

The correlation among subcutaneous lumbar spine index, paraspinal muscle parameters, and lumbar bone mineral density in patients with lumbar spondylolisthesis

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Abstract

Objectives: To analyze the correlation among subcutaneous lumbar spine index (SLSI), paraspinal muscle parameters, and lumbar bone mineral density (BMD), and to evaluate their predictive value on lumbar BMD for patients with lumbar spondylolisthesis.

Materials and methods: A total of 216 patients with lumbar spondylolisthesis were included. All of them were divided into groups of normal bone mass, osteopenia, and osteoporosis (OP) according to BMD of L1–4 measured by dual-energy X-ray absorptiometry (DXA). SLSI was obtained by computed tomography, and paraspinal muscle parameters were calculated by the Image J software. The differences between SLSI and paraspinal muscle parameters were compared in 3 groups. Correlation analysis and multiple linear regression were used to analyze the relationship between parameters and lumbar BMD.

Results: SLSI and paraspinal muscle parameters were analyzed among 3 groups. There was a significant difference in cross-sectional areas (CSAs) of psoas major (PS) and quadratus lumborum (QL), PS index, relative cross-sectional areas (rCSAs) of PS and QL, fatty infiltration (FI) of multifidus (MF) and erector spinae (ES) between normal bone mass group and osteopenia group, normal bone mass group and OP group ($p < 0.05$). Correlation analysis among body mass index (BMI), SLSI, paraspinal muscle parameters, and BMD was adopted for all included patients. There were positive correlations among BMI, CSAs of PS and QL, PS index, rCSAs of PS and QL, and lumbar BMD ($p < 0.05$). There were negative correlations among MF index, FI of PS, MF and ES, and lumbar BMD ($p < 0.05$). The regression equation of lumbar BMD: $BMD = -3.461 + 0.063 \times BMI + 0.943 \times rCSA \text{ of PS} - 3.871 \times FI \text{ of ES}$ ($R^2 = 0.111$).

Conclusions: For patients with lumbar spondylolisthesis, smaller CSAs of flexor muscle group and more FI of paraspinal muscles are related to less bone mass and lower lumbar BMD. Combined with BMI, rCSA of PS and FI of ES have predictive value on lumbar BMD. For patients with both lumbar spondylolisthesis and OP, those who have higher SLSI are estimated to have less bone mass.

Abbreviations: BMD = bone mineral density, BMI = body mass index, CSAs = cross-sectional areas, CT = computed tomography, DXA = dual energy X-ray absorptiometry, ES = erector spinae, FI = fatty infiltration, MF = multifidus, OP = osteoporosis, PS = psoas major, QL = quadratus lumborum, rCSAs = relative cross-sectional areas, SFT = subcutaneous fat thickness, SLSI = subcutaneous lumbar spine index, SPH = spinous process height

Keywords: bone mineral density, computed tomography, lumbar spondylolisthesis, paraspinal muscle parameters, subcutaneous lumbar spine index

1. Introduction

The important roles of adipose tissue and muscle tissue are supposed to be considered in the research on

osteoporosis (OP) for the reason that bone tissue is not isolated, and the development of OP is affected by both adipose and muscle. The influence of adipose on bone

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Spine Research (2026) 2:1;23–29

Received: 14 October 2025 / Accepted: 2 February 2026

Published online 23 March 2026

<http://dx.doi.org/10.1097/br9.0000000000000027>

tissue is sophisticated and controversial. Early research agreed that there might be a positive correlation between obesity and bone mineral density (BMD). Appropriate mechanical loading caused by body weight is beneficial for bone formation and the increase in bone strength. Therefore, proper obesity may have a potential preventive effect on the occurrence of OP.^[1] However, adipose tissue in different body parts exerts different effects on bone metabolism because other research found that the increasing content of visceral adipose tissue can be seen as a kind of risk factor of OP.^[2,3] Body mass index (BMI) and subcutaneous fat thickness (SFT) are normally used to describe the degree of obesity, while they cannot represent the specificity of fat distribution well; hence, it is necessary to select a proper parameter to describe the relationship between adipose tissue and bone tissue in a particular part of the body. Shaw et al. presented the subcutaneous lumbar spine index (SLSI) to quantify the correlation between SFT and spinous process height (SPH).^[4] SLSI links the subcutaneous fat tissue of the low back with the lumbar vertebra tissue well, which can be regarded as a suitable parameter for quantitative analysis of the relationship between fat tissue and bone tissue of the low back. The previous studies of SLSI were limited in its relationship with surgical site infection rather than OP.

Paraspinal muscle is vital to maintain spinal stability and function.^[5] The occurrence and development of several spinal disorders are always related to the degeneration of the paraspinal muscle. Previous research has identified significant atrophy and increased fat content in the paraspinal muscles of patients with lumbar spondylolisthesis.^[6] Other studies also demonstrate that the mass and fatty infiltration (FI) of paraspinal muscle are closely associated with OP.^[7] However, no studies pay attention to the relationship between paraspinal muscle parameters and OP in patients with lumbar spondylolisthesis. Whether paraspinal muscle parameters have predictive value on bone mass and strength is still not clear. Against this background, the research aims to analyze the correlation among SLSI, paraspinal muscle parameters, and lumbar BMD, and to evaluate their predictive value on lumbar BMD in patients with lumbar spondylolisthesis based on computed tomography (CT).

2. Methods

We reviewed patients with lumbar spondylolisthesis who were admitted to the department of orthopedics of the First Affiliated Hospital of Zhengzhou University from January 2020 to December 2022. We diagnosed lumbar spondylolisthesis through a combination of clinical history, physical examination, and radiological changes. Inclusion criteria were (1) aged ≥ 45 years old, (2) underwent lumbar CT and dual-energy X-ray absorptiometry (DXA) before surgery. Exclusion criteria were (1) previous or current lumbar compression fractures or pathologic fractures, (2) previous spinal surgery (including

spinal instrumentation, vertebroplasty, and kyphoplasty), (3) patients with bone tumor, ankylosing spondylitis, secondary OP, or other metabolic diseases, (4) previous or current hormone therapy or anti-OP treatment. A total of 216 patients were identified based on the above-mentioned criteria. With the institutional review committee's approval (protocol code 2023-KY-0346-002), we retrospectively collected patients' clinical data without interfering with their treatment in this study.

2.1. BMD measurement and grouping criteria

BMD was measured by DXA (Lunar Prodigy Advance, GE company) for all patients. *T* score of L1–4 was recorded from DXA. The World Health Organization criteria were utilized to distinguish OP ($T \leq -2.5$) from osteopenia ($-2.5 < T < -1.0$) and normal bone mass ($T \geq -1.0$).^[8] All included patients were divided into groups of normal bone mass (78 patients), osteopenia (79 patients), and OP (59 patients) according to the *T* score of L1–4.

2.2. SLSI and paraspinal muscle parameters evaluation based on CT

All patients underwent lumbar CT (Philips Brilliance iCT, 128 rows and 256 layers with a slice thickness of 1.0 mm). SPH and SFT were measured at the levels of the longest spinous processes of each vertebra on CT by picture archiving and communication system. $SLSI = (L1SFT/L1SPH + \dots + L5SFT/L5SPH)/5$ (Fig. 1). CT image at the median level of L3 was selected to measure paraspinal muscle parameters according to the guidance of the European Working Group on Sarcopenia.^[9] Image J (NIH Image J version 1.52c) software was used to calculate and

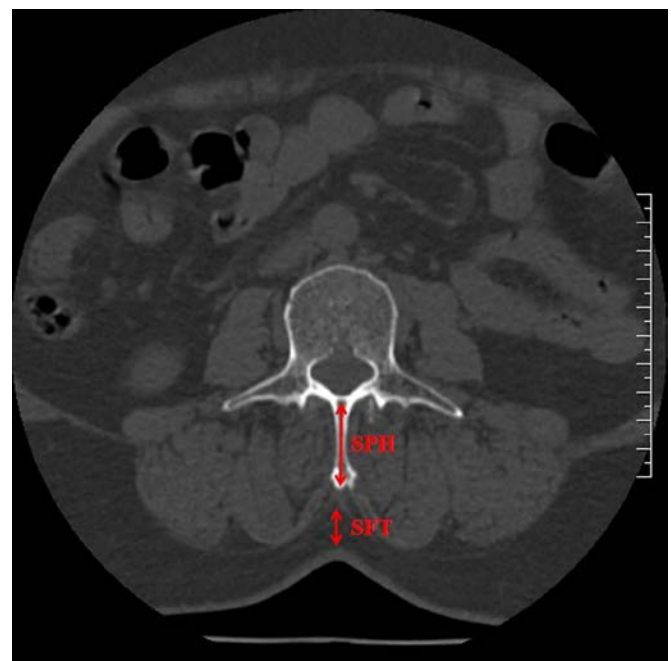


Figure 1. Measurement of spinous process height (SPH) and subcutaneous fat thickness (SFT).

analyze the parameters of different paraspinal muscles, including psoas major (PS), quadratus lumborum (QL), multifidus (MF), and erector spinae (ES). The cross-sectional areas (CSAs) of L3 and paraspinal muscles were measured firstly, and then paraspinal muscle index (the ratio of CSAs of paraspinal muscles to the square of the patient's height), related cross-sectional areas (rCSAs, the ratio of CSAs of paraspinal muscles to that of vertebra at the same level), and FI (the ratio of CSAs of fat in paraspinal muscles to that of the same muscles) of paraspinal muscles could be calculated subsequently (Fig. 2). All data were independently measured by 2 associate chief physicians. Three measurements were repeated, and the values were averaged.

2.3. Statistics

Chi-square test was used for enumeration data. The pairwise comparisons for statistical significance indicators were performed using Bonferroni correction.

Measurement data were described using mean \pm standard deviation ($x \pm s$). Differences among 3 groups were analyzed using 1-way analysis of variance followed by the (least significant difference) LSD-*t* post hoc test. Pearson correlation was selected for correlation analysis, and the stepwise regression method was used for statistical significance indicators to assess multiple linear regression and calculate the regression equation. Statistical significance was set at p value < 0.05 . All statistics were performed using SPSS 25.0 (IBM SPSS Inc.).

3. Results

3.1. General data of patients

The analysis of characteristics of included patients is presented in Table 1. Age of patients is significantly different and increase sequentially among normal bone mass group, osteopenia group, and OP group ($p < 0.05$). There is statistically significant difference in weight and BMI between OP group and normal bone mass group, OP

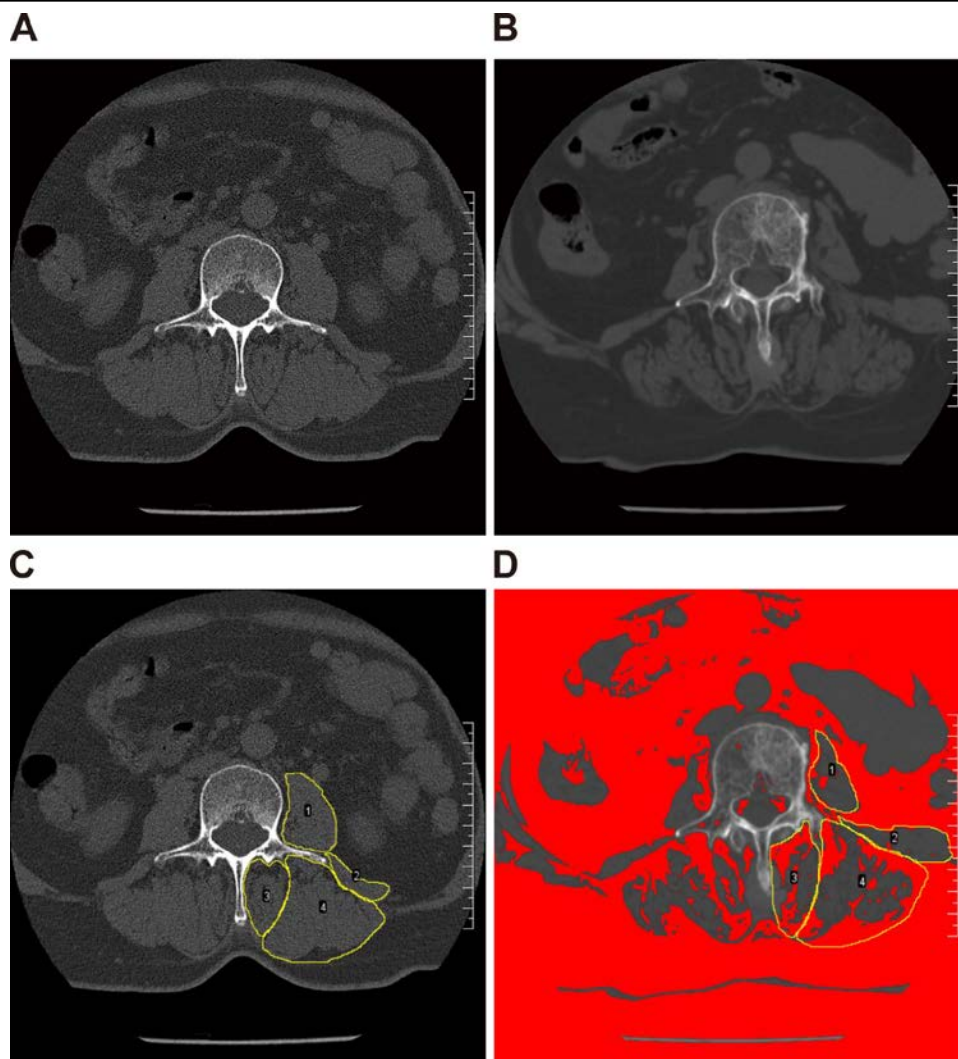


Figure 2. Cross-sectional areas (CSAs) and fatty infiltration (FI) of paraspinal muscle. (A, B) Computed tomography (CT) images at the median level of L3. (A) Paraspinal muscle with little FI. (B) Paraspinal muscle with much FI. (C) CSAs of paraspinal muscle: 1—psoas major (PS); 2—quadratus lumborum (QL); 3—multifidus (MF); 4—erector spinae (ES). (D) FI of paraspinal muscle.

Table 1**Comparison of general clinical data among normal bone mass group, osteopenia group, and OP group.**

	Normal bone mass group	Osteopenia group	OP group	<i>F</i> / χ^2	<i>p</i> Value
Age (year) ^{abc}	56.45 ± 10.288	60.28 ± 8.069	65.05 ± 6.974	16.501	0.000
Height (cm) ^b	162.147 ± 7.462	161.545 ± 6.010	159.696 ± 7.264	2.141	0.120
Weight (kg) ^{bc}	69.162 ± 9.908	67.712 ± 10.530	62.571 ± 9.679	7.374	0.001
BMI (kg/m ²) ^{bc}	26.299 ± 3.285	25.902 ± 3.511	24.537 ± 3.395	4.626	0.011
Gender ^a				10.318	0.006
Female, <i>n</i> (%)	54 (69.2)	70 (88.6)	50 (84.7)		
Male, <i>n</i> (%)	24 (30.8)	9 (11.4)	9 (15.3)		
Hypertension, <i>n</i> (%)	25 (32.1)	23 (29.1)	22 (37.3)	1.037	0.595
Coronary heart disease, <i>n</i> (%)	12 (15.4)	10 (12.7)	12 (20.3)	1.514	0.469
Diabetes, <i>n</i> (%)	8 (10.3)	7 (8.9)	3 (5.1)	1.221	0.543
Stroke, <i>n</i> (%) ^b	4 (5.1)	7 (8.9)	11 (18.6)	6.947	0.031

"a" represents there is statistically significant difference between normal bone mass group and osteopenia group ($p < 0.05$), "b" represents there is a statistically significant difference between normal bone mass group and OP group ($p < 0.05$), "c" represents there is a statistically significant difference between osteopenia group and OP group ($p < 0.05$). BMI = body mass index; OP = osteoporosis.

group, and osteopenia group ($p < 0.05$), while height is different only between OP group and normal bone mass group ($p < 0.05$). Besides, there is no difference in complications (including hypertension, coronary heart disease, and diabetes) among 3 groups ($p > 0.05$).

3.2. Comparison of SLSI and paraspinal muscle parameters among 3 groups

Using picture archiving and communication system and Image J, SLSI, and paraspinal muscle parameters are calculated and presented in Table 2. Although CSAs of PS and QL, PS index, rCSAs of PS and QL, and FI of MF and ES are significantly different between normal bone mass group and osteopenia group, normal bone mass group and OP group ($p < 0.05$), there is no statistically significant difference between osteopenia group and OP group ($p > 0.05$). The difference in QL index can only be found

between normal bone mass group and osteopenia group ($p < 0.05$). Additionally, there is no significant difference in SLSI and remaining parameters among 3 groups ($p > 0.05$).

3.3. Correlation analysis among BMI, SLSI paraspinal muscle parameters, and BMD

Correlation analysis among BMI, SLSI paraspinal muscle parameters, and BMD is adopted for all included patients, and the results are presented in Table 3. There are positive correlations among BMI, CSAs of PS and QL, PS index, rCSAs of PS and QL, and lumbar BMD ($p < 0.05$). Conversely, negative correlations are observed among MF index, FI of PS, MF and ES, and lumbar BMD ($p < 0.05$). Further, multiple linear regression is assessed by stepwise regression method and the regression equation of lumbar BMD: $BMD = -3.461 + 0.063 \times BMI + 0.943 \times rCSA \text{ of PS} - 3.871 \times FI \text{ of ES}$ ($R^2 = 0.111$).

Table 2**Comparison of SLSI and paraspinal muscle parameters among normal bone mass group, osteopenia group, and osteoporosis group.**

	Normal bone mass group	Osteopenia group	OP group	<i>F</i>	<i>p</i> Value
SLSI	0.511 ± 0.250	0.556 ± 0.315	0.520 ± 0.277	0.560	0.572
CSA of PS (mm ²) ^{ab}	1515.102 ± 460.011	1335.093 ± 360.904	1338.186 ± 448.952	4.443	0.013
CSA of QL (mm ²) ^{ab}	727.800 ± 265.840	641.996 ± 226.486	641.528 ± 184.211	3.440	0.034
CSA of MF (mm ²)	1358.343 ± 254.531	1363.283 ± 327.784	1376.162 ± 259.399	0.068	0.934
CSA of ES (mm ²)	3944.769 ± 896.605	3770.291 ± 731.864	3757.586 ± 832.135	1.198	0.304
PS index (mm ² /m ²) ^{ab}	573.305 ± 156.708	508.360 ± 121.192	521.102 ± 147.956	4.440	0.013
QL index (mm ² /m ²) ^a	273.932 ± 87.902	243.949 ± 79.525	253.254 ± 70.695	2.789	0.064
MF index (mm ² /m ²)	517.013 ± 97.369	523.917 ± 126.750	537.231 ± 103.284	0.551	0.577
ES index (mm ² /m ²)	1492.817 ± 290.216	1449.243 ± 261.323	1468.593 ± 296.443	0.465	0.629
rCSA of PS ^{ab}	1.268 ± 0.345	1.129 ± 0.273	1.096 ± 0.304	6.296	0.002
rCSA of QL ^{ab}	0.599 ± 0.180	0.542 ± 0.174	0.524 ± 0.128	4.024	0.019
rCSA of MF	1.146 ± 0.234	1.166 ± 0.302	1.144 ± 0.247	0.165	0.848
rCSA of ES	3.298 ± 0.664	3.213 ± 0.649	3.098 ± 0.693	1.508	0.224
FI of PS	0.099 ± 0.055	0.109 ± 0.053	0.117 ± 0.052	1.932	0.147
FI of QL	0.080 ± 0.067	0.084 ± 0.057	0.087 ± 0.050	0.196	0.822
FI of MF ^{ab}	0.190 ± 0.092	0.234 ± 0.113	0.232 ± 0.104	4.313	0.015
FI of ES ^{ab}	0.165 ± 0.071	0.196 ± 0.082	0.197 ± 0.085	4.016	0.019

"a" represents there is statistically significant difference between normal bone mass group and osteopenia group ($p < 0.05$), "b" represents there is statistically significant difference between normal bone mass group and OP group ($p < 0.05$). CSA = cross-sectional area; ES = erector spinae; FI = fatty infiltration; MF = multifidus; OP = osteoporosis; PS = psoas major; QL = quadratus lumborum; rCSA = relative cross-sectional area; SLSI = subcutaneous lumbar spine index.

Table 3
Correlation analysis among BMI, SLSI, paraspinal muscle parameters, and BMD.

	<i>r</i>	<i>p</i> Value
BMI (kg/m ²)	0.148	0.031
SLSI	-0.088	0.197
CSA of PS (mm ²)	0.179	0.008
CSA of QL (mm ²)	0.145	0.033
CSA of MF (mm ²)	-0.102	0.137
CSA of ES (mm ²)	0.050	0.464
PS index (mm ² /m ²)	0.157	0.022
QL index (mm ² /m ²)	0.101	0.145
MF index (mm ² /m ²)	-0.148	0.031
ES index (mm ² /m ²)	-0.015	0.825
rCSA of PS	0.242	0.000
rCSA of QL	0.186	0.006
rCSA of MF	-0.053	0.436
rCSA of ES	0.088	0.197
FI of PS	-0.147	0.031
FI of QL	-0.019	0.783
FI of MF	-0.182	0.007
FI of ES	-0.208	0.002

BMI = body mass index; CSA = cross-sectional area; ES = erector spinae; FI = fatty infiltration; MF = multifidus; PS = psoas major; QL = quadratus lumborum; rCSA = relative cross-sectional area; SLSI = subcutaneous lumbar spine index.

Moreover, correlation analysis is conducted within each group. In normal bone mass group, there is a negative correlation between CSA of MF and lumbar BMD ($r = -0.307$, $p = 0.006$) and the regression equation: $BMD = 1.178 - 0.001 \times \text{CSA of MF}$ ($R^2 = 0.094$). For patients in osteopenia group, there is a negative correlation between FI of ES and lumbar BMD ($r = -0.265$, $p = 0.018$) and the regression equation: $BMD = -1.426 - 1.475 \times \text{FI of ES}$ ($R^2 = 0.070$). Of note, negative correlation is also discovered between SLSI and lumbar BMD ($r = -0.382$, $p = 0.003$) and the regression equation: $BMD = -2.933 - 0.856 \times \text{SLSI}$ ($R^2 = 0.146$).

4. Discussion

Lipid metabolism takes part in the regulation of bone homeostasis.^[10] Increased weight and fat accumulation may be beneficial to bone strength to some extent for the reason that positive mechanical loading effects caused by them promote bone formation and suppress bone resorption by receptor activator of nuclear factor- κ B (RANK)/receptor activator of nuclear factor- κ B ligand (RANKL)/osteoprotegerin (OPG) axis.^[11] Compared with normal bone mass group and osteopenia group, patients in the OP group have lower weight and BMI. A definite positive correlation is confirmed between BMI and lumbar BMD among 3 groups, which is consistent with previous research findings and indicates that BMI can be seen as a protective factor of bone mass and strength. However, the influence of obesity to microstructure of bone is still not clear, and the effects of obesity on bone are not all positive. For instance, persistent low-level inflammation caused by obesity is supposed to damage bone tissue, and excessive adiposity may increase fracture risk. It seems that fat accumulation in different parts of the body plays distinct

roles in bone metabolism. High content of visceral adipose tissue is generally associated with low lumbar BMD in both perimenopausal and postmenopausal women.^[12,13] BMI only represents the overall fat condition of patients and is lack of describing the distribution of adipose tissue, because muscle and adipose contribute equally to weight, and it is difficult to distinguish them by BMI simply. Therefore, it is not comprehensive enough to consider BMI alone in the relationship between bone and adipose.

Although SFT is better than BMI in the evaluation of lumbar adipose tissue, it neglects the relationship between fat distribution and SPH. Besides, it has been convinced that there is no correlation between SFT and the initiation of OP.^[14] SLSI was presented as a risk factor of surgical site infection at the beginning. Higher SLSI is explained as patients with thicker SFT or shorter SPH, indicating stronger paraspinal muscle tone and more difficulties during surgical exposure.^[15] However, unlike SFT, lumbar adipose tissue is connected with bone tissue well by SLSI.

No research paid attention to the role of SLSI in OP in the past, while we demonstrate that there is a negative correlation between SLSI and lumbar BMD in patients with both lumbar spondylolisthesis and OP, meaning that the higher SLSI they have, the worse bone mass they suffer. Besides, the possibilities of intraoperative exposure difficulties and unstable internal fixation, postoperative surgical site infection, internal plant loosening, and pulling out greatly increase for OP patients with higher SLSI. However, there is no statistically significant difference in SLSI among the 3 groups, and no clear relationship between SLSI and lumbar BMD is discovered for all included patients, which can be explained by 2 aspects. First, lumbar sagittal images were used to measure SFT and SPH when Shaw et al. presented SLSI, but the specific measuring methods and positions were not defined exactly.^[4] Choosing different positions or levels may lead to discordant results. Besides, it is necessary to collect data from all lumbar segments to calculate SLSI. Measurement errors are unavoidable owing to excessive data. Considering this situation, this study adjusted measuring methods during the data collection stage. We used cross-sectional rather than sagittal images and selected the levels of the longest spinous processes of each vertebra to measure SPH and SFT for all patients. All data were averaged by several measurements to reduce the error, even if it cannot be eliminated. Second, spinal destabilization and relative displacement of adjacent vertebrae are typical characteristics of patients with lumbar spondylolisthesis. Instability of bone tissue has an impact on the surrounding muscle and adipose tissue, leading to the difference in data between slipped and nonslipped segments, thereby affecting the application of SLSI for this kind of patients.^[16] Although SLSI has limited predictive value on lumbar BMD for patients with lumbar spondylolisthesis according to this study, the clinical value of SLSI in other spinal disorders cannot be denied because of the potential relationship between bone tissue and adipose tissue. Further research and discussion for SLSI in different diseases are necessary.

It is confirmed that muscle tissue is closely related to both bone and fat tissue. Not only has great impact on the stability and function of the spine under physiological conditions, but paraspinal muscle also takes part in the occurrence and development of a variety of spinal diseases, including lumbar spondylolisthesis. The increased FI of paraspinal muscle is one of the most intuitive manifestation of the regulation capacity of lipid metabolism to muscle tissue.^[17] FI of muscle, which is caused by the increase of fat content in muscle, is the process by which original muscle tissue is replaced by adipose tissue without contractile function in essence, leading to the decrease in muscle function and muscle atrophy inevitably.^[18] Although SLSI has limited predictive value on BMD as described earlier, a high correlation between FI of paraspinal muscle and lumbar BMD for patients with lumbar spondylolisthesis is discovered. This is not paradoxical for the reason that the adipose tissue they represent is different. From another point of view, this phenomenon corroborates that fat in different parts of the body has different impacts on bone tissue again.

Atrophy and FI are supposed to influence the function of the paraspinal muscle in maintaining stability. Previous research has also illustrated that there is a significant correlation between CSA of the paraspinal muscle and spinal instability.^[19] Because the root cause of lumbar spondylolisthesis is the weakening of spinal stability, choosing patients with lumbar spondylolisthesis as subjects is able to reduce the effects on paraspinal muscle parameters caused by spinal instability to a certain extent. In addition, muscle index and rCSA, which are used in the study, are further processing of CSA and exclude the influence of body shape on paraspinal muscle parameters, making the results more reliable.^[20,21]

Paraspinal muscles can be divided into flexor muscle group (PS and QL) and extensor muscle group (MF and ES).^[22] According to our study, there is a positive correlation between CSAs of flexor muscle group and lumbar BMD for patients with lumbar spondylolisthesis. The conclusion of index and rCSAs of flexor muscle group is consistent with that of CSAs, meaning that body shape does not affect the correlation between CSAs of flexor muscle group and lumbar BMD. Besides, CSAs and rCSAs of flexor muscle group, PS especially, in the normal bone mass group are significantly different from another 2 groups, indicating that patients with larger CSAs of PS are relatively less likely to suffer from OP.

There are negative correlations between FI of PS, MF, ES, and lumbar BMD, and this result shows that increased FI of paraspinal muscle may be related to lower lumbar BMD. Compared with flexor muscle group, there is an obvious difference in FI of extensor muscle group for patients among 3 groups, meaning that patients with higher FI of extensor muscle group may have worse bone strength and lower BMD. It has been confirmed that the FI of ES has great predictive value on lumbar BMD in the osteopenia group. Considering both CSA and FI comprehensively, lumbar BMD can be predicted by

rCSA of PS, FI of ES, and BMI for patients with lumbar spondylolisthesis.

The following limitations have been recognized in the present study. To begin with, DXA has its own limitations in the measurement of BMD, and its results are easily affected by weight and fat distribution.^[23] Besides, all R^2 calculated in the study are small because only BMI, SLSI, and paraspinal muscle parameters are included. It is generally acknowledged that lumbar BMD is influenced by several other factors. Finally, severe degeneration of paraspinal muscle in imaging findings is not fully equivalent to poor function of muscle, which needs to be evaluated deeply by endurance of muscle, isometric muscle strength test, isokinetic muscle strength test, and so on.^[24]

5. Conclusion

For patients with lumbar spondylolisthesis, SLSI has limited predictive value on lumbar BMD. Smaller CSAs of flexor muscle group and more FI of paraspinal muscles are related to less bone mass and lower lumbar BMD. Combined with BMI, rCSA of PS and FI of ES have predictive value on lumbar BMD. For patients with both lumbar spondylolisthesis and OP, there is a negative correlation between SLSI and lumbar BMD. Those who have higher SLSI are estimated to have less bone mass. The results and data of the study can help clinicians evaluate the relationship among adipose, muscle, and lumbar BMD comprehensively to formulate more suitable surgical plans.

Acknowledgements

We thank the Translational Medical Center, First Affiliated Hospital of Zhengzhou University for technical support.

Ethical statement

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board of the First Affiliated Hospital of Zhengzhou University (protocol code 2023-KY-0346-002). The First Affiliated Hospital of Zhengzhou University Medical Science Research Ethics Committee granted a waiver of informed consent.

Conflicts of interest

The authors have no conflicts of interest to disclose.

Funding source

This work was supported by the National Natural Science Foundation of China (grant numbers: 82172484 and 82101451), Collaborative Innovation Project of Zhengzhou (grant number: XTCX2023003), the Young and Middle-aged Health Science and Technology

Innovation Talents Excellent Youth Project in Henan Province (grant number: YXKC2021058), and Henan Medical Science and Technology Research Project (grant number: LHGJ20190171).

Data availability statement

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

Author contributions

ZKL, HJL—design and supervised the review.
LYL, MCS, CFS, GWS, YHJ, SFC—wrote the manuscript.
XRC, HWK—read and edited the manuscript.
KYM, HT—edited the final version. All authors read and approved the final manuscript.

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How to cite this article: Li L, Song M, Leng Z, Shang C, Shang G, Ji Y, Chen S, Chen X, Kou H, Mao K, Tang H, Liu H. The correlation among subcutaneous lumbar spine index, paraspinal muscle parameters, and lumbar bone mineral density in patients with lumbar spondylolisthesis. *Spine Res*. 2026;2(1):e00027. doi: 10.1097/br9.000000000000027