Correlation Between Osteoporosis and Endplate Damage in Degenerative Disc Disease Patients: A Study Based on Phantom-Less Quantitative Computed Tomography and Total Endplate Scores

Yiming Zhang[1,4], Yiming Dou[1,4], Yuanzhi Weng[2], Chao Chen[1], Qingqian Zhao[1,4], Wentao Wan[1,4], Hanming Bian[1,4], Ye Tian[1], Yang Liu[1], Shan Zhu[3], Zhi Wang[3], Xinlong Ma[1,4], Xinyu Liu[5], Weijia William Lu[2], Qiang Yang[1,4]

■ BACKGROUND: **Osteoporosis and degenerative disc disease (DDD) are prevalent in the elderly population. Damage to the vertebral endplate, which impairs nutrient supply to the disc, serves as both a significant initiator and a hallmark of DDD. This study was aimed to explore the association between osteoporosis and endplate damage.**

■ METHODS: **This retrospective study included 205 patients with DDD who were treated at Tianjin Hospital from January 2019 to May 2023. We collected data on age, sex, body mass index, phantom-less quantitative computed tomography (PL-QCT) values, and total endplate scores (TEPS). The average PL-QCT value of L1–L4 and TEPS were used to represent volumetric bone mineral density (BMD) and the degree of endplate damage, respectively. Based on the average PL-QCT value of L1 and L2, patients were divided into 3 groups: normal group (BMD > 120 mg/cm^3), osteopenic group (80 mg/cm^3 ≤ BMD ≤ 120 mg/cm^3), and osteoporosis group (BMD < 80 mg/cm^3). Multiple linear regression models were used to identify independent factors associated with endplate damage.**

■ RESULTS: **The overall TEPS (4.3 ± 1.3 vs. 5.0 ± 1.0 vs. 5.9 ± 1.5, $P < 0.01$) and segment (L1/2–L4/5) TEPS ($P < 0.05$) in each group showed significant difference ($R = -0.5$), increasing in order from normal group to osteoporosis group. A significant negative correlation was found between TEPS and PL-QCT values in overall and each segment ($P < 0.001$). The PL-QCT values and age ($P < 0.05$) were independent factors influencing endplate damage. There were significant differences in the average number of TEPS ≥7 segments per patient among the 3 groups, with 1.16, 0.41, and 0.2 segments/person from osteoporosis group to normal group.**

■ CONCLUSIONS: **Our study showed a significant positive correlation between osteoporosis and endplate damage. Attention is warranted for patients with osteopenia to prevent progression to osteoporosis, potentially leading to exacerbated DDD. The management of patients with both DDD and osteoporosis necessitates comprehensive treatment strategies that address both the BMD and endplate aspects of these conditions.**

Key words
- Degenerative disc disease
- Endplate damage
- Osteoporosis
- Phantom-less quantitative computed tomography
- Total endplate scores
- Volumetric bone mineral density

Abbreviations and Acronyms
BMD: Bone mineral density
BMI: Body mass index
CT: Computed tomography
DDD: Degenerative disc disease
DXA: Dual-energy X-ray absorptiometry
MRI: Magnetic resonance imaging
PL-QCT: Phantom-less quantitative computed tomography
QCT: Quantitative computed tomography
ROI: Region of interest
TEPS: Total endplate scores
v-BMD: Volumetric bone mineral density

From the [1]Department of Spine Surgery, Tianjin Hospital, Tianjin University, Tianjin; [2]Department of Orthopaedics and Traumatology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong; [3]Department of Radiology Tianjin Hospital, Tianjin University, Tianjin; [4]Clinical School of Orthopedics, Tianjin Medical University, Tianjin; and [5]Department of Orthopaedics, Qilu Hospital, Shandong, China

Yiming Zhang and Yiming Dou contribute equally to this work as co-first authors.

To whom correspondence should be addressed: Qiang Yang, Ph.D., M.D. [E-mail: yangqiang1980@126.com]

Citation: World Neurosurg. (2024). https://doi.org/10.1016/j.wneu.2024.09.100

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***

INTRODUCTION

Osteoporosis and degenerative disc disease (DDD) are prevalent conditions among the elderly. Diminished bone mineral density (BMD) and microstructural deterioration are key features of osteoporosis, which contribute to chronic pain, fractures, and substantial lifestyle impairments.[1,2] In China, epidemiological data indicate osteoporosis affects approximately 5.0% of men and 20.6% of women aged 40 years and more.[3] The economic impact of osteoporosis-related conditions on families and society is substantial and projected to escalate significantly in the forthcoming decades.[4] Concurrently, DDD manifests in more than 90% of individuals aged 50 years and more, adversely affecting their functional capabilities.[5,6]

The vertebral endplate, positioned between the vertebral body and intervertebral disc, facilitates biomechanical stability and nutrient transport to the disc.[7-9] Previous studies have extensively examined the relationship between osteoporosis and disc degeneration. However, the impact of endplate damage, a significant factor in disc degeneration, has often been overlooked, and research in this area remains limited. In clinical investigations, endplate damage has been identified as an independent determinant of BMD. Li R et al. observed that patients with DDD who exhibited higher lumbar BMD were more likely to sustain greater endplate damage.[10] Conversely, findings from Zhuang C et al. presented contradictory results, indicating an inverse relationship between lumbar BMD and the prevalence of endplate damage.[11] These investigations have not used volumetric bone mineral density (v-BMD) as a more precise tool for assessing BMD and osteoporosis. This limitation has impeded a clearer understanding of the relationship between BMD and endplate damage.

Dual-energy X-ray absorptiometry (DXA) remains the clinical standard for assessing BMD and diagnosing osteoporosis.[12] However, its accuracy may be compromised in DDD patients due to interference from aortic calcification and osteophyte formation.[13,14] Compared to DXA, quantitative computed tomography (QCT) offers a more precise alternative, measuring v-BMD and circumventing areas of vertebral sclerosis.[15,16] This study employs phantom-less quantitative computed tomography (PL-QCT) software that calibrates using patients' muscle and fat, providing comparable accuracy to conventional QCT and using existing computed tomography (CT) images to assess v-BMD, thus minimizing costs and radiation exposure. For the evaluation of endplate damage, we referred to a quantified scoring system for total endplate scores (TEPS) proposed by Rajasekaran et al. The score system has been developed to evaluate the severity of damage on endplates based on T1-weighted magnetic resonance imaging (MRI) of the lumbar spine. This scoring system classifies endplates into 6 categories, enabling a detailed assessment of endplate integrity.[17]

This study aimed to elucidate the potential interplay between osteoporosis and endplate damage using advanced diagnostic tools such as PL-QCT and the TEPS, thereby contributing to a more integrated understanding of these conditions and their combined impact on the elderly population.

MATERIALS AND METHODS

Patient Population

This research based on data from the Tianjin Hospital, including hospitalized patients admitted from January 2019 to May 2023. Inclusion criteria: 1) age between 45 and 90 years; 2) DDD including degenerative lumbar spondylolisthesis, degenerative lumbar spinal stenosis, and degenerative lumbar disc herniation; and 3) maximum interval time between routine CT and MRI scans before surgery was 30 days. Exclusion criteria: 1) prior spinal surgery; 2) use medications that affect bone metabolism; 3) spinal fractures, tumors, infections, or severe spinal deformities; and 4) systemic metabolic bone diseases, including hypothyroidism, Paget's disease, etc. Demography characteristic, such as gender (M:F), age (years), and body mass index (BMI, kg/m^2), were recorded. Participants were required to provide both written and verbal informed consent before being enrolled in the study. The study protocol was approved by the institutional ethics committee of Tianjin Hospital (2022093) and was conducted in accordance with the Declaration of Helsinki.

Radiological Assessment of BMD

All patients underwent lumbar spine CT (General Electric Medical Systems, USA) in our hospital. QCT values for L1–L5 were obtained using the PL-QCT software (Bone's QCT, Bone's Technology [Shenzhen] Ltd., China).[15] According to the standards of the International Society for Clinical Densitometry, the average QCT value of the L1–L2 segment was used for the diagnosis and grouping of lumbar spine osteoporosis: normal group, BMD >120 mg/cm^3; osteopenia group, 80 mg/cm^3 $\leq$ BMD $\leq$120 mg/cm^3; osteoporosis group, BMD <80 mg/cm^3.[18] In the PL-QCT analysis software, the region of interest (ROI) was marked within the internal space of vertebral body, and adjusted to exclude the cortical bone and basivertebral vein. ROI was marked to include trabecular bones as much as possible, while avoiding islands or hardened areas (**Figure 1**). If the sclerotic lesions of the vertebral body are too diffuse and the affected area cannot be excluded from the ROI, then the vertebral body will be excluded from further analysis. We defined the BMD corresponding to each intervertebral disc segment as the average BMD of the upper and lower vertebral bodies.

Radiological Assessment of Endplate Damage

Each patient underwent lumbar spine MRI scans (1.5 T, General Electric Medical Systems, USA) and endplates were evaluated on T1-weighted images. Two authors (Y. M. Z. and Y. M. D.) classified endplate damage into 6 types according to previous studies[17] (**Figure 2**). The researchers were blinded to other patient data. The TEPS for each intervertebral disc were calculated by adding the damage score of the upper and lower endplates, and the average TEPS of L1/2–L4/5 were used to reflect the situation of endplate damage.

Statistical Analysis

Continuous variables were described using mean $\pm$ standard deviation, and categorical variables were described using frequency

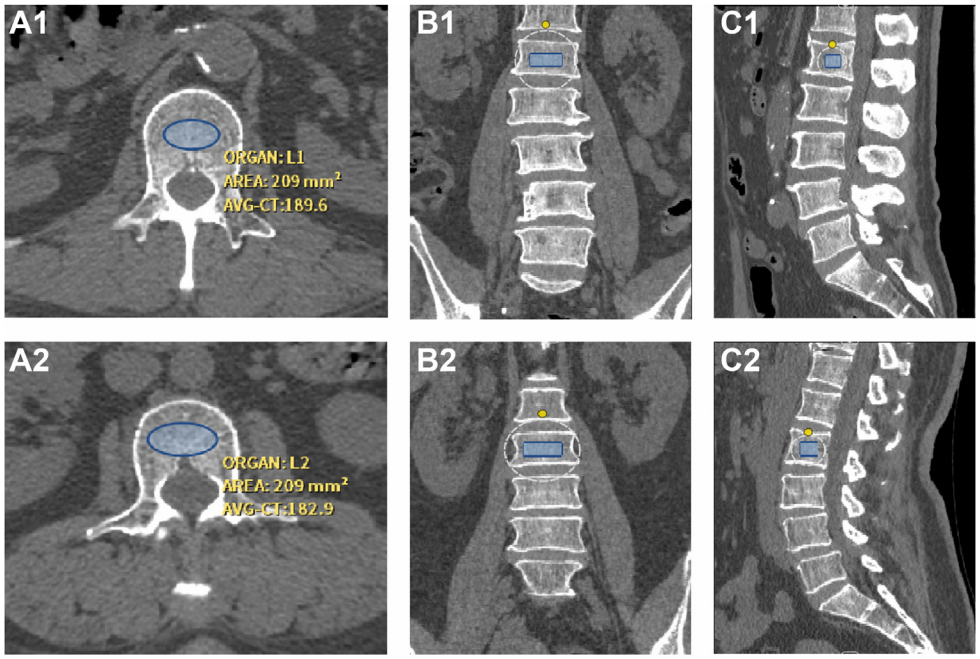

Figure 1. ROI selection of L1 and L2 vertebra in CT image; (**A**) axial plane of the vertebral ROI; (**B**) coronal plane of the vertebral ROI; (**C**) sagittal plane of the vertebral ROI. CT, computed tomography; ROI, region of interest.

and percentage. Baseline characteristics between patients with normal BMD, ostepenic, and osteoporosis were evaluated using analysis of variance, followed by multiple comparisons using least significant difference test. Categorical data analysis was performed using chi-squared test. Pearson's linear correlation plots and bivariate linear regression were used to assess the correlation between QCT and TEPS. Data analysis was performed with the SPSS Statistics version 26.0 (IBM Corporation, Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

RESULTS

Among 212 eligible patients, 6 patients were diagnosed with vertebral fractures and 1 patient was taking antiosteoporotic medications, and these 7 patients were excluded from further analysis. Therefore, in this study, demographic and imaging data of 205 patients were included. It is the results that the mean age of the 205 patients was 65.1 years, with a male-to-female ratio of 84:121. All 205 patients had complete imaging parameter data, with mean QCT and TEPS values of 93.3 ± 31.7 and 5.1 ± 1.3, respectively. And the mean value was BMI data 25.6 ± 4.2.

Differences in Demographic and Radiographic Parameters Between Different BMD Groups

Patients were divided into normal group (N = 50), osteopenia group (N = 91), and osteoporosis group (N = 64) based on their average L1–L2 QCT values. The comparison of baseline characteristics among the 3 groups is shown in Table 1. We found significant differences in TEPS among the normal, osteopenia, and osteoporosis groups (4.3 ± 1.1 vs. 5.0 ± 1.0 vs. 5.9 ± 1.2, $P < 0.01$). There was a significant difference in age between the normal group and the osteopenia and oste oporosis groups (60.8 ± 8.3 vs. 65.8 ± 7.3 and 60.8 ± 8.3 vs. 67.3 ± 5.8, $P < 0.01$), while there was no significant difference in age between the osteopenia and osteoporosis groups. There was no statistical difference in gender (male/female, 25/25 vs. 36/55 vs. 23/41) or BMI (27.3 ± 5.9 vs. 25.0 ± 3.9 vs. 24.9 ± 2.9) among the 3 groups.

Average QCT Value and TEPS Value

We conducted correlation and regression analyses on the average TEPS and QCT values of patients at L1/2–L4/5 and L1–L4 segments. The results showed a significant negative correlation between the average TEPS and QCT values at L1/2–L4/5 ($P < 0.001$) (Figure 3). To further determine the risk factors for endplate damage, we performed univariate and multivariate linear regression analyses on the correlation between TEPS and indicators such as age, sex, QCT values, and BMI. After controlling for other confounding factors, the results showed that QCT values and age were independent factors influencing endplate damage (Table 2).

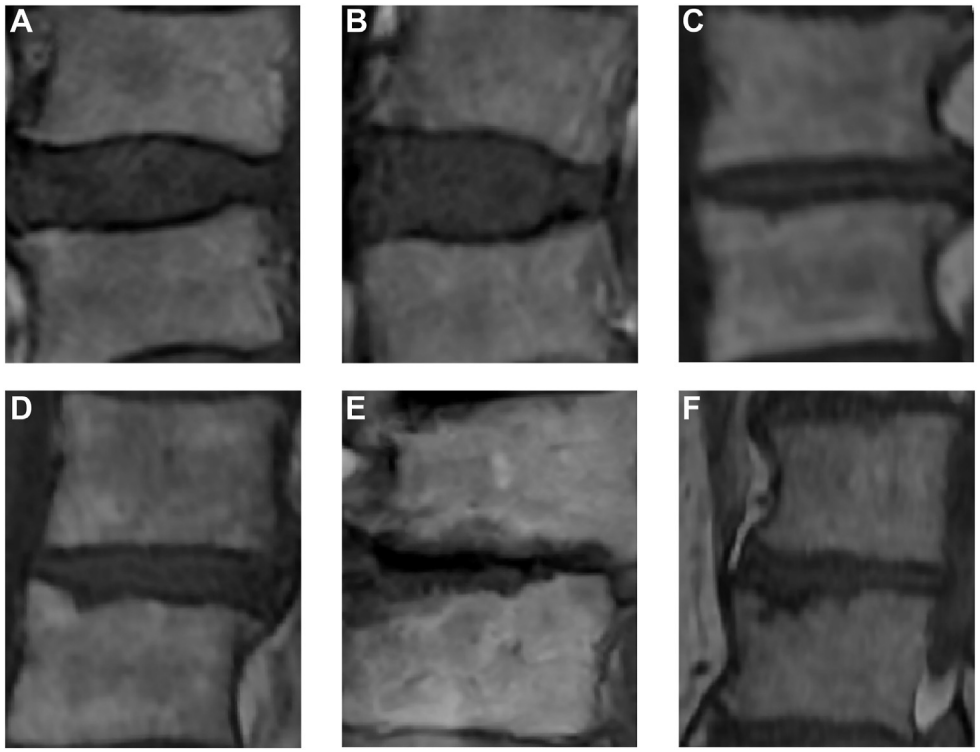

Figure 2. Example of the endplate classification and score system: (**A**) grade 1: no endplate breaks or defects; (**B**) grade 2: focal thinning of the endplate and no endplate breaks; (**C**) grade 3: focal disc marrow contacts and with normal contour of endplate maintained; (**D**) grade 4: damage upto 25% of width of endplate area; (**E**) grade 5: damage upto 50% of width of endplate area; (**F**) grade 6: complete endplate area damage.

Segment QCT Value and TEPS Value

For each vertebral segment, we explored the relationship between TEPS of the intervertebral disc and the QCT value (mean of the upper and lower vertebral bodies) of that segment. In L1/2–L4/5, there were significant differences in TEPS values for each segment among the 3 groups, with decreasing TEPS values from osteoporosis to normal groups ($P < 0.05$) (Table 3). We conducted correlation tests and regression analysis, which showed significant negative correlation ($P < 0.001$) between TEPS and QCT values for each segment from L1/2 to L4/5, with Pearson's correlation coefficients of 0.35–0.42. The strength of correlation was in the order of L4/5 > L3/4 > L1/2–L4/5 > L1/2 > L2/3 (Figure 4).

Proportion and Segment Distribution of Patients with High DDD Risk Segments

We compared the proportion of patients with TEPS ≥7 segments among the 3 groups. The proportion decreased from the

Table 1. Comparison of Patient Data Among the Normal, Osteopenia, and Osteoporosis Groups

Demographics	Total	Normal (N = 50)	Osteopenia (N = 91)	Osteoporosis (N = 64)
Age	65.1 ± 7.5	**60.8 ± 8.3**	**65.8 ± 7.3**	67.3 ± 5.8
Sex	84/121	25:25	36:55	23:41
BMI	25.6 ± 4.2	27.3 ± 5.9	25.0 ± 3.9	24.9 ± 2.9
TEPS	5.1 ± 1.3	**4.3 ± 1.1**	**5.0 ± 1.0**	**5.9 ± 1.2**
L1–L4 QCT valve	93.3 ± 31.7	**134.8 ± 20.5**	**92.7 ± 14.1**	**61.6 ± 16.1**

Boldface type indicates statistical significance ($P < 0.05$).
BMI, body mass index; TEPS, total endplate scores; QCT, quantitative computed tomography.

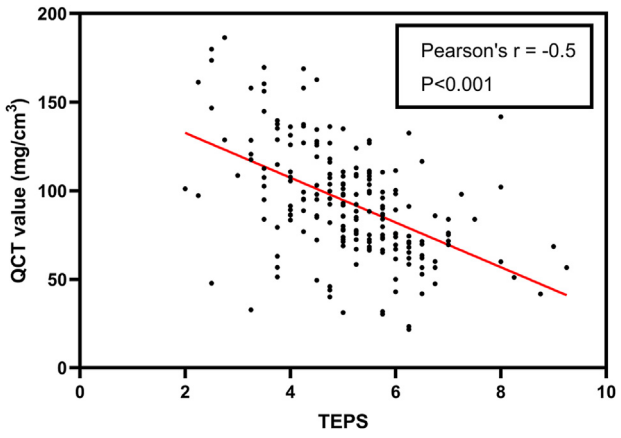

Figure 3. The relationship between average BMD and TEPS. BMD, bone mineral density; TEPS, total endplate scores.

osteoporotic group to the normal group, with percentages of 64%, 30%, and 16%, respectively. Additionally, there were significant differences in the average number of TEPS ≥7 segments per patient among the 3 groups, with 1.16 segments/person in the osteoporotic group, 0.41 segments/person in the osteopenia group, and 0.2 segments/person in the normal group. There were also differences in the mean number of TEPS ≥7 segments among patients who had TEPS ≥7 segments in the 3 groups, with 1.8 segments/person in the osteoporotic group, 1.37 segments/person in the ostepenic group, and 1.25 segments/person in the normal BMD group.

DISCUSSION

The deterioration of bone microstructure in patients with osteoporosis is evident in both cortical and trabecular bone, but is more severe in trabecular bone. Consequently, for individuals with spinal osteoporosis, PL-QCT offers a more precise measurement of v-BMD in trabecular bone compared to DXA, which measures areal BMD.[16,19,20] In this study, the PL-QCT system was used to assess v-BMD in patients hospitalized with DDD. We analyzed the variances in TEPS and additional parameters across the groups. The results showed that there were significant differences in TEPS across all groups, which decreased sequentially from the normal to the osteoporosis group ($P < 0.01$). In related research, Zhuang et al. categorized DDD patients into normal and osteoporotic groups based on the Hounsfield unit values from CT scans, noting that the osteoporosis group exhibited higher average TEPS, which aligns with the outcomes of this study.[11] Given the strong association between endplate damage and DDD, PL-QCT facilitates a more accurate assessment of v-BMD and aids in the precise diagnosis of osteoporosis.[15,16,21] Therefore, we speculated that patients with osteopenia and osteoporosis demonstrate higher average TEPS and an elevated risk of DDD compared to those in the normal group. Moreover, osteoporosis is an age-related disease; no significant age differences were found between the osteopenia and osteoporosis groups ($P > 0.05$), but it was significantly higher than the normal group ($P < 0.01$). This disparity could be attributed to the less pronounced variation in BMD with age among males compared to females, coupled with the varying gender ratios across groups, which might mask the true underlying differences.[22,23] Further studies are required to substantiate these findings. No statistical differences were observed in gender and BMI across the groups; however, a higher proportion of female patients was noted in both the osteoporosis and osteopenia groups, possibly due to postmenopausal estrogen decline, which renders women more susceptible to osteoporosis.[24]

The diagnosis of osteoporosis and osteopenia using QCT typically relies on standard average values derived from the L1–L2 vertebrae. However, in our study, we extended the measurement to include vertebrae L1–L4, providing a more comprehensive representation of the overall BMD in patients. Our data demonstrated a significant negative correlation between the average TEPS at the L1–L4 level and the patients' BMD, as illustrated in Figure 3. This finding aligns with Zhuang et al.'s research, which used CT Hounsfield unit values as a surrogate for BMD.[11] These results indicate that TEPS not only varies among different BMD groups but is also directly correlated with the BMD of patients. We postulate that more precise segmentation standards could enhance the assessment of endplate damage severity and the risk of developing DDD. Current diagnostic criteria based solely on L1–L2 QCT may not sufficiently identify patients at high risk for DDD. Further analysis through multiple linear regression revealed that age and BMD are the only independent factors influencing TEPS. This is attributable to the increased incidence of endplate fractures with age, which may heal with inflammation and sclerosis but still lead to a reduction in pore density, adversely affecting the nutritional pathways to the intervertebral disc.[25-28] In the trabecular bone of vertebral

Table 2. Multiple Linear Correlation Analysis of Risk Factors Associated With Total Endplate Scores

Variables	Standardized Coefficients	*P* Value
L1–L4 QCT valve	0.465	**< 0.001**
Sex	0.117	0.054
Age	0.132	**0.034**
BMI	0.135	0.484

Boldface type indicates statistical significance ($P < 0.05$).
BMI, body mass index; QCT, quantitative computed tomography.

Table 3. Comparison of Segment Total Endplate Scores Among the Normal, Osteopenic, and Osteoporosis Groups

Segment	Normal (N = 50)	Osteopenia (N = 91)	Osteoporosis (N = 64)
L1/2	4.24 ± 1.41	4.69 ± 1.55	6.02 ± 1.81
L2/3	4.26 ± 1.48	5.02 ± 1.57	5.95 ± 1.51
L3/4	4.22 ± 1.35	5.15 ± 1.37	5.70 ± 1.47
L4/5	4.40 ± 1.44	5.20 ± 1.37	5.98 ± 1.54

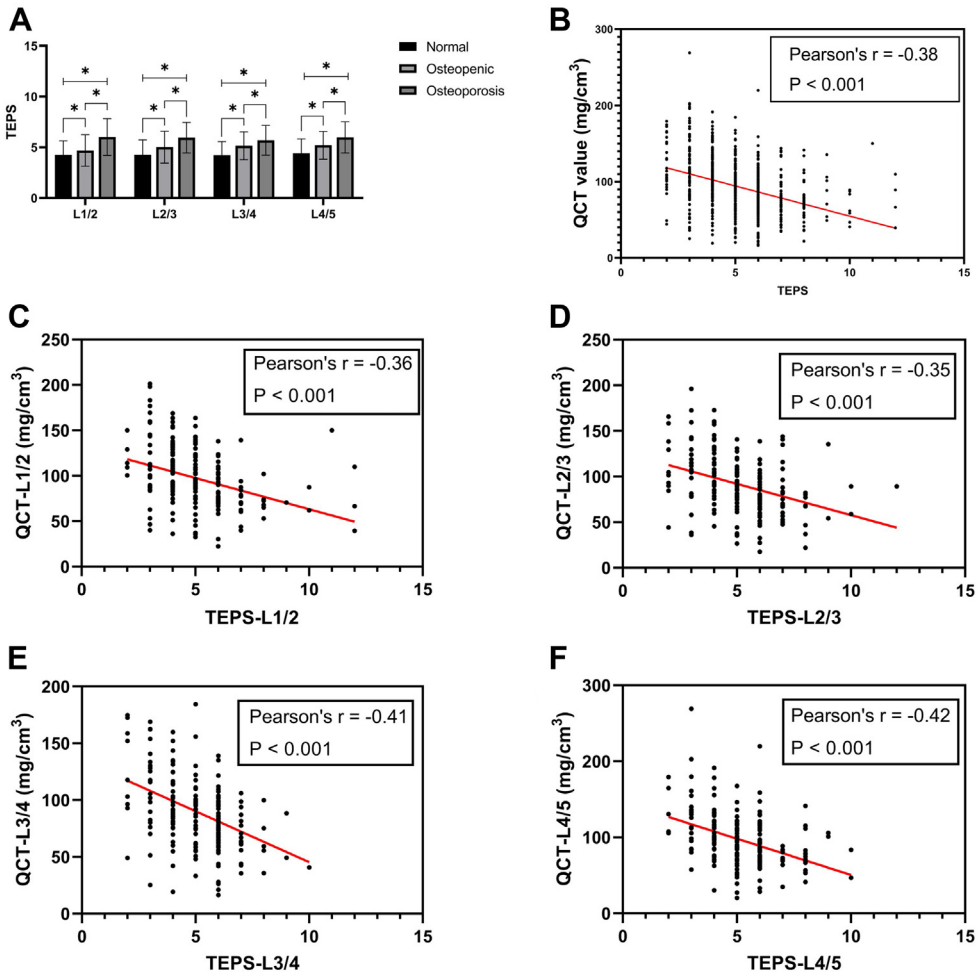

Figure 4. Scatter plot demonstrating a linear fit between QCT value and TEPS measurements. (**A**) Comparison with TEPS in each segment among all groups; (**B**–**E**) Linear fit in L1/2–L4/5 segment; (**F**) Linear fit in overall lumbar segments. TEPS, total endplate scores; QCT, quantitative computed tomography.

bodies, diminished BMD leads to a reduced number of trabecular support structures, causing fractures in the load-bearing portions of the vertebral body endplate, thus resulting in endplate damage.[29]

Our study observed variances in TEPS values across the segments from L1/2 to L4/5, with the osteoporosis group exhibiting higher TEPS values, which progressively decreased toward the normal group ($P < 0.05$). This stratification was further validated at the individual vertebral segment level. Employing PL-QCT software, we measured the v-BMD of individual segments and assigned the BMD corresponding to each intervertebral disc segment as the average v-BMD of the adjacent upper and lower vertebral bodies. Correlation and regression analyses confirmed a significant negative correlation ($P < 0.001$) between TEPS and QCT values from L1/2 to L4/5. The Pearson's correlation coefficients for each segment ranged from 0.35 to 0.42, with the strongest correlations observed at the L4/5 level, suggesting that endplate damage in the lower lumbar spine is more closely associated with segmental v-BMD. This corroborates previous findings that demonstrated a significant negative correlation between TEPS and QCT values in the lumbar spine.

Among the various factors implicated in the pathogenesis of DDD, diminished nutrient supply and structural damage that alter the mechanical environment of the intervertebral disc are recognized as 2 principal mechanisms driving disc degeneration.[30] In osteoporotic spines, the lack of vertebral trabecular bone support at the endplate can precipitate damage and disrupt nutrient transport to the intervertebral disc, as evidenced by histological findings in animal models.[31-33] While microscopic damage to the endplate structure may undergo self-repair, macroscopic structural impairments are likely to precipitate disc degeneration. Rajasekaran et al. have developed the TEPS, which leverages MRI imaging to

characterize macroscopic defects in the endplate structure. This scoring system is associated with the extent of disc degeneration, and a TEPS of 7 or higher has been identified as a critical threshold for a high incidence of DDD, as supported by Receiver Operating Characteristic curves demonstrating a strong correlation between TEPS and DDD severity.[17] In our study, we assessed the prevalence of TEPS $\geq$7 across different BMD groups. The results indicated a decreasing trend from the osteoporosis (64%), ostepenic (30%), to the normal BMD group (16%). Patients in the osteoporotic group not only exhibited a higher likelihood of having lumbar degeneration segments but also presented with a significantly greater average number of degenerated or potentially surgical segments (1.16 segments per person) compared to other groups. This finding underscores a greater economic and psychological burden on these individuals. Interestingly, a proportion of osteopenic patients also displayed segments with TEPS $\geq$7, albeit at a lower rate than in the osteoporotic group. Therefore, upon conducting PL-QCT screenings, heightened emphasis should be placed on protecting and educating osteopenic patients to prevent further bone density deterioration and avert the progression to osteoporosis, thereby reducing the incidence of additional lumbar disc degeneration segments.

This study elucidates the correlation between osteoporosis and endplate damage. Our findings demonstrate a significant association between the v-BMD, assessed through averaging values at L1—L2, L1—L4, or individual segments of the lumbar spine, and the TEPS of patients. These results provide an empirical foundation for further investigations into the link between osteoporosis and endplate deterioration. Sun et al. had shown that inhibiting osteoclast formation and activity, as well as osteoclast-mediated bone resorption, preserves the integrity of endplate cartilage as well as the microstructure and function of subchondral bone.[34] Conversely, Xiao et al. observed a marked increase in osteoclast activity within the endplates of ovariectomized mouse models.[35] Based on these findings, we hypothesize that osteoclasts activated in an osteopenic environment may compromise endplate integrity by adversely affecting chondrocytes within the endplate. This hypothesis warrants further investigation to substantiate its validity and explore its potential as a clinical strategy for addressing endplate damage associated with osteoporosis and DDD. The establishment of this connection could significantly inform the development of targeted therapeutic interventions for these conditions.

This study has several limitations. First, it is a retrospective and cross-sectional study, which limits our ability to establish a causal relationship between osteoporosis and endplate damage. Additionally, the TEPS used in this study was based on subjective measurements and analysis of radiological images. Despite systematic training of the measuring personnel, measurement errors are unavoidable. As most DDD patients did not undergo DXA measurement, we were unable to directly compare the accuracy of DXA and PL-QCT values in TEPS assessment. Finally, the sample population of this study consisted of DDD inpatients undergoing surgery; thus, the results of this study require further validation in a more diverse population.

CONCLUSION

Our study demonstrated a statistically significant positive correlation between osteoporosis and endplate damage. By employing a more nuanced classification of osteoporosis, our findings underscore the critical need for preventive measures in patients with osteopenia to mitigate progression to more severe bone loss. Furthermore, the management of patients with concurrent DDD and osteoporosis necessitates that clinicians devise and execute comprehensive treatment strategies, taking into account the multifaceted nature of these conditions.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Yiming Zhang: Writing — original draft, Writing — review & editing. **Yiming Dou:** Conceptualization, Data curation. **Yuanzhi Weng:** Methodology, Project administration. **Chao Chen:** Investigation, Methodology. **Qingqian Zhao:** Data curation, Formal analysis. **Wentao Wan:** Validation, Visualization. **Hanming Bian:** Software, Supervision. **Ye Tian:** Conceptualization, Data curation. **Yang Liu:** Supervision, Validation. **Shan Zhu:** Resources, Software. **Zhi Wang:** Methodology, Project administration. **Xinlong Ma:** Validation, Visualization. **Xinyu Liu:** Investigation, Methodology. **Weijia William Lu:** Resources, Software. **Qiang Yang:** Funding acquisition, Writing — original draft.

REFERENCES

1. Mo X, Zhao S, Wen Z, et al. High prevalence of osteoporosis in patients undergoing spine surgery in China. *BMC Geriatr*. 2021;21:361.
2. Andersen T, Christensen FB, Langdahl BL, et al. Fusion mass bone quality after uninstrumented spinal fusion in older patients. *Eur Spine J*. 2010;19:2200-2208.
3. Wang L, Yu W, Yin X, et al. Prevalence of osteoporosis and fracture in China: the China osteoporosis prevalence study. *JAMA Netw Open*. 2021;4:e2121106.
4. Si L, Winzenberg TM, Jiang Q, Chen M, Palmer AJ. Projection of osteoporosis-related fractures and costs in China: 2010-2050. *Osteoporos Int*. 2015;26:1929-1937.
5. Fujimoto K, Inage K, Orita S, et al. The nature of osteoporotic low back pain without acute vertebral fracture: a prospective multicenter study on the analgesic effect of monthly minodronic acid hydrate. *J Orthop Sci*. 2017;22:613-617.
6. Mallio CA, Vadalà G, Russo F, et al. Novel magnetic resonance imaging tools for the diagnosis of degenerative disc disease: a narrative review. *Diagnostics (Basel)*. 2022;12:420.
7. Holm S, Holm AK, Ekström L, Karladani A, Hansson T. Experimental disc degeneration due to endplate injury. *J Spinal Disord Tech*. 2004;17:64-71.
8. Lotz JC, Fields AJ, Liebenberg EC. The role of the vertebral end plate in low back pain. *Global Spine J*. 2013;3:153-164.
9. Ling Z, Crane J, Hu H, et al. Parathyroid hormone treatment partially reverses endplate remodeling and attenuates low back pain in animal models of spine degeneration. *Sci Transl Med*. 2023;15:eadg8982.
10. Li R, Zhang W, Xu Y, et al. Vertebral endplate defects are associated with bone mineral density in lumbar degenerative disc disease. *Eur Spine J*. 2022;31:2935-2942.
11. Zhuang C, Wang Z, Chen W, Tian B, Li J, Lin H. Osteoporosis and endplate damage correlation using a combined approach of Hounsfield unit values and total endplate scores: a retrospective cross-sectional study. *Clin Interv Aging*. 2021;16:1275-1283.
12. Munir S, Freidin MB, Rade M, Määttä J, Livshits G, Williams FMK. Endplate defect is heritable, associated with low back pain and

triggers intervertebral disc degeneration: a longitudinal study from TwinsUK. *Spine (Phila Pa 1976)*. 2018;43:1496-1501.

13. Donescu OS, Battié MC, Videman T. The influence of magnetic resonance imaging findings of degenerative disease on dual-energy X-ray absorptiometry measurements in middle-aged men. *Acta Radiol*. 2007;48:193-199.

14. Pan J, Lu X, Yang G, Han Y, Tong X, Wang Y. Lumbar disc degeneration was not related to spine and hip bone mineral densities in Chinese: facet joint osteoarthritis may confound the association. *Arch Osteoporosis*. 2017;12:20.

15. Liu ZJ, Zhang C, Ma C, et al. Automatic phantomless QCT system with high precision of BMD measurement for osteoporosis screening: technique optimisation and clinical validation. *J Orthop Translat*. 2022;33:24-30.

16. Kulkarni AG, Thonangi Y, Pathan S, et al. Should Q-CT Be the gold standard for detecting spinal osteoporosis? *Spine (Phila Pa 1976)*. 2022;47: E258-E264.

17. Rajasekaran S, Venkatadass K, Naresh Babu J, Ganesh K, Shetty AP. Pharmacological enhancement of disc diffusion and differentiation of healthy, ageing and degenerated discs : results from in-vivo serial post-contrast MRI studies in 365 human lumbar discs. *Eur Spine J*. 2008;17: 626-643.

18. Schuit SC, van der Klift M, Weel AE, et al. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. *Bone*. 2004;34:195-202.

19. Ravn P, Cizza G, Bjarnason NH, et al. Low body mass index is an important risk factor for low bone mass and increased bone loss in early postmenopausal women. Early Postmenopausal Intervention Cohort (EPIC) study group. *J Bone Miner Res*. 1999;14:1622-1627.

20. Löffler MT, Jacob A, Valentinitsch A, et al. Improved prediction of incident vertebral fractures using opportunistic QCT compared to DXA. *Eur Radiol*. 2019;29:4980-4989.

21. Moser M, Adl Amini D, Albertini Sanchez L, et al. The association between vertebral endplate defects, subchondral bone marrow changes, and lumbar intervertebral disc degeneration: a retrospective, 3-year longitudinal study. *Eur Spine J*. 2023;32:2350-2357.

22. Berger C, Langsetmo L, Joseph L, et al. Change in bone mineral density as a function of age in women and men and association with the use of antiresorptive agents. *CMAJ (Can Med Assoc J)*. 2008;178:1660-1668.

23. Tang H, Di W, Qi H, et al. Age-related changes in trabecular bone score and bone mineral density in Chinese men: a cross-sectional and longitudinal study. *Clin Interv Aging*. 2022;17:429-437.

24. Lin W, He C, Xie F, et al. Discordance in lumbar bone mineral density measurements by quantitative computed tomography and dual-energy X-ray absorptiometry in postmenopausal women: a prospective comparative study. *Spine J*. 2023;23: 295-304.

25. Boos N, Weissbach S, Rohrbach H, Weiler C, Spratt KF, Nerlich AG. Classification of age-related changes in lumbar intervertebral discs: 2002 Volvo Award in basic science. *Spine (Phila Pa 1976)*. 2002;27:2631-2644.

26. Rajasekaran S, Babu JN, Arun R, Armstrong BR, Shetty AP, Murugan S. ISSLS prize winner: a study of diffusion in human lumbar discs: a serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. *Spine (Phila Pa 1976)*. 2004;29:2654-2667.

27. Wang Y, Owoc JS, Boyd SK, Videman T, Battié MC. Regional variations in trabecular architecture of the lumbar vertebra: associations with age, disc degeneration and disc space narrowing. *Bone*. 2013;56:249-254.

28. Wang Y, Videman T, Battié MC. ISSLS prize winner: lumbar vertebral endplate lesions: associations with disc degeneration and back pain history. *Spine (Phila Pa 1976)*. 2012;37:1490-1496.

29. Twomey LT, Taylor JR. Age changes in lumbar vertebrae and intervertebral discs. *Clin Orthop Relat Res*. 1987;224:97-104.

30. Kirnaz S, Capadona C, Wong T, et al. Fundamentals of intervertebral disc degeneration. *World Neurosurg*. 2022;157:264-273.

31. Su Q, Li Y, Feng X, et al. Association and histological characteristics of endplate injury and intervertebral disc degeneration in a rat model. *Injury*. 2021;52:2084-2094.

32. Ding Y, Jiang J, Zhou J, et al. The effects of osteoporosis and disc degeneration on vertebral cartilage endplate lesions in rats. *Eur Spine J*. 2014; 23:1848-1855.

33. Zhong R, Wei F, Wang L, et al. The effects of intervertebral disc degeneration combined with osteoporosis on vascularization and microarchitecture of the endplate in rhesus monkeys. *Eur Spine J*. 2016;25:2705-2715.

34. Sun Q, Tian FM, Liu F, et al. Denosumab alleviates intervertebral disc degeneration adjacent to lumbar fusion by inhibiting endplate osteochondral remodeling and vertebral osteoporosis in ovariectomized rats. *Arthritis Res Ther*. 2021;23:152.

35. Xiao ZF, He JB, Su GY, et al. Osteoporosis of the vertebra and osteochondral remodeling of the endplate causes intervertebral disc degeneration in ovariectomized mice. *Arthritis Res Ther*. 2018;20: 207.

Conflict of interest statement: This study was supported by the National Key R&D Program of China (2023YFC2416900), National Natural Science Foundation of China (82372419, 82072435), NO.2021-NCRC-CXJJ-ZH-22 of Clinical Application-oriented Medical Innovation Foundation from National Clinical Research Center for Orthopedics, Sports Medicine & Rehabilitation Foundation, Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-026A), Applied Basic Research Multi-input Foundation of Tianjin (21JCZDJC01040), Tianjin Science and Technology Plan Project "Unveiling and Directing" Major Project (21ZXJBSY00130), and Scientific Foundation of Tianjin Hospital (TJYYQ2406).

Data availability: The datasets used and/or analysed during the present study are available from the corresponding author on reasonable request.

Received 27 August 2024; accepted 19 September 2024

Citation: World Neurosurg. (2024). https://doi.org/10.1016/j.wneu.2024.09.100

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***