

Caudal Sub-Endplate Bone Marrow Fat Fraction Is Associated With Early Biochemical Degeneration of Lumbar Intervertebral Discs: A Multiparametric Quantitative MRI Study

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Abstract

Objective

To investigate the spatial distribution of the sub-endplate bone marrow microenvironment and its association with biochemical degeneration of the nucleus pulposus (NP) in patients with lumbar disc degeneration (LDD) using multiparametric quantitative MRI.

Methods

This retrospective cross-sectional study included 72 patients with low back pain (aged 20–59 years), evaluation of 360 lumbar intervertebral discs. All discs were classified according to the five-grade Pfirrmann grade (PFG) system. NP-T1rho values, as well as the fat fraction (FF) and endplate bone quality (EBQ) index of both cranial and caudal sub-endplate bone marrow, were measured. Interobserver and intraobserver agreement was evaluated using intraclass correlation coefficients (ICCs). Cranial-caudal differences in FF and EBQ were compared across PFG categories and lumbar levels. Correlation analyses were performed to evaluate the relationships between NP-T1rho and sub-endplate bone marrow measures. Linear mixed-effects models, with patient identity specified as a random effect, were used to identify factors independently associated with NP-T1rho.

Results

Pfirrmann grading and quantitative MRI measurements showed good reproducibility, with kappa coefficients of 0.718–0.854 and ICCs of 0.817–0.912. NP-T1rho was strongly negatively correlated with PFG ($r = -0.857$, $p < 0.001$). Sub-endplate bone marrow FF and EBQ demonstrated marked cranial-caudal and lumbar-level heterogeneity. In general, caudal FF and EBQ were higher than their corresponding cranial values, particularly at the L1/2–L4/5 levels, and both measures progressively increased from L1/2 to L4/5 before decreasing at L5/S1. Significant negative correlations between NP-T1rho and both cranial and caudal FF were observed only in PFG grade II discs ($r = -0.283$ and -0.274 , respectively; both $p \leq 0.01$). After adjustment for covariates, caudal FF remained independently associated with lower NP-T1rho in PFG grade II discs ($\beta = -0.43$, $p = 0.031$), whereas cranial FF and EBQ were not independently associated with NP-T1rho. In the overall analysis, caudal FF and caudal EBQ were independently associated with NP-T1rho.

Conclusion

The sub-endplate bone marrow microenvironment exhibits marked cranial–caudal and level-specific heterogeneity. Increased caudal sub-endplate bone marrow FF is independently associated with lower

NP-T1rho during early disc degeneration, suggesting that caudal sub-endplate bone marrow fat infiltration may serve as a potential quantitative MRI marker of early biochemical degeneration in LDD.

1. Introduction

Lumbar disc degeneration (LDD) is the most common spinal degenerative disease and one of the leading causes of global workforce loss and increased healthcare burden [1]. Its pathological core begins with a decrease in the content of proteoglycan (PG) in the nucleus pulposus (NP) and a decline in water content, which subsequently leads to a disruption of the internal environment balance and biomechanical functions [2]. Although traditional morphological MRI can assess macroscopic structural changes, it lacks sensitivity for early and reversible molecular-level changes, limiting the identification of the early warning time and intervention window for LDD [3, 4]. In contrast, T1rho imaging shows significant advantages in the early diagnosis of LDD. By detecting interactions between water molecules and macromolecules such as PGs, it can non-invasively and quantitatively captures early PG loss in the NP, and is considered a highly sensitive imaging biomarker for early biochemical changes in LDD [4–6].

Disc health depends heavily on the integrity of the disc-endplate complex, which comprises the cartilaginous endplate and the sub-endplate bone [7]. The sub-endplate bone not only serves as the mechanical foundation for the disc but also acts as a critical pathway for nutrient diffusion and metabolic waste clearance [7, 8]. Previous studies examining the relationship between vertebral bone mineral density and LDD have yielded conflicting conclusions: some have reported that severe LDD correlates with higher bone density [9, 10], while another have found a significant negative association [11]. The research on the correlation between the local microenvironment of the sub-endplate bone and the intervertebral disc is highly anticipated [12]. Recently, the sub-endplate bone quality (EBQ) index has been proposed as a clinically accessible and cost-effective tool, which derived from signal intensity ratios on conventional T1-weighted imaging. It indirectly reflects subchondral trabecular microarchitecture and offers a novel quantitative imaging approach for noninvasive assessment of the local mechanical microenvironment [13, 14].

However, the sub-endplate microenvironment is not merely a mechanical scaffold; the bone marrow within it functions as an endocrine organ with secretory and metabolic activity [15]. With aging or under pathological conditions, excessive accumulation of bone marrow adipose tissue (BMAT) may reduce the space available for nutrient exchange and impair blood perfusion [16]. In addition, adipokines and proinflammatory mediators released by BMAT may disrupt local bone marrow homeostasis [15, 17]. Together, these changes can impair nutrient transport through the endplate and contribute to disc degeneration [18]. The pathogenesis of LDD should therefore be examined from both mechanical and metabolic perspectives. Although they are both considered potential upstream contributors to LDD, most previous studies have investigated them separately [9–11, 14, 16, 18]. Few studies have simultaneously quantified sub-endplate bone characteristics, including EBQ and fatty infiltration, and the biochemical composition of the NP within the same cohort. Importantly, the cranial and caudal endplates differ in their anatomy, biomechanical loading, and nutrient pathways [19]. LDD also varies across lumbar levels

[20]. This spatial heterogeneity supports separate evaluation of the cranial and caudal regions within the disc-endplate unit.

Thus, this study used multiparametric quantitative MRI to measure the sub-endplate bone marrow fat fraction (FF) and EBQ index within the same cohort. We aimed to characterize the cranial–caudal distribution of the sub-endplate bone marrow microenvironment according to sex, age, lumbar level, and degeneration grade, and to determine whether these measures were independently associated with early biochemical degeneration of the NP, as assessed using NP T1rho values.

2. Methods

2.1 Study Population

This retrospective cross-sectional study initially screened 104 patients with low back pain (LBP) who presented to the First Affiliated Hospital of Army Medical University between March 2024 and February 2025. presented with mild symptoms, as defined by an Oswestry Disability Index (ODI) score ≤ 20 [21], and underwent standardized lumbar quantitative MRI during the same period. Intervertebral disc degeneration was evaluated using the Pfirrmann grading (PFG) system [22, 23], with grade I defined as normal, grade II as early degeneration, grade III as moderate degeneration, and grade IV or higher as advanced degeneration.

The inclusion criteria were as follows: (1) age 20–59 years; (2) ODI score ≤ 20 ; (3) adequate-quality lumbar MRI including T1-weighted, T1rho, and multiecho water-fat separation fat analysis calculation technique (FACT) sequences. The exclusion criteria were as follows: (1) history of lumbar spine surgery, acute spinal trauma, or severe spinal deformity; (2) secondary causes of LBP or conditions affecting disc/bone metabolism (e.g., spinal tumors, infections, ankylosing spondylitis, or clinically diagnosed osteoporosis); (3) long-term use of medications affecting bone or cartilage metabolism; (4) severe systemic comorbidities (e.g., uncontrolled diabetes mellitus); (5) incomplete MRI sequence datasets or unsatisfactory image quality (e.g., severe motion artifacts).

As summarized in the recruitment flowchart (Fig. 1), 32 patients were excluded. The final cohort comprised 72 patients (34 men and 38 women; mean age, 38.86 ± 9.79 years, range 20–59 years), yielding a total of 360 lumbar intervertebral discs (L1/2–L5/S1) for quantitative analysis. Patients were categorized into four age groups by decade: 20–29 years ($n = 17$), 30–39 years ($n = 18$), 40–49 years ($n = 19$), and 50–59 years ($n = 18$) (Table 1). The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University (approval no. KY2025072). The requirement for informed consent was waived because of the retrospective study design.

2.2 MRI Image Acquisition

All lumbar MRI examinations were performed using a 3.0-T scanner (uMR 770; United Imaging Healthcare, Shanghai, China) with an eight-channel body surface coil. The imaging protocol included the following sequences: (1) Sagittal fast spin echo T2-weighted imaging: repetition time / echo time (TR/TE) = 3697 / 105.3 ms; slice thickness = 3.5 mm; field of view (FOV) = 200 × 300 mm²; matrix = 240 × 168; number of excitations = 1. (2) Sagittal fast spin echo T1-weighted imaging: TR/TE = 570/9.9 ms; slice thickness = 3.5 mm; FOV = 200 × 300 mm²; matrix = 240 × 168; number of excitations = 1. (3) Sagittal T1rho imaging: TR/TE = 8.6/3.9 ms, flip angle = 15°, spin lock frequency (FSL) = 300 Hz, spin lock times (TSL) = 0, 10, 35, and 65 ms, slice thickness = 3.5 mm, FOV = 300 × 160 mm², matrix = 320 × 320, number of excitations = 1. (4) Sagittal FACT (fat analysis calculation technique) imaging: TR = 11.3 ms, TEs = 1.71/3.2/4.69/6.18/7.67/9.16 ms, slice thickness = 3.5 mm, matrix = 224 × 168, FOV = 300 × 280 mm².

2.3 Image Assessment

All images were anonymized and then independently evaluated by two radiologists who were blinded to the patients' clinical and demographic information. The mean value of their measurements was used for final analysis. Inter-observer and intra-observer agreement were comprehensively assessed.

2.3.1 Qualitative and quantitative assessment of intervertebral discs

Two radiologists independently evaluated the mid-sagittal T2-weighted images to assess disc degeneration, assigning a five-grade PFG [21] to each of the five lumbar discs (L1/2, L2/3, L3/4, L4/5, and L5/S1). A third investigator documented the assessments. Any discrepancies were resolved through consultation with a senior spine surgeon until a consensus was reached.

Quantitative NP-T1rho values were measured on the mid-sagittal T1rho maps. As illustrated in Fig. 2c, each NP was divided into five equal sub-regions from the anterior to posterior margin along the orientation of the adjacent endplates. A circular region of interest (ROI) of equal size was placed in each sub-region. The mean T1rho value of the middle three ROIs was defined as the NP-T1rho value for that disc [24]. To evaluate intra-observer reliability, one radiologist repeated all measurements after a 2-week interval.

2.3.2 Measurement of sub-endplate bone marrow FF and EBQ

On the mid-sagittal T1-weighted images, a quasi-rectangular ROI (approximately 3 mm in height) was placed within the subchondral trabecular bone immediately adjacent to the cartilaginous endplate on both the cranial and caudal sides of each disc, strictly excluding cortical bone (Fig. 2a). The width of the ROI was customized to conform to the endplate morphology [14], and the mean signal intensity ($SI_{\text{sub-endplate}}$) was recorded. A circular reference ROI was placed within the cerebrospinal fluid (CSF) posterior to the L3 vertebral body to obtain $SI_{L3 \text{ CSF}}$ (Fig. 2a). The EBQ values were calculated separately

for the cranial and caudal endplates of each disc and recorded as EBQ_{cranial} and EBQ_{caudal} , respectively. The EBQ index was calculated as follows:

$$EBQ = \frac{SI(\text{sub} - \text{endplate bone})}{SI(L3 \text{ CSF})}$$

Sub-endplate bone marrow FF was measured on the quantitative FF maps derived from the FACT sequence. ROIs were redrawn at identical anatomical locations matching the T1-weighted images (Fig. 2b). The FF values for the cranial and caudal sides were directly obtained and recorded as FF_{cranial} and FF_{caudal} , respectively.

2.4 Statistical Analysis

Statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA) and GraphPad Prism (version 8.0; GraphPad Software, San Diego, CA, USA). Continuous variables were tested for normality using the Shapiro-Wilk test and for homogeneity of variance using Levene's test. Normally distributed data are presented as mean $\pm$ standard deviation (SD), and non-normally distributed data are expressed as median (interquartile range, IQR). Interobserver agreement between the two radiologists for PFG was assessed using Cohen's kappa coefficient. The reproducibility for quantitative MRI measurements (NP-T1rho, FF, and EBQ) was assessed using the intraclass correlation coefficients (ICCs), with an ICC > 0.75 indicating good agreement.

For normally distributed data with homogeneous variances, comparisons between two groups were performed using independent-samples or paired-samples t tests, as appropriate. Continuous variables were compared across age groups, lumbar levels and PFG grades using one-way analysis of variance. When the overall difference was statistically significant, Tukey's honestly significant difference test was used for post hoc pairwise comparisons, with an adjusted p value < 0.05 considered statistically significant. Correlations were evaluated using Pearson's correlation coefficient or Spearman's rank correlation coefficient, as appropriate for the variable distributions. Linear mixed-effects models were used to assess the effects of sub-endplate bone marrow FF and EBQ on NP-T1rho values [14], with NP-T1rho as the response variable, patients as random effects, and all other parameters as fixed effects.

3. Results

3.1 Distribution of Intervertebral Disc Degeneration and Assessment Reliability

A total of 72 patients with LBP, comprising 360 lumbar intervertebral discs, were evaluated. All patients had at least one disc with PFG $\geq$ II degeneration. The distribution of disc degeneration severity across all 360 discs was as follows: Grade I in 61 (16.94%), Grade II in 167 (46.39%), Grade III in 52 (14.44%), Grade IV in 69 (19.17%), and Grade V in 11 (3.06%). Regarding clinical presentation, 31 patients (43.06%)

exhibited single-segment involvement with PFG $\geq$ III, whereas 41 patients (56.94%) demonstrated multi-segment involvement (two or more segments with PFG $\geq$ III) (Table 1).

Assessment of inter-observer reliability for Pfirrmann grading yielded weighted Cohen's kappa coefficients of 0.769 for L1/2, 0.823 for L2/3, 0.854 for L3/4, 0.748 for L4/5, and 0.718 for L5/S1, indicating substantial to excellent agreement. For quantitative MRI metrics, the intra-observer and inter-observer ICCs for NP-T1rho measurements were 0.912 and 0.886, respectively. The inter-observer ICCs for sub-endplate bone marrow FF and EBQ measurements were 0.863 and 0.817, respectively, demonstrating robust reproducibility. Quantitative NP-T1rho values decreased progressively with advancing degeneration grades, showing a strong negative correlation with PFG grades ($r = -0.857$, $p < 0.001$) (Fig. 3).

3.2 Comparisons of NP-T1rho and Sub-Endplate Bone Microenvironment by Sex and Age

Mean NP-T1rho values differed significantly by sex in patients with LBP, with higher values in males than in females ($p = 0.015$) (Fig. 4a). Across age categories, Patients aged 20–29 years had significantly higher mean NP-T1rho values than those aged 30–39, 40–49, and 50–59 years (all post hoc $p < 0.05$), whereas no significant differences were observed among the latter three age groups (all $p > 0.05$) (Fig. 4b).

Regarding the sub-endplate bone microenvironment, mean sub-endplate bone marrow FF was significantly higher in males than in females ($p < 0.05$) and exhibited a progressive increase with advancing age. Post hoc pairwise comparisons revealed a sharp increase between the adjacent 30–39 and 40–49 age groups ($p < 0.001$) (Fig. 4c). In contrast, mean EBQ scores showed no significant difference between sexes ($p > 0.05$) (Fig. 4d). No significant difference in mean EBQ was observed between the 30–39 and 40–49 year age groups ($p > 0.05$), whereas differences among all other age cohorts remained statistically significant after correction for multiple comparisons (all adjusted $p < 0.001$) (Fig. 4e).

3.3 Cranial-Caudal Distribution of the Sub-Endplate Bone Microenvironment

Among discs classified as PFG grades I–V, both sub-endplate bone marrow FF and EBQ values were greater on the caudal side than on the cranial side. These differences were statistically significant for all grades except grade IV (all $p < 0.05$) (Table 2). With advancing Pfirrmann grades, mean cranial and caudal sub-endplate FF and EBQ initially increased, peaked at Grade III, and subsequently declined (Fig. 5a).

In comparisons between adjacent PFG categories, mean cranial and caudal FF and EBQ values showed no significant differences between grade I and grade II discs. However, caudal FF was significantly higher in Grade III discs than in Grade II discs ($p = 0.041$), whereas the increase in cranial FF did not

reach statistical significance ($p = 0.055$). Similarly, both cranial and caudal EBQ values were significantly higher in Grade III discs compared with Grade II discs ($p = 0.023$ and 0.022 , respectively). No significant differences in cranial or caudal FF or EBQ were observed between grade III and grade IV discs (all $p > 0.05$).

Grade-stratified correlation analyses between NP-T1rho and sub-endplate parameters revealed significant negative correlations exclusively in Grade II discs, where NP-T1rho was inversely correlated with both FF_{cranial} and FF_{caudal} ($r = -0.283$ and -0.274 respectively; both $p = 0.01$). No significant correlations were identified between NP-T1rho and any sub-endplate bone microenvironment parameter in the remaining Pfirrmann grades (Table 3).

Regionally, from the L1/2 through L4/5 levels, mean caudal sub-endplate FF and EBQ were significantly higher than their corresponding cranial values (all $p < 0.05$). At L5/S1 level, mean FF did not differ significantly between the cranial and caudal sides ($p = 0.682$), whereas mean caudal EBQ was significantly lower than mean cranial EBQ ($p = 0.016$) (Table 2). From L1/2 to L4/5, mean sub-endplate bone marrow FF and EBQ displayed a progressive upward trend, peaking at the L4/5 level before decreasing at L5/S1 (Fig. 5b).

3.4 Associations of the Sub-Endplate Bone Microenvironment With NP-T1rho

The results of the linear mixed-effects model for discs across all 360 lumbar discs are presented in Table 4. Variables with $p < 0.05$ in the univariable analyses were entered into the multivariable model. After adjustment for all covariates, caudal sub-endplate bone marrow FF ($\beta = -0.32$, 95% CI: -0.60 to -0.03 , $p = 0.030$), caudal EBQ ($\beta = -5.96$, 95% CI: -11.03 to -0.89 , $p = 0.022$), male sex ($\beta = 9.52$, $p < 0.001$), younger age ($\beta = -0.72$, $p < 0.001$), BMI ($\beta = -0.71$, $p = 0.045$), and lower lumbar level (L3/4, L4/5, and L5/S1; all $p < 0.01$) remained independently associated with NP-T1rho. In contrast, neither cranial sub-endplate bone marrow FF nor cranial EBQ was independently associated with NP-T1rho (both $p > 0.05$) (Table 4).

Stratified analyses according to Pfirrmann grades revealed grade-dependent variability in independent correlates (Table 5). In normal discs (PFG grade I), age ($\beta = -0.94$, $p < 0.001$) and male sex ($\beta = 11.09$, $p = 0.018$) were the only independent predictors of NP-T1rho. In discs with early degeneration (PFG grade II), caudal sub-endplate bone marrow FF was independently associated with lower NP-T1rho ($\beta = -0.43$, $p = 0.031$), alongside age ($\beta = -0.55$, $p < 0.001$) and male sex ($\beta = 6.32$, $p = 0.012$). In discs with intermediate degeneration (PFG grade III), only male sex remained significantly associated with NP-T1rho ($\beta = 4.49$, $p = 0.040$), whereas the association with sub-endplate bone marrow FF was no longer significant.

When advanced degeneration stages (PFG grades III–V) were analyzed, demographic parameters and sub-endplate microenvironmental measures were no longer independently associated with NP-T1rho. Instead, lower lumbar levels became the primary determinants of lower NP-T1rho values (Table 5).

4. Discussion

Using multiparametric quantitative MRI, this study simultaneously evaluated the association between biochemical alterations in the NP and the sub-endplate bone marrow microenvironment, as characterized by FF and EBQ, within the disc-endplate unit in patients with LDD. The results demonstrated marked cranial-caudal spatial heterogeneity in the sub-endplate bone marrow microenvironment. In particular, caudal sub-endplate bone marrow fat infiltration was independently associated with lower NP-T1rho values in early-stage LDD. These findings highlight sub-endplate bone marrow adiposity as a potential contributor to early LDD and provide objective imaging evidence that may improve our understanding of LDD pathophysiology and facilitate the exploration of novel therapeutic targets.

In patients with LDD aged 20–59 years (mean age, 38.86 ± 9.79 years), this study confirmed a strong negative correlation between NP-T1rho and PFG ($r = -0.857$, $p < 0.001$). This finding is highly consistent with the results reported by Zhou et al. [22] in both humans and a monkey model ($r = -0.681$ and -0.824 , respectively; both $p < 0.001$). Additionally, NP-T1rho measurements demonstrated excellent intra- and inter-observer reproducibility. A previous study [22] suggested that rapid biochemical progression of disc degeneration occurs between PFG grades II and III, a stage to which conventional morphological grading is insufficiently sensitive. Our findings further support this view, as NP-T1rho decreased sharply from PFG grade II to grade III. This suggests that rapid loss of proteoglycans within the NP may already be occurring when only mild signal heterogeneity is evident morphologically. Therefore, NP-T1rho may serve as a sensitive imaging biomarker for monitoring early molecular alterations in LDD and may provide an opportunity for intervention before irreversible structural damage develops. In a previous rhesus monkey study, Liu et al. [4] found that an NP-T1rho range of 80–95 ms represented the optimal window for hydrogel injection in the treatment of disc degeneration, providing preclinical evidence for the use of quantitative NP-T1rho assessment to guide early intervention strategies for LDD.

Unlike previous studies [13, 18, 26, 27] that analyzed the vertebral body as a whole, the present study focused on a 3-mm-thick trabecular bone region immediately adjacent to the endplate [14] and evaluated differences in the sub-endplate bone marrow microenvironment from an asymmetric cranial–caudal perspective. EBQ, which is closely related to bone strength, was also incorporated alongside sub-endplate bone marrow FF to provide a more comprehensive characterization of the sub-endplate bone marrow microenvironment. Significant negative correlations between NP-T1rho and both cranial and caudal sub-endplate FF were observed only during early degeneration (PFG grade II). After adjustment for potential confounders, only caudal FF remained independently associated with lower NP-T1rho in early-degenerative discs ($\beta = -0.43$, $p = 0.031$), suggesting that the relationship between sub-endplate bone marrow fat infiltration and disc degeneration is highly spatially specific. This result is consistent with previous quantitative MRI studies. Krug et al. [18] found significant negative correlations between adjacent vertebral marrow fat fraction and disc biochemical parameters (T1rho/T2), supporting the possibility that fatty conversion of hematopoietic bone marrow may accelerate the progression of LDD. Similarly, Ji et al. [28] observed that only at grade II did NP-T2 values correlate negatively with adjacent

vertebral fat fraction, implying that vertebral fat deposition occurs early in the degenerative process. Building on previous analyses of BMAT, the present study further localized this association to the caudal sub-endplate region, thereby revealing a spatially specific role of BMAT in LDD. This spatial specificity may be related to differences in lumbar biomechanical loading and endplate anatomy. The caudal lumbar endplate is thinner, has weaker trabecular support, and contains fewer nutrient channels [19]. During routine activities such as standing and bending, it is subjected to greater axial and shear stresses. These conditions may promote the differentiation of bone marrow mesenchymal stem cells into adipocytes, rendering the caudal sub-endplate region more susceptible to early fat infiltration and disruption of its mechanical microenvironment, which may subsequently contribute to early biochemical degeneration of the NP [26].

In the analysis of the entire sample, both caudal FF and caudal EBQ were independently associated with lower NP-T1rho. Previous studies have similarly demonstrated that caudal EBQ is closely related to the severity of disc degeneration, particularly in discs with PFG grade III or higher degeneration [14, 27], which is consistent with our findings. However, in the stratified analysis of early degeneration, caudal EBQ was not independently associated with NP-T1rho, suggesting that the changes in bone quality reflected by EBQ may predominantly be involved in the intermediate and advanced stages of LDD rather than in the early stage. Several factors may account for this difference. First, the study population consisted predominantly of young and middle-aged adults aged 20–59 years, and most discs were classified as PFG grade III or lower. Second, BMAT-related measures were simultaneously included in the mixed-effects model, allowing the overlapping contributions of BMAT and bone quality to be disentangled [30]. Although T1WI-based bone quality scores inherently incorporate some BMAT influence, chemical-shift imaging remains a more reliable technique for quantitative BMAT assessment [31]. Simultaneous adjustment for BMAT in the mixed-effects model may therefore have enabled a more accurate assessment of the independent association between EBQ and NP-T1rho. As an imaging measure primarily reflecting the trabecular microarchitecture and mechanical integrity of the sub-endplate bone [13], EBQ may have a greater role in the later stages of disc degeneration. During early degeneration, local mechanical remodeling may remain relatively mild, and changes in bone quality may occur later than abnormalities in fat metabolism. In contrast, BMAT, as a sensitive metabolic marker, may become altered earlier and may contribute to the biochemical degeneration of the NP. These findings suggest that bone marrow fat infiltration may have greater value than mechanical structural changes as an early warning marker of LDD.

Age was an important demographic factor associated with both sub-endplate bone marrow FF and NP-T1rho. Specifically, mean FF increased markedly between the age groups of 30–39 and 40–49 years in both men and women ($p < 0.0001$), suggesting that approximately 40 years of age may represent a critical period of accelerated bone marrow fat accumulation. This finding is consistent with that of Yu et al. [32], who reported a sharp increase in vertebral BMAT among women between 41 and 60 years. Previous studies have demonstrated that aging and obesity are major factors promoting the accumulation of ectopic adipocytes within the bone marrow cavity [33]. With respect to sex, mean NP-T1rho and FF were both significantly higher in men than in women. Previous studies have shown that

men generally have a higher bone marrow fat content than women throughout adulthood, with a relatively steady age-related increase [32], whereas rapid bone marrow fat accumulation in women occurs primarily after menopause, particularly after 60 years of age [32, 34]. Because the present study included young and middle-aged adults aged 20–59 years and relatively few postmenopausal women, this age distribution may partly explain the higher FF observed in men. In addition, mean NP-T1rho was significantly higher in patients aged 20–29 years than in the other age groups, was higher in men than in women, and progressively decreased with age. These findings suggest a higher proteoglycan content in the NP of young men, potentially related to a greater proteoglycan content or a larger reserve of notochordal cells [35]. Accordingly, sex and age were significantly associated with NP-T1rho in PFG grade I and II discs and in the overall sample. By contrast, EBQ did not differ significantly between men and women, suggesting that sex-related divergence in EBQ may not yet be apparent in predominantly young and middle-aged patients with LDD, most of whom had PFG grade III or less degeneration. EBQ may also be influenced by multiple interacting factors, including BMAT metabolism and mechanical loading; therefore, this finding requires validation in larger cohorts.

In PFG grade I–III discs and at the L1/2–L4/5 levels, both caudal sub-endplate bone marrow FF and EBQ were significantly higher than the corresponding cranial values, demonstrating a clear caudal predominance and level-specific distribution. In contrast, Ding et al. [14] reported a significant cranial-caudal difference in EBQ among PFG grade IV discs. This discrepancy may be related to differences in study populations, as their participants were predominantly older adults with a mean age of approximately 65 years and may therefore have had more pronounced age-related changes in endplate structure. Regarding lumbar level distribution, mean FF and EBQ progressively increased from L1/2 to L4/5 and peaked at L4/5, consistent with the greater axial loading borne by the lower lumbar spine [29]. At L5/S1, however, the cranial-caudal difference in FF disappeared, and caudal EBQ (2.99 ± 0.51) was significantly lower than cranial EBQ (3.09 ± 0.59). As a key level regulating both global and local mechanical loading of the trunk, L5/S1 contained a relatively high proportion of severely degenerated PFG grade IV/V discs. Under the combined and complex influences of BMAT metabolism, mechanical compensation, and inflammation, the sub-endplate bone marrow microenvironment at this level may undergo dynamic adaptation involving multiple structures [36]. Liu et al. [37] reported a similar level-dependent pattern: coupling between the vertebral body and intervertebral disc was more pronounced in the upper lumbar spine and gradually weakened toward the caudal levels, suggesting that disc degeneration at different lumbar levels may be influenced by distinct local environments. In a study of patients with osteoporosis [14], PFG grade V was independently associated with increased cranial EBQ, whereas PFG grades IV–V were independently associated with increased caudal EBQ. These findings further illustrate the complex relationship between advanced disc degeneration and the sub-endplate bone microenvironment and may partly explain the conflicting results of previous studies concerning the relationship between disc degeneration and bone mineral density. Collectively, these findings support the concept that the intervertebral disc, endplate, and vertebral bone marrow constitute an integrated morphological and functional unit that undergoes dynamic changes during degeneration [7,36–38].

Therefore, when interpreting an individual imaging measure in clinical practice, both the stage of degeneration and the lumbar level should be considered.

This study has several limitations. First, its retrospective cross-sectional design precludes determination of the temporal or causal relationship between bone marrow fat infiltration and disc degeneration, despite the observed independent association between caudal sub-endplate bone marrow FF and NP-T1rho. Longitudinal studies are needed to clarify their temporal sequence. Second, manually delineated ROIs may have introduced subjective measurement error. Furthermore, ROIs were drawn only on the central sagittal slice and therefore may not fully reflect the three-dimensional heterogeneity of the entire sub-endplate bone region. Third, several potential confounders, including serum lipid levels, bone mineral density, and menopausal status, were unavailable. These systemic metabolic factors may affect bone marrow adiposity. Fourth, no asymptomatic control group was included, limiting our ability to distinguish physiological aging of the sub-endplate bone microenvironment from pathological alterations associated with LDD. Finally, this was a single-center study with a limited sample size; therefore, the findings require further validation in larger multicenter cohorts.

5. Conclusion

In conclusion, multiparametric quantitative MRI demonstrated that early biochemical degeneration of the lumbar intervertebral disc is closely associated with alterations in the sub-endplate bone marrow microenvironment, which exhibits marked level specificity and caudal predominance. Increased caudal sub-endplate bone marrow FF was independently associated with lower NP-T1rho in early-degenerative discs. These findings suggest that caudal sub-endplate bone marrow fat infiltration may serve as a potential imaging marker for the early biochemical degeneration of LDD and provide a quantitative MRI basis for exploring early intervention targets.

Abbreviations

Abbreviations

BMI

body mass index

BMAT

bone marrow adipose tissue

CSF

cerebrospinal fluid

EBQ

sub-endplate bone quality

FACT

fat analysis calculation technique

FF

fat fraction

FI

fat infiltration

ICC

intraclass correlation coefficient

LBP

low back pain

LDD

lumbar disc degeneration

MRI

magnetic resonance imaging

NP

nucleus pulposus

ODI

Oswestry Disability Index

PFG

Pfarrmann grade

PG

proteoglycan

ROI

region of interest

T1WI

T1-weighted imaging

T2WI

T2-weighted imaging

Declarations

Ethics declarations

The study was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University (Approval No. KY2025072), with a waiver of informed consent.

Consent for publication:

All individuals included in this study have provided their consent for publication.

Competing interests:

The authors declare that they have no competing interests.

Contributions

Min He: Methodology, Investigation, Writing - Original Draft; Yali Deng: Investigation, Data Curation, Writing-Original Draft; Chuanghui Zhou: Software, Formal Analysis; Mengting Hu: Conceptualization, Writing - Review & Editing; Chunlun Xiao: Formal Analysis, Writing - Review & Editing; Wei Chen: Investigation, Supervision; Jiafei Chen: Project Administration, Funding Acquisition, Writing - Review & Editing. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Author Contribution

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Data Availability

The dataset used in this study can be obtained from the corresponding author upon reasonable request.

Tables

Table 1
General Clinical Characteristics of the Study Population

Characteristic	Value
Total patients (n = 72)	
Sex, male (n, %)	34 (47.22)
Age (years), mean $\pm$ SD	38.86 $\pm$ 9.79
BMI (kg/m ²), mean $\pm$ SD	23.94 $\pm$ 3.13
Age categories (n, %)	
20–29 years	17 (23.61)
30–39 years	18 (25.00)
40–49 years	19 (26.39)
50–59 years	18 (25.00)
Clinical diagnosis (n, %)*	
Lumbar disc degeneration	72 (100)
Lumbar disc herniation	31 (43.06)
Lumbar spinal stenosis	15 (20.83)
Multi-segment involvement (n, %)	
Single segment with PFG $\geq$ III	31 (43.06)
Two or more segments with PFG $\geq$ III	41 (56.94)
Intervertebral discs (n = 360 discs)	
PFG distribution (n, %)	
Grade I	61 (16.94)
Grade II	167 (46.39)
Grade III	52 (14.44)
Grade IV	69 (19.17)
Grade V	11 (3.06)
Segment-specific distribution (n, %)	
Upper levels (L1/2–L3/4) with PFG < III	170 (78.70)
BMI, body mass index; PFG, Pfirrmann grade.	

Characteristic	Value
Lower levels (L4/5–L5/S1) with PFG < III	105 (72.92)
BMI, body mass index; PFG, Pfirrmann grade.	

Table 2
Comparison of Cranial and Caudal Sub-Endplate FF and EBQ Across Lumbar Levels and Pfirrmann Grades

Category	FF _{cranial} (%)	FF _{caudal} (%)	p value	EBQ _{cranial}	EBQ _{caudal}	p value
PFG						
I	38.51 ± 9.48	41.48 ± 9.46	<0.001	2.88 ± 0.51	3.06 ± 0.46	<0.001
II	39.81 ± 10.64	41.40 ± 11.11	<0.001	3.05 ± 0.66	3.16 ± 0.59	<0.001
III	43.13 ± 8.86	45.30 ± 10.07	0.006	3.25 ± 0.51	3.38 ± 0.56	0.013
IV	42.79 ± 10.32	43.67 ± 10.22	0.160	3.20 ± 0.66	3.24 ± 0.64	0.408
V	37.49 ± 7.89	42.11 ± 11.15	0.039	2.77 ± 0.57	2.98 ± 0.44	0.021
Lumbar level						
L1/2	38.29 ± 10.16	40.67 ± 10.04	<0.001	2.78 ± 0.64	2.95 ± 0.58	<0.001
L2/3	40.28 ± 9.62	41.99 ± 10.47	0.003	3.09 ± 0.62	3.17 ± 0.53	0.030
L3/4	40.59 ± 10.20	42.91 ± 10.88	<0.001	3.17 ± 0.58	3.33 ± 0.56	<0.001
L4/5	41.49 ± 10.29	44.65 ± 10.55	<0.001	3.21 ± 0.60	3.47 ± 0.53	<0.001
L5/S1	41.76 ± 10.61	41.42 ± 11.07	0.682	3.09 ± 0.59	2.99 ± 0.51	0.016
EBQ, sub-endplate bone quality; FF, fat fraction; PFG, Pfirrmann grade.						

Table 3

Correlation Analysis Between NP-T1rho and Sub-Endplate Microenvironment Parameters Stratified by PFG.

PFG	FF _{cranial} (%)	FF _{caudal} (%)	EBQ _{cranial}	EBQ _{caudal}
Grade I (n = 61)	-0.160	-0.159	-0.240	-0.175
Grade II (n = 167)	-0.283**	-0.274**	-0.136	-0.139
Grade III (n = 52)	-0.037	-0.042	-0.095	-0.144
Grade IV (n = 69)	-0.118	-0.055	-0.167	-0.001
**, p < 0.01; EBQ, sub-endplate bone quality; FF, fat fraction; NP, nucleus pulposus; PFG, Pfirrmann grade.				

Table 4

Linear Mixed-Effects Model Analysis of Factors Associated with NP-T1rho Values in All Lumbar Discs

Variable	Univariate analysis		Multivariate analysis	
	β (95% CI)	p	β (95% CI)	p
Demographics				
Age (years)	-0.81 (-1.07, -0.56)	< 0.001	-0.72 (-0.98, -0.47)	< 0.001
Sex				
Female	Ref	-	Ref	-
Male	6.50 (1.28, 11.72)	0.015	9.52 (4.82, 14.22)	< 0.001
BMI (kg/m ²)	-1.36 (-2.19, -0.52)	0.002	-0.71 (-1.40, -0.02)	0.045
Lumbar level				
L1/2	Ref	-	Ref	-
L2/3	-1.76 (-8.59, 5.08)	0.615	-	-
L3/4	-8.33 (-15.17, -1.49)	0.017	-9.92 (-16.34, -3.50)	0.003
L4/5	-28.18 (-35.01, -21.34)	< 0.001	-30.03 (-36.62, -23.43)	< 0.001
L5/S1	-35.98 (-42.82, -29.14)	< 0.001	-37.05 (-42.24, -29.85)	< 0.001
Endplate parameters				
FF _{cranial} (%)	-0.54 (-0.80, -0.29)	< 0.001	-	-
FF _{caudal} (%)	-0.44 (-0.68, -0.19)	< 0.001	-0.32 (-0.60, -0.03)	0.030
EBQ _{cranial}	-8.66 (-12.79, -4.53)	< 0.001	-	-
EBQ _{caudal}	-7.00 (-11.50, -2.50)	0.002	-5.96 (-11.03, -0.89)	0.022
β , unstandardized regression coefficient; BMI, body mass index; CI, confidence interval; EBQ, sub-endplate bone quality; FF, fat fraction; Ref, reference category. Note: "-" indicates that the variable was not entered into the multivariate model.				

Table 5

Stratified Linear Mixed-Effects Model Analysis of Factors Associated with NP-T1rho Values by Pfirrmann Grade

PFG grade	n (discs)	Independent correlates	β (95% CI)	p value
Grade I (Normal)	61	Age (years)	-0.94 (-1.42, -0.46)	< 0.001
		Male sex	11.09 (2.14, 20.05)	0.018
Grade II (Early)	167	Male sex	6.32 (1.36, 11.28)	0.012
		Age (years)	-0.55 (-0.84, -0.26)	< 0.001
		FF _{caudal} (%)	-0.43 (-0.82, -0.04)	0.031
Grade III (Moderate)	52	Male sex	4.49 (0.33, 8.65)	0.040
Grade III–IV (Advanced)	132	L4/5 level (vs. L1/2)	-6.60 (-12.66, -0.55)	0.034
		L5/S1 level (vs. L1/2)	-9.29 (-15.29, -3.29)	0.003
β, unstandardized regression coefficient; CI, confidence interval; FF, fat fraction; NP, nucleus pulposus; PFG, Pfirrmann grade.				

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Figures

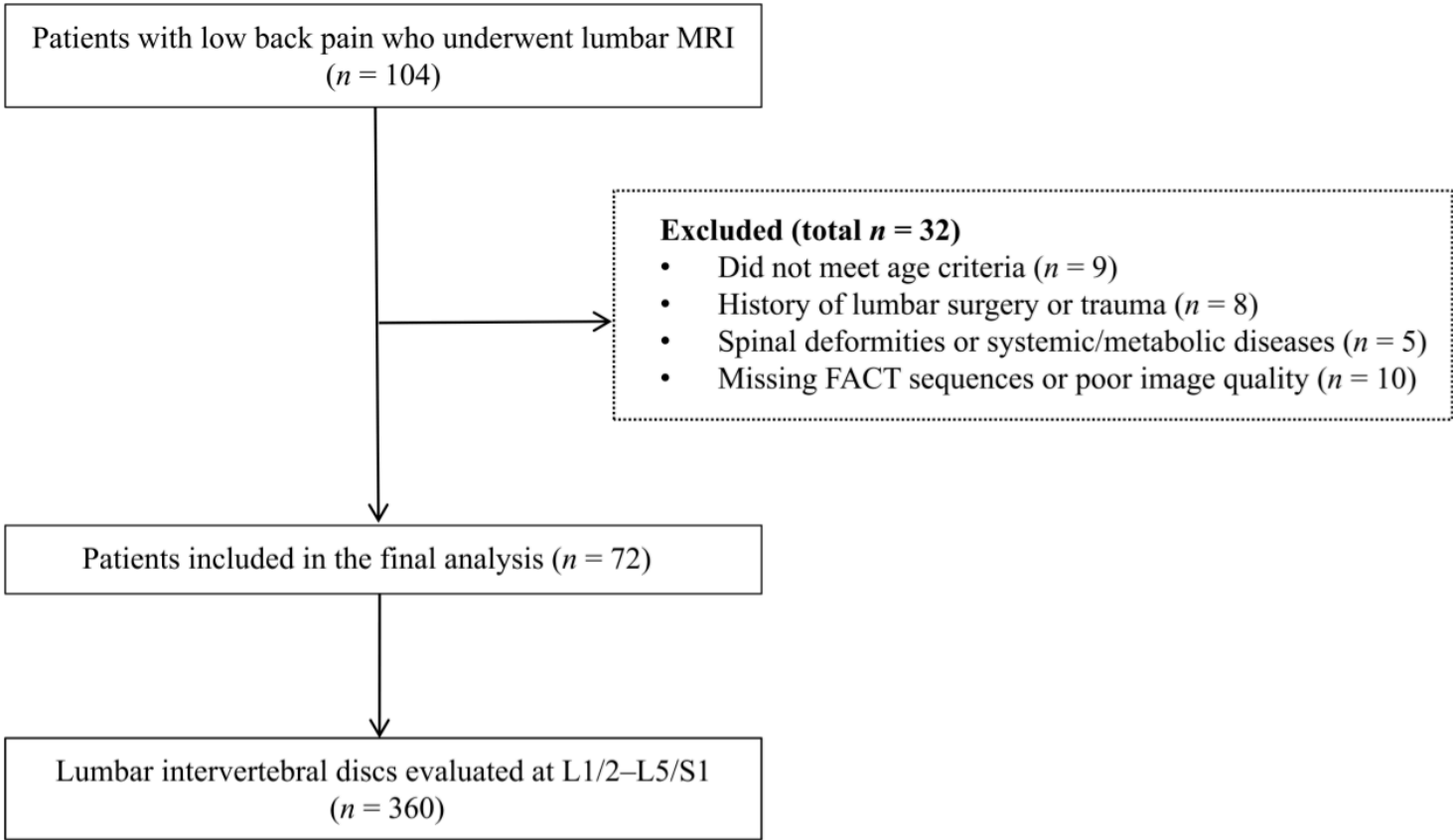


Figure 1

Flowchart of patient recruitment.

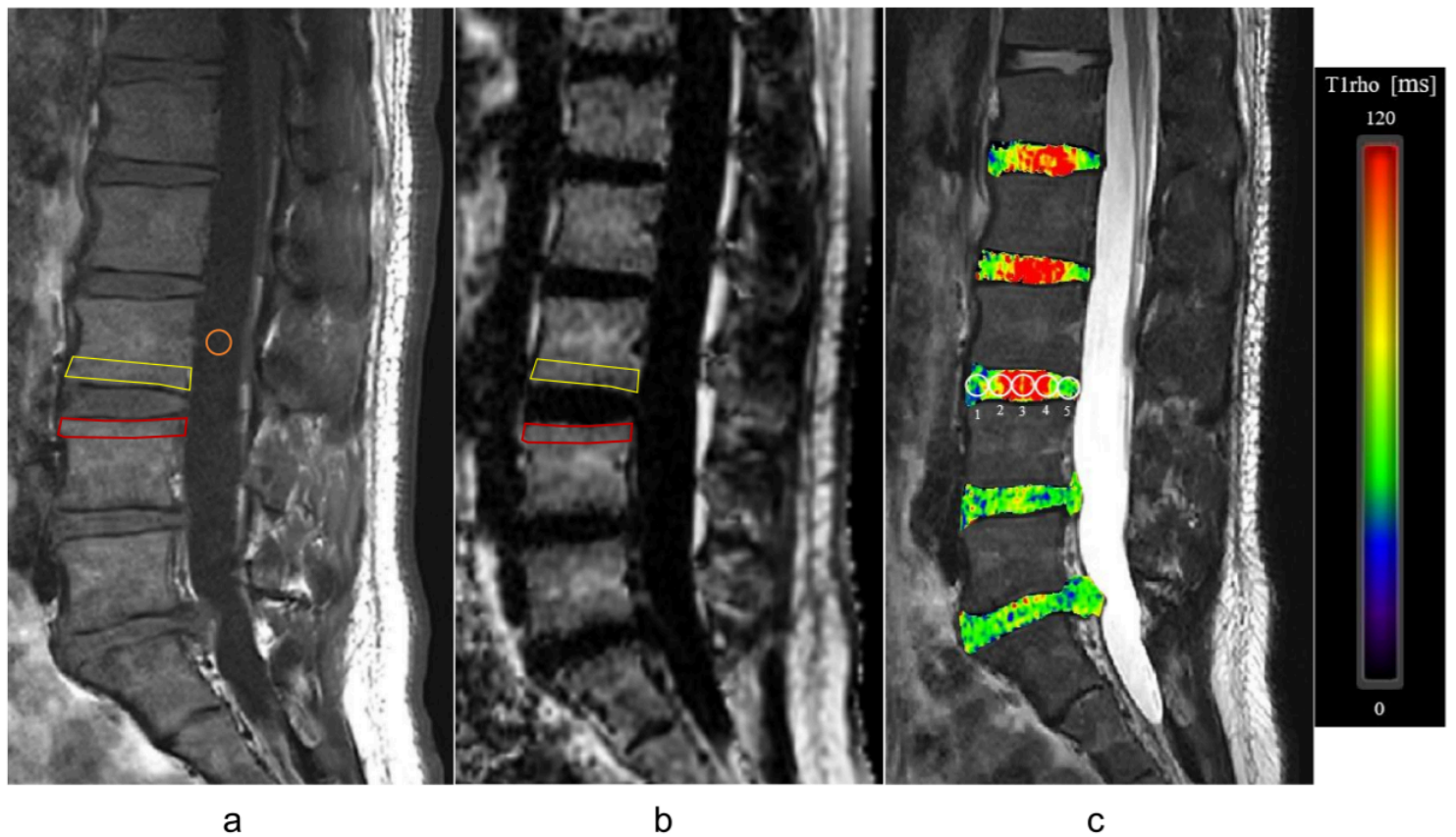


Figure 2

Schematic illustration of region of interest (ROI) placement for quantitative MRI measurements. (a) Sub-endplate bone quality (EBQ) ROI placement on the midsagittal T1-weighted image at the cranial (yellow outline) and caudal (red outline) endplates, with the reference ROI positioned in the cerebrospinal fluid (CSF, orange circle) at the L3 level. (b) Sub-endplate bone marrow fat fraction (FF) ROI placement on the corresponding FACT derived fat fraction map. (c) Nucleus pulposus (NP) T1rho ROI placement on the T1rho parametric map, with the disc divided into five equal partitions along the anterior-posterior axis and the middle three partitions (2, 3, and 4) used for final measurement.

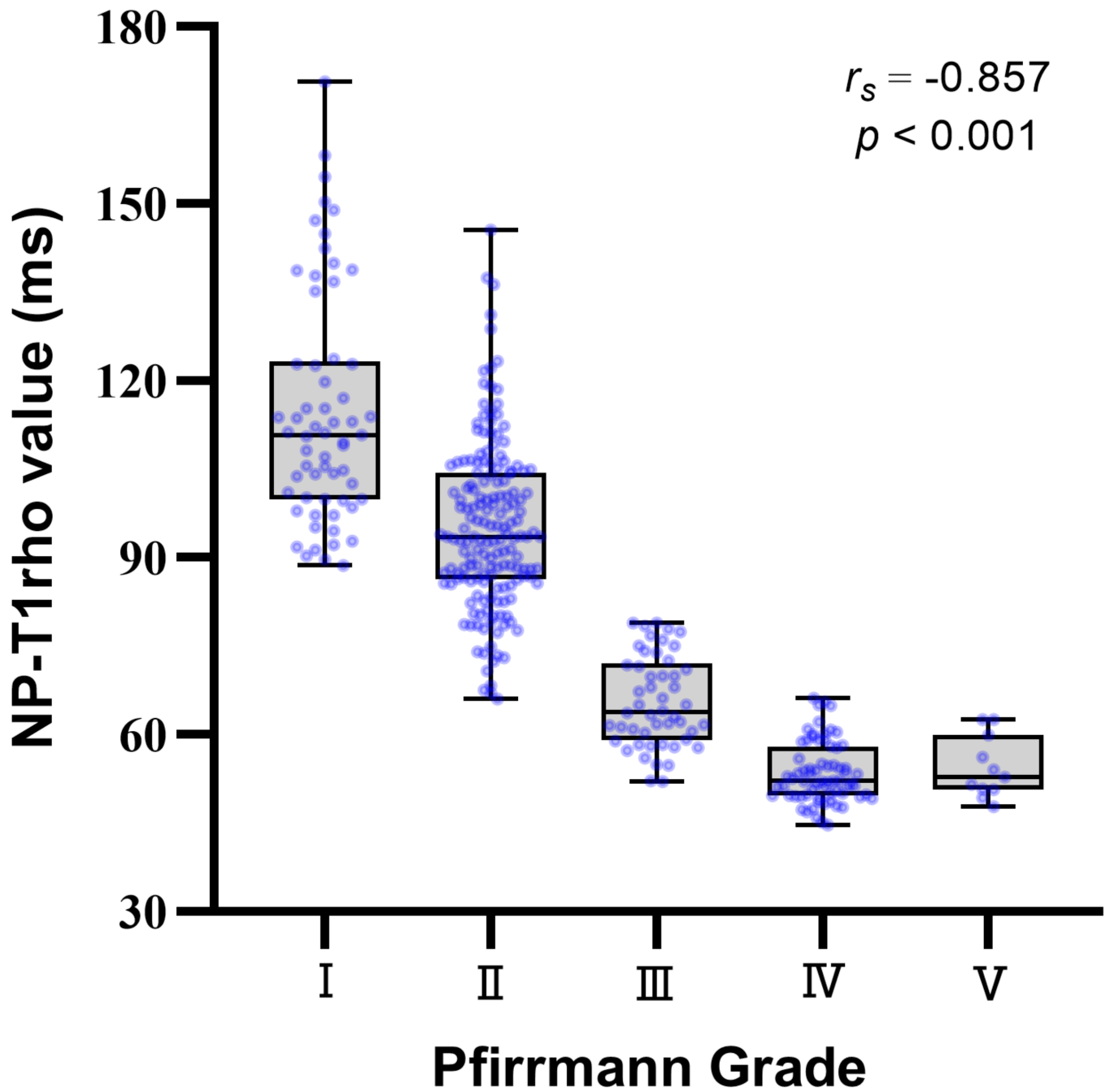


Figure 3

Correlation between NP-T1rho values and Pfirrmann degenerative grades. NP, nucleus pulposus; r_s , denotes the Spearman rank correlation coefficient.

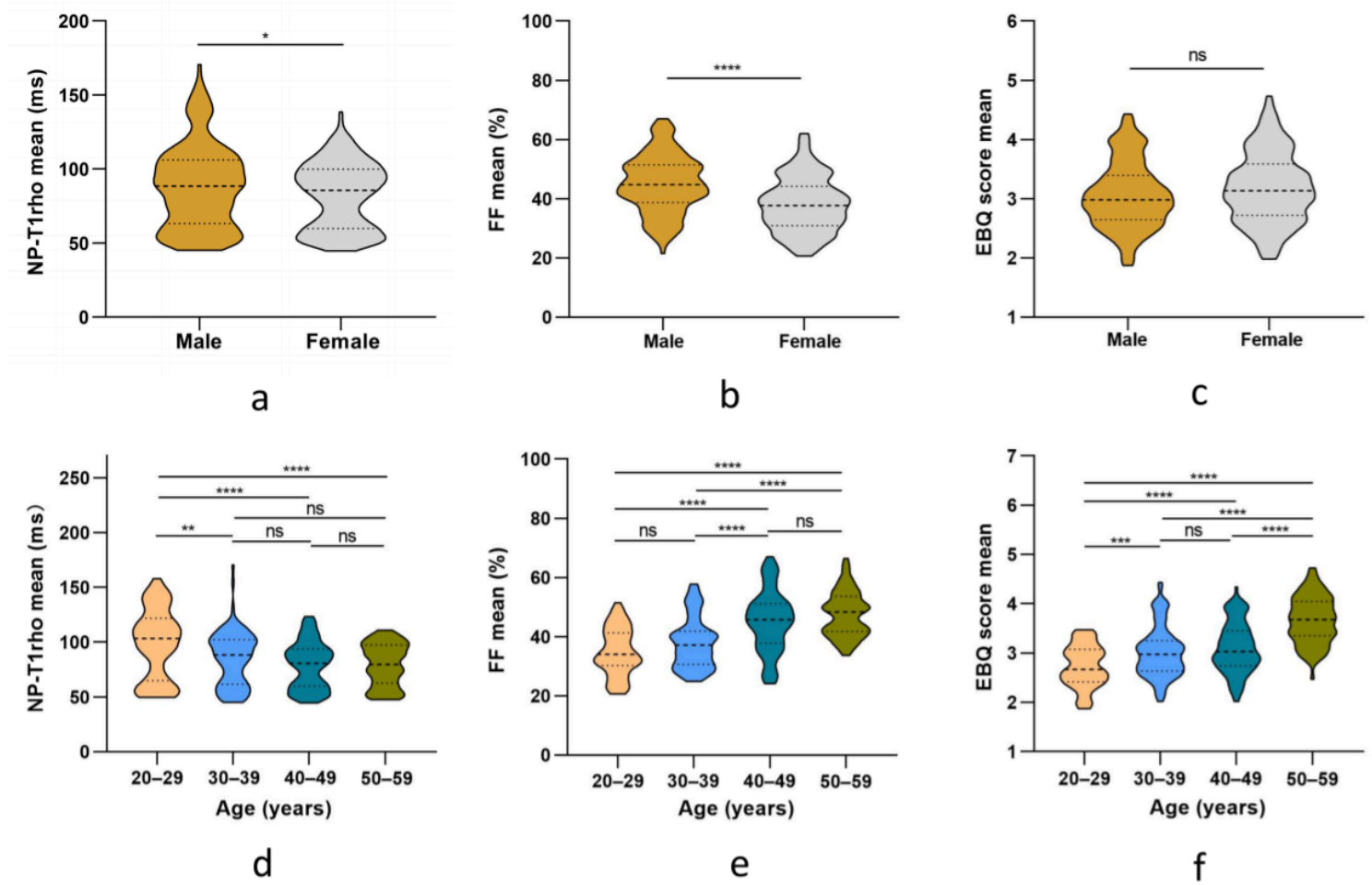


Figure 4

Comparison of NP-T1rho, sub-endplate FF, and EBQ values by sex and age group. (a-c) Sex-wise comparisons for NP-T1rho (a), FF (b), and EBQ (c); (d-f) Age group comparisons for NP-T1rho (d), FF (e), and EBQ (f). ns, not significant; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$; EBQ, sub-endplate bone quality; FF, fat fraction; NP, nucleus pulposus.

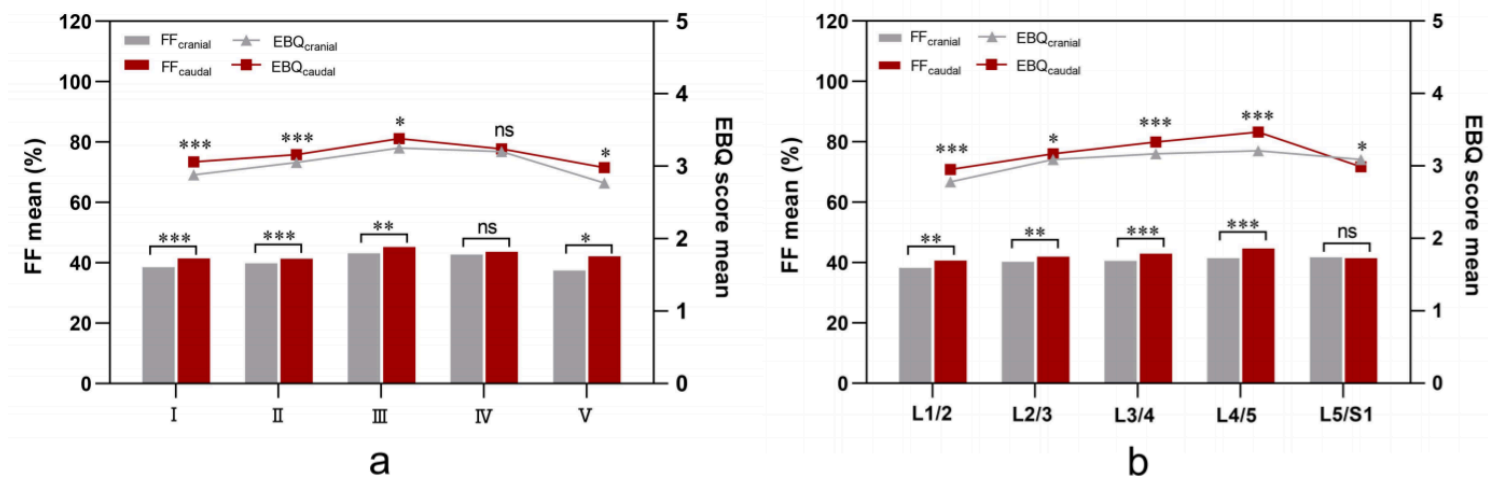


Figure 5

Distributions of cranial and caudal sub-endplate FF and EBQ across lumbar levels and Pfirrmann grades. (a) FF (bars, left y-axis) and EBQ (lines, right y-axis) distributions from L1/2 to L5/S1. (b) FF and EBQ distributions across Pfirrmann grades I to V. Data are presented as mean $\pm$ standard deviation. Asterisks denote statistically significant differences between the cranial and caudal sub-endplates within the same lumbar level or PFG. ns, not significant; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; EBQ, sub-endplate bone quality; FF, fat fraction; PFG, Pfirrmann grade.