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

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ABSTRACT

Background

Lumbar developmental spinal stenosis (DSS) describes pre-existing narrowed spinal canal at multiple lumbar levels, which predisposes subjects to develop compressive symptoms easier. However, the relationships between various MRI phenotypes and clinical outcomes are unclear.

Objective

To study the associations of demographics, lifestyle factors and different MRI phenotypes with low back pain (LBP) and radiating leg [JK1]pain~~radiculopathy~~.

Methods

This was a cross-sectional study of 2206 subjects with L1-S1 axial and sagittal magnetic resonance imaging (MRI). Clinical and radiological information regarding subjects' demographics, workload, smoking habit, anteroposterior (AP) vertebral canal diameter, Schmorl's nodes, spondylolisthesis, and other MRI phenotypes was assessed. Mann-Whitney *U* tests and Chi-square tests were conducted to search for differences between subjects with and without DSS.[DS2] Associations of intensity of LBP and presence of radiating pain [JK3]~~leg radiculopathy~~ in the past month and the past year with the clinical and radiological information were also investigated by utilizing univariate and multivariate logistic regressions.

Results

Subjects with DSS had more severe LBP intensity, higher prevalence of radiating leg pain ~~radiculopathy~~, more pain-related disability and lower quality of life (all $p<0.05$). In addition, subjects with spondylolisthesis had 1.5 (95% CI = 1.0-2.3; p=0.048) and 1.7 (95% CI = 1.0-3.0; p=0.033) times higher odds of experiencing LBP in the past month and the past year, respectively. Individuals with DSS had 1.4 (95% CI = 1.0-2.1; p=0.048) and 1.8 (95% CI = 1.3-2.6; p=0.001) times higher odds of having radiating leg pain ~~radiculopathy~~ in the past month and the past year, respectively. Schmorl's nodes were also significantly associated with leg radiculopathy in the past month (OR = 1.5; 95% CI = 1.1-1.9; p=0.006) and the past year (OR = 1.5; 95% CI = 1.2-2.0; p=0.002).

Conclusion

This is the first large-scale study that identified possible risk factors that were associated with LBP and leg radiculopathy. Multilevel DSS, spondylolisthesis and Schmorl's nodes are potential risk factors of acute and chronic pain. These MRI phenotypes should be assessed carefully in a clinical setting.

INTRODUCTION

Low back pain (LBP) and leg radiculopathy are two of the most common health problems around the world[1-3]. They bring about deterioration in one's quality of life, daily disability, absence from work, mental health disturbance, and increased public health burden[4-6]. However, LBP is generally nonspecific[7] and in these cases, the underlying cause is often unrecognizable. One of the leading causes of these symptoms is compression of the nerve roots in patients with stenotic lumbar canals[8,9]. Identification of their radiological phenotypes with magnetic resonance imaging (MRI) is currently the gold standard[10,11] and is imperative for identifying the potential source of LBP or leg radiculopathy. Many MRI phenotypes are postulated to be possible pain generators when studies investigated in their individual effects, including dural sac cross-sectional area[12], disc degeneration and herniation[7,13,14], facet joint degeneration[15], radial tears[16], high intensity zone (HIZ)[17], and Modic changes[18,19].

In addition to soft tissue changes, lumbar developmental spinal stenosis (DSS) may also play an important role in causing pain. Having a prevalence of 7.3%[20], it is suggested that DSS is not an uncommon pathology in the Chinese population. DSS is described as pre-existing narrowed vertebral canals at multiple lumbar levels[21-23]. It is an important factor to consider in spinal stenosis surgery as patients with DSS have a high reoperation rate of up to 22%[23-25]. A large amount of studies focused on defining DSS radiologically[22,26-31], but only a few investigated its clinical course and clinical presentation[9,32]. Subjects with DSS are found to have earlier onset of symptoms during their fourth or fifth decades[33] as mild degenerative changes of the lumbar spine are already sufficient to compress the neural elements. Although DSS and other MRI phenotypes were observed to be closely related, their interactions in causing pain are still poorly understood. The contribution of DSS in generating pain alone is also unknown. Furthermore, there is little consensus on what radiological abnormalities of the lumbar spine contribute most to LBP, leg pain or disability. Systematic reviews by Brinjikji *et*

al[34,35] commented that high proportions (>29%) of asymptomatic subjects had some abnormal changes of the spine although they were less prevalent than among patients with LBP.

Therefore, this study was designed to address the aforementioned incomprehensive understanding on the interaction of DSS and different MRI phenotypes in producing different clinical outcomes namely LBP, leg radiculopathy and disability.

METHODS

Study Design and Population

This was a cross-sectional large-scale study of 2206 Chinese subjects from the Hong Kong Disc Degeneration Cohort Study[17,22,26,36-38]. All subjects were openly recruited via newspapers advertisement, posters and e-mails, regardless of their social and economic status. Participants with prior surgical treatment of the spine, spinal tumours, and marked spinal deformities were excluded from the study. Subjects selected were not based on the presence or absence of clinical symptoms. All qualified subjects underwent T1-weighted axial MRI and T2-weighted sagittal MRI of the lumbosacral spine (L1-S1) after informed consent was obtained from participants and ethics was approved by a local institutional board.

Low Back Pain and Leg Radiculopathy

Information related to LBP and leg radiculopathy was recorded as follows: age of onset, any pain experienced in the past month (30 days) and the past year (365 days). LBP was defined as pain localizing in the lower back and/or buttocks. Leg radiculopathy was defined as pain radiating from the lower back/buttocks to one or both lower extremities beyond the knee in a dermatomal pattern that may be associated with numbness and paresthesia[39][JK4]. Visual analog scale (VAS) was utilized to measure the worst LBP experience since the day of onset. The

severity of LBP was subdivided into 3 categories according to previously published criteria[17,40]: no or mild pain (VAS < 3), moderate pain (VAS 3 – 5.9), and severe pain (VAS ≥ 6).

Lifestyle Factors and Disability

Age, gender, height and weight were obtained on the day with MRI. Body mass index (BMI) was calculated by weight/height^2 (kg/m^2). Information on previous lumbar spine injury, smoking habit, regular exercise and occupation was surveyed. Previous lumbar spine injury was a closed-ended question for subjects to recall any prior back injury regardless of severity. Occupation was characterized into different subgroups based on the physical workloads[17,19]: 1 = sedentary work (lifting 10 lbs); 2 = light work (lifting 20 lbs); 3 = medium work (lifting 50 lbs); 4 = heavy or very heavy work (lifting ≥100 lbs). Pain-related disability was assessed by the Oswestry Disability Index (ODI)[41] and the Roland Morris Disability Questionnaire (RMQ)[42]. Quality of life was assessed by the 36-Item Short Form Survey (SF-36)[43]. An ODI of ≥15% was noted as pain-related disability[40].

MRI Protocol

1.5T or 3T ~~HD~~ MRI [DS5]machines were used for axial and sagittal imaging at L1-S1. Subjects were oriented in the supine position. For T1-weighted axial scans, the field of view was 21cm×21cm, slice thickness was 4mm, slice spacing was 0.4mm, and imaging matrix was 218×256. For T2-weighted sagittal scans, the field of view was 28cm×28cm, slice thickness was 5mm, slice spacing was 1mm, and imaging matrix was 448×336. The repetition time for T1- and T2-weighted MRI were 500ms-800ms and 3320ms respectively, and their echo time was 9.5ms and 85ms. According to the pedicle and disc levels, 11 parallel slices were made at each spinal level. The MRI protocol has been described in further details elsewhere[22].

MRI Measurements[DS6]

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

The cut with the thickest pedicle diameter, pedicle, lamina and vertebral body was utilized for every T1-weighted axial MRI. The following measurements were obtained for L1-S1 axial MRI: anteroposterior (AP) vertebral canal diameter (Figure 1) and left and right facet joint angle (Figure 2). Facet joint angle was the angle made by a line joining the corners of the facet joint and the transverse plane. Facet joint angulation of greater than 58º at L4-L5 was regarded as abnormal[44]. Facet joint tropism was noted if the absolute difference between left and right facet joint angle was greater than 8 degrees based on the definition by Samartzis *et al* [44].

T2-weighted sagittal MRI was acquired at the midsagittal cut with the most prominent lumbar spinous processes. The following measurements were obtained for L1-S1: presence of disc herniation, disc degeneration[45], Schmorl's nodes[46] (Figure 3), endplate irregularity, [DS7]high intensity zone (HIZ)[17,47] (Figure 4), radial tear, spondylolisthesis (Figure 4), Modic change and anterior marrow change[48]. Disc herniation was further divided into 4 categories: 0 = no disc herniation; 1 = posterior disc bulging (disc displaced beyond a virtual line connecting the posterior edges of two adjacent vertebrae); 2 = disc extrusion (distance between the edge of the protruded disc into the spinal canal was greater than the distance between edges of the base of the disc); 3 = disc sequestration[17,18,49]. The scores of each lumbar level were added up as disc herniation score and further categorized into two subgroups[17]: disc herniation score of <2 (no or mild disc herniation) and disc herniation score of ≥3 (moderate to several disc herniation).

Disc degeneration was evaluated using the Pfirrmann grading[45]: 1 = homogeneous bright white disc; 2 = inhomogeneous white disc and/or horizontal bands; 3 = inhomogeneous grey disc; 4 = inhomogeneous grey to black disc; 5 = inhomogeneous black disc. The scores of each lumbar level were added up as disc degeneration score and further categorized into two subgroups: disc degeneration score of <16 (no or mild disc degeneration) and disc degeneration score of ≥16 (moderate to severe disc degeneration)[50]. Schmorl's node was defined as herniation of the nucleus pulposus into the adjacent vertebral body. [DS8]Endplate irregularity was described as an irregular surface at the endplates. [DS9]HIZ was defined as a high-intensity area of the anterior or posterior annulus fibrosus[17,51,52]. Radial tear was noted as a hyperintense line in the annulus fibrosus. Spondylolisthesis was characterized by anterior displacement of the cranial vertebral body on the caudal vertebra. Modic change was described as ~~high~~ signal intensity change involving the whole or middle posterior of the vertebral body adjacent to the endplates, while anterior marrow change was described as high-signal intensity change at the anterior vertebral body adjacent to the endplates. The presence of Schmorl's nodes, endplate irregularity, HIZ, radial tear, spondylolisthesis, Modic change and anterior marrow change were defined as one or more radiological findings of their respective entities throughout the entire lumbar spine. Dichotomizing these variables are more relevant to a clinical setting.

Definition of Lumbar Developmental Spinal Stenosis

Subjects were noted to have multilevel DSS if their axial AP vertebral canal diameters were below the proposed cut-offs at 3 or more lumbosacral levels[20]: L1<19mm, L2<19mm, L3<18mm, L4<18mm, L5<18mm, S1<16mm. This criterion was utilized as it recognizes the importance of multilevel stenosis in patients with DSS.

Statistical Analysis

Frequency and descriptive statistics were performed for all variables. Normality testing was performed. For detecting differences between DSS and non-DSS subjects, Mann-Whitney *U* tests were performed for continuous independent variables including age, BMI, ~~average~~ mean ODI, mean ~~average~~ RMQ, mean ~~average~~ SF-36, axial AP vertebral canal diameter, and left and right facet joint angle, while chi-square tests were used for categorical independent variables including gender, previous spinal injury, smoking habit, regular exercise, physical workload, LBP within the past month and the past year, LBP intensity, leg radiculopathy within the past month and the past year, pain-related disability, abnormal left and right facet joint angulation, facet joint tropism, disc herniation score, disc degeneration score, presence of Schmorl's nodes, endplate irregularity, HIZ, radial tear, spondylolisthesis, Modic change, and anterior marrow change. Means and ranges were also calculated for all T1-weighted axial MRI measurements. Intraobserver and interobserver reliability assessments were based on Cronbach α analysis: α values of 0.90 to 1.00 was noted to have excellent reliability; α values of 0.80 to 0.89 was noted to have good reliability[53].

Univariate logistic regressions were then conducted to detect any association between individual independent variables and clinical outcomes (LBP in the past month and the past year, and leg radiculopathy in the past month and the past year). All demographics, lifestyle factors and MRI measurements except AP vertebral canal diameter were included as independent variables as it was used to dichotomize subjects into DSS and non-DSS. Variables that were statistically significant ($p<0.05$) in the univariate logistic regressions were included to build four multivariate logistic regression models based on the four clinical outcomes (LBP in past month and year, and leg radiculopathy in past month and year), after controlling for age, gender, and BMI. These[DS10] models were used to assess the association of lifestyle factors together with MRI phenotypes with LBP and leg radiculopathy [JK11]experienced in the past month and the past year. As no published article demonstrated the best prediction equation in a similar

situation, stepwise regression was used in these models to explore for possible impactful factors. Adjusted odds ratios (OR) and 95% confidence interval (CI) were obtained from these models.

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

RESULTS

Among 2206 subjects, 153 were identified to have multilevel DSS. Descriptive and frequency statistics in subjects with and without multilevel DSS were presented in Table 1 and Table 2. Excellent interobserver (α = 0.90 – 0.96) and intraobserver reliability (α = 0.92 – 0.99 and α = 0.92 – 0.99) between the two independent investigators were noted. Associations of multilevel DSS with demographics, lifestyle factors, and MRI phenotypes were also presented. Subjects with multilevel DSS were noted to have narrower spinal canals and more likely to be females (75.8%). They also have higher VAS which inferred more severe pain, higher incidence of leg radiculopathy both in past month and past year, higher average ODI, RMQ, and higher physical component score in SF-36. In addition, abnormal right facet joint angulation, higher disc herniation score and higher disc degeneration score were associated with multilevel DSS.

Table 3 showed the results of the univariate logistic regressions on LBP. Statistically significant associations of LBP in the past month with previous lumbar injury and spondylolisthesis were observed. These independent variables were used to conduct a multivariate logistic regression analysis (Table 4) which reached statistical significance (Chi square (5, n=2160) = 185.911; p<0.001). After adjusting for gender, age and BMI, subjects with previous lumbar injury (adjusted OR = 3.663; 95% CI = 2.994-4.480[DS12]; p<0.001) and spondylolisthesis (adjusted OR = 1.526; 95% CI = 1.004-2.322[DS13]; p=0.048) had higher odds of LBP in the past month.

Age, previous lumbar injury, and spondylolisthesis were associated with LBP in the past year (Table 3). These independent variables were used to conduct a multivariate logistic regression analysis (Table 4) which reached statistical significance (Chi square (5, n=2163) = 220.918; p<0.001). After adjusting for gender, age and BMI, subjects with previous lumbar injury (adjusted OR = 5.627; 95% CI = 4.291-7.380; p<0.001) and spondylolisthesis (adjusted OR = 1.762; 95% CI = 1.047-2.963; p=0.033) had higher odds of LBP in the past month.

Similarly, Table 5 showed the results of the univariate analyses on leg radiculopathy. Gender, age, BMI, previous lumbar injury, workload, multilevel DSS, and Schmorl's nodes were associated with leg radiculopathy in the past month. These independent variables were included in a multivariate logistic regression analysis (Table 6) which reached statistical significance (Chi square (9, n=2209) = 157.899, p<0.001). After adjusting for gender, age and BMI, subjects with previous lumbar injury (adjusted OR = 2.715; 95% CI = 2.231-3.303; p<0.001), heavy workload (adjusted OR = 1.743; 95% CI = 1.053-2.887; p=0.031), multilevel DSS (adjusted OR = 1.439; 95% CI = 1.004-2.063; p=0.048) and Schmorl's nodes (adjusted OR = 1.458; 95% CI = 1.113-1.911; p=0.006) had higher odds of leg radiculopathy in the past month.

Gender, age, BMI, previous lumbar injury, multilevel DSS, and Schmorl's nodes were associated with leg radiculopathy in the past year (Table 5). Table 6 shows the results of the multivariate logistic regression analysis of these significant independent variables with leg radiculopathy in the past year, which reached statistical significance (Chi square (9, n=2088) = 170.615, p<0.001). After adjusting for gender, age and BMI, subjects with previous lumbar injury (adjusted OR = 2.714; 95% CI = 2.243-3.284; p<0.001), multilevel DSS (adjusted OR = 1.811; 95% CI = 1.262-2.600; p=0.001) and Schmorl's nodes (adjusted OR = 1.510; 95% CI = 1.158-1.970; p=0.002) had higher odds of leg radiculopathy in the past month. If the

significant factors were removed from the above models, their effects were shown by the changes in -2 log likelihood (all $p<0.05$).

DISCUSSION

LBP and leg radiculopathy are common health conditions that one may experience during his/her lifetime. It is observed that the periphery of the annulus fibrosus and endplates are highly innervated, while the nucleus pulposus and inner annulus fibrosus of the disc are free of innervation[54,55]. Pain is generated when the intact structure of the vertebral disc is disrupted or when nociceptors are stimulated by compression. However, these clinical presentations are often poorly associated with the imaging profiles, except for HIZ and Modic changes which are relatively well-documented[51,56]. In addition, patients with multilevel DSS have pre-existing narrowed vertebral canals which predisposed them to a lower threshold of neural compression. This was further proven by our results which showed these subjects were associated with a shorter AP vertebral canal diameter at L1-S1 ($p<0.001$). They may experience LBP and leg radiculopathy even if a milder degree of degenerative changes of the lumbar spine is present. Yet, to date, there is no research on their interactions in causing pain. The contribution of multilevel DSS in generating pain is also unknown. Therefore, our study was the first to show that subjects with spondylolisthesis had higher risks of LBP in the past month and the past year, while subjects with multilevel DSS and Schmorl's nodes had higher risks of leg radiculopathy in the past month and the past year.

We compared the clinical outcomes in subjects with and without multilevel DSS. The former group had more severe LBP ($p = 0.013$) and higher prevalence of leg radiculopathy in the past month ($p = 0.008$) and the past year ($p = 0.001$). This might be attributed to the narrowed spinal canal that causes the subject more prone to nerve root compression, leading to pain radiating to the legs. However, LBP was not found to be significantly different between

the two groups even though nerve root compression could also lead to LBP. This could be due to its nonspecific characteristics[7,57]. LBP can be caused by many other pathologies such as intervertebral disc disruption, facet joint and sacroiliac joint disruption, ligament or muscle strain, and idiopathic causes. A clinical study by Dai *et al*[8] examining the preoperative clinical symptoms in patients with DSS also realized more patients experienced leg radiculopathy or sciatica than LBP. Furthermore, this group was also associated with higher pain-related disability scores (ODI and RMQ) and lower quality of life (SF-36), specifically for the physical component score. Similarly, Lee et al[58] observed the majority of the patients with DSS undergoing surgery had lower quality of life and poorer clinical presentation including more severe and incapacitating pain, shorter walking distance, poorer sitting endurance, and muscle weaknesses. It was also found that subjects with DSS were more prone to disc herniation and disc degeneration, as suggested by their higher scores. Although statistically significant, the absolute differences between groups were small and might not be clinically relevant.

Pain lasting for less than 6 weeks is defined as acute, while pain lasting for more than 12 weeks is noted to be chronic[59]. Our large-scale study was able to obtain this clinical information for both LBP and leg radiculopathy. The predicting variables appeared to be the same in both LBP in the past month and the past year, but subjects with spondylolisthesis were found to have a higher risk of having LBP for a longer period of time after adjusting for demographic confounders (adjusted OR = 1.762; 95% CI = 1.047-2.963). Among all of its etiologies, degeneration is the most common form of spondylolisthesis seen in adults[60]. Acute causes such as trauma could also lead to fractures and dislocation at the posterior elements, but this is more likely in a children cohort[61]. Therefore, chronic pain is more likely to be found in these patients. [DS14]Our findings are also supported by a meta-analysis of 28 articles consisting of 26,107 subjects conducted by Raastad *et al*[62]. They noticed significant association between

spondylolisthesis and LBP in both occupational-based studies (OR = 2.21; 95% CI = 1.44-3.39) and community-based studies (OR = 1.12; 95% CI = 1.03-1.23).

On the other hand, subjects with leg radiculopathy were associated with older age, larger BMI, [DS15]and they were more likely to be females. Predictor variables were also found to be the same for both leg radiculopathy in the past month and the past year. After adjusting for demographics, subjects with multilevel DSS and subjects with Schmorl's nodes had higher risks of having chronic leg radiculopathy compared to acute leg radiculopathy. Our multivariate analysis was consistent with the results in Table 1 and this could be attributed to the developmental origin of DSS, as the canal size is reported to be unchanged after puberty and skeletal maturity[33], and hence subjects with narrower spinal canals are more likely to experience nerve roots compression and lead to chronic pain. Furthermore, Schmorl's nodes were found to be associated with leg radiculopathy. However, this is poorly documented in current literature and is more likely to be associated with LBP[46] as Schmorl's node locates in the disc-vertebral junction without affecting the spinal canal. Scatter researches[63] reported radicular pain in patients with Schmorl's nodes as the only radiological finding but they are of low level of evidence. Schmorl's node [DS16]is possibly a result of maldevelopment of the vertebrae which is similar to DSS[64]. Patients with DSS are more likely to have Schmorl's nodes (15.7% vs 13.2%) although it is found to be statistically insignificant (P = 0.386) in our study. This might be influenced by our small sample size (n = 24) in those who had both DSS and Schmorl's nodes. However, this association is still preliminary and require future longitudinal studies to justify. Nevertheless, multilevel DSS is more likely to be a significant risk factor in causing nerve root compression and leg radiculopathy.

Some relatively well-documented associations of clinical outcomes with MRI phenotypes such as Modic changes[56] and HIZ[17] were found to be insignificant in this study. The methodologies in those studies were different from our study as they examined the

individual effect of the MRI phenotypes on pain. In contrast, our study attempted to search for possible predictors that contributed to generating pain by covering the majority of MRI phenotypes that are commonly seen in the population. Due to these considerations, our study is the first to integrate demographics with lifestyle factors and MRI phenotypes and examine their relationship with clinical outcomes. [DS17]

There are several limitations to this study. Firstly, our results may not be generalizable in other ethnicities as only Chinese subjects were recruited. However, this is beneficial to the strength of exploration as it limits potential unknown confounders between ethnic groups. Secondly, as with other cross-sectional studies, we cannot conclude any causative relationships between the independent variables and clinical outcomes. Thirdly, as subjects were openly recruited via advertisements, the proportion of males and females were not equally distributed. [DS18]In addition, this method of sampling subjects may not be representative of the true population as individuals who respond to advertisements may be inherently biased. It will be useful to follow-up these subjects to observe the impact of lifestyle factors and MRI phenotypes on clinical outcomes in the long run. Changes in intensity of pain across time is also of interest to understand the complete picture.

CONCLUSION

This is the first large-scale study that examined the associations of lifestyle factors, DSS, and different MRI phenotypes with LBP and leg radiculopathy. Our study observed that subjects with spondylolisthesis had higher likelihood~~risks~~ of LBP [JK19]in the past month and the past year, while subjects with multilevel DSS and Schmorl's nodes had higher likelihood~~risks~~ of leg radiculopathy in the past month and the past year. These should be assessed carefully in a clinical setting. Future longitudinal studies are necessary to understand the associations

between different phenotypes and pain, and to observe the changes in clinical presentation over time.

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FIGURE LEGENDS

Figure 1. Axial magnetic resonance imaging measurement: (A) anteroposterior (AP) vertebral body diameter.

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

Figure 3. Sagittal magnetic resonance imaging: (C) Schmorl's nodes (herniation of the nucleus pulposus into the adjacent vertebral body).

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