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Possible predictive markers in surgical decision making in patients with degenerative or isthmic lumbar spondylolisthesis

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Keywords
degenerative spondylolisthesis, isthmic spondylolisthesis, surgery

ABSTRACT

Background: Although age, comorbidity, duration and severity of symptoms, slippage degree, and flexion-extension slipping stability during X-ray imaging are effective in making a surgical decision in patients with spondylolisthesis, these factors are rarely based on definitive evidence. The aim of this study was to determine the efficacy of clinical, radiological and biochemical findings in surgical decision making in these patients.

Materials and methods: Patients' data including age, gender, degree and type (i.e. degenerative or isthmic) of the spondylolisthesis, urinary incontinence, neurogenic claudication were recorded. Radiological imaging studies (lumbar dynamic X-ray, computed tomography, magnetic resonance imaging), serum glucose, C-reactive protein and erythrocyte sedimentation rate values of the patients obtained during hospital admissions were evaluated.

Results: Forty patients were followed conservatively and 12 patients were treated surgically. Degenerative spondylolisthesis was seen in 22 patients. Nine patients had neurogenic urinary incontinence and 19 patients had neurogenic claudication. When the patients were divided into two groups with and without surgical treatment, the presence of the pars defect, slipping distance in a neutral position and slipping distance in flexion position was significantly different between groups. A positive correlation was found between pars defect and surgical treatment. Likelihood ratio test results revealed that the presence of pars defect, neurogenic claudication and neurogenic urinary incontinence could be the best parameters in decision making the surgical treatment.

Conclusion: The presence of pars defect, neurogenic claudication and urinary incontinence could be the best parameters that may help the surgeon to make the surgical treatment decision.

INTRODUCTION

Lumbar spondylolisthesis which described as slipping of a vertebral body over the adjacent vertebral body may be caused by a combination

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of osteoarthritis and degenerative changes in the disc and facet joints. This slipping may lead to varying degrees of spinal stenosis, resulting in mechanical low back pain associated with hip and leg pain clinically (1).

In literature, it is advocated that these patients should be treated with conservative treatment as the first choice, but surgical treatment should be applied when this treatment fails (2-5). Today, surgical treatment options include decompression and fusion to slipping vertebrae with instrumentation (6-11). However, other clinical studies have demonstrated that there will be no difference in spine fusion between instrument use and non-use (12), some of the systematic reviews have reported that the use of instrumentation can increase the likelihood of obtaining spinal fusion (1).

In clinical practice, it is generally reported that the patient's age, comorbidity, duration and severity of the symptoms, degree of slippage, and flexion-extension slipping stability during X-ray imaging are effective on making of the surgical decision, but these factors are rarely based on definitive evidence. It is generally believed that patients with symptoms of neural compression due to spondylolisthesis can be useful for simple decompression and less extensive fusion surgery, and extensive fusion surgery is generally recommended when serious "instability" is detected (12).

This study aimed to determine the efficacy of clinical, radiological and biochemical findings in surgical decision making in patients with degenerative or isthmic lumbar spondylolisthesis.

Materials and methods

Patient groups

This single-center retrospective study was conducted after approval by the Local Ethics Committee for Clinical Trial. In this study, the information of patients who were treated with conservatively and surgically was included between January 2015 and December 2018. ICD-10 (International Statistical Classification of Diseases and Related Health Problems) coding was used to scan hospital records.

Patients were divided into groups according to gender, whether there was a pars defect, according to the degree of spondylolisthesis, and whether surgical treatment was performed.

Patients with missing data, patients coded with the wrong ICD-10 code, patients with pathological spondylolisthesis due to a tumor, rheumatic disease, and infection, and patients in the pediatric age group (<16 years) were excluded from the study. Furthermore, patients with cauda equine syndrome which is considered as an emergency procedure, patients who underwent spinal surgery including unilateral or bilateral fenestration, hemilaminectomy, laminectomy, laminarthrectomy, laminotomy, foraminotomy, discectomy, flavectomy, sequestrectomy including anterior interbody fusion between adjacent vertebrae, instrumented fusion (with/without decompression) including intervertebral stabilization such as transforaminal interbody fusion (TLIF), anterior lumbar interbody fusion (ALIF) or posterior lumbar interbody fusion (PLIF), extreme lateral lumbar interbody fusion (XLIF) were ruled out from the study. Moreover, vascular claudication and other conditions/ joint problems limiting walking capacity have been ruled out

Materials

The patients' parameters including the age, gender, degree of spondylolisthesis according to Meyerding grade, type of the spondylolisthesis (degenerative or isthmic spondylolisthesis according to the evidence of the pars defect), presence of the radiculopathy pain, urinary incontinence and neurogenic claudication were recorded. Radiological images (lumbar dynamic X-ray, computed tomography (CT), magnetic resonance imaging (MRI), serum glucose, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values of the patients obtained during hospital admissions were evaluated. The approach for measurements acquisition was adopted after review of available literature (13,14).

Surgical method

After general anesthesia applied to the patients who were considered surgery, paravertebral muscles were dissected by midline incision while the stabilization level was determined by scopy while in prone position and stabilization was applied to the vertebrae using transpedicular screws. A standard laminectomy was performed to remove spinal cord compression. Following hemostasis, surgical layers were closed according to anatomy and the operation was terminated. The patients walked on the first postoperative day after wearing a lumbosacral corset.

Biochemical analysis

Study results were obtained from the venous blood samples of the patients taken at their initial admission to the hospital. ESR (reference range <20 mm / h) was measured using an analyzer (ESR 40, Cystate Diagnostics). Serum glucose (reference range 74-109 mg/dL) and CRP (reference range 0.15-5 mg/dL) levels were obtained by the immunoturbidimetric method using an analyzer (Roche Diagnostic COBAS c501).

Table 1. Table shows the patients' data according to the gender. *Chi-Square test, Mann Whitney U test, p<0.05*

		GENDER			
Variable		**Male**	**Female**	**X^2 / Z**	**p**
Pars defect	Degenerative	4 (18.2%)	18 (81.8%)	0.229*	0.632
	Isthmic	4 (13.3%)	26 86.7%)		
Meyerding grade	1	3 (27.3%)	8 (72.7%)	3.453*	0.178
	2	5 (17.2%)	24 (82.8%)		
	3	0 (0.0%)	12 (100.0%		
Treatment modality	Conservative	7 (17.5%)	33 (82.5%)	0.596*	0.440
	Surgery	1 (8.3%)	11 (91.7%)		
Number of screws	0	7 (17.5%)	33 (82.5%)	0.916*	0.633
	4	0 (0.0%)	4 (100.0%)		
	6	1 (12.5%)	7 (87.5%)		
Incontinence	no	6 (14.0%)	37 (86.0%)	0.391*	0.532
	yes	2 (22.2%)	7 (77.8%)		
Radiculopathy pain	no	7 (26.9%)	19 (73.1%)	5.318*	**0.021**
	yes	1 (3.8%)	25 (96.2%)		
Claudication	no	5 (15.2%)	28 (84.8%)	0.004*	0.951
	yes	3 (15.8%)	16 (84.2%)		
Glucose		93.50 (81-206)	95.00 (79-140)	-0.038	0.970
C-reactive protein		2.61 (0-28)	4.36 (1-54)	-0.311	0.755
ESR		10 (9-46)	19 (5-71)	-0.210	0.834

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

Statistical analysis

The power analysis for the results of this study was performed using the "Gpower 3.1" package program and it was concluded that the patients included in the study were sufficient to form the study.

Chi-Square test, Kruskal Wallis test, and Mann-Whitney U test was used to compare the nonparametric data between the groups (p <0.05). Parametric data were analyzed using Independent Samples t-test (p<0.05).

Spearman's rho Correlation test was used to determine the relationship between the parameters (p <0.05).

ROC-Curve test and Logistic Regression test were used to determine the predictive markers in the decision of surgical treatment. The likelihood ratio test was used to estimate the "best" variable in decision-making in patients undergoing surgery (p <0.05).

Results

Fifty-two patients (male = 8, female = 44) were included in the study. Nine patients (17.31%) had neurogenic urinary incontinence and 19 patients (36.54%) had neurogenic claudication. Twenty six patients (50%) suffered from radiculopathy pain. Serum glucose median values were 94.5 (79-205) mg / dL, CRP median values were 4.29 (0-54) mg / dL, and ESR median values were 19 (5-71) mm / hour.

When the patients were divided into two groups according to their gender, no statistically significant difference was found in terms of study parameters except radiculopathy pain (X2 = 5.318, p = 0.021) (Table 1).

Forty of the patients were followed conservatively and 12 patients were treated surgically. When the patients were divided into two groups with and without surgical treatment, there was found a statistically significant difference in terms of pars

defect (X2 = 4.202, p = 0.040) (Table 2). On the other hand, there was a statistically different between the two groups in terms of the slipping distance in the neutral position of the patient (t = 3.113, p = 0.006) and slipping distance in flexion position of the patient (t = 3.380, p = 0.003). However, changing the degree of the slippage angle was not different between the groups. In non-operated patients, the median slipping distance position was 0.22 ± 0.18 mm and the slippage angle was 7.03 ± 9.1 degrees in the neutral position while the mean slipping level was 0.24 ± 0.22 mm and the slippage angle was 7.26 ± 0.31 degrees in the flexion position (Figure 1 and Figure 2). In operated patients, the median slipping distance was 15.52 ± 13.78 mm and the slippage angle was 6.78 ± 5.49 degrees in the neutral position while the mean slipping distance was 17.26 ± 14.11 mm and the slippage angle was 4.93 ± 5.61 degrees in the flexion position (Figure 3 and Figure 4).

Figure 1. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slipping distance of patient who was not operated.

Table 2. Table shows the data of patients who were treated surgically and conservatively. *Chi-Square test and Mann Whitney U test, p<0.05*

		TREATMENT MODALITY			
Variable		**Conservative**	**Surgery**	**X^2 / Z**	**p**
Gender	male	7 (87.5%)	1 (12.5%)	0.596*	0.440
	female	33 (75.0%)	11 (25.0%)		
Pars defect	Degenerative	20 (90.9%)	2 (9.1%)	4.202*	**0.040**
	Isthmic	20 (66.7%)	10 (33.3%)		
Meyerding grade	1	9 (81.8%)	2 (18.2%)	0.953*	0.621
	2	23 (79.3%)	6 (20.7%)		
	3	8 (66.7%)	4 (33.3%)		
Number of screw s	0	40 (100.0%)	0 (0.0%)	52.000*	**<0.001**
	4	0 (0.0%)	4 (100.0%)		
	6	0 (0.0%)	8 (100.0%)		
Incontinence	no	33 (76.7%)	10 (23.3%)	0.004*	0.947
	yes	7 (77.8%)	2 (22.2%)		

Radiculopathy pain	no	22 (84.6%)	4 (15.4%)	1.733*	0.188
	yes	18 (69.2%)	8 (30.8%)		
Claudication	no	27 (81.8%)	6 (18.2%)	1.219*	0.270
	yes	13 (68.4%)	6 (31.6%)		
Glucose		94 (79-206)	98 (83-139)	-1.055	0.292
C-reactive protein		4.33 (0-28)	4.03 (1-54)	-0.421	0.673
ESR		19 (5-71)	10 (6-51)	-0.941	0.347

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

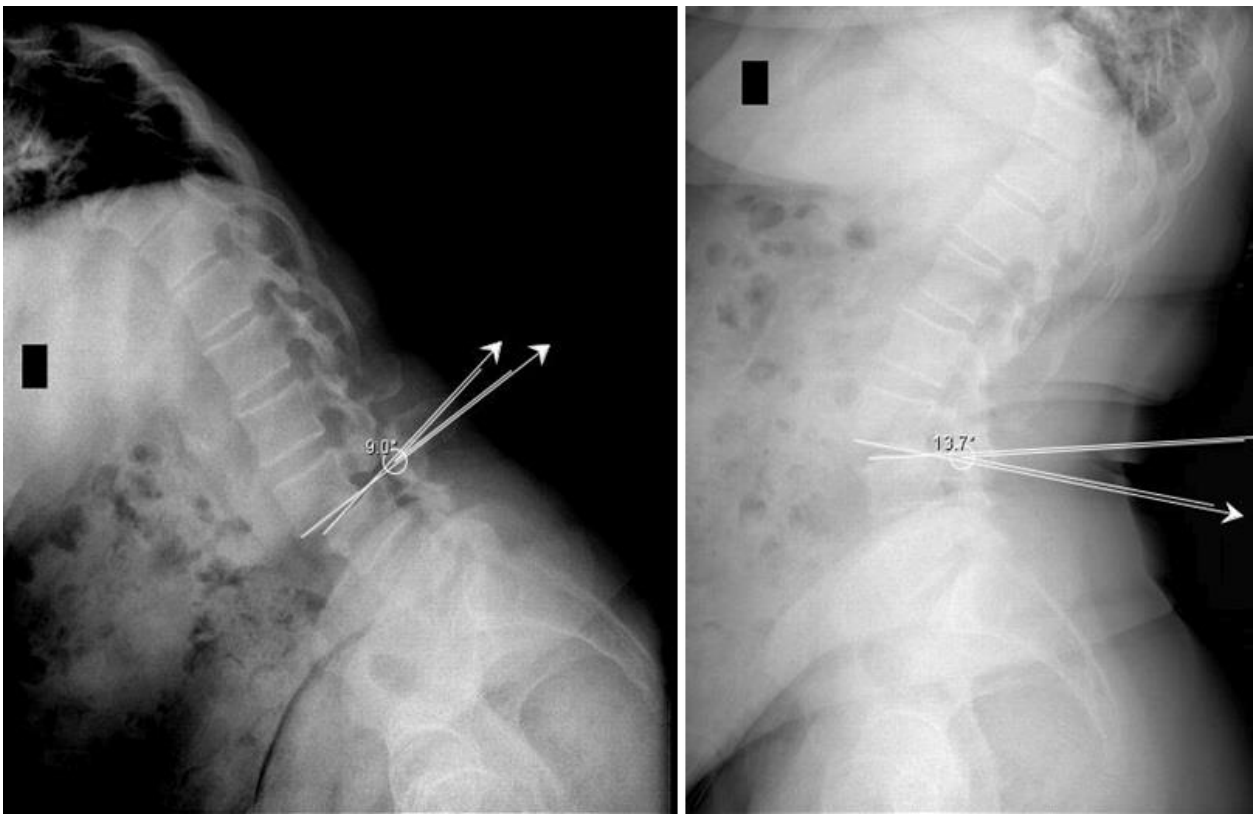

Figure 2. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slippage degrees of patient who was not operated

Table 3. Table shows the patients' data according to the type (i.e. degenerative and isthmic type) of spondylolisthesis. *Chi-Square test and Mann Whitney U test, p<0.05*

		TYPE OF SPONDYLOLISTHESIS			
Variable		**Degenerative**	**Isthmic**	**X^2 / Z**	**p**
Gender	male	4 (50.0%)	4 (50.0%)	-0.229*	0.632
	female	18 (40.9%)	26 (59.1%)		
Meyerding grade	1	10 (90.9%)	1 (9.1%)	14.605*	**<0.001**
	2	10 (34.5%)	19 (65.5%)		
	3	2 (16.7%)	10 (83.3%)		
Treatment modality	Conservative	20 (50.0%)	20 (50.0%)	4.202*	**0.040**
	Surgery	2 (16.7%)	10 (83.3%)		
Number of screw s	0	20 (50.0%)	20 (50.0%)	4.885*	0.087
	4	0 (0.0%)	4 (100.0%)		
	6	2 (25.0%)	6 (75.0%)		

Incontinence	no	22 (51.2%)	21 (48.8%)	7.981*	**0.005**
	yes	0 (0.0%)	9 (100.0%)		
Radiculopathy pain	no	13 (50.0%)	13 (50.0%)	1.261*	0.262
	yes	9 (34.6%)	17 (65.4%)		
Claudication	no	12 (36.4%)	21 (63.6%)	1.307*	0.253
	yes	10 (52.6%)	9 (47.4%)		
Glucose		93.00 (79-139)*	96.5 (83-206)*	-1.076	0.282
C-reactive protein		3.96 (1-17)*	4.58 (0-54)*	-0.771	0.441
ESR		19 (5-71)*	14 (6-68)*	-0.600	0.548

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

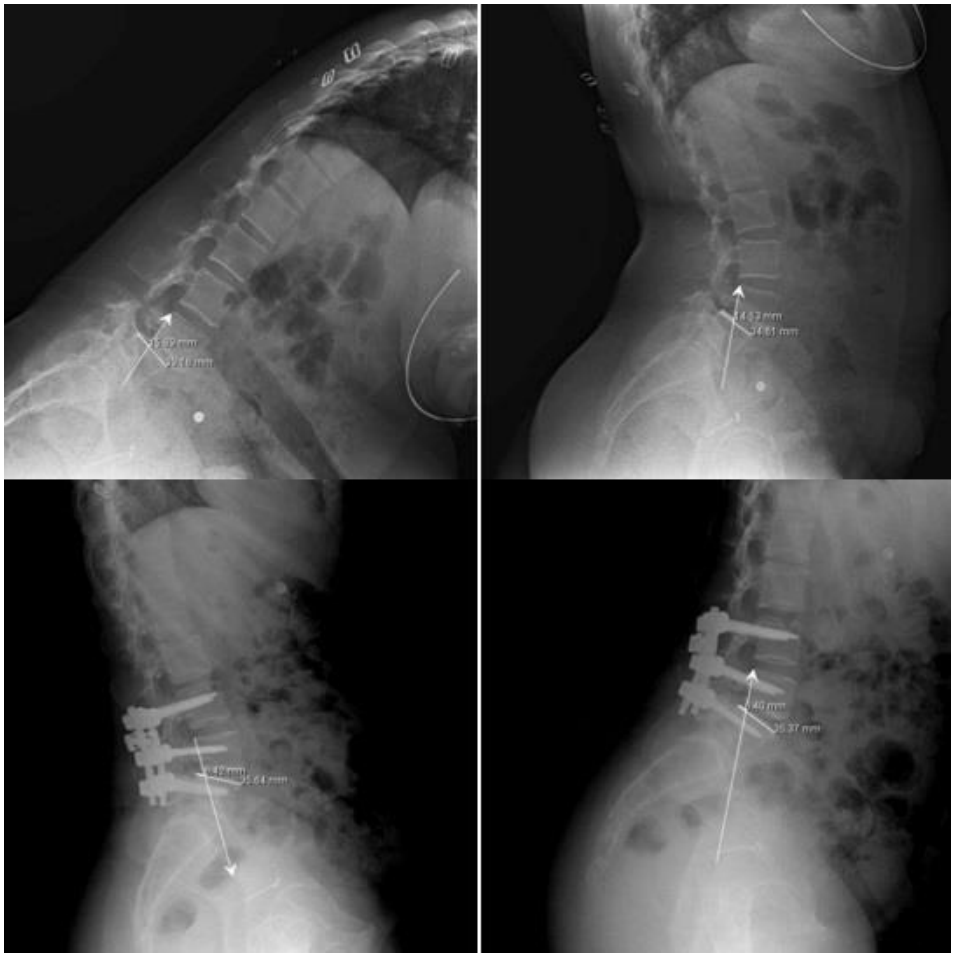

Figure 3. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slipping distance of patient who was operated.

Table 4. Table shows the data of patients according to the grade (i.e. Meyerding grade) of spondylolisthesis. *Chi-Square test and Kruskal Wallis test, p<0.05*

		GRADE OF THE SPONDYLOLISTHESIS				
Variable		**1**	**2**	**3**	**X^2 / Z**	**p**
Gender	male	3 (37.5%)	5 (62.5%)	0 (0.0%)	3.453*	0.178
	female	8 (18.2%)	24 (54.5%)	12 (27.3%)		
Pars defect	Degenerative	10 (45.5%)	10 (45.5%)	2 (9.1%)	14.605*	**0.001**
	Isthmic	1 (3.3%)	19 (63.3%)	10 (33.3%)		
Treatment modality	Conservative	9 (22.5%)	23 (57.5%)	8 (20.0%)	0.953*	0.621

	Surgery	2 (16.7%)	6 (50.0%)	4 (33.3%)		
Screw s Number	0	9 (22.5%)	23 (57.5%)	8 (20.0%)	7.319*	0.120
	4	0 (0.0%)	4 (100.0%)	0 (0.0%)		
	6	2 (25.0%)	2 (25.0%)	4 (50.0%)		
Incontinence	no	11 (25.6%)	23 (53.5%)	9 (20.9%)	3.030*	0.220
	yes	0 (0.0%)	6 (66.7%)	3 (33.3%)		
Radiculopathy pain	no	8 (30.8%)	13 (50.0%)	5 (19.2%)	2.916*	0.233
	yes	3 (11.5%)	16 (61.5%)	7 (26.9%)		
Claudication	no	4 (12.1%)	21 (63.6%)	8 (24.2%)	4.539*	0.103
	yes	7 (36.8%)	8 (42.1%)	4(21.1%)		
Glucose		92 (81-139)	94 (79-206)	97 (80-125)	0.375	0.829
C-reactive protein		4 (1-17)	2.61 (0-54)	5 (1-28)	0.539	0.764
ESR		20.50 (9-59)	19 (5-71)	10 (5-68)	0.978	0.613

(*) Chi-Square test
Number of patients (%) or median (minimum-maximum) value
X^2: Chi-Square score, Z: Z score, ESR: erythrocyte sedimentation rate

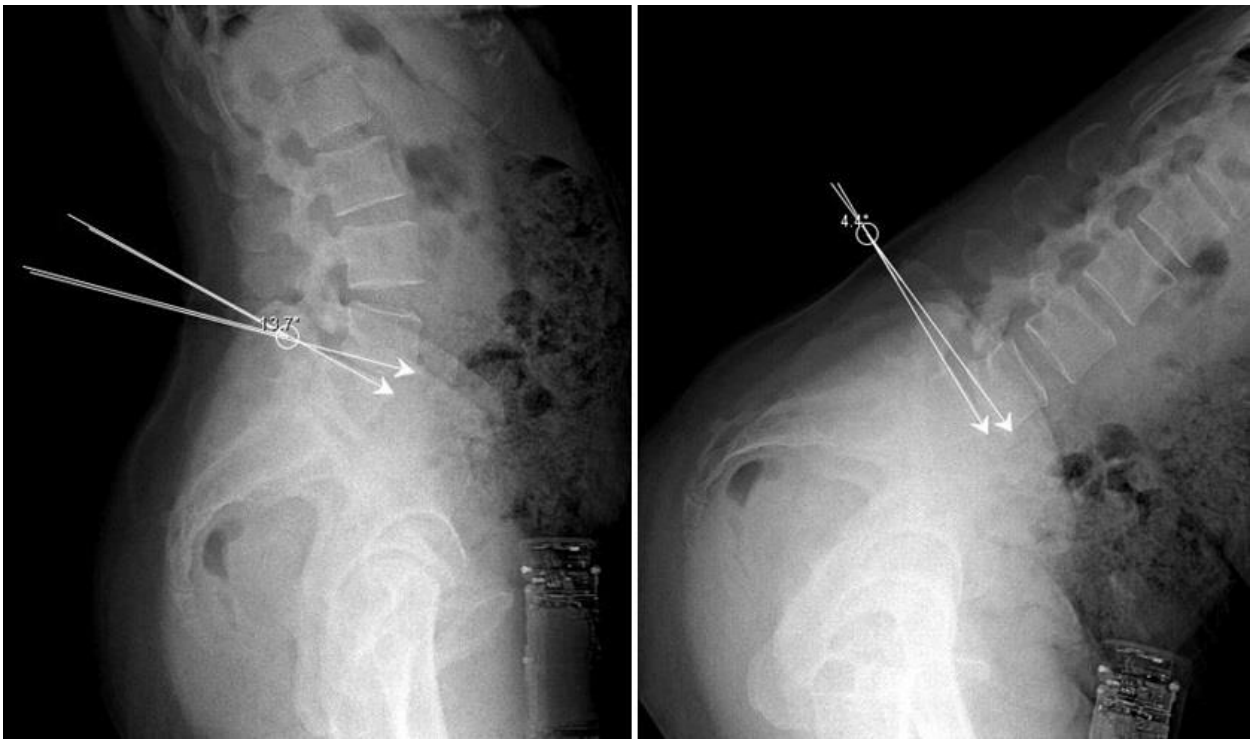

Figure 4. Lumbar dynamic X-ray images which were obtained in the neutral position and in flexion position showing the slippage degrees of patient who was operated

Degenerative spondylolisthesis was seen in 22 patients (male=4, female=18) and isthmic spondylolisthesis was found in 30 patients (male=4, female=26). When the patients were divided into two groups according to their pars defect (degenerative spondylosisthesisvs isthmic spondylolisthesis), the grade of spondylolisthesis (X2= 14.605, p <0.001), surgical treatment (X2= 4.202, p = 0.040) and urinary incontinence (X2= 7.981, p = 0.005) was found to be different between the groups (Table 3).

Eleven patients (21.15%) had grade 1, 29 patients (55.77%) had grade 2 and 12 patients (23.08%) had grade 3 spondylolisthesis. When the patients were divided into three groups according to the degree of spondylolisthesis, only the pars defect was found to be different between the groups (X2= 14.605, p = 0.001) (Table 4).

At the end of the correlation analysis applied to the data of all patients, a positive correlation was found between the gender and radiculopathy pain (r

= 0.320, p = 0.021), between pars defect and the grade of spondylolisthesis(r = 0.491, p <0.001), between the pars defect and receiving the surgical treatment (r = 0.284, p = 0.041), between the pars defect and urinary incontinence (r=0.392, p=0.004), between the urinary incontinence and radiculopathy pain (r=0.356, p=0.010) and between urinary incontinence and neurogenic claudication (r = 0.392, p = 0.004). However, a negative correlation was seen between the age and pars defect (r = -0.390, p = 0.004).

At the end of the ROC-Curve test and Logistic Regression tests, it was determined that no parameter could be a sensitive and specific predictive marker in the decision of surgical treatment. However, the likelihood ratio test results revealed that the presence of pars defect (X2 = 10.576, p = 0.001), the presence of neurogenic urinary incontinence (X2 = 8.203, p = 0.004) and the presence of neurogenic claudication (X2 = 8.003, p = 0.005) could be auxiliary parameters in decision making the surgical treatment (Table 5). Besides, it was considered that the angulation change or slipping distance in the slipping spine segment detected on dynamic X-Ray images was not sensitive or specific or an auxiliary parameter in decision making the surgical treatment.

Table 5. Table shows the best possible markers to make a decision of the surgery in patients with spondylolisthesis. *ROC-Curve test and Likelihood Ratio test, p<0.05*

	***ROC-Curve* test**		***Likelihood Ratio* test**	
Variable	**Area**	**p**	**X^2**	**p**
Pars defect	0.667	0.082	10.576	**0.001**
Meyerding grade	0.575	0.434	0.001	0.973
Incontinence	0.496	0.965	8.203	**0.004**
Radiculopathy pain	0.608	0.259	1.468	0.226
Claudication	0.588	0.362	8.003	**0.005**

Discussion

It has been shown in the literature that loss of height in the disc space, facet joint hypertrophy, hypertrophic ligamentumflavum, subchondral sclerosis, the presence of osteophyte, multifudis atrophy and presence of the “pars interarticularis” fracture may cause either severe canal stenosis and foraminal stenosis and anterior and / or lateral slipping in the vertebrae (3-5). Isthmic spondylolisthesis may result from a stress fracture, acute fracture or elongation defect. It is typically seen in children aged 5-7 years, but the defect can reach and be seen in adulthood. Lesions often occur in L5 - S1 but in trauma cases above the L5 level. It may be asymptomatic or may cause low back pain, hamstrings stiffness, knee contractures, and bladder and bowel incontinence (15).

In a study, degenerative changes in the lumbar spine were examined in 3 groups and group 1 patients had transient dysfunction; Group 2 patients had an unstable spine and group 3 patients had re-stabilization. It was reported that group 1 patients benefited more from conservative treatment, conservative approaches were applied to those in the early stage of group 2 patients, while conservative treatments were inadequate and fusion surgery was performed in late group 2 patients. Group 3 patients had severe stenosis and these patients underwent spinal decompression with or without instrumentation (16). In another study, it was suggested that the micro-instability period could be unnoticed. Therefore, a classification was formed by scoring the changes in X-ray, CT, and MRI for a decision on which the treatment would be done in these patients. According to the classification, it was aimed to provide early diagnosis and treatment to the patient in the period of micro-instability (17,18).

In our study, it was thought that the complaint of radiculopathy pain occurred mostly in women, but gender did not affect other study parameters. On the other hand, it was found that most of the patients (n = 30) had pars defect and 10 of them had surgical treatment. Most of the patients had grade 2 spondylolisthesis (n = 19) and most of them (n = 40) were treated conservatively, whereas surgical treatment was preferred in patients with pars defects (n = 10), and most patients (n = 43) did not have urinary incontinence.

Most of the patients (n = 30) had pars defect and 19 patients had grade 2 and 10 patients had grade 3 spondylolisthesis. Surgical treatment was applied to 2 patients without pars defect and 10 patients with pars defect; 6 of these patients had grade 2 and 4 had grade 3 spondylolisthesis. Although it was seen that most of the patients with grade 2-3 isthmic spondylolisthesis underwent surgery, it was thought that type or grade of spondylolisthesis could not be a criterion for deciding on the surgical treatment because of a small number of patients.

Correlation analysis showed that pars defect may be an important factor in the formation of spondylolisthesis and neurogenic urinary incontinence. It was also thought that urinary incontinence may also occur if the patient had symptoms and signs of radiculopathy pain or neurogenic claudication. However, it was argued that there was no statistical relationship between the degree of spondylolisthesis and the findings of radiculopathy pain, neurogenic claudication or urinary incontinence. ESR or CRP values, which are known as acute and / or chronic inflammation markers, could not be correlated with any parameters. With this result, it was argued that pars defect and / or spondylolisthesis detected in patients could not be the result of an inflammatory process.

On the other hand, at the end of the ROC-Curve analysis, it was concluded that none of the parameters evaluated in this study could be a predictive marker in deciding on surgical treatment. However, Likelihood Ratio test results demonstrated that the presence of pars defect in the patient, the presence of neurogenic claudication and urinary incontinence findings could be the parameters that may help the surgeon to decide on surgical treatment. However, it was thought that the degree of spondylolisthesis could be ineffective in deciding for surgical treatment.

Some limitations of this study are as follows: First, the retrospective character of this study limited the discussion of the mid-term or long-term follow up results of the patients. Second, the number of the study population was very small. Nevertheless, it can be easily said that the results of this study were very impressive and novel to discuss the predictive markers in deciding on surgical treatment. Third, in some cases, determining the correct level to identify spondylolisthesis was a challenge due to the difficulty in counting spinal levels with the possibility of lumbar-sacral segments or sacralized lumbar segments or a variable total number of spine levels. Fourth, because some MR and / or CT images were from external institutions, they could not be evaluated retrospectively. Therefore, the relationship between the X-Ray images and CT / MR images which could support more relevant data was not investigated. Finally, the present study included computerized abstracted information that required personal measurements that could be prone to random error.

Conclusion

At the end of this study, it was seen that the presence of pars defect (isthmic spondylolisthesis) in the patient, the presence of neurogenic claudication and urinary incontinence findings could be the parameters that may help the surgeon to make the surgical treatment decision. However, it was considered that the presence of the radiculopathy suffering of the patient or the grade of spondylolisthesis could be ineffective in the decision of surgical treatment.

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