

Prevalence and causing factors of
skipped level in multiple degenerative
lumbar patients

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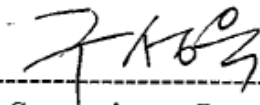
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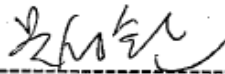
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ABSTRACT

Prevalence and causing factors of skipped level in multiple degenerative lumbar patients

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(Directed by Professor Sung Uk Kuh)

Background: Disc degeneration has been attributed to the accumulation of environmental effects, mechanical injuries and insults, imposed on normal aging changes in general. Mostly there are confined to the effects of age and biomechanics associated with disc degeneration. Most common lesions of disc degeneration L4/5 level in lumbar spine and also adjacent lesions to the above level are frequently involved anatomically. Sometimes degenerative disc disease is not consecutive, but the cause is not known yet. Especially, it is difficult to determine the extent of surgery in skipped level disc degeneration patients. We investigated the causing factors of skipped level in multiple degenerative lumbar disc patients.

Methods: We evaluated 1353 outpatients who were visited to Gangnam Severance Spine Hospital from January 2010 to April 2010 (mean age 47.5 years old, range 13–85 years). The exclusion criteria were scoliosis, trauma, previous spine operation, infection, and spinal tumor patients. All 474 patients without excluded patients took whole sagittal T2-weighted MRI scans. We measured pfirrmann classification for each level and checked the presence of Schmorl's node, spondylolisthesis, spondylolysis, ossification of ligamentum flavum, ossification of posterior longitudinal ligament, and bony spur for each level.

Results: The total skipped lesion patients (Group S) were 105 (men; 65,

women; 40) and non-skipped lesions patients (Group NS) were 369 (men; 179, women; 190). Group S consisted of more males compared to group NS. Group S was significantly associated with the presence of bony spur ($p=0.002$), instability ($p=0.030$), schmorl's nodule ($p<0.05$), and male ($p=0.021$). Other MRI findings did not significantly differ between groups ($p>0.05$). In group S, disc degeneration increased at age 50 to 60 years old, while in group NS, disc degeneration abruptly increased from age 60.

Conclusion: Although many factors associated with degeneration have been studied, there are few regarding non-contiguous disc degeneration. In our study, male sex, presence of bony spur, spinal instability, and presence of Schmorl's nodule were significantly associated with skipped lesion disc degeneration. Our results may provide further evidence in the pathogenesis of lumbar disc degeneration.

Key words: disc degeneration; pfirrmann classification; skipped lesion; lumbar spinal pathology; whole sagittal MR image

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I. INTRODUCTION

Intervertebral disc degeneration of the lumbar spine is a common manifestation typically attributed to age progression and excessive physical loading, and contributes to structural compromise and biochemical degradation of discs.¹⁻³ In recent years, several additional etiologic factors have been reported suggesting that a complex, multifactorial process may play an underlying role in disc degeneration. Moreover, many factors that influence disk degeneration include a genetic component.⁴⁻⁷ Due to the effects of degeneration, patients often develop lower back pain, which is one of the most common health issues worldwide.

“Skipped” or non-contiguous levels of disc degeneration (SLDD) is a unique occurrence of the spine, which appear as healthy normal discs between degenerated discs on magnetic resonance imaging (MRI).⁴ A skipped lesion is defined as a Pfirrmann classification of more than one between adjacent discs in MRI. SLDD shows different pattern of disc degeneration that are commonly observed, in that when they typically involve the 2 lowest levels of the lumbar spine, with single level or contiguous, multilevel involvement.⁵

Furthermore, it has been proposed that when disc degeneration does occur, it may alter the biomechanical environment of the involved and adjacent vertebral segments, resulting in contiguous levels of disc pathology.

Degeneration generally occurs contiguously, however, in some patients, it manifests as a skipped lesion. Multilevel contiguous degeneration is more common, usually occurring in older patients. Interestingly, several distinct patterns of disc degeneration have been observed, the causes of which are not yet entirely clear. In addition, it is especially difficult to determine the extent of surgery needed for patients with skipped level disc degeneration.

In an effort to further elaborate on the clinical implications of skipped levels of disc degeneration, we compared the clinical relevance and MRI findings of patients with skipped lesion degeneration (Group S) with that of patients with non-skipped lesion disc degeneration (Group NS).

II. MATERIALS AND METHODS

Study population

Following institutional ethics board approval and patient consent, 1353 outpatients who visited Gangnam Severance Spine Hospital from January 2010 to April 2010 (mean age 47.5 years, range 13–85 years) were included in this study. Complete radiographic and clinical data was available for review for all of the patients in this study. We excluded patients who had a history of lumbar spine surgery, spinal deformities, bony spinal tumors, spinal infections, known symptomatic vertebral fractures, or inflammatory disease of the spine.

Radiographic assessment

Whole T2-weighted sagittal MRI of the lumbar spine was performed for all subjects. Images were evaluated by a physician who was blinded to the clinical assessment. We measured the Pfirrmann classification for each level (Table 1, Fig. 1) and also checked each level for the presence of Schmorl's node, spondylolisthesis, spondylolysis, ossification of the ligamentum flavum, ossification of posterior longitudinal ligament, and bony spurs.⁶

Statistical Analysis

Statistical analysis was performed using the computer program SPSS (version 14, SPSS Inc., Chicago, IL, USA), and values were expressed as the mean \pm standard deviation. Student's t-test was performed with a significance level of 0.05. Pearson's chi-squared and Fisher's exact tests were performed where appropriate. Univariate logistic regression analysis was performed to assess the effects of various covariates on the presence of skipped lesion degeneration (i.e. being in Group S). Following these analyses, logistic regression modeling was performed; P-values less than 0.05 were considered significant, and the corresponding 95% confidence intervals (95% CIs) of P-values were assessed.

III. RESULTS

Patient characteristics

Our study population (n=1353) consisted of 613 males (45.3%) and 740 females (54.7%). Of the 1353 patients, 897 were excluded leaving 474 individuals. We divided the remaining patients into two groups, namely, Group S consisting of patients with skipped lesion disc degeneration, and Group NS, which consisted of patients with non- skipped lesion disc degeneration. There were 105 patients (65 males and 40 females) in Group S (Fig. 2) and 369 patients (179 males and 190 females) in group NS. Group S consisted of more males compared to Group NS (P=0.028). The mean age of the subjects was 47.5 years (range 13–85 years) (Fig. 2).

Table 1. Grading System for Lumbar Disc Degeneration proposed by Pfirrmann

Grade	Nucleus Signal Intensity	Nucleus Structure	Distinction of Nucleus and Annulus	Disc Height
I	Hyperintense	Homogenous, white	Clear	Normal
II	Hyperintense	Homogenous with horizontal band, white	Clear	Normal
III	Intermediate	Inhomogeneous, gray to black	Unclear	Normal to decreased
IV	Hypointense	Inhomogeneous, gray to black	Lost	Normal to decreased
V	Hypointense	Inhomogeneous, gray to black	Lost	Collapsed



Figure 1. Whole sagittal T2-weighted images of the spine illustrating various skipped lesion disc patterns.

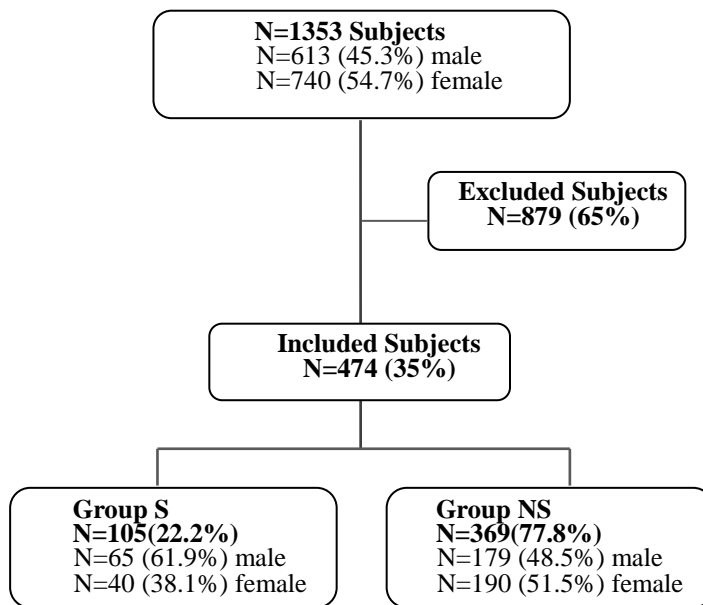


Figure 2. Flow diagram of the study, illustrating derivation of sample size and group stratification. (Group S=skipped lesion, Group NS=non-skipped lesion)

Comparison of disc degeneration severity

Of all disc degeneration levels, L4/5 (mean grade 4.2) was the most severe, followed by L5/S1 (mean grade 3.53), L3/4 (mean grade 3.32), L2/3 (mean grade 3.18), and L1/2 (mean grade 3.01), respectively. Degeneration was most severe in the L4/5 level for both males and females. However, upon comparing levels, females showed more severe disc degeneration at the L3/4 and L4/5 levels ($P < 0.05$) (Fig. 3, Table 2).

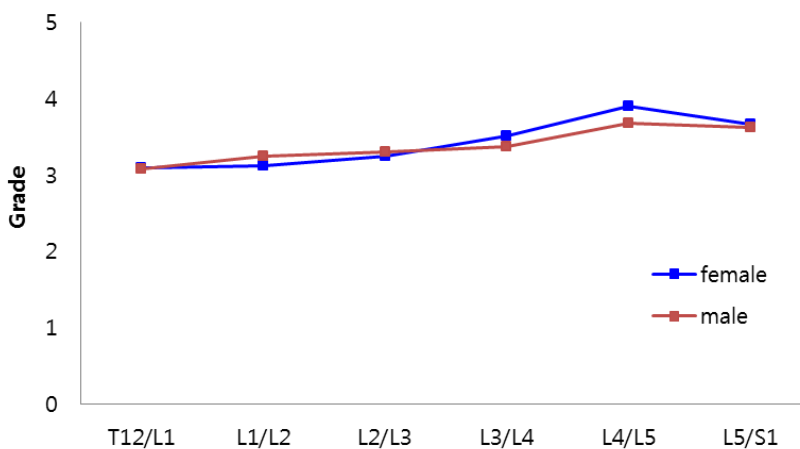


Figure 3. Pfirrmann classification grades according to sex and level of degeneration. Degeneration was most severe at the L4/5 level for both males and females (Male 3.91 ± 0.66 , Female 3.68 ± 0.79). A significant difference was noted between females and males at the L1/L2 (3.12 ± 0.55 vs. 3.25 ± 0.64 respectively, $P = 0.046$) and L4/L5 levels (3.68 ± 0.79 vs. 3.91 ± 0.66 respectively, $P = 0.002$).

Table 2. Comparison of Pfirrmann classification grades according to sex and level of degeneration.

Levels of degeneration	Female (N=201)	Male (N=186)	<i>P</i>-value
T12/L1	3.10±0.51	3.08±0.68	0.759
L1/L2	3.12±0.55	3.25±0.64	0.046
L2/L3	3.25±0.60	3.30±0.66	0.467
L3/L4	3.52±0.65	3.38±0.68	0.048
L4/L5	3.91±0.66	3.68±0.79	0.002
L5/S1	3.67±0.73	3.63±0.73	0.620

We next compared the Pfirrmann classification grades between Group S and Group NS according to age. Significant differences were noted at 30-39 years between NS and S groups (3.14 ± 0.31 vs. 2.83 ± 0.36 respectively, $P=0.024$) and at 40-49 years (3.25 ± 0.23 vs. 3.04 ± 0.47 respectively, $P=0.041$). In these younger age ranges of patients, patients with skipped lesion disc degeneration (Group S) had a lower Pfirrmann classification grade compared to patients with non-skipped lesion disc degeneration (Group NS) (Fig. 4, Table 3).

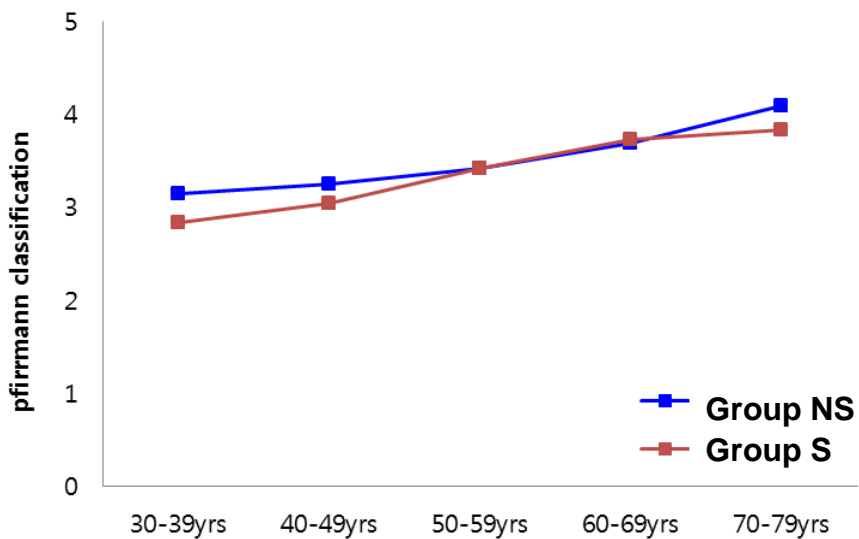


Figure 4. Comparison of Pfirrmann classification grades between group NS and group S according to age. Significant differences were noted at 30-39 years (3.14 ± 0.31 vs. 2.83 ± 0.36 , $P=0.024$), and 40-49 years (3.25 ± 0.23 vs. 3.04 ± 0.47 , $P=0.041$).

Table 3. Comparison of Pfirrmann classification grades between group S and group NS according to age.

	Group NS		Group S		P-value
	N	Mean	N	Mean	
30-39 yrs	58	3.14±0.31	6	2.83±0.36	0.024
40-49 yrs	70	3.25±0.23	27	3.04±0.47	0.041
50-59 yrs	89	3.41±0.24	37	3.41±0.44	0.993
60-69 yrs	52	3.69±0.35	20	3.73±0.38	0.666
70-79 yrs	19	4.09±0.46	9	3.83±0.44	0.168

We also compared the Pfirrmann classification grade at each disc level between Group S and Group NS according to age. At the T12/L1 level, significant differences were noted at 30-39 years (2.93±0.31 vs. 2.33±0.51, P=0.036) and 40-49 years 3.07±0.42 vs. 2.74±0.76, P=0.041) (Fig. 5, Table 4).

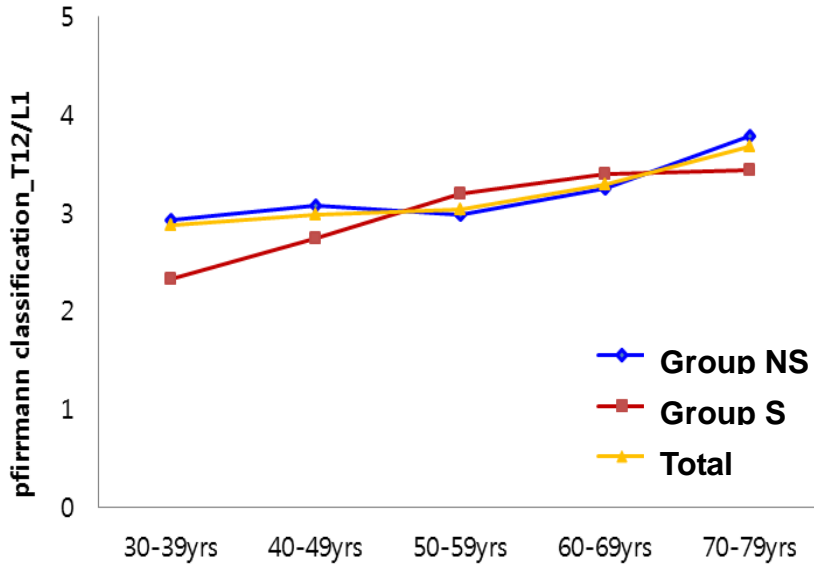


Figure 5. Comparison of Pfirrmann classification grades between group S and group NS at the T12/L1 level according to age. Significant differences were noted at 30-39 years (2.93±0.31 vs. 2.33±0.51, P=0.036) and 40-49 years (3.07±0.42 vs. 2.74±0.76, P=0.041).

Table 4. Comparison of Pfirrmann classification grades between group S and group NS at the T12/L1 level according to age.

	Group NS		Group S		<i>P</i> -value
	N	Mean	N	Mean	
30-39 yrs	58	2.93±0.31	6	2.33±0.51	0.036
40-49 yrs	70	3.07±0.42	27	2.74±0.76	0.041
50-59 yrs	89	2.98±0.26	37	3.19±0.87	0.157
60-69 yrs	52	3.25±0.55	20	3.40±0.94	0.509
70-79 yrs	19	3.79±0.71	9	3.44±0.72	0.245

At the L3/4 level, significant differences between NS and S groups were noted at 50-59 years (3.57±0.60 vs. 3.32±0.62, P=0.039) (Fig. 6, Table 5). In addition, for the L4/5 level, significant differences were noted at 30-39 years (3.57±0.65 vs. 2.83±0.75, P=0.012), 40-49 years (3.70±0.57 vs. 3.00±0.92, P<0.001), and 50-59 years (3.98±0.60 vs. 3.59±0.83, P=0.014) (Fig. 7, Table 6). However, no significant differences were observed at level L1/2, L2/3, and L5/S1 between NS and S groups.

In addition, we compared the presence of Schmorl's nodules among patients. More extensive degeneration was noted in patients with Schmorl's node and the degeneration was more evident in older patients. Specifically, Schmorl's node was most prominent at the L1/2 level followed by L2/3, T12/L1, L3/4, L4/5 and L5/S1, respectively. In Group S, Schmorl's nodule was most prominent at the L1/2 level followed by L2/3, T12/L1, L3/4, L4/5, and L5/S1, respectively. In Group NS, Schmorl's nodule was most commonly seen at the L2/3 level followed by L4/5, T12/L1, L1/2, L3/4, and L5/S1, respectively.

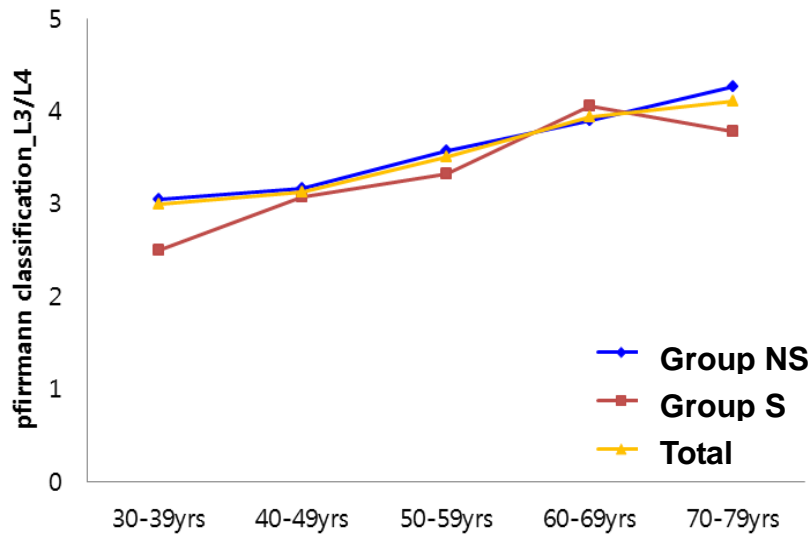


Figure 6. Comparison of Pfirrmann classification grades between group S and group NS at L3/L4 according to age. Significant differences were noted at 50-59 years (3.57 ± 0.60 vs. 3.32 ± 0.62 , $P=0.039$).

Table 5. Comparison of Pfirrmann classification grades between group S and group NS at the L3/L4 level according to age

	Group NS		Group S		<i>P</i> -value
	N	Mean	N	Mean	
30-39 yrs	58	3.05±0.34	6	2.50±0.83	0.168
40-49 yrs	70	3.16±0.40	27	3.07±0.67	0.553
50-59 yrs	89	3.57±0.60	37	3.32±0.62	0.039
60-69 yrs	52	3.90±0.53	20	4.05±0.60	0.319
70-79 yrs	19	4.26±0.65	9	3.78±1.09	0.244

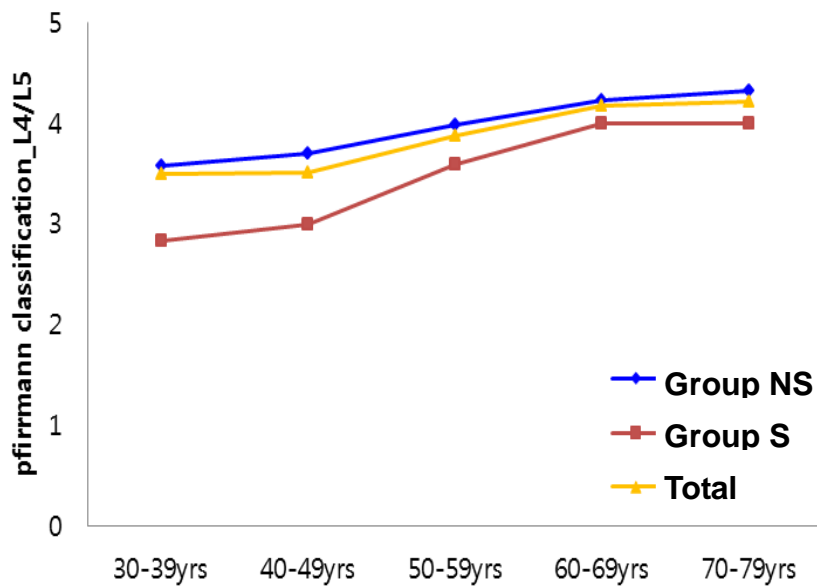


Figure 7. Comparison of Pfirrmann classification grades between group S and group NS at the L4/L5 level according to age. Significant differences were noted at 30-39 years (3.57 ± 0.65 vs. 2.83 ± 0.75 , $P=0.012$), 40-49 years (3.70 ± 0.57 vs. 3.00 ± 0.92 , $P<0.001$), and 50-59 years (3.98 ± 0.60 vs. 3.59 ± 0.83 , $P=0.014$).

Table 6. Comparison of Pfirrmann classification grades between group S and group NS at the L4/L5 level according to age.

	Group NS		Group S		P-value
	N	Mean	N	Mean	
30-39 yrs	58	3.57±0.65	6	2.83±0.75	0.012
40-49 yrs	70	3.70±0.57	27	3.00±0.92	<0.001
50-59 yrs	89	3.98±0.60	37	3.59±0.83	0.014
60-69 yrs	52	4.23±0.54	20	4.00±0.64	0.132
70-79 yrs	19	4.32±0.58	9	4.00±0.86	0.263

Comparison between Group S and Group NS

There were no statistically significant differences between Group S and Group NS with respect to spondylolisthesis, spondylolysis, and ossification of the ligamentum flavum. However, statistically significant differences were noted with respect to sex ($P=0.028$), instability ($P=0.030$), presence of bony spur ($P<0.001$), and presence of Schmorl's node at levels T12/L1, L1/2, L2/3, L3/4 ($P<0.05$), with all of these factors being more prominent in Group S (Table 7). Logistic regression analysis revealed that there was a significant association of sex (OR 2.493, $P=0.042$), Schmorl's node on L1/2 (OR 1.128, 95% CI, $P<0.001$), and bony spur (OR 1.848, $P=0.002$) with having skipped lesion degeneration (Group S). Specifically, patients in Group S were more likely to be male, present with Schmorl's nodule at the high lumbar level (L1/2), and exhibit bony spurs (Table 8).

Table 7. Age distribution and comparison of study groups according to sex and other clinical parameters.

		Frequency		<i>P</i> -value
		Group NS	Group S	
Age (30-39 yrs)		58	6	0.028
(40-49 yrs)		70	27	
(50-59 yrs)		89	37	
(60-69 yrs)		52	20	
(70-79 yrs)		19	9	
Sex	M	127	59	0.008
	F	161	40	
Instability	-	270	86	0.030
	+	18	13	
Spondylolisthesis	-	270	86	0.030
	+	18	13	
Spondylolysis	-	276	92	0.249
	+	12	7	
OLF	-	277	91	0.061
	+	10	8	
Bony spur	-	178	37	<0.001
	+	110	62	
Schmorl's nodule T12/L1	-	273	86	0.009
	+	15	13	
Schmorl's nodule L1/L2	-	274	73	<0.001
	+	14	26	
Schmorl's nodule L2/L3	-	271	83	0.002
	+	17	16	
Schmorl's nodule L3/L4	-	273	88	0.043
	+	15	11	
Schmorl's nodule	-	269	90	0.409

L4/L5				
	+	19	9	
Schmorl's nodule	-	276	95	0.927
L5/S1				
	+	11	4	

NS, non-skipped lesion; S, skipped lesion; M, male; F, female; OLF, ossification of the ligamentum flavum.

Table 8. Univariate logistic regression analysis of the occurrence of skipped level disc degeneration.

Variable	Odds ratio	<i>P</i>-value
Sex	2.493	0.042
Schmorl's nodule L1/L2	1.218	<0.001
Bony spur	1.848	0.002

IV. DISCUSSION

Hsu et al. first described the occurrence of skipped lesion disc degeneration of the lumbar spine in 1992,⁴ and since then several reports have been published.^{7,8} In their initial report, Hsu et al. reported that the prevalence of skipped lesion disc degeneration in the Hong Kong population was 1.8%.⁴ In another study, the prevalence of skipped lesion disc degeneration in the overall population was reported to be 8.1%.⁷ Several etiologic factors, such as preexisting end plate deficiencies, abnormal biomechanics, developmental factors, and genetic predisposition have been postulated.⁸ Therefore, in our study, we investigated causative factors of skipped lesions in Korean patients with multiple degenerative lumbar discs.

Degenerative disc disease is a prevalent health concern that generally increases with age. Disc degeneration commences as early as the second decade of life;⁹ however, due to a lack of data in the present study, we were unable to observe the prevalence of degenerative disc disease in patients younger than 20. Thus, we only investigated degenerative disc disease patients aged 30 to 70 years. Usually, L4/L5 and L5/S1 have the highest prevalence of all disc findings with the exception of Schmorl's nodes, which are most commonly observed at the L1/L2, L2/L3, and L3/L4 levels.¹⁰⁻¹³ Our observation that the L4/S1 lumbar discs were more degenerated than L1–L4 discs was consistent with previous studies suggesting that lifetime physical exposure plays a role in disc pathogenesis, as both “pure” aging genes and systemic factors would be expected to affect discs similarly.¹⁴ Specifically, we found that L4/5 was the most degenerated level in both male and female patients. In the higher L1/2 level, males showed more degeneration compared to opposite sex whereas females showed more severe degeneration at the L3/4/5 level. In group S, degeneration gradually progressed through 50-60 years of age, with less degeneration noted in patients aged 70 years and older. In group NS, degeneration gradually increased from 30 to 60 years of age, but

increased abruptly beginning at 70 years of age.

Cheung KM et al.⁷ performed a study of intervertebral disc degeneration based on a skipped level disc degeneration in 174 patients with a mean age of 39 years by MRI, and demonstrated that male sex was more highly associated than female sex with the presence of Schmorl's nodes, and also that skipped level degeneration patterns were multiregional. Therefore, they proposed that repetitive loading of the spine with excessive forward bending, possibly related to occupation or lifestyle, was a significant risk factor of disc degeneration. We also found out that degeneration was more severe in the transitional zone T12/L1 in group NS patients aged 30 to 40 years old. When the two groups were compared, the degeneration was more severe in group NS in 30-40 year old patients while degeneration was more severe in group S in 50-60 year old patients. However, statistical significance was only seen in 30-40 year old patients. Indeed, the propensity for disc degeneration to occur at such regions may suggest excessive, abnormal loading and bending due to daily activities or potential stress induction from the thoracolumbar transition zone.⁴ Such regional effects may also be associated with the manifestation of end plate alterations, such as Schmorl's nodes, that are known to occur at the high and mid levels of the lumbar spine.¹⁵ With respect to Schmorl's nodes, some reports have suggested that improper or excessive anterior column loading may contribute to such lesions. However, recent evidence also suggests that some individuals may be genetically predisposed to develop Schmorl's nodes.¹⁵

In our study, a statistically significant difference was noted between group S and group NS. Based on logistic regression analysis, our study identified a significant association of male sex, presence of bony spurs, spinal instability, and presence of Schmorl's nodes with skipped lesion degeneration. Since patients with these factors are prone to fall into the group S category, clinicians should be aware of these risk factors and use X-rays to correlate

MRI findings. Specifically, in group S patients, degeneration increased significantly at ages 50 to 60 years of age in the middle area of the L3/4 level. Therefore, when encountering patients with skipped lesions aged 50 to 60 years, more education regarding bad posture and repetitive movement should be provided to prevent further degeneration.

V. CONCLUSIONS

We identified several characteristic findings for skipped lesion disc degeneration in Korean patients. Skipped lesion disc degeneration was significantly associated with male sex, presence of bony spurs, spinal instability, and presence of Schmorl's nodes. Despite our findings, the overall pattern and variety of factors that influence skipped lesion degeneration remains unclear. Further investigation regarding the etiology of skipped lesion disc degeneration is warranted.

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ABSTRACT(IN KOREAN)

다발성 퇴행성 요추부 디스크 질환 환자에서 skipped 병변의
유병률과 원인인자 분석

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배경 : 디스크 퇴행성은 일반적으로 환경적인 요인, 물리적 사고와 노화로 인해 생긴다고 알려져 왔다. 대부분 나이와 생체학적 영향에 국한되어 졌다. 요추에서 요추4번/5번간 디스크가 가장 흔한 퇴행성 변화를 보였고 해부학적으로 인접마디에 영향을 미쳤다. 때때로 퇴행성 디스크 질환은 연속적으로 생기지 않았고 skipped (건너뛰기) 현상을 보였는데 그 원인은 밝혀진 바가 적다. 특히 디스크 퇴행성에 건너뛰기 현상이 있을 경우 수술적 범위를 결정하기란 힘들었다. 본 연구에서는 요추부 디스크 퇴행성 변화에서 디스크 건너뛰기 현상을 일으키는 요인을 분석하였다.

결과 : 2010년 1월부터 4월까지 강남세브란스 척추병원을 내원한 총1353명(평균나이 47.5세, 13세에서 85세까지)을 분석 하였다. 이중 척추측만증, 사고, 이전 수술한 과거력, 감염, 척추종양, 선천성 기형 환자는 제외하였다. Pfirrmann classification을 이용하여 각각의 디스크를 측정하였고 쉬모를 결절, 척추 전방전위증, 척추분리증, 황색인대골화증, 후종인대골화증, 뼈돌기의 유무를 확인하였다. 디스크 퇴행성에 건너뛰기 현상을 보인

환자(Group S)는 총105명 (남자65명, 여자40명) 이었고 연속적인 퇴행성 변화를 보인 환자(Group NS)는 369명(남자179명, 여자190명) 이었다. Group S는 남자($p=0.021$), 뼈돌기($p=0.002$), 척추불안정증 ($p=0.030$), 쉬모를 결절($p<0.05$)이 연관되었다.

결론 : 디스크 퇴행성 변화에 여러 연구가 보고 되었지만 건너뛰기 현상에 관한 연구는 아직까지 많지 않다. 우리는 디스크 퇴행성 변화에서 건너뛰기 현상에 영향을 미치는 요인으로는 남자, 뼈돌기, 척추불안정증, 쉬모를 결절이 관여한다고 밝혀내었다. 우리의 연구로 인해 요추부 디스크 퇴행성에 관여하는 병태학적 원인을 더욱 밝혀낼 것이다.

핵심되는 말 : 요추부 디스크; 퇴행성 변화; 건너뛰기 현상;
Pfirrmann classification; skipped lesion; lumbar spinal pathology;
whole sagittal MR image