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Clinical implications of lumbar developmental spinal stenosis on back pain, leg pain and disability

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1

2 **ABSTRACT**

3 **Aims**

4 To study the associations of lumbar developmental spinal stenosis (DSS) with low back pain  
5 (LBP), radicular leg pain and disability.

6

7 **Patients and Methods**

8 This was a cross-sectional study of 2206 subjects with L1-S1 axial and sagittal magnetic  
9 resonance imaging (MRI). Clinical and radiological information regarding subjects'  
10 demographics, workload, smoking habit, anteroposterior (AP) vertebral canal diameter,  
11 spondylolisthesis, and other MRI phenotypes was assessed. Mann-Whitney *U* tests and Chi-  
12 square tests were conducted to search for differences between subjects with and without DSS.  
13 Associations of LBP and radicular pain in the past month and the past year with the clinical  
14 and radiological information were also investigated by utilizing univariate and multivariate  
15 logistic regressions.

16

17 **Results**

18 Subjects with DSS had higher prevalence of radicular leg pain, more pain-related disability and  
19 lower quality of life (all  $p < 0.05$ ). Subjects with DSS had 1.5 (95% CI: 1.0-2.1;  $p = 0.027$ ) and  
20 1.8 (95% CI: 1.3-2.6;  $p = 0.001$ ) times higher odds of having radicular leg pain in the past month  
21 and the past year, respectively. However, DSS was not associated with LBP. Instead, subjects

1 with spondylolisthesis had 1.7 (95% CI: 1.1-2.5; p=0.011) and 2.0 (95% CI: 1.2-3.2; p=0.008)  
2 times more likely to experience LBP in the past month and the past year, respectively.

3

#### 4 **Conclusion**

5 This large-scale study identified DSS as a possible risk factor of acute and chronic radicular  
6 leg pain. There is an increased likelihood of nerve root compression due to a pre-existing  
7 narrowed canal. These subjects are also more likely to have poorer disability and quality of life.

8

9 **Key Words:** Lumbar; developmental spinal stenosis; spondylolisthesis; back pain; leg pain

10 **Level of Evidence:** Type I prognostic study

11

#### 12 **Clinical relevance**

13 1. Developmental spinal stenosis is a risk factor for acute and chronic radicular leg pain, and  
14 worse disability

15 2. Developmental spinal stenosis is a predictor of radicular pain, and spondylolisthesis is a  
16 predictor of low back pain

## 1 INTRODUCTION

2 Lumbar developmental spinal stenosis (DSS) is described as pre-existing narrowed  
3 vertebral canals at multiple lumbar levels<sup>1-4</sup>. The prevalence of DSS in the general population  
4 is unknown, and diagnostic cut-offs from imaging has been variable<sup>2,4-6</sup>. A large amount of  
5 studies also focused on defining DSS radiologically<sup>2,5-10</sup>, but only a few investigated its clinical  
6 course and implications<sup>11,12</sup>. Subjects with DSS are often found to have earlier onset of  
7 symptoms during their fourth or fifth decades<sup>13</sup>. Due to the canal narrowing, mild degenerative  
8 changes are already sufficient to compress the neural elements leading to an earlier onset of  
9 symptoms. As DSS is likely a developmental problem, there is a risk for multi-level  
10 compression. This is an important factor to consider in spinal stenosis surgery as patients with  
11 DSS have a high reoperation rate at nonoperative levels of up to 22%<sup>3,14,15</sup>. Nonoperated DSS  
12 levels may predispose to symptoms at a later stage even if they are considered asymptomatic  
13 at the index operation.

14 Low back pain (LBP) and radicular leg pain are two of the most common health  
15 problems around the world<sup>16-18</sup>. They bring about deterioration in one's quality of life, mental  
16 health disturbance, and increased public health burden<sup>19-21</sup>. However, LBP is generally  
17 nonspecific<sup>22</sup> and in these cases, the underlying cause is often unrecognizable. One of the  
18 leading causes of these symptoms is compression of the nerve roots in patients with stenotic  
19 lumbar canals<sup>12,23</sup>. Identification of their radiological phenotypes with magnetic resonance  
20 imaging (MRI) is currently the gold standard<sup>24,25</sup> and is imperative for identifying the potential  
21 source of LBP or radicular leg pain. Many MRI phenotypes are found to be possible pain  
22 generators when studies investigated in their individual effects, including dural sac cross-  
23 sectional area<sup>26</sup>, disc degeneration and herniation<sup>22,27,28</sup>, facet joint degeneration<sup>29</sup>, radial tears<sup>30</sup>,  
24 high intensity zone (HIZ)<sup>31</sup>, and Modic changes<sup>32,33</sup>. However, the contribution of DSS in  
25 generating pain is obscure.

1           Therefore, this study was designed to address the aforementioned unknowns regarding  
2 the contribution of DSS to different clinical outcomes namely LBP, radicular leg pain and  
3 disability.

## 4 5 **METHODS**

### 6 *Study Design and Population*

7           This was a prospective large-scale study of 2206 Chinese subjects from the Hong Kong  
8 Disc Degeneration Cohort Study<sup>2,6,31,34-36</sup>. All subjects were openly recruited via newspapers  
9 advertisement, posters and e-mails, regardless of their social and economic status. The study  
10 call was for any participant who agreed to a study on the lumbosacral spine with MRI, clinical  
11 questionnaires and follow-up assessments. Participants with prior surgical treatment of the  
12 spine, spinal tumours and fractures, and marked spinal deformities were excluded from the  
13 study. Subjects selected were not based on the presence or absence of clinical symptoms. All  
14 qualified subjects underwent T1-weighted axial MRI and T2-weighted sagittal MRI of the  
15 lumbosacral spine (L1-S1) after informed consent was obtained from participants and ethics  
16 was approved by a local institutional board.

### 17 18 *Low Back Pain and Radicular Leg Pain*

19           Information related to LBP and radicular leg pain was recorded as follows: age of onset,  
20 any pain experienced in the past month (30 days) and the past year (365 days). Symptoms in  
21 the past month was considered acute pain and symptoms in the past year was considered  
22 chronic pain. LBP was defined as pain localizing in the lower back and/or buttocks. Radicular  
23 leg pain was defined as any pain radiating from the lower back/buttocks which can reach one  
24 or both lower extremities, can be beyond the knee, and usually in a dermatomal pattern that  
25 may be associated with numbness and paresthesia<sup>37</sup>. Visual analog scale (VAS) was utilized to

1 measure the worst LBP experience since the day of onset. The severity of LBP was subdivided  
2 into 3 categories according to previously published criteria<sup>31,38</sup>: no or mild pain (VAS < 3),  
3 moderate pain (VAS 3 – 5.9), and severe pain (VAS ≥ 6).

#### 4 5 *Lifestyle Factors and Disability*

6 Age, gender, height and weight were obtained on the day of MRI. Body mass index  
7 (BMI) was calculated by weight/height<sup>2</sup> (kg/m<sup>2</sup>). Information on smoking habit, regular  
8 exercise and occupation was surveyed. Occupation was characterized into different subgroups  
9 based on the physical workloads<sup>31,33</sup>: 1 = sedentary work (lifting 10 lbs); 2 = light work (lifting  
10 20 lbs); 3 = medium work (lifting 50 lbs); 4 = heavy or very heavy work (lifting ≥100 lbs).  
11 Pain-related disability was assessed by the Oswestry Disability Index (ODI)<sup>39</sup> and the Roland  
12 Morris Disability Questionnaire (RMQ)<sup>40</sup>. Quality of life was assessed by the 36-Item Short  
13 Form Survey (SF-36)<sup>41</sup>. An ODI of ≥15% was noted as pain-related disability<sup>38</sup>.

#### 14 15 *MRI Protocol*

16 1.5T or 3T MRI machines were used for axial and sagittal imaging at L1-S1. Subjects  
17 were oriented in the supine position. For T1-weighted axial scans, the field of view was  
18 21cm×21cm, slice thickness was 4mm, slice spacing was 0.4mm, and imaging matrix was  
19 218×256. For T2-weighted sagittal scans, the field of view was 28cm×28cm, slice thickness  
20 was 5mm, slice spacing was 1mm, and imaging matrix was 448×336. The repetition time for  
21 T1- and T2-weighted MRI were 500ms-800ms and 3320ms respectively, and their echo time  
22 was 9.5ms and 85ms. According to the pedicle and disc levels, 11 parallel slices were made at  
23 each spinal level. The MRI protocol has been described in further details elsewhere<sup>2</sup>.

#### 24 25 *MRI Measurements*

1 Two independent investigators were blinded to all demographical and clinical data  
2 before and during MRI measurements. Methodologies on obtaining the measurements were  
3 aligned before the assessment. Forty MRI films were randomly selected by a third independent  
4 investigator for repeated measurements which were at least 4 weeks after the initial  
5 measurements. This data was used to assess the intraobserver and interobserver reliability.

6 The cut with the thickest pedicle diameter, pedicle, lamina and vertebral body was  
7 utilized for every T1-weighted axial MRI. The following measurements were obtained for L1-  
8 S1 axial MRI: anteroposterior (AP) vertebral canal diameter (Figure 1) and left and right facet  
9 joint angle (Figure 2). Facet joint angle was the angle made by a line joining the corners of the  
10 facet joint and the transverse plane. Facet joint angulation of greater than  $58^\circ$  at L4-L5 was  
11 regarded as abnormal<sup>42</sup>. Facet joint tropism was noted if the absolute difference between left  
12 and right facet joint angle was greater than  $8^\circ$  based on the definition by Samartzis *et al*<sup>42</sup>.

13 T2-weighted sagittal MRI was acquired at the midsagittal cut with the most prominent  
14 lumbar spinous processes. The following measurements were obtained for L1-S1: presence of  
15 disc herniation, disc degeneration<sup>43</sup>, endplate irregularity, high intensity zone (HIZ)<sup>31,44</sup> (Figure  
16 3), radial tear, spondylolisthesis (Figure 3), Modic change and anterior marrow change<sup>45</sup>. Disc  
17 herniation was further divided into 4 categories: 0 = no disc herniation; 1 = posterior disc  
18 bulging (disc displaced beyond a virtual line connecting the posterior edges of two adjacent  
19 vertebrae); 2 = disc extrusion (distance between the edge of the protruded disc into the spinal  
20 canal was greater than the distance between edges of the base of the disc); 3 = disc  
21 sequestration<sup>31,32,46</sup>. The scores of each lumbar level were added up as disc herniation score  
22 and further categorized into two subgroups<sup>31</sup>: disc herniation score of  $<2$  (no or mild disc  
23 herniation) and disc herniation score of  $\geq 3$  (moderate to several disc herniation). Disc  
24 degeneration was evaluated using the Pfirrmann grading<sup>43</sup>: 1 = homogeneous bright white disc;  
25 2 = inhomogeneous white disc and/or horizontal bands; 3 = inhomogeneous grey disc; 4 =



1 inhomogeneous grey to black disc; 5 = inhomogeneous black disc. The scores of each lumbar  
2 level were added up as disc degeneration score and further categorized into two subgroups:  
3 disc degeneration score of <16 (no or mild disc degeneration) and disc degeneration score of  
4  $\geq 16$  (moderate to severe disc degeneration)<sup>47</sup>. Endplate irregularity was described as an  
5 irregular surface at the endplates. HIZ was defined as a high-intensity area of the anterior or  
6 posterior annulus fibrosus<sup>31,48,49</sup>. Radial tear was noted as a hyperintense line in the annulus  
7 fibrosus. Spondylolisthesis was characterized by anterior displacement of the cranial vertebral  
8 body on the caudal vertebra but all patients in this cohort were grade 1<sup>50</sup>. Modic change was  
9 described as signal intensity change involving the whole or middle posterior of the vertebral  
10 body adjacent to the endplates, while anterior marrow change was described as high-signal  
11 intensity change at the anterior vertebral body adjacent to the endplates. The presence of  
12 endplate irregularity, HIZ, radial tear, spondylolisthesis, Modic change and anterior marrow  
13 change were defined as one or more radiological findings of their respective entities throughout  
14 the entire lumbar spine. Dichotomizing these variables are more relevant to a clinical setting.

15

#### 16 *Definition of Lumbar Developmental Spinal Stenosis*

17 The definition of DSS used in this study was developed by using “multi-level” values  
18 generated from those proposed by Cheung *et al*<sup>2</sup>. We wanted to establish a multi-level cut-off  
19 as patients with DSS often have multi-level stenosis. Subjects with AP vertebral canal diameter  
20 below those proposed values in 3 or more levels were considered as DSS cases. Three levels  
21 were decided because for multiple levels of decompression for example a L4-S1  
22 decompression surgery, two stenotic levels are included which equates to three vertebral levels  
23 of L4, L5 and S1. After identifying the subjects who fulfilled the proposed canal diameters at  
24 multi-levels, new cut-off values were defined by the level-specific median of these cases with  
25 the best sensitivity and specificity. Hence, the proposed cut-off for DSS was inclusion of 3 or

1 more lumbosacral levels with L1<19mm, L2<19mm, L3<18mm, L4<18mm, L5<18mm,  
2 S1<16mm.

3

#### 4 *Statistical Analysis*

5         Frequency and descriptive statistics were performed for all variables. Normality testing  
6 was performed. For detecting differences between DSS and non-DSS subjects, Mann-Whitney  
7 *U* tests were performed for continuous independent variables including age, BMI, mean ODI,  
8 mean RMQ, mean SF-36, axial AP vertebral canal diameter and left and right facet joint angle,  
9 while chi-square tests were used for categorical independent variables including gender,  
10 smoking habit, regular exercise, physical workload, LBP within the past month and the past  
11 year, LBP intensity, radicular leg pain within the past month and the past year, pain-related  
12 disability, abnormal left and right facet joint angulation, facet joint tropism, disc herniation  
13 score, disc degeneration score, presence of endplate irregularity, HIZ, radial tear,  
14 spondylolisthesis, Modic change, and anterior marrow change. Means and ranges were also  
15 calculated for all T1-weighted axial MRI measurements. Intraobserver and interobserver  
16 reliability assessments were based on Cronbach  $\alpha$  analysis:  $\alpha$  values of 0.90 to 1.00 was noted  
17 to have excellent reliability;  $\alpha$  values of 0.80 to 0.89 was noted to have good reliability<sup>51</sup>.

18         Univariate logistic regressions were then conducted to detect any association between  
19 individual independent variables and clinical outcomes (LBP in the past month and the past  
20 year, and radicular leg pain in the past month and the past year). All demographics, lifestyle  
21 factors and MRI measurements except AP vertebral canal diameter were included as  
22 independent variables as it was used to dichotomize subjects into DSS and non-DSS. Variables  
23 that were statistically significant ( $p<0.05$ ) in the univariate logistic regressions were included  
24 to build four multivariate logistic regression models based on the four clinical outcomes (LBP  
25 in past month and year, and radicular leg pain in past month and year), after controlling for age,

1 gender, and BMI. These models were used to assess the association of lifestyle factors together  
2 with MRI phenotypes with LBP and radicular leg pain experienced in the past month and the  
3 past year. As no published article demonstrated the best prediction equation in a similar  
4 situation, stepwise regression was used in these models to explore for possible impactful factors.  
5 Adjusted odds ratios (OR) and 95% confidence interval (CI) were obtained from these models.

6 A P-value of less than 0.05 was considered as statistically significant. All statistical  
7 analyses were performed by SPSS Statistics 26 (IBM SPSS Inc., Chicago, Illinois).

## 9 **RESULTS**

10 Among 2206 subjects, 153 were identified to have DSS. Descriptive and frequency  
11 statistics in subjects with and without DSS were presented in Table 1 and Table 2. Excellent  
12 interobserver ( $\alpha = 0.90 - 0.96$ ) and intraobserver reliability ( $\alpha = 0.92 - 0.99$  and  $\alpha = 0.92 -$   
13  $0.99$ ) between the two independent investigators were noted. Associations of DSS with  
14 demographics, lifestyle factors, and MRI phenotypes were also presented. Subjects with DSS  
15 were noted to have narrower spinal canals and more likely to be females (75.8%). They also  
16 have higher VAS which inferred more severe pain, higher incidence of radicular leg pain both  
17 in the past month and past year, higher average ODI, RMQ, and higher physical component  
18 score in SF-36. In addition, abnormal right facet joint angulation, higher disc herniation score  
19 and higher disc degeneration score were associated with DSS. When stratified by age, subjects  
20 with DSS had more endplate irregularity in the >50 age group but otherwise had similar  
21 prevalence of other MRI features, LBP and radicular leg pain (Table 3).

22 The results of the univariate logistic regressions on LBP are listed in appendix A.  
23 Statistically significant association of LBP in the past month with spondylolisthesis was  
24 observed. The significant variable was used to conduct a multivariate logistic regression  
25 analysis (Table 4) which reached statistical significance (Chi square (4, n=2160) = 10.605;

1 p=0.031). After adjusting for gender, age and BMI, subjects with spondylolisthesis (adjusted  
2 OR: 1.683; 95% CI: 1.125-2.517; p=0.011) had higher odds of LBP in the past month. Similarly,  
3 age and spondylolisthesis were associated with LBP in the past year. These independent  
4 variables were used to conduct a multivariate logistic regression analysis (Table 4) which  
5 reached statistical significance (Chi square (4, n=2163) = 17.061; p=0.002). After adjusting for  
6 gender, age and BMI, subjects with spondylolisthesis (adjusted OR: 1.967; 95% CI: 1.191-  
7 3.248; p=0.008) also had higher odds of LBP in the past year.

8 The results of the univariate analyses on radicular leg pain is listed in appendix B.  
9 Gender, age, BMI, workload and DSS were associated with radicular leg pain in the past month.  
10 These independent variables were included in a multivariate logistic regression analysis (Table  
11 5) which reached statistical significance (Chi square (7, n=2209) = 50.314, p<0.001). After  
12 adjusting for gender, age and BMI, subjects with heavy workload (adjusted OR: 1.822; 95%  
13 CI: 1.118-2.970; p=0.016) and DSS (adjusted OR: 1.482; 95% CI: 1.047-2.097; p=0.027) had  
14 higher odds of radicular leg pain in the past month. Similarly, gender, age, BMI and DSS were  
15 associated with radicular leg pain in the past year. Table 5 shows the statistically significant  
16 multivariate logistic regression analysis involving these significant independent variables with  
17 radicular leg pain in the past year (Chi square (7, n=2088) = 54.570, p<0.001). After adjusting  
18 for gender, age and BMI, subjects with DSS (adjusted OR: 1.807; 95% CI: 1.276-2.559;  
19 p=0.001) had higher odds of radicular leg pain in the past year. If the significant factors were  
20 removed from the above models, their effects were shown by the changes in -2 log likelihood  
21 (all p<0.05).

22

## 23 **DISCUSSION**

24 LBP and radicular leg pain are common health conditions that one may experience  
25 during his/her lifetime. It is observed that these clinical presentations are often poorly

1 associated with the imaging profiles<sup>52,53</sup>, except for HIZ and Modic changes which are  
2 relatively well-documented<sup>48,54</sup>. Besides, patients with DSS have multiple pre-existing  
3 narrowed vertebral canals which predisposed them to a lower threshold of neural compression.  
4 This was further proven by our results which showed these subjects were associated with a  
5 shorter AP vertebral canal diameter at L1-S1 ( $p < 0.001$ ). It is thought that these patients are  
6 more likely to experience pain even if a milder degree of degenerative changes of the lumbar  
7 spine is present. Our large-scale study shows that subjects with DSS had higher risks of  
8 radicular leg pain in the past month and the past year.

9 We compared the clinical outcomes in subjects with and without DSS. The former  
10 group had higher prevalence of radicular leg pain in the past month ( $p = 0.008$ ) and the past year  
11 ( $p = 0.001$ ). This may be attributed to the narrowed spinal canal that is more prone to nerve root  
12 compression, leading to radicular pain. Besides, these subjects were also associated with higher  
13 pain-related disability scores (ODI and RMQ) and lower quality of life (SF-36), specifically  
14 for the physical component score. Similarly, Lee et al<sup>55</sup> observed the majority of the patients  
15 with DSS undergoing surgery had lower quality of life and poorer clinical presentation  
16 including more severe and incapacitating pain, shorter walking distance, poorer sitting  
17 endurance, and muscle weaknesses. Regarding other MRI phenotypes, we observed several  
18 associations such as an abnormal right facet joint angulation with DSS. However despite  
19 reaching statistical significance, the left facet joint angulation and any facet joint tropism were  
20 not associated with DSS. Due to the small number of subjects between each group ( $n = 2$  and  
21  $n = 3$ ), the association of one side facet joint angulation with DSS is likely spurious. It was also  
22 found that subjects with DSS were more prone to disc herniation and disc degeneration, as  
23 suggested by their higher scores. Although statistically significant, the absolute differences  
24 between groups were small and might not be clinically relevant.

1           Our large-scale study was also able to obtain clinical information for both acute and  
2 chronic LBP and radicular leg pain. Pain lasting for less than 6 weeks is defined as acute, while  
3 pain lasting for more than 12 weeks is noted to be chronic<sup>56</sup>. DSS appeared to be one of the  
4 significant predictive factors for acute and chronic radicular leg pain, along with female gender,  
5 older age, and larger BMI. After adjusting for demographics, subjects with DSS had higher  
6 odds of having chronic radicular leg pain (adjusted OR: 1.807; 95% CI: 1.276-2.559; p=0.001)  
7 compared to acute radicular leg pain (adjusted OR: 1.482; 95% CI: 1.047-2.097; p=0.027). Our  
8 multivariate analysis was consistent with the results in Table 1 and this could be attributed to  
9 the developmental origin of DSS, as the canal size is reported to be unchanged after puberty  
10 and skeletal maturity<sup>13</sup>. DSS leads to a circumferential constriction of the neural tissue<sup>57</sup> and  
11 as such is an event that occurs at young age. Patients are predisposed to acute events such as  
12 disc herniation or chronic events such as facet joint hypertrophy. These are individuals with  
13 worse disability and pain scores, and may benefit from early intervention. It is fortunate to have  
14 a cohort of individuals without previous spine interventions to identify these associations.  
15 Although not a true population cohort due to the advertised recruitment, its large-scale nature  
16 reflects the importance of DSS in radicular symptoms. This is especially important as the  
17 prevalence of DSS is not small. Patients with DSS have been shown to develop multi-level  
18 stenosis and high reoperation rate at adjacent non-operated levels.<sup>3</sup> Individuals who may have  
19 screening radiographs or MRI should be informed of this risk factor.<sup>6</sup> Subjects with narrower  
20 spinal canals are more likely to experience nerve root compression and chronic pain.

21           DSS was not found to be associated with LBP in the past month and the past year  
22 despite more likely to develop VAS  $\geq 6$  (p=0.013). Unlike radicular pain which essentially  
23 means nerve root compression, LBP is not as clear in its character or presentation<sup>22,58</sup>. LBP can  
24 be caused by many other pathologies such as intervertebral disc disruption, facet joint and  
25 sacroiliac joint disruption, ligament or muscle strain, and idiopathic causes. It can also be

1 caused by nerve root compression.<sup>59</sup> A clinical study by Dai *et al*<sup>23</sup> examining the preoperative  
2 clinical symptoms in patients with DSS observed similar results, in which they realized more  
3 patients experienced radicular leg pain or sciatica than LBP. The cause for LBP must be  
4 investigated carefully. Interventions for disc herniations and other degenerative disorders often  
5 do not lead to favorable outcomes.<sup>60,61</sup> For spondylolisthesis, it is important to identify any  
6 mechanical instability before attributing the cause of LBP to it. Dynamic radiographs capture  
7 excessive motion, which reflects the mechanical LBP patients experience clinically during  
8 movement. The concept of instability in spondylolisthesis is crucial for the success of any  
9 intervention. Stable slips may not require fusion surgery but unstable slips documented by  
10 dynamic radiographs may fare better with fusion surgery.<sup>62,63</sup> Stabilizing an unstable segment  
11 may lead to better relief of LBP.<sup>64</sup> Instead, subjects with spondylolisthesis were found to have  
12 a higher risk of having chronic LBP after adjusting for demographics. Among all of its  
13 etiologies, degeneration is the most common form of spondylolisthesis seen in adults due to  
14 facet joint strain<sup>65</sup>. Acute causes such as trauma could also lead to fractures and dislocation at  
15 the posterior elements, but this is more likely in a children cohort<sup>66</sup>. Therefore, chronic pain is  
16 more likely to be found in our study cohort. Our findings are also supported by a meta-  
17 analysis<sup>67</sup> that noticed significant association between spondylolisthesis and LBP in both  
18 occupational-based studies (OR: 2.21; 95% CI: 1.44-3.39) and community-based studies (OR:  
19 1.12; 95% CI: 1.03-1.23).

20       There are several limitations to this study. Firstly, our results may not be generalizable  
21 in other ethnicities as only Chinese subjects were recruited. However, this is beneficial to the  
22 strength of exploration as it limits potential unknown confounders between ethnic groups.  
23 Secondly, we cannot conclude any causative relationships between the independent variables  
24 and clinical outcomes. Thirdly, as subjects were openly recruited via advertisements, the  
25 proportion of males and females were not equally distributed. However, we have adjusted for

1 this in our analyses. In addition, this method of sampling subjects may not be representative of  
2 the true population as individuals who respond to advertisements may be inherently biased. It  
3 will be useful to follow-up these subjects to observe the impact of lifestyle factors and MRI  
4 phenotypes on clinical outcomes. Changes in intensity of pain across time is also of interest to  
5 understand the complete picture.

6

## 7 **CONCLUSION**

8 This large-scale study examined the associations of DSS with LBP and radicular leg  
9 pain. After adjusting for demographics, subjects with DSS had higher likelihood of radicular  
10 leg pain in the past month and the past year. They are also associated with greater pain-related  
11 disability. The multi-level involvement in subjects with DSS should be identified early as these  
12 patients are prone to developing nerve compression symptoms. Individuals should know of  
13 their risk for radicular pain as these symptoms may require surgical intervention. Future  
14 longitudinal studies are necessary to understand the associations between different phenotypes  
15 and pain, and to observe the changes in clinical presentation over time.



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1 Table 1. Associations of Developmental Spinal Stenosis with Subjects' Demographics, Lifestyle Factors, and MRI Phenotypes

	DSS	Non-DSS	P-value
Number of Subjects	n=153	n=2053	
Gender (N, %)			
Male	37 (24.2%)	810 (39.5%)	<0.001*
Female	116 (75.8%)	1243 (60.5%)	
Mean Age, years (range)	51.9 (22.9-71.9)	51.1 (16.7-86.3)	0.307
Mean Body Mass Index, kg/m <sup>2</sup> (range)	23.7 (15.9-33.6)	23.2 (14.2-39.6)	0.121
Smoking Habit (N, %)			
Smoker	10 (6.6%)	234 (11.4%)	0.067
Non-smoker	142 (93.4%)	1817 (88.6%)	
Regular exercise (N, %)			
Yes	40 (26.8%)	641 (31.5%)	0.232
No	109 (73.2%)	1391 (68.5%)	
Workload (N, %)			
Sedentary Work	8 (5.6%)	132 (6.6%)	0.177
Light work	82 (57.3%)	984 (49.5)	
Medium Work	48 (33.6%)	727 (36.6%)	
Heavy Work	5 (3.5%)	145 (7.3%)	
LBP in Past Year (N, %)			
Yes	120 (78.4%)	1470 (71.6%)	0.069
No	33 (21.6%)	583 (28.4%)	
LBP in Past Month (N, %)			
Yes	92 (60.5%)	1159 (56.6%)	0.351
No	60 (39.5%)	887 (43.4%)	
LBP Intensity (N, %)			
No or Mild Pain (VAS < 3.0)	40 (27.0%)	699 (34.8%)	0.013*

Moderate Pain (VAS 3.0-5.9)	25 (16.9%)	436 (21.7%)	
Severe Pain (VAS $\geq$ 6.0)	83 (56.1%)	876 (43.6%)	
Radicular Leg Pain in the Past Year (N, %)			
Yes	83 (54.2%)	821 (40.0%)	0.001*
No	70 (45.8%)	1232 (60.0%)	
Radicular Leg Pain in the Past Month (N, %)			
Yes	61 (40.1%)	611 (29.9%)	0.008*
No	91 (60.0%)	1435 (70.1%)	
Average Oswestry Disability Index (ODI)	13.7 (0.0-75.6)	10.2 (0.0-86.0)	0.012*
Average Roland Morris Disability Score	3.4 (0.0-23.0)	2.5 (0.0-21.0)	0.042*
Average 36-Item Short Form Survey Score			
Physical Component Score	28.5 (15.4-38.1)	29.9 (13.2-78.0)	0.001*
Mental Component Score	41.4 (27.6-51.6)	41.1 (21.4-52.0)	0.588
Physical Functioning	46.9 (21.5-57.1)	49.2 (15.2-57.2)	<0.001*
Physical Role Functioning	44.7 (28.0-56.2)	46.9 (6.2-56.2)	0.035*
Bodily Pain	45.4 (19.9-62.7)	46.7 (19.9-62.7)	0.137
General Health Perception	40.5 (17.2-62.6)	41.9 (17.2-64.0)	0.095
Vitality	48.6 (23.0-70.4)	49.1 (5.2-70.4)	0.457
Social Role Functioning	47.3 (19.1-57.1)	48.0 (13.7-67.1)	0.540
Emotional Role Function	43.6 (23.7-55.3)	44.4 (23.7-66.3)	0.696
Mental Health	45.0 (16.4-64.1)	45.1 (9.6-64.1)	0.783
Pain-related Disability			
ODI < 0.15	47 (31.8%)	518 (26.0%)	0.125
ODI $\geq$ 0.15	101 (68.2%)	1475 (74.0%)	
MRI Phenotypes			
Presence of Abnormal Right Facet Joint Angulation; N (%)	2 (1.3%)	3 (0.1%)	0.004*

Presence of Abnormal Left Facet Joint Angulation; N (%)	1 (0.7%)	3 (0.1%)	0.155
Presence of Facet Joint Tropism; N (%)	40 (26.1%)	546 (26.6%)	0.903
Average Disc Herniation Score (range)	2.5 (0-10)	2.1 (0-12)	0.029*
Presence of Moderate to Severe Disc Herniation ( $\geq 3$ )	71 (46.4%)	811 (39.5%)	0.093
Average Disc Degeneration Score (range)	15.6 (7-21)	15.0 (5-23)	0.011*
Presence of Moderate to Severe Disc Degeneration ( $\geq 16$ )	87 (57.6%)	931 (45.8%)	0.005*
Presence of Endplate Irregularity; N (%)	41 (26.8%)	443 (21.6%)	0.132
Presence of High Intensity Zone; N (%)	52 (34.0%)	679 (33.1%)	0.817
Presence of Radial Tear; N (%)	12 (7.8%)	151 (7.4%)	0.824
Presence of Spondylolisthesis; N (%)	11 (7.2%)	106 (5.2%)	0.347
Presence of Modic Change; N (%)	36 (23.5%)	458 (22.3%)	0.727
Presence of Anterior Marrow Change; N (%)	28 (18.3%)	356 (17.3%)	0.765

*\*Statistically significant at 0.05 level.*

n, number of subjects; LBP, low back pain; VAS, visual analog scale.

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1 Table 2. Associations of Developmental Spinal Stenosis with Continuous Axial MRI Phenotypes

	DSS (range)	Non-DSS (range)	P-Value of Mann-Whitney <i>U</i> Tests
Number of Subjects	n=153	n=2053	
Mean Anteroposterior Vertebral Canal Diameter, <i>mm</i>			
L1	19.4 (16.7-22.0)	21.3 (17.2-29.6)	<0.001*
L2	18.8 (15.3-22.7)	21.0 (17.1-30.2)	<0.001*
L3	18.1 (14.7-22.4)	20.5 (15.5-29.3)	<0.001*
L4	17.5 (14.9-21.4)	20.2 (14.1-28.9)	<0.001*
L5	17.4 (14.1-24.4)	20.3 (12.7-32.3)	<0.001*
S1	16.1 (11.2-21.4)	18.8 (9.4-30.3)	<0.001*
Mean Right Facet Joint Angle, °			
L1-L2	57.1 (38.5-69.2)	56.1 (35.4-74.7)	0.029*
L2-L3	53.7 (31.6-68.4)	53.0 (31.8-69.4)	0.100
L3-L4	47.1 (31.0-66.0)	46.2 (23.7-65.6)	0.116
L4-L4	40.8 (25.4-62.1)	38.1 (16.1-61.0)	<0.001*
L5-S1	35.6 (14.3-54.2)	34.1 (12.8-62.9)	0.006*
Mean Left Facet Joint Angle, °			
L1-L2	58.1 (38.8-69.9)	57.0 (38.1-72.5)	0.032*
L2-L3	54.6 (34.3-70.6)	53.7 (33.1-72.7)	0.040*
L3-L4	48.1 (30.1-65.0)	46.6 (24.7-67.5)	0.005*
L4-L4	41.7 (27.7-59.3)	38.9 (12.0-60.1)	<0.001*
L5-S1	36.3 (18.0-58.6)	34.7 (11.0-60.0)	0.008*
*Statistically significant at 0.05 level. n, number of subjects; DSS: Developmental spinal stenosis.			

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1 Table 3. Presence of MRI phenotypes and pain in DSS subjects stratified by age

Age groups (years)	≤40 (n=17)	41 – 50 (n=33)	51 – 60 (n=87)	61 – 75 (n=16)	p-value <sup>^</sup>
MRI Phenotypes	Counts (n) per group				
Presence of Abnormal Right Facet Joint Angulation	0	1	1	0	0.678
Presence of Abnormal Left Facet Joint Angulation	0	0	1	0	1.000
Presence of Facet Joint Tropism	7	6	26	1	0.069
Disc Herniation Score (≥ 3)	8	17	40	6	0.834
Disc Degeneration Score (≥ 16)	9	19	50	9	0.975
Presence of Endplate Irregularity	1	6	24	10	0.002*
Presence of High Intensity Zone	7	11	30	4	0.823
Presence of Radial Tear	3	0	6	3	0.027*
Presence of Spondylolisthesis	2	1	7	1	0.692
Presence of Modic Change	1	8	21	6	0.181
Presence of Anterior Marrow Change	5	4	14	5	0.220
Pain	Counts (n) per group – n (column percentage)				
LBP in Past Year					
Yes	15 (88.2%)	24 (72.7%)	69 (79.3%)	12 (75.0%)	0.617
No	2 (11.8%)	9 (27.3%)	18 (20.7%)	4 (25.0%)	
LBP intensity					
No or Mild Pain (VAS < 3.0)	4 (26.7%)	9 (27.3%)	24 (28.6%)	3 (18.8%)	0.670
Moderate Pain (VAS 3.0-5.9)	2 (13.3%)	3 (9.1%)	15 (17.9%)	5 (31.3%)	
Severe Pain (VAS ≥ 6.0)	9 (60.0%)	21 (63.6%)	45 (53.6%)	8 (50.0%)	
Radicular Leg Pain in the Past Year					
Yes	11 (64.7%)	11 (33.3%)	52 (59.8%)	9 (56.3%)	0.053
No	6 (35.3%)	22 (66.7%)	35 (40.2%)	7 (43.8%)	
LBP in the Past Month					
Yes	9 (52.9%)	19 (57.6%)	56 (52.9%)	9 (9.7%)	0.737
No	8 (47.1%)	14 (42.4%)	31 (35.6%)	7 (43.8%)	

Radicular Leg Pain in the Past Month					1
Yes	6 (35.3%)	8 (24.2%)	41 (47.1%)	7 (43.8%)	0.141 2
No	11 (64.7%)	25 (75.8%)	46 (52.9%)	9 (56.3%)	3 4 5
					6

7 ^ Chi-square test or Fisher's exact test if expected cell count < 5

1 Table 4. Multivariate Binary Logistic Regression Analysis of the Association of LBP with Lifestyle Factors and MRI Phenotypes

Predictors	Regression Coefficient	Wald Chi-square	P-values	Odds ratio	95% CI	Change in -2 log likelihood
<b>Low Back Pain in the Past Month</b>						
Gender (Reference: Male)	-0.078	0.734	0.392	0.925	0.774-1.105	N/A
Age	-0.008	2.568	0.109	0.993	0.983-1.002	N/A
Body Mass Index	-0.002	0.020	0.887	0.998	0.973-1.024	N/A
Spondylolisthesis	0.520	6.412	0.011*	1.683	1.125-2.517	6.753*
<b>Low Back Pain in the Past Year</b>						
Gender (Reference: Male)	0.000	0.000	0.999	1.000	0.820-1.219	N/A
Age	-0.015	8.348	0.004*	0.985	0.974-0.995	N/A
Body Mass Index	0.014	0.908	0.341	1.014	0.985-1.044	N/A
Spondylolisthesis	0.676	6.978	0.008*	1.967	1.191-3.248	7.965*
*Statistically significant at 0.05 level.						
MRI; magnetic resonance imaging; CI, confidence interval; N/A, not available; DSS, developmental spinal stenosis.						

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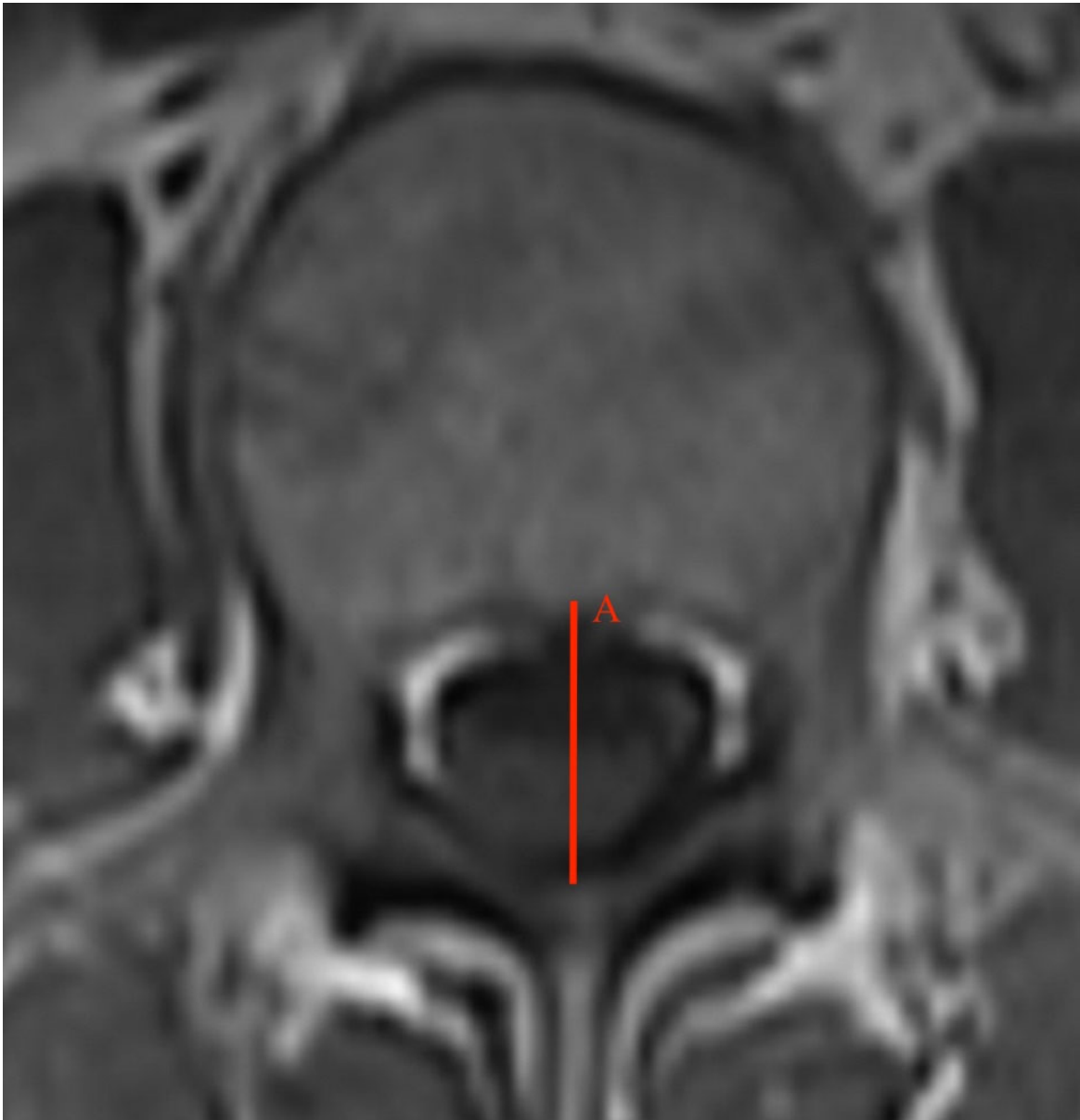
1 Table 5. Multivariate Binary Logistic Regression Analysis of the Association of Radicular Leg Pain with Lifestyle Factors and MRI Phenotypes

Predictors	Regression Coefficient	Wald Chi-square	P-values	Odds ratio	95% CI	Change in -2 log likelihood
<b>Radicular Leg Pain in the Past Month</b>						
Gender	-0.341	11.447	0.001*	0.711	0.583-0.866	N/A
Age	0.012	5.405	0.020*	1.013	1.002-1.023	N/A
Body Mass Index	0.034	5.796	0.016*	1.035	1.006-1.064	N/A
Workload (Reference: Sedentary Work)		16.901	0.001*			16.650*
Light work	-0.088	0.198	0.656	0.916	0.621-1.351	
Medium Work	0.169	0.713	0.398	1.185	0.799-1.755	
Heavy Work	0.600	5.803	0.016*	1.822	1.118-2.970	
Presence of DSS	0.393	4.922	0.027*	1.482	1.047-2.097	4.800*
<b>Radicular Leg Pain in the Past Year</b>						
Gender	-0.252	7.065	0.008*	0.777	0.645-0.936	N/A
Age	0.009	2.966	0.085	1.009	0.999-1.019	N/A
Body Mass Index	0.045	10.831	0.001*	1.046	1.019-1.075	N/A
Workload (Reference: Sedentary Work)		16.690	0.001*			16.745*
Light work	-0.359	3.768	0.052	0.698	0.486-1.003	
Medium Work	-0.116	0.380	0.538	0.890	0.616-1.288	
Heavy Work	0.278	1.342	0.247	1.321	0.825-2.115	
Presence of DSS	0.592	11.128	0.001*	1.807	1.276-2.559	11.214*
*Statistically significant at 0.05 level.						
MRI; magnetic resonance imaging; CI, confidence interval; N/A, not available; DSS, developmental spinal stenosis.						

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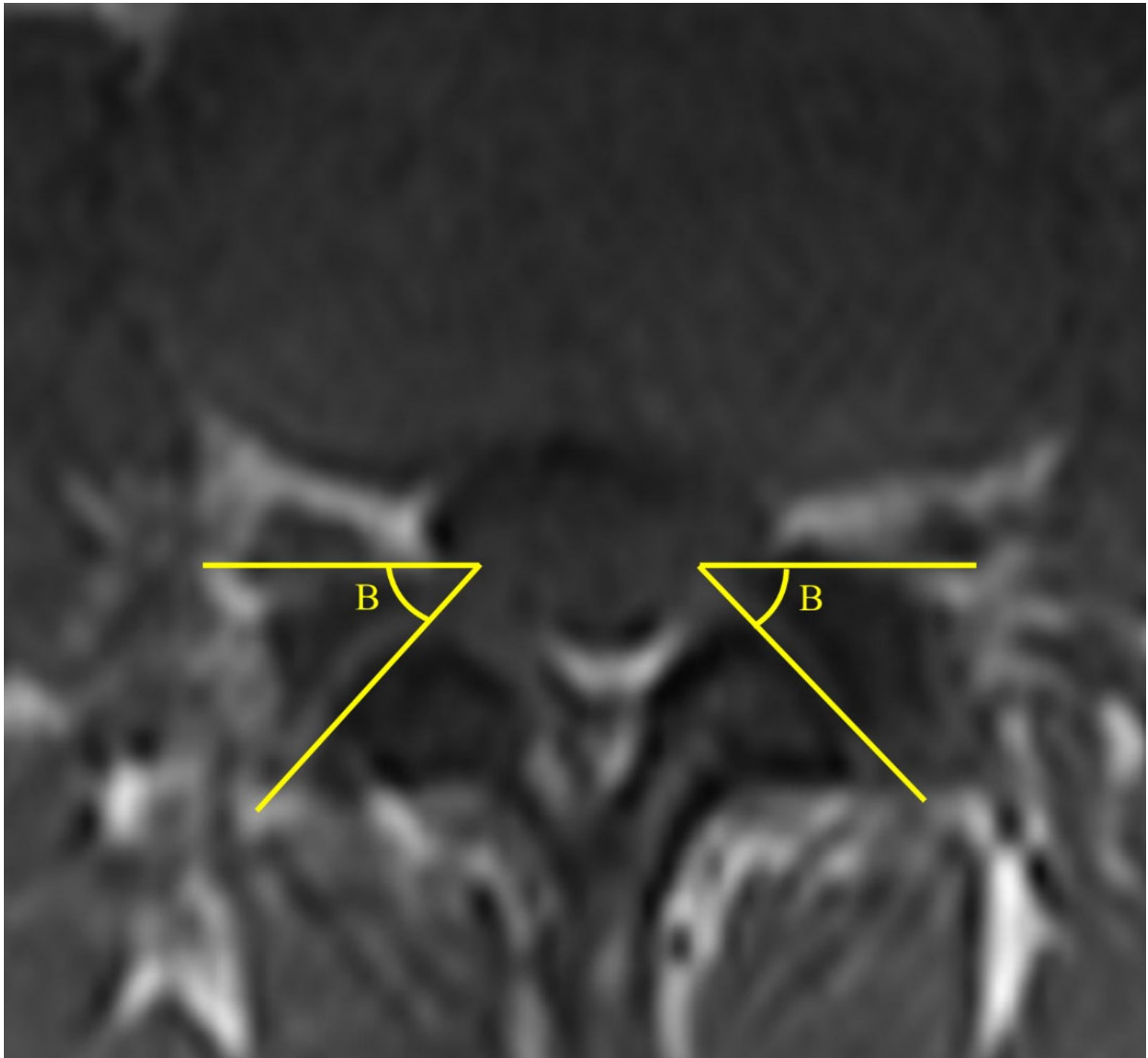
1 **FIGURE LEGENDS**



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3 **Figure 1:** Axial magnetic resonance imaging measurement: (A) anteroposterior (AP) vertebral

4 body diameter.



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2 **Figure 2:** Axial magnetic resonance imaging measurement: (B) left and right facet joint angle  
3 (made by a line joining the corners of the facet joint and the transverse plane).

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3 **Figure 3:** Sagittal magnetic resonance imaging: (C) High intensity zones (high-intensity area  
4 of the anterior or posterior annulus fibrosus); (D) Spondylolisthesis (anterior displacement of  
5 the cranial vertebral body on the caudal vertebra).

1 Appendix A. Univariate Binary Logistic Regression for Association between Independent Variables and Low Back Pain

Imaging Parameters	With or Without LBP in this Month			With or Without LBP in this Year		
	Yes, N (%)	No, N (%)	Unadjusted Odds Ratio (95% CI)	Yes N (%)	No N (%)	Unadjusted Odds Ratio (95% CI)
Number of Subjects	n=1257	n=949		n=1589	n=617	
<b>Demographics</b>						
Gender (Reference: Male)	471 (37.5%)	378 (39.8%)	0.905 (0.761-1.076)	611 (38.5%)	239 (38.7%)	0.988 (0.816-1.195)
Mean Age (years)	50.9	51.5	0.993 (0.984-1.002)	50.8	51.9	0.987 (0.977-0.997)*
Mean Body Mass Index (kg/m <sup>2</sup> )	23.2	23.3	0.993 (0.969-1.018)	23.2	23.2	1.007 (0.980-1.035)
Smoker	147 (11.7%)	98 (10.3%)	1.154 (0.880-1.513)	181 (11.4%)	65 (10.5%)	1.094 (0.811-1.477)
Regular Exercise	381 (30.3%)	299 (31.5%)	0.938 (0.781-1.126)	489 (30.8%)	194 (31.4%)	0.950 (0.777-1.162)
Workload (Reference: Sedentary Work)	81 (6.4%)	66 (7.0%)		101 (6.4%)	40 (6.5%)	
Light work	595 (47.3%)	494 (52.1%)	0.981 (0.694-1.387)	760 (47.8%)	306 (49.6%)	0.984 (0.666-1.452)
Medium Work	479 (38.1%)	320 (33.7%)	1.220 (0.856-1.739)	564 (35.5%)	200 (32.4%)	1.143 (0.766-1.704)
Heavy Work	91 (7.2%)	62 (6.5%)	1.196 (0.756-1.891)	111 (7.0%)	39 (6.3%)	1.127 (0.672-1.890)
<b>MRI Phenotypes</b>						
Presence of DSS	94 (7.5%)	61 (6.4%)	1.177 (0.843-1.643)	121 (7.6%)	35 (5.7%)	1.370 (0.929-2.020)
Presence of Abnormal Right Facet Joint Angulation	4 (0.3%)	1 (0.1%)	3.026 (0.338-27.120)	4 (0.3%)	1 (0.2%)	1.554 (0.173-13.932)
Presence of Abnormal Left Facet Joint Angulation	2 (0.2%)	2 (0.2%)	0.755 (0.106-5.367)	3 (0.2%)	1 (0.2%)	1.165 (0.121-11.220)

Presence of Facet Joint Tropism	330 (26.3%)	257 (27.1%)	0.959 (0.792-1.160)	412 (25.9%)	176 (28.5%)	0.877 (0.712-1.079)
Disc Herniation Score ( $\geq 3$ )	505 (40.2%)	378 (39.8%)	1.014 (0.854-1.205)	633 (39.8%)	251 (40.7%)	0.965 (0.799-1.166)
Disc Degeneration Score ( $\geq 16$ )	590 (46.9%)	430 (45.3%)	1.066 (0.900-1.264)	739 (46.5%)	283 (45.9%)	1.035 (0.859-1.248)
Presence of Endplate Irregularity	289 (23.0%)	195 (20.5%)	1.154 (0.940-1.417)	359 (22.6%)	126 (20.4%)	1.137 (0.905-1.428)
Presence of High Intensity Zone	404 (32.1%)	329 (34.7%)	0.893 (0.747-1.067)	519 (32.7%)	214 (34.7%)	0.913 (0.751-1.111)
Presence of Radial Tear	90 (7.2%)	72 (7.6%)	0.939 (0.681-1.296)	124 (7.8%)	39 (6.3%)	1.254 (0.864-1.820)
Presence of Spondylolisthesis	81 (6.4%)	36 (3.8%)	1.745 (1.167-2.608)*	98 (6.2%)	19 (3.1%)	2.065 (1.252-3.405)*
Presence of Modic Change	282 (22.4%)	211 (22.2%)	1.012 (0.826-1.239)	352 (22.2%)	142 (23.0%)	0.952 (0.762-1.188)
Presence of Anterior Marrow Change	232 (18.5%)	153 (16.1%)	1.176 (0.940-1.472)	286 (18.0%)	99 (16.0%)	1.149 (0.895-1.475)
*Statistically significant at 0.05 level and included in the multivariate binary logistic regression. CI, confidence interval; N/A, not available; DSS, developmental spinal stenosis; LBP: low back pain.						

1 Appendix B. Univariate Binary Logistic Regression for Association between Independent Variables and Radicular Leg Pain

Imaging Parameters	With or Without Radicular Leg Pain in this Month			With or Without Radicular Leg Pain in this Year		
	Yes, N (%)	No, N (%)	Unadjusted Odds Ratio (95% CI)	Yes, N (%)	No, N (%)	Unadjusted Odds Ratio (95% CI)
Number of Subjects	n=672	n=1534		n=901	n=1305	
<b>Demographics</b>						
Gender (Reference: Male)	226 (33.6%)	622 (40.5%)	0.744 (0.615-0.899)*	320 (35.5%)	530 (40.6%)	0.808 (0.678-0.963)*
Mean Age (years)	52.2	50.7	1.018 (1.008-1.028)*	51.9	50.6	1.014 (1.005-1.023)*
Mean Body Mass Index (kg/m <sup>2</sup> )	23.5	23.1	1.037 (1.010-1.065)*	23.5	23.0	1.046 (1.020-1.073)*
Smoker	77 (11.5%)	168 (11.0%)	1.058 (0.795-1.409)	98 (10.9%)	148 (11.3%)	0.960 (0.732-1.258)
Regular Exercise	206 (30.7%)	474 (30.9%)	0.989 (0.812-1.204)	285 (31.6%)	397 (30.4%)	1.055 (0.878-1.268)
Workload (Reference: Sedentary Work)	42 (6.3%)	104 (6.8%)	*	63 (7.0%)	77 (5.9%)	*
Light work	291 (43.3%)	804 (52.4%)	0.896 (0.611-1.314)	394 (43.7%)	677 (51.9%)	0.711 (0.499-1.015)
Medium Work	268 (39.9%)	526 (34.3%)	1.262 (0.856-1.858)	344 (38.2%)	434 (33.3%)	0.969 (0.675-1.391)
Heavy Work	66 (9.8%)	89 (5.8%)	1.836 (1.137-2.966)*	79 (8.8%)	72 (5.5%)	1.341 (0.845-2.127)
<b>MRI Phenotypes</b>						
Presence of DSS	61 (9.1%)	93 (6.1%)	1.548 (1.106-2.167)*	83 (9.2%)	72 (5.5%)	1.741 (1.255-2.416)*
Presence of Abnormal Right Facet Joint Angulation	1 (0.1%)	4 (0.3%)	0.570 (0.064-5.113)	1 (0.1%)	4 (0.3%)	0.362 (0.040-3.245)
Presence of Abnormal Left Facet Joint Angulation	0 (0.0%)	4 (0.3%)	0.0 (N/A)	1 (0.1%)	3 (0.2%)	0.483 (0.050-4.653)

Presence of Facet Joint Tropism	178 (26.5%)	407 (26.5%)	0.999 (0.813-1.226)	232 (25.7%)	354 (27.1%)	0.934 (0.771-1.133)
Disc Herniation Score ( $\geq 3$ )	261 (38.8%)	619 (40.4%)	0.940 (0.781-1.131)	353 (39.2%)	529 (40.5%)	0.948 (0.797-1.128)
Disc Degeneration Score ( $\geq 16$ )	316 (47.0%)	702 (45.8%)	1.064 (0.886-1.277)	426 (47.3%)	595 (45.6%)	1.086 (0.916-1.288)
Presence of Endplate Irregularity	135 (20.1%)	350 (22.8%)	0.851 (0.681-1.064)	190 (21.1%)	296 (22.7%)	0.913 (0.743-1.122)
Presence of High Intensity Zone	207 (30.8%)	523 (34.1%)	0.861 (0.709-1.047)	291 (32.3%)	441 (33.8%)	0.938 (0.783-1.123)
Presence of Radial Tear	47 (7.0%)	116 (7.6%)	0.920 (0.647-1.308)	72 (8.0%)	91 (7.0%)	1.161 (0.842-1.601)
Presence of Spondylolisthesis	40 (6.0%)	77 (5.0%)	1.198 (0.808-1.775)	53 (5.9%)	64 (4.9%)	1.213 (0.835-1.764)
Presence of Modic Change	143 (21.3%)	348 (22.7%)	0.922 (0.740-1.149)	200 (22.2%)	295 (22.6%)	0.979 (0.799-1.201)
Presence of Anterior Marrow Change	128 (19.0%)	255 (16.6%)	1.180 (0.933-1.493)	163 (18.1%)	221 (16.9%)	1.085 (0.868-1.356)
<p><i>*Statistically significant at 0.05 level and included in the multivariate binary logistic regression.</i>  CI, confidence interval; N/A, not available; DSS, developmental spinal stenosis.</p>						