Critical Values of Facet Joint Angulation and Tropism in the Development of Lumbar Degenerative Spondylolisthesis: An International, Large-Scale Multicenter Study by the AOSpine Asia Pacific Research Collaboration Consortium

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Abstract

Study Design An international, multicenter cross-sectional image-based study performed in 33 institutions in the Asia Pacific region.

Objective The study addressed the role of facet joint angulation and tropism in relation to L4–L5 degenerative spondylolisthesis (DS).

Methods The study included 349 patients (63% females; mean age: 61.8 years) with single-level DS; 82 had no L4–L5 DS (group A) and 267 had L4–L5 DS (group B). Axial computed tomography and magnetic resonance imaging were utilized to assess facet joint angulations and tropism (i.e., asymmetry between facet joint angulations) between groups.

Results There was a statistically significant difference between group A (left mean: 46.1 degrees; right mean: 48.2 degrees) and group B (left mean: 55.4 degrees; right mean: 57.5 degrees) in relation to bilateral L4–L5 facet joint angulations ($p < 0.001$). The mean bilateral angulation difference was 7.4 and 9.6 degrees in groups A and B, respectively ($p = 0.025$). A critical value of 58 degrees or greater significantly increased the likelihood of DS if unilateral (adjusted OR: 2.5; 95% CI: 1.2 to 5.5; $p = 0.021$) or bilateral facets (adjusted OR: 5.9; 95% CI: 2.7 to 13.2; $p < 0.001$) were involved. Facet joint tropism was found to be relevant between 16 and 24 degrees angulation difference (adjusted OR: 5.6; 95% CI: 1.2 to 26.1; $p = 0.027$).

Conclusions In one of the largest studies assessing facet joint orientation in patients with DS, greater sagittal facet joint angulation was associated with L4-L5 DS, with a critical value of 58 degrees or greater increasing the likelihood of the condition for unilateral and bilateral facet joint involvement. Specific facet joint tropism categories were noted to be associated with DS.

Keywords

- degenerative
- spondylolisthesis
- facet
- joints
- angulation
- orientation
- tropism
- AOSpine

Introduction

The lumbar facet joint provides stability of the spinal motion segments against shearing, rotation, and flexion forces. The biomechanical role of the facet joints includes supporting 33% of the dynamic compressive load and 35% of the static load of the spine.[1,2] Disruption of the facet joint function by degenerative processes may lead to translation of the vertebral body or degenerative spondylolisthesis (DS; ►**Fig. 1**).[3] Spinal stenosis can result from DS when combined with ligamentum flavum hypertrophy and foraminal narrowing due to the impingement of a prominent superior articular process.[4] Lower back pain may develop in addition to other symptoms.[5] As such, a better understanding of the mechanisms of DS may assist in implementing preventive and prognostic strategies.

The epidemiology of DS is complex and variable among populations. DS mainly manifests at L4–L5,[6,7] is more common in patients over 50 years of age,[8] primarily occurs in female patients, and is associated with sagittal spinal malalignment.[9,10] Other risk factors include general joint laxity, increased pedicle facet angle, and increased/abnormal sagittal alignment of the facet joints.[7]

Studies have shown that DS is closely related to greater sagittally oriented facet joint angulation,[6,7,11–15] which may be attributed to developmental origins or the outcome of a remodeling process.[6,16] Grobler et al and Fujiwara et al have both shown that facet joint degeneration is related to facet joint sagittalization; however, a critical cutoff value in relation to facet joint angulation in relation to DS has yet to be proposed.[7,8] Furthermore, the significance of facet joint tropism (i.e., bilateral facet joint angulation asymmetry) upon the development of DS remains controversial. Some studies have proposed that facet joint tropism increases the risk of disk degeneration and rotational instability of the spine, which may lead to DS.[17–20] Facet joint tropism in cases of DS is quoted to be 2.3 degrees greater than in normal subjects and also correlates with the extent of disk degeneration.[13] Biomechanical studies have noted that facet joint tropism may be more susceptible to anterior sheer force.[21] Yet other studies have concluded that no association exists between DS and facet joint tropism.[8,22–24] According to a recent systematic review, there is still insufficient evidence regarding the relationship of facet joint tropism and the development of DS,[25] which can be attributed to the definition of the tropism phenotype, insufficient statistical analyses, small sample sizes and lack of statistical power, and possibly ethnic heterogeneity.

Understanding the role of facet joint angulation and tropism on the development of DS may further refine the comprehension of the facet joint phenotype and may potentially assist in predicting as well as designing more personalized interventions. To date, no large-scale studies have been conducted to address the role of facet joint angulation and tropism in relation to DS, in particular among an Asian population. As such, this large-scale, international multicenter study, initiated by the AOSpine Asia Pacific (AOSAP) Research Collaboration Consortium, addressed the role of lumbar facet joint angulation and tropism in relation to L4–L5 DS in the Asia Pacific region.

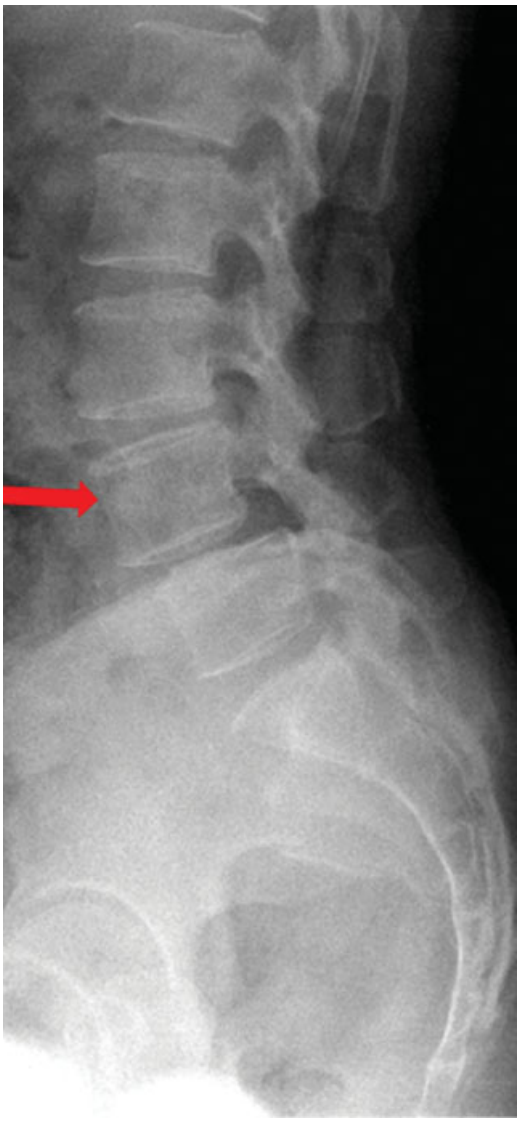

Fig. 1 Lateral standing plain radiograph illustrating a L4–L5 degenerative spondylolisthesis (arrow).

Methods

The study was an international, multicenter, cross-sectional imaging study of patients with DS in the Asia Pacific region. Thirty-three centers were identified based on their involvement with the AOSAP Research Collaboration Consortium and were invited to participate.[15] This consortium was established to promote international collaboration in spinal research throughout the Asia Pacific region.[15] Approval from the local institutional review boards was obtained prior to the commencement of the study where applicable, and informed consent was acquired from each patient.

The inclusion criteria was patients older than 18 years of age who were diagnosed with DS and living in the Asia Pacific region. DS was defined as nonisthmic with a 3-mm or greater slip on lateral standing plain radiographs. For the purpose of the current study, the patients who had single-level DS were included for assessment, with a focus on the L4–L5 vertebral segment. The exclusion criteria included patients with previous or current spinal surgery, congenital anomalies, transitional vertebrae, previous infection, trauma, tumors, isthmic spondylolisthesis, and unsatisfactory imaging.

Demographic information was obtained from each patient, which included age (years), sex, weight (kilograms), height (meters), body mass index (kilograms per square meter), and ethnicity. Standing lateral radiographs and axial magnetic resonance images (MRI) or computed tomography (CT) scans of the lumbar spine were obtained. The level of DS of the caudal vertebrae in comparison to the rostral vertebrae was assessed radiographically (►**Fig. 1**). The patients were stratified into those presenting without (group A) or with (group B) L4–L5 DS. Axial images were selected based on the level that most closely bisected the facet joints at each segmental level. The imaging cut sequences were at least 3-mm thick. Axial slices were preferred if they included the posterior/superior corner of the caudal vertebral body. This slice most closely bisected the facet joint and was utilized for measuring the facet joint geometry. If this exact slice was not available from the scans performed, the most closely situated slice was used. If the selected slice was more than 2 mm cranial or caudal to the ideal slice cut, a new scan was ordered. On axial imaging, left and right facet joint angulations in degrees were obtained digitally. The angulation degree was obtained based on line of the posterior border of the vertebral body in the coronal plane intersecting the line bisecting the inferior and superior tips of the facet joint process (►**Fig. 2**). Based on the initial description by Grogan et al,[22] facet joint tropism was defined as asymmetry between the left and right facet joint angles, with

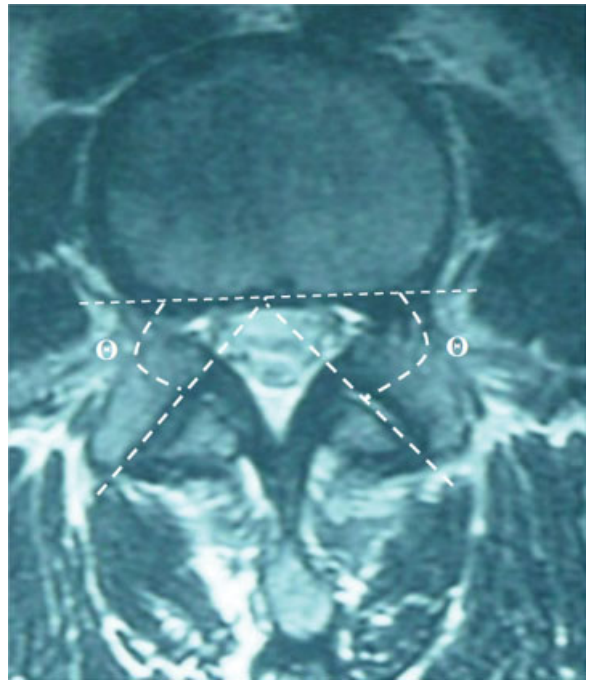

Fig. 2 Axial lumbar magnetic resonance image illustrating the assessment of facet joint angulation. Dashed lines are intersecting lines to denote the sagittal facet joint angulation in relation to the coronal plane.

Table 1 Patient demographics

	L4–L5 degenerative spondylolisthesis		
Variable	No (group A), $n = 82$	Yes (group B), $n = 267$	p Value
Sex-type (% female)	58.5	64.7	0.315
Mean age, y (± SD, range)	57.0 (13.8, 24.0–82.0)	63.2 (11.6, 28.0–90.0)	0.001
Mean BMI, kg/m^2 (± SD, range)	24.9 (4.2, 15.4–36.5)	25.8 (4.1, 17.3–43.9)	0.179

Abbreviations: BMI, body mass index; SD, standard deviation; y, years.
Note: $p < 0.05$ is considered statistically significant.

one joint having ≥7-degree sagittal orientation difference in comparison with the other. An independent observer who was not participating in the clinical management of these patients assessed all the images. All images were digitized and assessed on Image J (Version 1.46h, 2012; U.S. National Institutes of Health, Bethesda, Maryland, United States). This imaging protocol has been previously reported.[15]

SPSS version 21 statistical software (Chicago, Illinois, United States) was utilized to perform the statistical analyses. Analyses assessed the parametricity of the data. Univariate analyses were conducted, and parametric and nonparametric tests were utilized where appropriate. Multivariate logistic regression analyses were performed to assess the strength of the covariates in relation to the development of L4–L5 DS, with emphasis placed upon the impact of facet joint angulation and tropism. The covariates for inclusion in the regression modeling were selected based on the univariate analyses. The variables noting an association on the univariate analyses in relation to L4–L5 DS with p values of 0.200 or less were included in the regression modeling. The backward stepwise elimination method was used in the model building. The interaction effects between the variables in the model were also assessed. The Hosmer-Lemeshow goodness-of-fit test was considered to assess model stability, whereby a larger p value indicated greater stability. Odds ratios (ORs) and their 95% confidence interval (CI) bounds were assessed; 95% CIs crossing the value of 1 were not statistically significant. Furthermore, the receiver operating characteristic (ROC) of the curve were also performed to assess the area under the curve (AUC) of the bilateral facet joint angulations and tropism in relation to L4–L5 DS. Higher AUC values correspond to better ability of the parameter to discriminate regarding its association strength with the outcome (DS). An AUC of 0.50 or less indicates unsatisfactory or poor predictive value. ROC analyses were also used to select critical values of these aforementioned parameters that demonstrated at least 50% sensitivity. Such critical values were then included in the multivariate logistic regression modeling. A threshold for statistical significance was also established at $p < 0.05$.

Results

Three hundred forty-nine patients were included (63% women), all of whom were symptomatic at initial presentation. The patients had a mean age of 61.8 years (standard deviation [SD]: ± 12.4; range: 24.0 to 90.0) and a mean body mass index of 25.6 kg/m^2 (SD: ± 4.2; range: 15.4 to 43.9). There were 82 patients (23.5%) without L4–L5 DS (group A) and 267 patients (76.5%) with L4–L5 DS (group B). The patient demographics with respect to the presence of DS are noted in ►**Table 1**.

Univariate Analyses

In the group A patients, the mean left and right facet joint angulations were 46.1 degrees (SD: ± 12.9; range: 22.0 to 86.0) and 48.2 degrees (SD: ± 13.7; range: 20.0 to 85.0), respectively (►**Fig. 3**). In the group B patients, the mean left and right facet joint angulations were 55.4 degrees (SD: ± 14.2; range: 29.0 to 101.0) and 57.5 degrees (SD: ± 14.8, range: 20.0 to 99.0), respectively (►**Fig. 3**). There was a statistically significant greater left ($p < 0.001$) and right ($p < 0.001$) facet joint angulation in group B compared with group A (►**Fig. 3**). The mean differences in facet joint angulation between group A and group B were 7.4 degrees (SD: ± 7.3, range: 0 to 33) and 9.6 degrees (SD: ± 9.0; range: 0 to 48), respectively ($p = 0.025$; ►**Fig. 4**). Based on the definition of facet joint tropism (i.e., ≥7 degrees asymmetry) as proposed by Grogan et al,[22] 40.2% of patients in group A and 50.6% in group B had tropism ($p = 0.102$).

ROC and Multivariate Analyses

Based on the ROC analyses (►**Fig. 5**), the AUCs for left and right facet joint angulations in relation to L4–L5 DS were 0.70 (95% CI: 0.63 to 0.76; $p < 0.001$) and 0.69 (95% CI: 0.62 to 0.75; $p < 0.001$), respectively. According to the analyses, the

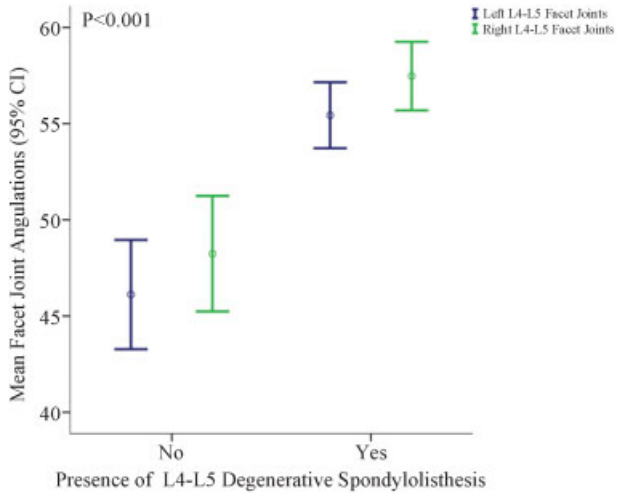

Fig. 3 Error bars demonstrating the association between mean facet joint angulation and the presence of L4–L5 degenerative spondylolisthesis. Abbreviation: CI, confidence interval.

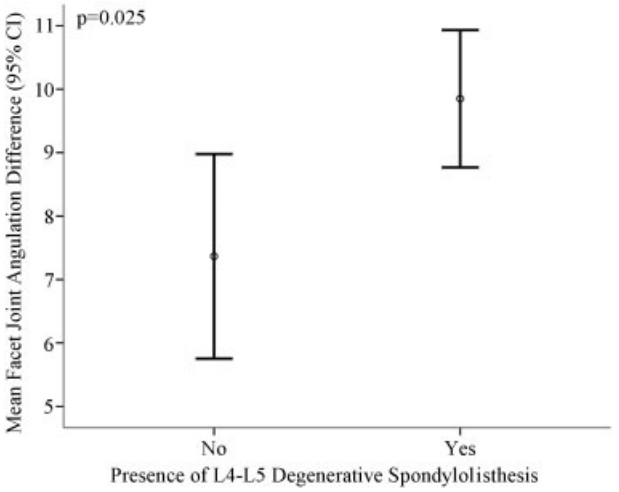

Fig. 4 Error bars demonstrating the association of mean facet joint angulation difference and the presence of L4–L5 degenerative spondylolisthesis. Abbreviation: CI, confidence interval.

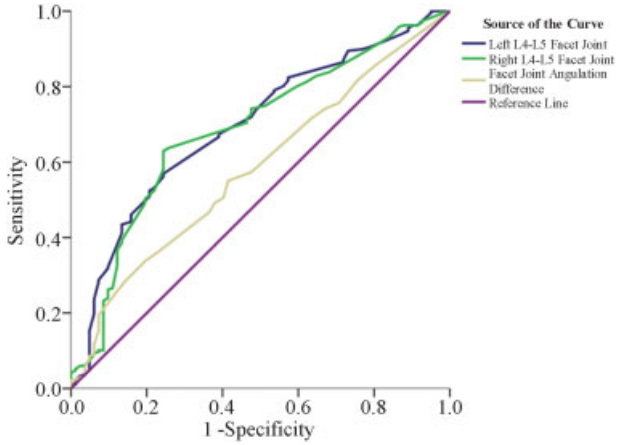

Fig. 5 Receiver operating characteristic curves of the left and right facet joint angulations and angulation difference in relation to L4–L5 degenerative spondylolisthesis.

left and right facet joint angulations that fulfilled 50% sensitivity presented with values of 55 and 58 degrees, respectively. As such, a 58-degree minimum cutoff value was adopted for the bilateral facet joint angulations. According to ROC analysis of the difference between bilateral facet joint angulations, the AUC was 0.58 (95% CI: 0.51 to 0.65; $p = 0.026$; ►**Fig. 5**). The analyses noted that an adopted critical value of 8-degree difference (50% sensitivity) corresponded to the minimum threshold for facet joint tropism in relation to L4–L5 DS. Based on the angulation values from the ROC analyses, the patients were further stratified to the following categories: (1) bilateral facet joint angulations less than 58 degrees, (2) unilateral facet joint angulation of 58 degrees or greater, and (3) bilateral facet joint angulations greater than 58 degrees. Tropism was further stratified into the following categories: (1) 0 to 7.9 degrees (normal), (2) 8 to 15.9 degrees, (3) 16 to 23.9 degrees, and (4) 24 or greater degrees.

Based on the multivariate model, adjusted for age and facet joint angulation categories, facet joint tropism of 8 degrees or greater was not found to be significant ($p = 0.444$). However, facet joint tropism of 16 degrees or greater was noted to be significantly associated with group B (adjusted OR: 2.9; 95% CI: 1.1 to 7.6; $p = 0.032$). According to an alternative model adjusting for age and facet joint angulation categories, tropism of 16 to 23.9 degrees may have an independent effect upon DS (adjusted OR: 5.6; 95% CI: 1.2 to 26.1; $p = 0.027$), whereas other ranges were not significant in relation to L4–L5 DS. Based on this multivariate regression model, there was a statistically significant increase in the likelihood of having DS in the presence of unilateral (adjusted OR: 2.5; 95% CI: 1.2 to 5.5; $p = 0.021$) or bilateral (adjusted OR: 5.9; 95% CI: 2.7 to 13.2;

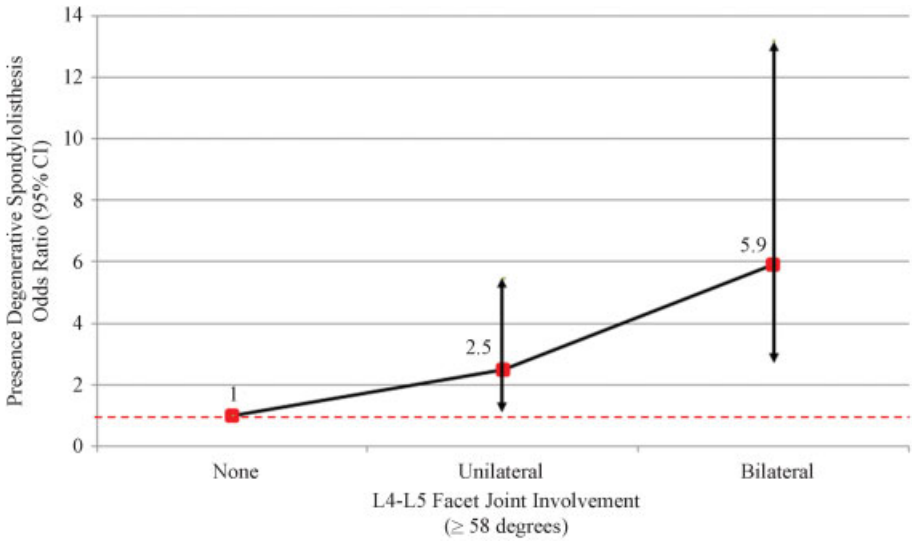

Fig. 6 The multivariate regression model noting association of facet joint angulation critical value and the likelihood of L4–L5 degenerative spondylolisthesis. Model adjusted for age and facet joint tropism. Hosmer-Lemeshow goodness-of-fit test was $p = 0.348$. Note that if the 95% confidence interval (CI) crosses the value of 1, the factor is not statistically significant.

$p < 0.001$) facet joints having an angulation of 58 degrees or greater in comparison to both joints having an angulation less than 58 degrees (►**Fig. 6**).

Discussion

This study was the largest and first international multicenter work focusing upon the role of facet joint angulation and tropism in relation to L4–L5 DS, in particular in an Asian population. Our findings indicated for the first time that a critical value (i.e., 58 degrees or greater) of facet joint angulation is significantly related to the likelihood of having L4–L5 DS. We proposed a simple three-tier classification scheme based on the number of facet joints involved and their association of DS. Furthermore, our study is the first to note that facet joint tropism may have a role in DS, but largely pertaining to specific bilateral angulation asymmetry ranges that may affect the mechanics and facilitate gliding of the vertebral segment to spondylolisthesis.

Advanced imaging, such as MRI and CT, allows one to appreciate the constitution and changes of the facet joints in relation to DS by assessing their geometrical orientation. With more sagittally aligned facet joints in patients with DS, a reduction in the resistance of anterior shearing occurs.[6,7,12,26,27] In a study of 111 subjects, Fujiwara et al showed that individuals with L4–L5 DS had more sagittally oriented facet joints compared with those without DS (mean 62.9 degrees versus mean 48.2 degrees).[8] In a study of 140 subjects (27 with DS) of heterogenic origin, Boden et al noted that individuals with L4–L5 DS had a mean facet joint orientation of 60 degrees versus 41 degrees in those with no DS.[6] The authors further noted that individuals who had sagittal angulation of 45 degrees or greater in relation to the coronal plane involving both facet joints were 25 times more likely to have DS. However, previous studies failed to address critical values based on a systematic assessment of the data in relation to DS, did not account for the aging process, were small in sample size, and possessed other methodological limitations as previously noted in the introduction section of this article. Our large-scale study of 349 individuals (82 controls and 267 with L4–L5 DS) from the Asia Pacific region further supported the notion that more sagittally oriented facet joints were associated with L4–L5 DS. Our study further proposed, after accounting for patient demographics and the effect of tropism, a critical value of 58 degrees or greater with individualized risk assessment based on unilateral or bilateral facet joint involvement in the development of DS (►**Fig. 6**). Our study noted an almost threefold and sixfold increase in the likelihood of L4–L5 DS when one or both facet joints reached that critical threshold, respectively.

The role of facet joint tropism in the development of DS remains controversial. In a recent systematic review by Devine et al,[25] the role of facet joint tropism in relation to DS was deemed "inconclusive." This discrepancy may depend on the definition of the phenotype of tropism, improper analytical assessment, or perhaps the ethnic/racial variations among many other factors. For example, according to a Caucasian study by Berlemann et al,[11] there was no relationship between facet joint tropism and the development of DS. Conversely, according to Dai,[13] in a study addressing a Japanese cohort of 53 subjects, facet joint tropism in cases of DS was 2.3 degrees greater than in cases without DS. Gao et al showed in their study of 156 patients that facet joint tropism was significantly greater in DS patients compared with control subjects.[28] However, in a heterogeneous population of 188 subjects, Kalichman et al did not find facet joint tropism to be related to DS.[24] Our study, based on the propagated definition of facet joint tropism ($\geq$7 degrees angulation asymmetry) as proposed by Grogan et al,[22] did not find facet joint tropism to be related to L4–L5 DS. Alternatively, based on our ROC assessment and multivariate analyses, we found that specific tropism ranges were more clinically relevant, such as 16 to 23.9 degrees of facet joint angulation differences. In our study, such a tropism category was associated with a sixfold increase in the likelihood of L4–L5 DS. As such, we propose a clinically relevant approach to the phenotype of facet joint tropism and note specific critical values that may warrant further consideration. Theoretically, such tropism may further lead to more severe forms of disk degeneration and segmental destabilization by compromise of the posterior column leading to greater facet joint degeneration. Nonetheless, future studies are needed to understand the interplay between such tropism and specific facet joint angulation parameters.

As with any clinical and multicenter study, inherent limitations existed with our work. For one, our sample was composed of patients who presented with DS at a single level from L3 to S1. We stratified those without L4–L5 DS to those with L4–L5 involvement; thereby, subjects acted as their own controls. Because studies have been published noting that facet joint orientation differences may be more localized to the level of DS involvement, our approach seemed acceptable. In addition, we found significant facet joint orientation variations between those patients with and without L4–L5 DS, facilitating comparisons. Furthermore, our study in large part was composed of Asian subjects and may be used for comparison to other populations in Western cultures. Our previous study assessing ethnic variations between Asian populations and facet joint angulation did not yield any substantial variations.[15] Also, the large sample of our study facilitated more in-depth statistical analyses to account for patient demographics, such as age, sex, and body mass index, which may play a role in facet joint orientation parameters. In addition, our findings are limited to the L4–L5 level and not to any other lumbar segments. However, because DS mainly manifests at the L4–L5 segment,[6,7] we felt that focusing on this level would be applicable, which was further facilitated by our sample size allowing for proper group stratification. In addition, our study was cross-sectional, providing an "association" of facet joint orientation and L4–L5 DS. However, it is highly likely that such facet joint orientation was pre-existent to the DS and played a role in its "development." Nonetheless, future prospective studies are needed to assess the cause and effect of such phenotypes and to determine their role in DS progression and changes of other spinal

phenotypes (e.g., disk degeneration, herniations, Modic changes, end plate irregularities, etc.), as well as outcomes of treatment management.

Conclusions

To our knowledge, our study is the largest to assess the role of facet joint angulation and tropism in the development of L4–L5 DS, particularly in an Asian population. Because it remains questionable whether facet joint angulation and/or tropism is developmental in origin or a secondary cause of the remodeling process with age and degenerative changes, our findings further raise attention to the phenotype of facet joint orientation. Our study has redefined the phenotype of facet joint orientation critical values in relation to DS and proposes a risk profile of DS based on these parameters. Such findings may warrant specific consideration of a "facet joint angulation and tropism classification" in the future. Therefore, such an understanding may facilitate ethnic and racial comparisons, possess potential clinical utility to identify the individuals who may be predisposed to developing such facet joint orientations, assist in management protocols, and be a tool for prognostic purposes on more personalized platforms. In addition, in an age whereby genomics has a role in numerous musculoskeletal conditions, such as disk degeneration[29,30] and knee osteoarthritis,[31,32] having a clearer understanding of the phenotype of the facet joints in spinal disorders may introduce a new approach to prevention and lifestyle modification as well as understanding the phenotype for future "omics" studies.

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