Journal of Athletic Training 2021;56(11):1173–1179
doi: 10.4085/1062-6050-0458.20

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Changes in Infrapatellar Fat Pad Volume 6 to 12 Months After Anterior Cruciate Ligament Reconstruction and Associations With Patient-Reported Knee Function

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Context: Hypertrophy of the infrapatellar fat pad (IFP) in idiopathic knee osteoarthritis has been linked to deleterious synovial changes and joint pain related to mechanical tissue impingement. Yet little is known regarding the IFP's volumetric changes after anterior cruciate ligament reconstruction (ACLR).

Objectives: To examine changes in IFP volume between 6 and 12 months after ACLR and determine associations between patient-reported outcomes and IFP volume at each time point as well as the volume change over time. In a subset of individuals, we examined interlimb IFP volume differences 12 months post-ACLR.

Study Design: Prospective cohort study.

Setting: Laboratory.

Patients or Other Participants: We studied 26 participants (13 women, 13 men, age = 21.88 ± 3.58 years, body mass index = 23.82 ± 2.21 kg/m^2) for our primary aims and 13 of those participants (8 women, 5 men, age = 21.15 ± 3.85 years, body mass index = 23.01 ± 2.01 kg/m^2) for our exploratory aim.

Main Outcome Measure(s): Using magnetic resonance imaging, we evaluated the IFP volume change between 6 and 12 months post-ACLR in the ACLR limb and between-limbs differences at 12 months in a subset of participants. International Knee Documentation Committee subjective knee evaluation (IKDC) scores were collected at 6-month and 12-month follow-ups, and associations between IFP volume and patient-reported outcomes were determined.

Results: The IFP volume in the ACLR limb increased from 6 months (19.67 ± 6.30 cm^3) to 12 months (21.26 ± 6.91 cm^3) post-ACLR. Greater increases of IFP volume between 6 and 12 months were significantly associated with better 6-month IKDC scores ($r = .44$, $P = .03$). The IFP volume was greater in the uninjured limb (22.71 ± 7.87 cm^3) than in the ACLR limb (20.75 ± 9.03 cm^3) 12 months post-ACLR.

Conclusions: The IFP volume increased between 6 and 12 months post-ACLR; however, the IFP volume of the ACLR limb remained smaller than that of the uninjured limb at 12 months. In addition, those with better knee function 6 months post-ACLR demonstrated greater increases in IFP volume between 6 and 12 months post-ACLR. This suggests that greater IFP volumes may play a role in long-term joint health after ACLR.

Key Words: magnetic resonance imaging, posttraumatic osteoarthritis, knee

Key Points

- The infrapatellar fat pad (IFP) is a dynamic structure that demonstrates volume changes from 6 to 12 months post–anterior cruciate ligament reconstruction (ACLR).
- Greater increases in IFP volume over time correlated with better self-reported knee function at 6 months post-ACLR.
- The IFP volume in the ACLR limb was smaller than that of the uninjured limb at 12 months post-ACLR.

Approximately one-third of those who sustain an anterior cruciate ligament (ACL) injury and undergo ACL reconstruction (ACLR) will develop posttraumatic osteoarthritis (PTOA) of the knee within a decade of ACL injury.[1] Although the precise cause of PTOA remains unknown, pathogenic changes to multiple joint tissue structures are recognized as contributing to PTOA onset and progression.[2] Synovitis of the knee joint is often present early after injury,[2] and changes to joint synovium have been identified as a contributor, or potential trigger, to the early development of PTOA.[3] The joint synovium is known to contain and release a host of cartilage-degrading cytokines and joint-remodeling macrophages early and throughout the progression of osteoarthritis (OA).[4] In addition, synovial inflammation persists after traumatic knee injury and throughout PTOA development.[5] Therefore, early evaluation of the structures associated with synovial changes may improve our understanding of pathologic processes associated with early PTOA onset.

The infrapatellar fat pad (IFP), also known as the Hoffa fat pad, is an intracapsular, extrasynovial adipose structure located in the anterior compartment of the knee.[6,7] The posterior surface of the IFP is lined with synovial tissue, making the IFP a relevant structure for assessing synovial changes at the knee.[8] Similar to the synovium, the IFP is known to be highly vascularized and richly innervated with nociceptor nerve fibers, as well as capable of producing and releasing numerous proinflammatory mediators directly into the joint.[7,9] Synovitis in the anterior infrapatellar region has been strongly associated with patient-reported knee pain in individuals diagnosed with idiopathic OA.[10] In addition, synovitis after ACL injury and ACLR has been shown to induce inflammation and hypertrophy of the IFP.[11] Because inflammation of the IFP and synovial membrane increases after joint trauma, mechanical impingement of the soft tissue is common.[12] Impingement of the IFP may lead to further inflammation, producing a harmful positive-feedback loop of increased IFP hypertrophy, tissue impingement, knee pain, and inflammatory biochemical release.[7,11] It has been hypothesized that mechanical impingement of the IFP after ACLR may be associated with knee-related symptoms and deleterious changes to knee tissues, which may lead to the development of PTOA.[3,5,8]

Evidence is emerging that the IFP functions as an exocrine tissue that contributes to the metabolic processes at the joint.[8,9,11] However, it remains unknown whether the exocrine function is protective or promotes joint tissue breakdown. Results from rodent[13] and sheep[14] models suggested that proinflammatory cells in the IFP may contribute to swelling and fibrosis of the IFP, prolonged synovitis, and development of PTOA after ACLR. Yet researchers[15–18] have hypothesized that healthy IFP tissue may play a protective, energy-absorbing, and lubricating role in those with idiopathic OA, as well as those at risk of PTOA development after knee trauma. Therefore, understanding the role of the IFP after injury may result in the development of novel treatment strategies that target the IFP for the purpose of mitigating degenerative processes after ACL injury. Unfortunately, the early time course of changes to the IFP after ACL injury and ACLR is still unclear. Understanding early, longitudinal changes in IFP volume and how volume associates with patient-reported outcomes is critical for understanding the potential clinical relevance of this structure after ACL injury. Thus, the primary purposes of our study were to determine (1) volume changes of the IFP in the ACLR limb from 6 months to 12 months after unilateral ACLR and (2) associations between IFP volume and patient-reported outcomes at 6 and 12 months post-ACLR. In addition, we investigated associations between IFP volume change and changes in patient-reported outcomes from 6 to 12 months post-ACLR. As an exploratory aim, we sought to examine between-limbs IFP volume differences in a subset of individuals 12 months after unilateral ACLR. We hypothesized that the IFP volume would be greater at 6 months post-ACLR and that the volume would decrease from 6 to 12 months as inflammation subsided. Due to the potential for tissue impingement, we proposed that greater IFP volume would be associated with worse patient-reported outcomes, and a greater decrease in IFP size from 6 to 12 months would be associated with better patient-reported outcomes. For our exploratory aim, we hypothesized that the IFP volume would be greater in the ACLR limb than in the contralateral limb at 12 months post-ACLR due to IFP inflammation and tissue swelling.

METHODS

Study Design

For this longitudinal cohort study, participants were recruited into a larger prospective study of individuals identified on presentation in the orthopaedic clinic with ACL injury and scheduled to undergo ACLR (26 $\pm$ 17 days between consent and ACLR). The data presented in this investigation were collected at 6- and 12-month post-ACLR follow-up visits (195 $\pm$ 21 days and 369 $\pm$ 17 days post-ACLR, respectively). Only participants who attended both the 6- and 12-month follow-ups were included in this study. Magnetic resonance imaging (MRI) of the ACLR limb was obtained at these testing sessions. The MRI scans of the contralateral, uninjured limb were collected on a subset of individuals at the 12-month follow-up examination. Scans of the contralateral limb were not collected for all participants due to time constraints and restrictions in funding. International Knee Documentation Committee subjective knee evaluation (IKDC) scores were collected at the 6- and 12-month follow-up examinations to determine the self-reported function of the cohort. All participants provided informed consent, and the university's institutional review board approved all aspects of this study.

Participants

Participants were between the ages of 18 and 35 years and had sustained an ACL injury within 14 days of consenting to the study (5 $\pm$ 3 days between injury and consent). All participants ($N = 26$, exploratory aim subset $n = 13$; Table 1) underwent unilateral arthroscopic ACLR (31 $\pm$ 17 days after ACL injury) using a bone–patellar tendon–bone autograft, performed by 1 of 3 participating orthopaedic surgeons (G.M.K., R.A.C., J.T.S.). We excluded individuals with a history of ACL injury to either limb and those who sustained a second ACL injury at any point during the study. In addition, we excluded participants who had a previous diagnosis of any form of arthritis, those in need of multiligament reconstruction, and those who sustained a concomitant bone fracture at the time of ACL injury. We also excluded participants who were pregnant at the time of consent or were planning on becoming pregnant during the 12-month observational period.

Patient-Reported Outcomes

The IKDC is a reliable and valid outcome measure for detecting changes in symptoms, sports activity, and function after a knee injury.[19] We administered and

Table 1. Participant Demographics and Outcome Measures

Characteristic		Mean ± SD[a]
Sex, females/males		13/13
Age, y		21.88 ± 3.58
Height, cm		177.70 ± 11.65
Weight, kg		75.69 ± 13.02
Body mass index, kg/m^2		23.82 ± 2.21
Infrapatellar fat pad volume, ACLR limb (n = 26)		
	6 mo, cm^3	19.67 ± 6.30
	12 mo, cm^3	21.26 ± 6.91
	6- to 12-mo percentage change	8.44 ± 9.70
Exploratory aim subset		
Sex, females/males		8/5
Age, y		21.15 ± 3.85
Height, cm		175.06 ± 13.57
Weight, kg		71.09 ± 14.16
Body mass index, kg/m^2		23.01 ± 2.01
Infrapatellar fat pad volume, cm^3		
	12-mo, ACLR limb (n = 13)	20.75 ± 9.03
	12-mo, uninjured limb (n = 13)	22.71 ± 7.87
International Knee Documentation Committee subject knee evaluation score, %		
6 mo (n = 24)		73.35 ± 11.63
12 mo (n = 23)		86.06 ± 11.46
Δ 6 to 12 mo (n = 21)		13.00 ± 10.62

Abbreviation: ACLR, anterior cruciate ligament reconstruction.

[a] Unless otherwise indicated.

collected IKDC outcomes using an electronic internet-based health care informatics system (Socrates GP; Healthcare Ltd) and provided a computer for completion of the questionnaires at the 6- and 12-month follow-up examinations. The IKDC scores were calculated electronically to minimize error and were normalized to 100%, with higher scores indicating better knee function.

Magnetic Resonance Imaging

Magnetic resonance imaging is a valid[20] and widely used imaging modality for measuring IFP volume.[17,18,21] Scans of the contralateral, uninjured limb were also collected for 13 of the 26 participants at the 12-month follow-up. Consistent with methods previously published by our research team,[22] upon arrival to the imaging center, participants were instructed to remain seated for 30 minutes to unload the knee before scanning. For all scans, the participant's knees were positioned in full extension, wrapped with a 4-channel Siemens large flex coil or an XR 80/200 gradient coil, and supported with a cushion as needed.[22] Proton density-weighted, fat-suppressed scans were acquired using a 3-dimensional variable flip angle turbo-spin-echo sequence on 3 Tesla Siemens scanners in our Biomedical Research Imaging Center (Magnetom TIM Trio 3T scanner and Siemens Magnetom Prisma 3T PowerPack scanner). The following sequence specifications were used: repetition time = 1300 milliseconds, echo time = 21 to 22 milliseconds, echo train length = 700 ms/161 echos, slice thickness = 0.5 mm, field of view = 173 × 173 mm^2, matrix = 320 × 320 pixels, and bandwidth = 504 Hz/pixel. The number of slices was adjusted for each participant to cover the whole knee while keeping the slice thicknesses constant.

Segmentation of the IFP

We determined the IFP volume using ITK-SNAP software (version 3.6; http://www.itksnap.org).[23] The IFP volume was first segmented using semiautomated methods based on voxel intensity and then manually edited slice by slice. Manual editing of the semiautomated segmentations was primarily performed in the sagittal view with particular care to exclude the patellar tendon, articular cartilage of the femur and tibia, and menisci. The superior boundary of the IFP was determined at the midpoint between the inferior and superior poles of the patella on its middle slice. In addition, the lateral and medial boundaries of the IFP were identified by locating the medial and lateral edges of the patella. Portions of the IFP extending farther laterally and medially past the patella in the sagittal view were excluded from volume measurements, as described in previous work.[17] Consistent with published methods[17,24] for volumetric analysis of the IFP, anterior and posterior protrusions of the IFP were included but recesses and clefts were excluded in segmentations. Small alterations in the IFP that were completely surrounded by adipose tissue were included in the volume measurements. Segmentations of the IFP generated a 3-dimensional image of the adipose structure (Figure), and overall volumetric outcomes of the IFP (cm^3) were exported for analysis. Segmentations were performed by a single investigator (K.G.W.) with anatomical accuracy confirmed by a fellowship-trained musculoskeletal radiologist (D.N.). Intrarater reliability was established by resegmenting participants' IFPs at least 1 month after initial segmentation (n = 8, intraclass correlation coefficient = 0.99).

Statistical Analyses

Based on the results of a previous study[18] of IFP volume and patient-reported knee function in patients with patellofemoral OA, we estimated that IFP volume and patient-reported knee function would be moderately associated ($r = .50$). We determined a minimum of 19 participants would be needed to detect a statistically significant association with a similar effect ($1–\beta = 0.8$, $\alpha = .05$; G*Power, version 3.1.9.2).[25] We recruited a total of 26 participants to account for an attrition rate of 25%. The level of significance for all analyses was determined a priori at $P \leq .05$.

Before any analyses, we calculated the percentage of change in IFP volume as well as the absolute change in IKDC scores from 6 to 12 months. Means and SDs were calculated for participant demographics, 6- and 12-month IFP volumes, percentage of change of IFP volumes, IKDC scores, and IKDC change scores. A dependent *t* test was used to assess differences between IFP volumes in the ACLR limb at the 6- and 12-month follow-up examinations. Pearson product moment correlations were conducted to determine associations between IFP volume in the ACLR limb at the 6- and 12-month follow-up visits and IKDC scores at these time points. Next, we calculated Pearson product moment correlations to assess the association between percentage of change in IFP volume and absolute

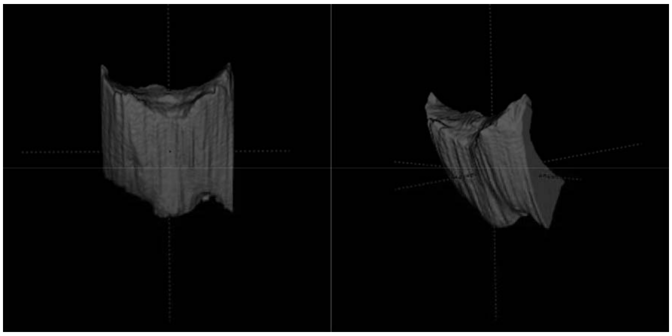

Figure. Example of a 3-dimensional rendering of an infrapatellar fat pad (IFP) segmentation. The segmentation clearly depicts the boundaries established at the medial and lateral edges of the patella. Anterior and posterior protrusions as well as small alterations within the IFP that were completely surrounded by adipose tissue were included. Recesses and clefts in the IFP were excluded.

change in IKDC scores from 6 to 12 months post-ACLR. Before our exploratory analysis, an independent *t* test was used to determine whether statistical differences existed between injured IFP volumes of the subsample with bilateral MRI scans and those with only a unilateral scan at the 12-month follow-up. Then a dependent *t* test was performed to assess interlimb differences of IFP volume between the ACLR limb and contralateral uninjured limb in the cohort with bilateral 12-month scans. Associations were classified as *negligible* (0.0–0.3), *low* (0.31–0.5), *moderate* (0.51–0.7), *high* (0.71–0.9), and *very high* (0.9–1.0).[26] We considered all analyses to be statistically significant with *P* values $\leq$ .05. All statistical analyses were performed using SPSS (version 21.0; IBM Corp).

Post Hoc Analyses

Separate stepwise linear regression models controlling for participant body mass index (BMI) and sex were conducted to assess associations of 6- and 12-month IFP volumes and volume change with patient-reported outcomes at corresponding time points. Earlier evidence[27,28] indicated that IFP volume may be influenced by these 2 factors. Previous authors have also accounted for participant age in IFP volume measurements; however, we did not control for age in these analyses owing to the relatively young age and narrow age range of our cohort. In addition, due to our relatively small sample size and in order to avoid overfitting our model, regressions accounting for BMI and sex were conducted separately. For each stepwise linear regression, the first predictor variable that was entered was participant BMI or sex. The IKDC scores at 6 and 12 months post-ACLR and the absolute change in IKDC scores between 6 and 12 months were used as the criterion variables. We evaluated the change in R^2 to determine the unique associations of IFP volume and volume change with IKDC scores after separately accounting for BMI and sex.

RESULTS

Mean IFP Volume Change in the ACLR Limb and Interlimb Mean Differences

For the 26 participants in the entire cohort, IFP volume increased by an average of 8.4% from the 6- to 12-month

Table 2. Associations Between Infrapatellar Fat Pad Volume and Volume Change (Anterior Cruciate Ligament Reconstruction Limb) and International Knee Documentation Committee Scores

International Knee Documentation Committee Subject Knee Evaluation Score	Infrapatellar Fat Pad Volume, *r* (*P* Value)		
	6 mo	12 mo	Percentage Δ
6 mo (n = 24)	−0.12 (.57)	<0.001 (.99)	0.44 (.03)[a]
12 mo (n = 23)	−0.09 (.67)	−0.06 (.78)	0.11 (.62)
Δ 6 to 12 mo (n = 21)	0.01 (.96)	−0.10 (.66)	−0.39 (.08)

[a] Denotes statistically significant association ($P < .05$).

follow-up examinations ($t_{25} = -3.92$, $P = .001$). For our bilateral IFP analysis, no differences were found in injured IFP volume between the cohort with bilateral MRI scans (n = 13) and those with unilateral scans (n = 13) at the 12-month follow-up ($t_{24} = 0.370$, $P = .715$). In this subset of participants, we observed that IFP volume was on average 13.4% greater in the uninjured limb than in the ACLR limb at 12 months post-ACLR ($t_{12} = -2.53$, $P = .03$; Table 1).

Associations of IFP Volume and Volume Change in the ACLR Limb With IKDC Scores

The IKDC was completed by 24 participants at 6 months and 23 at 12 months. A total of 21 participants completed the survey at both time points and, therefore, 21 participants were included in this analysis. A significant association was present between a greater increase in IFP volume from 6 to 12 months and a better 6-month IKDC score ($r = 0.44$, $P = .03$). Albeit not significant, a notable association occurred between a greater increase in IFP volume from 6 to 12 months and smaller increase in IKDC score from 6 to 12 months ($r = -0.39$, $P = .08$). No other associations between 6- or 12-month IFP volume and IKDC score at any time point or change in IKDC scores were demonstrated (Table 2).

Post Hoc Analyses

After accounting for BMI, a greater increase in IFP volume from 6 to 12 months post-ACLR was associated with a better 6-month IKDC score ($\Delta R^2 = 0.17$, standardized β coefficient = 0.42, $P = .04$). In addition, after accounting for sex, a greater increase in IFP volume from 6 to 12 months post-ACLR was associated with a better 6-month IKDC score ($\Delta R^2 = 0.19$, standardized β coefficient = 0.44, $P = .04$). Although not significant, notable associations existed between a greater increase in IFP volume from 6 to 12 months and a smaller IKDC score increase from 6 to 12 months after separately accounting for BMI ($\Delta R^2 = 0.11$, standardized β coefficient = −0.34, $P = .12$) and sex ($\Delta R^2 = 0.15$, standardized β coefficient = −0.39, $P = .08$; Table 3).

DISCUSSION

Contrary to our hypothesis, IFP volume in the ACLR limb increased from 6 to 12 months post-ACLR. In addition, a greater increase in IFP volume between 6 and 12 months was associated with a better patient-reported outcome at 6 months. In the cohort that underwent bilateral MRI scans, IFP volume was larger in the uninjured limb than in the ACLR limb at the 12-month follow-up. Our study was the first to examine changes in the IFP volume in humans at early and clinically relevant time points after

Table 3. Post Hoc Analyses Accounting for Body Mass Index or Sex, Anterior Cruciate Ligament Reconstruction Limb

Controlled For International Knee Documentation Committee Subject Knee Evaluation Score	Infrapatellar Fat Pad Volume, ΔR^2 (Standardized β)					
	6 mo		12 mo		Percentage Δ	
	BMI	Sex	BMI	Sex	BMI	Sex
6 mo (n = 24)	0.00 (−0.06)	0.03 (−0.18)	0.01 (0.07)	0.00 (−0.04)	0.17[a] (0.42)	0.19[a] (0.44)
12 mo (n = 23)	0.02 (−0.15)	0.00 (−0.06)	0.01 (−0.10)	0.00 (−0.03)	0.02 (0.14)	0.01 (0.11)
Δ 6 to 12 mo (n = 21)	0.01 (−0.10)	0.01 (0.13)	0.04 (−0.21)	0.00 (−0.00)	0.11 (−0.34)	0.15 (−0.39)

Abbreviation: BMI, body mass index.

[a] Denotes significant ΔR^2 value ($P \leq .05$).

ACL injury and ACLR. Furthermore, this was the first to demonstrate changes in IFP volume over time and associations with patient-reported outcomes of knee function. Last, our work provides a novel between-limbs comparison demonstrating smaller IFP volume in the ACLR limb than in the contralateral uninjured limb at 12 months post-ACLR. Our finding that the IFP is a dynamic structure after ACLR can be used to justify the need for further examination of the role of the IFP in promoting long-term joint health.

It is unclear whether the increases (1.59 cm^3, 8.4%) in IFP volume between 6 and 12 months after ACLR reflected a return to presurgical volume or hypertrophy that exceeded the presurgical IFP volume in the injured limb. Our exploratory between-limbs comparison showed that the IFP in the ACLR limb remained smaller than in the uninjured limb at 12 months post-ACLR. The overall smaller IFP of the ACLR limb may negate the biomechanical mechanism behind our initial hypothesis that greater IFP volume after ACLR leads to impingement and pain in the ACLR limb. The mechanisms related to the smaller IFP volumes in the ACLR limb remain unknown, yet they may be due to tissue damage or removal of a portion of the IFP during ACLR surgery. Partial IFP excision may occur while harvesting the bone–patellar tendon–bone graft from the middle third of the tendon and is common during routine surgical debridement for easier access to the intercondylar notch.[29] Different theories have been proposed regarding the efficacy of IFP resection during ACLR and arthroplasty for the purpose of alleviating anterior knee pain resulting from IFP tissue impingement. Some fully embrace the procedure as a means of removing damaged tissue or relieving intra-articular pressure,[7,30] whereas many warn against removal of the adipose tissue because it may have negative biomechanical or metabolic implications.[16,21,31] Our results suggest the need to determine whether smaller IFP volumes after ACLR may be linked to deleterious changes to joint tissue. Furthermore, future researchers should examine IFP volumes bilaterally and include presurgical baseline assessments of IFP volume because surgical procedures may directly affect IFP volume in the ACLR limb. Investigating bilateral changes in IFP volumes at time points before and after ACLR, including time points beyond 12 months, will provide a more accurate characterization of whether IFP volumes increase to normal volumes or continue to excessively hypertrophy after ACLR.

Although we did not find associations between 6- or 12-month IFP volume and IKDC scores, we did find significant associations between a greater IFP volume change from 6 to 12 months and a better 6-month IKDC score. Thus, perhaps those with greater subjective knee function at 6 months post-ACLR also experience a greater increase in IFP volume from 6 to 12 months. In addition, it is possible that these participants had a larger increase in IFP volume from the time of ACLR to the 6-month examination, but without a presurgical volume measure, this explanation remains speculative. Our study was not designed to determine the mechanistic nature linking IFP volume and IKDC score after ACLR; however, the IFP can be considered an active exocrine tissue[9] that contributes to the secretion of different inflammatory mediators that may affect the healing process after ACLR or progression of knee OA. Recent work[32] demonstrated that IFP abnormalities noted on MRI after ACL injury were associated with higher synovial fluid concentrations of inflammatory cytokines and markers related to cartilage breakdown,[32] suggesting a link between alterations in the IFP and joint tissue metabolism. Furthermore, Cai et al[15] determined that a greater IFP volume of 1 cm^3 was associated with greater knee cartilage volume (30–80 cm^3) and a reduced prevalence of knee cartilage defects (10%–12%), bone marrow lesions (9%–12%), and osteophyte formation (12%) in individuals with idiopathic OA. Moreover, Bastiaansen-Jenniskens et al[33] concluded that the IFP of patients with idiopathic OA was capable of inhibiting catabolic mediators while promoting collagen type II gene expression in the cartilage. However, the potential chondroprotective influence of the IFP should be interpreted with caution on the basis of the Cai et al[15] and Bastiaansen-Jenniskens et al[33] results, because their patients were already diagnosed with idiopathic OA. Yet evidence is emerging to suggest that MRI-assessed IFP abnormalities may be associated with deleterious compositional changes in the articular cartilage of the femoral trochlea consistent with decreased proteoglycan density and disorganization of type II collagen linked with PTOA development.[32] Therefore, suboptimal functioning of the IFP may be linked to PTOA-related changes in other joint tissues. Future research is needed to better characterize the role of the IFP in PTOA development and whether changes in IFP volume indicate biological changes associated with joint tissue metabolism after ACLR.

This investigation provided important preliminary information regarding IFP volume changes in young adults after ACLR, but it is important to consider the limitations of the study. Due to the relatively small sample size of this cohort, we focused our analyses on simple associations of IFP volume and volume change with patient-reported outcomes. In addition, in our post hoc analyses, and to avoid overfitting our model, we were only able to control for BMI and sex in separate regressions. A larger sample size would allow us to better understand the associations between IFP volume and subjective knee function by controlling for multiple confounding variables in a multivariate model. Also, we were only able to acquire bilateral MRI scans on a relatively small subset of our participants (n = 13) and only at the 12-month follow-up examination. Previous authors[17] demonstrated no difference in IFP volume between uninjured control individuals and patients 2 to 3 years post-ACLR, suggesting that IFP volume may normalize in patients with ACLR over time. Future researchers should perform longitudinal studies to examine bilateral differences at earlier time points, as well as before ACLR. In addition, we were unable to control for the time of day when the MRI was obtained. Investigators should evaluate possible diurnal effects on the IFP after ACLR. Furthermore, we acknowledge that a lack of presurgical IFP volume measurements is a limitation of this study, but we were able to demonstrate changes in IFP volume over time and at clinically relevant time points post-ACLR. For subsequent studies, a presurgical assessment of the IFP will be critical to elucidate the exact morphology of the IFP after ACL injury and ACLR. Although a strength of this study was the uniform surgical technique and ACLR autograft selection, given that the entire cohort received bone–patellar tendon–bone autografts, future researchers may also wish to evaluate whether different graft types affect IFP volume after ACLR. We believe that researchers can build upon this preliminary study to longitudinally track bilateral IFP volume change from presurgery to time points beyond 12 months. In addition, this preliminary study examined only subjective, patient-reported knee function, and it will be important to understand how IFP volume post-ACLR correlates with measurable patient biomechanics and functional activity as well as potential biochemical changes. These future explorations will help to determine the importance of the IFP in PTOA development and potentially promoting long-term joint health after ACLR.

CONCLUSIONS

The IFP volume in the ACLR limb increased from 6 to 12 months after ACLR. Also, the IFP was larger in the contralateral uninjured limb than in the ACLR limb at the 12-month examination. Last, although we did not find any significant associations between IFP volume and patient-reported knee function at 6 or 12 months, the change in IFP volume between those time points was significantly associated with patient-reported outcomes at 6 months post-ACLR. These findings do not rule out the potential that greater IFP volume protects the knee and highlight the importance of maintaining IFP volume after ACLR.

ACKNOWLEDGMENTS

Research reported in this original manuscript was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health (1R03AR066840-01A1), North Carolina Translational and Clinical Sciences (TRaCS) Institute, and National Athletic Trainers' Association Research and Education Foundation (No. 14NewInv001).

REFERENCES

1. Luc B, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. *J Athl Train*. 2014;49(6):806–819. doi:10.4085/1062-6050-49.3.35
2. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. *Arthritis Rheum*. 2012;64(6):1697–1707. doi:10.1002/art.34453
3. Berenbaum F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis Cartilage*. 2013;21(1):16–21. doi:10.1016/J.JOCA.2012.11.012
4. Hügle T, Geurts J. What drives osteoarthritis?—synovial versus subchondral bone pathology. *Rheumatology*. 2016;56(9):1461–1471. doi:10.1093/rheumatology/kew389
5. Lieberthal J, Sambamurthy N, Scanzello CR. Inflammation in joint injury and post-traumatic osteoarthritis. *Osteoarthritis Cartilage*. 2015;23(11):1825–1834. doi:10.1016/j.joca.2015.08.015
6. Biedert RM, Sanchis-Alfonso V. Sources of anterior knee pain. *Clin Sports Med*. 2002;21(3):335–347, vii. doi:10.1016/s0278-5919(02)00026-1
7. Dragoo JL, Johnson C, McConnell J. Evaluation and treatment of disorders of the infrapatellar fat pad. *Sports Med*. 2012;42(1):51–67. doi:10.2165/11595680-000000000-00000
8. Macchi V, Stocco E, Stecco C, et al. The infrapatellar fat pad and the synovial membrane: an anatomo-functional unit. *J Anat*. 2018;233(2):146–154. doi:10.1111/joa.12820
9. Clockaerts S, Bastiaansen-Jenniskens YM, Runhaar J, et al. The infrapatellar fat pad should be considered as an active osteoarthritic joint tissue: a narrative review. *Osteoarthritis Cartilage*. 2010;18(7):876–882. doi:10.1016/j.joca.2010.03.014
10. Hill CL, Hunter DJ, Niu J, et al. Synovitis detected on magnetic resonance imaging and its relation to pain and cartilage loss in knee osteoarthritis. *Ann Rheum Dis*. 2007;66(12):1599–1603. doi:10.1136/ard.2006.067470
11. Eymard F, Chevalier X. Inflammation of the infrapatellar fat pad. *Joint Bone Spine*. 2016;83(4):389–393. doi:10.1016/j.jbspin.2016.02.016
12. Lapègue F, Sans N, Brun C, et al. Imaging of traumatic injury and impingement of anterior knee fat. *Diagn Interv Imaging*. 2016;97(7–8):789–807. doi:10.1016/j.diii.2016.02.012
13. Wang CY, Tsai PH, Siow TY, et al. Change in T2* relaxation time of Hoffa fat pad correlates with histologic change in a rat anterior cruciate ligament transection model. *J Orthop Res*. 2015;33(9):1348–1355. doi:10.1002/jor.22914
14. Solbak NM, Heard BJ, Achari Y, et al. Alterations in Hoffa's fat pad induced by an inflammatory response following idealized anterior cruciate ligament surgery. *Inflamm Res*. 2015;64(8):615–626. doi:10.1007/s00011-015-0840-y
15. Cai J, Xu J, Wang K, et al. Association between infrapatellar fat pad volume and knee structural changes in patients with knee osteoarthritis. *J Rheumatol*. 2015;42(10):1878–1884. doi:10.3899/jrheum.150175
16. Han W, Cai S, Liu Z, et al. Infrapatellar fat pad in the knee: is local fat good or bad for knee osteoarthritis? *Arthritis Res Ther*. 2014;16(4):R145. doi:10.1186/ar4607
17. Van Ginckel A, Fortin K, Bennell KL, et al. Associations between infra-patellar fat pad volume and knee joint structure in young adults at 2–3 years after anterior cruciate ligament reconstruction and healthy controls: a cross-sectional analysis. *Osteoarthritis Cartilage*. 2017;25(suppl 1):S228–S229. doi:10.1016/j.joca.2017.02.392
18. Cowan SM, Hart HF, Warden SJ, Crossley KM. Infrapatellar fat pad volume is greater in individuals with patellofemoral joint osteoarthritis and associated with pain. *Rheumatol Int*. 2015;35(8):1439–1442. doi:10.1007/s00296-015-3250-0
19. Higgins LD, Taylor MK, Park D, et al. Reliability and validity of the International Knee Documentation Committee (IKDC) Subjective Knee Form. *Joint Bone Spine*. 2007;74(6):594–599. doi:10.1016/j.jbspin.2007.01.036

20. Chuckpaiwong B, Charles HC, Kraus VB, Guilak F, Nunley JA. Age-associated increases in the size of the infrapatellar fat pad in knee osteoarthritis as measured by 3T MRI. *J Orthop Res*. 2010;28(9):1149–1154. doi:10.1002/jor.21125
21. Roemer FW, Jarraya M, Felson DT, et al. Magnetic resonance imaging of Hoffa's fat pad and relevance for osteoarthritis research: a narrative review. *Osteoarthritis Cartilage*. 2016;24(3):383–397. doi:10.1016/j.joca.2015.09.018
22. Pietrosimone B, Pfeiffer SJ, Harkey MS, et al. Quadriceps weakness associates with greater T1ρ relaxation time in the medial femoral articular cartilage 6 months following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(8):2632–2642. doi:10.1007/s00167-018-5290-y
23. Yushkevich PA, Piven J, Hazlett HC, et al. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage*. 2006;31(3):1116–1128. doi:10.1016/j.neuroimage.2006.01.015
24. Ruhdorfer AS, Wirth W, Dörrenberg J, Kwoh CK, Hunter DJ, Eckstein F. Longitudinal change in infrapatellar fat pad volume and MRI signal prior to total knee replacement—data from the osteoarthritis initiative. *Osteoarthritis Cartilage*. 2017;25(suppl 1):S74–S75. doi:10.1016/j.joca.2017.02.131
25. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39(2):175–191. doi:10.3758/BF03193146
26. Mukaka MM. Statistics corner: a guide to appropriate use of correlation coefficient in medical research. *Malawi Med J*. 2012;24(3):69–71.
27. Burda B, Steidle-Kloc E, Dannhauer T, Wirth W, Ruhdorfer A, Eckstein F. Variance in infra-patellar fat pad volume: does the body mass index matter?—Data from Osteoarthritis Initiative participants without symptoms or signs of knee disease. *Ann Anat*. 2017;213:19–24. doi:10.1016/J.AANAT.2017.04.004
28. Diepold J, Ruhdorfer A, Dannhauer T, Wirth W, Steidle E, Eckstein F. Sex-differences of the healthy infra-patellar (Hoffa) fat pad in relation to intermuscular and subcutaneous fat content—data from the Osteoarthritis Initiative. *Ann Anat*. 2015;200:30–36. doi:10.1016/j.aanat.2014.12.004
29. Sonnery-Cottet B, Archbold P, Zayni R, et al. High lateral portal for sparing the infrapatellar fat-pad during ACL reconstruction. *Orthop Traumatol Surg Res*. 2011;97(8):870–873. doi:10.1016/J.OTSR.2011.08.007
30. Doner GP, Noyes FR. Arthroscopic resection of fat pad lesions and infrapatellar contractures. *Arthrosc Tech*. 2014;3(3):e413–e416. doi:10.1016/j.eats.2014.04.002
31. Teichtahl AJ, Wulidasari E, Brady SR, et al. A large infrapatellar fat pad protects against knee pain and lateral tibial cartilage volume loss. *Arthritis Res Ther*. 2015;17(1):318. doi:10.1186/s13075-015-0831-y
32. Heilmeier U, Mamoto K, Amano K, et al. Infrapatellar fat pad abnormalities are associated with a higher inflammatory synovial fluid cytokine profile in young adults following ACL tear. *Osteoarthritis Cartilage*. 2020;28(1):82–91. doi:10.1016/j.joca.2019.09.001
33. Bastiaansen-Jenniskens YM, Clockaerts S, Feijt C, et al. Infrapatellar fat pad of patients with end-stage osteoarthritis inhibits catabolic mediators in cartilage. *Ann Rheum Dis*. 2012;71(2):288–294. doi:10.1136/ard.2011.153858

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