

RESEARCH

Open Access



Correlation analysis between the mDIXON-quant fat quantification parameters of the infrapatellar fat pad and the severity of knee osteoarthritis

Bao-Gen Zhao¹, Yu-Jin Zhang¹, Meng Wang¹, Ning Wang¹, Yong Wang¹, Ting Gao^{1*} and Li Zhang^{1*}

Abstract

Purpose This study aimed to explore the correlation between the proton density fat fraction (PDFF) of the infrapatellar fat pad and the severity of knee osteoarthritis (KOA), with a focus on identifying potential imaging biomarkers for KOA progression.

Methods Seventy patients with KOA and forty-four healthy controls (HCs) were prospectively recruited for conventional MR and mDIXON-Quant sequence scanning. The mDIXON-Quant technique was selected for its precision in fat quantification and ability to provide three-dimensional water-fat separation, offering superior accuracy in assessing fat content compared to traditional methods. The severity of KOA was assessed via the whole-organ magnetic resonance imaging score (WORMS). Intraclass correlation coefficients (ICCs) were calculated to assess interobserver agreement for the PDFF measurements. Differences in the PDFF between KOA patients and HCs were compared. Additionally, the correlations between the PDFF of the infrapatellar fat pad in KOA patients and scores of the characteristic areas included in the knee WORMS were analyzed.

Results The PDFF of the infrapatellar fat pad in KOA patients was significantly lower than in HCs. PDFF in KOA patients was negatively correlated with multiple aspects of total knee WORMS scores (e.g., articular cartilage integrity, etc.; r from -0.94 to -0.25 ; $P < 0.05$), except for medial or lateral collateral ligament integrity ($r = 0.27$, $P \geq 0.05$). Interobserver agreement was excellent ($ICC = 0.793$, $P < 0.001$).

Conclusions The PDFF of the infrapatellar fat pad is significantly associated with KOA severity, demonstrating a progressive decrease as the disease advances. These findings suggest that PDFF holds promise as a potential objective biomarker for evaluating KOA severity. However, further validation in larger and more diverse cohorts is required to confirm its clinical applicability. This study is a prospective investigation that adhered to the Declaration of Helsinki and was approved by the Ethics Committee of the First Hospital of Hebei Medical University (Approval No. [2024] Research Review No. 056).

*Correspondence:

Ting Gao
315747721@qq.com
Li Zhang
leo054@163.com

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Keywords Knee joint, Osteoarthritis, mDIXON-Quant, Infrapatellar fat pad, Magnetic resonance imaging

Introduction

As the proportion of the elderly population continues to grow, the incidence of knee osteoarthritis (KOA) has also increased [1]. Recent research has expanded beyond the traditional focus on articular cartilage and subchondral bone damage, recognizing that KOA is a multifaceted joint disease involving various tissues [2]. These tissues include the articular cartilage, subchondral bone, synovium, ligaments, menisci, loose bodies, and periarthicular muscles, including the infrapatellar fat pad [3–5].

The role of the meniscus in the progression of KOA has also garnered significant attention. The meniscus, a crucial component of the knee joint, plays a vital role in load distribution, shock absorption, and joint stability. Pathological changes in the meniscus, such as tears or degeneration, are closely associated with the development and progression of KOA. Studies have shown that meniscus pathologies can exacerbate cartilage damage and contribute to the inflammatory microenvironment within the joint, further accelerating the degenerative process [6]. Recent research has highlighted the strong relationship between meniscus pathologies and KOA, demonstrating that meniscus injuries are not only a consequence of KOA but also a contributing factor to its progression [7]. This interplay between meniscus damage and KOA underscores the importance of considering meniscus health in the broader context of KOA management and research.

The infrapatellar fat pad, another critical structure in the knee joint, has also been implicated in the etiology and progression of KOA. Beyond its mechanical role in cushioning and lubrication, the infrapatellar fat pad is increasingly recognized as an active endocrine organ that secretes pro-inflammatory cytokines and adipokines, such as interleukin-6 (IL-6), leptin, and adiponectin, which contribute to synovial inflammation and cartilage degradation [8,9]. Magnetic resonance imaging (MRI) offers significant advantages in visualizing and quantitatively assessing the infrapatellar fat pad, particularly through fat quantification analysis. Previous methods for assessing changes in the signal intensity of the infrapatellar fat pad have included semiquantitative/quantitative T2-weighted imaging (T2WI) [6,8,9], enhancement [10], dynamic contrast-enhanced (DCE) quantitative imaging [11,12], and radiomics [13]. However, these methods have limitations in terms of precision and reproducibility, particularly in quantifying fat content changes associated with inflammation and fibrosis.

To address these limitations, this study employs the mDIXON-Quant technique [14], a state-of-the-art fat quantification method based on a three-dimensional

multiecho water-fat separation approach. Unlike traditional Chemical Shift Encoded (CSE) MRI methods [15], mDIXON-Quant offers superior accuracy and reproducibility in measuring PDFF, making it particularly suitable for assessing subtle fat content changes in the infrapatellar fat pad [16,17]. This technique has been successfully applied in other areas, such as hepatic steatosis and spinal fat quantification [18,19], but its application in evaluating KOA severity through infrapatellar fat pad fat quantification remains underexplored.

This study aims to fill this research gap by investigating the correlation between PDFF alterations in the infrapatellar fat pad and KOA severity. We hypothesize that decreased PDFF in the infrapatellar fat pad correlates with increased KOA severity due to inflammatory and fibrotic changes, which may serve as a potential imaging biomarker for disease progression. By elucidating the underlying mechanisms of PDFF changes, including fat content reduction, inflammatory responses, and tissue proliferation, this study seeks to provide new insights into the role of the infrapatellar fat pad in KOA pathogenesis and its potential as a therapeutic target.

Methods

Study participants

This study is a prospective investigation that adhered to the Declaration of Helsinki and was approved by the Ethics Committee of our hospital (Approval No. [2024] Research Review No. 056). Informed consent was obtained from all participants. The inclusion criteria for the KOA group were as follows: (1) had recurrent knee pain; (2) had an X-ray (standing or weight-bearing position) demonstrating KOA; (3) had a morning stiffness of ≤ 30 min; and (4) had a high degree of compliance, were informed about the study, and voluntarily signed the informed consent form. The exclusion criteria were as follows: (1) history of knee trauma or surgery; (2) infectious or noninfectious (e.g., rheumatoid) inflammatory lesions of the knee; and (3) poor patient cooperation or the presence of artifacts on MRI. The inclusion criteria for HCs were as follows: (1) age- and sex-matched with those with KOA and (2) no knee-related diseases or clinical symptoms. The exclusion criteria were as follows: (1) history of knee trauma or surgery; (2) presence of diseases affecting the components of the knee joint; (3) poor image quality that could not meet the requirements; and (4) presence of contraindications to MRI examination.

MRI acquisition

Knee joint imaging was performed using a 3.0T MR scanner (Philips, Ingenia 3.0T CX) equipped with a body

coil. The mDIXON-Quant sequence, a multi-echo gradient-echo CSE-MRI technique, was selected for its ability to provide precise PDFF. This technique offers several advantages over traditional CSE-MRI methods, including multi-echo acquisition, improved correction for magnetic field inhomogeneities, and superior fat-water separation, which are critical for accurate fat quantification in tissues such as the infrapatellar fat pad. The 3.0T field strength was chosen to ensure high signal-to-noise ratio and enhanced fat quantification accuracy, which are particularly important for detecting subtle changes in fat content associated with KOA progression. The scanning sequences and parameters used were as follows: sagittal FSE-T1WI: repetition time (TR) 560.00 ms, echo time (TE) 20.00 ms, field of view (FOV) 180 mm×161 mm, flip angle (FA) 90°, slice thickness (ST) 4.00 mm, and slice gap (SG) 0.40 mm. Sagittal FS-PDWI: TR 1723.00 ms, TE 30.00 ms, FOV 159 mm×182 mm, FA 90°, ST 4.00 mm, SG 0.40 mm. Coronal FS-PDWI: TR, 1804.00 ms; TE, 25.00 ms; FOV, 180 mm×161 mm; FA, 90°; ST, 4.00 mm; SG, 0.40 mm. Axial FS-T2WI: TR 2152.00 ms, TE 60.00 ms, FOV 160 mm×160 mm, FA 90°, ST 4.00 mm, SG 1.00 mm. Sagittal mDIXON-Quant: TR 5.70 ms, TE 0.99 ms, FOV 180 mm×180 mm, FA 3°, ST 6.00 mm, SG 0.00 mm. The scan was centered on the lower edge of the patella, with the body coil positioned to maintain the knee in its natural state. Sandbag fixation was used to minimize motion artifacts.

PDFF measurement of the subpatellar fat Pids in the knee joint

In this study, PDFF measurements of the infrapatellar fat pad were performed using sagittal T1WI and PDFF fusion images. The boundaries of the infrapatellar fat pad were manually delineated at the largest level of the patella, as well as at the left and right levels. Efforts were made to exclude the synovium, ligaments, subcutaneous fat, and effusion as much as possible. This approach was chosen to ensure consistency and reproducibility in PDFF measurements, as the central slices are less prone to partial volume effects and provide a representative sample of the fat pad's fat content. The final PDFF of the infrapatellar fat pad was obtained by averaging three measurements to minimize inter-observer variability. The postprocessing software used was IntelliSpace Portal Philips on an Ingenia 3.0T MRI system. Image postprocessing was conducted independently and in a blinded fashion by two trained radiologists.

Whole-Organ MRI scoring (WORMS) of the knee joint

WORMS is a semiquantitative, multifeature assessment method used to evaluate the severity of KOA on the basis of conventional MRI. This method involves scoring 11 distinct articular features across 15 different knee

regions. The assessed features include cartilage signal and morphology, subarticular bone marrow abnormalities, subarticular cysts, subarticular bone attrition, marginal osteophytes, medial and lateral meniscal integrity, anterior and posterior cruciate ligament integrity, medial and lateral collateral ligament integrity, synovitis, loose bodies, and periarticular cysts/bursae [20]. Higher WORMS scores indicate more severe KOA. Scores for each feature, as well as the total WORMS score (derived by summing the individual feature scores), were independently obtained through a double-blind process by two trained radiologists.

Statistical analysis

Statistical analysis was conducted via IBM SPSS Statistics 26.0. Data are presented as the means ± standard deviations or medians with interquartile ranges for continuous variables and as frequencies and percentages for categorical variables. Descriptive statistics were performed on general information (age, sex, knee joint side, and body mass index (BMI), defined as weight (kg)/(height (m)²), reported as the means with 95% confidence intervals. The chi-square test was used to evaluate categorical variables, whereas the t test or Mann-Whitney U test was used for continuous variables. Pearson or Spearman correlation tests were applied to analyze the relationship between WORMS scores and total WORMS scores of each knee joint region with the PDFF of the infrapatellar fat pad. ICCs were calculated to assess the reproducibility of the measured PDFF. The criteria proposed by Cicchetti and Sparrow were used as references, where an ICC ≤ 0.40 indicates poor reliability, between 0.40 and 0.58 indicates fair reliability, between 0.59 and 0.75 indicates good reliability, and ≥ 0.75 indicates excellent reliability. The significance level was set at $\alpha = 0.05$. A power analysis was conducted to justify the sample size, ensuring adequate statistical power to detect significant differences in PDFF between KOA patients and healthy controls. Potential confounding factors, such as age and BMI, were controlled through matching and statistical adjustment.

Results

Participant characteristics

A total of 70 participants (54 [77.14%] females; 36 [51.43%] with a right knee) with an average age of 63.17 ± 7.26 years and a BMI of 27.54 ± 2.71 kg/m² were included in the KOA group. The HCs comprised 44 participants (33 [75.00%] females; 25 [56.82%] with a right knee), with an average age of 64.36 ± 8.43 years and a BMI of 27.66 ± 2.87 kg/m². There were no statistically significant differences between the KOA patients and HCs in terms of age, sex, side, or BMI (Table 1).

Table 1 Patient characteristics between the HCs and KOA

	control	KOA	t/ χ^2	P
Age, year	64.36 ± 8.43	63.17 ± 7.26	0.80	0.42
Sex, n(male/female)	11/33	16/54	2.16	0.15
Side, n(left/right)	19/25	34/36	0.32	0.57
BMI, kg/m ²	27.54 ± 2.71	27.66 ± 2.87	0.23	0.82

KOA: Knee Osteoarthritis; BMI: Body Mass Index

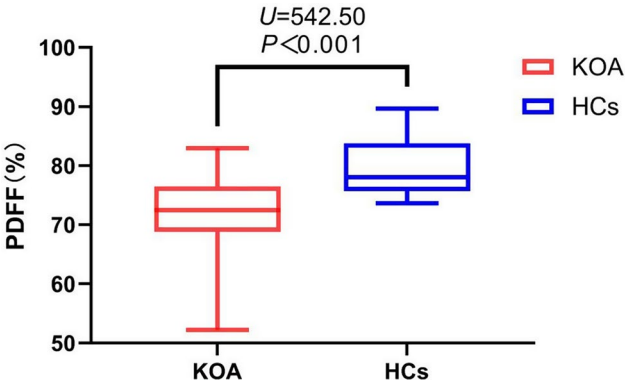


Fig. 1 shows the box plot of the proton density fat fraction (PDFF) of the infrapatellar fat pad in patients with knee osteoarthritis (KOA) compared with HCs. The PDFF of the infrapatellar fat pad in the KOA patients was significantly lower than that in the HCs

Interobserver consistency in PDFF measurement

Interobserver consistency in the PDFF measurements of the infrapatellar fat pad was excellent (ICC = 0.793, 95% CI: 0.667–0.875, $P<0.001$).

PDFF comparison between patients with KOA and HCs

The PDFF of the infrapatellar fat pad was significantly lower in the KOA patients than in the HCs (72.11 ± 6.45 vs. 78.07 ± 8.11 , Mann–Whitney $U=542.50$, $P<0.001$;

Fig. 1). The effect size (Cohen’s d) for this difference was 0.82, indicating a large effect.

In the fused images of the infrapatellar fat pad PDFF with T1WI, color changes from yellow to violet were observed, indicating a gradual decrease in the PDFF. An increase in the WORMS score was associated with this color change from yellow to purple, whereas a decrease in the WORMS score corresponded to a change from purple to yellow in the PDFF imaging (Fig. 2).

Correlation between PDFF and WORMS parameters in patients with KOA

In KOA patients, the PDFF of the infrapatellar fat pad was significantly negatively correlated with the total knee WORMS score and various WORMS parameters, including articular cartilage integrity, marginal osteophytes, and subarticular bone abnormalities ($P<0.05$; Fig. 3; Table 2). However, no significant correlation was observed with medial or lateral collateral ligament integrity ($r=0.027$, $P=0.826$).

Discussion

The infrapatellar fat pad was first described by Albert Hoffa in 1904 and is therefore referred to as Hoffa’s fat pad [21]. Owing to its unique spatial location and composition, the infrapatellar fat pad plays a protective role in the knee joint by restricting hypermobility, secreting lubrication to reduce friction, and cushioning oscillations. However, in patients with KOA, the infrapatellar fat pad often becomes edematous, hemorrhagic, and fibrotic, diminishing its protective function and facilitating the progression of KOA.

Previous studies have focused on how changes in the high signal intensity of the infrapatellar fat pad impact KOA, with few investigations into the structural

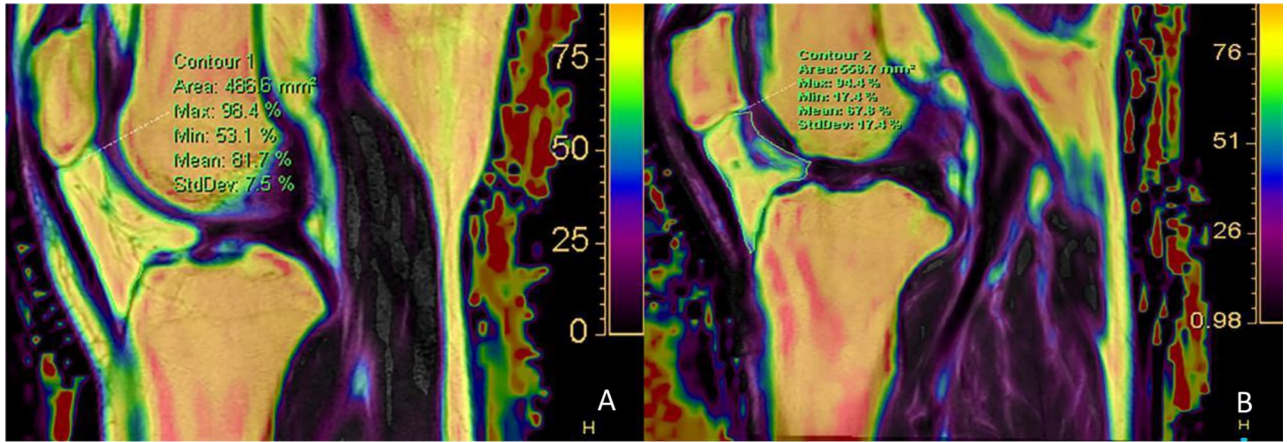


Fig. 2 **A** depicts a fused images of the infrapatellar fat pad proton density fat fraction (PDFF) with T1WI of the infrapatellar fat pad of the knee in a participant with healthy controls (HCs)(female, 55 years old)with a total Whole Organ Magnetic Resonance Imaging Score (WORMS) of 33 and a PDFF of 81.7%. **B** depicts a fused images of the infrapatellar fat pad PDFF with T1WI of the infrapatellar fat pad of the knee in a patient with KOA (female, 59 years old) with a total WORMS score of 154 and a PDFF of 67.8%

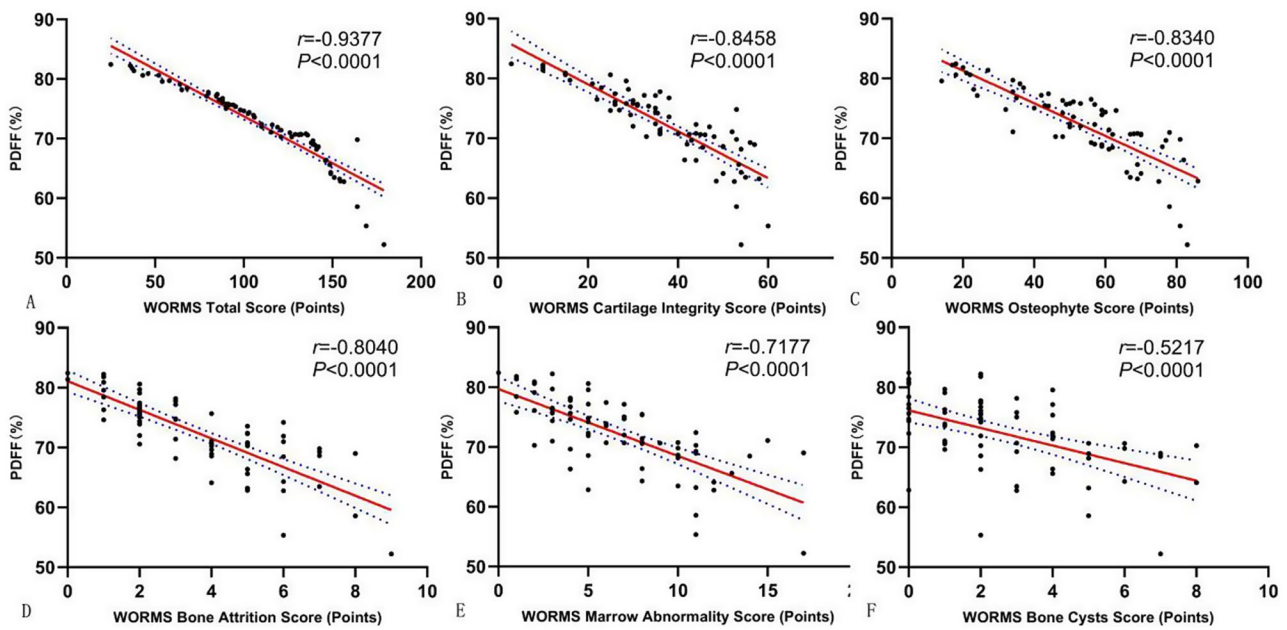


Fig. 3 A-F show negative correlations between the proton density fat fraction (PDFF) and the total whole-organ magnetic resonance imaging score (WORMS), articular cartilage integrity, marginal osteophytes, subarticular bone attrition, subarticular bone marrow abnormality, and subarticular cyst WORMS score scatterplots

Table 2 Correlation of PDFF with WORMS scores in each region and total WORMS scores

	<i>r/p</i>	Total Worms	Collateral Ligament	Cartilage	Bone Attrition	Bone Cysts	Marrow Abnormality
PDFF	<i>r</i>	-0.94	0.27	-0.85	-0.80	-0.52	-0.72
	<i>P</i>	<0.001	0.83	<0.001	<0.001	<0.001	<0.001
	<i>r/p</i>	Loose Bodies	Cruciate Ligament	Menisci	Periarticular Cysts/Bursitis	Osteophytes	Synovitis/Effusion
	<i>r</i>	-0.54	-0.27	-0.54	-0.80	-0.83	-0.25
	<i>P</i>	<0.001	0.043	<0.001	0.017	<0.001	0.030

WORMS: Whole-Organ MRI Scoring. PDFF: Proton Density Fat Fraction

alterations in the knee joint associated with low signal intensity (e.g., chronic inflammation, such as hemorrhage and fibrosis) [6,18]. The present study investigated the PDFF, which quantifies the signal intensity contributed by adipose tissue in the infrapatellar fat pad as a more objective measure. We employed the mDIXON-Quant technique to assess alterations in the PDFF in the infrapatellar fat pad and their correlation with the severity of KOA. Additionally, this study aimed to elucidate the underlying mechanisms and pathological basis for the observed PDFF modifications in the infrapatellar fat pad of the knee joint.

Pathology of the infrapatellar fat pad in patients with end-stage KOA reveals neovascularization, fibrosis, and chronic inflammation. Studies have shown that infrapatellar fat pad synovitis at baseline is associated with the development of KOA over a four-year follow-up period [19]. Furthermore, the Multicenter Osteoarthritis Study demonstrated that infrapatellar fat pad synovitis is an independent causal factor in the development of KOA at the 84-month follow-up [22].

Patients with KOA secrete higher levels of inflammatory and adipokine substances from the infrapatellar fat pad than from the subcutaneous fat pad. These substances include interleukin 6 (IL-6), adipsin, adiponectin, and visfatin [23–25]. Other studies have confirmed that the infrapatellar fat pads of KOA patients also secrete increased levels of leptin [26]. Compared with those in controls, leptin levels in the synovial fluid and serum of KOA patients are elevated.

Leptin, a proinflammatory factor, has been shown to promote synovial inflammation, exacerbate joint damage, influence adipose tissue metabolism, and participate in bone remodeling. It also affects osteoblast activity, contributing to osteophyte formation.

Han et al. [18]. identified a low-signaling component within the infrapatellar fat pad on T2WI, which is considered a consequence of chronic synovitis and tissue fibrosis/hemorrhage. These changes lead to a reduction in the signal intensity contributed by the adipose tissue, resulting in a decreased PDFF. It is hypothesized that inflammatory edema, fibrosis, and hemorrhage in the

infrapatellar fat pad contribute to the observed reduction in the PDFF in KOA patients. As KOA severity increases, the PDFF of the infrapatellar fat pad likely further decreases.

KOA is a multifaceted disease that affects various tissues and structures, including cartilage [27], subchondral bone [28], synovium, ligaments [29], bursa, meniscus [30], and the infrapatellar fat pad [31–34]. Alterations in these structures not only reflect the progression of KOA but also may influence the PDFF measurements of the infrapatellar fat pad.

Han et al. [35] reported a positive correlation between high signal intensity in the infrapatellar fat pad and increased cartilage damage and subarticular bone marrow abnormalities on the basis of semiquantitative assessment of these high signal modifications [8,35]. Although this is different from the negative correlation observed in this study, the actual reflected content is different. Specifically, we found that as the high signaling component of the infrapatellar fat pad increased, the proportion of signal intensity attributable to adipose tissue decreased, which contributed to the observed negative correlation. Furthermore, our study included pathological components of the infrapatellar fat pad with iso/low signals, such as chronic inflammation (e.g., hemorrhage and fibrosis), in the PDFF analysis and assessed their impact on articular cartilage damage and subchondral bone marrow abnormalities.

We found that there was a significant difference in PDFF% between KOA patients and the control group. Based on existing evidence, we believe it may be related to the following reasons. Firstly, KOA is a complex multifactorial disorder with varying pathological processes among different patients. During the progression of the disease, the extents and rates of pathological alterations such as articular cartilage damage, synovial inflammation, and osteophyte formation differ. These factors interact and jointly influence the microenvironment of the infrapatellar fat pad, resulting in different degrees of metabolic and structural changes in the fat cells within the fat pad, ultimately leading to significant differences in PDFF%. Previous studies have demonstrated that the degree of articular cartilage degeneration is closely associated with the inflammatory response of the infrapatellar fat pad [8], and synovial inflammation can induce a series of pathological changes in the fat pad [36], which indirectly support our contention that the pathological heterogeneity of KOA affects PDFF%.

Secondly, individual variations among patients, including age, gender, body mass index (BMI), and lifestyle factors, may also have an impact on PDFF%. Despite our efforts to match the KOA patients and HC for age, gender, and BMI in this study, the subtle differences in these factors at the individual level might still interfere with the

PDFF% measurement results. For instance, the fat metabolism capacity varies among patients of different ages, and age advancement may be accompanied by changes in fat tissue function [32], thereby affecting the fat content and PDFF% of the infrapatellar fat pad.

Degenerative and chronic injury in the knee joint contributes to the development of osteophytes, which can result in microvascular dilation, tissue congestion, local hemorrhage, fatty interstitial edema, inflammatory cell infiltration, and even synoviocyte hyperplasia and synovial chorioallantoic hyperplasia on the infrapatellar fat pad surface [37]. Chuckpaiwong et al. [38] reported a significant positive correlation between altered signal intensity in the infrapatellar fat pad and the formation of osteophytes at various sites. This finding supports the observed decrease in the PDFF of the infrapatellar fat pad with increasing severity of KOA in our study and highlights the potential of the PDFF as a marker for structural joint changes.

This study revealed a negative correlation between the PDFF of the infrapatellar fat pad and synovitis/effusion, indicating that the synovial status significantly affects the PDFF. Previous studies have shown that hemoperfusion of the infrapatellar fat pad increases in the presence of knee effusion, which may be related to inflammation of the infrapatellar fat pad associated with KOA [9,12,38]. This study employed the mDIXON-Quant technique to quantitatively assess changes in the PDFF, further confirming that the PDFF of the infrapatellar fat pad decreases with increasing severity of KOA. Klein-Wieringa et al. [24] revealed similarities in immune cell composition between synovial tissue and the infrapatellar fat pad, as well as potential interactions between them. This finding aligns with the negative correlation between the PDFF and synovitis/effusion observed in this study, suggesting that synovial inflammation may lead to an inflammatory response in the infrapatellar fat pad, thereby reducing the proportion of signal intensity contributed by fat tissue. This study provides direct quantitative evidence supporting this theory through objective PDFF measurements.

Additionally, this study revealed a negative correlation between the integrity of the medial and lateral menisci and the anterior and posterior cruciate ligaments and the PDFF of the infrapatellar fat pad. The integrity of these structures is crucial for maintaining knee stability and function. This damage may exacerbate the progression of KOA, leading to increased secretion of inflammatory cytokines. The presence of crosstalk between synovial tissue and the infrapatellar fat pad could further result in inflammatory infiltration, edema, hemorrhage, and even fibrosis of the infrapatellar fat pad, ultimately leading to a decreased PDFF.

Compared with previous studies, this research provides more accurate PDFF measurements through the advanced mDIXON-Quant technique, offering a more precise reflection of the physiological changes in the infrapatellar fat pad during progression.

This study has several limitations. First, the sample size was relatively small, with a significant sex imbalance. While this allowed for preliminary observations, it may not fully capture the variability and heterogeneity present in larger populations. A larger, more balanced sample would have increased the statistical power, potentially reducing the risk of type II errors and enhancing the generalizability of our findings. Second, the PDFF measurement of the infrapatellar fat pad was not based on its entire volume but rather on the mean values of selected slices. This approach lacks assessment of the fat pad margins, potentially overlooking important spatial variations in the PDFF distribution. Future studies should consider whole-volume PDFF analysis to provide a more comprehensive and accurate evaluation of the infrapatellar fat pad. Third, this study did not include the measurement or analysis of other fat pads. Future studies could further explore the changes in PDFF of these fat pads and their correlation with KOA severity to provide a more comprehensive understanding of the role of fat pads in KOA. Future studies could further explore the changes in PDFF of these fat pads and their correlation with KOA severity to provide a more comprehensive understanding of the role of fat pads in KOA. Fourth, While mDIXON-Quant has been validated for PDFF quantification in other tissues (e.g., liver, muscle), no direct validation against a reference method (e.g., MR spectroscopy or histology) has been performed for the infrapatellar fat pad. This represents a gap in the current study, and future research should aim to validate PDFF measurements in the infrapatellar fat pad using these reference methods.

Conclusion

This study demonstrates the capability of the MR mDIXON-Quant technique in enabling precise quantitative assessment of PDFF alterations in the infrapatellar fat pads of patients with KOA. As the severity of KOA progresses, the PDFF in the infrapatellar fat pad decreases. Thus, the PDFF of the infrapatellar fat pad emerges as a potential objective marker for assessing the severity of KOA. Nevertheless, despite the promising potential of PDFF in evaluating KOA severity, its clinical applicability requires further validation in larger, multicenter studies. Additionally, the lack of reference validation in the infrapatellar fat pad currently limits its immediate clinical use. Future research should aim to validate the effectiveness of PDFF as a biomarker for KOA in a broader context and explore its potential applications in supporting clinical decision-making.

Abbreviations

PDFF	Proton density fat fraction
KOA	Knee Osteoarthritis
HCS	Healthy controls
MR	Magnetic Resonance
CSE	Chemical Shift Encoded
WORMS	Whole-Organ Magnetic Resonance Imaging Score
ICC	Intraclass correlation coefficient
MRI	Magnetic Resonance Imaging
T2WI	T2-weighted imaging
DCE	Dynamic contrast-enhanced
TR	Repetition time
TE	Echo Time
FOV	Field of View
FA	Flip angle
ST	Slice thickness
SG	Slice Gap
BMI	Body mass index

Acknowledgements

Not applicable.

Author contributions

BaoGen Zhao conceived study design and conceived the content concept; BaoGen Zhao, Yulin Zhang and Meng Wang performed the data collection, extraction and analyzed the data. BaoGen Zhao, Ning Wang and Yong Wang interpreted and reviewed the data and drafts. All authors were involved in literature search, writing the paper and had final approval of the submitted and published versions. Li Zhang and Ting Gao contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

This research was funded by the Medical Science Research Project of Hebei (No. 20250355).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study was approved by Committee of Internal Review Board "Approval No. [2024] Research Review No. 056" of the First Hospital of Hebei Medical University. The study protocol was in accordance with the Declaration of Helsinki.

Human ethics and consent to participate declarations

The study was approved by Committee of Internal Review Board "Approval No. [2024] Research Review No. 056" of the First Hospital of Hebei Medical University. All patients agreed to participate in this experiment. Written informed consent for publication was obtained from all participants.

Consent of publication

All the others have agreed to publish in this journal and take responsibility of the manuscript.

Clinical trial number

Not applicable.

Author details

¹Department of radiology and nuclear medicine, The First Hospital of HeBei Medical University, Shijiazhuang 050000, China

Received: 2 December 2024 / Accepted: 6 March 2025

Published online: 17 March 2025

References

- Steinmetz JD, Culbreth G T, Haile L M, et al. Global, regional, and National burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the global burden of disease study 2021[J]. *Lancet Rheumatol*. 2023;5(9):e508–22. [https://doi.org/10.1016/S2665-9913\(23\)00163-7](https://doi.org/10.1016/S2665-9913(23)00163-7).
- Ye Z, Lin J, He C, et al. Polydatin protects against articular cartilage degeneration by regulating autophagy mediated by the AMPK/mTOR signaling pathway[J]. *Histol Histopathol*. 2024;39(11):1505–15. <https://doi.org/10.14670/HH-18-739>.
- Chen L, Zhou H, Gong Y, et al. How do muscle function and quality affect the progression of KOA? A narrative review[J]. *Orthop Surg*. 2024;16(4):802–10. <https://doi.org/10.1111/os.14022>.
- Taniguchi M, Umehara J, Yamagata M, et al. Understanding muscle coordination during gait based on muscle synergy and its association with symptoms in patients with knee osteoarthritis[J]. *Clin Rheumatol*. 2024;43(2):743–52. <https://doi.org/10.1007/s10067-023-06852-w>.
- Törnblom M, Bremander A, Allt K, et al. Development of radiographic knee osteoarthritis and the associations to radiographic changes and baseline variables in individuals with knee pain: a 2-year longitudinal study[J]. *BMJ Open*. 2024;14(3):e081999. <https://doi.org/10.1136/bmjopen-2023-081999>.
- Fontanella C G, Belluzzi E. Quantitative MRI analysis of infrapatellar and Suprapatellar fat pads in normal controls, moderate and end-stage osteoarthritis[J]. *Annals Anat - Anatomischer Anzeiger*. 2019;221:108–14. <https://doi.org/10.1016/j.aanat.2018.09.007>.
- Atik I, Gul E. Evaluation of the relationship between knee osteoarthritis and meniscus pathologies[J]. *Malawi Med J*. 2024;36(1):48–52. <https://doi.org/10.4314/mmj.v36i1.8>.
- Han W, Aitken D. Association between quantitatively measured infrapatellar fat pad high signal-intensity alteration and magnetic resonance imaging-assessed progression of knee osteoarthritis[J]. *Arthritis Care Res*. 2019;71(5):638–46. <https://doi.org/10.1002/acr.23713>.
- Ruan G, Lu S, Zhang Y, et al. Quantitatively measured infrapatellar fat pad signal intensity alteration is associated with joint effusion-synovitis in knee osteoarthritis[J]. *Curr Med Imaging Former Curr Med Imaging Reviews*. 2023;20:e100323214543. <https://doi.org/10.2174/1573405619666230310093402>.
- Ballegaard C, Riis R G C Bliddal, et al. Knee pain and inflammation in the infrapatellar fat pad estimated by conventional and dynamic contrast-enhanced magnetic resonance imaging in obese patients with osteoarthritis: a cross-sectional study[J]. *Osteoarthr Cartil*. 2014;22(7):933–40. <https://doi.org/10.1016/j.joca.2014.04.018>.
- De Vries B A, Van Der Heijden R A, POOT D H J, et al. Quantitative DCE-MRI demonstrates increased blood perfusion in Hoffa's fat pad signal abnormalities in knee osteoarthritis, but not in patellofemoral pain[J]. *Eur Radiol*. 2020;30(6):3401–8. <https://doi.org/10.1007/s00330-020-06671-6>.
- Van Der Heijden R A, DE VRIES B A, POOT D H J, et al. Quantitative volume and dynamic contrast-enhanced MRI derived perfusion of the infrapatellar fat pad in patellofemoral pain[J]. *Quant Imaging Med Surg*. 2021;11(1):133–42. <https://doi.org/10.21037/qims-20-441>.
- Fischer MA. From morphology to biomarker: quantitative texture analysis of the infrapatellar fat pad reliably predicts knee osteoarthritis[J]. *Radiology*. 2022;304(3):622–3. <https://doi.org/10.1148/radiol.221094>.
- P K, V K. Assessment of lumbar paraspinal muscle morphology using mDixon quant magnetic resonance imaging (MRI): a cross-sectional study in healthy subjects[J]. *Quant Imaging Med Surg*. 2024;14(8). <https://doi.org/10.21037/qims-23-1796>. <https://pubmed.ncbi.nlm.nih.gov/39144006/>. [2025-03-04].
- Nv A, Am O. Deep network and multi-atlas segmentation fusion for delineation of thigh muscle groups in three-dimensional water-fat separated MRI[J]. *J Med Imaging (Bellingham Wash)*. 2024;11(5). <https://doi.org/10.1117/1.JMI.1.5.054003>. <https://pubmed.ncbi.nlm.nih.gov/39234425/>. [2025-03-04].
- Fan Z, Wang T, Wang Y, et al. Risk factors in patients with low back pain under 40 years old: quantitative analysis based on computed tomography and magnetic resonance imaging mDIXON-quant[J]. *J Pain Res*. 2023;16:3417–31. <https://doi.org/10.2147/JPR.S426488>.
- Klauke F, Zänker K, Schenk P, et al. Comparison of the zonal distribution of calcium salt density and fat marrow in bone-healthy and osteoporotic sacra: an image data analysis using quantitative computed tomography and magnetic resonance imaging[J]. *Eur J Trauma Emerg Surg*. 2024;50(4):1765–73. <https://doi.org/10.1007/s00068-024-02507-w>.
- Han W, Zhu Aitken. Hypointense signals in the infrapatellar fat pad assessed by magnetic resonance imaging are associated with knee symptoms and structure in older adults: a cohort study[J]. *Arthritis Res Therapy*. 2016;18(1):234. <https://doi.org/10.1186/s13075-016-1130-y>.
- Atukorala I, Kwok C K, Guermazi A, et al. Synovitis in knee osteoarthritis: a precursor of disease? [J]. *Ann Rheum Dis*. 2016;75(2):390–5. <https://doi.org/10.1136/annrheumdis-2014-205894>.
- Peterfy C G, Guermazi A, Zaim S, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis[J]. *Osteoarthr Cartil*. 2004;12(3):177–90. <https://doi.org/10.1016/j.joca.2003.11.003>.
- Mace J, Bhatti W. Infrapatellar fat pad syndrome: a review of anatomy, function, treatment and dynamics[J]. *Acta Orthop Belg*. 2016;82(1):94–101.
- Felson D T, Niu J, Neogi T, et al. Synovitis and the risk of knee osteoarthritis: the MOST study[J]. *Osteoarthr Cartil*. 2016;24(3):458–64. <https://doi.org/10.1016/j.joca.2015.09.013>.
- Ilia I, Ciordas P D, Nitusca D, et al. Analysis of the level of adiponectin and selected cytokines in patients with knee osteoarthritis[J]. *Medicina*. 2024;60(4):571. <https://doi.org/10.3390/medicina60040571>.
- Klein-Wieringa I R Kloppenburg, Bastiaansen-Jenniskens Y M, et al. The infrapatellar fat pad of patients with osteoarthritis has an inflammatory phenotype[J]. *Ann Rheum Dis*. 2011;70(5):851–7. <https://doi.org/10.1136/ard.2010.140046>.
- Zhang J, Li K, Qiu X. Exploring causal correlations between inflammatory cytokines and knee osteoarthritis: a two-sample Mendelian randomization[J]. *Front Immunol*. 2024;15:1362012. <https://doi.org/10.3389/fimmu.2024.1362012>.
- De Boer T N, Van Spil W E, Huisman A M, et al. Serum adipokines in osteoarthritis: comparison with controls and relationship with local parameters of synovial inflammation and cartilage damage[J]. *Osteoarthr Cartil*. 2012;20(8):846–53. <https://doi.org/10.1016/j.joca.2012.05.002>.
- Amesbury R, Ragati-Haghi H, Mathiessen A, et al. Osteoarthr Cartil. 2024;32(9):1149–53. <https://doi.org/10.1016/j.joca.2024.04.010>. Gender differences in patterns of cartilage loss: data from the osteoarthritis initiative[J].
- Ponnusamy R, Zhang M, Wang Y, et al. Automatic segmentation of bone marrow lesions on MRI using a deep learning method[J]. *Bioengineering*. 2024;11(4):374. <https://doi.org/10.3390/bioengineering11040374>.
- Luo P, Wang Q, Cao P, et al. The association between anterior cruciate ligament degeneration and incident knee osteoarthritis: data from the osteoarthritis initiative[J]. *J Orthop Translation*. 2024;44:1–8. <https://doi.org/10.1016/j.jot.2023.09.005>.
- Guo H, Li Q, Zhang Z et al. Better clinical outcomes and return to sport rates with additional medial meniscus root tear repair in high tibial osteotomy for medial compartmental knee osteoarthritis[J]. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2024, 32(7): 1753–1765. <https://doi.org/10.1002/ksa.12180>.
- Abramoff B, Caldera FE. Osteoarthritis[J]. *Med Clin North Am*. 2020;104(2):293–311. <https://doi.org/10.1016/j.mcna.2019.10.007>.
- Cen H, Yan Q, Meng T, et al. Quantitative infrapatellar fat pad signal intensity alteration as an imaging biomarker of knee osteoarthritis progression[J]. *RMD Open*. 2023;9(1):e002565. <https://doi.org/10.1136/rmdopen-2022-002565>.
- Martel-Pelletier J, Tardif G, Pelletier JP. An open debate on the morphological measurement methodologies of the infrapatellar fat pad to determine its association with the osteoarthritis process[J]. *Curr Rheumatol Rep*. 2022;24(3):76–80. <https://doi.org/10.1007/s11926-022-01057-7>.
- Van Den Langenbergh J, Bastiaansen-Jenniskens Y M, VAN OSCH G J V M, et al. PLOD2 gene expression in infrapatellar fat pad is correlated with fat mass in obese patients with end-stage knee osteoarthritis[J]. *Osteoarthr Cartil Open*. 2024;6(2):100469. <https://doi.org/10.1016/j.ocarto.2024.100469>.
- Han W, Zhu Aitken. Signal intensity alteration in the infrapatellar fat pad at baseline for the prediction of knee symptoms and structure in older adults: a cohort study[J]. *Ann Rheum Dis*. 2016;75(10):1783–8. <https://doi.org/10.1136/annrheumdis-2015-208360>.
- Klein-Wieringa I R, De Lange-Brokaar B J E Yusuf, et al. Inflammatory cells in patients with endstage knee osteoarthritis: a comparison between the synovium and the infrapatellar fat pad[J]. *J Rheumatol*. 2016;43(4):771–8. <https://doi.org/10.3899/jrheum.151068>.
- Jaraya M, Guermazi A, Felson D T, et al. Is superolateral Hoffa's fat pad hyperintensity a marker of local patellofemoral joint disease? – the MOST study[J]. *Osteoarthr Cartil*. 2017;25(9):1459–67. <https://doi.org/10.1016/j.joca.2017.05.020>.

38. CHUCKPAIWONG B, CHARLES H C, KRAUS V B, et al. Age-associated increases in the size of the infrapatellar fat pad in knee osteoarthritis as measured by 3T MRI[J]. *J Orthop Res*. 2010;28(9):1149–54. <https://doi.org/10.1002/jor.21125>.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.