

# Hyperechoic and Low Morphological Changes in the Prefemoral Fat Pad in Individuals with Knee Osteoarthritis Based on Ultrasonographic Findings

Kazuyuki Shibata<sup>1\*</sup>, Masahiko Wakasa<sup>2</sup>, Akira Saito<sup>2</sup>, Minoru Kimoto<sup>2</sup>, Yusuke Takahashi<sup>3</sup>, Hiromichi Sato<sup>4</sup>, Tetsuaki Kamada<sup>4</sup>, Takuto Shinde<sup>1</sup>, Hitomi Takahashi<sup>5</sup>, Yoshiaki Kimura<sup>6</sup>, Kyoji Okada<sup>2</sup>

<sup>1</sup>Department of Rehabilitation, Akita City Hospital, Akita, Japan, <sup>2</sup>Department of Physical Therapy, Akita University Graduate School of Health Sciences, Akita, Japan, <sup>3</sup>Department of Rehabilitation Medicine, Akita University Hospital, Akita, Japan, <sup>4</sup>Department of Rehabilitation, Akita Kousei Medical Center, Akita, Japan, <sup>5</sup>Department of Physical Therapy, School of Health Sciences, International University of Health and Welfare, Tochigi, Japan, <sup>6</sup>Department of Orthopedic Surgery, Akita City Hospital, Akita, Japan

## Abstract

**Background:** To clarify the changes in the echo intensity (EI) in the prefemoral fat pad (PFP) and identify the relationship between the PFP and clinical features of knee osteoarthritis (OA). **Methods:** Twenty-six women with knee OA (mean age: 76 years) and 17 healthy women (mean age: 73 years) were enrolled. The Kellgren and Lawrence grading scale was used for the radiographic evaluation of knee OA. The EI of the PFP was measured as grayscale values. The change ratio of the anteroposterior PFP length during quadriceps contraction was measured. Knee range of motion and pain (100-mm visual analog scale) were evaluated. **Results:** The EI was significantly higher in the OA group than in the healthy group ( $P < 0.001$ ). The change ratio of the PFP in the OA group was significantly lower than that in the healthy group ( $P < 0.001$ ). The ranges of knee flexion and extension were correlated with the EI of the PFP (both  $P < 0.01$ ) and the change ratio of the PFP (both  $P < 0.01$ ). There was no significant correlation observed with knee pain. **Conclusion:** Hyperechoic changes and a decreased change ratio of the PFP were observed in the patients with knee OA. High EI and decreased morphological PFP changes were associated with decreased ranges of motion.

**Keywords:** Adipose tissue, knee osteoarthritis, ultrasonography

## INTRODUCTION

There are three anterior fat pads in the knee joint: infrapatellar or Hoffa's fat pad (IFP) located at the anterior surface of the synovium and the inferior pole of the patella superiorly, quadriceps fat pad (QFP), and prefemoral fat pad (PFP). The suprapatellar joint recess, an upward extension of the knee joint cavity, separates the QFP and PFP.<sup>[1]</sup>

It has recently been recognized that the obesity-related risk of incidence and progression of knee osteoarthritis (OA) may be conveyed not only by biomechanical factors (i.e., increased body weight) but also by endocrinological mechanisms.<sup>[2]</sup> The IFP has become a focus of OA research, as it has been found to be a local source of leptin, interleukin-6, and other pro-inflammatory cytokines.<sup>[3-7]</sup>

Conversely, a few reports have suggested the presence of PFP impingement as a cause of anterior knee pain.<sup>[8-10]</sup> However, the mechanical and endocrinological role of the PFP is unclear. As the PFP is an intra-articular adipose tissue located in the knee joint, as is the IFP, it may have a negative effect on OA. However, there are a few studies reporting a relationship of OA with the PFP,<sup>[11]</sup> hence, the role of the PFP in knee symptoms and structure is largely unknown. Therefore, evaluation of the PFP, as well as the existing suprapatellar soft tissue, is important.

In recent years, ultrasonographic evaluation has been widely used to evaluate not only morphological changes but also the

**Address for correspondence:** Dr. Kazuyuki Shibata, Department of Rehabilitation, Akita City Hospital, 4-30 Kawamoto-Matsuoka-cho, Akita 010-0933, Japan. E-mail: [siva.kzyk1113@gmail.com](mailto:siva.kzyk1113@gmail.com)

Received: 27-04-2020 Revised: 17-07-2020 Accepted: 24-08-2020 Available Online: 22-01-2021

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**DOI:**  
10.4103/JMU.JMU\_85\_20

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**How to cite this article:** Shibata K, Wakasa M, Saito A, Kimoto M, Takahashi Y, Sato H, *et al.* Hyperechoic and low morphological changes in the prefemoral fat pad in individuals with knee osteoarthritis based on ultrasonographic findings. *J Med Ultrasound* 2021;29:105-10.

echo intensity (EI). The EI has been reported to be able to evaluate changes in intramuscular adipose tissue and muscle fibers, particularly those of the skeletal muscle.<sup>[12-14]</sup> Thus, changes in the EI have been recently evaluated. The EI may be able to indicate biological tissue changes, and therefore, its evaluation may reveal histological changes in the fat pad itself.

The aims of this study were to compare the EI changes in the PFP between patients with knee OA and healthy older adults and to clarify the relationship between the PFP and the clinical features and structures around OA knees.

## MATERIALS AND METHODS

### Participants

This study evaluated two groups: a group of patients with knee OA and a control group. Twenty-six women with knee OA were enrolled. They were diagnosed with knee OA based on clinical knee symptoms and radiographic findings, namely, knee pain, swelling, poor range of motion, loss of joint space, deformities, and osteophytes. Based on the radiographic findings, cases with a Kellgren and Lawrence (KL) grade of 2, 3, or 4 were included.<sup>[15]</sup> Among the 26 patients, 16 had bilateral knee OA, and 10 had unilateral knee OA. Consequently, 42 OA knees were examined.

Seventeen healthy older women (34 knees) were classified as the control group. In this group, individuals having any symptoms or deformity around the knees, knee pain, orthopedic or neuromuscular disorder in the lower limb, or any wear or irregularity of the femoral cartilage identified through ultrasonography were excluded.

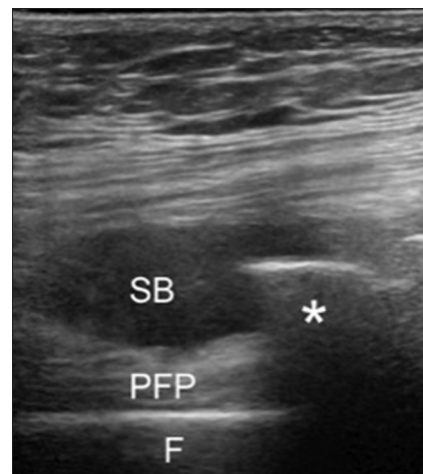
This study was conducted in accordance with the Helsinki Declaration (October 2008, Seoul; revised). In addition, personal information was handled in accordance with the Personal Information Protection Law, and participant privacy was protected. We confirmed that the participants understood the study's purpose and obtained written informed consent. This study was approved by the Akita City Hospital Ethical Review Board in 2014 (approval number 12).

### Image acquisition using ultrasonography

Quantitative ultrasonographic scans and image capture were completed using a diagnostic sonography machine (HI VISION Noblus, Hitachi Aloka Medical, Mitaka City, Tokyo, Japan) with a 13-4-MHz linear array transducer and B-mode scanning. The long axial view was obtained by placing the transducer on the line from the anterosuperior iliac spine to the center of the patella, and minimal pressure was applied to the transducer to limit tissue deformation [Figure 1].<sup>[11]</sup> In the supine position, the participants' knees were placed on a rolled-up towel. We instructed them to hold their thigh muscle contraction. The PFP was examined at rest and during maximum isometric quadriceps contraction.

### Image analysis of the prefemoral fat pad

We measured the echogenicity of the PFP in the long axis view. The mean grayscale values were obtained using an



**Figure 1:** Long-axis PFP image. The PFP is located between the anterior femoral surface and SB. There are osteophytes on the patellar surface of the femur between the femoropatellar joints. SB: Suprapatellar bursa, F: Femur, PFP: Prefemoral fat pad, \*: Osteophyte

image editing program: ImageJ (National Institutes of Health, Bethesda, MD, USA, version 1.48).<sup>[16]</sup> We selected the region of interest for the images using the freehand tool. The grayscale histogram values were obtained from the region of interest within the superior and inferior surfaces of the PFP and the lateral borders of the PFP defined by the field of view. The mean values of all grayscale measurements were used for the data analysis. The grayscale values ranged from 0 to 255 (scale black = 0; white = 255). Further, the gain and focus setting was fixed for all measurements. The anteroposterior length of the PFP was measured as the maximum distance from the femur to the suprapatellar bursa [Figure 2].<sup>[11]</sup> Thereafter, the difference between the length at rest and during quadriceps contraction was calculated and expressed as “the change ratio of the PFP” using the following equation:

Change ratio of the PFP (%) = (Anteroposterior length during contraction – anteroposterior length at rest)/anteroposterior length at rest × 100

### Assessment of the range of motion, knee pain, and severity of osteoarthritis

The maximum knee range of flexion/extension was measured using a standard goniometer (OG Giken, Okayama City, Okayama, Japan), with the greater trochanter, lateral condyle of the femur, head of the fibula, and lateral malleolus as bony landmarks.<sup>[17]</sup> The angular notation was in 5° increments. Knee pain was evaluated using the 100-mm visual analog scale (VAS).<sup>[18]</sup> The participants marked the point on the scale that indicated their most recent maximum intensity of knee pain. Our hospital orthopedic surgeon graded the severity of knee OA as a KL grade 2, 3, or 4 based on the radiographic findings.

### Statistical analysis

Statistical analyses were performed using SPSS Statistics ver. 21 (IBM, Chuo Ward, Tokyo, Japan). The assumption of normality was assessed using the Shapiro–Wilk test. The EI of

the PFP, anteroposterior length of the PFP at rest and during quadriceps contraction, and change in the PFP ratio were compared between the OA and normal knees using Student's *t*-test. Spearman and Pearson's correlation coefficient (*r*) tests were used to assess the relationship between the PFP variables and clinical features (KL grade, VAS pain score, and knee range of motion). In addition, the effect size of each difference was obtained. The level of significance was set at  $P < 0.05$ .

## RESULTS

The demographic characteristics of the study participants are shown in Table 1. There were significant differences in the mean age between the knee OA group ( $76 \pm 6$  years) and control group ( $73 \pm 5$  years) ( $P = 0.019$ ). The mean body mass index (BMI) in the knee OA group was significantly higher than that in the control group ( $26.8 \pm 4.49$  kg/m<sup>2</sup> vs.  $21.1 \pm 1.9$  kg/m<sup>2</sup>,  $P < 0.001$ ). The EI of the PFP was higher in the knee OA group than in the control group and was whiter

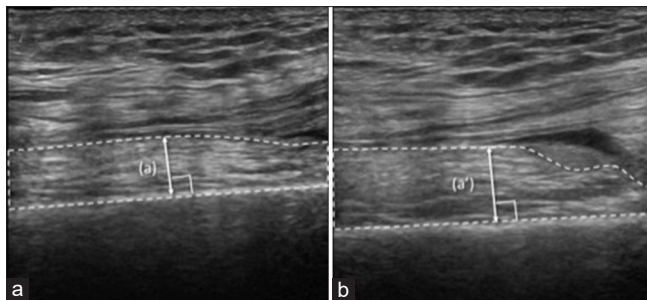
on the screen when visualized with hyperintensity. There was no significant difference in the anteroposterior length of the PFP at rest between the groups. Conversely, the anteroposterior length during contraction and the change ratio of the PFP were shorter and lower in the knee OA group than in the control group, respectively. In the knee OA group, the range of extension was  $-11.0^\circ \pm 5.5^\circ$ , and the range of flexion was  $129.5^\circ \pm 14.3^\circ$ . The mean VAS pain score was  $41.8 \pm 25.0$  mm. Among the 42 OA knees, 13 were classified under Grade 2, 12 under Grade 3, and 17 under Grade 4.

The correlation coefficients for the EI of the PFP, anteroposterior length of the PFP, and clinical features are listed in Table 2. Age, BMI, the KL grade, and the VAS pain score were not correlated with the PFP variables.

There were significant findings between the anteroposterior length and EI of the PFP [Table 3].

## DISCUSSION

In this study, the PFP in the OA knees was visualized as whiter areas based on the high-intensity EI observed in comparison with that in the healthy knees. There have been no reports regarding the quantitative evaluation of the EI of the intra-articular fat pads around the knee joint. On magnetic resonance imaging (MRI), patellofemoral joint degeneration has been reported to significantly increase over 48 months in subjects with signal alterations in the QFP, suggesting an association between QFP abnormalities and the progression of patellofemoral OA.<sup>[19]</sup> Such changes in the MRI of the fat pad were also visualized in the ultrasonographic images. Chronically inflamed adipose tissues can lead to the development of fatty fibrosis with associated pain, synovitis, and loss of range of motion.<sup>[20,21]</sup> Inflammation and mechanical stress may have a similar effect on the PFP of patients with knee OA.



**Figure 2:** PFP analysis. (a) Long-axis image at rest. (b) Long-axis image during isometric contraction. (a) or (a') the anteroposterior PFP length. The increase in the anteroposterior length during isometric contraction was expressed as a percentage of the anteroposterior length at rest (Change ratio of the PFP =  $(a' - a)/a$ ). The echo intensity was measured in the grayscale image. PFP: Prefemoral fat pad

**Table 1: Demographic and basic differences between the patients with osteoarthritis and healthy participants**

|                                     | OA group (n=42) | Control group (n=34) | P      | t      | Effect size |
|-------------------------------------|-----------------|----------------------|--------|--------|-------------|
| Age (y)                             | 76±6            | 73±5                 | 0.019  | 2.40   | 0.27        |
| BMI (kg/m <sup>2</sup> )            | 26.8±4.4        | 21.1±1.9             | <0.001 | 7.28   | 0.71        |
| KL grade                            |                 |                      |        |        |             |
| 2 (%)                               | 13 (6)          | NA                   | -      | -      | -           |
| 3 (%)                               | 12 (38)         | NA                   | -      | -      | -           |
| 4 (%)                               | 17 (56)         | NA                   | -      | -      | -           |
| Visual analog scale pain score (mm) | 52.70±22.14     | NA                   | -      | -      | -           |
| Knee range of motion                |                 |                      |        |        |             |
| Flexion (°)                         | 129.5±14.3      | 150.0±2.7            | <0.001 | -8.62  | 0.79        |
| Extension (°)                       | -11.0±5.5       | 0.0±0.0              | <0.001 | -12.79 | 0.89        |
| Anteroposterior length of the PFP   |                 |                      |        |        |             |
| Rest (mm)                           | 5.72±1.91       | 5.57±2.12            | 0.752  | 0.32   | 0.04        |
| Isometric contraction (mm)          | 6.35±2.33       | 8.68±3.00            | <0.001 | 3.82   | 0.41        |
| Change ratio (%)                    | 10.55±0.15      | 60.88±0.38           | <0.001 | 7.80   | 0.67        |
| Echo intensity of the PFP           | 113.62±22.11    | 96.13±15.94          | <0.001 | 3.87   | 0.41        |

Comparisons between the OA and healthy knees were performed using Student's *t*-test. In addition, the effect size of each difference was obtained. Values are presented as means±SDs. The level of significance was set at  $P < 0.05$ . OA: Osteoarthritis, PFP: Prefemoral fat pad, NA: Not applicable, SD: Standard deviation, KL: Kellgren and Lawrence

**Table 2: Relationship between the prefemoral fat pad variables and clinical assessment**

| Variables                         | Range of extension (°) | Range of flexion (°) | VAS pain score (mm) | KL grade |
|-----------------------------------|------------------------|----------------------|---------------------|----------|
| Anteroposterior length of the PFP |                        |                      |                     |          |
| Rest (mm)                         | -0.111                 | -0.090               | -0.166              | -0.083   |
| Isometric contraction (mm)        | 0.313*                 | 0.400*               | -0.269              | -0.135   |
| Change ratio (%)                  | 0.551*                 | 0.701*               | -0.324              | -0.137   |
| Echo intensity of the PFP         | -0.495*                | -0.354*              | 0.285               | 0.105    |

Spearman and Pearson's correlation coefficient tests were used to assess the relationship between the PFP variables (echo intensity, anteroposterior length at rest and during contraction, and change ratio) and clinical features (KL grade, VAS pain score, and knee ROM). ROM and VAS pain score: Pearson's correlation coefficient. KL grade: Spearman correlation coefficient. The level of significance was set at  $P < 0.05$ . \* $P < 0.01$ . ROM: Range of motion, VAS: Visual analog scale, KL: Kellgren and Lawrence, PFP: Prefemoral fat pad

**Table 3: Relationship between the anteroposterior length and echo intensity of the prefemoral fat pad**

| Variables                  | Echo intensity      |
|----------------------------|---------------------|
| Anteroposterior length     |                     |
| Rest (mm)                  | -0.267 <sup>†</sup> |
| Isometric contraction (mm) | -0.462*             |
| Change ratio (%)           | -0.380*             |

Pearson correlation coefficient: \* $P < 0.01$ , <sup>†</sup> $P < 0.05$

The anteroposterior length of the PFP during isometric quadriceps contraction was shorter in the OA knees than in the healthy knees. Shibata *et al.*<sup>[11]</sup> reported that the change in the anteroposterior length of the PFP during quadriceps contraction was smaller in patients with knee OA than in older and younger adults without OA based on ultrasonographic findings. Since the PFP is located anterior to the distal surface of the femur and posterior suprapatellar bursa, it prevents direct contact between those surfaces and may also support the motion of the suprapatellar bursa. Furthermore, individuals with knee OA exhibited atrophic changes and dysfunctions of the articularis genus muscle, which is assumed to retract and elevate the suprapatellar bursa during knee extension,<sup>[22]</sup> thereby preventing entrapment of the bursa between the patella and the femur. Therefore, the PFP cannot change in correspondence with quadriceps contraction.

There was a significant correlation between the EI of the PFP and the knee range of motion in this study. The decrease in the range of extension/flexion is well known as a feature of OA knees and is considered to be attributed to articular deformation and/or changes in the soft tissues around the knee joint, such as the muscle, ligament, skin, and adipose tissue. In knee OA progression, knee effusion is a common symptom in the suprapatellar bursa and is thought to be the cause of the decrease in knee range of flexion. Postoperative arthrofibrosis affecting the suprapatellar bursa after total knee arthroplasty and arthroscopy reduces knee flexion.<sup>[23,24]</sup> Therefore, the high EI of the PFP located in the deep layer of the suprapatellar bursa indicates fibrosis, and the decreased change in the anteroposterior length indirectly affected the decrease in the range of motion.

Chronic knee pain is a hallmark feature of knee OA and other joint structural abnormalities, such as bone marrow lesions,

osteophyte formation, meniscal tears, synovitis, and cartilage defects.<sup>[25-27]</sup> Since the local fat pads are highly innervated, they can be responsible for knee pain.<sup>[28]</sup> Borja *et al.*<sup>[9]</sup> reported anterior knee pain that was caused by PFP impingement within the patellofemoral joint. Roth *et al.*<sup>[21]</sup> reported that a QFP mass effect was associated with anterior knee pain in knee MRI examinations and suggested that the knee pain could be explained by impingement caused by an enlarged and edematous QFP. Wang *et al.*<sup>[29]</sup> reported that a QFP mass effect and a signal intensity alteration were associated with the Western Ontario and McMaster University OA Index. In contrast, Tsavalas and Karantanas<sup>[30]</sup> reported that a QFP mass effect was not significantly associated with anterior knee pain. In this study, there was no association between the EI of the PFP and the VAS pain score. However, some studies suggest that a mass effect and/or signal intensity change in the intra-articular fat pads of the knee, as identified on MRI, is related to pain.

The severity of OA (determined radiographically) was not significantly correlated with the EI and anteroposterior length of the PFP. There has been no report on the relationship between signal changes and knee OA severity or progression with regards to the PFP. Wang *et al.*<sup>[29]</sup> reported that the QFP mass effect and signal intensity alteration were related not only to the Western Ontario and McMaster University Osteoarthritis Index but also to OA, osteophyte formation, and joint space narrowing. Relationships between intra-articular fat pad enlargement or edema and severity of knee OA were reported.<sup>[31]</sup> The IFPs of individuals with patellofemoral OA were reported to be significantly larger than that of healthy controls.<sup>[32]</sup> In contrast, there are some reports that the IFP size was not associated with the progression of knee OA and knee pain,<sup>[33]</sup> and the QFP mass effect was not related to patellofemoral OA.<sup>[30]</sup> A high EI and a decrease in the anteroposterior length change in the PFP were found to be features of knee OA; however, no association was observed for the severity of OA. The severity of knee OA must be determined not only by the KL grade based on radiographic images but also by the evaluation of subchondral deformities, cartilage defects, and bone marrow lesions based on MRI findings.

There was a significant correlation found between the EI and the change in the anteroposterior length of the PFP during quadriceps contraction. Based on pathological specimens,



the intra-articular fat pads, such as the IFP and PFP in OA knee joints, differ from the subcutaneous adipose tissue, smaller fat cells, and fibrous tissue, and in vascular are increased.<sup>[34]</sup> Maculé *et al.*<sup>[35]</sup> reported that the adipose tissue of the IFP was composed of approximately 33% fibrosis and 36% inflammatory cells. Taken together, it is considered that one cause of the decrease in the anteroposterior length change in the PFP is the fibrosis of the adipose tissue. The histological changes observed in the EI and the decrease in the anteroposterior length change in the PFP are unclear but may be similar to the histological changes described in the IFP, which are characterized by inflammation, swelling, hypertrophy, and fibrosis and/or calcification.<sup>[36,37]</sup> To date, there are no reports quantifying the change in the EI of the intra-articular fat pads using ultrasonography. Based on the results of this study, the ultrasonic diagnostic imaging apparatus can reveal changes in the EI of the PFP in OA knees.

### Limitation

Some limitations exist in this study. First, all enrolled participants were women, which may yield a sex bias. Second, the EI of the PFP was not compared with MRI or pathology findings. The reason why the EI of the PFP represents a hyperechoic change in knee OA cannot be determined and requires further study.

### CONCLUSION

We assessed the echogenicity and the anteroposterior length of the PFP using ultrasonography and compared the knees of older women with OA with those of healthy older women. The PFPs of those with knee OA were hyperechoic and had a decreased anteroposterior length change, which was associated with the decrease in the knee range of motion.

### Acknowledgments

We would like to thank Editage ([www.editage.jp](http://www.editage.jp)) for English language editing and the staff in our hospital for useful discussions.

### Financial support and sponsorship

All authors have (completed the authorship disclosure form) and declare that: NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

### Conflicts of interest

There are no conflicts of interest.

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