

## Original Articles

Determinants of Hypertension Treatment Adherence during the COVID-19 Pandemic: Lesson Learned from Various Studies Sites in Indonesia

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## Correlation between Vertebral Slippage in Spondylolisthesis with Ligamentum Flavum Thickening in Dr. Soebandi Hospital, Jember, East Java, Indonesia

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### Abstract

**Background:** Spondylolisthesis is a vertebral slip condition that compromises the body's axial alignment and structures such as ligamentum flavum. The ligamentum flavum thickening may play a role in spondylolisthesis. The purpose of this study was to investigate the correlation between the slippage of vertebral body (spondylolisthesis) with ligamentum flavum thickening as a tissue response regarding increased mechanical stress.

**Methods:** An analytical retrospective radiological observational was used a cross-sectional study from the results of MRI examination in Dr. Soebandi Hospital, Jember, Indonesia, collected from 2018-2021 using the simple random sampling method. Ligamentum flavum thickness and the degree of vertebral slip were measured using T2-weighted MR imaging and the correlation was analyzed using Fisher's exact test.

**Results:** Of 102 spondylolisthesis data records, 34 were taken, being female was the most prevalent cases in the age group above 60 years, with the most vertebral segment shift occurring at the L4-L5 level. There was a significant correlation. ( $p = 0.02$ ;  $RR = 4.8$ ) between ligamentum flavum thickening and vertebral slip in spondylolisthesis.

**Conclusion:** The significant correlation between ligamentum flavum thickening and vertebral slip in spondylolisthesis suggest that mechanical stress has caused spondylolisthesis, by inducing chronic inflammation that results in hypertrophy of ligamentum flavum. Lumbar segmental instability due to spondylolisthesis is a factor contributing to the development of ligamentum flavum hypertrophy.

**Keywords:** Ligamentum flavum thickening, magnetic resonance imaging, spondylolisthesis

### Introduction

Ligamentum flavum (LF) plays a crucial role in intervertebral motion and intrinsic spinal stability in sitting and standing postures, as well as the protector of the posterior wall of the spinal canal and neural foramina.<sup>1-3</sup> In abnormal conditions such as increased mechanical stress and chronic inflammation, the LF undergoes several changes, such as hypertrophy.<sup>4-5</sup>

Spondylolisthesis is a slipping of the vertebra, however, the neural arch is still

intact. Spondylolisthesis may compromise the stability of spine and increase axial load that may stress surrounding structures. Previous studies have investigated the causes of spondylolisthesis, especially degenerative spondylolisthesis (DS). The most common potential risk factors identified are gender, activity level, body mass index (BMI), facet joint's sagittal orientation, mechanical stress in LF, and ligament hyperlaxity.<sup>6,7</sup> Tissue damage due to mechanical stress can be the initial trigger of the inflammatory reaction, which then develops into scar tissue, and

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accumulation of the scar tissue will result in LF hypertrophy.<sup>8,9</sup>

The stability of the spine is influenced by many things, one of which is the integrity of the ligamentous structures in the vertebrae. The ligamentum flavum (LF) is one of several ligaments that help support the stability of the vertebrae. In the event of spinal instability, the supporting elements of the vertebrae try to maintain spinal stability in various ways, one of which is tissue hypertrophy.<sup>10,11</sup>

This study was conducted to investigate whether there was a correlation between increasing slip degree of spondylolisthesis and LF thickening to prove that spondylolisthesis has caused LF hypertrophy.

## Methods

An analytical retrospective observational study was conducted in Dr. Soebandi Hospital, Jember, Indonesia, in January 2022. Data from MRI of patients diagnosed with spondylolisthesis by a radiologist from 2018 to 2021 were collected. The exclusion criteria were data from patients with incomplete medical records, spinal disorders other than spondylolisthesis (such as tumors, infection, and inflammatory spondylitis previous lumbar surgery), and traumatic spondylolisthesis.

Data were chosen using a simple random sampling method, with total sample size of 34 data patients for one-tailed correlation analysis with type 1 error ( $\alpha$ ) and type 2 error ( $\beta$ ) allowed up to 5% and 20%, respectively. The data were collected using the data collecting form by the variable investigator. Two independent investigators participated in this study and were educated to use the same measurement standards before the start of the study.

The vertebral slippage was measured using the mid-sagittal view of T2-weighted MRI images. Vertebral slippage was the relative horizontal displacement of the superior vertebral body over the inferior vertebral body. Meyerding classification was used to categorize the degree of slip. If more than 2 different levels were involved, the segment with the largest degree of slip was chosen. Conflicting results from two investigators were resolved by the third investigator.

Ligamentum flavum thickening was measured using axial view of T2-weighted MRI images, as shown in Figure 1. The level measuring by the investigator was the same as where the vertebral slippage was measured, in line with the facet joint of

the two vertebral bodies involved. LF was considered as thickened if its length was >4 mm. If there were more than 2 different levels involved, the segment with the largest degree of slip was chosen. Conflicting results from two investigators were resolved by the third investigators.

Research data were then tabulated into a Microsoft Excel worksheet (Microsoft Corp., Washington, USA) and statistically analyzed using Statistical Package for Social Science (SPSS) for Windows (version 24.0; IBM Corp., Armonk, NY). The continuous variables were categorized into pre-determined groups. Vertebral slip was categorized into 4 groups based on Meyerding Classification (grade I–IV). Ligamentum flavum thickening was categorized into 2 groups that is thickened (> 4 mm) and non-thickened group ( $\leq 4$  mm). The Fisher's exact test was used to analyze the correlation between LF thickening and vertebral slip in spondylolisthesis.

This study was approved by the Ethical Review Board of the Medical Faculty University of Jember, registration number 1573/H25.1.11/KE/2021. This study adhered to STROBE guidelines for reporting observational studies.

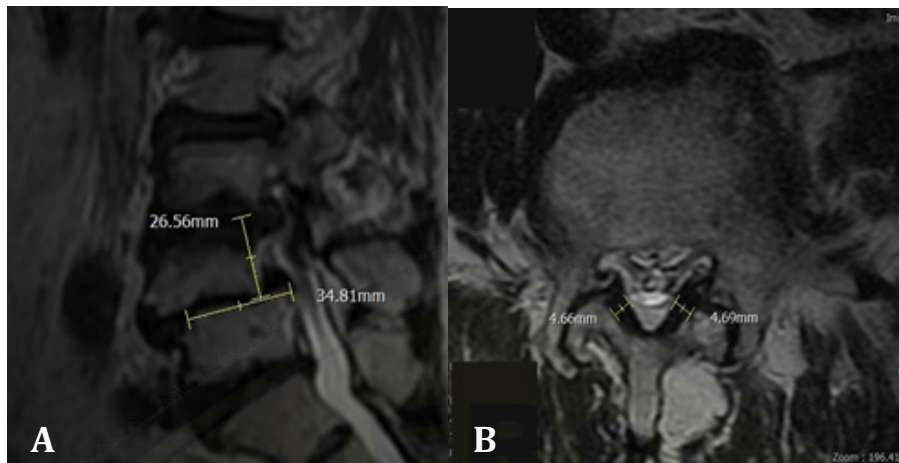
## Results

The spondylolisthesis cases between year 2018 and 2021 included 24% males and 76% females. The age group with the most spondylolisthesis cases was individuals over 60 years old (65%), followed by 41–60 years old patients (35%), and none were under 40

**Table 1 Characteristics of Patients with Spondylolisthesis in Dr. Soebandi Hospital, Jember, Indonesia year 2018 to 2021 (n=34)**

Characteristics	n (%)
Gender	
Male	8 (24)
Female	26 (76)
Age	
41–60	12 (35)
> 60	22 (65)
Level of slip	
L3–L4	5 (15)
L4–L5	23 (67)
L5–L6	1 (3)
L5–S1	5 (15)





**Figure 1 Lumbar MRI Demonstrated Anterior Vertebral Slippage (A) with Grade II Slippage, and Ligamentum Flavum Thickening (B) with 4.66 mm (Left Ligamentum Flavum) and 4.69 mm (Right Ligamentum Flavum) Thickness**

**Table 2 Vertebral Slip and LF Thickening Measurement Result**

Vertebral Slip Degree	Ligamentum Flavum Thickening		Total	p value	Risk Ratio
	Yes	No			
II	5 (100%)	0 (0%)	5	0.02	4.8
I	6 (20.7%)	23 (79.3%)	29		

years old. The level of vertebral slip mostly inflicted by spondylolisthesis was L4-L5 (67%), as shown in Table 1.

Measurement of vertebral slip and LF thickening showed that grade I spondylolisthesis was mostly non-thickened (79.3%). Interestingly, in grade II spondylolisthesis, all samples were thickened. The results showed a significant difference ( $p < 0.02$ ; Fisher's exact test), indicating a significant correlation between the increase in the degree of vertebral slip and the thickening of the LF. The risk ratio result showed that the degree of vertebral slip had a risk factor of 4.8 times for LF thickening (Table 2).

**Discussion**

Our study has shown that most spondylolisthesis patients are female (76%), consistent with the demographics of degenerative spondylolisthesis. This result might be due to ligament laxity and hormonal effects. Post-menopausal women experience an increased expression of estrogen receptors in their vertebral facet joints, therefore, in

post-menopausal women with degenerative spondylolisthesis, facet arthritis is more common than spinal stenosis. In addition, pregnancy is also thought to play a role in the occurrence of degenerative spondylolisthesis. During pregnancy, the spine stability is compensated due to an increased in body weight, and the center of mass of the body moves forward. Increased body mass will also increase stress on the facet joints, ligaments around the vertebrae, and the vertebrae themselves.<sup>13</sup>

Furthermore, the age of the patient plays a significant role, as shown in the result that the age group above 60 years is the highest incidence (65%), followed by the age group 41-60 years (35%).

The degenerative type of spondylolisthesis often occurs at over 40 and most commonly occurs in the sixth decade of life. The cause of spondylolisthesis might be due to a degenerative process that occurs later in life. The degenerative processes include degeneration of the intervertebral discs, arthritis of the facet joints, osteoporosis of the senile vertebrae, and degeneration of the ligaments that

support the spine. The degeneration process will cause instability in the spine, thus the alignment, especially the sagittal alignment, is disturbed. Impaired sagittal alignment is a state of spondylolisthesis.<sup>14</sup>

The location of the vertebral shift has shown that the most vertebral segment shift occurred at the L4–L5 level (67%). Spondylolisthesis, especially the degenerative type, mostly occurs at the L4–L5 level.<sup>15</sup> The anatomical reason that the L4–L5 is the most common location for degenerative spondylolisthesis is due to the orientation of the facet joints at that level. The facet joints at the L4–L5 level, which are sagittal oriented at an angle of more than 45 degrees, increase the risk of developing degenerative spondylolisthesis by 25 times. The occurrence of sacralization at L5 also increases the chance of dysplastic type spondylolisthesis at the L4–L5 level.<sup>7,15,16</sup>

Our study shows that there is a correlation between vertebral segment shift and ligamentum flavum thickening (p-value <0.05; Fisher's exact test), indicating that the greater the displacement of the vertebral segments, the greater the likelihood of thickening of the ligamentum flavum (RR= 4.8). The cadaveric study has shown that the integrity of the intervertebral disc and the strength of the ligaments supporting the spine must be compromised for significant spine instability to occur.<sup>17</sup> The integrity of the intervertebral disc is considered to have a more significant influence than the strength of the ligaments that support the spine.

The ligamentum flavum, especially in the lumbar spine, is prone to inflammation. The axial load of the lumbar spine is greater than the other segments. If there is instability in the spine, the ligamentous structure would be exposed to mechanical stress, and inflammation. Inflammation that occurs continuously or chronically will trigger the process of hypertrophy of the ligamentum flavum. Hypertrophy of the ligamentum flavum is the main cause of ligamentum flavum thickening.<sup>2,5,18–21</sup>

The distribution of vertebral displacement degrees found in this study consist of grade I and II and none in grade III and IV groups. This finding is in line with the findings found in degenerative spondylolisthesis. The slipping of the vertebral segments will be obstructed due to the intact posterior vertebral elements, in this case the neural arch.<sup>15</sup>

This study has several limitations that must be considered in the interpreting of the outcomes. Numerous factors contribute

to spondylolisthesis, including gender, age, body mass index, and history of pregnancy. To better understand the pathogenesis of spondylolisthesis, these additional factors should be included in future analyses.

In conclusion, there is a significant correlation between ligamentum flavum thickening and vertebral slip in spondylolisthesis, suggesting that mechanical stress has caused spondylolisthesis, by inducing chronic inflammation that results in hypertrophy of ligamentum flavum. Lumbar segmental instability due to spondylolisthesis is a factor contributing to the development of ligamentum flavum hypertrophy.

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