The efficacy of quantitative magnetic resonance imaging in the diagnosis of unstable L4/L5 degenerative spondylolisthesis

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Abstract. Lumbar degenerative spondylolisthesis (LDS) is a common degenerative disease that particularly affects the elderly. LDS can occur in any segment of the spine but is most commonly found in the L4/L5 segment. In the present study, a quantitative study of lumbar MRI measurements was conducted to identify predisposing factors indicative of spinal instability in patients with L4/L5 LDS. In total, 81 patients [58 patients in the stable group (SG) and 23 patients in the unstable group (UG)] who were diagnosed with L4/L5 LDS on X-ray and MRI between January 2021 and January 2022 were included in this study. Disk height, disk signal intensity on T1-weighted (T1W) and T2-weighted (T2W) images, facet joint fluid thickness, and ligamentum flavum thickness were measured on MRI, and the differences in these parameters between the two groups were evaluated. The receiver operating characteristic curve was generated, and the area under the curve (AUC), cut-off value, sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were calculated for parameters found to be significantly different between the two groups. The facet joint fluid was significantly thicker in the UG than in the SG (P<0.01), and a cut-off value of 1.45 mm was found to have an AUC of 0.77 and an SE, SP, PPV, and NPV of 73.9, 67.2, 69.3, and 69.77%,

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respectively. No significant differences were identified between the two groups for mean disk height, ligamentum flavum thickness, or disk signal intensity on T1W or T2W images. The facet joint fluid thickness on axial T2W images may represent a useful predictor of spinal instability in patients with LDS. Therefore, spinal instability should be assessed, and additional evaluation methods, such as standing lateral flexion-extension radiographs, should be performed when facet fluid is detected on lumbar MRI.

Introduction

Lumbar degenerative spondylolisthesis (LDS) is defined as the excessive displacement of one vertebral body relative to another due to degenerative changes in spinal support structures, such as disks, ligaments, and facet joints (1-3). LDS can occur in any segment of the spine but is most commonly found in the L4/L5 segment, which may be due to the large range of flexion-extension motion that involves this segment (3,4). Lumbar instability refers to any abnormal movements of the spine beyond its normal range. Mechanical instability due to spinal degeneration can cause clinical symptoms, such as back pain or nerve compression, presenting as leg pain, leg weakness, and cauda equina syndrome (1,5,6). When clinical symptoms worsen, surgical treatments should be considered. Early and accurate diagnosis can promote the initiation of appropriate treatment strategies and improve clinical outcomes in this patient population. The treatment strategies include surgery with decompression or decompression with fusion and conservative treatment (7.8). Standing lateral flexion-extension (SLFE) radiographs are used as the gold standard for diagnosing spinal instability (1,2,5). Previously, several studies have reported that disk degeneration and signs of facet joint effusion detected on T2-weighted (T2W) MRI can be indicators of potential lumbar spine instability (8,9). However, qualitative MRI evaluations are highly dependent on the subjective judgments of the radiologist. In this study, quantitative value assessments including disk height, facet fluid thickness, ligamentum flavum thickness, and disk signal intensity on T1-weighted (T1W) and T2W MRI were assessed to identify potential factors and their efficacy in the diagnosis of unstable L4/L5 degenerative spondylolisthesis.

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Materials and methods

Study subjects. A retrospective study was conducted on 81 patients (age range, 39 to 85 years old, median age, 59 years old) diagnosed with L4/L5 LDS based on X-ray and MRI evaluations at the Viet Duc Hospital between January 2021 and January 2022. The patients were divided into 2 groups, the stable group (SG) which included 39 women and 19 men and the unstable group (UG) which included 20 women and 3 men. The institutional review board of Hanoi Medical University approved this retrospective study (approval no. 2444/QĐ-ĐHYHN, dated 13 July 2021). Due to the retrospective nature of this study, the requirement for informed consent was waived by the institutional review board of Hanoi Medical University. The study was performed in accordance with the ethical standards of the responsible committee on human experimentation and in line with the guidelines described in the Declaration of Helsinki 1975, as revised in 2013 (10). All patients underwent 4 postural lumbar spine X-rays and lumbar spine MRI with basic pulse sequences. Exclusion criteria included spondylolisthesis with trauma, tumor, infection, spondylolysis, surgical history, and congenital hypoplasia of the joints.

Plain film technique. X-rays of the lumbar spine were obtained for all cases in 4 positions: anteroposterior, lateral, maximal flexion, and maximal extension while standing. X-rays were performed using GE Definium XR120 (75-80 kV, 20-25 mAs, 100 cm).

MRI technique. All MRI scans were performed using either a Siemens 1.5 T Magnetom Essenza (Siemens Healthineers) or a Philips Ingenia 1.5 T (Philips Medical Systems) using basic sequences, including sagittal T1W, sagittal and axial T2W, and coronal short tau inversion recovery. The parameters of these sequences are described in Table I.

Image analysis. X-rays and MRI data were stored using the INFINITT PACS system (INFINITT Healthcare) and analyzed retrospectively by a radiologist with >10 years of experience with musculoskeletal imaging.

The Tailliard method was used to measure the slip distance on dynamic radiographs and MRI (11): The first line passes through the dorsal edges of the L5 vertebral body (line a), whereas the second line passes through the lower posterior margin of the L4 vertebral body and is parallel to the first line (line b). The distance between two lines where they pass through the upper ends of the lower vertebra is recorded as the slip distance (Figs. 1 and 2).

On dynamic radiographs, dynamic translation is calculated as the difference in displacement distance between maximal flexion and maximal extension in the same position; angular displacement is calculated as the difference in angle between the lower ends of the L4 vertebral body and the upper ends of the L5 vertebral body comparing maximal flexion and maximal extension in the same position (Fig. 1). Dynamic translation >5 mm or angular displacement >10° is defined as an unstable vertebral body slip (12-15). Based on these criteria, the study subjects were divided into two groups: The UG and the SG. The disk height was determined by calculating the Farfan Index, as the sum of the anterior and posterior border heights divided by the disk width as measured on the sagittal plane of T2W images (Fig. 2) (16). Facet fluid was measured perpendicular to the joint at the site of greatest volume on axial T2W images (Fig. 3) (17,18). The ligamentum flavum was measured at the joint surface level on axial T2W images (Fig. 3) (19). Quantitative values for disk signal, including minimum, maximum, and mean signal values, were obtained by placing a region of interest (ROI) ellipse in the center of the intervertebral disk on sagittal T1W and T2W images (Fig. 2).

Statistical analysis. Statistical analysis was performed using SPSS version 20 (IBM Corp). Quantitative variables are presented as the mean \pm SD. Qualitative variables are presented as the frequency and percentage. Differences between two quantitative variables were compared using an independent-samples Student's t-test. Normality was evaluated using the Kolmogorov-Smirnov test. A χ^2 test or Fisher's exact test were used to compare the distribution of sexes. P<0.05 was considered to indicate a statistically significant difference.

Receiver operating characteristic (ROC) curve analysis was used to evaluate quantitative variables that can be used to differentiate between two groups, and a cut-off value, the area under the curve (AUC), sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were obtained for significant predictive variables.

Results

Clinico-radiological characteristics of the patient population. A total of 58 patients with a definitive diagnosis of L4/L5 LDS without instability, as assessed using SLFE radiographs (SG, 58 cases, 71.6%), and 31 patients with instability based on SLFE radiographs (UG, 23 cases, 28.4%) were identified for study inclusion (Table II).

No significant differences were identified in the age or sex distribution between the SG and UG. X-ray-based measurements of dynamic translation and angular displacement were significantly higher in the UG than in the SG. The slip distance measured on MRI in the UG was 5.44±1.9 mm, which was larger than the distance measured in the SG of 5.11±2.2 mm; however, this difference was not significant.

MRI characteristics. The mean disk height of the UG was lower than that of the SG, but the difference was not significant. The mean facet joint was significantly thicker in UG than in the SG. The UG also displayed a thicker mean ligamentum flavum than the SG, but the difference was not significant. No significant differences in the minimum, maximum, or mean disk signal intensity values were measured on either T1W or T2W images between the UG and SG. However, these values tended to be lower in the UG than in the SG (Table III).

Based on the significant difference observed in the mean value of facet joint fluid thickness between the UG and SG, the ROC curve was analyzed, as shown in Fig. 4.

The mean facet fluid thickness was a significant predictor of the differential diagnosis between the SG and UG, with moderate accuracy (0.7<AUC=0.77<0.8) with Se, Sp, PPV, and NPV values of 73.9, 67.2, 69.3, and 69.77%. respectively.

Parameters	Repetition time, ms	Echo time, ms	Slice thickness, mm	Field of view, mm	Matrix
Sagittal T1W	600-700	20-30	4	160-250	256x256
Sagittal T2W	2000-3000	90-100	4	160-250	256x256
Coronal short tau inversion recovery	3000-3200	90-100	4	160-250	256x256
Axial T2W	2000-3000	90-100	4	160-250	256x256
T1W. T1-weighted imaging: T2W. T2-weig	hted imaging.	20 100	т	100 250	

Table I. Lumbar MRI parameters.



Figure 1. Dynamic translation on maximal extension and maximal flexion X-rays from one patient. The slip distances on (A) maximal extension and (B) maximal flexion X-rays were measured. The difference in the slip distance between the 2 positions was defined as the dynamic translation. Angular displacement on (C) maximal extension and (D) maximal flexion X-rays were measured. The angle created between the lower ends of the L4 vertebral body and the upper ends of the L5 vertebral body on extension and flexion X-rays was measured. The difference between the 2 positions was defined as the angular displacement.

Discussion

In the present study, the quantitative values obtained from MRI scans were analyzed to determine their relevance in the diagnosis of unstable L4/L5 degenerative spondylolisthesis. Although only facet joint fluid factor was the only statistically significant factor, other quantitative values between the two groups were compared, including the mean disk height, ligamentum flavum thickness, or disk signal intensity on T1W or T2W images. This study used ROC curves for mean facet joint fluid thickness assessment, which provided the area under the curve, cut-off value, Se, Sp, PPV, and NPV of quantitative values from MRI scans in the diagnosis of unstable L4/L5 degenerative spondylolisthesis.

LDS is a common cause of spondylolisthesis (20) that can occur in any spinal segment, but typically affects the L4/L5 level; 69% of cases, according to Cho et al (9) and 71.05% of cases according to Even et al (21) due to the large range of motion experienced at this spinal level. Kirkaldy-Willis and Farfan (22) proposed that lumbar degenerative diseases progress in three clinical stages: Transient dysfunction, followed by instability, and culmination in restability. A spinal instability diagnosis in LDS patients is essential for developing an appropriate treatment plan and evaluating the prognosis of the patient (23). Lumbar spinal instability is an independent risk factor for spinal surgery failure (24). Previous reports have defined the unstable LDS stage (also known as mobile LDS) according to changes in the slip distance and angular displacement on SLFE radiographs (12-15). In a study of 91 patients with LDS by Cho et al (9), the study sample was divided into two groups (SG and UG), with unstable LDS defined as a dynamic translation >5 mm or angular displacement $>10^{\circ}$ based on SLFE radiographs. Thus, this definition was applied to the 81 patients in the present study, resulting in 58 patients being categorized into the SG and 23 in the UG.

The present study showed that the mean age of the SG was higher than that of the UG, but this difference was not significant. This outcome is similar to that reported by Kuhns *et al* (8), who reported mean ages for the SG and UG of 67 and 64 years, respectively. However, Cho *et al* (9) showed a significant difference in age between the SG and UG, which were 62.2 and 65.3 years, respectively.

According to the present study, no significant difference was identified in the mean disk height. However, the UG had a larger mean disk height than the SG. This result was similar to that reported by Kuhns et al (8), who reported a larger mean disk height for the UG (0.70 mm) than for the SG (0.67 mm), although the difference was not significant. Disk height is correlated with the disk degeneration grade, with a larger degeneration grade associated with a smaller disk height. Cho et al (9) demonstrated that the average disk degeneration grade in the SG was significantly higher than that in the UG. Fujiwara et al (25) showed that the greatest range of motion was observed on SLFE films associated with grade III and IV disk degeneration, whereas spinal motion was reduced in patients with grade V disk degeneration. Hypertrophy of the ligamentum flavum is significantly correlated with disk and facet joint degeneration, which may be a predisposing factor for spinal instability (19). In the study by Yoshiiwa et al (19), the group with a ligamentum flavum thickness ≥ 4 mm

Characteristics	Stable group, n=58	Unstable group, n=23	P-value	
Age, years	58.93±10.2	57.22±9.7	0.486	
Sex, n (%)				
Male	19 (32.75)	3 (13.04)	0.422	
Female	39 (67.25)	20 (86.96)	0.432	
Plain films				
Dynamic translation, mm	1.93 ± 1.2	4.97±1.5	≤0.001ª	
Angular displacement, °	4.17±2.3	7.85±4.1	≤0.001ª	
Slip distance on the MRI scan, mm	5.11±2.2	5.44±1.9	0.53	
*P<0.001				

Table II. Clinico-radiological characteristics of the patient population.



Figure 2. Representative measurements from one patient. (A) Sagittal T2W images. The Tailliard method was used to measure the slip distance. (B) Sagittal T2W image. The Farfan Index was used to calculate disk height. Farfan Index=(anterior disk height-posterior disk height)/disk width. (C) Sagittal T1W image and (D) Sagittal T2W image. Regions of interest were placed in the center of the disks and the minimum, maximum, and mean signal values were obtained. T1W, T1-weighted; T2W, T2-weighted.



Figure 3. Facet fluid and ligamentum flavum thickness measurement. (A) Facet fluid thickness was measured as the length of a line perpendicular to the joint surface at the site of the thickest fluid on axial T2W. (B) The ligamentum flavum was measured at the joint surface level on axial T2W. T2W, T2-weighted image.

showed greater angular displacement than the group with a ligamentum flavum thickness <4 mm, although this difference was not significant. The authors concluded that hypertrophy of the ligamentum flavum may be a useful sign for diagnosing spinal instability on MRI scans. These results are similar to

the results of the present study. Although no significant difference was observed for the thickness of the ligamentum flavum between the UG and SG, the ligamentum flavum in the UG $(4.09\pm1.02 \text{ mm})$ was thicker on average than that of the SG $(3.70\pm1.17 \text{ mm})$.

Characteristics	Stable group, n=58	Unstable group, n=23	P-value	
Mean disk height, mm	0.45±0.15	0.52±0.58	0.381	
Mean facet fluid thickness, mm	0.89 ± 1.11	2.15±1.23	≤0.001ª	
Mean ligamentum flavum thickness, mm	3.70±1.17	4.09±1.02	0.144	
Disk signal T1W				
Min	226.66±135.9	189.70±162.98	0.342	
Max	341.55±171.96	306.39±168.53	0.405	
Mean	287.41±150.95	245.98±163.61	0.300	
Disk signal T2W				
Min	66.36±53.54	57.52±45.47	0.458	
Max	231.29±112.34	210.26±105.86	0.433	
Mean	171.34±225.36	145.27±69.99	0.591	

Table III. MRI characteristics.

^aP≤0.001. T1W, T1-weighted; T2W, T2-weighted; Min, minimum; Max, maximum.



Figure 4. ROC curve for mean facet joint fluid thickness (blue line). ROC, receiver operating characteristic.

In the present study, the mean facet joint fluid in the UG was significantly thicker than that in the SG. This result is in agreement with the results reported in previous studies. Chaput *et al* (17) demonstrated that facet joint fluid thickness ≥ 1 mm on MRI scans was indicative of an unstable LDS on SLFE radiographs. According to the study by Snoddy *et al* (26), an increase of 1 mm in facet joint fluid thickness increased the risk of spinal instability by 41.6% (95% CI: 1.8-97.0%), by contrast, facet joint fluid thickness ≤ 0.5 mm was associated with a 90% chance of spinal stability. Moreover, this previous study also reported a PPV of 30% for facet joint fluid thickness in detecting spinal instability (26). The study results reported by Kuhns *et al* (8) showed a significant difference in the facet joint fluid thickness between the UG and SG, with mean

values of 2.0 and 1.2 mm, respectively. The PPV of the facet joint fluid thickness for detection of an unstable lumbar spine increased from 52% with an effusion width >1 mm to 100% with an effusion width >3.5 mm. In addition, in the study by Lattig *et al* (18), the unstable LDS group had a larger mean facet joint fluid thickness value than the stable LDS group (1.77 vs. 0.10 mm). The results of the present study showed that the mean value of the facet joint fluid thickness could be used to differentiate the SG from the UG using a cut-off value of 1.45 mm with an AUC of 0.77, and a Se, Sp, PPV, and NPV of 73.9, 67.2, 69.3, and 69.77%, respectively. It is thus hypothesized that an increase in the facet joint fluid may be related to changes in spinal kinematics in weight-bearing positions, leading to an increased probability of spinal instability.

According to the present study, the minimum, maximum, and mean disk signal intensity values on both T1W and T2W images were lower in the UG than in the SG. However, these differences were not significant. By contrast, in the study by Cho *et al* (9), examining qualitative levels of disk degeneration described a significantly higher disk degeneration grade for the SG (3.96+0.88) than for the UG (3.0+0.77). Disk degeneration is caused by dehydration in the nucleus disk, leading to a reduced disk signal on T2W. A higher disk degeneration grade is associated with a lower disk signal on T2W (1).

The present study has some limitations. First, the study was performed using a small cohort, which may not be sufficiently representative of the overall population of individuals with LDS. Second, the use of a single L4/L5 evaluation may represent another weakness. Although this is the most common level associated with LDS, the conclusions drawn may not apply to patients with LDS at other levels or patients with multistage LDS. In addition, the measurement of facet joint fluid thickness on axial T2W images does not reflect the true 3D volume of facet joint fluid (17,18). The quantitative measurements of ROI signals were performed by a single radiologist in this study and may thus be subject to measurement error. In the future, similar studies with larger cohorts, and with data analysis performed by at least 2 radiologists, with the inclusion of assessments of different lumbar levels will be performed.

In conclusion, facet joint fluid thickness measured on axial T2W images may be predictive of an unstable LDS, especially if >1.45 mm. Therefore, when LDS is clinically suspected, the use of SLFE and MRI are recommended for diagnosis.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

NDHung, NTH, NTHA, NDM, and NDHue were the patient's physicians, and they reviewed the literature search, and contributed to acquisition, analysis and interpretation of data, and manuscript drafting. NDHung and NMD contributed to manuscript drafting and acquisition of data. NTH and NTHA analyzed and interpreted the imaging findings. NDHung and NDHue confirm the authenticity of all the raw data. All authors read and approved final version of this manuscript for publication.

Ethics approval and consent to participate

The institutional review board of Hanoi Medical University approved this retrospective study (approval no. 2444/QĐ-ĐHYHN). Due to the retrospective nature of this study, the requirement for informed consent was waived by institutional review board of Hanoi Medical University. The study was performed in accordance with the ethical standards of the responsible committee on human experimentation and in accordance with the guidelines described in the Declaration of Helsinki 1975, as revised in 2013.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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