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Age, pelvic incidence, facet joint angle and pedicle-facet angle as correlative factors for isthmic spondylolisthesis: a retrospective case control study

Qian Kong^{1†}, Bohan Wei^{1†}, Shuoqun Niu¹, Jiawen Liao¹, Yuliang Zu^{2*} and Tao Shan^{3*}

Abstract

Background Isthmic spondylolisthesis (IS) is a common clinical disease with a high incidence rate. However, most current researches explain the clear pathogenesis from a single perspective. The aim of our study was to explore the relationships between multiple parameters in patients and find the potential risk factors of this disease.

Methods Our study retrospectively included 115 patients who were diagnosed with isthmic spondylolisthesis and the same number of individuals without spondylolisthesis. The following parameters were measured or collected: age, pelvic incidence (PI), facet joint angle (FJA) and pedicle-facet angle (P-F angle). The radiographic files were imported into Mimics Medical 20.0 and all collected data were analyzed using SPSS, version 26.0, statistical software.

Results The age was higher in IS group than in control group. PI was also higher in the IS group (50.99 ± 7.67) than in the control group (43.77 ± 9.30) significantly ($P = 0.009$). There was significant difference in cranial and average FJA tropism in L3-L4 level ($P = 0.002$, $P = 0.006$, respectively) and in L4-L5 level ($P < 0.001$). P-F angle of L4-L5 level showed significantly larger in IS group than in control group ($P = 0.007$). The logistic regression analysis showed a larger age, a greater L3-L4 cranial FJA tropism, and a greater L4-L5 cranial FJA tropism were potential predictors of IS, with an OR of 1.07, 1.28, and 1.39 respectively. The thresholds of the predictors were 60 years, 5.67° , and 8.97° according to the ROC curve. The linear regression equation was established: degree of slippage (%) = $0.220 * \text{age} - 0.327 * \text{L3-4 cranial FJA tropism} - 0.346 * \text{L4-5 average FJA tropism}$ ($F = 3.460$, $P = 0.011$, $r = 0.659$).

Conclusions Our study revealed that isthmic spondylolisthesis may be related to multiple factors rather than a single factor. Age, PI, PJA and P-F angle are potentially associated with spondylolisthesis.

Keywords Facet joint, Spinopelvic balance, Pelvic incidence, Spondylolisthesis, Computed tomography

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Background

Spondylolisthesis is a common pathological condition with an estimated 3–5% incidence rate [1, 2]. Isthmic spondylolisthesis (IS) is one of the main types of spondylolisthesis defined as the anterior translation of one vertebral body relative to the next caudal segment as a result of an abnormality of the pars interarticularis [3] that appears most commonly at the L5–S1 level, with a grade of slippage of I–IV. The hamstring tightness and lower back or buttock pain as well as disability such as intermittent claudication associated with IS [4, 5] cause a significant burden of patients' quality of life. The related factors of IS are thought to be complex and multifactorial [6, 7], believed to involve both integral factors like sagittal spinopelvic alignments and partial elements like the morphology of lumbar facet joints [8, 9]. Some researchers reported an increase in pelvic incidence (PI) among patients with IS compared to healthy volunteers [10–12]. The facet joint of slippery segment appears to be structurally asymmetrical and have a more transverse orientation, that is to say an increase in difference between the left and right facet joint angles (FJA), and an increase in pedicle-facet angle (P-F angle) [9, 13].

However, published studies focus mostly on the respective relationship between IS and one certain factor while the relationship between multiple parameters involving several vertebral segments of IS patients has rarely been reported. What's more, the few studies discussing the correlation between the parameters and the grade of slippage is controversial.

Most previous studies used 2D sagittal radiographs to measure the spinopelvic parameters such as PI in the standing position, which leads to difficulties to obtain the superposition of the two femoral heads in practice because of the rotation of the pelvic and nonvertical projection of the X-ray. As a result, some researchers pick the midpoint on the line connecting the centers of the femoral heads as the reference point to measure PI, causing the appearance of systematic error [14]. It is crucial for pre-and-post operative evaluation of IS patients to obtain accurate PI. Therefore, the CT scans is used for PI measurement in this study.

The aim of this study is to use 3D reconstructed models from CT images to evaluate PI and the morphological change of facet joint, as well as the relationships between multiple parameters in IS patients.

Materials and methods

Our study was designed as a retrospective study for clinical research. With the approval of institutional review board, we included 115 patients who were diagnosed with isthmic spondylolisthesis in Qilu Hospital of Shandong University (Qingdao) from June 30th, 2017 to October 30th, 2021 (85 Meyerding grade I patients, 30 Meyerding

grade II patients). The diagnosis is made according to the imaging which indicates the cone moves forward. The Meyerding grade of the spondylolisthesis was defined based on the degree of slippage in the lumbar spine (grade 0, no slip; grade I, a 1–25% slip; grade II, a 25–50% slip; grade III, a 51–75% slip; and grade IV, a 75–100% slip) [5]. The same number of individuals without IS over the same period were considered as the control group.

The inclusion criteria were: (1) 18 years of age or older. (PI increases during childhood and then remains unchanged throughout adolescence and adulthood [15]) (2) The imaging data and case notes of all study subjects were reserved completely. (3) The structures such as the femoral head, the sacrum endplate surface, and the facet joints can be clearly seen in the image.

The exclusion criteria were: (1) Congenital spinal deformities including congenital failure of formation or segmentation. (2) History of spinal and pelvic surgery. (3) Diagnosis of lumbar scoliosis, lumbar trauma or infection, lumbar facet joint infection or invasive tumour. (4) Other types of spondylolisthesis, such as degenerative, isthmic, traumatic, dysplastic, or pathologic spondylolisthesis (according to the Wiltse Classification).

Image data was exported as Digital Imaging and Communications in Medicine (DICOM) files (ABD=1 mm) and the DICOM format files was imported into Mimics Medical 20.0 for measurement.

Measurement of radiographic parameters

CT images of the subjects were saved in DICOM format. These DICOM files were imported into Mimics Medical 20.0 (Materialise NV, Belgium). All radiographic parameters were measured by four researchers using this software, and the average value was obtained for analysis. The radiographic parameters include:

Pelvic Incidence PI was measured using 3D reconstruction. We first marked the midpoint of sacral endplate using “point” tool, and created the approximate spheres of bilateral femoral heads using “sphere” tool in sagittal view. Then view was switched to 3D reconstruction to make sure the superposition of the left and right femoral heads. PI was measured by the complementary angle between the line parallel to the sacral endplate and the line connecting the midpoint of sacral endplate to the midpoint of the femoral heads [16] (Fig. 1).

Facet Joint Angle FJA was measured on an axial cut parallel to the vertebral endplate. The angle was formed by a midsagittal line through the vertebral body and a line connecting the anteromedial point to the posterolateral point of the facet joint [17]. Both left and right side of the angles were measured (Fig. 2). The FJA measured in the plane that was parallel to endplate of the inferior verte-

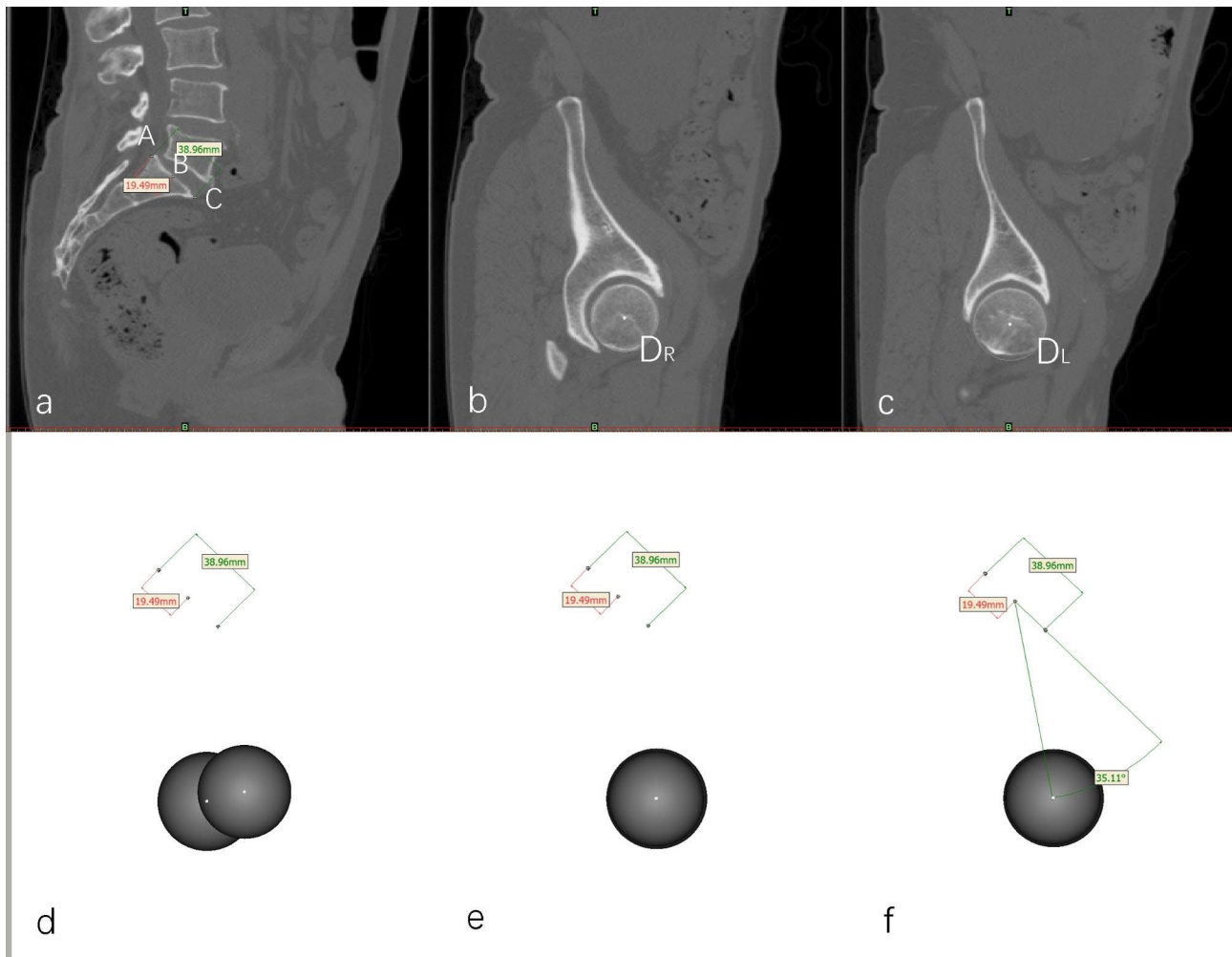


Fig. 1 Measurement of pelvic incidence. **a** The posterior edge(A), midpoint(B) and anterior edge(C) of the sacral endplate are marked respectively in the sagittal view. **b-c** The approximate spheres of the left and right femoral heads are created using “sphere” tool, with which center of sphere(D_L and D_R) could be automatically calculated. **d-e** In 3D view, the superposition of bilateral femoral heads was assured by rotating until the two centers coincide. **f** The angle between the line parallel to the sacral endplate and the line connecting the midpoint of sacral endplate to the center of femoral heads was measured, which is the complementary angle of PI.

bral body was defined as cranial FJA, while its counterpart measured in the plane that was parallel to endplate of the superior vertebral body was defined as caudal FJA. Both left and right, cranial and caudal FJA of L3-L4, L4-L5, and L5-S1 levels were measured.

Pedicle-facet Angle P-F angle was measured on a sagittal cut in which the facet joint was clearly visualized. The angle between the line connecting the midpoint of the anterior and posterior vertebral body cortices and the line parallel to the facet joint was defined as P-F angle [18] (Fig. 3). P-F angle of L3-L4, L4-L5, and L5-S1 levels were measured.

Degree of slippage The severity of isthmic spondylolisthesis can be described by degree of slip on the sagittal view. A line perpendicular to the upper endplate of the

caudal vertebra was drawn from posterior border of the cranial vertebra. The distance posterior to the line divided by the width of caudal vertebra was defined as degree of slip [19]. We measured the degree of slippage on L5 level and expressed them as a percentage.

Statistical analysis

All collected data were analyzed using SPSS (version 26.0) and R (version 4.2.1), statistical software. Measures were expressed as the mean ± standard deviation. The between-group difference for PI, FJA and P-F angle of the spinal segments were analyzed using Student’s t-test. Pearson correlation analysis was performed in IS group to analyze the relationship between parameters and degree of slippage. Logistic regression analysis was used to analyze the potential predictors. Receiver operating characteristic curve (ROCC) and Youden index were

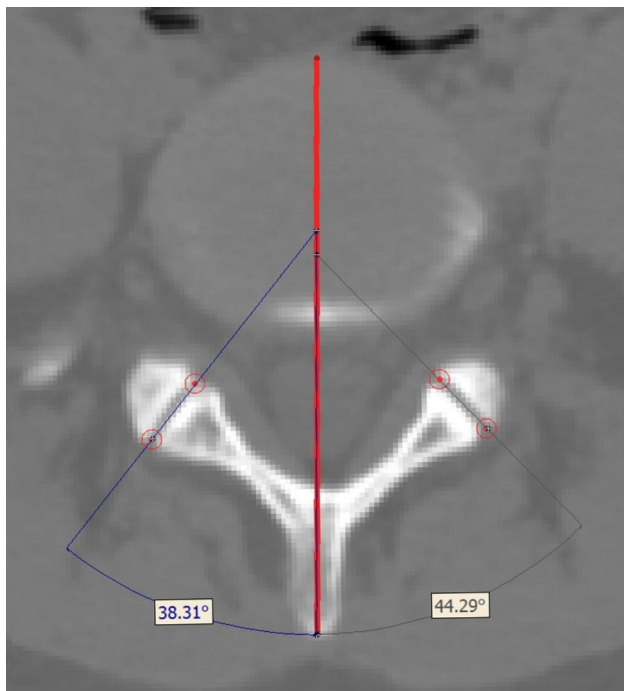


Fig. 2 Measurement of facet joint angle. On an axial cut parallel to the vertebral endplate the FJA was measured. A line represents the sagittal axis of vertebra was drawn (the red line), then the anteromedial and posterolateral points of facet joint on both sides are marked. Connecting the anteromedial and posterolateral points, the angle between this line and the sagittal axis was measured as FJA.

used to analyze threshold for factors associated with lumbar IS. Linear regression analysis was performed to figure out the relationship between radiologic parameters and degree of slippage. Intraobserver and interobserver reliabilities were determined by intraclass correlation coefficient analysis. A probability (P) value of <0.05 was considered statistically significant.

Results

The IS group included 115 patients (53 male patients, 62 female patients) with an average age of 53.60 ± 16.24 years. We matched the same patients (53 male patients, 62 female patients) with an average of 62.25 ± 12.30 years. ICC analysis showed high intraobserver and interobserver reliabilities in the measurement of all parameters (0.855–0.959).

Comparison of control and IS group

Age was higher in IS group than in control group (62.25 ± 12.46 vs. 53.60 ± 16.44 , $P=0.010$). PI was higher in the IS group than in the control group significantly ($50.99 \pm 7.67^\circ$ vs. $43.77 \pm 9.30^\circ$, $P=0.009$). The FJA tropism shows different results in each segment. In L3-L4 level, there was significant difference in cranial and average FJA tropism ($P=0.002$, $P=0.006$, respectively). In L4-L5 level, there was also significant difference in cranial



Fig. 3 Measurement of pedicle-facet angle. In the sagittal view in which the facet joint was clearly visualized, the midpoints of anterior and posterior vertebral cortices were connected. The angle between this line and the line parallel to the facet joint was defined as P-F angle

and average FJA tropism ($P<0.001$). However, in L5-S1 level, no significant differences were observed in FJA tropism. P-F angle of L4-L5 level showed significantly larger in IS group than in control group ($111.47 \pm 7.57^\circ$ vs. $106.74 \pm 7.49^\circ$, $P=0.007$) (Table 1).

Logistic regression analysis and threshold of the predictors

Logistic regression analysis showed a larger age, a greater L3-L4 cranial FJA tropism, and a greater L4-L5 cranial FJA tropism were potential predictors of IS, with an OR of 1.07, 1.28, and 1.39 respectively (Table 2). The thresholds of the predictors were 60 years, 5.67° , and 8.97° according to the ROC curve (Fig. 4). See Table 3 for details.

Correlation between parameters and degree of slippage

Age was positively related with degree of slippage. There was a negative correlation between L3-L4 cranial FJA tropism and degree of slippage ($r=-0.343$, $P=0.024$). A negative correlation could also be observed between L4-L5 average FJA tropism and degree of slippage ($r=-0.318$, $P=0.033$). To further analyze the relationship between these parameters and degree of slippage, a linear regression equation was established as follows: degree of slippage (%) = $0.220 \times \text{age} - 0.327 \times \text{L3-4 cranial FJA tropism}$

Table 1 t-test of PI, FJA tropism, and P-F angle between IS and control group

			IS	control	t	P
Age			62.25 ± 12.46	53.60 ± 16.44	-2.652	0.010
PI			50.99 ± 7.67	43.77 ± 9.30	2.681	0.009
FJA tropism						
	L3-L4	cranial	9.80 ± 9.50	4.39 ± 4.08	3.286	0.002
		caudal	8.13 ± 8.26	5.53 ± 3.80	1.583	0.118
		average	8.82 ± 7.66	5.09 ± 3.05	2.855	0.006
	L4-L5	cranial	11.95 ± 7.35	5.10 ± 4.39	5.236	0.000
		caudal	7.90 ± 7.12	6.10 ± 5.54	2.310	0.194
		average	9.81 ± 6.01	5.49 ± 4.32	3.806	0.000
	L5-S1	cranial	9.26 ± 8.23	9.81 ± 7.23	-1.426	0.158
		caudal	7.58 ± 6.40	9.69 ± 6.70	-0.315	0.754
		average	8.40 ± 5.51	9.70 ± 5.83	-1.038	0.302
P-F angle						
	L3-L4		104.77 ± 5.75	104.39 ± 5.30	-0.303	0.763
	L4-L5		111.47 ± 7.57	106.74 ± 7.49	-2.772	0.007
	L5-S1		111.77 ± 7.28	110.60 ± 7.20	-0.671	0.505

The numbers in bold represented that there was significant difference between the two groups. FJA tropism was defined as the difference between left and right side on the same level (cranial or caudal). Average FJA tropism was defined as the average of cranial and caudal FJA tropism in a certain segment.

Table 2 Logistic regression analysis of potential predictors

	β	OR	95% CI	P
Age	0.071	1.07	(1,1.15)	0.047
L3-L4 cranial FJA tropism	0.243	1.28	(1.06,1.54)	0.011
L4-L5 cranial FJA tropism	0.327	1.39	(1.13,1.7)	0.001

Table 3 Threshold of predictors of IS

	Sensitivity	Specificity	Youden Index	AUC	Threshold
Age	0.625	0.675	0.650	0.650	60.000
L3-L4 cranial FJA tropism	0.595	0.725	0.320	0.701	5.670
L4-L5 cranial FJA tropism	0.676	0.850	0.526	0.805	8.970

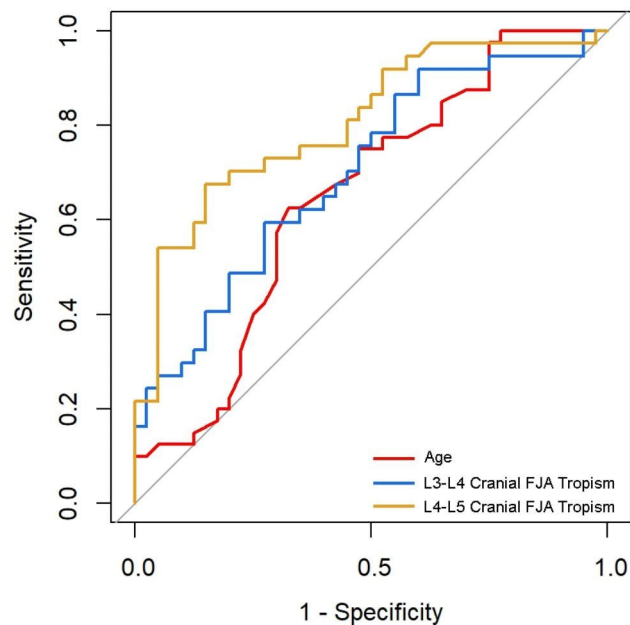


Fig. 4 The ROC curve of predictors of IS. Age, L3-L4 cranial FJA tropism, and L4-L5 cranial FJA tropism were included in the ROC curve according to logistic regression analysis. The thresholds of the predictors were 60 years, 5.67°, and 8.97° respectively

-0.346* L4-5 average FJA tropism (F=3.460, P=0.011, r=0.659) (Table 4).

Discussion

In this study, we found the progression of IS may correlate with multiple factors, involving both integral factors like sagittal spinopelvic alignments and partial elements like the morphology of lumbar facet joints. Previous studies have mainly tended to be uni-factorial, with fewer studies looking at the factors associated with IS as a whole.

First, we found that FJA might have an impact on isthmic spondylolisthesis. In this study, the FJA of different vertebral segments were measured and the difference values were calculated. It was found that the L3-L4 cranial FJA tropism and the L4-L5 cranial FJA tropism in the spondylolisthesis group were significantly different from those in the control group, and the values of the relevant parameters in the spondylolisthesis group were higher than those in the control group. The risk of isthmic spondylolisthesis is possibly increased when the FJA tropisms were larger, especially if the L3-L4 cranial

Table 4 Correlation coefficients between PI, FJA tropism, P-F angle and the degree of slippage in the 115 IS group

		r	P
Age		0.450	0.007
PI		-0.280	0.109
FJA tropism			
L3-L4	cranial	-0.343	0.024
	caudal	0.036	0.421
	average	-0.192	0.139
L4-L5	cranial	-0.145	0.068
	caudal	0.074	0.222
	average	-0.318	0.033
L5-S1	cranial	-0.001	0.497
	caudal	-0.004	0.481
	average	-0.003	0.487
P-F angle			
L3-L4		0.135	0.440
L4-L5		0.084	0.643
L5-S1		-0.040	0.841

FJA tropism > 5.67, the L3-L4 cranial FJA tropism > 8.97 and age > 60 years. We proposed that the increase in FJA tropism may be related to the progression of IS. If excessive angle is repositioned below this threshold, it may improve the pelvic balance of the spine and provide guidance for clinical work.

In 1967, Farfan et al. proposed the concept of articular synovial asymmetry was that the synovial joint angle was increased on one side (tilted towards the coronal position) [20]. Ahmet Eroğlu et al. indicated that facet angle tropism could be seen in a high proportion of patients with IS. Masharaw YM also indicated that individuals with more frontally oriented facets in the lower lumbar vertebrae incorporated with facet tropism were at a greater risk for developing isthmic spondylolysis at L5 segment [21].

Further, the spondylolisthesis patients showed the significantly larger P-F angle of the L4-L5 segments and a larger PI than the normal group, which is consistent with the results of previous studies [22, 23]. T Iguchi and Fei Gao et al. certified the same conclusion that the P-F angle was significantly higher in the spondylolisthesis group than in the control group and it occurred more often in the L4-L5 segments [18, 24]. However, PI and P-F angle were only statistically significant in the Student's t-test, but not in the logistic regression. The results may suggest that the PI and P-F angle have not directly impact the disease, but play an indirect indication of a tilted pelvis, resulting in a forward shift of the centre of gravity and a corresponding increase in the biological forces on the spine. It increases the isthmus shear forces and thus the risk of slipping. PI represents the anatomical position of

the sacrum and the pelvis and has individual variability, so it becomes the reliable evaluation of the spinal-pelvic sagittal balance parameter. Previously, researchers believed that PI was the only anatomical and constant parameter while the others were positional parameters and remained constant in adults [25, 26]. However, the correlation between age and PI was observed significant in recent studies [27]. These findings might indicate that the occurrence of lumbar spondylolisthesis is not only correlated with a single related factor but a multifactorial interaction between related factors.

Our study shows that IS may be not merely related to the independent influence of a single relevant factor or the simple accumulation of multiple single factors. A possible process of how these parameters interact and contribute to lumbar spondylolisthesis is as follows. Patients with high PI have increased shear stresses at the lumbo-sacral junction, causing more tension on the pars interarticularis L5 segment, making the weak isthmus of the vertebral arch vulnerable to fatigue fractures [8, 28]. Similarly, Manon Sterba et al. [29] built a comprehensive osseo-disco-ligamentous L4-S1 finite element model to compute the Von Mises stress, L5-S1 facet contact force and resultant internal loads at the sacral endplate for each simulation and confirmed that the lumbosacral stresses increased with the higher PI, the posterior articular joint stresses of the vertebral body and the lumbosacral shear forces increased [30].

Meantime, the degeneration of the synovial joint probably increases after shear stress increasing in different lumbar segments, leading to the articular synovial asymmetry. One study has reported that disc degeneration predisposed to intersegmental instability and rotational strain, which resulted in secondary osteoarthritic change of the articular processes and segmental canal stenosis [31]. A possible explanation for this phenomena might be that symmetric lumbar changes in the synovial joints may lead to disc disruption and reduced stability of the spine, while disruption of the disc may further cause an increase in intervertebral space-induced shear forces, resulting in isthmus fracture [32].

Li et al. measured the lamina angle on the L3 and L4 segments (the angle between the midline of the lower edge of the lamina and the posterior edge of the vertebral body). Both the lamina angle and the P-F angle reflect the degree of lamina tilt, and the values of the lamina angle were higher in the case group [32]. It is probably a result of the fact that the higher P-F angle, the greater inclination of the vertebral plate plane. The forces are more likely to be exerted at the level of the pedicle and the potential for fracture increases [33].

Our findings reveals that the IS is highly likely to be associated with a combination of factors. According to our study, the regression equation for slippage was

obtained as: degree of slippage (%) = $0.220 * \text{age} - 0.327 * \text{L3-L4 cranial FJA tropism} - 0.346 * \text{L4-L5 average FJA tropism}$, which indicates that IS is not a disease just related with a single factor changes. It needs to be viewed from a multifactorial perspective. There was no significance in FJA between the two groups at L5-S1 segments, though all patients in this study had a slipped lumbar spine with an isthmic cleft at the L5 segments. Differences were found between the FJA in the L3-L4 and L4-L5 segments, and differences were found to be significant between the cranial FJA tropism in the L3-L4 and the L5-S1 segments. This suggests that parameters may interact with each other during the process of IS.

While the previous studies have reported differences in various spinal-pelvic parameters between IS and normal subjects, the disease progression of IS has rarely been analyzed from a holistic, multi-stage perspective. In our study, the ROCC showed that age, L3-L4 cranial FJA tropism, L4-L5 cranial FJA tropism were risk factors for IS, and the cut-off(threshold) values were obtained. The development of IS was investigated in terms of the integral factors of the spinal-pelvic sagittal balance, the local factors of the synovial joint angle and the P-F angle and the regression equation for the degree of slippage was further derived: degree of slippage (%) = $0.220 * \text{age} - 0.327 * \text{L3-L4 cranial FJA tropism} - 0.346 * \text{L4-L5 average FJA tropism}$, indicating that isthmic lumbar spondylolisthesis is a multifactorial disease process. This is where the present study differs from most studies. Based on the clinical reference to our results. Future studies further conduct relevant prospective trials to derive the causative relationship so that preventive treatment through intervention may be helpful to slow down the progression of IS or recover spinal-pelvic stability. Furthermore, the imaging technique of CT is used and has advantages in terms of the accuracy of the parameters results, which is different from the X-ray measurement method used in previous studies. Tomaz and Rob used CT scan methods to investigate the differences in PI between patients with lumbar scoliosis and normal subjects in order to provide increased reliability of the results [34, 35]. Another study compared PI obtained from lateral XR, standard CT scan and CT scan with 3D reconstruction and found PI measurements on repeated imaging of the same individual demonstrated that CT methods produced more consistent measurements than XR [36].

The present study has some limitations. First, this study is a retrospective study without including post-operative spinal-pelvic parameters to validate our structure, which might cause the bias. The study also needs to be tested in clinical practice to validate the results. Second, in order to get a more comprehensive understanding of the progression of IS, changes in micro-osseous structures [37] such as the pedicle and non-osseous structures[38] such

as the intervertebral disc and ligaments should also be studied. Future retrospective analyses with larger sample sizes and multicentre large-scale randomized prospective clinical studies are awaited to verify the reliability of the results.

Conclusion

IS is probably related to a combination of multiple factors. The age, L3-L4 cranial FJA tropism, L4-L5 cranial FJA tropism were possibly correlated with the process of isthmic lumbar spondylolisthesis and the regression equation was obtained as follows: degree of slippage (%) = $0.220 * \text{age} - 0.327 * \text{L3-L4 cranial FJA tropism} - 0.346 * \text{L4-L5 average FJA tropism}$. However, the study needs to be put into clinical practice to verify the results.

List of abbreviations

IS	Isthmic spondylolisthesis
CT	Computed tomography
PI	Pelvic incidence
FJA	Facet joint angle
P-F angle	Pedicle-facet angle
ROCC	Receiver Operating Characteristic Curve
XR	X-ray
OR	Odds ratio
95%CI	95% Confidence interval
AUC	Area under the curve

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Authors' contributions

QK and JL conceived the project. QK and BW analyzed the data. BW and SN prepared tables and figures. TS and YZ provided the data and revised the manuscript. All authors wrote the manuscript. All authors have read and approved the final version of the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Qilu Hospital of Shandong University (Qingdao) and Qingdao University (No. QDU-HEC-2022229). As the retrospective nature of the study and conducted anonymously, the data was obtained from the medical records of discharged patients and no identifiable information was included in the data, thus the informed consent was waived off by the Ethics Committee of Qilu Hospital of Shandong University (Qingdao) and the Ethics Committee of Qingdao University. All procedures were performed in accordance with relevant guidelines.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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