Journal of Research in Medical and Dental Science
2018, Volume 6, Issue 6, Page No: 121-127

Available Online at: www.jrmds.in
eISSN No.2347-2367: pISSN No.2347-2545

Evaluation of the Relationship between Ligamentum Flavum Thickness and Degenerative Changes in Lumbar Spinal Canal in MRI

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ABSTRACT

Background and Aims: Low back pain caused by degenerative diseases of the lumbosacral spinal canal and spinal canal stenosis is one of the major causes of disability and loss of one's efficiency. One of the abnormalities in the spinal canal structures is an increase in the thickness of ligamentum flavum. The aim of this study was to evaluate the relationship between ligamentum flavum thickness and degenerative changes in the lumbar spinal canal in MRI.

Materials and Methods: This cross-sectional and descriptive-analytical study was conducted on 225 patients who had MRI due to low back pain. The images of the patients were examined in different sequences and the degenerative changes and the ligamentum flavum thickness were measured at L1 to L5 levels. Then, the relationship of the ligamentum flavum with the two variables of gender and age in two groups of patients with and without degenerative changes as well as the relationship between the ligamentum flavum thickness and degenerative changes were evaluated.

Results: A total of 225 patients (127 males and 98 females) with a mean age of 47.63 ± 14.19 years participated in this research. The results of statistical tests revealed that ligamentum flavum thickness, except for L1-2 and L2-3, had a direct and significant correlation with patients with spinal canal degenerative changes and the levels were directly and significantly correlated with the variable of age. However, no significant relationship was found between the ligamentum flavum thickness and gender. The statistics also confirmed that patients with spinal canal degeneration had significantly higher LF thickness.

Conclusion: Increased thickness of LF is associated with exacerbated aging and spinal canal degeneration.

Key words: Degenerative changes, Ligamentum flavum, Spinal canal stenosis

HOW TO CITE THIS ARTICLE: Babak Shekarchi, Mohammad Momeni*, Evaluation of the relationship between ligamentum flavum thickness and degenerative changes in lumbar spinal canal in MRI, J Res Med Dent Sci, 2018, 6(6): 121-127

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Received: 09/11/2018
Accepted: 20/11/2018

INTRODUCTION

Low back pain caused by degenerative diseases of the lumbosacral spinal canal and spinal canal stenosis is a major cause of death, disability, and loss of individual efficiency [1]. Spinal canal abnormalities, such as an increase in ligamentum flavum thickness (yellow ligament), play an important role in spinal stenosis [2,3]. The ligamentum flavum covers a large part of the back wall and the lateral walls of the spinal canal [4]. Ligamentum flavum is composed of connective tissue and plays an important role in stabilizing the spinal canal, controlling the vertebral movement, and creating a smooth surface for the posterior rotation of the spinal canal [5]. As ligamentum flavum thickness can reduce the diameter of the spinal canal. This thickening is considered one of the causes of spinal canal stenosis [6]. The canal stenosis mechanically imposes pressure on the nerve roots and Cauda equina and this process can lead to low back pain and sciatic pain even in the absence of intervertebral disk pathologies [7].

With increasing the lifespan of the Iranian population and as a result of an increase in the proportion of middle-aged and elderly people, the spinal canal pain becomes a serious health problem. Given the slow progression of the disease, its diagnosis may be significantly delayed. Given the potential and destructive effects of this disease, its early diagnosis and treatment to achieve positive results is essential [1]. The pathogenesis of thickening of ligamentum flavum is not clear and it is not still clear that the thickening of the ligamentum flavum is due to hypertrophy or due to the protrusion of these ligaments into the canal, following the narrowing of the controversy inter-vertebral space [8]. In a normal ligamentum flavum, elastic fibers contain 70% of the ingredients, but in the hypertrophic ligament, the level of collagen is dominant [5]. The reason for the ligamentum flavum thickening is multifactorial, and it seems that changes in factors such as activity level, aging, and the level of mechanical stress to be involved in its development, but its definitive causes are still unclear [9,10]. Histopathological and immunological studies have investigated and identified

different mechanisms, involved in the development of hypertrophy. Mechanical stresses can cause tissue damage, followed by infiltration of inflammatory factors and the formation of scar. They can finally lead to ligamentum hypertrophy [5]. Cases such as intervertebral disk pathologies and osteoarthritis of fast joints are among the mechanical stresses, which affect soft tissues such as ligamentum flavum [3,11]. According to a search on databases of Pubmed Medline, Science Direct, Google Scholar and Scopus, limited studies have been conducted to evaluate the potential impact of factors such as age, gender, and degenerative changes on the ligamentum flavum thickness. This study was conducted to assess the effect of these factors on the degree of thickening of the ligamentum. A similar study in this regard was not found in Iran. Hence, the objective of this study was to evaluate the different demographic and pathologic factors around ligamentum flavum to clarify the effect of these factors on the degree of ligamentum thickening.

MATERIALS AND METHODS

The present study is a cross-sectional type of descriptive-analytical study. This study was conducted from 2016 to 2017 on 225 patients underwent MRI due to low back pain and admitted to Golestan Hospital. Patients with a history of surgery or did not have good quality images due to the artifact were excluded from the study. Based on the previous studies and after applying the inclusion and exclusion criteria, 225 people were selected and included in the study. Subjects included in the study voluntarily and by observing the principles of medical ethics and after obtaining consent form from all patients and with full knowledge of the research process. The patient's MR images were evaluated by an experienced radiologist on a digital workstation. LF thickness measurement and intervertebral disc degeneration were reviewed for all patients at levels of L1-L2, L2–L3, L3–L4, L4–L5, and L5–S1. The maximum thickness of the LF was measured bilaterally on axial T2W images at the facet joint level. To reduce measurement errors the measurements were repeated three times and mean values were used. In cases of asymmetrical LF thickness, we used the thicker value. Intervertebral disc degeneration was characterized by a reduction in disc height and signal intensity and evaluated by the same radiologist from L1–L2 to L5–S1 levels on the T2 sequence at midsagittal images. The raw data were entered into IBM SPSS Statistics 23 software. Then, the data normality was examined for all variables and suitable statistical tests were used based on the normality state. In this study, Independent Samples T-Test and Pearson Correlation were used to analyzing the data. Non-parametric Mann-Whitney U test and Spearman Correlation tests were used and significant level was considered less than 0.05 (P-value<0.05). The sample size in this study was calculated to be at least 225 patients based on the statistical formula (1) of the sample size calculation and considering the variability of the prevalence of findings in different studies and considering the maximum number of samples in descriptive-analytical studies and by considering confidence level of 95% (Z1-α/2=1.96) and the error level of 0.05.

$$n=[Z2 \times P(1-P)]/d^2 \quad (1)$$

RESULTS

Out of 225 patients participated in this study, 127 were male and 98 others were female. The mean age of male subjects (the age range of them was between 16 years and 89 years) was reported in this study to be 48.42 ± 14.97 years. In the present study, the age range of females was 19 to 79 years with a mean age of 46.61 ± 15.03 years. The level of ligamentum flavum thickness at different levels of the lumbar spinal canal was evaluated based on age in patients with and without degenerative spinal canal changes. After determining the normality of the data, KS test was used and correlation test was used to measure the correlation between the quantitative data of age and ligamentum flavum thickness at this level and the results were determined separately at five levels of L1 to L5.

At level 1 (L1), 21 patients had degenerative changes and 204 patients had no degenerative changes in the spinal canal. Individuals without degenerative changes in the spinal canal were classified into different age groups and the mean thickness of the right and left L1 ligamentum flavum was calculated. The results of this nonparametric Spearman test showed that there is a significant correlation between age and right and left level 1 ligamentum flavum in patients without degenerative changes (P-value<0.05). This means that with increasing the age, the ligamentum flavum thickness also significantly increases in these patients (Table 1 and Figure 1).

Table 1: Descriptive data on ligamentum flavum thickness in level 1 (L1) lumbar spinal canal based on age in patients without degenerative changes in spinal canal

Level	Age Groups	N	Mean	SD	Min	Max
Right L1 thickness	10-20	3	1.7667	0.23094	1.5	1.9
	21-30	29	1.8621	0.37836	1.2	3.2
	31-40	47	2.0447	0.45674	1.2	4.2
	41-50	52	2.2173	0.30788	1.3	3.2
	51-60	34	2.2706	0.30104	1.2	2.8

	61-70	26	2.4692	0.26649	2.1	3.1
	71 through highest	13	2.6692	0.3146	2.3	3.3
	Total	204	2.1902	0.41177	1.2	4.2
Left L1 thickness	10-20	3	1.7667	0.35119	1.4	2.1
	21-30	29	1.7759	0.3952	1.1	3.1
	31-40	47	1.9638	0.38189	1.2	3.6
	41-50	52	2.2442	0.32018	1.2	3.4
	51-60	34	2.2794	0.33465	1.1	2.8
	61-70	26	2.5	0.26382	2.1	3.2
	71 through highest	13	2.6	0.37859	1.9	3.2
	Total	204	2.1672	0.42479	1.1	3.6

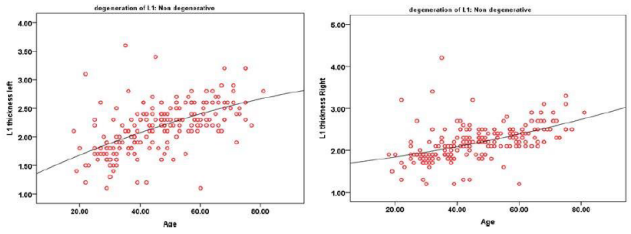

Figure 1: Distribution of ligamentum flavum thickness in level 1 (L1) of lumbar spinal canal based on age in patients

The ligamentum flavum thickness in different levels of the lumbar spinal canal was also followed up based on age of patients with degenerative changes in the spinal canal. Accordingly, based on the group with no degenerative changes in the spinal canal, the subjects were first divided into different age groups with age interval of 10 years and the mean thickness of the ligamentum flavum in the L1 to L5 level was investigated. Then, the correlation between the quantitative variables of age and the quantitative variable of the Ligamentum flavum thickness was analyzed by statistical tests. After examining the descriptive data, the correlation between the age and thickness of the ligamentum flavum in the left and right L1 levels was evaluated using Pearson correlation parametric statistic. The results of this statistical test showed that in patients with degenerative changes in the spinal canal, there was no significant correlation between age and thickness of ligamentum flavum in L1 (P-Value>0.05). This finding suggests that in this group of patients, age variations did not have much effect on the thickness of the flavum (Table2).

Table 2: Correlation between the ligamentum flavum thickness in the level 1 (L1) lumbar spinal canal and age variable in patients with and without degenerative changes in spinal canal

Correlation: degenerative (L1)			
Age variable		**L1 thickness Right**	**L1 thickness left**
Age	Pearson Correlation	-0.1	-0.282
	P-Value	0.667	0.216
	N	21	21
Correlations: Non degenerative (L1)			
Age variable		**Right L1 thickness**	**Left L1 thickness**
Age	Correlation Coefficient	0.615	0.616
	P-Value	0	0
	N	204	204

At level 2 (L2), 35 patients had degenerative changes and 190 patients had no degenerative changes in the spinal canal. The results of the Spearman non-parametric statistical test indicate that there is a significant correlation between age and ligamentum flavum thickness in the left and right L2 in patients without degenerative changes (P-value<0.05). In other words, it can be stated that with increasing age, the ligamentum flavum thickness also significantly increases in these patients (Table 3).

Table 3: Correlation between the level of ligamentum flavum thickness in the level 2 (L2) of lumbar spinal canal and age variable in patients without degenerative changes of spinal canal

Correlations: Non degenerative (L2)			
Correlation		**Right L2 thickness**	**Left L2 thickness**
Spearman	Correlation Coefficient	0.634	0.643
	P-Value	0	0
	N	190	190

To evaluate the L2 level, the normal distribution of data was first examined by the K-S test. Then, to examine the correlation between the age and ligamentum flavum thickness in the right level 2 (L2), the Pearson correlation test was used and to test the correlation between the age and ligamentum flavum thickness in the left level 2 (L2), Spearman's non-parametric statistical test. After examining the descriptive data, it was found that there was no significant correlation between age and ligamentum flavum thickness in the left and right L1 in patients with degenerative changes in the spinal canal (P-value>0.05).

At level 3 (L3), 119 patients had degenerative changes and 106 patients had no degenerative changes in the spinal canal. Based on the results, with increasing age, the ligamentum flavum thickness also significantly increased in these patients, indicating that there is a significant correlation between age and L3 (left and right) ligamentum flavum thickness in patients without degenerative changes (P-value<0.05). In addition, the results of the Spearman nonparametric test showed a significant correlation between age and flavum thickness in the left and right L3 level in patients with degenerative changes (P-value<0.05). In other words, with increasing age, the ligamentum flavum thickness also significantly increases in these patients.

At level 4 (L4), 156 patients had degenerative changes and 69 patients had no degenerative changes in the spinal canal. The results of this statistical test showed a significant correlation between age and left level 4 ligamentum flavum thickness in patients without degenerative changes (P-value<0.05). Moreover, the results of the Spearman test showed a significant correlation between the age and right and left level 4 ligamentum flavum thickness in patients with degenerative changes in the spinal canal (P<0.05). At level 5 (L5), 135 patients had degenerative changes and 90 patients had no degenerative changes in the spine. The results of non-parametric statistical test revealed a significant correlation between age and left and right L5 ligamentum flavum in patients without degenerative changes (P-value<0.05) and with increasing the age, ligamentum flavum thickness also significantly increases in this group of patients, indicating a significant correlation between age and L5 (left and right) ligamentum flavum thickness in patients with degenerative changes (P-Value<0.05).

Overall, mean thickness of ligamentum flavum in patients with degenerative changes was more than 3 mm, except for L1 level, while in patients with non-degenerative changes it was lower than 3 mm (Table 4).

Table 4: The relationship between ligamentum flavum thickness at all lumbar levels and degenerative changes in spinal canal

Level of ligamentum flavum thickness	Degeneration state of Lumbar level	N	Mean	SD	Mean Rank	P-Value
Right L1 thickness	Non degenerative	204	2.1902	0.41177	105.9	0.001
	degenerative	21	2.8095	0.53376	181.93	
left L1 thickness	Non degenerative	204	2.1672	0.42479	104.91	0.001
	degenerative	21	2.8952	0.47273	191.6	
Right L2 thickness	Non degenerative	190	2.3405	0.38885	98.18	0.001
	degenerative	35	3.1543	0.43274	193.43	
left L2 thickness	Non degenerative	190	2.3047	0.41061	97.92	0.001
	degenerative	35	3.1429	0.42515	194.87	
Right L3 thickness	Non degenerative	106	2.3405	0.36924	62.87	0.001
	degenerative	119	3.1543	0.45535	157.65	
left L3 thickness	Non degenerative	106	2.3047	0.35856	62.45	0.001
	degenerative	119	3.1429	0.46346	158.03	
Right L4 thickness	Non degenerative	69	2.4565	0.26979	41.29	0.001
	degenerative	156	3.4929	0.65255	144.72	

left L4 thickness	Non degenerative	69	2.3348	0.30861	42.02	0.001
	degenerative	156	3.3846	0.63012	144.39	
Right L5 thickness	Non degenerative	90	2.37	0.31138	57.81	0.001
	degenerative	135	3.3452	0.71045	149.8	
left L5 thickness	Non degenerative	90	2.31	0.2953	54.21	0.001
	degenerative	135	3.2963	0.68463	152.19	

After determining the normality of the data using KS test, independent t-test and non-parametric Mann-Whitney U test were used for measuring the ligamentum flavum thickness in different levels of lumbar spinal canal based on gender in patients with and without degenerative changes in the spinal canal. The results of this statistical analysis in both the degenerative and non-degenerative groups at each of the 5 levels revealed that there was no significant difference between females and males in the ligamentum flavum thickness variable (P value>0.05). This result suggests that the gender variable does not play a role in determining the ligamentum flavum thickness and these two variables are completely independent of each other.

Finally, the relationship between the level of ligamentum flavum thickness (at L1 to L5 levels) and degenerative changes of the spinal canal was investigated. In this regard, the data at L1 to L5 levels were evaluated in terms of normal distribution of data using K-S test. Then, Mann-Whitney U non-parametric test was used to examine the relationship between ligamentum flavum thickness and degenerative changes in spinal canal. The results of this statistical test show a significant difference between the level of ligamentum flavum thickness (L1 to L5 levels) and degenerative changes of the spinal canal (P-value <0.05). The highest level of ligamentum flavum thickness at different levels in both groups belongs to the L4 and L5 levels (Table 4).

DISCUSSION

The complication of degenerative changes in the spinal canal means gradual loss of the structure and function of the spinal canal over time [12]. These problems usually increase with increasing the age [13]. However, it might be developed as a result of some other factors, such as tumor, infection, or arthritis [14]. Among the common causes of low back pain is the spinal canal stenosis (LSS) seen more in middle-aged and elderly people [15]. Congenital canal stenosis, disc herniation, increased ligamentum flavum thickness, vertebral osteoarthritis and spondylolisthesis are among the most important factors in the development of stenosis in the spinal canal [16]. The results of this study showed that at level 1 (L1), 21 patients had degenerative changes and 204 patients had no degenerative changes in the spinal canal. The results of the statistical test showed a significant correlation between the age and thickness of the left and right L1 ligamentum flavum thickness in patients without degenerative changes, while statistical analyses showed that in patients with degenerative changes in the spinal canal, there is no significant correlation between age and ligamentum flavum thickness in left and right l1.

At level 2 (L2), 35 patients had degenerative changes and 190 patients had no degenerative changes in the spinal canal. Investigations suggest that with increasing age, the ligamentum flavum thickness is significantly increased in these patients. In other words, in this group of patients, there is a significant correlation between the age and left and right L2 ligamentum flavum thickness in patients without degenerative changes, but the studies showed that there was no significant correlation between age and ligamentum flavum thickness in the right and left L2 of patients with degenerative changes in the spinal canal. At level 3 (L3), 119 patients had degenerative changes and 106 patients had no degenerative changes in the spinal canal. At level 4 (L4), 156 patients had degenerative changes in the spinal canal and 69 patients had no degenerative changes in spinal canal. At level 5 (L5), 135 patients had degenerative changes in the spinal canal and 90 patients had no degenerative changes in the spinal canal. At these three levels, the results of the statistical test showed that there is a significant correlation between age and left and right ligamentum flavum thickness in patients with and without degenerative changes.

In the second stage of the analyses, the ligamentum flavum thickness at different levels of the lumbar spinal canal was investigated in male and female patients with and without degenerative changes of spinal canal. Thus, people with degenerative changes in the spinal canal were first separated from subjects without these changes. Then, in each group, the ligamentum flavum thickness was measured at the five levels of the lumbar spinal canal between males and females. The results of this statistical investigation in both degenerative group and the non-degenerative group at all levels (L1 to L5) revealed that there was no statistically significant difference between females and males in the ligamentum flavum thickness variable. In the third stage, this study investigated the relationship between the level of ligamentum flavum in different levels and degenerative changes in spinal canal. The results of this study showed a significant difference between ligamentum flavum thickness (L1 to L5 levels) and degenerative changes in the spinal canal. Ligamentum flavum thickness was significantly increased in subjects with degenerative changes in spinal canal compared with other subjects.

Mattar et al. conducted a study in 2014 entitled "Ligamentum flavum thickness" and its association with

disk degeneration. This study was conducted on 98 patients with chronic pain in low back and MRI was used to measure LF thickness. The degree of disk degeneration was measured by using Pfirrmann grading system in the mentioned study. In the mentioned study, the relationship between LF hypertrophy, disk degeneration, age and gender was evaluated. They reported the highest thickness between L4-L5. They also reported that women in L3 and L4 have more ligamentum thickness than men. However, they stated that there was no statistically significant relationship between the LF thickness and disk degeneration [7]. In our study, both degenerative and non-degenerative groups showed the highest thickness between L4 and L5, and only in the patients with degenerative changes, women had thicker ligamentum in L3 and L4 compared to men. Hence, the results of these two studies are in line with each other. In another part of their study, they reported that there was no statistically significant relationship between the LF thickness and disk degeneration, while a significant relationship was found between LF thickness and disk degeneration at all levels in our study.

Cheung et al. in 2016 published reports of an original research under the title of "The relationship between hypertrophy of ligamentum flavum and lumbar spinal stenosis". In his research, patients who had surgery for lumbar spinal stenosis were included in the study. The diameter of the spinal canal was measured in MRI. In addition, the degree of disk degradation and thickness of LF were measured from L1 to S1, and LF samples of surgery were studied for the histological evaluation of fibrotic degree and the fibrosis level. Their results showed a strong correlation between the thickness of LF and the spinal canal diameter in the non- progressive canal stenosis (NON-DSS) (right: $r=0.98$ and $p<0.001$) (left: $r=0.92$ and $p<0.01$). Data indicated that there the correlation is poor in people with weaker DSS (only in L5-S1) and in people with severe DSS, there is no statistically significant correlation between LF thickness and spinal canal diameter. The results of their study showed a significant negative correlation between LF thickness and the fibrotic degree in both severe DSS and relative DSS groups. Conversely, in the NON-DSS group, there was a positive and significant correlation between LF thickness and fibrosis [11].

Although the variables and research design of the study conducted by Cheung et al. [11] are similar with those of the current study, it can be discussed in one aspect. In their study, in subjects with a weaker DSS, a significant relationship was found between the LF thickness and spinal canal diameter only in L5-S1, and in our study, LF thickness in patients group was associated with degenerative changes, that is, lower levels of L3, 4, 5 were associated with age. This can mean that the size of the LF thickness at lower lumbar levels can provide a clearer picture with greater differentiation power and it would better reveal the relationship between the LF thickness and the other variables examined.

Safak et al. evaluated the effect of age and gender on the thickness of LF at lower lumbar levels using magnetic resonance imaging (MRI) in an analytical study. They determined the thickness of 1280 ligaments in 320 patients at L4-L5 and L5-S1 levels using MRI. At the end of the study, the researchers observed that no significant difference among the males and females in LF thickness ($P>0.05$). They also reported a correlation between age and LF thickness. In addition, the LF thickness in the two-way L5-S1 was significantly higher than the corresponding L4-L5 side ($P<0.05$) [17]. This study is similar to our study in many aspects. In our study, except for L1 and L2 levels in patients with degenerative changes, there was a statistically significant relationship between age of patients and LF thickness, so that with increasing age, the LF thickness also increases. In addition, in our study, no significant difference was found between males and females in the thickness of LF. While this study is in line with some other studies, some significant differences are seen, especially in the relationship between disc degeneration and LF thickness. These differences can be attributed to factors such as sample size, technical parameters in the measurement, the studied population, exclusion, and inclusion criteria, diagnostic limits, measurement errors and analyses, and so on.

CONCLUSIONS

It is concluded that LF thickness is directly correlated with age variable, so that with increasing the age, the LF thickness also increases and this increase occurs more in lower levels of spinal canal. In addition, an increase in LF thickness is correlated with spinal canal degeneration, so that patients with spinal canal degeneration had LF with more thickness. The research results also suggest that gender has no role in LF thickness change, meaning that there is no difference between males and females in measured thickness.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests.

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