An International Multicenter Study Assessing the Role of Ethnicity on Variation of Lumbar Facet Joint Orientation and the Occurrence of Degenerative Spondylolisthesis in Asia Pacific: A Study from the AOSpine Asia Pacific Research Collaboration Consortium

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Abstract

Study Design A multinational, multiethnic, cross-sectional image-based study was performed in 33 institutions, representing 10 countries, which were part of the AOSpine Asia Pacific Research Collaboration Consortium.

Objective Lumbar facet joint orientation has been reported to be associated with the development of degenerative spondylolisthesis (DS). The role of ethnicity regarding facet joint orientation remains uncertain. As such, the following study was performed across a wide-ranging population base to assess the role of ethnicity in facet joint orientation in patients with DS in the Asia Pacific region.

Methods Lateral standing X-rays and axial magnetic resonance imaging scans were obtained for patients with lumbar DS. The DS parameters and facet joint angulations were assessed from L3–S1. Sex, age, body mass index (BMI), and ethnicity were also noted.

Results The study included 371 patients with known ethnic origin (mean age: 62.0 years; 64% males, 36% females). The mean BMI was 25.6 kg/m^2. The level of DS was most prevalent at L4–L5 (74.7%). There were 28.8% Indian, 28.6% Japanese, 18.1% Chinese, 8.6% Korean, 6.5% Thai, 4.9% Caucasian, 2.7% Filipino, and 1.9% Malay patients. Variations in facet joint angulations were noted from L3 to S1 and between patients with and without DS ($p < 0.05$). No differences were noted with regards to sex and overall BMI to facet joint angulations ($p > 0.05$); however, increasing age was found to increase the degree of angulation throughout the lumbar spine ($p < 0.05$). Accounting for age and the presence or absence of DS at each level, no statistically significant differences between ethnicity and degree of facet joint angulations from L3–L5 were noted ($p > 0.05$). Ethnic variations were noted in non-DS L5–S1 facet joint angulations, predominantly between Caucasian, Chinese, and Indian ethnicities ($p < 0.05$).

Conclusions This study is the first to suggest that ethnicity may not play a role in facet joint orientation in the majority of cases of DS in the Asia-Pacific region. Findings from this study may facilitate future comparative studies in other multiethnic populations. An understanding of ethnic variability may assist in identifying those patients at risk of postsurgical development or progression of DS. This study also serves as a model for large-scale multicenter studies across different ethnic groups and cultural boundaries in Asia.

Keywords
- degenerative
- spondylolisthesis
- facet
- joints
- morphology
- ethnicity
- Asia
- AOSpine

Introduction

Lumbar degenerative spondylolisthesis (DS) is sagittal plane translation of a lumbar vertebral body resulting from the destabilizing influence of progressive spondylosis (►**Fig. 1**).[1–3] Progressive change in the intervertebral disk, thickening of the ligamentum flavum, and translation of the vertebra all contribute to the compromise of the canal and central spinal stenosis. The process may also cause foraminal narrowing due to the impingement of the superior articular process in the neuroforamina. In symptomatic patients with DS whose condition can be debilitating and nonresponsive to conservative management, surgical intervention is performed, which is not without inherent complications and is often associated with tenuous outcomes.[3–7] As such, understanding the development of DS is essential to design preventative measures as well as for patient management and outcomes.

Numerous risk factors are associated with DS. For example, DS occurs up to four times more frequently in females.[8] It is more common in individuals in their sixth decade of life,[9] occurring in 29% of the female population over the age of 65.[10] Other predisposing factors for DS include parity, general joint laxity, oophorectomy, increased pedicle facet angle, and sagittal alignment of the facet joints.[11]

The facet joints control motion between the adjacent vertebrae. They provide stability to spinal segments and they protect the neural elements. The lumbar facet joint

Fig. 1 Lateral standing plain radiograph. Arrow illustrates L4–L5 degenerative spondylolisthesis.

accommodates 33% of the dynamic compressive load and 35% of the static load at each lumbar motion segment.[12,13] The sagittal orientation of the facet joints limits axial rotation, increases torsional strength, and resists anterior shearing forces.[14]

The development of the sagittal orientation and morphology of the lumbar facet joints are debated. Boden et al reported that greater sagittal facet joint orientation was seen in subjects without DS, suggesting a developmental etiology rather than secondary to the degenerative process.[15] An alternative theory relates to a remodeling process associated with degenerative change. The anterior third of the facet joint receives loading stress and the posterior two-thirds of the facet joint is mainly under shear stress, which some authors believe may lead the facet joints to become more sagittally oriented over time.[16] In a small Asian population, Fujiwara et al have postulated that osteoarthritis of the facet joints is the precursor lesion to sagittal orientation rather than spondylolisthesis itself.[9] In a Caucasian population, Grobler et al have shown a relationship between the facet joint sagittal orientation and DS.[11] Although the issue of cause and effect regarding facet orientation and slippage remains, these small cohort studies imply that there may be a difference in the occurrence of DS based on ethnicity.

The notion that DS may have an ethnic proclivity is further substantiated by numerous studies that have noted ethnic variations for pain, function, and skeletal morphologies affecting the hand, hip, and knee.[17–21] Ethnic variations are also noted between the osteoarthritic changes of the knee and the degenerative changes of the intervertebral disk.[22] Moreover, the genetic factors associated with various musculoskeletal conditions may also vary between ethnic groups.[23–25]

Understanding the impact of ethnicity upon the development of DS may shed light as to its risk profile and in devising proper patient management guidelines that may be more ethnicity-specific rather than generalized. To date, no large-scale studies have addressed the role of ethnicity upon lumbar facet joint orientation and its association with DS. As such, the AOSpine Asia Pacific (AOSAP) Research Collaboration consortium conducted a large-scale, international multicenter study to address the role of ethnicity in the variation of lumbar facet joint orientation and the development of DS in the Asia Pacific region.

Methods

The study was an international, multicenter, cross-sectional radiographic assessment of patients with DS in the Asia Pacific region. Thirty-three centers representing 10 countries were identified based on their involvement with the AOSAP Research Collaboration Consortium and were invited to participate. This consortium was established as a mechanism to promote international collaboration in spinal research throughout the Asia Pacific region. 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.

Patients greater than 18 years of age with DS residing in the Asia Pacific region were recruited. No individuals of mixed or unknown ethnic origin were included in this study. DS was defined as nonisthmic with a 3-mm or greater slip on lateral standing plain radiographs at any level from L3 to S1. Exclusion criteria included previous or current spinal surgery, congenital anomaly, transitional vertebrae, infection, trauma, tumor, isthmic spondylolisthesis, and inadequate imaging.

Standing lateral plain radiographs and axial T2-weighted lumbar magnetic resonance images (MRI) of the lumbar spine were obtained. The level of DS and the degree of slip in millimeters was assessed on plain radiographs (►**Fig. 1**). Axial MRIs 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 (►**Fig. 2**). MRI slices (►**Fig. 3**) were selected if they included the posterior/superior corner of the caudal vertebral body. This slice most closely bisects the facet joint and as such was utilized for measuring the fact 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. Because DS mainly affects the lower lumbar spine, the imaging assessment focused on the bilateral facet joints from L3 to S1. For the purposes of the following study, MRI was used to assess the facet joint angulation, noted as the angle representing the anteroposterior facet joint borders to that of the border of the posterior rim of the vertebral body (►**Fig. 3**). All imaging was independently assessed. Reliability estimates of facet joint orientations have been reported elsewhere.[26] In

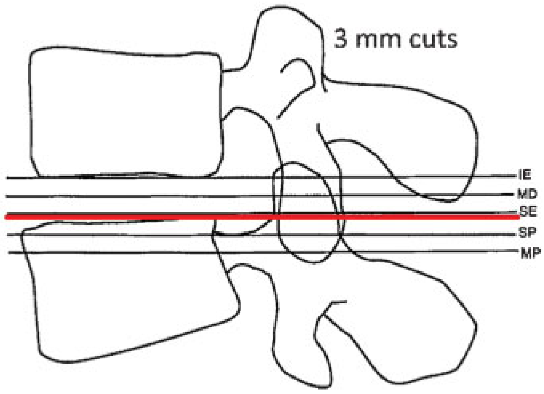

Fig. 2 The 3-mm cuts made for axial images. The best cut is the bisector of the facet joint (denoted as SE here). Other cuts here include the inferior end plate (IE), middle of disk (MD), superior aspect of pedicle (SP), and midpedicle (MP).

addition, age (years), sex, weight (kilograms), height (meters), body mass index (kg/m^2), and ethnicity were recorded. In the event both parents were not of the same ethnic background, the patient was regarded as having "mixed" ethnicity and were excluded from study.

All imaging was collected at each respective site, anonymized, and forwarded to a central location for data analysis. All data was entered unto a spreadsheet. 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 appropriate parametric and nonparametric tests were utilized where appropriate. Chi-square tests were performed to assess categorical data. Analysis of variance tests were performed to assess the variations between patient demographics and ethnicity to facet joint angulations. Post hoc multiple-comparison Tukey tests were performed to assess the association between ethnicity types to facet joint angulations while controlling for applicable confounders. A threshold for statistical significance was established at $p < 0.05$.

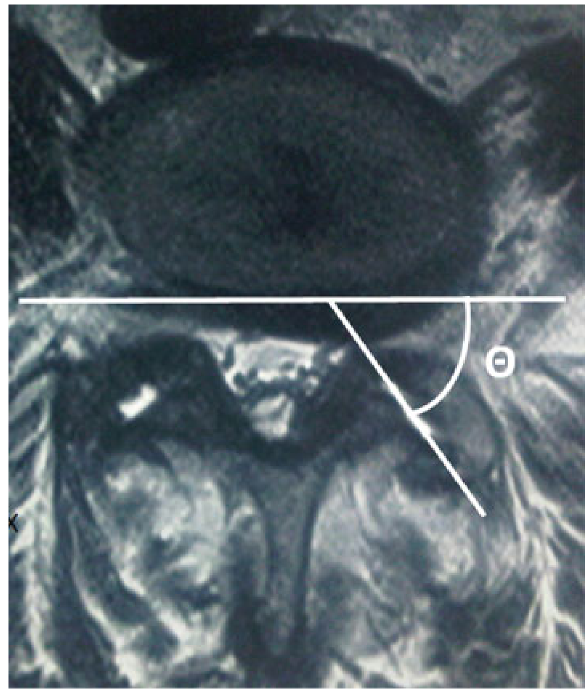

Fig. 3 Axial magnetic resonance imaging noting the assessment of facet joint angulation. "Θ" denotes degrees.

Results

The study consisted of 371 patients with DS who presented with known ethnic origin. The mean age was 62.0 years (standard deviation [SD]: ± 12.4; range: 24.0 to 90.0) with a mean BMI of 25.6 kg/m^2 (SD: ± 4.2; range: 15.4 to 43.9). There were 64% females and 36% males. Of the cases, 28.8% were Indian; 28.6%, Japanese; 18.1%, Chinese; 8.6%, Korean; 6.5%, Thai; 4.9%, Australian Caucasian; 2.7%, Filipino; and 1.9%, Malay. Patient demographics stratified to ethnic type are noted in ►**Table 1**. The DS level most commonly involved was L4–L5, occurring with single-level L4–L5 involvement in 74.7% of the cases, followed by L5–S1 in 12.9% of the cases, and L3–L4 in 12.4% of the cases.

Table 1 Demographics of patients with degenerative spondylolisthesis stratified to ethnic origin

Ethnicity	Females (%)	Age (y), mean, SD (range)	BMI (kg/m^2), mean, SD (range)
Caucasian	27.8	68.5, 9.0 (49.0–82.0)	25.9, 3.6 (21.3–34.0)
Chinese	72.3	65.0, 9.9 (39.0–88.0)	28.0, 5.5 (16.9–43.9)
Filipino	80.0	64.0, 12.4 (48.0–81.0)	24.8, 3.3 (19.5–29.1)
Indian	62.6	66.7, 10.9 (28.0–83.0)	24.7, 3.3 (17.3–34.7)
Japanese	59.4	54.8, 12.6 (24.0–90.0)	25.5, 3.8 (15.4–34.9)
Korean	78.1	63.9, 9.4 (46.0–82.0)	24.3, 3.3 (15.6–30.5)
Malay	85.7	52.1, 10.3 (37.0–65.0)	25.4, 7.2 (21.1–41.6)
Thai	62.5	59.0, 13.9 (32.0–81.0)	26.1, 3.4 (18.1–36.2)
Overall	64.0	62.0, 12.4 (24.0–90.0)	25.6, 4.2 (15.4–43.9)

Abbreviations: BMI, body mass index; SD, standard deviation.

Overall Facet Joint Angulations

The mean left and right facet joint angulations at L3–L4 were 55.4 degrees (SD: ± 13.7; range: 4.0 to 97.0) and 55.6 degrees (SD: ± 15.7; range: 0 to 173.0), respectively. The mean left and right facet joint angulations at L4–L5 were 53.0 degrees (SD: ± 14.9; range: 1.2 to 101.0) and 55.6 degrees (SD: ± 15.6; range: 8.0 to 125.0), respectively. The mean left and right facet joint angulations at L5–S1 were 43.2 degrees (SD: ± 13.2; range: 3.5 to 120.0) and 42.9 (SD: ± 12.5; range: 0 to 95.0), respectively. Sex and BMI did not statistically significantly differ between the L3–S1 bilateral facet joint angulations ($p > 0.05$); however, increasing age was related to increasing facet joint angulation ($p < 0.05$). Further stratification of bilateral facet joint angulations from L3–S1 according to ethnicity is illustrated in ►**Table 2**.

Facet Joint Angulations at L3–L4

Of the 371 patients, 46 individuals presented with L3–L4 DS and 325 without L3–L4 DS. Of the patients with no DS at L3–L4, the mean left and right facet joint angulations were 55.0 degrees (SD: ± 12.6; range: 24.0 to 97.0) and 54.3 degrees (SD: ± 13.1; range: 10.0 to 100.0), respectively. Of the patients with DS, the mean left and right facet joint angulations were 61.4 degrees (SD: ± 14.5; range: 33.0 to 85.0) and 67.1 degrees (SD: ± 22.9; range: 30.0 to 173.0), respectively. The left ($p = 0.002$) and right ($p < 0.001$) facet joint angulations statistically differed regarding the presence or not of DS. Based on post hoc multiple comparison tests and further controlling for the factor of age, no statistically significant difference was noted between bilateral facet joint angulations and different ethnicity at levels without L3–L4 DS ($p > 0.05$; ►**Fig. 4A**). However, the small sample size of individuals who had DS at L3–L4 prevented robust analytical assessment to determine the role of ethnicity upon facet joint angulation at those levels (►**Fig. 4B**).

Facet Joint Angulations at L4–L5

Of the overall patients, 277 presented with L4–L5 DS and 94 without L4–L5 DS. Of the patients with no DS at L4–L5, the mean left and right facet joint angulations were 47.8 degrees (SD: ± 13.0; range: 24.0 to 86.0) and 50.0 degrees (SD: ± 14.0; range: 20.0 to 85.0), respectively. Of the patients with DS, the mean left and right facet joint angulations were 55.4 degrees (SD: ± 14.1; range: 29.0 to 101.0) and 57.7 degrees (SD: ± 15.4; range: 20.0 to 125.0), respectively. Left ($p < 0.001$) and right ($p < 0.001$) facet joint angulations statistically differed regarding the presence of DS. Based on post hoc multiple comparison tests and further controlling for the factor of age, no statistically significant difference was noted between bilateral facet joint angulations and different ethnicity at levels without (►**Fig. 5A**) or with (►**Fig. 5B**) L4–L5 DS ($p > 0.05$).

Facet Joint Angulations at L5–S1

Forty-eight individuals presented with L5–S1 DS and 327 without L5–S1 DS. Of the patients with no DS at L5–S1, the mean left and right facet joint angulations were 42.6 degrees (SD: ± 12.2; range: 10.0 to 80.0) and 42.8 degrees (SD:

Table 2 Overall bilateral facet joint angulations from L3–S1 based on ethnicity

Ethnicity	L3–L4, mean, SD (range)		L4–L5, mean, SD (range)		L5–S1, mean, SD (range)	
	Left	Right	Left	Right	Left	Right
Caucasian	55.4, 11.1 (36.0–85.0)	60.9, 31.9 (36.0–173.0)	48.4, 17.2 (25.0–70.0)	55.1, 14.7 (32.0–85.0)	52.6, 14.1 (29.0–80.0)	50.7, 10.8 (32.0–75.0)
Chinese	59.1, 13.5 (30.0–97.0)	57.0, 15.6 (15.0–85.0)	58.0, 14.1 (29.0–84.0)	58.0, 14.8 (20.0–90.0)	45.5, 12.0 (17.0–73.0)	44.8, 14.5 (0–76.0)
Filipino	47.0, 11.9 (27.0–68.0)	54.7, 10.3 (35.0–68.0)	53.0, 14.2 (30.0–76.0)	51.7, 9.5 (38.0–67.0)	42.2, 8.0 (31.0–52.0)	37.7, 12.3 (5.0–51.0)
Indian	57.5, 11.2 (30.0–84.0)	55.3, 12.7 (10.0–86.0)	55.5, 14.1 (24.0–95.0)	58.0, 14.4 (23.0–89.0)	40.4, 11.5 (10.0–70.0)	41.2, 11.3 (13.0–80.0)
Japanese	52.4, 13.3 (30.0–88.0)	53.4, 15.0 (27.0–100.0)	49.0, 13.3 (30.0–88.0)	51.1, 15.8 (20.0–125.0)	42.4, 14.5 (10.0–120.0)	41.1, 12.2 (10.0–95.0)
Korean	62.8, 12.0 (40.0–91.0)	61.4, 11.9 (45.0–88.0)	57.9, 14.0 (40.0–101.0)	62.0, 17.1 (35.0–99.0)	44.2, 12.3 (25.0–73.0)	43.4, 10.6 (25.0–70.0)
Malay	55.1, 10.1 (39.0–70.0)	62.1, 8.6 (54.0–78.0)	49.4, 12.4 (34.0–66.0)	53.3, 15.9 (32.0–75.0)	44.7, 13.2 (25.0–60.0)	41.3, 11.9 (21.0–57.0)
Thai	48.2, 12.2 (24.0–75.0)	54.3, 14.0 (23.0–75.0)	50.9, 14.9 (31.0–86.0)	53.3, 17.8 (8.0–83.0)	46.1, 14.2 (20.0–87.0)	48.7, 13.6 (27.0–85.0)
Overall	55.8, 13.0 (24.0–97.0)	55.9, 15.3 (10.0–173.0)	53.5, 14.3 (24.0–101.0)	55.6, 15.6 (8.0–125.0)	43.3, 13.0 (10.0–120.0)	43.1, 12.5 (10.0–95.0)

Abbreviation: SD, standard deviation.

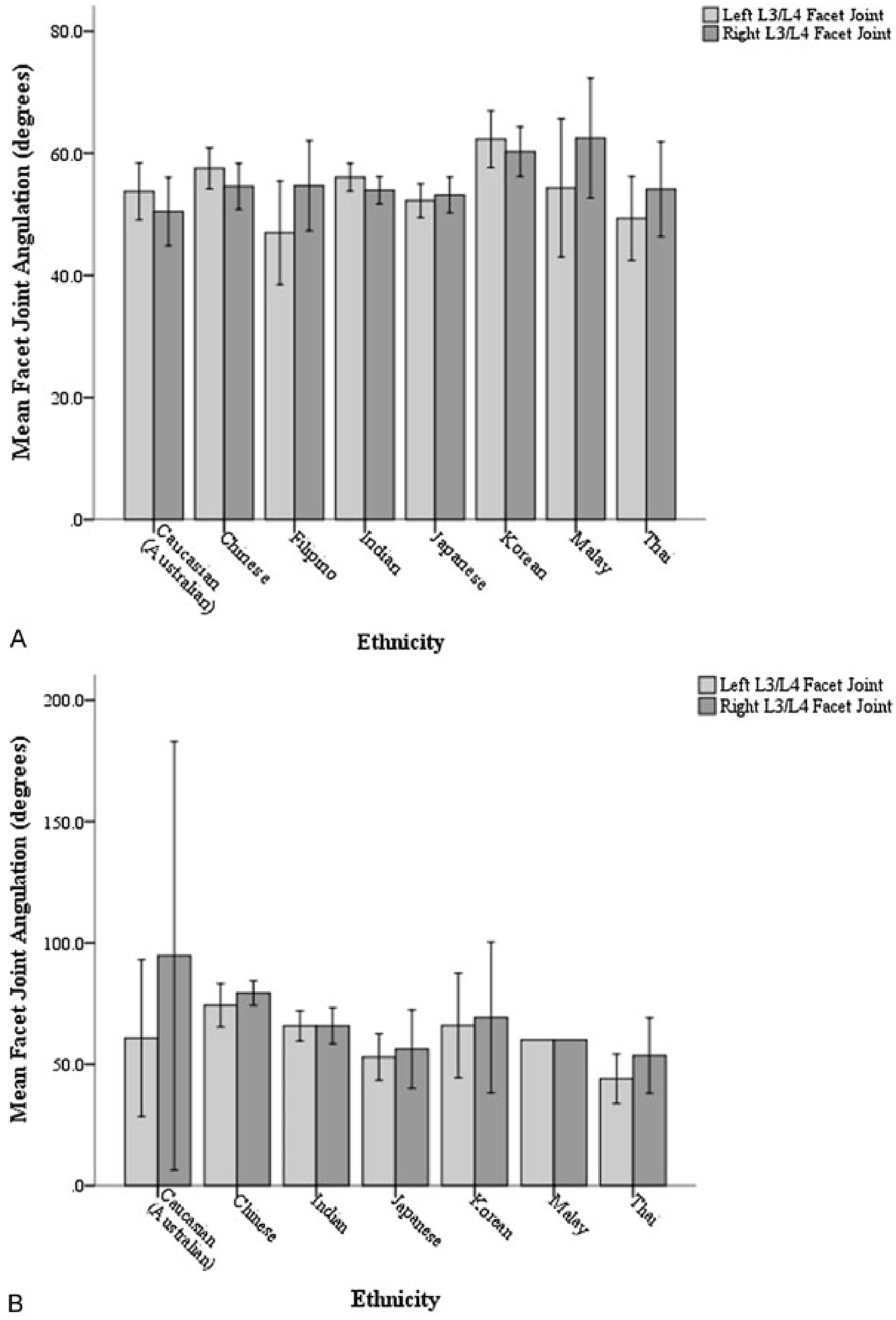

Fig. 4 Left and right mean facet joint angulations with 95% confidence intervals at L3–L4 in individuals (A) who had no degenerative spondylolisthesis and (B) who had spondylolisthesis at that level.

$\pm$ 12.0; range: 10.0 to 80.0), respectively. Of the patients with DS, the mean left and right facet joint angulations were 48.2 degrees (SD: $\pm$ 17.3; range: 20.0 to 120.0) and 45.2 degrees (SD: $\pm$ 13.4; range: 10.0 to 95.0), respectively. Left facet joint angulation was statistically greater in patients with L5–S1 DS ($p = 0.006$), but a statistically significant difference was not noted for the right facet joint ($p = 0.209$). Based on post hoc multiple comparison tests and further controlling for the factor of age, no statistically significant difference was noted between bilateral facet joint angulations and different ethnicity at levels without L5–S1 DS ($p > 0.05$) with the exception of significant variations between Caucasians, Chinese, and Indian ethnicities ($p < 0.05$; ►**Fig. 6A**). Due to the small sample size of individuals with DS at L5–S1, the role of ethnicity upon facet joint angulation could not be discerned (►**Fig. 6B**).

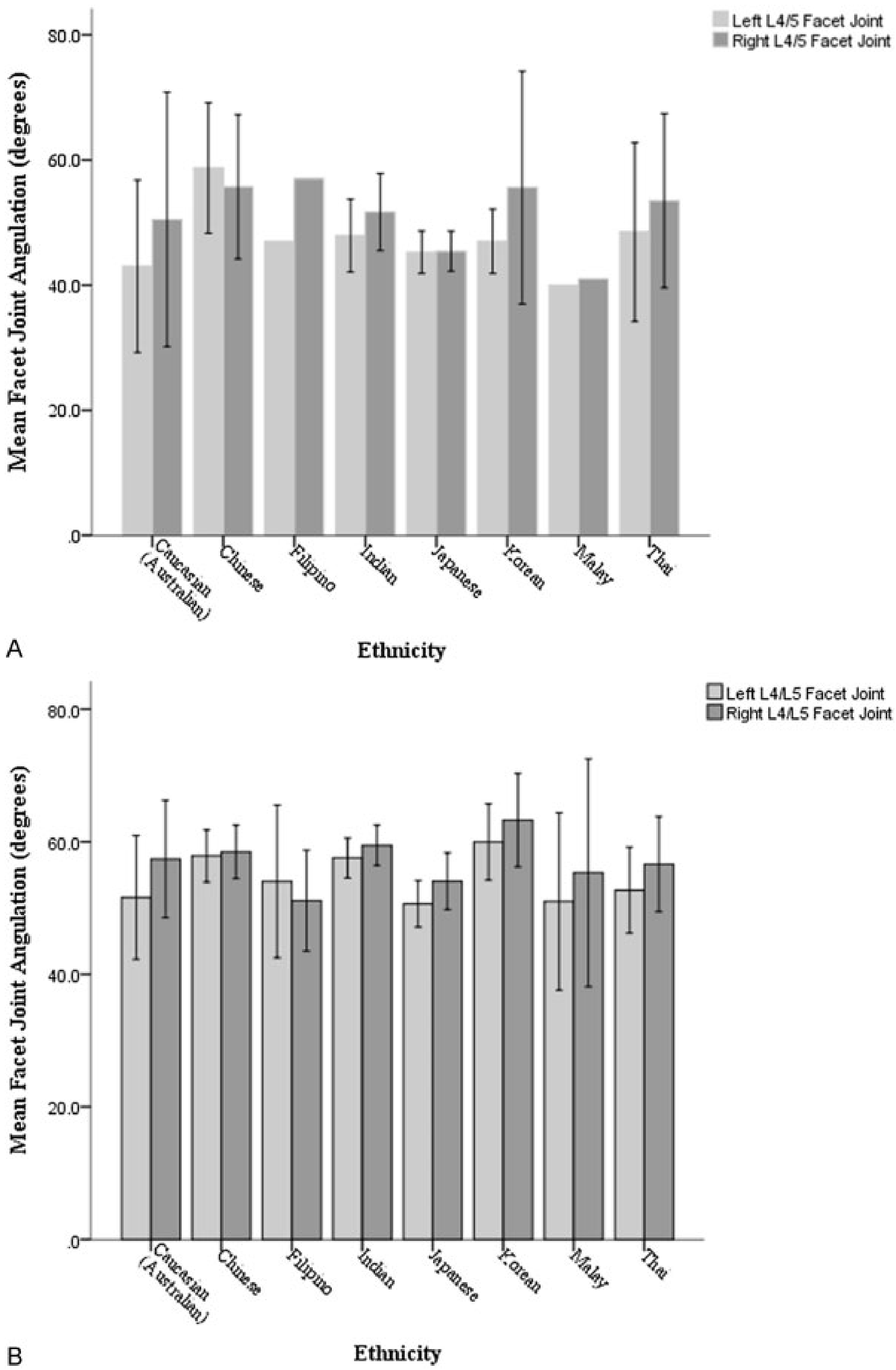

Fig. 5 Left and right mean facet joint angulations with 95% confidence intervals at L4–L5 in individuals (A) who had no degenerative spondylolisthesis and (B) who had spondylolisthesis at that level.

Discussion

We believe our study to be the first international multicenter study created to assess the role of ethnicity upon lumbar facet joint orientation in patients with DS in the Asia Pacific region. This collaborative study offered better understanding of the prevalence, gender, and ethnic variations of lumbar facet joint orientation and DS in the Asia Pacific region. Although ethnic variation did not seem to play a role in facet joint angulation from L3 to L5, distinct ethnic variations between Caucasians, Chinese, and Indian ethnicities were noted at the L5–S1 joints. Ethnic variations are commonly found in osteoarthritis. Management decisions should be tailored toward the respective population group because the indications and outcomes may differ across different ethnicities. Ethnicity affects the clinical presentation, symptom severity, and

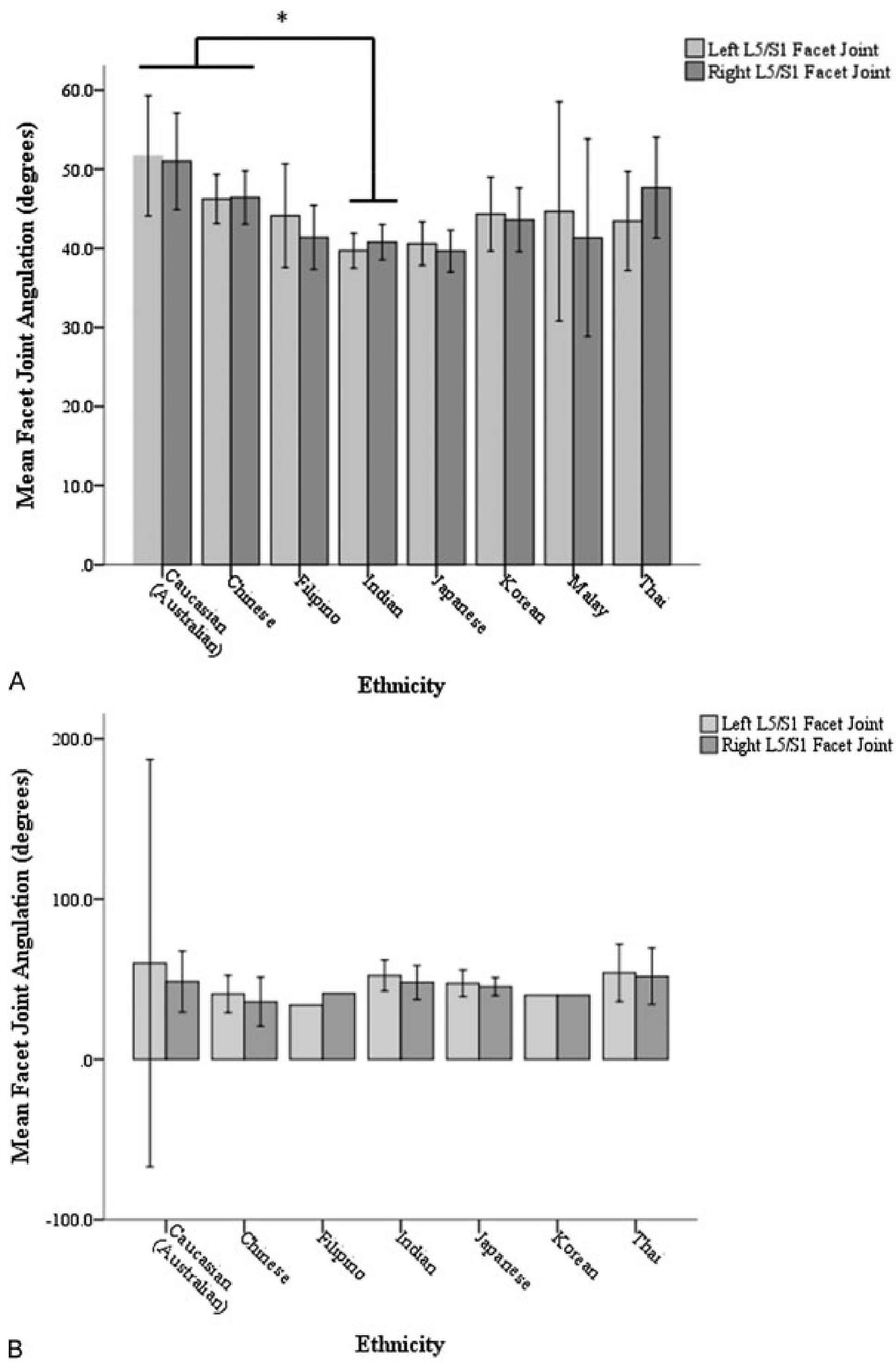

Fig. 6 Left and right mean facet joint angulations with 95% confidence intervals at L5–S1 in individuals (A) who had no degenerative spondylolisthesis and (B) who had spondylolisthesis at that level. *Statistically significant difference based on multiple-comparison post hoc tests adjusting for age ($p < 0.05$).

management options and outcomes in osteoarthritis of the hand, hip, and knees.[17–20]

For the spine, the lumbar facet joints are also influenced by ethnicity. Fujiwara et al have shown in a Japanese population that patients with DS had more sagittally oriented facet joints versus controls with 62.9 versus 48.2 degrees and 68.6 versus 41.9 degrees for L4–L5 and L5–S1, respectively.[9] In this study, no differences were noted for L3–L4. In a Caucasian population, Grobler et al have shown that the most distal facet joints, especially L4–L5, were usually in coronal alignment.[11] The L3–L4 was most sagittal, followed by L5–S1, and the L4–L5 was most coronal. These findings differed from the study by Fujiwara et al indicating ethnic differences between Caucasian and Asian facet joint orientation.[9] Boden et al conducted a similar study in the United States and found that individuals with DS at L4–L5 had a facet orientation of 60 versus 41 degrees for those without slip.[15] Further difference was noted in a United Kingdom study where sagittally oriented facet joints were only associated with osteoarthritis and DS at L4–L5.[27] In our study, greater sagittal orientation was noted in patients with DS between L3 and S1. The difference was considerable at L4–L5 but less so at L5–S1. In general, there was a similar spread for facet joint angulation across all ethnic groups with the only exception being at L5–S1 between Caucasians, Chinese, and Indian ethnicities.

In addition to ethnicity, gender may also play a role in the development of DS. There is a predominance of females with DS despite comparable facet joint orientation between males and females. In one study of Caucasian subjects,[11] Kalichman et al also found that the facet orientation was similar in males and females.[27] In our study, 63.3% of patients with DS were females but gender did not affect facet joint orientation. Thus, gender is likely to contribute to DS development, but its role may not be related to sagittal alignment of the facet joints. Although this rationale is unproven, some have suggested that a higher expression of the estrogen receptor may correlate with more severe facet joint arthritis and DS.[28]

MRI is useful to assess facet joint orientation and tropism without the risk of ionizing radiation.[15] In the same setting, the severity of disk degeneration, facet joint arthritis, and end plate changes can also be assessed. Although inconclusive, disk degeneration may adversely affect facet joint function orientation, and the shape of the lumbar facet joints can also be related to their biomechanical function. The more curved L3–L4 joint gives multidirectional stabilization resisting both anterior and lateral translations, and the L5–S1 is flat and is more coronally oriented, giving greater resistance to anterior shearing loads. With more sagittally aligned facet joints, there is a reduction in the coronal dimension of the joint resulting in reduced area for resisting the anterior shearing forces, which is more commonly found in DS.[11,15,29–31] The relationship between the L5–S1 segment and the development of DS is not fully understood. It is believed that the iliolumbar ligament contributes materially to the stability of the L5–S1 segment, preventing or minimizing the predisposition to DS.[32,33] Also, although increased BMI has also been linked to disk degeneration and back pain, no obvious association between BMI and facet joint orientation was observed.

As with any multicenter study, there were some inherent issues regarding study limitations. For one, age at presentation of DS varied. There could be an age-related effect of facet joint osteoarthritis leading to the development of DS, and its contribution as a risk factor to the sagittal orientation of the facet joints remains debatable. Sagittally oriented facet joints may be observed in cases without osteoarthritis or DS, indicating a possible developmental cause rather than a remodeling effect. Longitudinal studies are necessary to resolve this issue. Nonetheless, we attempted to stratify our sample size into various age categories to control for the factor of age in the assessment between ethnicity and facet joint angulation. Gene association studies may also be useful in understanding the genetic architecture behind facet joint morphology. Future studies should also assess the degree of disk degeneration and disk height loss as they correlate with the facet joint orientation, because these parameters may predispose to DS. The overall global alignment was another element not addressed in this study, which may answer some of the questions regarding spine biomechanics and the development of sagittal facet orientation and DS.

Despite the limitations discussed, this study has shown that ethnicity may have level-specific influences upon facet joint orientation, particularly at L5–S1, and may influence the occurrence and severity of DS. Moreover, this study is the largest to assess the role of ethnicity on lumbar facet joint orientation in patients with DS and is a model for collaborative, multicenter studies across different countries, ethnic groups, and cultural boundaries in the Asia Pacific region. We have shown important baseline facet joint characteristics among different ethnic groups in this region and as such have further refined the phenotype of facet joint angulation in this population and its subethnicities.

Conclusions

This article describes the largest study with collaboration of multiple countries in the Asia Pacific region to address the role of ethnicity upon lumbar facet joint orientation in DS. Moreover, this study further elaborated upon the phenotype of facet joint orientation of the lumbar spine in a predominantly Asian population. As a result, this study is the first to identify the level-specific ethnic associations regarding facet joint angulations, mainly affecting L5–S1. Although ethnicity may play a role in facet joint orientation and may influence the occurrence and severity of DS, numerous factors are present that preclude any robust position that ethnicity does indeed affect facet joint orientation. As such, further studies are required to fully distinguish ethnic variations. An understanding of ethnic variability may be one factor that assists in identifying those patients at risk of postsurgical development or progression of DS. In addition, this study has proposed an overall model of multicenter collaboration composed of different spine institutes throughout Asia Pacific, whose structure can be utilized for future spine research initiatives.

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