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Effects on patellar chondromalacia of the size of the infrapatellar fat pad**Abuzer Uludag¹, Mehmet Sirik²**¹Adiyaman University, Faculty of Medicine, Department of Orthopaedics and Traumatology, Adiyaman, Turkey²Adiyaman University, Faculty of Medicine, Department of Radiology, Adiyaman, TurkeyReceived 14 February 2019; Accepted 18 February 2019
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Abstract

Infrapatellar fat tissue (IPFP), which is placed in the anterior compartment, has a vital role in the biomechanics of knee. It is thought that infrapatellar fat pad, which also functions as a storage for repair cells after injury, has a protective effect in mechanical and inflammatory knee pain. In this study, the relationship between patellar chondromalacia, which is among significant causes of anterior knee pain, and the sizes of IPFP was investigated. MRI images of patients over 18 years of age, who underwent MRI examination in June 2017 - December 2017, were examined retrospectively by recovering from the electronic patient registration system in the hospital. Eighty-three cases had patellar chondromalacia with normal-healthy IPFP tissue in the examination of knee MRI, and 53 cases without chondromalacia were included in the study. The average age of all evaluated 134 patients was 37.8 (22-68) years. The degree of chondromalacia patella was made according to Outerbridge classification. The height and depths of IPFP in all cases were measured from the widest site on the T1-weighted MRI images in the sagittal plane. The relationship among age, gender, the degree of patellar chondromalacia and IPFP sizes were evaluated. While the average of 51 patients without patellar chondromalacia was 29.04 (22-51) years, the average of 83 patients with chondromalacia was 43.20 (27-68) years. According to Outerbridge classification, patellar chondromalacia grade 3 in 14 patients, grade 2 in 41 patients, grade 1 in 26 patients and grade 4 in 2 patients were observed. It was not seen a significant difference between the groups in terms of gender ($p = 0.78$). It was seen a significant increase in between patellar chondromalacia and increasing age ($p < 0.001$). It was observed that while IPFP height was averagely 35.33 mm and IPFP anteroposterior width was 17.29 mm in the patients with patellar chondromalacia, IPFP height was averagely 38.65 mm, and IPFP anteroposterior width was averagely 19.49 (15-37) mm in the patients without chondromalacia. It was observed a statistically significant increase in the frequency of patellar chondromalacia as the size of the IPFP tissue decreased ($p < 0.001$). Incidence of patellar chondromalacia increases both with increasing age and a decrease in IPFP sizes. We consider that IPFP tissue has a contribution to joint cartilage in both biomechanical and physiological levels. For this reason, protection of IPFP tissue is required in both the prevention of patellofemoral joint degeneration and in the decrease of anterior knee pain during knee arthroscopy or arthroplasty interventions.

Keywords: Infrapatellar fat pad, chondromalacia, effect, volume, size**Introduction**

IPFP (infrapatellar fat pad), which is also known as Hoffa's fat pad, is an intra-capsular and extrasynovial structure filling the anterior knee compartment [1,2]. Gallagher et al.[3] stated that the anatomical border of this structure consists of the inferior pole of the patella in superior, anterior tibia, an intermeniscal ligament, meniscus horns and infrapatellar bursa in inferior, a patellar tendon in anterior, a femoral condyle and an intercondylar notch in posterior.

Chondromalacia patella is a cartilage disease which is seen related to a disorder of hyaline cartilage covering the joint surface of the bone. It begins with the softening of the cartilage and then

it results with tearing, fissuring and erosion. It is called patellar chondromalacia, patellofemoral syndrome or runners knee. It may lead to chondromalacia many causes including post-traumatic injuries, micro trauma, wear and tear, axial patella disorders, and iatrogenic injections. It may also be observed as immobilization and the complication of surgical procedures [4]. Patellar chondromalacia, which is seen mostly in the 2nd-3rd decades of life, is among the most common causes of mechanical anterior knee pain [5]. Women are affected more than man due to increased Q angle. It is observed in high incidence related to increased stress on patellofemoral joint due to especially repetitive jumping and knee bending movements in young adult runners and workers [4].

Magnetic resonance imaging (MRI) and knee arthroscopy are helpful in the diagnosis of patellar chondromalacia. MRI is a non-invasive and radiation-free gold standard procedure. Knee arthroscopy is an invasive technique which provides the direct view of patellar cartilage [5].

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The main complaint in these patients is anterior knee pain. Other reasons of anterior knee pain are Hoffa's disease, osteochondritis dissecans of the patellofemoral joint, patellar tendinitis, patella alta, patella baja, plica and bi-partite patella [4]. IPFP pathologies are one of the common causes of anterior knee pain. Recurrent local micro-traumas, impingement, local bleeding after surgery and inflammation are the most common causes of IPFP pain, and these may lead to various arthrofibrotic lesions. Abnormalities and edema observed in IPFP on MRI are often symptomatic, but some such types of changes can be observed in asymptomatic persons [6].

IPFP tissue of the patients with osteoarthritic knees have macrophages, lymphocytes, and granulocytes alongside adipocytes, and these may contribute to the progression of knee osteoarthritis. Furthermore, there are nociceptive nerve fibers in IPFP, which are thought as responsible for some of the anterior knee pain in patients with osteoarthritic knees. These nerve fibers secrete substance P which induces immune responses and causes vasodilatation in response to inflammation. This substance P may cause extravasation of immune cells and edema in IPFP. Besides, IPFP tissue secretes substances such as cytokines, interleukins, growth factors, and adipokines, which affect cartilage. These secreted substances regulate the production of matrix metalloproteinases (MMPs), stimulates the expression of pro-inflammatory cytokines, and inhibits the production of cartilage matrix proteins [1].

IPFP is a flexible structure which can adjust to different degrees of flexion and extension of the knee. The primary function of IPFP is reducing friction among patella, patellar tendon, and deep skeletal structures. It also prevents the impingement of the synovial membrane and facilitates the vascularization of adjacent structures [6].

It is evident that the biomechanics of this area are altered with IPFP extent. It was evaluated the relationship between patellar chondromalacia and the dimensions of the infrapatellar fat pad which is among the significant reasons for anterior knee pain in this study.

Material and Methods

MRI images of patients over 18 years of age, who underwent MRI examination in June 2017 - December 2017, were examined retrospectively by recovering from the electronic patient registration system in the hospital. The study protocol was established according to the principles of the Helsinki Declaration by obtaining approval from Adiyaman University Clinical Ethics Committee (2018/8-5) for this study. The patients who have edema, inflammation, scar and fibrosis in their IPFP tissue were excluded from the study. Eighty-three cases had patellar chondromalacia with normal-healthy IPFP tissue in the examination of knee MRI, and 53 cases without chondromalacia were included in the study. The degree of chondromalacia patella was made according to Outerbridge classification [7]. Infrapatellar fat pad height and depths in all cases were measured from the widest site on the T1-weighted MRI images in the sagittal plane (Figure 1). An experienced radiologist performed all measurements. The relationship among age, gender, the degree of patellar chondromalacia and IPFP sizes of cases were evaluated.

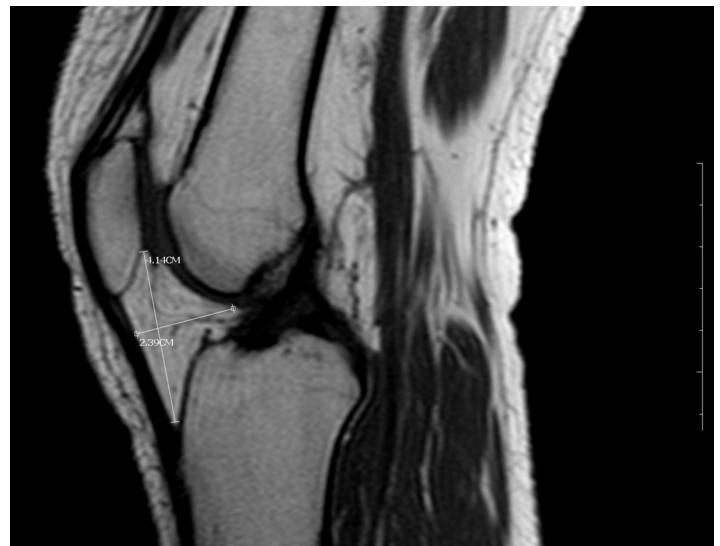


Figure 1. Measurement of the height and depth of the Infrapatellar fat pad

MRI protocol

All MRI examinations were performed on a 1.5 T Achieva scanner (Philips, Best, The Netherlands). Sequences used for knee MR examination; 1- Axial, coronal and sagittal plane PD SPAIR (proton density, spectral attenuated inversion recovery), 2- sagittal T1W TSE image. SPAIR sequences; 1- Sagittal plane: Repetition Time (TR) 3034 ms, Echo Time (TE) 30 ms, 3.5 mm slice thickness, Gap 0.3 mm, 2- Coronal plane: Repetition Time (TR) 3034 ms, Echo Time (TE) 30 ms, 3.5 mm slice thickness, Gap 0.3 mm, 3- Axial plane: Repetition Time (TR) 3034 ms, Echo Time (TE) 30 ms, 3.5 mm slice thickness, Gap 0.3 mm, T1W TSE(turbo spin-echo) Coronal plane: Repetition Time (TR) 560 ms, Echo Time (TE) 17 ms, 3.5 mm slice thickness, Gap 0.6 mm.

Statistical analysis

Statistical analyses were obtained using the IBM SPSS Statistics 22 (Chicago, IL, USA) software program. A Student's t-test was used to compare the normally distributed continuous parametric data between groups. Normally distributed continuous parametric data were shown as mean $\pm$ standard deviation. Non-parametric data were investigated using by the Mann-Whitney U, Chi-Square and Fisher's exact tests. The p-values <0.05 were considered statistically significant.

Results

The average age of a total of 134 cases was 37.8 (22-68) years. The gender of the cases which were included in the study were 70 males and 74 females. The study involved 83 patients with chondromalacia patella and 51 patients without chondromalacia. The average age of 51 patients, 32 of them were females, and 29 were males, without chondromalacia was 29.04 ± 7.5 (22-51) years. The average age of totally 83 patients, 41 of them were males, and 42 were females, with patellar chondromalacia was 43.20 ± 9.6 (27-68) years. It was not seen a significant difference between the groups in terms of gender ($p = 0.78$). An increase in the rate of patellar chondromalacia was specified with increasing age. A statistically significant difference was observed between the patients with patellar chondromalacia and without patellar chondromalacia in terms of age. It was seen a significant increase in between patellar chondromalacia and increasing age ($p < 0.001$).

According to Outerbridge classification, patellar chondromalacia grade 3 in 14 patients, grade 2 in 41 patients, grade 1 in 26 patients and grade 4 in 2 patients were observed.

When considering all patients, the average height of the IPFP was measured as 36.58 mm, and the anteroposterior width of the IPFP was measured as 17.69 mm. It was observed that while IPFP height was averagely 35.33 ± 4.06 (26-48) mm in the patients with patellar chondromalacia, it was averagely 38.65 ± 3.59 (32-48) mm in the patients without chondromalacia. It was observed that while IPFP anteroposterior width was averagely 17.29 ± 2.76 (9-26) mm in the patients with patellar chondromalacia, it was averagely 19.49 ± 3.32 (15-37) mm in the patients without chondromalacia. A statistically significant increase ($p < 0.001$) was observed in the incidence of patellar chondromalacia as the sizes of IPFP tissue decreases.

Discussion

Knee osteoarthritis is a joint disease, which affects the individuals' daily life activities and reducing their quality of life, with its chronic and progressive trend [8], and it is characterized by joint cartilage loss and osteophyte formation in old ages [9,10]. This event is not only limited to joint cartilage, but it is a process which also covers menisci, ligaments, subchondral bone, capsule, synovium, and periarticular muscles. Although the etiology of this disease cannot be fully defined, are known to have affected many factors such as genetically, metabolic and mechanical [9,10]. Osteoarthritis not only affects the medial and lateral compartments of the tibiofemoral joint but it is also observed in patellofemoral joint (PFJ). PFJ [8] osteoarthritis (PFJ OA) is observed as in the rate of %26 by being isolated in individuals with knee pain below 50 years of age, and as in the rate of %29 with tibiofemoral joint involvement [11]. In our study, it is seen that there is a linear relationship between the incidence of patellar chondromalacia and increasing age.

There are relatively few studies investigating PFJ OA. Mainly, the source of pain in PFJ OA could not be detected entirely [12]. Cowan et al. [12] searched the relationship between IPFP volume and pain in the patients with and without PFJ OA. They reported that IPFP volume was more significant in the group with PFJ OA compared to the control group by 26% without adding variables and 19.6% after the variables were added. They also stated that there is a correlation between pain and volume size in patients with PFJ OA. They indicated that large-volume IPFP has a role in the development of PFJ OA. They also expressed that this coincidental relationship between PFJ changes and IPFP should be supported with further studies. IPFP protects joint against mechanical damage by its shock absorption effect [13]. Pan et al. [14] reported that every 1cm² increase in IPFP, which is over 2.6 years, decreases total knee pain score in 0.86 in women. When the cartilage volume was considered in female patients, they informed that there was a positive correlation between the medial and lateral condyle cartilage thickness and the size of IPFP except for patella. They stated that this clinical finding indicated that the IPFP site showed a protective effect on mechanical and inflammatory knee pain. They also urged that the decrease of IPFP during knee surgery may cause an increase in knee pain in women and for this reason, it should be protected during knee surgery. However, in another study, it was reported that resection of IPFP did not affect knee

pain and its function during total knee replacement. This situation should be interpreted with caution as there are limited studies. It was indicated that IPFP tissue has both protective and disease-enhancing effect in OA [15].

It is thought that IPFP tissue plays a role in the biomechanics of knee or functions as a storage for repair cells after injury. Various arthrofibrotic lesions such as Hoffa's disease, infrapatellar contracture syndrome, anterior interval scarring can be observed in IPFP due to inflammation and fibrosis. It was expressed that while positive results were obtained with arthroscopic partial resection in IPFP impingement and Hoffa's disease, concurrent total excision with arthroplasty caused terrible results compared to partial excision [2]. Han et al. [16] reported that the IPFP site is averagely 7.59 cm² (range 4.56 to 12.14), and less OA is seen radiographically in those with large IPFP site. They stated that there was only a correlation between osteophyte and IPFP, but there was no statistical significance. They also indicated that the knee is protective in terms of OA. Therefore the resection of normal IPFP should be avoided in knee surgeries, and special attention should be paid to IPFP in clinical events.

It is observed that there are different evaluations in the above-mentioned studies. In our study, it was observed that there was a decrease in the frequency of patellar chondromalacia as IPFP sizes increased. We think that IPFP tissue with its large volume in normal (healthy) structure has an especially protective effect in terms of patellar chondromalacia, and for this reason, IPFP tissue should be protected not only in arthroscopic interventions but also during arthroplasty.

IPFP has long been thought of as a structural fat tissue having minimal or no metabolic response. However, it is estimated that it contributes to the expansion of the synovial space when considering its anatomical structure, and for this reason, it may increase the distribution of lubrication of the knee joint [17]. In the meta-analysis, Clockaerts et al. [1] reported that infrapatellar adipose tissue has the capacity to modify inflammatory and destructive responses in knee osteoarthritis due to its metabolic properties, containing nerve fibers, adipocytes and immune cell combinations. Furthermore, they also informed that it contributes to the disease process with the production and release of inflammatory mediators. IPFP with large-volume may cause pathological results by changing the release of cytokines from adipocytes and other potential pro-arthritis mediators or distribution and size of PFJ forces. On the contrary, it may also lead to the extension of IPFP by causing the change of environment with osteoarthritis molecular and local mechanical effect which first developed in PFJ. Although the cause and effect relationship between PFJ OA and IPFP volume is not entirely known, it was shown that there was a linear relationship between volume size and pain scores [12]. Gallagher et al. [3] stated in the cadaver study between 80-95 years of age that the volume of IFP is averagely 24 ml (12-36), there may be averagely 4ml difference between the right and left knees. Culvenor et al. [18] reported that IPFP volume is quite significant in the patients with chronic patellar tendinitis compared to a healthy control group. Although a whole relationship between IPFP diseases and cartilage problems is not known, it was indicated that hypertrophy and fibrosis of IPFP induce degeneration by causing an increase in cartilage contact pressure [19].

The potential role of IPFP on the development of osteoarthritis (OA) originates from the local production of adipocytokines [20]. Inflammatory adipokines, including high levels of interleukin 6, adipsin, adiponectin and visfatin, and cytokines are secreted from adipose tissue in IPFP in patients with OA [21]. Meanwhile, lipid mediators such as multiple oxylipins may play a role in the pathogenesis of OA by being secreted [22]. Favero et al. [20] reported that they observed inflammatory infiltration, vascularization, increase in interlobular septa thickness, fibrosis, and hyperplasia in the content of IPFP tissue in the patients with OA compared to control group. They indicated that they observed VEGF, MCP-1 and IL-6 proteins as higher in the content of IPFP in patients with osteoarthritis compared to the control group. They urged that while VEGF protein levels are correlated with increased vascularity, MCP-1 and IL-6 protein levels are correlated with excessive inflammatory infiltration.

There is a direct relationship between anterior knee pain and IPFP. IPFP has rich vascularization and nerve innervation. The degree of nerve stimulation in inflammatory pathologies, the ratio of fibrils containing substance-P and its relationship with posterior synovial sheath affects infrapatellar knee pain [2]. Bennell et al. [23] reported that they created anterior knee pain with nociceptive stimulation in the study in which they performed hypertonic saline solution injection to demonstrate the presence and sensitivity of sensory fibers in IPFP. Pressure changes due to anterior interval volume are observed throughout the movement of the knee joint. The presence of edema in IPFP causes irritation of the adjacent tissues and an increase in pressure [2]. Ballegaard et al. [24] indicated that the amount of inflammation observed in IPFP tissue in the examination of MRI in osteoarthritic knees and perfusion changes are correlated with pain level. No relationship was found between the volume of IPFP and BMI, and total body fat [24]. Adipose tissue produces cytokines, interleukins, and growth factors through paracrine, endocrine and autocrine mechanisms. IPFP plays a role in the beginning and progression of osteoarthritis linked to its role in the release and activation of pro-inflammatory mediators. Degenerative joint disease is considered as an inflammatory process. The relationship between obesity and joint degeneration is not only correlated with the biomechanical disorder but also adipose tissue with the ability to activate the inflammatory process. It has a direct effect on the composition of synovial fluid due to IPFP localization, and it is thought that it has also effect on other elements of joint. Pro-inflammatory cytokines activate the substance P fibers that stimulate anterior knee pain. They have a direct effect in the formation of chemokines, cytokines and growth factors together with fat tissue, immune and nervous system in IPFP. All of these effects influence the metabolism and function of the synovial membrane and articular cartilage. They stated that it is essential to investigate the complex relationship among nervous system, immune system and adipose tissue in the light of this information [25].

Evaluating the role of IPFP in the knee joint involves difficulties for several reasons. When it is intended to be evaluated through arthroscopy, access to information related to pathology, physiology, and composition of pathological changes in this tissue will be restricted.

Information regarding IPFP can be achieved through examining the

specimen which was excised during knee replacement or obtained from cadaver studies. Other information is often obtained from non-invasive techniques such as ultrasound and MRI, and these examinations may specify inflammatory changes in tissue other than the information related to molecular and cellular mechanisms [15]. Sagittal MRI is the most common imaging technique to evaluate IPFP pathologies which include mass-like lesions, edema, inflammation, and fibrosis [2]. IPFP tissue is observed as predominantly hyper intense in T1-and T2-weighted MRI images, and it is structurally similar to subcutaneous fat tissue [6]. Signal changes in IPFP may be observed in noncontrast-enhanced MRI [15].

As seen in the studies reported above, PFJ arthrosis or anterior knee pain is observed in patients with large-volume IPFP tissue, who were observed with inflammation infiltration, edema, and vascularity increase. This may be explained with the process caused by mediators released from IPFP tissue. However, all patient groups had healthy IPFP tissue in our study. In this manner, we consider that healthy IPFP tissue contributes positively both to lubrication and shock absorption of the knee. This study shows the relationship only between patellar chondromalacia and IPFP sizes in the patients with healthy IPFP tissue in MRI examination. Therefore, the effect of IPFP tissue on chondromalacia or joint degeneration should be analyzed in radiological, histopathological and biochemical respects.

Although there are some studies concerning the volume of IPFP tissue in the literature, as far as we know there is no study evaluating the relationship between its sizes and chondromalacia. However, this study has many potential restrictions such as its being a retrospective study, the absence of different parameter measurements such as extremity axis measurements in the knee, the lack of clinical history and examination information of patients.

Conclusions

Consequently, an increase in the risk of patellar chondromalacia and decrease in IPFP sizes are observed with increasing age. We can state that there is a linear relationship between the reduction of IPFP volume and chondromalacia. Therefore, we consider that IPFP tissue should be protected in both the prevention of patellofemoral joint degeneration and reduction of anterior knee pain during the interventions of knee arthroscopy or arthroplasty.

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Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

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Ethical approval

The study protocol was established according to the principles of the Helsinki Declaration by obtaining approval from Adiyaman University Clinical Ethics Committee (2018/8-5) for this study.

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