pompili A, Caroli F, Crispo F, Giovannetti M, Raus L, Vidiri A, et al. Unilateral Laminectomy Approach for the Removal of Spinal Meningiomas and Schwannomas: Impact on Pain, Spinal Stability, and Neurologic Results. World Neurosurg. 2016;85:282-91.
7. Ahn DK, Park HS, Choi DJ, Kim KS, Kim TW, Park SY. The surgical treatment for spinal intradural extramedullary tumors. Clin Orthop Surg. 2009;1:165-72.
8. Angevine PD, Kellner C, Haque RM, McCormick PC. Surgical management of ventral intradural spinal lesions. J Neurosurg Spine. 2011;15:28-37.
9. Canbay S, Hasturk AE, Basmaci M, Erten F, Harman F. Management of Thoracal and Lumbar Schwannomas Using a Unilateral Approach without Instability: An Analysis of 15 Cases. Asian Spine J. 2012;6:43-9.
10. Chen R, Xiao A, Xing L, You C, Liu J. A rare thoracic intraspinal schwannoma in twin pregnancy with aggravated clinical presence: A case report following CARE. Medicine (Baltimore). 2017;96:e6327.
11. Klekamp J. Treatment of intramedullary tumors: analysis of surgical morbidity and long-term results. J Neurosurg Spine. 2013;19:12-26.
12. Gloth FM 3rd, Scheve AA, Stober CV, Chow S, Prosser J. The Functional Pain Scale: reliability, validity, and responsiveness in an elderly population. J Am Med Dir Assoc. 2001;2:110-4.
13. Safavi-Abbasi S, Senoglu M, Theodore N, Workman RK, Gharabaghi A, Feiz-Erfan I, et al. Microsurgical management of spinal schwannomas: evaluation of 128 cases. J Neurosurg Spine. 2008;9:40-7.
14. Yaşargil MG, Tranmer BI, Adamson TE, Roth P. Unilateral partial hemi-laminectomy for the removal of extra- and intramedullary tumours and AVMs. Adv Tech Stand Neurosurg. 1991;18:113-32.
15. Ottenhausen M, Ntoulias G, Bodhinayake I, Ruppert FH, Schreiber S, Förschler A, et al. Intradural spinal tumors in adults-update on management and outcome. Neurosurg Rev. 2019;42:371-88.
16. McGirt MJ, Garcés-Ambrossi GL, Parker SL, Sciubba DM, Bydon A, Wolinksy JP, et al. Short-term progressive spinal deformity following laminoplasty versus laminectomy for resection of intradural spinal tumors: analysis of 238 patients. Neurosurgery. 2010;66:1005-12.

17. Dobran M, Paracino R, Nasi D, Aiudi D, Capece M, Carrassi E, et al. Laminectomy versus Unilateral Hemilaminectomy for the Removal of Intraspinal Schwannoma: Experience of a Single Institution and Review of Literature. J Neurol Surg A Cent Eur Neurosurg. 2021;82:552-5.
18. Sario-glu AC, Hanci M, Bozkuş H, Kaynar MY, Kafadar A. Unilateral hemilaminectomy for the removal of the spinal space-occupying lesions. Minim Invasive Neurosurg. 1997;40:74-7.
19. Sim JE, Noh SJ, Song YJ, Kim HD. Removal of intradural-extramedullary spinal cord tumors with unilateral limited laminectomy. J Korean Neurosurg Soc. 2008;43:232-6.

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THE EFFECT OF ANTI-INFLAMMATORY, ANTIOXIDATIVE, AND NEUROPROTECTIVE CHARACTERISTICS OF ALOPERINE ON EXPERIMENTAL ACUTE SPINAL CORD INJURY IN A RAT MODEL

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ABSTRACT

Objective: Spinal cord injury (SCI) disrupts nerve axons with devastating neurological consequences. However, there is no effective clinical treatment. The purpose of this study was to investigate the effects of the anti-inflammatory, antioxidative, and neuroprotective characteristics of alverine on traumatic spinal injury in a rat model.

Materials and Methods: A total of 36 Wistar albino rats, each weighing 300-400 g, were divided into four treatment groups. In Group 1 (sham/control, n=9), only laminectomy was performed. In Group 2 (SCI, n=9), SCI was simulated after laminectomy. In Group 3 (SCI + saline, n=9), physiological saline solution was injected after SCI was induced. In Group 4 (SCI + aloperine), aloperine was administered after SCI was induced. SCI was established using the weight drop technique after laminectomy.

Results: Neurological examination scores were significantly better in the aloperine-treated group than in Groups 2 and 3. SCI significantly increased serum and spinal cord tissue glutathione peroxidase, total oxidant status, 8-hydroxiguanosine, and interleukin-6 levels. These levels were successfully reduced with alverine administration. Interleukin-10 and total antioxidant status levels also decreased with alverine administration. Increased histopathological spinal cord damage score and apoptotic index in Groups 2 and 3 were significantly decreased in Group 4.

Conclusion: Aloperine reduced apoptosis and increased anti-inflammatory and antioxidative mediator levels, which protected the SCI rat model against secondary nerve injury.

Keywords: Aloperine, antioxidant, inflammation, reactive oxygen species, spinal cord injury

INTRODUCTION

Spinal cord injury (SCI) accounts for 11.5-53.4 cases per million annually[1]. SCI causes varying degrees of loss of work and psychological effects among the patients and their relatives. Primary damage occurs at the time of injury, and there is no cure other than prevention. However, secondary damage occurs due to the accumulation of free oxygen radicals, cord ischemia, ionic imbalance, and cellular excitotoxicity[2]. Trauma causes neural ischemia, nerve compression, thrombosis, and vasospasm. Thus, it is important to manage this part of the injury by increasing cord perfusion and reducing reactive oxygen species (ROS)[3,4].

Aloperine (ALO) has been used to treat various neurological diseases. For example, it has been used in a cell model of Alzheimer's disease to reduce ROS and the resultant cell apoptosis[5]. In one study, ALO reduced inflammatory infiltration and tubular cell apoptosis, and protected the mice against renal injury[6]. In another study, ALO protected against oxygen-glucose deprivation and cultured rat hippocampal[7]. In an energy-deficient environment, ALO can diffuse across the blood-brain barrier[7]. Therefore, we hypothesized that ALO may protect a patient against cerebrospinal injury. Thus, in this study, we aimed to demonstrate the effects of ALO in terms of anti-inflammation, antioxidation, and anti-apoptosis.

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MATERIALS AND METHODS

Groups

Four study groups were created. In Group 1, only laminectomy was performed. In Group 2, SCI was mimicked after laminectomy. In Group 3, after SCI, a physiological saline solution was administered. In group 4, ALO was administered.

Anesthesia and Surgical Technique

Saline containing 10% acetic acid (2.5 mg/mL) was used to dissolve ALO (Kmaels, Shanghai, China)[6]. ALO (150 mg/kg) was administered intraperitoneally 2 and 24 hours after induction of the SCI model in Group 4[8]. Analyses involved western blotting, immunohistochemistry (IHC), terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) staining, assessment of neurological deficits, and enzyme activity assays.

Intraperitoneal injections of 10 mg/kg of ketamine (Ketalar; Parke-Davis, Eczacıbaşı, Turkey) and 50 mg/kg of xylazine (Alfazyne; Egevet, İzmir, Turkey) were used to anesthetize all rats. A midline incision was made between T7 and T12, and total laminectomy at T10 and T11 were performed. After the total laminectomy, a 10-g impact weight was dropped from a predetermined height of 25 mm onto the thoracic spinal cord in the SCI group. In Group 3, 150 mg/kg of 10% acetic acid solution was administered intraperitoneally. In Group 4, 150 mg/kg of ALO was intraperitoneally administered.

Two weeks after SCI, all animals were decapitated under deep anesthesia. The spinal cord was removed for histopathological examination and blood samples were drawn for biochemical analyses.

Biochemical Analysis

Blood samples were stored at -40 ˚C. Mechanical and ultrasonic homogenizers were used to thaw the tissue samples. Tissue levels of 8-hydroxiguanosine (8-OHG) (Sinogeneclon Co., Ltd.), glutathione peroxidase (GPx) (Sinogeneclon Co., Ltd., Hangzhou, China), interleukin (IL)-6 and IL-10 were determined from plasma and spinal cord samples using ELISA. The tissue protein levels, total antioxidant status (TAS), and total oxidant status (TOS) (RelAssay Diagnostics, Gaziantep, Turkey) were determined using spectrophotometry (ThermoScientific, Chicago, Illinois, USA).

Histopathological Investigations

The tissue samples were fixed using 10% (v/v) formaldehyde. Histopathological changes were graded between 0 and 3. Hemorrhage, edema, inflammation, and necrosis were scored as follows: 0, absent; 1, mild; 2, moderate; and 3, frequent[9].

TUNEL Assay

The apoptotic cells were labeled using the ApopTag *In Situ* Apoptosis Detection Kit (Millipore, Burlington, Massachusetts, USA). The terminal deoxynucleotidyl transferase modified the DNA fragments. In selective fields, the terminal TUNEL-positive neurons and the total number of neurons were counted[10].

Neurological Examination

The modified Tarlov scoring system and inclined plane test were used to evaluate neurological status[9]. A score of 0-5 was allocated. The rate included the following: no voluntary extremity movement, perceptible joint movement, active movement but an inability to sit without assistance, ability to sit but unable to jump, or a weak jump.

Statistical Analysis

SPSS (version 20.0; IBM Corp., Armonk, New York, USA) was used for all the data analyses. The Kruskal-Wallis test was used for comparisons. The Mann-Whitney U test was used to evaluate differences between the groups. A p-value <0.05 was considered statistically significant. The histopathological semiquantitative scoring system and Tukey's test were used to compare TUNEL-positive cell counts.

Ethics Statement

The study protocol was approved by the Necmettin Erbakan University KONÜDAM Experimental Medicine Application and Research Centering (decision no: 191518001, date: 19/10/2018). The study was conducted in conformance with the ethical and humane principles of research.

RESULTS

Biochemical Evaluation

The GPx, 8-OHG, TOS, and IL-6 levels significantly increased after SCI. The TAS and IL-10 levels significantly decreased after SCI. ALO treatment significantly decreased the plasma and spinal cord tissue levels of GPx, 8-OHG, TOS, and IL-6 and increased the levels of TAS and IL-10 (Tables 1 and 2).

TUNEL Assay

TUNEL-positive cells increased significantly in Group 2 (Figure 1B) and Group 3 (Figure 1C) than in Group 1 (Figure 1A). However, in Group 4 (Figure 1D), ALO significantly decreased the number of TUNEL-positive cells when compared with Group 3 (Figure 2).

Histopathological Evaluation

Hematoxylin-eosin staining revealed that the rats in Groups 2 and 3 had the most severe statistically significant SCI (Figure 3). The damaged area decreased in Group 4 (Figures 3 and 4).

Rats in Group 1 had normal spinal cord histology (Figures 5A, 6A). Hemorrhage, necrosis, loss of myelin, axon degeneration, necrosis in the gray matter, and loss of Nissl bodies were observed in Groups 2 and 3 (Figures 5B, 5C, 6B, 6C). The severity of these findings decreased in Group 4 (Figures 5D, 6D).

Table 1. Comparison of serum IL-6, 8-OHG, IL-10, Gpx, TAS, and TOS levels

Pg/mL	Group 1	Group 2	Group 3	Group 4	p-value
IL-6	4.12±0.53	5.61±1.08	5.73±2.09	4.74±1.66	0.023
8-OHG	26.73±6.12	29.84±4.14	30.9±5.98	28.21±6.32	0.001
IL-10	10.38±2.46	8.62±4.52	8.47±3.44	9.40±3.38	0.012
Gpx	3.41±0.36	2.98±0.32	3.01±0.42	3.21±0.65	0.036
TOS	19.23±36.35	31.74±42.65	32.32±51.23	24.10±37.31	0.021
TAS	0.97±0.83	0.83±0.59	0.76±0.61	0.92±0.72	0.001

IL-6: Interleukin-6, 8-OHG: 8-hydroxyguanosine, IL-10: Interleukin-10, Gpx: Glutathione peroxidase, TAS: Total antioxidant status, TOS: Total oxidant status, pg/mL: Picograms per milliliter

Table 2. Comparison of tissue IL-6, 8-OHG, IL-10, Gpx, TAS, and TOS levels

Pg/mL	Group 1	Group 2	Group 3	Group 4	p-value
IL-6	16.32±5.19	18.83±6.59	19.36±7.95	17.32±6.29	0.016
8-OHG	26.57±5.36	28.13±5.21	29.36±6.35	27.81±7.65	0.024
IL-10	19.79±8.13	15.21±6.32	16.84±6.98	17.93±4.92	0.002
Gpx	3.61±0.83	2.86±0.68	2.91±0.36	3.41±0.65	0.001
TOS	22.14±26.63	28.84±39.87	32.19±47.36	26.115±37.31	0.002
TAS	0.31±0.57	0.20±0.25	0.18±0.45	0.28±0.63	0.001

IL-6: Interleukin-6, 8-OHG: 8-hydroxyguanosine, IL-10: Interleukin-10, Gpx: Glutathione peroxidase, TAS: Total antioxidant status, TOS: Total oxidant status, pg/mL: Picograms per milliliter

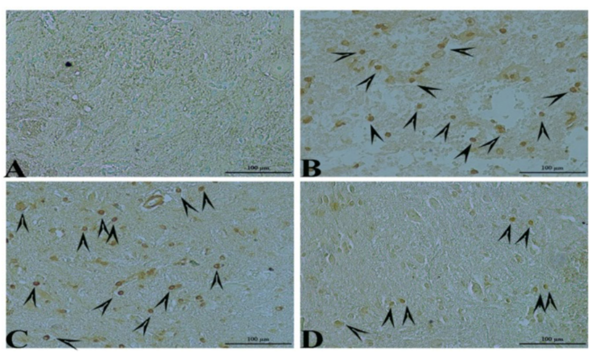

Figure 1. TUNEL-positive cells (black arrowheads) in samples from **(A)** Group 1, **(B)** Group 2, **(C)** Group 3, and **(D)** Group 4
TUNEL: Transferase dUTP nick-end labeling

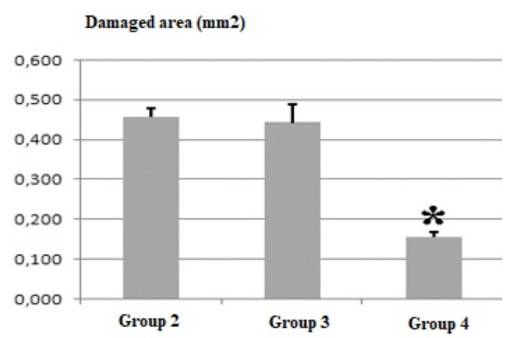

Figure 3. Evaluation of the damaged area measurements
*p<0.05 than in Groups 2 and 3

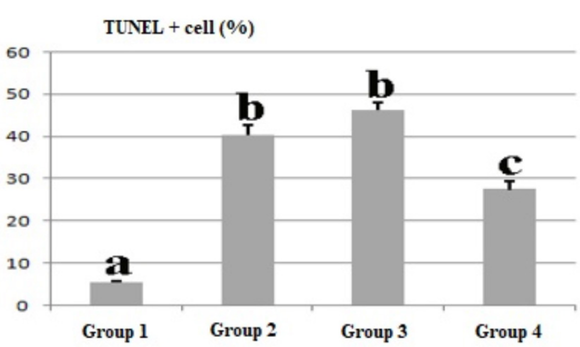

Figure 2. Comparison of the treatment groups with respect to TUNEL-positive cells. Different letters on the columns indicate that the means are significant compared to the others (p<0.05)
TUNEL: Transferase dUTP nick-end labeling

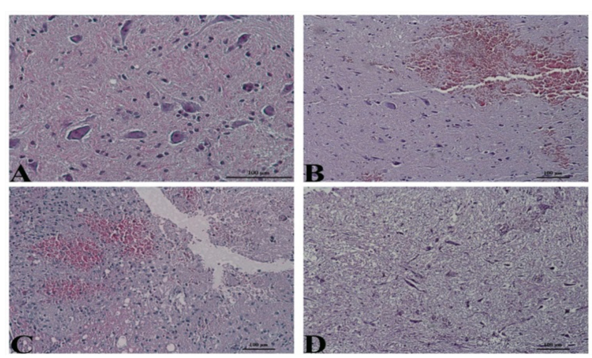

Figure 4. Hematoxylin-eosin stained tissue sections from rats in **(A)** Group 1, **(B)** Group 2, **(C)** Group 3, and **(D)** Group 4

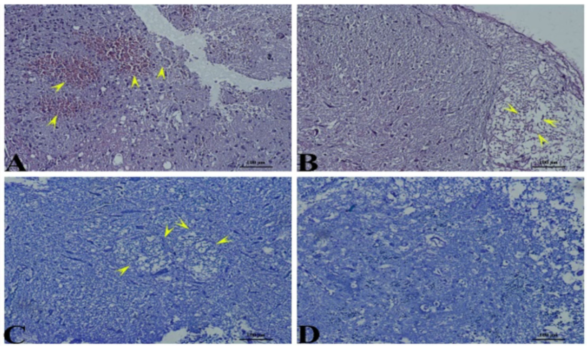

Figure 5. HE-stained sections from rats in Group 3 revealed **(A)** hemorrhage and necrosis (arrowheads) and **(B)** myelin loss and axon degeneration (arrowheads). Toluidine blue-stained sections demonstrate **(C)** vacuolization in the neuropil (arrowheads) and **(D)** neuron loss
HE: Hematoxylin-eosin

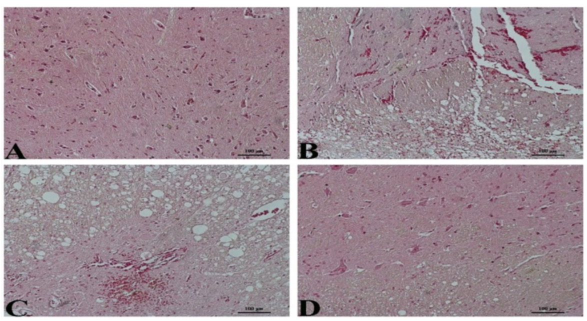

Figure 6. Masson Trichrome-stained tissue sections from rats in **(A)** Group 1, **(B)** Group 2, **(C)** Group 3, and **(D)** Group 4

Neurological Evaluation

Inclined plane score: The measurements obtained on days 1 and 7 in each group were as follows: Group 1, 58.6°±6.7° vs. 57.9°±8.2°; Group 2, 58.3°±5.3° vs. 38.7°±4.7°; Group 3, 59.2°±5.1° vs. 37.2°±6.3°; and Group 4, 58.3°±5.4 vs. 43.8°±6.5°.

On day 1, there was no significant difference in the angle between the groups. In Group 1, there was no significant difference in the angle between the first and seventh days. However, the angle at which the subjects could hold decreased on day 7 in all the other groups. There was no significant difference in the angle between Groups 2 and 3. However, Group 4 could hold at a significantly higher angle than Groups 2 and 3.

Drummond-Moore test: In our study, while the Drummond-Moore test score was 4 in all the rats before the experiment was performed, on day 7, the mean score was 4 points in Group 1, 1.3±0.3 points in Group 2, 1.2±0.2 points in Group 3, and 1.9±0.6 points in Group 4. The score in Group 4 was statistically higher than in Groups 2 and 3.

DISCUSSION

After mechanically inflicting primary damage to the tissue, trauma continues to inflict secondary damage, which includes inflammation, apoptosis, and oxidative stress-induced tissue damage[11]. Minimizing the effects of secondary injury on the central nervous system is important in trauma treatment[9,12]. Studies on spinal cord damage are ongoing.

Human SCI is the most convenient model for determining the mechanism of post-traumatic injury, its pathogenesis, and treatment of cellular and tissue damage[10]. In most human SCIs, the primary injury is at least two-sided and develops because of different movements. A combination of different forces causes an injury in humans[13]. Following a trauma, the point at which medical management needs to be switched to surgical treatment may vary. In animal experiments, the post-traumatic treatment process begins in the first hour[13]. In addition to trauma, vascular damage and ischemic injury may occur at different rates and uncontrollable levels[14]. Because we wanted to produce a standard effect in all the groups and exclude additional factors, we induced the SCI model in rats in our study using the weight drop method.

After a primary injury, secondary damage begins to develop within a few hours and it can continue to occur for weeks. It includes physiological responses to trauma, hypoxia, and ischemia. Local edema, formation of free radicals, and release of excitatory neurotransmitters are associated with increased oxidative stress. Additionally, increased inflammatory processes indirectly stimulate the apoptotic mechanisms[15]. Therefore, steroids, opioid antagonists, calcium channel blockers, volume expanders, Thyrotropin-Releasing Hormone, trilazad mesylate, and especially methylprednisolone are commonly used in the treatment of SCIs[16,17]. Although the primary injury due to a mechanical insult to the spinal cord cannot be treated, the effects of the secondary injuries, such as ischemia, inflammation, increased oxidative stress, the destructive effect of excitatory neurotransmitters, and programmed cell death, should be reduced[18,19]. The changes in the levels of inflammatory cytokines, which are involved in the secondary damage processes and treatment, and oxidative stress and changes at the tissue level are the result of all pathological processes. Cytokines are usually maintained at low levels under physiological conditions[20]. In the microenvironment of the central nervous system, cytokines are activated by glial cells following infection, trauma, or ischemia[21,22]. In a SCI model, systemic inflammation reportedly decreases after systemic IL-10 administration 30 minutes after injury[23].

Although several molecules have been used to assess oxidative stress in tissues and cells, TAS and TOS analyses allow us to obtain reliable, sensitive results easily, immediately, and cost-effectively using long-life reagents[24]. Furthermore, GPx prevents oxidative damage and determines the levels of 8-OHG[25]. Therefore, in our study, we compared the 8-OHG, GPx, TAS, and TOS levels with the oxidative stress levels of IL-10 and IL-6. In our study, we observed myelin loss and axonal degeneration following SCI; these are the most prominent indicators of neuron damage. Furthermore, we also identified neuropil vacuolization in the gray matter, necrotic neurons in the gray matter, presence of Nissl bodies, and TUNEL-positive cells, which are histological indicators of apoptosis[26]. A histopathological scale (Malinowsky score) was used to assess cell damage under a microscope[27].

Zhou et al.[28] demonstrated the anti-allergic and anti-inflammatory effects of ALO in an animal model. Fan et al.[29] demonstrated that ALO significantly decreased the IL-1 and IL-6 levels and that it has anti-inflammatory effects. Yuan et al.[30] demonstrated that ALO significantly decreased IL-1b, IL6, and TNF-a levels in mice models of allergic contact dermatitis. In our study, the serum IL-6 levels were significantly higher in Groups 2 and 3 than in Group 1. Although the IL-6 level was higher in the mice administered ALO than in the sham group, the ALO administered was lower in group 4 than in the other groups in which SCI was induced. This difference was statistically significant. At the serum as well as the tissue level, the mice in Group 4 had significantly higher IL-6 levels than the mice in the sham group but lower IL-6 than mice in Groups 2 and 3[31].

In our study, we found a decrease in the inflammatory cascade, which is consistent with those of previous studies on ALO. This may be attributed to the effect on some cytokines, such as TNF-a and IL-1b, which are involved in initiating the inflammatory process. We did not examine these cytokines in our study.

Studies on ALO have mostly focused on the IL-10 level. Zhou et al.[32], in their experimental colitis model, found a significant increase in the IL-10 levels and improvement in colitis findings following ALO administration. Li et al.[33] stated that during the inflammatory process, which plays a role in endothelial damage, ALO administration increases the IL-10 level. In our study, the IL-10 levels were low in Groups 2 and 3 due to spinal trauma. Following ALO administration, the serum and tissue IL-10 levels were significantly higher in Group 4 than in Groups 2 and 3. Although the IL-10 level was the highest in both the serum and tissue samples in the sham group, where spinal damage had not occurred, its levels were the lowest in Group 3. Studies have demonstrated that ALO administration effectively prevents oxidative stress. Wu et al.[7] demonstrated a significant decrease in oxidative damage following ALO administration in patients with pulmonary hypertension. In the study by Hu et al.[6] ALO administration to mice with ischemic damage demonstrated an antioxidant effect and decreased cell damage. In our study, the TOS, an indicator of oxidative stress, was the lowest in the sham group. However, the TOS was significantly higher in Group 4 than in Groups 2 and 3. Additionally, we observed that the TAS was the highest in the sham group and the lowest in Group 3, indicating an antioxidant level. According to the trauma groups, the administration of ALO had a significantly higher TAS level. These TAS findings were confirmed at the enzymatic level based on the GPx and 8-OHG levels. In our study, the serum and tissue levels of 8-OHG were the lowest in the sham group and were the highest level in Group 3. Although it was significantly lower in Group 4 than in Groups 2 and Group 3, it was significantly higher than that in the sham group. Our study findings confirmed the hypothesis that ALO administration may improve the inflammatory and oxidative processes that develop after cord injury at the serum and tissue levels. Because the correction produced by the active substance in the serum values in experimental studies does not indicate improvement, a histological study should be performed to confirm this effect. Statistically, the sham group had the lowest levels of apoptotic cells according to the TUNEL test. In Groups 2 and 3, hemorrhagic and necrotic areas, loss of myelin, axon degeneration, neuropil in the gray matter, and necrosis were observed. Additionally, the Nissl bodies had disappeared. The decrease in the severity of these findings in Group 4 indicates that the antioxidant and anti-inflammatory effects of ALO treatment were successful. Although the pathologies concerning the nervous system occur at the tissue level, because they are reflected in physical activity, a treatment method can be considered valid if the biochemical and histological improvements affect motor functions. The Drummond-Moore test was performed to assess the neurological state. Because this test was performed on the 7th day before and after the damage, we did not observe any motor damage in the sham group. This indicates that we did not cause nerve tissue damage in the sham group. We also demonstrated that Group 4 had significantly higher scores on the Drummond-Moore test than Groups 2 and 3. The inclined plane test was also used to examine motor functions. Although there was no difference in the inclined plane test angle in the sham group before and after the experiment, the angles were similar in Groups 2 and 3, and they were significantly lower.

Study Limitations

This is the first study till date that investigated the effectiveness of ALO treatment in an SCI model and demonstrated its effect on the biochemical and histological results of motor functions. This study has some limitations. Creating a situation similar to SCI in humans is not possible. The trauma is unidirectional, the treatment starts on the first day, and ALO is administered as a single dose.

CONCLUSION

ALO has neuroprotective effects and prevents the degree of secondary cord damage following SCI via its antioxidative, anti-inflammatory, and antiapoptotic characteristics. It demonstrates promising results regarding its future applications in the clinic.

Ethics

Ethics Committee Approval: The study protocol was approved by the Necmettin Erbakan University KONÜDAM Experimental Medicine Application and Research Centering (decision no: 191518001, date: 19/10/2018).

Informed Consent: Informed consent is not required.

Authorship Contributions

Surgical and Medical Practices: E.S., F.H.Y., Concept: E.S., Y.K., G.C., D.A., Design: E.S., Y.K., G.C., D.A., Data Collection or Processing: E.S., D.A., F.H.Y., Analysis or Interpretation: E.S., Y.K., G.C., D.A., F.H.Y., Literature Search: E.S., M.Z.Y., C.İ.G., Writing: E.S., M.Z.Y., C.İ.G.

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REFERENCES

1. Botterell EH, Jousse AT, Kraus AS, Thompson MG, WynneJones M, Geisler WO. A model for the future care of acute spinal cord injuries. Can J Neurol Sci. 1975;2:361-80.
2. Takigawa T, Yonezawa T, Yoshitaka T, Minaguchi J, Kurosaki M, Tanaka M, et al. Separation of the perivascular basement membrane provides a conduit for inflammatory cells in a mouse spinal cord injury model. J Neurotrauma. 2010;27:739-51.
3. Witiw CD, Fehlings MG. Acute Spinal Cord Injury. J Spinal Disord Tech. 2015;28:202-10.
4. Eckert MJ, Martin MJ. Trauma: Spinal Cord Injury. Surg Clin North Am. 2017;97:1031-45.
5. Zhao J, Zhang G, Li M, Luo Q, Leng Y, Liu X. Neuro-protective effects of aloperine in an Alzheimer's disease cellular model. Biomed Pharmacother. 2018;108:137-43.
6. Hu S, Zhang Y, Zhang M, Guo Y, Yang P, Zhang S, et al. Aloperine Protects Mice against Ischemia-Reperfusion (IR)-Induced Renal Injury by Regulating PI3K/AKT/mTOR Signaling and AP-1 Activity. Mol Med. 2016;21:912-23.
7. Wu F, Hao Y, Yang J, Yao W, Xu Y, Yan L, et al. Protective effects of aloperine on monocrotaline-induced pulmonary hypertension in rats. Biomed Pharmacother. 2017;89:632-41.
8. Xu YQ, Jin SJ, Liu N, Li YX, Zheng J, Ma L, et al. Aloperine attenuated neuropathic pain induced by chronic constriction injury via anti-oxidation activity and suppression of the nuclear factor kappa B pathway. Biochem Biophys Res Commun. 2014;451:568-73.
9. Hulsebosch CE. Recent advances in pathophysiology and treatment of spinal cord injury. Adv Physiol Educ. 2002;26:238-55.
10. Ducker TB, Hamit HF. Experimental treatments of acute spinal cord injury. J Neurosurg. 1969;30:693-7.
11. Simpson LA, Eng JJ, Hsieh JT, Wolfe DL; Spinal Cord Injury Rehabilitation Evidence Scire Research Team. The health and life priorities of individuals with spinal cord injury: a systematic review. J Neurotrauma. 2012;29:1548-55.
12. Busto R, Dietrich WD, Globus MY, Valdés I, Scheinberg P, Ginsberg MD. Small differences in intraischemic brain temperature critically determine the extent of ischemic neuronal injury. J Cereb Blood Flow Metab. 1987;7:729-38.
13. Scheff SW, Rabchevsky AG, Fugaccia I, Main JA, Lumpp JE Jr. Experimental modeling of spinal cord injury: characterization of a force-defined injury device. J Neurotrauma. 2003;20:179-93.
14. Khan M, Griebel R. Acute spinal cord injury in the rat: comparison of three experimental techniques. Can J Neurol Sci. 1983;10:161-5.
15. Carlson SL, Parrish ME, Springer JE, Doty K, Dossett L. Acute inflammatory response in spinal cord following impact injury. Exp Neurol. 1998;151:77-88.
16. Bracken MB, Shepard MJ, Hellenbrand KG, Collins WF, Leo LS, Freeman DF, et al. Methylprednisolone and neurological function 1 year after spinal cord injury. Results of the National Acute Spinal Cord Injury Study. J Neurosurg. 1985;63:704-13.
17. Kwon BK, Tetzlaff W, Grauer JN, Beiner J, Vaccaro AR. Pathophysiology and pharmacologic treatment of acute spinal cord injury. Spine J. 2004;4:451-64.
18. Amar AP, Levy ML. Pathogenesis and pharmacological strategies for mitigating secondary damage in acute spinal cord injury. Neurosurgery. 1999;44:1027-39; discussion 1039-40.
19. Tator CH, Fehlings MG. Review of the secondary injury theory of acute spinal cord trauma with emphasis on vascular mechanisms. J Neurosurg. 1991;75:15-26.
20. Chaudhari N, Talwar P, Parimisetty A, Lefebvre d'Hellencourt C, Ravanan P. A molecular web: endoplasmic reticulum stress, inflammation, and oxidative stress. Front Cell Neurosci. 2014;8:213.
21. Sansbury BE, Spite M. Resolution of Acute Inflammation and the Role of Resolvins in Immunity, Thrombosis, and Vascular Biology. Circ Res. 2016;119:113-30.
22. Bollaerts I, Van Houcke J, Andries L, De Groef L, Moons L. Neuroinflammation as Fuel for Axonal Regeneration in the Injured Vertebrate Central Nervous System. Mediators Inflamm. 2017;2017:9478542.
23. Bethea JR, Dietrich WD. Targeting the host inflammatory response in traumatic spinal cord injury. Curr Opin Neurol. 2002;15:355-60.
24. Birer S, Arda H, Kilic D, Baskol G. Systemic oxidative stress in non-arteritic anterior ischemic optic neuropathy. Eye (Lond). 2019;33:1140-4.
25. Michiels C, Raes M, Toussaint O, Remacle J. Importance of Se-glutathione peroxidase, catalase, and Cu/Zn-SOD for cell survival against oxidative stress. Free Radic Biol Med. 1994;17:235-48.
26. Streeter KA, Sunshine MD, Brant JO, Sandoval AGW, Maden M, Fuller DD. Molecular and histologic outcomes following spinal cord injury in spiny mice, Acomys cahirinus. J Comp Neurol. 2020;528:1535-47.
27. Gibson-Corley KN, Olivier AK, Meyerholz DK. Principles for valid histopathologic scoring in research. Vet Pathol. 2013;50:1007-15.
28. Zhou CC, Gao HB, Sun XB, Shi HB, Liu W, Yuan HN, et al. [Anti-inflammatory and anti-allergic action of aloperine]. Zhongguo Yao Li Xue Bao.). 1989;10:360-5.
29. Fan L, Yanchun S, Honglan H, Zhongqiu L, Shaolun Z. Effect of aloperine on the immune cells in mice. J Norman Bethune Univ Med Sci. 1997;23:603-5.
30. Yuan XY, Liu W, Zhang P, Wang RY, Guo JY. Effects and mechanisms of aloperine on 2, 4-dinitrofluorobenzene-induced allergic contact dermatitis in BALB/c mice. Eur J Pharmacol. 2010;629:147-52.
31. Wang H, Yang S, Zhou H, Sun M, Du L, Wei M, et al. Aloperine executes antitumor effects against multiple myeloma through dual apoptotic mechanisms. J Hematol Oncol. 2015;8:26.
32. Zhou Y, Wang H, Liang L, Zhao WC, Chen Y, Deng HZ. Total alkaloids of Sophora alopecuroides increases the expression of CD4+ CD25+ Tregs and IL-10 in rats with experimental colitis. Am J Chin Med. 2010;38:265-77.
33. Li W, Li Y, Zhao Y, Ren L. The protective effects of aloperine against ox-LDL-induced endothelial dysfunction and inflammation in HUVECs. Artif Cells Nanomed Biotechnol. 2020;48:107-15.

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DECOMPRESSION WITH INSTRUMENTATION IN THE TREATMENT OF UPPER-LEVEL DISC HERNIATIONS

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ABSTRACT

Objective: The aim of this study was to compare the results of microdiskectomy + fusion and microdiskectomy + dynamic instrumentation, which are 2 different methods used for treating upper-level lumbar disk herniations, and to share the data obtained with our colleagues.

Materials and Methods: In this study, 51 patients who underwent surgery for upper-level disk herniation between 2019 and 2021 were retrospectively analyzed. The study group was divided into two groups. Patients who underwent microdiscectomy with fusion and those who underwent microdiscectomy with dynamic instrumentation were examined. In both groups, demographic data, such as age and gender, as well as quality of life scores, such as preoperative visual pain scoring and Oswestry disability index, etc. were examined and compared with the postoperative values at the end of 1 year. Complications were noted.

Results: There was no significant difference between both groups in terms of gender and age distribution (p=0.676, p=0.992). After 1 year of follow-up, both groups showed significant improvement in both the back-leg visual pain score and Oswestry disability values. When back-leg visual pain and Oswestry disability score change between the groups were analyzed, there was no significant difference in terms of pain, whereas Oswestry disability change was better in the fusion group (p=0.76, p=0.354, p=0.037 respectively). Complications were observed in 7 (13.7%) patients, and superficial wound infection was the most common complication in five (71.4%) patients. Dural tears and hematomas were detected in one patient each. None of the patients required revision surgery.

Conclusion: Both techniques can be used for treating upper-level disk herniations. After one year of follow-up, we believe that there is no significant difference between the two groups, although the fusion group appears to be superior in terms of ODI recovery.

Keywords: Dynamic instrumentation, posterior fusion, upper-level disk herniation

INTRODUCTION

Lumbar disc herniation is one of the most common pathologies encountered by spine surgeons. Medical and conservative treatments are applied in treatment strategies primarily. Different surgical treatment strategies ranging from minimally invasive surgery to instrumented fusion surgery are applied in cases that do not respond to conservative treatment. Many variable parameters play a role in the surgical method to be chosen. In addition to the patients' age, the level and location of the pathology in the lumbar region are decisive at this point. As a matter of fact, the treatment of upper lumbar disc herniations and lower lumbar disc herniations may be different[1-4]. When we review the literature, it can be easily evaluated as lower lumbar disc herniation for L4-5 and L5-S1 levels and upper lumbar disc herniation for L1-2 and L2-3 levels[4]. However, there is no definite consensus for the L3-4 level[4]. Considering the placement of the facet joints and the apex of the lumbar region, some sources describe this level as a gray zone and state that its anatomical features are more similar to the upper lumbar region[4]. In our practice, we consider the L3-4 region as the upper level and apply our surgical strategy in this context. Decompression with microdiscectomy, endoscopic surgery, hybrid instrumentation applications, and fusion surgery are the applied methods for upper-level lumbar disc herniations[4-11]. In this study, we aimed to compare the clinical results of 2 different methods, microdiscectomy + unilateral posterior instrumentation + fusion (MDPF) and microdiscectomy + unilateral dynamic instrumentation (MDD), and to share the information we obtained with our colleagues.

MATERIALS AND METHODS

This study had been carried out in accordance with principles of the Declaration of Helsinki, informed patient consent was granted from all patients and approved by the Ethics Committee of Adana City Training and Research Hospital (136/2846).

In this study, patients operated between 2019 and 2021 for upper-level disc herniation were retrospectively analyzed. Inclusion criteria for the study: Adult patients who were operated for the first time for single-level upper disc herniation and underwent instrumentation. The surgical decision was made according to magnetic resonance imaging. Surgery was

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recommended for patients who did not respond to conservative treatment lasting longer than 6 months or who had a loss of motor strength. Patients were randomly selected according to which procedure to perform. Patients who were under 18 years of age, who underwent recurrent lumbar disc surgery or who underwent only decompression were excluded from the study. Patients who underwent MDPF and MDD were divided into 2 groups. All operations were performed by the same senior spine surgeon. The sequence of surgical procedures performed was similar in both groups. In the MDPF group, a microdiscectomy was performed after pedicle screws were placed, and a titanium rod was used (Figure 1). Posterolateral grafting was performed with autografts obtained from the area. In the MDD group, the same surgical algorithm was followed and polyetheretherketone (PEEK) rods were used instead of titanium rods (Figure 2). Posterolateral grafting was not performed in the MDD group. In both groups, demographic data such as age, and gender, as well as quality of life scores such as preoperative visual pain scoring, Oswestry disability index were examined and compared with the postoperative values at the end of 1 year. Complications were noted. All the assessors and patients were blinded to the procedure at follow-up.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 25.0 package program was used for statistical analysis of the data. Categorical measurements were presented as numbers and percentages, and continuous measurements were summarized as mean and standard deviation [median (mean) or minimum-maximum, as appropriate]. Chi-square and Fisher's exact tests were used for comparisons of categorical expressions. Kolmogorov-Smirnov test was used to determine whether the parameters in the study showed normal distribution. For parameters that did not show normal distribution, Mann-Whitney U tests were used. The statistical significance level was taken as 0.05 in all tests.

RESULTS

Twenty-six in the MDPF group and 25 in the MDD group, a total of 51 patients were included in the study. The mean age of the patients was 48.9±9.7 years, and 26 (51%) of them were female and 25 (49%) of them were male. The level distribution was L1-2 in 12 (23.5%), L2-3 in 14 (27.5%), and L3-4 in 25 (49%) patients, respectively. There was no significant difference between both groups in terms of gender and age distribution (p=0.676, p=0.992) (Table 1).

After 1-year follow-up, significant improvement was observed in both back-leg VAS and ODI values in both groups. When the back-leg VAS and ODI changes between the groups were analyzed, there was no significant difference in terms of VAS, while ODI change was better in the MDPF group (p=0.76, p=0.354, p=0.037 respectively). Complications were observed in 7 (13.7%) patients and superficial wound infection was the most common complication in 5 patients (71.4%). Dural tear and haematoma were detected in one patient each. None of the patients required revision surgery. Patients with superficial wound infection were treated with appropriate antibiotherapy.

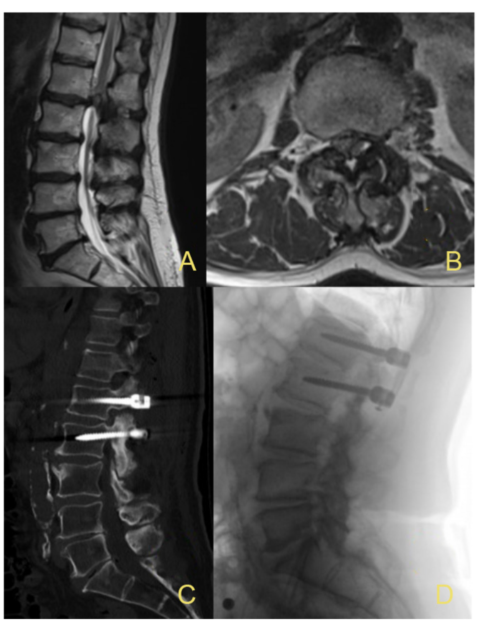

Figure 1. Images of a patient with L2-3 right posteromedial disc herniation, **A)** preoperative sagittal MRI, **B)** preoperative axial section of MRI, **C)** posterior fusion and titanium rod instrumentation is observed in postoperative coronal CT, **D)** axial section of pedicle inserted screw on CT

MRI: Magnetic resonance imaging, CT: Computed tomography

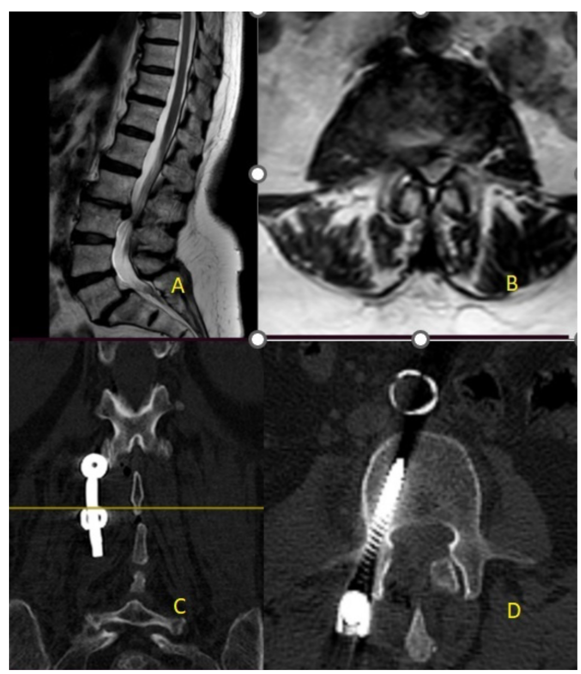

Figure 2. Images of a patient with L1-2 left posteromedial disc herniation, **A)** preoperative sagittal MRI, **B)** preoperative axial section of MRI, **C)** posterior dynamic peek rod instrumentation is observed on postoperative sagittal CT, **D)** lateral view of instrumentation on X-ray

MRI: Magnetic resonance imaging, CT: Computed tomography

Table 1. Comparison of patient data between groups

	MDPF (n=26)	MDD (n=25)	Total (n=51)	p-value
Gender [n (%)]				
Female	14 (53.8)	12 (48)	26 (51)	0.676
Male	12 (46.2)	13 (52)	25 (49)	
Level [n (%)]				
L1-2	7 (26.9)	5 (20)	12 (23.5)	0.838
L2-3	7 (26.9)	7 (28)	14 (27.5)	
L3-4	12 (46.2)	13 (52)	25 (49)	
Complication [n (%)]	4 (15.4)	3 (12)	7 (13.7)	0.725
Age (Mean ± SD)	48.8±9.0	49.2±10.5	48.9±9.7	0.992
Preop back VAS (Mean ± SD)	5.12±1.7	4.68±1.3	4.90±1.5	0.312
Postop back VAS (Mean ± SD)	2.50±1.1	2.24±1.0	2.37±1.1	0.464
Preop leg VAS (Mean ± SD)	8.04±1.1	8.44±1.0	8.24±1.1	0.186
Postop leg VAS (Mean ± SD)	2.58±1.3	2.48±1.4	2.53±1.3	0.816
Preop ODI (Mean ± SD)	62.4±10.9	53.9±13.3	58.2±12.8	0.016*
Postop ODI (Mean ± SD)	19.0±8.4	18.2±8.4	18.6±8.3	0.755
ΔBack VAS	-2.61±2.0	-2.44±1.6	-2.52±1.8	0.760
ΔLeg VAS	-5.46±1.8	-5.96±1.7	-5.70±1.8	0.354
ΔDelta ODI	-43.4±12.6	-35.8±13.5	-39.6±13.5	**0.037***

*p<0.05, a: Chi-square and Fisher's exact, b: Mann-Whitney U, Δ: Change of parameters at the end of 1 year, MDPF: Microdiscectomy + unilateral posterior instrumentation + fusion, MDD: Microdiscectomy + unilateral dynamic instrumentation, SD: Standard, VAS: Visual Analog Scale

Table 2. Distribution of complications between groups

	MDPF	MDD
Superficial wound infection	3	2
CSF fistula	1	-
Haemotoma	-	1

MDPF: Microdiscectomy + unilateral posterior instrumentation + fusion, MDD: Microdiscectomy + unilateral dynamic instrumentation, CSF: Cerebrospinal fluid fistula

There was no statistical difference in terms of complications between the groups and no implant-related complications were observed (p=0.725) (Table 2). At the end of 1-year follow-up, no recurrent disc herniation was observed in both groups.

DISCUSSION

Upper-level lumbar disc herniations are encountered more rarely than distal-level disc herniations (L4-5, L5-S1)[3]. However, it can create similar symptoms like distal level disc herniations by causing back pain and radicular findings. Urinary problems are observed more frequently due to its proximity to the conus medullaris[8]. Conservative treatments are the primary choice in patients without neurological deficit. However, surgical interventions are performed in the presence of loss of muscle strength and severe neural compression. It is worth mentioning a few important points here. In the treatment of upper-level lumbar disc herniations, the anatomical differences of the lumbar region from distal to proximal should be known. The close neighborhood of the conus medullaris and the smaller diameter of the spinal canal in the upper lumbar region necessitates the application of different surgical options[3,9]. The orientation of the facet joints varies as they move from the distal to the proximal. In the thoracic region, facet joints that are sagittally positioned at lower lumbar levels are oriented coronally[12]. At the transition from the lower lumbar region to the upper lumbar and thoracolumbar regions, the facet joints are actually in an anatomical transition zone. Therefore, in the surgical treatment of upper lumbar disc herniation, in the presence of a broad-based herniation, more than 50% of the facet joint may unintentionally be resected, which can lead to segmental instability[4,9]. In this context, we apply unilateral instrumentation in addition to microdiscectomy in our surgical strategy to prevent both instability and recurrent disc herniations. In this study, we compared the results of two different instrumentation we applied.

MDPF and MDH are technically similar methods. In fusion surgery, a titanium rod is used, and posterolateral grafting is performed for fusion, while in the hybrid method, a PEEK rod is used, and no grafting was performed. While motion-preserving surgery is aimed with PEEK rods[5,6], fusion is intended with MDPF. Both methods are known in the literature as treatment strategies that have been applied for many years[5,13-15]. In the study on lumbar disc herniations by Sezer and Acikalin[16], 20 patients who underwent unilateral dynamic instrumentation showed significant improvement in both VAS and ODI scores at the end of 1 year. In a study on lumbar disc herniations and various spinal pathologies by Karakoyun et al.[17], they reported the results of unilateral dynamic instrumentation and reported a significant decrease in VAS and ODI scores at the end of 1 year. And in the study of Bozkus et al.[18], patients who underwent decompression and unilateral facetectomy for various spinal pathologies underwent unilateral dynamic instrumentation, and significant improvement reported in ODI and VAS scores at the end of 12 months (p<0.01). In our study, in addition to the above data, significant improvement was observed in both VAS scores and ODI scores at the end of 1 year in the MDD group.

We think that applying fusion along with decompression in upper-level disc herniations may prevent the development of instability and reduce the recurrence rate[9]. As a matter of fact, in the study of Sanderson et al.[1], 11 out of 19 patients (58%) who underwent surgery at the L1-2 and L2-3 levels had previously undergone surgery in the same area. In the same study, fusion was performed on 4 patients (20%) and 4 patients (20%) required re-operation at a later time[1]. In another study, unilateral fusion surgery was performed for broad-based disc herniations, and the patients' ODI score decreased from 68.74±8.99 to 24.17±7.55 one year after the surgery[19].

In the study of Lin et al.[9], patients who underwent only decompression and those who underwent decompression+fusion were divided into 2 groups. At the end of the study, patients who underwent decompression with fusion had a significant improvement in ODI scores and higher satisfaction rates (p=0.034).

In our study, we found similar results to those mentioned above. At the end of a year, we achieved improvement in both VAS and ODI scores. When we made an evaluation between the groups, we did not find any significant statistical difference related to back and leg VAS change (p=0.750, p=0.354 respectively). When ODI scores were examined, ODI values were found to be similar at the end of 1 year in both groups (19.0±8.4 18.2±8.4). However, regarding the ODI change, we observed that the improvement was statistically better in the MDD group (p=0.037). We believe that the reason for this is that the preoperative ODI score was lower in the MDD group, thus a mathematical difference occurred. Nevertheless, studies in large groups may provide a more objective opinion.

Study Limitations

The limitation of our study is that it was a retrospective study, the follow-up period was short, and the group was small. Nevertheless, we think that the comparison of 2 different surgical techniques in a rare pathology will contribute to the literature.

CONCLUSION

As a result, both techniques can be used in the treatment of upper-level disc herniations. After one year of follow-up, we believe that although the fusion group was superior in terms of ODI recovery, there was no significant difference between the two groups.

Ethics

Ethics Committee Approval: This study had been carried out in accordance with principles of the Declaration of Helsinki, and approved by the Ethics Committee of Adana City Training and Research Hospital (136/2846).

Informed Consent: Informed patient consent was granted from all patients.

Authorship Contributions

Surgical and Medical Practices: Z.B., S.K.O., Y.G., Concept: Z.B., S.K.O., Y.G., Design: Z.B., S.K.O., Y.G., Data Collection or Processing: Z.B., S.K.O., Y.G., Analysis or Interpretation: Z.B., S.K.O., Y.G., Literature Search: Z.B., S.K.O., Y.G., Writing: Z.B., S.K.O., Y.G.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Sanderson SP, Houten J, Errico T, Forshaw D, Bauman J, Cooper PR. The unique characteristics of "upper" lumbar disc herniations. Neurosurgery. 2004;55:385-9; discussion 389.
2. Albert TJ, Balderston RA, Heller JG, Herkowitz HN, Garfin SR, Tomany K, et al. Upper lumbar disc herniations. J Spinal Disord. 1993;6:351-9.
3. Kim DS, Lee JK, Jang JW, Ko BS, Lee JH, Kim SH. Clinical features and treatments of upper lumbar disc herniations. J Korean Neurosurg Soc. 2010;48:119-24.
4. Echt M, Holland R, Mowrey W, Cezayirli P, De la Garza Ramos R, Hamad M, et al. Surgical Outcomes for Upper Lumbar Disc Herniations: A Systematic Review and Meta-analysis. Global Spine J. 2021;11:802-13.
5. Ormond DR, Albert L Jr, Das K. Polyetheretherketone (PEEK) Rods in Lumbar Spine Degenerative Disease: A Case Series. Clin Spine Surg. 2016;29:E371-5.
6. Ogrenci A, Koban O, Yaman O, Yilmaz M, Dalbayrak S. Polyetheretherketone Rods in Lumbar Spine Degenerative Disease: Mid-term Results in a Patient Series Involving Radiological and Clinical Assessment. Turk Neurosurg. 2019;29:392-9.
7. Yüce I, Kahyaoğlu O, Mertan P, Çavuşoğlu H, Aydın Y. Analysis of clinical characteristics and surgical results of upper lumbar disc herniations. Neurochirurgie. 2019;65:158-63.
8. Karaaslan B, Aslan A, Börcek AÖ, Kaymaz M. Clinical and surgical outcomes of upper lumbar disc herniations: a retrospective study. Turk J Med Sci. 2017;47:1157-60.
9. Lin TY, Wang YC, Chang CW, Wong CB, Cheng YH, Fu TS. Surgical Outcomes for Upper Lumbar Disc Herniation: Decompression Alone versus Fusion Surgery. J Clin Med. 2019;8:1435.
10. Erdoğan U. The Results of Using a Transforaminal Lumbar Interbody Fusion Cage at the Upper Lumbar Level. Cureus. 2021;13:e15496.
11. Wu J, Zhang C, Zheng W, Hong CS, Li C, Zhou Y. Analysis of the Characteristics and Clinical Outcomes of Percutaneous Endoscopic Lumbar Discectomy for Upper Lumbar Disc Herniation. World Neurosurg. 2016;92:142-7.
12. Kapetanakis S, Gkantsinikoudis N. Anatomy of lumbar facet joint: a comprehensive review. Folia Morphol (Warsz). 2021;80:799-805.
13. Mavrogenis AF, Vottis C, Triantafyllopoulos G, Papagelopoulos PJ, Pneumaticos SG. PEEK rod systems for the spine. Eur J Orthop Surg Traumatol. 2014;24 Suppl 1:S111-6.

14. Abode-Iyamah K, Kim SB, Grosland N, Kumar R, Belirgen M, Lim TH, et al. Spinal motion and intradiscal pressure measurements before and after lumbar spine instrumentation with titanium or PEEK rods. J Clin Neurosci. 2014;21:651-5.
15. Qi L, Li M, Zhang S, Xue J, Si H. Comparative effectiveness of PEEK rods versus titanium alloy rods in lumbar fusion: a preliminary report. Acta Neurochir (Wien). 2013;155:1187-93.
16. Sezer C, Acikalin R. Unilateral Dynamic Stabilization in Recurrent Lumbar Disc Herniation. Turk Neurosurg. 2023;33:334-40.
17. Karakoyun DO, Baydar AT, Hazar NU, Uzlu O, Dalgic A. Clinical Results of Unilateral Dynamic Rod Application in the Short-Medium Period. Turk Neurosurg. 2021;31:545-53.
18. Bozkus H, Sasani M, Oktenoglu T, Aydin AL, Ozer AF. Unilateral dynamic stabilization for unilateral lumbar spinal pathologies; a new surgical concept. Turk Neurosurg. 2012;22:718-23.
19. Zhao CQ, Ding W, Zhang K, Zhao J. Transforaminal lumbar interbody fusion using one diagonal fusion cage with unilateral pedicle screw fixation for treatment of massive lumbar disc herniation. Indian J Orthop. 2016;50:473-8.

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THE EFFECT OF INTERFERENTIAL CURRENTS AND TENS ON PAIN AND FUNCTIONALITY IN PATIENTS WITH CHRONIC MECHANICAL LOW BACK PAIN

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ABSTRACT

Objective: This study aimed to compare the effects of interferential current (IFC) and transcutaneous electrical nerve stimulation (TENS) on pain, disability, and flexibility for treating patients with chronic low back pain (CLBP).

Materials and Methods: This study included 50 volunteer patients diagnosed with CLBP randomly assigned to IFC and TENS treatment. In addition to electrical stimulation, therapeutic ultrasound, hot packs, and exercise were administered to both groups. All patients underwent 20 sessions of treatment for 4 weeks and 5 days on weekdays. The Numerical Pain Scale, Oswestry Scale (ODI), and sit-and-reach test were used for evaluation. Patients were evaluated 3 times: before treatment, at the 10th session, and after treatment. The paired t-test was used for statistical analysis.

Results: Significant improvement was seen in both treatment groups' pain levels when the levels of pain before and after treatment were compared. Before and after treatment, both groups in the sit-and-reach test and Oswestry evaluation showed a significant improvement ($p>0.05$). The change in pain and disability scores did not show superiority in the TENS and IFC groups ($p>0.05$). Only in the sit-and-reach test did the IFC group show significantly more improvement after the 20th session treatment ($p=0.026$).

Conclusion: IFC and TENS should be used in patients with CLBP to control pain and improve function. However, studies with electrical currents determined by different biophysical parameters are needed to determine the superiority of TENS and IFC in terms of treatment outcome measures.

Keywords: Low back pain, TENS, interferential current, rehabilitation

INTRODUCTION

Approximately to 23% of people worldwide suffer from chronic low back pain, with an estimated 24-80% of patients experiencing recurrence every year(1). Low back pain comprises an average of 9.6% of all emergency department visits and 0.9% of all hospital admissions(2).

Numerous factors can contribute to low back pain, and mechanical low back pain is the most prevalent type of chronic pain. Mechanical low back pain can also be defined as nociceptive pain. Back pain that originates intrinsically from the spine, intervertebral discs, or surrounding soft tissues is referred to as mechanical low back pain(2,3).

In addition to medical treatment, many physiotherapy and rehabilitation methods are used in the treatment of chronic low back pain (CLBP). Electrotherapy modalities are often preferred for pain control. Transcutaneous Electrical Nerve Stimulation (TENS), ultrasound (US), and interferential currents (IFC) are commonly preferred electrotherapy modalities in low back pain(2-4).

IFCs are amplitude-modulated currents resulting from the superposition of two or more medium-frequency sinusoidal type currents with a frequency of approximately 4000 Hz. The frequency of the resulting current is equal to the difference of the frequencies of two medium-frequency sinusoidal alternating currents, so its effect on tissue is similar to the effect of low-frequency currents. The most important feature of interference is that it encounters minimum skin resistance, unlike low-frequency currents, because it has a medium frequency during the entry of the current into the tissue. With this advantage, it can be applied to deep tissues without disturbing the patient(5,6). It was stated in the literature that IFC provides a significant reduction in pain in low back pain(7).

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Transcutaneous electrical nerve stimulation can be considered as the most widely used low-frequency analgesic current in clinical practice by physiotherapists. It was first developed in 1965 based on the control theory by Razak Özdinçler[5]. Conventional TENS application produces inhibitory effects on nociceptive nerve conduction when used at high frequency (>100 Hz) and low intensity[5,8]. The gate control theory is based on the principle that both pain and superficial sensations are transported to the central nervous system via the substantia gelatinosa. Accordingly, if neurons entering the medulla spinalis from the same location are stimulated with painless stimuli, the transmission of pain to the higher centers are inhibited[5,6,8]. Meta-analyses indicate that there is moderate evidence that pain intensity during or immediately after TENS application is lower compared to placebo and that there are no serious adverse events[9].

Although IFC and TENS are the most commonly used methods in the treatment of low back pain, there are limited studies investigating and comparing their efficacy in the literature. Although the physiological mechanisms of TENS and IFC are similar, their superiority over each other when used for a certain period of time as traditional physiotherapy applications is limited in the literature[10]. The aim of this study was to compare the effects of IFC and TENS on pain, disability, and flexibility in patients with chronic mechanical low back pain.

MATERIALS AND METHODS

This prospective clinical interventional study was approved by the Clinical Research Ethics Committee of Marmara University (07/12/2018). The patients were informed verbally and written about the purpose, duration, and methods to be used before the study. All participants read and approved the "Informed Voluntary Consent Form" prepared in accordance with the standards set by the Ethics Committee.

Patients who were diagnosed with CLBP who applied to Private Tepe Medical Center Physical Therapy and Rehabilitation outpatient clinic between August and December 2019 were included in the study. Patients with mechanical low back pain for more than 12 weeks, literate and volunteered to participate in the study were included in the study. Patients with pacemakers and neurostimulators, diagnosed cancer, previous pelvic or spinal surgery or spinal cord injury, peripheral vascular disease and uncontrolled comorbid conditions, and pregnant or suspected pregnancy were excluded. Patients were not receiving any other treatment (including medication) that would affect the treatment program.

The numerical pain scale (NPS) was used to assess pain intensity. In this scale, "0" defines painlessness and "10" defines the highest pain[11]. Pain intensity during activity, at rest and during sleep was questioned.

Oswestry Scale was used to evaluate functional disability. The Turkish validity and reliability study was conducted by Yakut et al.[11]. The Oswestry scale includes 10 questions evaluating different activities of daily living and 6 options for each question. A score of 0-4 is considered as no disability, 5-14 as mild, 15-24 as moderate, 25-34 as severe and 35-50 as complete functional disability. The minimum score obtained from the scale is 0 and the maximum score is 50. A score of 50 indicates the highest level of functional disability[12].

The Sit and Reach Test was used to evaluate trunk flexibility. A ruler was placed on a 30 cm fixed wooden block. The individual was asked to reach forward with both hands in a long sitting position with the feet resting on the block and the knees in extension. The edge of the block was taken as 0, the 3rd finger of the right hand was taken as the reference point and the values passing the board were recorded as positive and the values failing to pass were recorded as negative. The test was repeated three times and the mean value was recorded[13]. The treatment programme was carried out by an experienced physiotherapist. The evaluation of outcome measurements and the treatment programme were performed by two physiotherapists. No blinding was used between those who implemented the treatment programme and those who evaluated the outcome measures.

In order to design the study group, the patients were divided into two groups by block randomization according to the order of arrival. Both groups received 20 sessions of treatment for a total of 4 weeks. In addition to therapeutic US, hot pack, and exercise treatment, participants in the IFC group received IFC for 20 minutes and those in the TENS group received TENS for 20 minutes.

In both groups, treatment was started with therapeutic US application. Therapeutic US (Chattanooga, Intelect Mobile, 2012 Taiwan) was calibrated at a frequency of 1 MHz and an intensity of 1.5 Watt/cm^2 for 5 minutes on the lumbar region (T12 to S1 paravertebral) in both groups. Then, a 30x30 cm hot pack (Çelenmed, 2019) heated in a 70 °C hot water boiler was wrapped in four layers of cotton towel and placed on the lumbar region and applied for 20 minutes. The IFC (Chattanooga, Intelect Combine Physiotherapy, 2012, Taiwan) was applied to the painful area (T12 to S1 paravertebral) with vacuum electrodes for 20 minutes with 4000 Hz (Channel-1) and 4100 Hz (Channel-2) frequency to create ΔF of 100 Hz interferential current in the tissues. The TENS (SPort, X32, 2019, China); 2 channels were applied over the lumbar region (T12 to S1) with 5x5 cm self-adhesive 4 electrodes were placed in a quadripolar arrangement for 20 minutes (pulse width: 50-100 μs and frequency: 60-120 Hz). Current intensity was applied at a strong but comfortable intensity in both groups. Before each session, skin preparation with alcohol was done to lower the skin's resistance to the current transmission.

The same exercise program was applied to both groups: (1) To stretch the lumbar extensor muscles, bilateral hip knee flexion was performed in the supine position with the help of the hands. The stretched position was maintained for 5 seconds. (2) To stretch the hip flexor muscles, one leg was in extension in the supine position, while the other side was maximally flexed at the hip and knee and held in the stretched position for 5 seconds. (3) To strengthen the lumbar extensor muscles isometrically, the patient was taught to perform isometric contraction with the knees and hips in bilateral flexion, hands in the waist cavity, and the contraction was continued for 5 seconds (If the patient's lordosis was decreased, care was taken not to decrease the lordosis during the exercise). (4) To strengthen the abdominal muscles, the abdominal muscles were exercised isotonically with a half sit-up movement by extending the hands towards the knees in the hook position, and the patient was asked to count to 5 when he/she got up from the floor. (5) To stretch the hamstring muscles, straight leg raises were performed in the supine position with the help of a belt, and the patient was asked to wait 5 seconds at the endpoint. All exercises were performed as 10 repetitions, 1 set. Patients were evaluated before the treatment, after the 10th session, and 20th sessions. Clinical and demographic information was recorded on the evaluation form prepared by the investigators.

The type I error was taken to be α=0.05 and the type II error was taken to be β=0.10, with a confidence interval of 95%, assuming a 95% likelihood of demonstrating a 15% difference in the TENS and IFC groups. To achieve this, the sample size was set at 43 participants. The data were evaluated with the SPSS 15.0 statistical program. The Kolmogorov-Smirnov test was used to evaluate normality of data. The percentage distributions, standard deviation, and arithmetic mean were used to evaluate the demographic characteristics of the subjects. The Freidman's test was used for the comparison of within-group changes. "Mann-Whitney U" test was used for intergroup comparisons. $p<0.05$ was considered significant.

RESULTS

A total of 50 patients with CLBP were included in the study. Six patients did not continue the treatment programme and the study was completed with 44 patients. In the IFC group, there were 20 females (86.9%) and 3 males, while in the TENS group, there were 17 females (80.9%) and 4 males. There is no significant difference between the gender distribution in both groups (p=0.587). No significant difference was found between the mean age, height, weight, and body mass index values of the participants in the groups (p>0.005) (Table 1).

At the beginning of the study, there was no significant difference between the two groups except for activity pain scores (p=0.002), resting and nocturnal pain, Oswestry scores indicating functionality and mean scores of sit and reach test evaluating trunk flexibility (Table 2).

Between the 10th and 20th session, the reduction in rest, activity and night pain scores was higher in the TENS group than in the IFC group (p=0.004, p=0.002, p=0.006). The reduction in mean activity pain scores in the first 10 sessions was higher in the IFC group (p=0.014). In addition, the mean baseline activity pain levels of the patients in the IFC group were higher than the participants in the TENS group (Table 3, Figure 1). Evaluation of the changes obtained in the mean Oswestry scores showed that the IFC group was superior in terms of the changes that occurred in the first 10 sessions compared to baseline (Table 3). The TENS group was superior in the mean changes in Oswestry scores between the 10th and 20th sessions. The IFC group was superior in terms of both 10th and 20th session changes and baseline and 20th session changes when the amount of change obtained in the mean scores of the sit-reach test was compared.

Table 1. Demographic characteristics of the patients

	IFC Group n=23 Mean ± SD Min.-max	TENS Group n=21 Mean ± SD Min.-max	p-value
Age (years)	54.78±12.27 33-79	53.23±12.08 36-79	0.672
Weight (kg)	79.08±10.45 60-100	79.8±10.74 61-100	0.750
Height (cm)	163.47±6.90 155-180	163.14±9.21 148-187	0.804
BMI (kg/m^2)	29.70±4.56 23.44-41.62	30.03±3.89 25.39-38.29	0.690

IFC: Interferential currents, TENS: Transcutaneous Electrical Nerve Stimulation, SD: Standard deviation, Min.-max: Minumum-maximum, BMI: Body mass index

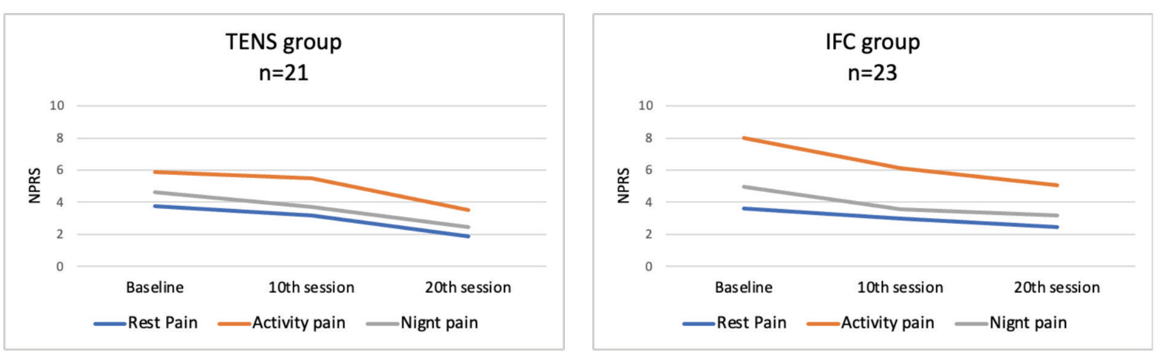

Figure 1. Change of pain scores in the groups

NPRS: Numeric Pain Rating Score, TENS: Transcutaneous Electrical Nerve Stimulation, IFC: Interferential currents

DISCUSSION

The results of this study showed that combined physiotherapy and rehabilitation approaches including IFC and TENS applications in the treatment of patients with chronic mechanical low back pain have similar effects in reducing pain scores and improving functionality at the end of treatment. After a 20-session treatment program, more improvement was obtained in the flexibility scores in the IFC group than in the TENS group.

Chronic mechanical back pain has significant functional and financial implications. Effective treatment is necessary for this pain syndrome, which affects a sizable portion of the population[1,14,15]. Pain has been identified as an important area to be evaluated in low back pain[2,16,17]. In individuals with low back pain, pain assessment is performed based on verbal expressions. These subjective data expressed by patients are transformed into objective data with the help of scales and instruments to provide feedback to patients and to provide measurements for clinicians. The NPS is a valid method widely used in the assessment of pain severity in low back pain. Dias et al.[17] evaluated the pain intensity of patients with low back pain immediately after 30 minutes of IFC application at 4 different frequencies and TENS application at 2 different frequencies by NPS and reported that IFC and TENS currents had similar effects in reducing pain[18]. The researchers also reported that both types of currents had a superior effect compared to the placebo treatment[18]. Facci et al.[18] applied 20 Hz, 330 msec TENS, and 2 Hz IFC for 30 min for 10 sessions after patient education in patients with low back pain. The researchers reported that the pain intensity of both currents decreased significantly in patients with both current types and that TENS and IFC currents

Table 2. Pain, disability and flexibility characteristics of patients at baseline: comparison between 10th and 20th session conclusion

Assessment Parameters			IFC group n=23 Mean ± SD Min.-max	TENS group n=21 Mean ± SD Min.-max	p-value
Numeric pain scale	Rest pain score	Baseline	3.60±2.67 (0-10)	3.76±1.99 (1-8)	0.686
		10th session	3.00±2.02 0-7	3.19±2.01 (0-8)	0.840
		20th session	2.47±1.97 0-6	1.85±1.62 (0-6)	0.312
	Activity pain score	Baseline	8±1.90 (5-10)	5.9±1.90 (3-10)	**0.002**
		10th session	6.13±1.93 (3-10)	5.47±1.93 (3-10)	0.207
		20th session	5.04±2.09 (1-8)	3.52±1.80 (1-8)	**0.012**
	Night pain score	Baseline	4.95±3.29 (0-10)	4.61±2.29 (3-7)	0.603
		10th session	3.56±2.87 (0-9)	3.71±2.47 (0-10)	0.822
		20th session	3.17±2.96 (0-9)	2.47±1.99 (0-7)	0.635
Oswestry Disability Score (%)		Baseline	47.04±15.65 (16-72)	48.47±11.07 (24-68)	0.962
		10th session	35.82±15.75 (8-66)	47.52±14.44 (24-72)	**0.024**
		20th session	30.60±33.17 (2-60)	33.14±11.92 (16-52)	0.416
Sit & Reach Test (cm)		Baseline	-(-0.26)±8.20 [(-17)-16]	1.16±6.21 [(-15)-13]	0.604
		10th session	0.97±8.23 (-25)-15	1.61±6.46 (-15)-14	0.934
		20th session	2.93±7.55 (-20)-15	1.90±6.65 (-15)-15	0.294

Bold value denote statistical significance at the p<0.05 level, TENS: Transcutaneous Electrical Nerve Stimulation, IFC: Interferential currents, Min.-max: Minumum-maximum

Table 3. Comparison of changes in pain, functionality and flexibility at baseline, 10th and 20th session between groups

			IFC group n=23 Mean ± SD min.-max.	TENS group n=21 Mean ± SD min.-max.	p-value
Numeric Pain Scale	Rest Pain Score	C1	-0.60±1.85 (-6)-2	-0.57±0.92 (-2)-1	0.660
		C2	1.13±1.93 (-5)-2	-1.33±0.85 (-3)-0	0.051
		C3	-0.52±1.20 (-4)-2	-1.90±1.04 (-4)-0	**0.004**
	Activity Pain Score	C1	-1.86±1.79 (-6)-0	-0.47±1.16 (-2)-2	**0.014**
		C2	-2.95±1.42 (-6)-0	-2.42±0.81 (-4)-(-1)	0.195
		C3	-1.08±1.08 (-4)-0	-1.95±0.86 (-4)-(-1)	**0.002**
	Night Pain Score	C1	-1.39±2.46 (-9)-1	-0.90±2.04 (-4)-7	0.318
		C2	-1.78±2.59 (-10)-1	-2.14±1.82 (-5)-4	0.121
		C3	-0.39±1.07 (-3)-2	-1.23±0.83 (-3)-0	**0.006**
Oswestry Disability Score (%)		C1	-11.21±8.54 (-32)-2	-0.95±7.76 (-16)-18	**0.000**
		C2	-16.43±10.01 (-38)-2	-15.33±8.51 (-36)-6	0.494
		C3	-5.21±8.77 (-26)-8	-14.38±8.63 (-34)-0	**0.001**
Sit & Reach Test (cm)		C1	1.23±3.63 (-8)-8	0.45±0.66 (-1)-2	0.259
		C2	3.19±4.37 (-3)-13.5	0.73±0.88 (-1)-2	**0.026**
		C3	1.95±1.78 (0-6.5)	0.28±0.64 (-1)-2	**0.000**

Bold value denote statistical significance at the p<0.05 level, C1: Mean change from baseline to week 10, C2: Mean change from baseline to week 20, C3: Mean change from baseline to week 10 to session 20, TENS: Transcutaneous Electrical Nerve Stimulation, IFC: Interferential currents, Min.-max: Minumum-maximum

were similar in reducing pain[19]. They also reported that both current applications were superior in pain reduction compared to the control group[19]. Grabiańska et al.[19] reported that pain intensity decreased significantly in patients with low back pain after two weeks of IFC and TENS treatment and this change was similar in the two treatment groups[20]. Rajfur et al.[20] divided patients with low back pain into 6 groups as conventional TENS (100 Hz, 100 µs), acupuncture-like TENS (200 Hz, 10 µs), IFC (50-100 Hz, 100 µs). Diadynamic current, high-voltage electrical stimulation and control group and applied electrotherapy for 15 sessions in addition to exercise therapy[21]. Unlike other researchers, Rajfur et al.[20] reported that the reduction in pain intensity at the end of 15 sessions was greater in the IFC group and provided superior effect compared to two different TENS applications. The researchers attributed this effect to the fact that IFC application is a medium frequency current and acts on deeper tissues[21].

In this study, similar to the studies of Dias et al.[17], Facci et al.[18] and Grabiańska et al.[19], were determined that IFC and TENS applications had similar effects in terms of pain intensity reduction values after a 20-session treatment program.

Functional/disability measures, pain severity measures, and measures for how pain affects social life and general mental health are all used to assess low back pain (LBP). Physicians and patients use both generic and condition-specific measures as functional measures for LBP management[21]. The Oswestry Disability Index is one of the most widely used scales for the assessment of symptoms and functionality of patients with chronic low back pain[14]. In their study, Rajfur et al.[20] found that interferential current application resulted in more improvement in Oswestry-assessed functioning than TENS current as a result of 15 sessions of different electrotherapy applications. In their study, Facci et al.[18] questioned the disability of the patients with the Rolland-Morris Disability Questionnaire[19]. The researchers reported that disability improved at a similar level in the TENS and IFC groups, but did not change in the control group[19]. In this study, there was a significant improvement in Oswestry scores in both IFC and TENS groups after the treatment program, but it was determined that the two groups showed similar changes before and after treatment.

Low back pain is frequently linked to the spine's reduced flexibility[22,23]. In this study, sit-reach test was used to evaluate spinal flexibility. Rajfur et al.[20] evaluated spinal flexibility with the Schober test in their study. The researchers reported that IFC and TENS currents applied in addition to a 15-session exercise program had a similar effect on improving flexibility. In the present study, flexibility improved in both groups after the treatment program, but the increase in flexibility in the IFC group was found to be superior to the TENS group.

In a recent study, it was determined that patients with low back pain wanted to know the problems that caused the pain, a decrease in pain, and an increase in the ability to perform activities of daily living, respectively[24]. According to the results of this study, IFC and TENS currents applied in addition to the basic exercise program in patients with chronic mechanical low back pain significantly reduced the pain at night, rest, and activity and improved disability levels of the patients.

Study Limitations

It is noteworthy that our study has some limitations, such as the absence of a control group and the fact that the electrical current intensity applied to the participants for each session was not recorded. Another limitation of the study is that although pain parameters such as rest, activity, and night pain were examined in detail, the participants were not questioned about how much they were exposed to functional activities that stimulate pain. Future studies with larger sample sizes are needed to examine the effects of different biophysical properties of these electrotherapy methods.

CONCLUSION

It has been determined that two different electrotherapy modalities, which are applied for analgesic and pain modulation in addition to exercise therapy in patients with chronic low back pain and which are most frequently preferred for this purpose in the clinic, are not different from each other. Our results support the results of the studies in the literature which aimed to evaluate shorter-term and immediate effects.

Ethics

Ethics Committee Approval: This prospective clinical interventional study was approved by Marmara University Clinical Research Ethics Review Board with approval number: 879, approval date: 07.12.2018.

Informed Consent: Written informed consent was obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: T.K.Ç., Concept: T.K.Ç., N.S., Design: T.K.Ç., N.S., Data Collection or Processing: N.S., B.S., A.A., Analysis or Interpretation: T.K.Ç., B.S., A.A., Literature Search: T.K.Ç., N.S., B.S., A.A., Writing: T.K.Ç., N.S., B.S., A.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Will JS, Bury DC, Miller JA. Mechanical Low Back Pain. Am Fam Physician. 2018;98:421-8.
2. Melman A, Lord HJ, Coombs D, Zadro J, Maher CG, Machado GC. Global prevalence of hospital admissions for low back pain: a systematic review with meta-analysis. BMJ Open. 2023;13:e069517.
3. Casiano VE, Sarwan G, Dydyk AM, Varacallo M. Back Pain. 2023 Feb 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2023.
4. Can H, Kuru Çolak T, Acar G. Nonspesifik Bel Ağrısında Konservatif Tedavi Yaklaşımları. Haliç Üniversitesi Sağlık Bilimleri Dergisi. 2020;3:1-14.
5. Razak Özdinçler A (ed). Elektroterapi ve Fiziksel Modaliteler kanıtlar ve Olgular Eşliğinde. İstanbul Tıp Kitabevi, İstanbul, 2019.
6. Bahçacı U, Kuru Çolak T, Acar G. Low back pain approaches by physiotherapists. JETR. 2021;8:152-9.
7. Rampazo ÉP, Liebano RE. Analgesic Effects of Interferential Current Therapy: A Narrative Review. Medicina (Kaunas). 2022;58:141.
8. Karacan İ, Koyuncu H. Fiziksel Tıp ve Rehabilitasyonda Elektroterapi. Güneş Kitabevi, İstanbul. 2003:pp:115-117.
9. Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults: a systematic review and meta-analysis of 381 studies (the meta-TENS study). BMJ Open. 2022;12:e051073.
10. Haefeli M, Elfering A. Pain assessment. Eur Spine J. 2006;15 Suppl 1:S17-24.
11. Yakut E, Düger T, Oksüz C, Yörükan S, Ureten K, Turan D, et al. Validation of the Turkish version of the Oswestry Disability Index for patients with low back pain. Spine (Phila Pa 1976). 2004;29:581-5; discussion 585.
12. Liu H, Shen Y, Xiong Y, Zhou H, Mao Y, Shen Q, et al. Psychometric Properties of Four Common Clinical Tests for Assessing Hamstring Flexibility in Young Adults. Front Physiol. 2022;13:911240.
13. Herndon CM, Zoberi KS, Gardner BJ. Common questions about chronic low back pain. Am Fam Physician. 2015;91:708-14.
14. Weiner DK, Haggerty CL, Kritchevsky SB, Harris T, Simonsick EM, Nevitt M, et al. How does low back pain impact physical function in independent, well-functioning older adults? Evidence from the Health ABC Cohort and implications for the future. Pain Med. 2003;4:311-20.
15. Mannion AF, Balagué F, Pellisé F, Cedraschi C. Pain measurement in patients with low back pain. Nat Clin Pract Rheumatol. 2007;3:610-8.
16. Shafshak TS, Elnemr R. The Visual Analogue Scale Versus Numerical Rating Scale in Measuring Pain Severity and Predicting Disability in Low Back Pain. J Clin Rheumatol. 2021;27:282-5.
17. Dias LV, Cordeiro MA, Schmidt de Sales R, Dos Santos MMBR, Korelo RIG, Vojciechowski AS, et al. Immediate analgesic effect of transcutaneous electrical nerve stimulation (TENS) and interferential

current (IFC) on chronic low back pain: Randomised placebo-controlled trial. J Bodyw Mov Ther. 2021;27:181-90.

18. Facci LM, Nowotny JP, Tormem F, Trevisani VF. Effects of transcutaneous electrical nerve stimulation (TENS) and interferential currents (IFC) in patients with nonspecific chronic low back pain: randomized clinical trial. Sao Paulo Med J. 2011;129:206-16.
19. Grabiańska E, Leśniewicz J, Pieszyński I, Kostka J. Porównanie działania przeciwbólowego prądów interferencyjnych i TENS u pacjentów z dolegliwościami bólowymi w części lędźwiowo-krzyżowej kregosłupa [Comparison of the analgesic effect of interferential current (IFC) and TENS in patients with low back pain]. Wiad Lek. 2015;68:13-9.
20. Rajfur J, Pasternok M, Rajfur K, Walewicz K, Fras B, Bolach B, et al. Efficacy of Selected Electrical Therapies on Chronic Low Back Pain: A Comparative Clinical Pilot Study. Med Sci Monit. 2017;23:85-100.
21. Dohnert MB, Bauer JP, Pavao TS. Study of the effectiveness of interferential current as compared to transcutaneous electrical nerve stimulation in reducing chronic low back pain. Braz. J Pain. 2015;16:27-31.
22. Laird RA, Kent P, Keating JL. How consistent are lordosis, range of movement and lumbo-pelvic rhythm in people with and without back pain? BMC Musculoskelet Disord. 2016;17:403.
23. Šarabon N, Vreček N, Hofer C, Löfler S, Kozinc Ž, Kern H. Physical Abilities in Low Back Pain Patients: A Cross-Sectional Study with Exploratory Comparison of Patient Subgroups. Life (Basel). 2021;11:226.
24. Smuck M, Barrette K, Martinez-Ith A, Sultana G, Zheng P. What does the patient with back pain want? A comparison of patient preferences and physician assumptions. Spine J. 2022;22:207-13.

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LOW-ENERGY VERTEBRAL COMPRESSION FRACTURES: DIFFERENTIAL DIAGNOSIS BETWEEN OSTEOPOROTIC AND MALIGNANT FRACTURES BY INFLAMMATORY BIOMARKERS

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ABSTRACT

Objective: Spontaneous or low-energy vertebral compression fractures are encountered in clinical practice and pose a diagnostic challenge. This study aimed to determine the role of systemic inflammatory markers in the differential diagnosis of malignant and osteoporotic vertebral fractures (MVF and OVF).

Materials and Methods: Patients who underwent surgical treatment for OVF and MVF at our center were retrospectively analyzed. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammatory index (SII) values were calculated using complete blood count data obtained before treatment. Optimal cut-off values were determined for the differentiation of OVF and MVF. The results were correlated with the histopathological and surgical findings.

Results: The study was conducted with 72 patients, 73.6% (n=53) of whom were women and 26.4% (n=19) were men. Of the patients participating in the study, 63.9% (n=46) had OVF and 36.1% (n=26) had MVF. The mean age of the OVF group (69.93±15.52) was significantly higher than that of the MVF group (56.38±19.76) ($p=0.001$; $p<0.01$). Furthermore, the ratio of women in the OVF group (84.8%) was significantly higher than that in the MVF group (53.8%) ($p=0.006$; $p<0.01$). The lymphocyte measurements of the MVF group were significantly lower than those of the OVF group ($p=0.029$; $p<0.05$). The PLR ($p=0.026$; $p<0.05$), NLR ($p=0.009$; $p<0.01$), and SII ($p=0.007$; $p<0.01$) measurements were significantly higher in the MVF group than in the OVF group.

Conclusion: Our study found significantly elevated levels of inflammatory markers (NLR, PLR, SII) in MVF compared with OVF. These findings suggest that NLR, PLR, and SII hold promise as concise and effective tools for the differential diagnosis of low-energy vertebral compression fractures.

Keywords: Vertebral fractures, Neutrophil-to-Lymphocyte ratio, Platelet-to-Lymphocyte ratio, Metastasis, inflammatory markers

INTRODUCTION

Vertebral compression fractures occur because of various reasons, such as trauma, osteoporosis, infection, and tumor. While these fractures can occur with high energy, such as in trauma, they can also occur with low energy in the presence of osteoporosis, infection, and malignancy. In low-energy vertebral compression fractures, it is necessary to determine whether the underlying cause is malignancy or a benign cause, such as osteoporosis or infection.

Identifying whether a vertebral fracture is due to a benign or malignant cause is important for approaching the patient because the clinical course, prognosis, and treatment strategies vary greatly. Moreover, early detection of malignancy can profoundly improve the success of the treatment and increase the overall survival[1]. The differential diagnosis is usually based on anamnesis, physical examination, clinical findings, localization, and radiological imaging findings. Magnetic resonance imaging (MRI) plays an important role in the differential diagnosis of such lesions. However, primary malignant tumors, metastatic malignancies, acute benign and malignant vertebral fractures (MVF), and infectious conditions present with similar signal changes on routine MRI[2]. A definitive diagnosis can be made in this case using pathological examination via biopsy. However, it is an invasive procedure.

In addition to the clinical and radiological approach, laboratory tests that can be used in the diagnosis of malignancy have long been the subject of research. So far, researchers have explored various sources of blood-based biomarkers in their quest to identify the most suitable biomarker for early-stage cancer detection[3]. Although there has been no consensus on a definitive and reliable parameter so far, the presence and role

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of inflammatory biomarkers in tumor physiopathology have been widely studied in recent years.

The importance of chronic inflammation in the pathogenesis and progression of various cancers has been demonstrated in many studies(4-6). Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic inflammatory index (SII) are known markers of the systemic inflammatory response and have been used to determine the diagnosis and prognosis of several musculoskeletal tumors(7-11), as well as being associated with spinal tumoral pathologies(12). Similarly, there are studies on biomarkers for early diagnosis of osteoporosis(13-17). However, the importance of inflammatory markers in differentiating MVF from osteoporotic vertebral fracture (OVF) has not been evaluated. Therefore, this study aimed to differentiate MVF from OVF of the spine using inflammatory biomarkers.

MATERIALS AND METHODS

Ethics committee approval of Atlas University Non-interventional Scientific Research (approval number: E-22686390-050.99-28169/14.06.2023) was obtained, and the study was conducted according to the principles of the Declaration of Helsinki.

Inclusion criteria: Low energy or spontaneous OVFs and MVFs were included in the study. The exclusion criteria are as follows: Vertebral fractures due to infection and other benign causes, leukocytosis and elevated C-reactive protein levels, absence of pathological data, rheumatologic, hematologic, or inflammatory diseases, steroid and anti-inflammatory drug use, non-vertebral invasion or metastasis, and previous diagnosis and treatment of malignancy.

A total of 123 low-energy or spontaneous vertebral fractures diagnosed and surgically treated in our hospital between 2011 and 2022 were retrospectively analyzed. Accordingly, 51 patients who did not meet the inclusion criteria were excluded from the study. A total of 72 patients with fracture were included in the study and evaluated.

Age, sex, pathological diagnosis, cause of fracture, and blood parameters before treatment were analyzed. Clinical and demographic data of the patients were obtained from hospital records.

Neutrophil, lymphocyte, and platelet counts obtained from a complete blood count taken before the treatment were evaluated. NLR was obtained by dividing the neutrophil count by the lymphocyte count, and PLR was obtained by dividing the platelet count by the lymphocyte count. SII was obtained by multiplying the neutrophil count and platelet count and dividing this value by the lymphocyte count. The patients were categorized into two groups, i.e., OVF and MVF. Results were correlated with histopathological and surgical findings.

Statistical Analysis

While evaluating the findings obtained in the study, Statistical Package for the Social Sciences, Version 26, program was used for statistical analysis. For descriptive statistics, quantitative variables were represented as mean, standard deviation, median, and minimum and maximum values. On the contrary, qualitative variables were represented as frequency and percentage. Shapiro-Wilk test and box plot graphs were used to evaluate the conformity of the data to normal distribution. Student's t-test was used to evaluate quantitative data with normal distribution between two groups. Mann-Whitney U test was used to evaluate non-normally distributed variables between two groups. Receiver operating characteristic curve (ROCC) analysis was used to predict malignancy. Chi-square test was used to compare qualitative data. Results were evaluated at a 95% confidence interval, and p<0.05 was accepted as statistically significant in all analyses.

RESULTS

This study was conducted at the Atlas University Medicine Hospital between 2012 and 2022 with a total of 72 patients, 73.6% (n=53) of whom were women and 26.4% (n=19) were men. The age of the patients ranged between 17 years and 98 years, with a mean of 62.48±17.65 years. When the diagnoses of the patients who participated in the study were analyzed, 63.9% (n=46) were OVF and 36.1% (n= 26) were MVF (Table 1). The OVF group had a significantly higher age (p=0.001; p<0.01) and a significantly higher female: male ratio (p=0.006; p<0.01) (Table 1).

Of the patients with MVF, 4 (12.5%) were cervical, 15 (46.8%) were thoracic, and 17 (53.1%) were lumbar. Four patients had involvement of multiple vertebrae. Of the patients with OVF, 27 (50.0%) were thoracic and 30 (55.5%) were lumbar. Seven patients had multiple fractures.

In the MVF group, the cause of fractures was determined to be metastasis in 19 patients, primary bone tumor in 4 patients, and multiple myeloma in 3 patients. In the OVF group, 5 patients underwent instrumented fusion and 41 patients underwent

Table 1. Comparison of descriptive characteristics by diagnosis

		Total (n=72)	OVF (n=46)	MVF (n=26)	p-value
Sex	**Women**	53 (73.6)	39 (84.8)	14 (53.8)	[a]**0.006****
	Men	19 (26.4)	7 (15.2)	12 (46.2)	
Age (years)	Mean ± SD	62.48±17.65	69.93±15.52	56.38±19.76	[b]**0.026**
	Median (min.-max.)	64.5 (17-98)	67.5 (19-98)	58 (17-87)	

[a]Pearson chi-square test, [b]Student's t-test, **p<0.01, SD: Standard deviation, OVF: Osteoporotic vertebral fracture, MVF: Malignant vertebral fracture, min.: Minimum, max.: Maximum

vertebroplasty. In the MVF group, 20 patients underwent instrumented fusion and 6 patients underwent vertebroplasty.

The lymphocyte measurements of the MVF group were statistically significantly lower than those of the OVF group ($p=0.029$; $p<0.05$). PLR ($p=0.026$; $p<0.05$), NLR ($p=0.009$; $p<0.01$), and SII ($p=0.007$; $p<0.01$) values were statistically significantly higher in the MVF group than those in the OVF group. According to the diagnoses, platelet and neutrophil counts of the patients did not show a statistically significant difference ($p>0.05$) (Table 2).

For predicting malignancy, a cut-off value of 1.76 for lymphocyte count had a sensitivity of 76.92%, specificity of 67.39%, positive predictive value of 57.10%, and negative predictive value of 83.80%. In the receiver operating characteristic ROOC obtained, the underlying area was 68.1% with a standard error of 6.7%. There was a statistically significant correlation between lymphocyte count with a cut-off value of 1.76 and malignancy ($p=0.011$; $p<0.05$). However, there was no statistically significant correlation between PLR value and malignancy ($p=0.053$; $p>0.05$).

For predicting malignancy, a cut-off value of 2.42 for NLR had a sensitivity of 53.85%, specificity of 78.26%, positive predictive value of 58.30%, and negative predictive value of 75%. In the ROCC obtained, the underlying area was 67.1% with a standard error of 6.8%. There was a statistically significant correlation between NLR level with a cut-off value of 2.42 and malignancy ($p=0.017$; $p<0.05$).

For predicting malignancy, a cut-off value of 483.52 for SII had a sensitivity of 69.23%, specificity of 60.87%, positive predictive value of 50%, and negative predictive value of 77.80%. In the ROCC obtained, the underlying area was 65.1% with a standard error of 7.2%. There was a statistically significant correlation between SII with a cut-off value of 483.52 and malignancy ($p=0.035$; $p<0.05$) (Table 3) (Figure 1).

DISCUSSION

In this study, the role of inflammatory markers in the differential diagnosis between MVF and OVF was investigated. The results showed that systemic inflammatory biomarkers measured in peripheral blood samples collected before treatment had an important diagnostic value in this differentiation.

When malignancy develops, the immune system components, including neutrophils, platelets, and lymphocytes, can be impacted[18]. Tumors induce an inflammatory response, triggering increased neutrophil production and release into the bloodstream, potentially contributing to neutrophilia in cancer patients[19,20]. In our series, the neutrophil count was higher in the MVF group compared to the OVF group, although not statistically significant. Platelets play a crucial role in malignancy by influencing tumor angiogenesis, growth, and metastasis. The intricate interaction between platelets and

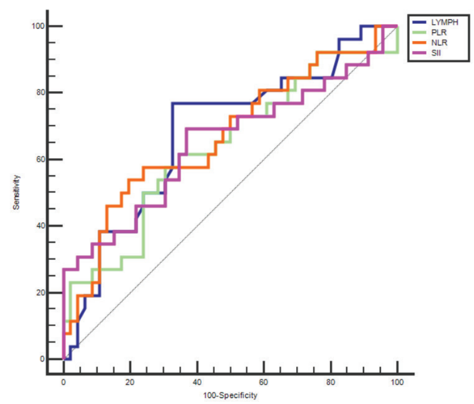

Figure 1. ROCC for predicting malignancy

LYMPH: Lymphocyte, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic inflammatory index, ROCC: Receiver operating characteristic curve

Table 2. Comparison of measurement values according to diagnoses

		Total	OVF (n=46)	MVF (n=26)	p-value
PLT	Mean ± SD	233.45±74.24	239.63±78.37	222.53±66.35	[a]0.351
	Median (min.-max.)	214 (85-458)	223.5 (85-458)	208 (107-370)	
LYMPH	Mean ± SD	1.87±0.71	2.01±0.71	1.63±0.66	[a]0.029*
	Median (min.-max.)	1.8 (0.5-3.6)	1.9 (0,5-3.6)	1.6 (0.6-2.9)	
NEUT	Mean ± SD	3.66±1.57	3.48±1.42	3.99±1.78	[a]0.183
	Median (min.-max.)	3.5 (0.3-7.5)	3.4 (0.3-6.4)	4.2 (1.2-7.5)	
PLR	Mean ± SD	137.65±54.15	127.04±39.13	156.42±70.69	[a]0.026*
	Median (min.-max.)	122.5 (43.2-368.3)	119 (71.2-220.6)	149.1 (43.2-368.3)	
NLR	Mean ± SD	2.30±1.55	1.95±1.07	2.93±2.02	[b]0.009**
	Median (min.-max.)	2 (0.2-9.4)	1.7 (0.2-5.6)	2.6 (0.4-9.4)	
SII	Mean ± SD	522.35±336.65	442.97±204.69	662.80±462.97	[a]0.007**
	Median (min.-max.)	483.1 (32.7-1987.5)	464.9 (32.7-754.1)	590.3 (51.9-1987.5)	

[a]Student's t-test, *$p<0.05$, **$p<0.01$, SD: Standard deviation, OVF: Osteoporotic vertebral fracture, MVF: Malignant vertebral fracture, PLT: Platelet, LYMPH: Lymphocyte, NEUT: Neutrophil, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic inflammatory index, min.: Minimum, max.: Maximum

malignant diseases leads to altered platelet function and properties, contributing to an accelerated progression of cancer[21,22]. Lymphocytes, essential for antitumor immunity, engage in attacking and eliminating tumor cells within the microenvironment. Prolonged exposure to this environment may lead to lymphocyte depletion, impacting their effectiveness and correlating with poor prognostic outcomes in cancer, although some inconsistencies exist in pre-treatment lymphocyte counts' predictive value[21].

In the light of this information, markers such as NLR, PLR, and SII are expected to vary in inflammation-related events, including malignancy. Indeed, NLR and other values have been reported to be high in many studies on malignancy. However, some studies have reported that the reason for the increase in NLR in these multicomponent ratios is the decrease in lymphocytes rather than neutrophils[23,24]. Similarly, in the present study, lymphocyte ratios were found to be significantly lower in the MVF group.

Studies have shown that inflammatory biomarkers can be used in the diagnosis and prognosis of malignancy[9,10,25,26]. In a study evaluating all spinal tumors, including bone and soft tissue tumors, in 503 patients, NLR and PLR were found to be valuable markers for preoperative diagnosis and differentiation of primary and secondary tumors. Cut-off values for NLR (>3.19) and PLR (>141) were also reported to be associated with a high risk of malignancy[12]. In their study, Caliskan and Korkmaz[7] analyzed patients for whom scintigraphy was recommended for suspected bone metastasis and compared the results with NLR values. Accordingly, NLR was found to be higher in the group with bone metastasis. In this group, the median neutrophil count was 4.9 (range: 3.1-10.8), median lymphocyte count was 1.6, and NLR was 2.5[7]. In our series, the median neutrophil count was 4.2 (1.2-7.5), median lymphocyte count was 1.6 (0.6-2.9), and median NLR was 2.6 (0.4-9.4).

In addition to malignancies, different biomarkers have been investigated for the early detection of osteoporosis[27]. The pathogenesis of postmenopausal osteoporosis (PMO) has long been recognized to be closely related to immune system dysfunction and systemic inflammation, with T cells, neutrophils, and platelets playing a role in the mechanism of the relationship between osteoporosis and immunity[28-30]. Several publications have reported that NLR levels are elevated in elderly people with osteoporosis[16,17,31-33]. T cells, notably Th17 cells promoting osteoclast formation and Treg cells inhibiting bone loss, play a crucial role in the regulation of bone resorption[34,35]. These findings indicate that an imbalance in the immune system contributes to bone loss by fostering osteoclast formation[36]. There is literature evidence that platelets are active in osteoporosis. Elevated inflammatory stimuli initiate platelet activation[37], and activated platelets influence osteoclast formation via receptor activation, which affects prostaglandin and RANKL signaling[38]. Furthermore, thromboxanes and other mediators secreted by activated platelets can increase inflammation as a result of this process[37].

The literature encompasses numerous studies investigating the association between osteoporosis and various biomarkers. Yolaçan and Guler[39] assessed 148 Turkish women with PMO and observed an inverse correlation between NLR, PLR, MLR, and SII values and alterations in bone mineral density (BMD), suggesting their potential role in early diagnosis. While some authors reported a correlation, others did not detect any significant association[13-17,32,33,39]. Koseoglu[15], categorizing postmenopausal patients into normal and low BMD groups, found an inverse relationship between PLR and BMD. However, no statistically significant relationship was observed between NLR and BMD[15]. In our present study, the mean PLR was 119 (range: 71.2-220.6) in the OVF group and 149.1 (range: 43.2-368.3) in the MVF group. Additionally, the mean NLR was 1.95±1.07 in the OVF group and 2.93±2.02 in the MVF group.

A review of the literature showed that NLR, PLR, and SII are increased in both malignancy and osteoporosis. In Tables 4 and 5, our results in osteoporosis and malignancy groups are compared with similar studies in the literature[40-45]. Of the studies in the literature investigating the relationship between several biomarkers and osteoporosis and bone malignancies, a considerable number of studies have reported that certain biomarkers are not associated with osteoporosis and malignancy[14,17]. In the present study, the primary comparison was not based on normal values but rather on the distinction in biomarker ratios resulting from the two pathologies. In other words, we compared the NLR, PLR, and SII values between OVF and MVF. The findings revealed statistically significant elevations in NLR, PLR, and SII in MVF compared to OVF. In

Table 3. Diagnostic screening tests and ROCC results for lymphocyte, PLR, NLR, and SII in predicting malignancy

	Diagnostic scan					ROCC		
	Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area	95% confidence interval	p-value
LYMPH	≤1.76	76.92	67.39	57.10	83.80	0.681	0.550-0.812	0.011*
PLR	≥137.98	57.69	67.39	50.00	73.80	0.638	0.500-0.776	0.053
NLR	≥2.42	53.85	78.26	58.30	75.00	0.671	0.536-0.805	0.017*
SII	≥483.52	69.23	60.87	50.00	77.80	0.651	0.509-0.792	0.035*

*p<0.05, LYMPH: Lymphocyte, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic inflammatory index, ROCC: Receiver operating characteristic curve

Table 4. Comparison of malignant cases in our sample with similar studies in the literature. Measurements are shown in the table as mean ± SD, median (min.-max.), and median (Q1-Q3)

Author of the article	Disease	Number of patients	NLR	PLR	SII
Caliskan and Korkmaz[7] median (min.-max.)	Various malignancies with bone metastases	25	2.83 (1.56-31.8)		
Li et al.[12]	Malignant spine tumors	262	3.31 (0.41, 18.82)	150.31 (16.84, 548.00)	
Chen et al.[40]	Hepatocellular carcinoma bone metastases	239	4.73 (IQR, 2.38-6.00)	163.56 (IQR, 95.12-196.67)	705.05 (IQR, 298.28-783.23)
Xia et al.[41] median (min.-max.)	Osteosarcoma	359	3.19 (0.79-74.49)	142 (5.4-3111)	
Thio et al.[8]	Various malignancies with bone metastases	1012	6.4 (IQR 3.6-11.8)	283 (IQR, 174-452)	
Wang et al.[42] Mean ± SD	Bone metastasis in patients with prostate cancer	67	2.83±0.55	127.89±29.28	
Yapar et al.[9] median (min.-max.)	Enchondroma and low-grade chondrosarcoma	101	2.54 (1.12-7.46)		
This study mean ± SD median (min.-max.)	Various malignancies, pathological vertebral fracture	26	2.93±2.02 2.6 (0.4-9.4)	156.42±70.69 149.1 (43.2-368.3)	662.80±462.97 590.3 (51.9-1987.5)

SD: Standard deviation, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic inflammatory index, IQR: Interquartile range, min.: Minimum, max.: Maximum

Table 5. Comparison of osteoporosis cases in our sample with similar studies in the literature. Measurements are shown in the table as mean ± SD, median (min-max), and median (Q1-Q3)

Author of the article	Disease	Number of cases	NLR	PLR	SII
Eroglu and Karatas[13]	PMO	48	1.71 (0.81-8.9)	134 (52.89-385)	
Yolaçan and Guler[39]	PMO	148	2.3±0.81	149.9±54.9	641.2±362.7
Kale[43]	PMO	48	1.91±0.74	132.83±29.4	
Al Salmani et al.[44]	PMO	221	1.19 (0.20-4.43)	131.47 (39.74-256.92)	
Onalan and Gokalp[45]	Osteoporosis	169	3.5±4.2	179.2±130.7	
Qin et al.[31]	Osteoporosis	29	2.11±0.73		
Huang and Li[14]	PMO	122	2.74±1.06		
Koseoglu[15]	PMO	179	1.9±0.7	136.3±50.4	
This study mean ± SD median (min.-max.)	Osteoporosis	46	1.95±1.07 1.7 (0.2-5.6)	127.04±39.13 119 (71.2-220.6)	442.97±204.69 464.9 (32.7-754.1)

SD: Standard deviation, PLR: Platelet-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic inflammatory index, PMO: Postmenopausal osteoporosis, min.: Minimum, max.: Maximum

general, when examining NLR, PLR, and SII values in literature series, it is evident that NLR, PLR, and SII values of patients with malignancy are higher than those of patients with osteoporosis. This observation supports the conclusions reached in the present study.

This study has important strengths. To the best of our knowledge, this is the first study to examine the association of inflammatory markers with spontaneous low-energy vertebral fractures. Furthermore, the association between osteoporotic and pathological fractures and inflammatory markers was also evaluated. Lastly, the study examined the role of inflammatory markers in differentiating osteoporosis from malignancy in the etiology of this type of vertebral fractures.

Study Limitations

The number of patients with MVF evaluated in this study was relatively low, which is due to the rarity of such cases. Furthermore, we could not create more similar groups in terms of age, sex, and comorbidity. Working with a larger dataset and selecting groups with similar characteristics are necessary for the results to be more reliable and meaningful.

Furthermore, although statistically significant, the sensitivity and specificity of inflammatory biomarkers are low. Systemic inflammatory biomarkers are non-specific predictors of MVF and OVF, which is one of their main disadvantages. Lastly, the study was retrospective and conducted in a single center. Multicenter prospective studies are required.

CONCLUSION

This study showed that MVF has a higher level of increased inflammation than OVF. The main aim of this study was to investigate the usefulness of such a relationship in distinguishing between MVF and OVF. Our results support that such an approach can be used for the differential diagnosis of MVF and OVF. In conclusion, systemic inflammatory biomarkers have diagnostic value in differentiating MVF from OVF. Although these markers are not reliable on their own, when used in combination with other medical tests, they can make an important contribution to pretreatment assessment. Moreover, they have practical and cost advantages, making them preferred markers.

When faced with a low-energy vertebral fracture, it is important to examine parameters such as NLR, PLR, and SI, which can be easily measured in any medical center. If these values are high, the probability of an underlying malignancy increases.

Ethics

Ethics Committee Approval: Ethics committee approval of Atlas University Non-interventional Scientific Research (approval number: E-22686390-050.99-28169/14.06.2023) was obtained, and the study was conducted according to the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: H.D., A.O.M., D.A., N.D., H.A., Concept: H.D., Design: H.D., D.A., Data Collection or Processing: N.D., Analysis or Interpretation: H.A., Literature Search: H.D., A.O.M., Writing: H.D., A.O.M.

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REFERENCES

1. Etzioni R, Urban, N, Ramsey S, McIntosh, Schwartz S, Reid B, et al. The case for early detection. Nat Rev Cancer. 2003;3:243-52.
2. Romeo V, Ugga L, Stanzione A, Cocozza S, Cuocolo R, Brunetti A. Differential diagnosis of benign and malignant vertebral compression fractures using conventional and advanced MRI techniques. BJR Open. 2019;1:20180033.
3. Uttley L, Whiteman BL, Woods HB, Harnan S, Philips ST, Cree IA. Building the Evidence Base of Blood-Based Biomarkers for Early Detection of Cancer: A Rapid Systematic Mapping Review. EBioMedicine. 2016;10:164-73.
4. Goertzen C, Mahdi H, Laliberte C, Meirson T, Eymael D, Gil-Henn H, et al. Oral inflammation promotes oral squamous cell carcinoma invasion. Oncotarget. 2018;9:29047-63.
5. Lasfar A, Zloza A, Silk AW, Lee LY, Cohen-Solal KA. Interferon Lambda: Toward a Dual Role in Cancer. J Interferon Cytokine Res. 2019;39:22-9.
6. Berger E, Delpierre C, Hosnijeh FS, Kelly-Irving M, Portengen L, Bergdahl IA, et al. Association between low-grade inflammation and Breast cancer and B-cell Myeloma and Non-Hodgkin Lymphoma: findings from two prospective cohorts. Sci Rep. 2018;8:10805.
7. Caliskan B, Korkmaz AN. Can Neutrophil/Lymphocyte Ratio be a Predictor for Bone Metastases of Solid Tumors? World J Nucl Med. 2016;15:196-9.
8. Thio QCBS, Goudriaan WA, Janssen SJ, Paulino Pereira NR, Sciubba DM, Rosovksy RP, Schwab JH. Prognostic role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients with bone metastases. Br J Cancer. 2018;119:737-43.
9. Yapar A, Ulucaköy C, Sezgin EA, Atalay İB, Ekşioğlu MF. Diagnostic role of neutrophil-to-lymphocyte ratio and monocyte-to-lymphocyte ratio in patients with enchondroma and low-grade chondrosarcoma. Jt Dis Relat Surg. 2020;31:286-90.
10. Xia X, Li K, Wu R, Lv Q, Deng X, Fei Z, et al. Predictive value of neuron-specific enolase, neutrophil-to-lymphocyte-ratio and lymph node metastasis for distant metastasis in small cell lung cancer. Clin Respir J. 2020;14:1060-6.
11. Vano YA, Oudard S, By MA, Têtu P, Thibault C, Aboudagga H, et al. Optimal cut-off for neutrophil-to-lymphocyte ratio: Fact or Fantasy? A prospective cohort study in metastatic cancer patients. PLoS One. 2018;13:e0195042.
12. Li Y, Wang B, Zhou S, Jiang L, Yang S, Liu X, et al. Do routine blood test results help in the diagnosis of spine tumors? A retrospective study of the significance of pretreatment neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios from 503 spine tumor patients. Medicine (Baltimore). 2019;98:e14902.
13. Eroglu S, Karatas G. Platelet/lymphocyte ratio is an independent predictor for osteoporosis. Saudi Med J. 2019;40:360-6.
14. Huang C, Li S. Association of blood neutrophil lymphocyte ratio in the patients with postmenopausal osteoporosis. Pak J Med Sci. 2016;32:762-5.
15. Koseoglu SB. Bone loss & platelet-to-lymphocyte ratio. Biomark Med. 2017;11:5-10.
16. Tang Y, Peng B, Liu J, Liu Z, Xia Y, Geng B. Systemic immune-inflammation index and bone mineral density in postmenopausal women: A cross-sectional study of the national health and nutrition examination survey (NHANES) 2007-2018. Front Immunol. 2022;13:975400.
17. Chen S, Sun X, Jin J, Zhou G, Li Z. Association between inflammatory markers and bone mineral density: a cross-sectional study from NHANES 2007-2010. J Orthop Surg Res. 2023;18:305.
18. Borregaard N. Neutrophils, from marrow to microbes. Immunity. 2010;33:657-70.
19. Rosales C. Neutrophil: A Cell with Many Roles in Inflammation or Several Cell Types? Front Physiol. 2018;9:113.
20. Nagata H, Komatsu S, Takaki W, Okayama T, Sawabe Y, Ishii M, et al. Granulocyte colony-stimulating factor-producing hepatocellular carcinoma with abrupt changes. World J Clin Oncol. 2016;7:380-6.
21. Plantureux L, Crescence L, Dignat-George F, Panicot-Dubois L, Dubois C. Effects of platelets on cancer progression. Thromb Res. 2018;164:S40-7.
22. Lin RJ, Afshar-Kharghan V, Schafer AI. Paraneoplastic thrombocytosis: the secrets of tumor self-promotion. Blood. 2014;124:184-7.

23. Saroha S, Uzzo RG, Plimack ER, Ruth K, Al-Saleem T. Lymphopenia is an independent predictor of inferior outcome in clear cell renal carcinoma. J Urol. 2013;189:454-61.
24. Joseph N, Dovedi SJ, Thompson C, Lyons J, Kennedy J, Elliott T, et al. Pre-treatment lymphocytopaenia is an adverse prognostic biomarker in muscle-invasive and advanced bladder cancer. Ann Oncol. 2016;27:294-9.
25. Mısırlıoğlu M, Yapar A, Sezgin EA, Bulut EK, Beltir G, Güngör BŞ. Are preoperative complete blood count parameters in peripheral nerve sheath tumors useful diagnostic tools? Jt Dis Relat Surg. 2021;32:340-6.
26. Zhang JY, Ge P, Zhang PY, Zhao M, Ren L. Role of Neutrophil to Lymphocyte Ratio or Platelet to Lymphocyte Ratio in Prediction of Bone Metastasis of Prostate Cancer. Clin Lab. 2019;65.
27. Jackson RD, Mysiw WJ. Insights into the epidemiology of postmenopausal osteoporosis: the Women's Health Initiative. Semin Reprod Med. 2014;32:454-62.
28. Barbour KE, Boudreau R, Danielson ME, Youk AO, Wactawski-Wende J, Greep NC, et al. Inflammatory markers and the risk of hip fracture: the Women's Health Initiative. J Bone Miner Res. 2012;27:1167-76.
29. Poubelle PE, Chakravarti A, Fernandes MJ, Doiron K, Marceau AA. Differential expression of RANK, RANK-L, and osteoprotegerin by synovial fluid neutrophils from patients with rheumatoid arthritis and by healthy human blood neutrophils. Arthritis Res Ther. 2007;9:R25.
30. Chakravarti A, Raquil MA, Tessier P, Poubelle PE. Surface RANKL of Toll-like receptor 4-stimulated human neutrophils activates osteoclastic bone resorption. Blood. 2009;114:1633-44.
31. Qin Q, Yan S, Yang Y, Chen J, Yan H, Li T, et al. The Relationship Between Osteoporosis and Intestinal Microbes in the Henan Province of China. Front Cell Dev Biol. 2021;9:752990.
32. Yilmaz H, Uyfun M, Yilmaz TS, Namuslu M, Inan O, Taskin A, et al. Neutrophil-lymphocyte ratio may be superior to C-reactive protein for predicting the occurrence of postmenopausal osteoporosis. Endocr Regul. 2014;48:25-33.
33. Liu YC, Yang TI, Huang SW, Kuo YJ, Chen YP. Associations of the Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio with Osteoporosis: A Meta-Analysis. Diagnostics (Basel). 2022;12:2968.
34. Li Y, Toraldo G, Li A, Yang X, Zhang H, Qian WP, et al. B cells and T cells are critical for the preservation of bone homeostasis and attainment of peak bone mass in vivo. Blood. 2007;109:3839-48.
35. Weitzmann MN, Ofotokun I. Physiological and pathophysiological bone turnover - role of the immune system. Nat Rev Endocrinol. 2016;12:518-32.
36. Zhang W, Dang K, Huai Y, Qian A. Osteoimmunology: The Regulatory Roles of T Lymphocytes in Osteoporosis. Front Endocrinol (Lausanne). 2020;11:465.
37. Koupenova M, Clancy L, Corkrey HA, Freedman JE. Circulating Platelets as Mediators of Immunity, Inflammation, and Thrombosis. Circ Res. 2018;122:337-51.
38. Clowes JA, Riggs BL, Khosla S. The role of the immune system in the pathophysiology of osteoporosis. Immunol Rev. 2005;208:207-27.
39. Yolaçan H, Guler S. Inverse Correlation Between Bone Mineral Density and Systemic Immune Inflammation Index in Postmenopausal Turkish Women. Cureus. 2023;15:e37463.
40. Chen J, Huang W, Xu X, Fan S, Zhang Q, Li X, et al. Prognostic implications of systemic immune-inflammation index in patients with bone metastases from hepatocellular carcinoma treated with radiotherapy. Front Oncol. 2023;13:1076428.
41. Xia WK, Liu ZL, Shen D, Lin QF, Su J, Mao WD. Prognostic performance of pre-treatment NLR and PLR in patients suffering from osteosarcoma. World J Surg Oncol. 2016;14:127.
42. Wang Z, Sun Y, Ren W, Guan Z, Cheng J, Pei X, Dong Q. Establishment and validation of a predictive model for bone metastasis in prostate cancer patients based on multiple immune inflammatory parameters. Am J Transl Res. 2023;15:1502-9.
43. Kale I. The predictive role of monocyte-lymphocyte ratio and platelet-lymphocyte ratio in postmenopausal osteoporosis. J Clin Investig Surg. 2021;6:141-7.
44. Al Salmani A, Al Shidhani A, Al-Alawi NM, Al Sulaimi AA, Al-Hashemi MA. Inflammatory Markers as a Predictor of Postmenopausal Osteoporosis: Cross-sectional study from Sultan Qaboos University Hospital. Sultan Qaboos Univ Med J. 2022;22:508-14.
45. Onalan E, Gokalp Y. The relationship between bone mineral density and hematological parameters in the geriatric age group. Fam Pract Palliat Care. 2020;5:1-5.

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OSTEOPOROTIC VERTEBRAL FRACTURE; COMPARATIVE ANALYSIS OF UNILATERAL AND BILATERAL VERTEBROPLASTY RESULTS

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ABSTRACT

Objective: Osteoporotic vertebral fracture (OVF) results in increased morbidity and mortality, primarily in the elderly, leading to severe limitation of movement. In this study, we evaluated the results of unilateral and bilateral vertebroplasty (VP) procedures in OVF.

Materials and Methods: Two hundred fifty-seven patients who underwent VP for OVF were retrospectively studied and divided into two groups: unilateral (204 patients) and bilateral (53 patients) VP. The visual Analogue Scale (VAS) pain score and kyphotic angle were comparatively analyzed between the two groups.

Results: There was no statistically significant difference between the groups (unilateral and bilateral VP) in terms of VAS preop/postop variables and kyphosis.

Conclusion: We believe that unilateral VP is sufficient for significantly reducing the complication rate with anesthesia and radiation exposure and reducing the cost of the surgical procedure.

Keywords: Unilateral vertebroplasty, osteoporotic fracture, osteoporotic vertebral fracture, vertebroplasty, vertebral fracture

INTRODUCTION

Osteoporosis is a systemic bone disease that is usually seen in elderly individuals, characterized by loss of bone mass due to deterioration in bone tissue and increased likelihood of fracture[1]. Vertebral fractures are one of the most common complications of osteoporosis[2].

Osteoporotic vertebral fracture (OVF) results in increased morbidity and mortality, primarily in the elderly, leading to severe limitation of movement[3]. A significant portion of the pain that occurs as a result of vertebral fracture is due to the instability caused by the fracture. The pain increases significantly when the patient is moving and it is less at rest. The symptoms of OVF may result in loss of height due to vertebral collapse, spinal instability, and even kyphotic deformity. Therefore, rapid relief of pain and restoration of mobility and sagittal contour allows the patient to normalize[1,4]. Since the bones are osteoporotic in patients undergoing stabilization surgery, the use of long supports to increase strength and the use of anterior and posterior surgery together increase the surgical risks in patients. For these reasons, percutaneous vertebroplasty (VP), which is described as minimally invasive, has been used in recent years. The risk of complications is lower compared to radical surgical interventions[5]. This method usually relieves fracture pain effectively in elderly patients[6].

Recently, unilateral interventions have been recommended by some authors because they shorten the duration of surgery and anesthesia, reduce the cost of the procedure and the radiation dose received during the operation, reduce the risk of escape from the cement used, and avoid complications of placing a second working cannula[7,8]. In this study, we evaluated the clinical and radiologic results of unilateral and bilateral VP procedures in OVF.

MATERIALS AND METHODS

This study included 257 patients who underwent VP for OVFs in our clinic between 2011 and 2022 (204 patients with unilateral and 53 patients with bilateral VP). The patients were studied retrospectively. Detailed informed consent was obtained from

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all patients for these interventions. All patients underwent a detailed physical and neurologic examination. Bone mineral density was evaluated by the T-Score method. Routine perop specimen for pathology was obtained from all patients. Primary bone tumors and metastatic tumors were excluded based on preoperative evaluation and/or postoperative pathology results. In addition, patients receiving radiation, those with active infection in the region, and chemotherapy patients were excluded from the study. A visual analog scale (VAS) score was used for preoperative and postoperative pain assessment. Angle measurements were performed for kyphotic angle restoration before and after surgery. Cobb angle measurements were used for this. The measurements were evaluated as segmenter Cobb angle on standing lateral radiographs. Cobb measurements were made using the software in Picture Archiving and Communication Systems.

Surgical Technique

Prophylactic antibiotics were administered to all patients preoperatively. All VP procedures were performed percutaneously in the operating room in the prone position under fluoroscopy guidance. Kyphosis was attempted to be corrected by placing two transverse plane cylinders under the chest and iliac crest. Local anesthesia and sedation were preferred. In 12 cases, general anesthesia was used due to a lack of cooperation and failure of sedation. Local anesthesia was performed with 1% lidocaine before surgical intervention. During unilateral VP, we preferred to enter 5 mm lateral from the normal entry site to centralize the targeted point. Polymethylmethacrylate (PMMA) bone cement (Aditus Medical GmbH Berlin Germany) was used in all cases. Patients were continuously monitored for possible complications. The patients were mobilized with a brace 3 hours after surgery. Patients who had no problems were discharged the next day after a control X-ray and a control computed tomography (CT) if needed (according to the X-ray image).

This study was approved by the Kayseri Governorship Provincial Directorate of Health (approval number: E-75717723-619, date: 11.04.2023).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 21.0 (SPSS Inc, Chicago, IL, USA). Shapiro-Wilk test was used (data were found to be suitable for normal distribution using the Shapiro-Wilk test, histogram, and Q-Q graphs). Data were expressed as mean and expressed as standard deviation. Independent Samples t-test (alternative; Mann-Whitney U test) was used for intergroup comparisons. Paired Samples t-test was used for comparisons between times (preoperative and postoperative). The relationship between categorical variables was evaluated using Pearson's chi-square (χ^2) test and Fisher's exact test. A p-value <0.05 was considered statistically significant.

RESULTS

Of the 257 patients operated on, 161 were female (62%) and 96 were male (37%). Their ages ranged between 50 and 90 years (mean: 68.2). Ninety seven of the patients had a significant history of trauma. Eighty six had a compelling movement that could be defined as trauma, while 74 had no history of trauma. Most fractures occurred at the L1 level and the least and above level at the T7 (Table 1). The pain was the presenting complaint in all patients and was the main reason for hospitalization. Of all patients, 88% had low back pain, 41% back pain, 56% low back and back pain, and 21% low back and leg pain.

In addition, 43% of the patients had difficulty walking and postural disturbance, and 5% had numbness and loss of sensation in the legs. Physical and neurologic examinations of all patients revealed no deficits originating from the OVF except partial limitation of movement due to pain, posture disorder, and variable sensory deficits. Bone densimetry showed varying degrees of osteoporosis (T-score: -2.5 to -5). Two hundred thirteen fractures were in the lumbar region and 88 in the thoracic region. One hundred forty nine patients had a single-level vertebral fracture, 31 patients had two-level vertebral fractures and 30 patients had three or more level vertebral fractures. Unilateral VP was performed in 204 patients and bilateral VP in 53 patients. On average, 2-3.5 mL of PMMA was used for unilateral and 3.5-4 mL for bilateral VP. In the postoperative controls, the low back pain had disappeared in 214 of 228 patients and it had decreased in 14. Of the 107 patients with back pain, pain disappeared in 102, decreased in 3, and remained unchanged in 2. Of the 112 patients with posture disorder and difficulty in walking, 94 had improvement, 7 had partial improvement and 11 had no change (Table 1, Figure 1).

The median VAS postop score [3.0 (2.0-4.0)] was statistically significantly lower than the VAS preop score [7.5 (6.0-9.0)] in patients operated through unilateral VP (p<0.001). Similarly, the median VAS postop score [3.0 (2.0-4.0)] was statistically significantly lower than the VAS preop score [7.0 (6.0-8.0)] in patients operated through bilateral VP (p<0.001). There was no statistically significant difference between the groups in terms of VAS preop/postop variables (Table 2). Similarly, there was no statistically significant difference between the groups in terms of kyphosis restoration variables (Figure 2, Table 3).

One patient with a single-level vertebral fracture and one patient with four or more levels of vertebral fractures died in the early postoperative period. Thromboembolism was considered as the cause of death. In two patients, the cement was found

Table 1. Distribution of fractures level

Levels	L5	L4	L3	L2	L1	T10-12	T7-9	T5-6
Unilateral VP	4	16	34	34	88	61	8	2
Bilateral VP	-	2	9	12	17	15	2	-

VP: Vertebroplasty

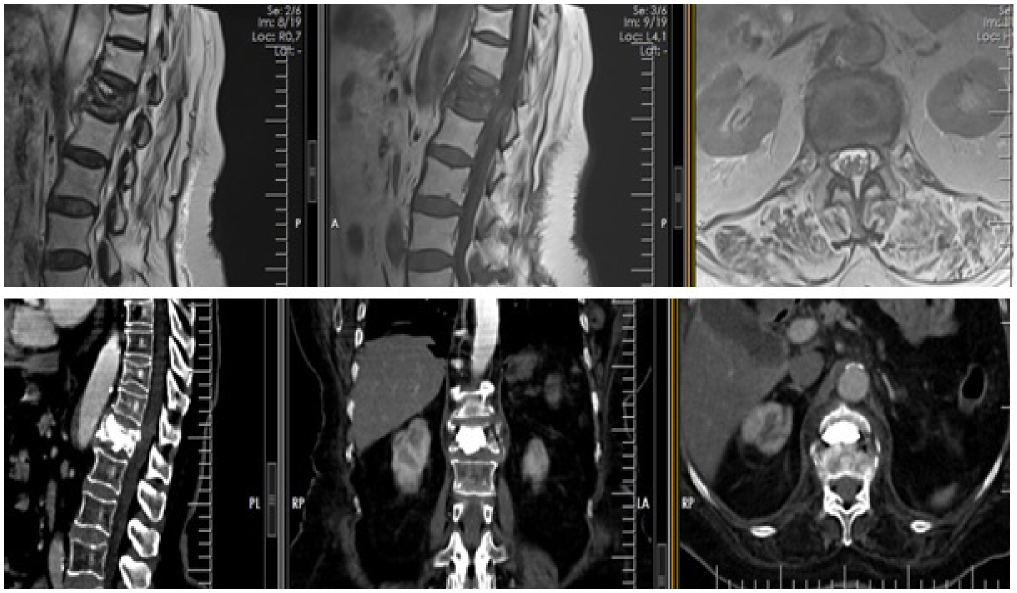

Figure 1. T12 unilateral VP. It was observed that the corpus can be completely filled with VP performed from a single pedicle
VP: Vertebroplasty

Table 2. Comparison of VAS preop and VAS postop scores between groups

	Unilateral VP (n=204)	Bilateral VP (n=53)	p-values
Preop VAS	7.6±0.9 7.5 (6.0-9.0)	7.4±0.6 7.0 (6.0-8.0)	0.218
Postop VAS	3.2±0.5 3.0 (2.00-4.0)	3.1±0.5 3.0 (2.0-4.0)	0.109
p-values	<0.001	<0.001	

Data were expressed as mean ± standard deviation and median (minimum-maximum). Different lowercase letters in the same column indicate differences between groups, VP: Vertebroplasty, VAS: Visual analog scale

Table 3. Comparison of kyphosis restoration between groups

	Unilateral VP (n=204)	Bilateral VP (n=53)	p-values
Kyphosis restoration	6.1° ± 1.2 5.9° (4.0-9.1)	5.8° ± 1.2 5.8 (4.1-8.0)	0.057

Data were expressed as mean ± standard deviation and median (minimum-maximum). Different lowercase letters in the same column indicate differences between groups, VP: Vertebroplasty

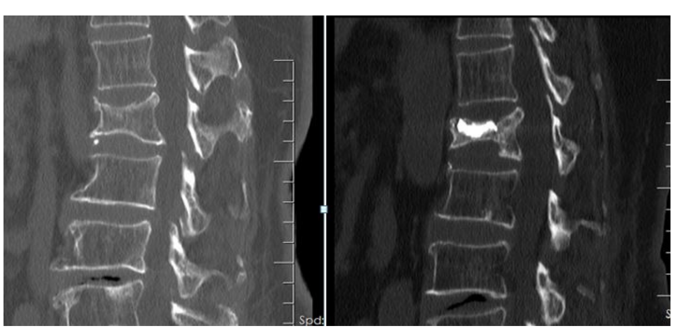

Figure 2. Restoration of kyphosis

to have escaped into the canal. Although they did not cause a neurologic deficit, they were surgically removed. Two patients had a postoperative transient loss of strength in the lower extremity, which resolved during follow-up (no compression of the canal or root was detected on radiographs and CT scans). It was thought that the local anesthetic used was absorbed into the epidural region. In one patient who underwent VP with unilateral and single level, a new fracture occurred at the sixth upper level. Scoliosis was detected in one patient 19 months after unilateral VP. In 107 patients (42%), postoperative X-rays and CT scans showed small cement leaks at various sites with no clinical significance. Most of the leaks occurred in the disc space, paravertebral region, epidural space, and pedicle (Figure 3, Table 4). No infection was observed in any patient.

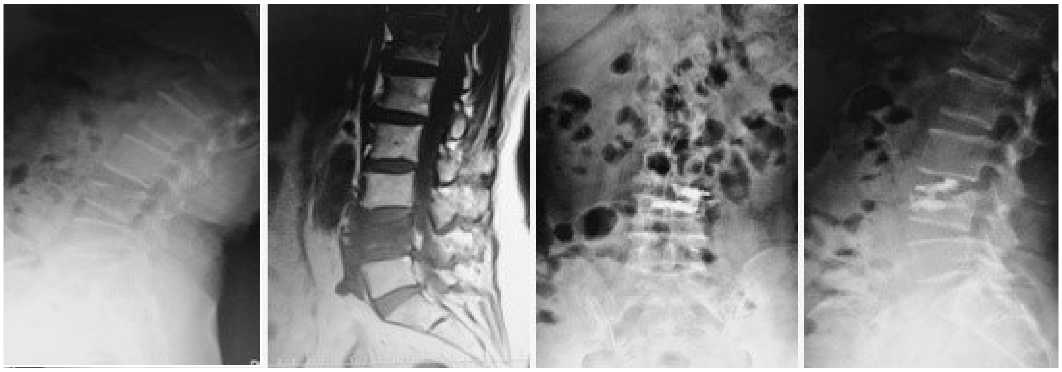

Figure 3. Escape of cement into the pedicle and disc space

Table 4. Distribution of complaints

	Unilateral VP (n=204)	Bilateral VP (n=53)	χ2 p-values
Low back pain	90.2 (184/204)	83.0 (47/53)	0.165 0.112
Back pain	42.6 (87/204)	37.7 (20/53)	0.314 0.418
Low/leg pain	18.6 (38/204)	30.2 (16/53)	3.388 0.052
Difficulty walking/ posture disorders	41.2 (84/204)	52.8 (28/53)	2.324 0.086
Numbness	4.9 (10/204)	7.5 (4/53)	0.572 0.321

Data expressed as % (n/total), VP: Vertebroplasty

DISCUSSION

Vertebroplasty is a procedure in which cement is applied to the fractured vertebra at high pressure. Mostly PMMA is used. This method was first applied in 1987 by Galibert et al.[9] for the minimally invasive treatment of painful hemangiomas. In recent years, it has been widely used in the treatment of OVF causing severe pain and limitation of movement[10]. VP is a widely preferred technique for the stabilization of vertebral fractures, especially those that develop due to osteoporosis, and for the treatment of pain[1]. This method is also widely used in hemangiomas and malignant tumors of the spine[7]. This method also has complication risks. There may be risks related to anesthesia, surgical technique, and cement. The cement may escape into the epidural veins or epidural space, neural foramen, intervertebral disc, perivertebral venous plexus, or paravertebral soft tissues[11-13]. In addition, complications such as pneumothorax, pedicle fracture, pulmonary embolism, and infection may occur[14].

In this technique, it is thought that the pain is controlled by filling the fractured vertebral body with cement, preventing gradual collapse and stabilizing micro-movements. However, it should not be ignored that thermal and chemical nerve ablation may also be effective. Aebli et al.[15] showed that intravertebral temperature levels caused thermal necrosis after the use of intervertebral PMMA cement. Hulme et al.[10] reported in a study that VP gave 87% positive results on pain. In our study, VAS scores decreased postoperatively, and similar values were obtained in terms of the change in VAS scores between unilateral (7.6 to 3.2) or bilateral (7.4 to 3.1) VP and there was no statistical difference between them. In a published meta-analysis, both techniques provided excellent pain relief and improved quality of life. They encouraged the use of the unipedicular approach as the preferred surgical technique for the treatment of osteoporotic compression fractures due to shorter operative time, limited X-ray exposure, and minimal cement ingress and extravasation[16].

In a biomechanical study, the distribution of cement in the corpus was investigated in unilateral and bilateral VP. As a result, it was shown that the stress of the vertebral body could be better balanced in bilateral VP, the maximum stress of the intervertebral disc was reduced and this was advantageous in terms of stability[17].

While publications are indicating that VP has positive effects on height loss and improvement of kyphotic deformity, there are also publications showing that it has no effect[18]. Generally, studies have shown that the mean kyphotic angle restoration is 5-8.4 degrees for VP[18]. In our study, the effects of the unilateral or bilateral VP on kyphotic angle restoration were similar in preop and postop measurements, and no statistical difference was found between them. In addition to the relief of the patient's pain, we think that the fact that kyphosis was recovered to a certain extent with pillows during the operation and the osteoporotic vertebra was filled in this form contributed to this. Berlemann et al.[19] reported that fracture stage was an important determinant in achieving correction in their study, while Phillips et al.[20] reported that there was no relationship between fracture stage and deformity correction. It is thought that better results can be obtained in VP applications in single-level osteoporotic fractures compared to multilevel fractures. Chen et al.[7] reported that the clinical and radiologic results of unilateral or bilateral VP interventions were very similar.

Various studies have tried to reduce the effectiveness and complications of unilateral VP. Zhang and Deng[21] reported that a unilateral extrapedicular puncture route was used to ensure good distribution of bone cement and prevent leakage of cement into the spinal canal. Hu et al.[22] also reported that unilateral VP using a curved diffusion needle in osteoporotic vertebral compression fractures provided a good distribution of bone cement and was safe.

McKiernan et al.[23] stated that the height loss of mobile fractures resulting from osteoporosis can be partially corrected, but there is no improvement in height loss with VP in immobile fractures. There is no mechanical method that provides kyphosis reduction in VP, so correction of the deformity is not possible. In order to reduce the kyphotic angle and maintain vertebral height, the patient can be positioned during the procedure, or support pads can be used. Cement injected after positioning may be effective in maintaining this position[1]. In our study, two transverse plane cylinders under the chest and iliac crest was placed in an attempt to correct kyphosis. We think that this procedure is effective in correcting fracture-related kyphosis.

CONCLUSION

Unilateral VP provides fast and effective pain relief with local anesthesia and low surgical risk, especially in the treatment of patients with OVF. It is an effective method for preventing kyphosis and improving quality of life. The clinical and radiologic results of unilateral access and bilateral access are similar. Improvement in VAS scores and kyphotic angle restoration rates are similar in both techniques. No statistical difference was found between them. We believe that a unilateral approach is sufficient in terms of significantly reducing the complication rate with anesthesia and radiation exposure and reducing the cost of the surgical procedure.

Ethics

Ethics Committee Approval: This study was approved by the Kayseri Governorship Provincial Directorate of Health (approval number: E-75717723-619, date: 11.04.2023).

Informed Consent: The patients were studied retrospectively. Detailed informed consent was obtained from all patients for these interventions.

Authorship Contributions

Surgical and Medical Practices: M.M., M.O., E.B., Es.B., R.K.K., Concept: M.M., R.K.K., Design: M.M., R.K.K., Data Collection or Processing: M.M., M.O., E.B., Es.B., Analysis or Interpretation: M.M., R.K.K., Literature Search: M.M., R.K.K., Writing: M.M.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Kiraz İ, Dağtekin A. Osteoporotik vertebra kırıkları vertebraplasti/kifoplasti-Avantajları/dezavantajları. Türk Nöroşir Derg. 2020;30:516-20.
2. Melton LJ 3rd, Atkinson EJ, Cooper C, O'Fallon WM, Riggs BL. Vertebral fractures predict subsequent fractures. Osteoporos Int. 1999;10:214-21.
3. Fribourg D, Tang C, Sra P, Delamarter R, Bae H. Incidence of subsequent vertebral fracture after kyphoplasty. Spine (Phila Pa 1976). 2004;29:2270-6.
4. Bademci G, Aydın Z, Batay F, Attar A, Çağlar Ş. Yaşlılarda ağrılı osteoporotik vertebra çökme kırıklarının tedavisinde kifoplasti, vertebroplasti etkinliğinin değerlendirilmesi. Türk Geriatri Dergisi. 2005;8:5-9.
5. Çopuroğlu C, Çopuroğlu E, Çiftdemir M, Özcan M, Yalnız E. Vertebroplasty can intraoperative systemic complications be prevented. J Turk Spinal Surg. 2011;22:195-203.
6. Lieberman IH, Dudeney S, Reinhardt MK, Bell G. Initial outcome and efficacy of "kyphoplasty" in the treatment of painful osteoporotic vertebral compression fractures. Spine (Phila Pa 1976). 2001;26:1631-8.
7. Chen L, Yang H, Tang T. Unilateral versus bilateral balloon kyphoplasty for multilevel osteoporotic vertebral compression fractures: a prospective study. Spine (Phila Pa 1976). 2011;36:534-40.
8. Yilmaz A, Çakir M, Yücetaş CŞ, Urfali B, Üçler N, Altaş M, et al. Percutaneous kyphoplasty: Is bilateral approach necessary? Spine (Phila Pa 1976). 2018;43:977-83.
9. Galibert P, Deramond H, Rosat P, Le Gars D. Note préliminaire sur le traitement des angiomes vertébraux par vertébroplastie acrylique percutanée [Preliminary note on the treatment of vertebral angioma by percutaneous acrylic vertebroplasty]. Neurochirurgie. 1987;33:166-8.
10. Hulme PA, Krebs J, Ferguson SJ, Berlemann U. Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. Spine (Phila Pa 1976). 2006;31:1983-2001.
11. Deramond H, Dion JE, Chiras J. Complications. IN: Mathis JM, Deramond H, Belkoff SM (Eds). Percutaneous vertebroplasty. 1st ed. Newyork: Springer-Verlac Inc. 2002;p:165-74.
12. Katsanos K, Sabharwal T, Adam A. Percutaneous cementoplasty. Semin Intervent Radiol. 2010;27:137-47.
13. Perez-Cruet MJ, Fessler RG, Perin NI. Review: complications of minimally invasive spinal surgery. Neurosurgery. 2002;51(5 Suppl):S26-36.
14. Hacıyakupoğlu E, Kınalı B, Oktay K, Yılmaz DM, Hacıyakupoğlu S. Vertebroplasti. Arşiv Kaynak Tarama Dergisi. 2012;21:283-98.
15. Aebli N, Goss BG, Thorpe P, Williams R, Krebs J. In vivo temperature profile of intervertebral discs and vertebral endplates during vertebroplasty: an experimental study in sheep. Spine (Phila Pa 1976). 2006;31:1674-8.
16. Sun H, Li C. Comparison of unilateral and bilateral percutaneous vertebroplasty for osteoporotic vertebral compression fractures: a systematic review and meta-analysis. J Orthop Surg Res. 2016;11:156.
17. Dai H, Liu Y, Han Q, Zhang A, Chen H, Qu Y, et al. Biomechanical comparison between unilateral and bilateral percutaneous vertebroplasty for osteoporotic vertebral compression fractures: A finite element analysis. Front Bioeng Biotechnol. 2022;10:978917.
18. Kim DY, Lee SH, Jang JS, Chung SK, Lee HY. Intravertebral vacuum phenomenon in osteoporotic compression fracture: report of 67 cases with quantitative evaluation of intravertebral instability. J Neurosurg. 2004;100(1 Suppl Spine):24-31.
19. Berlemann U, Franz T, Orler R, Heini PF. Kyphoplasty for treatment of osteoporotic vertebral fractures: a prospective non-randomized study. Eur Spine J. 2004;13:496-501.
20. Phillips FM, Ho E, Campbell-Hupp M, McNally T, Todd Wetzel F, Gupta P. Early radiographic and clinical results of balloon kyphoplasty for the treatment of osteoporotic vertebral compression fractures. Spine (Phila Pa 1976). 2003;28:2260-5.
21. Zhang T, Deng Y. A design of a targeted puncture trajectory applied to unilateral extrapedicular percutaneous vertebroplasty. BMC Musculoskelet Disord. 2023;24:268.
22. Hu H, Lin X, Tan L. Thoracolumbar osteoporotic vertebral compression fracture treatment by unilateral percutaneous vertebroplasty using curved diffusion needle. Indian J Orthop. 2023;57:899-906.
23. McKiernan F, Faciszewski T, Jensen R. Does vertebral height restoration achieved at vertebroplasty matter? J Vasc Interv Radiol. 2005;16:973-9.

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COEXISTENCE OF SPINAL DYSRAPHISM AND EXTRARENAL WILMS TUMOUR: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Extrarenal Wilms tumor is rare, but its association with spinal dysfraism is even rarer, and to our knowledge, there is no association with meningomyelocele sac in the literature. Our case was a 36-month-old baby with a meningomyelocele sac in the lumbar region. No additional anomaly was detected, and the baby had no leg movements. Magnetic resonance imaging examination revealed a 24x10 mm meningomyelocele sac and an 18x30x27 mm contrast-forming mass in the sac. Mass resection was performed during sac repair. Histological examination revealed a three-phase tumor consisting of a stromal component containing fibrous and fatty tissue, an epithelial component containing primitive glomeruli and tubule structures consisting of papillary structures with fibrovascular nuclei within cystic structures, and a blastemal component containing oval primitive cells between epithelial areas. Immunohistochemically, the blastemal and epithelioid components were stained positively with WT1, the stromal component with vimentin, and the epithelial component with PanCK and EMA. In this form, the case was defined as an extrarenal Wilms tumor associated with a meningocolocele. This case was valuable in terms of showing that Wilms tumor should be included in the differential diagnosis of masses with meningomyelocele and the importance of total resection of these lesions.

Keywords: Extrarenal wins tumor, spinal dysraphism, meningomyelocele

INTRODUCTION

Wilms tumour is the most common primary kidney tumour in children, accounting for 5% of all childhood cancers[1,2]. Although the prognosis of Wilms tumour, which has three histological subtypes, varies according to stage, 4-year survival rates reportedly range from 85-100% for favourable histology, 70-100% for focal anaplastic type, and 30-35% for diffuse anaplastic type[3].

Extrarenal Wilms tumour is exceedingly rare. So much so that Shojaeian et al.[4], in their 2015 study in which they excluded cases coexisting with teratoma, stated that a total of 80 cases were published under the age of 14, the first of which was in 1961.

In patients with extrarenal Wilms tumour, localization is often the retroperitoneal, inguinal, lumbosacral regions, the genital organs, and mediastinum[4,5]. However, to our knowledge, the association of extrarenal Wilms tumour with spinal midline defect is very rare[6] and our literature review did not reveal any reported association with a meningomyelocele sac. In this case report, we present a case who had a postpartum mass with a meningomyelocele sac, which was later revealed to be a Wilms tumour as confirmed by pathological analysis.

CASE REPORT

A 36-week-old term female baby was evaluated because of a possible meningomyelocele sac in the lumbar region (Figure 1). There was no additional anomaly detected, and the infant did not have leg movements. Whole spinal and cranial magnetic resonance imaging (MRIs) were ordered to detect accompanying spinal pathologies in the patient who did not have cerebrospinal fluid (CSF) leakage from the meningomyelocele sac.

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Radiological Findings

In the evaluation of cranial and spinal MRIs, a defect in the posterior elements of the vertebrae in the lower thoracic-lumbar region, as well as a CSF-filled myelomeningocele sac measuring 24×10 mm characterized by neural elements in its lumen, were observed. At this level, abnormal osseous structures and fusion appearance in the vertebral bodies were recorded as additional findings. Finally, a mass lesion measuring 18×30×27 mm with lobulated contour and causing compression in the pouch was observed in the right lateral neighbourhood of the sac. It demonstrated heterogeneous features and relative hyperintensity in T2AGs, hypointensity in T1AGs, and was well-enhanced after intravenous gadolinium injection (Figure 2). In the differential diagnosis, meningioma was considered primarily with respect to imaging features and localization.

Urinary ultrasonography examination, which was performed later with regard to the primary tumour, did not reveal any remarkable findings, and the kidneys included in the MRI examination area were also natural in appearance.

Figure 1. Preoperative view of the spinal defect

Surgical Intervention

The procedure was performed with the patient in the prone position. After total excision of the well-cleaved mass (Figure 3), the borders of which were clearly defined, the bone spur was excised and determined to be within the dura mater defect. Then, the duraplasty was completed by sectioning the filum, the skin was repaired, and the surgical intervention was completed.

Pathological Findings

Macroscopically, the specimen was observed to be a well-circumscribed lesion with an off-white fibrillary appearance, measuring 25×23×17 mm. Histological examination revealed a triphasic tumour consisting of a stromal component containing fibrous and adipose tissue, an epithelial component containing primitive glomeruli and tubule structures consisting of papillary structures with fibrovascular cores within cystic structures, and a blastemal component containing oval primitive cells between epithelial areas. There were no signs of anaplasia (Figure 4).

Immunohistochemically, the blastemal and epithelioid components were stained positively with WT1, the stromal component with vimentin, and the epithelial component with PanCK and EMA. The Ki-67 proliferation index was observed to be increased in focal areas.

Follow-up

The patient was started on chemotherapy and there are no long-term follow-up results as of writing.

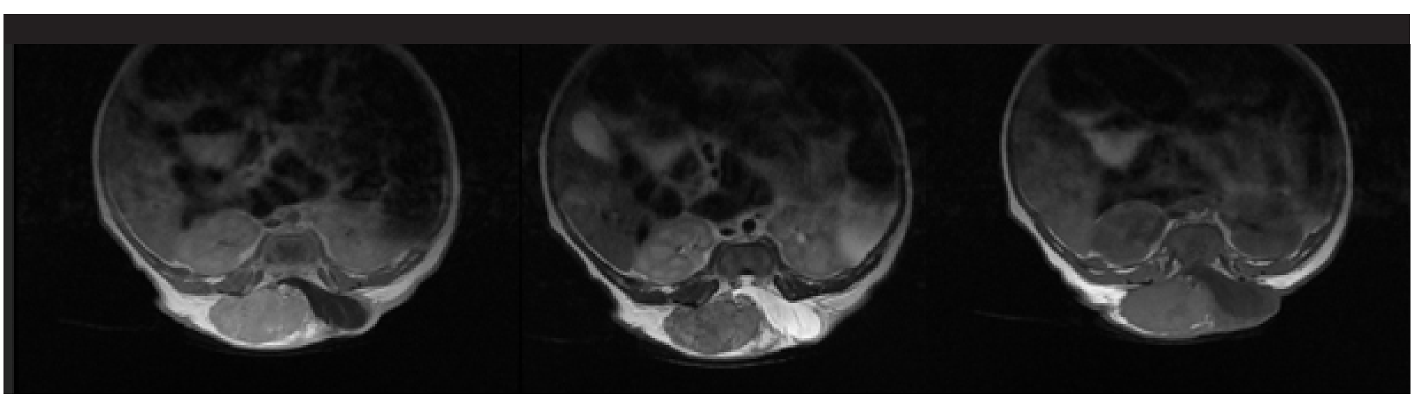

Figure 2. MRI image of the case

MRI: Magnetic resonance imaging

DISCUSSION

Extrarenal Wilms tumours are exceedingly rare, but the most common site is the retroperitoneum. Although it was previously reported with spinal midline defects such as diastematomyelia, tethered cord syndrome, and bone closure defects, to the best of our knowledge, this is the first report in the literature demonstrating an association with meningomyelocele.

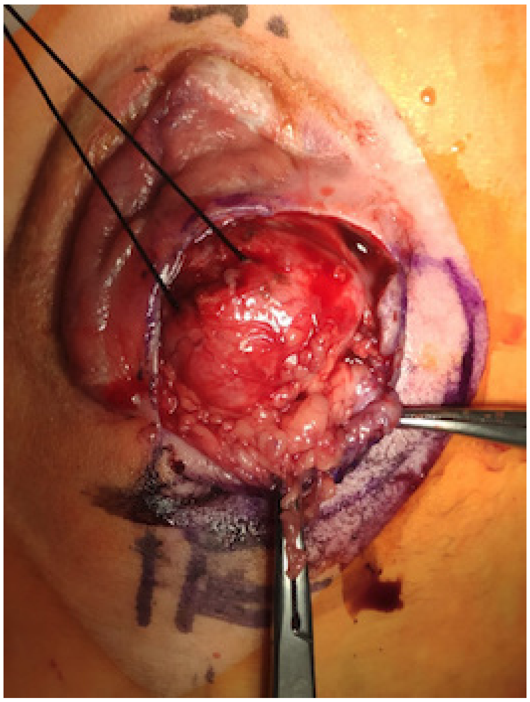

Figure 3. Perioperative view of the mass

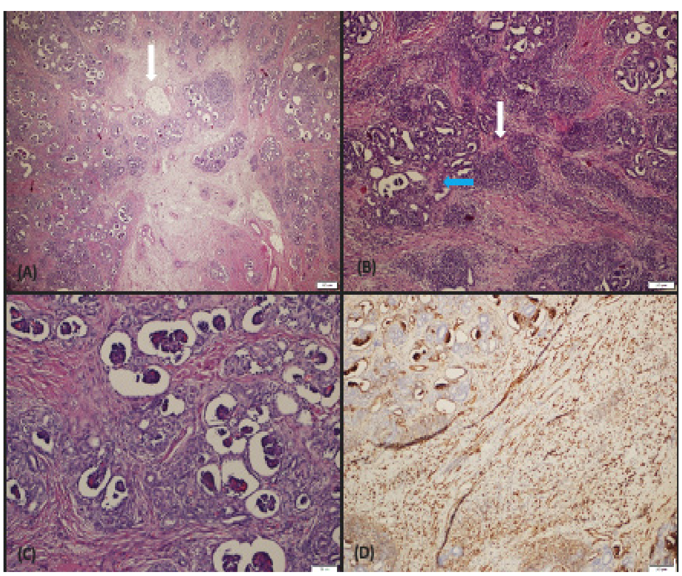

Figure 4. A: Mesenchymal component (arrow) containing loose myxoid stroma and adipose tissue, (H&E, x40), **B:** Blastemal (white arrow) and epithelioid (blue arrow) component (H&E, x100), **C:** Primitive glomerular structures formed by papillary structures containing fibrovascular cores within the cystic areas (H&E, x200), **D:** Positivity in epithelioid and blastemal component with WT-1 (x40)

Igbaseimokumo et al.[7], in their 2017 study in which they included patients with extrarenal Wilms tumour associated with spinal dysraphism, described a total of seven cases (together with their own). When these cases were examined, it was found that five cases had swelling in the lumbar region accompanied by hypertrichosis, while there were no morphological changes in the other two cases. Among these seven patients reported by the authors, we did not include the cases reported by Deshpande et al.[13] and Fahner et al.[14] in the present study because they did not have any anomalies that could be considered as spinal dysraphism. In addition, in the review of Govender et al.[9] one of the cases was mentioned as a teratocarcinoma and the outcome pathology was evaluated as Wilms tumour; however, we excluded this case because it was considered controversial in its reportedstate. Besides, unlike these, in the study of four cases titled, "Extrarenal Nephroblastic Proliferation in Spinal Dysraphism" presented by Abrahams et al.[10], one of the cases was a 4-week-old girl with a bifid lamina in the L5 vertebra and a 35×35 mm mass in this region, and therefore, was included in our assessment because the mass pathology was Wilms tumour. To conclude, we defined our case as the seventh case adding to a total of previously-reported six patients with extrarenal Wilms tumour associated with spinal dysraphism, and we believe the association with a meningomyelocele sac in our study was a valuable finding (Table 1).

The generally accepted view regarding Wilms tumour occurrence outside of renal tissue is that mesenchymal remnants transform into nephrogenic remnants, which in turn undergo malignant transformation[15-17].

Wilms tumour has no specific radiological features, and therefore, pathological examination is critical. When other cases in the literature are examined, it is understood that in the preoperative evaluation of extrarenal Wilms tumours, other diagnoses are considered possible by physicians with respect to the patient's age, clinical findings, and tumour localization[7]. In addition, neuroblastoma, teratoma, embryonal rhabdomyosarcoma and other rare sarcomas are included in the radiological differential diagnosis of extrarenal Wilms tumours[5].

However, in the pathological examination of our case, the tumour was considered compatible with the diagnosis of Wilms tumour without anaplasia, since the tumour had triphasic morphology including blastemal, epithelial, and mesenchymal components, was immunohistochemically positive for WT-1, had a blastemal component, was immunohistochemically positive for WT-1, and did not have a typical teratoma area.

Since there is no specific radiological feature of Wilms tumour and the diagnosis can only be made pathologically, it should be considered in the differential diagnosis when a mass lesion accompanying meningomyelocele is encountered.

Table 1. Literature of extrarenal Wilms tumour cases associated with spinal dysraphism and their characteristics

					Treatment			
Study	**Age**	**Sex**	**Level**	**Spinal dysraphism**	**Surgery**	**ChT**	**RT**	**Follow-up**
Present case	New-born	Female	T12-L5	Meningomyelocele	Complete excision	Yes	No	2 months
Igbaseimoku et al.[7] 2017	New-born	Female	L5	Dysraphic lamina + lipoma	Complete excision	Yes	No	No recurrence at 1 year
Sharma et al.[8] 2005	18 months	Female	L1	Diastematomyelia + lipoma	Complete excision	Yes	No	3 months
Govender et al.[9] 2000	4 years	Female	T10-coccyx	Spina Bifida	Biopsy	Yes	Yes	Palliative care
Abrahams et al.[10] 1999	4 weeks	Female	L5	Bifid lamina	Complete excision	Yes	No	4 years disease-free after 10 weeks of chemotherapy
Mirkin et al.[11] 1990	2 years	Female	T12-L4	Diastematomyelia + lipoma	Complete excision	Yes	Yes	Cerebellar metastasis 1 year after diagnosis, no recurrence 20 months after cerebellar mass excision
Fernbach et al.[12] 1984	2 years	Female	L1	Diastematomyelia + lipoma	Near total excision	Yes	Yes	No recurrence at 1 year

ChT: Chemotherapy, RT: Radiotherapy

Ethics

Informed Consent: Written informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: A.T., T.T., B.Y., Z.Ç.G., Y.Ç., Ö.Ö., Concept: A.T., T.T., Design: A.T., T.T., Data Collection or Processing: B.Y., Z.Ç.G., Analysis or Interpretation: A.T., Y.Ç., Ö.Ö., Literature Search: A.T., T.T., B.Y., Z.Ç.G., Y.Ç., Ö.Ö., Writing: A.T., T.T., Y.Ç., Ö.Ö.

Conflict of Interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review (CSR) 1975-2018. National Cancer Institute. 2021. https://seer.cancer.gov/archive/csr/1975_2018/index.html
2. Breslow N, Olshan A, Beckwith JB, Green DM. Epidemiology of Wilms tumor. Med Pediatr Oncol. 1993;21:172-81.
3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021 Jan;71(1):7-33. doi: 10.3322/caac.21654. Epub 2021 Jan 12. Erratum in: CA Cancer J Clin. 2021;71:359.
4. Shojaeian R, Hiradfar M, Sharifabad PS, Zabolinejad N. Extrarenal Wilms' Tumor: Challenges in Diagnosis, Embryology, Treatment and Prognosis. In: van den Heuvel-Eibrink MM, editor. Wilms Tumor [Internet]. Brisbane (AU): Codon Publications. 2016.
5. Liang H, He Y, Fu L, Tian J, Sun N, Yu T, et al. Extrarenal Wilms tumor in children: A retrospective observational case series. J Pediatr Urol. 2020;16:664.e1-664.e7.
6. Itoshima R, Kobayashi R, Sano H, Hori D, Kishimoto K, Suzuki D, et al. Extrarenal Nephroblastoma of the Retroperitoneal Space in Children: A Case Report and Review of the Literature. J Pediatr Hematol Oncol. 2017;39:296-8.
7. Igbaseimokumo U, Cartwright C, Lewing K, Hutchison L, Habeebu S. The Rare Association of Spina Bifida and Extrarenal Wilms Tumor: A Case Report and Review of the Literature. World Neurosurg. 2017;104:1046.e1-1046.e5.
8. Sharma MC, Sarat Chandra P, Goel S, Gupta V, Sarkar C. Primary lumbosacral Wilms tumor associated with diastematomyelia and occult spinal dysraphism. A report of a rare case and a short review of literature. Childs Nerv Syst. 2005;21:240-3.
9. Govender D, Hadley GP, Nadvi SS, Donnellan RB. Primary lumbosacral Wilms tumour associated with occult spinal dysraphism. Virchows Arch. 2000;436:502-5.
10. Abrahams JM, Pawel BR, Duhaime AC, Sutton LN, Schut L. Extrarenal nephroblastic proliferation in spinal dysraphism. A report of 4 cases. Pediatr Neurosurg. 1999;31:40-4.
11. Mirkin LD, Azzarelli B, Seo IS. Extrarenal Wilms' tumor with cerebellar metastasis in a four-year-old girl with spina bifida. Am J Clin Pathol. 1990;93:805-9.
12. Fernbach SK, Naidich TP, McLone DG, Leestma JE. Computed tomography of primary intrathecal Wilms tumor with diastematomyelia. J Comput Assist Tomogr. 1984;8:523-8.
13. Deshpande AV, Gawali JS, Sanghani HH, Shenoy AS, Patankar JZ, Borwankar SS. Extrarenal Wilm's tumour - a rare entity. Pediatr Surg Int. 2002;18:543-4.
14. Fahner JB, Switzer R, Freyer DR, Mann JD, Mann RJ. Extrarenal wilms' tumor: Unusual presentation in the lumbosacral region. Journal of Pediatric Hematology/Oncology. 1993;15:117-9.
15. Roberts DJ, Haber D, Sklar J, Crum CP. Extrarenal Wilms' tumors. A study of their relationship with classical renal Wilms' tumor using expression of WT1 as a molecular marker. Lab Invest. 1993;68:528-36.
16. Ratajczak MZ, Schneider G, Sellers ZP, Kucia M, Kakar SS. The embryonic rest hypothesis of cancer development–an old XIX century theory revisited. J Cancer Stem Cell Res. 2014;2:e1001.
17. Sell S. On the stem cell origin of cancer. Am J Pathol. 2010;176:2584-494.

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EPIDURAL ANESTHESIA FOR POSTOPERATIVE ANALGESIA FOLLOWING ANTERIOR VERTEBRAL BODY TETHERING

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Keywords: Epidural anesthesia, VATS, anterior vertebral body tethering

To editor:

Idiopathic scoliosis is a condition characterized by an abnormal curvature of the spine that typically emerges during adolescence and lacks an identifiable cause. It is more frequently observed in adolescent girls between the ages of 10 and 18[1]. The treatment of juvenile scoliosis cases is determined based on factors such as the severity of the spinal curvature, the patient's age, gender, overall health, and other considerations. Anterior vertebral body tethering (VBT) has recently become a popular surgical technique in the treatment of idiopathic scoliosis. This technique involves providing a non-fusion treatment using flexible spinal implants, allowing the spine to continue growing (Figure 1). The curvature gradually improves as the patient continues to grow[2].

Video-assisted thoracic surgery (VATS) is a routinely and successfully applied minimally invasive method in many thoracic surgical procedures. The first publication related to VATS in spine surgeries was in 1993 by Mack et al.[3] In surgeries involving anterior VBT, VATS is a preferred minimal-invasive approach. Its advantages include smaller incisions, less blood loss, reduced risk of infection, and shorter hospital stays. Although the combination of VBT with VATS is minimally invasive, pain remains a commonly encountered issue. In scoliosis surgery and thoracoscopy, the best analgesia method involves the use of epidural anesthesia along with a multimodal approach[4]. We aimed to share our experience with epidural anesthesia used for postoperative analgesia in VBT surgery performed with VATS.

Anterior VBT with VATS was planned for a 14-year-old female patient weighing 53 kg, diagnosed with idiopathic scoliosis. The patient's scoliosis radiograph revealed a 37-degree right thoracic scoliosis at the level of thoracic vertebra T7-T8 and a 23-degree

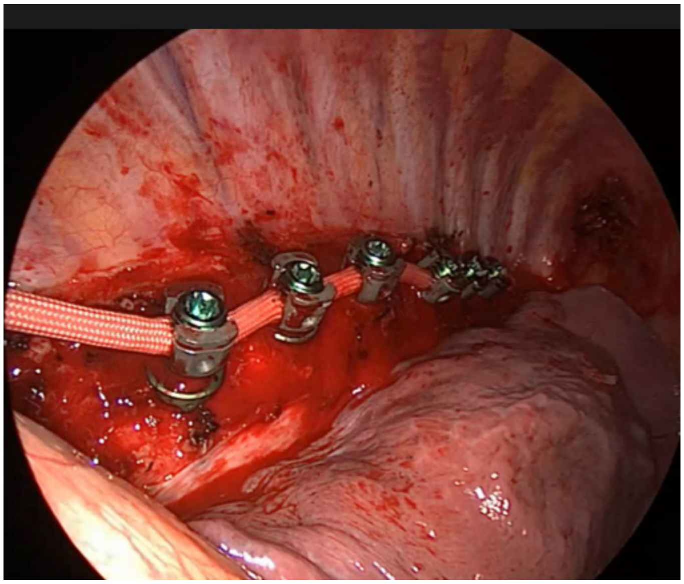

Figure 1. Technique of anterior vertebral body tethering

left thoracic scoliosis at the lumbar vertebra L3-L4 level (Figure 2). A thoracic epidural catheter was planned for postoperative pain management. A thoracic epidural was placed around the 6-7th thoracic vertebraL level, in the lateral decubitus position with intravenous sedation with fentanyl 25 mcg and midazolam 2 mg, using the loss of resistance to air technique. Appropriate epidural placement (B. Braun 22 g) was assessed by negative catheter aspiration for blood or cerebrospinal fluid. An epidural catheter was placed at the 6-7th thoracic vertebral level. A bolus dose of 8 mL of 0.25% bupivacaine was administered. Selective endobronchial intubation was performed, and the operation was performed under general anesthesia. 1 MAC

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Figure 2. Scoliosis levels

L: Left

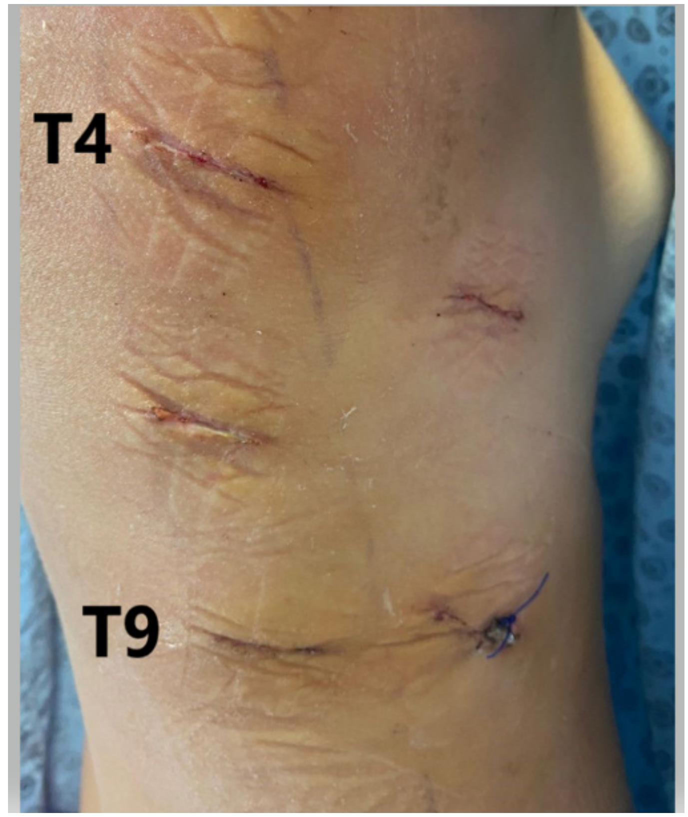

Figure 3. VATS trocar entry sites

VATS: Video-assisted thoracic surgery

of desflurane and remifentanil infusion at a rate of 0.5-2 μg/kg/min were used for anesthesia maintenance. VATS trocar entry sites are shown in Figure 3. Before extubation, 10 mg of meperidine hydrochloride iv and 500 mg of paracetamol iv were administered. For the postoperative analgesia, an epidural patient-controlled anesthesia was prepared with 0.125% Marcaine, 2 mL infusion, 8 mL bolus dose, and a 15-minute lockout period. After the 6-hour-long operation, the patient was extubated and the Visual Analog Scale (VAS) for pain was 0 in the recovery room. During the 24-hour follow-up in the intensive care unit, Paracetamol 500 mg every 6 hours and dexketoprofen 25 mg every 4 hours with maximum daily dose of 75 mg was ordered as a rescue analgesic, and the VAS score was seen at most 3. The epidural chatheter was removed on the third day after surgery. No additional opioid analgesics were needed in the postoperative period.

After scoliosis surgeries, the occurrence of severe pain is a commonly encountered condition and even if the procedure is minimally invasive and performed with VATS, the pain following the surgery requires treatment(5). The reduction of postoperative pain intensity is crucial, particularly for the rapid improvement of respiratory functions. Epidural anesthesia is known to be effective in reducing pain in VATS procedures(6). In our case involving anterior VBT performed with VATS, we observed that the use of an epidural catheter for pain control was a suitable solution. As this surgical procedure is increasingly performed, we believe that more comprehensive studies are needed to demonstrate the true effectiveness of the epidural catheter as part of multimodal anesthesia.

Ethics

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REFERENCES

1. Konieczny MR, Senyurt H, Krauspe R. Epidemiology of adolescent idiopathic scoliosis. J Child Orthop. 2013;7:3-9.
2. Szapary HJ, Greene N, Paschos NK, Grottkau BE, Braun JT. A Thoracoscopic Technique Used in Anterior Vertebral Tethering for Adolescent Idiopathic Scoliosis. Arthrosc Tech. 2021;10:e887-95.
3. Mack MJ, Regan JJ, Bobechko WP, Acuff TE. Application of thoracoscopy for diseases of the spine. Ann Thorac Surg. 1993;56:736-8.
4. Lowry KJ, Tobias J, Kittle D, Burd T, Gaines RW. Postoperative pain control using epidural catheters after anterior spinal fusion for adolescent scoliosis. Spine (Phila Pa 1976). 2001;26:1290-3.
5. Costanzo S, Pansini A, Colombo L, Caretti V, Popovic P, Lanfranchi G, et al. Video-Assisted Thoracoscopy for Vertebral Body Tethering of Juvenile and Adolescent Idiopathic Scoliosis: Tips and Tricks of Surgical Multidisciplinary Management. Children (Basel). 2022;9:74.
6. Coşarcan SK, Manici M, Yörükoğlu HU, Gürkan Y. Toraks duvarı fasyal plan bloklar [Ultrasound guided thoracic wall blocks]. Agri. 2021;33:205-14.