Recreational Runners with Patellofemoral Pain Exhibit Elevated Patella Water Content

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Recreational runners with patellofemoral pain exhibit elevated patella water content

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Abstract

Increased bone water content resulting from repetitive patellofemoral joint overloading has been suggested to be a possible mechanism underlying patellofemoral pain (PFP). To date, it remains unknown whether persons with PFP exhibit elevated bone water content. The purpose of this study was to determine whether recreational runners with PFP exhibit elevated patella water content when compared to pain-free controls. Ten female recreational runners with a diagnosis of PFP (22 to 39 years of age) and 10 gender, age, weight, height, and activity matched controls underwent chemical-shift-encoded water-fat magnetic resonance imaging (MRI) to quantify patella water content (i.e., water-signal fraction). Differences in bone water content of the total patella, lateral aspect of the patella, and medial aspect of the patella were compared between groups using independent t tests. Compared with the control group, the PFP group demonstrated significantly greater total patella bone water content (15.4 ± 3.5% vs. 10.3 ± 2.1%; P = 0.001), lateral patella water content (17.2 ± 4.2% vs. 11.5 ± 2.5%; P = 0.002), and medial patella water content (13.2 ± 2.7% vs. 8.4 ± 2.3%; P < 0.001). The higher patella water content observed in female runners with PFP is suggestive of venous engorgement and elevated extracellular fluid. In turn, this may lead to an increase in intraosseous pressure and pain.

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1. Introduction

Patellofemoral pain (PFP) is the most common overuse injury in runners, and accounts for 25% of injuries treated in orthopedic clinics [1]. In spite of the high prevalence of PFP in persons who are physically active, little is known about the mechanism(s) underlying the development of PFP. It has been hypothesized that PFP is the result of chronic overloading of highly innervated subchondral bone [2]. For example, previous work from our group has shown that individuals with PFP exhibit greater patellofemoral joint stress during weight-bearing activities when compared to persons without pain [3]. Elevated loading of the patellofemoral joint has been hypothesized to result in articular cartilage breakdown [4], elevated subchondral bone metabolic activity [2], and increased bone water content [5]. Hejgaard and Arnoldi [6] have reported that elevated intraosseous pressure within the patella is associated with pain in persons with patellofemoral joint osteoarthritis. Elevated intraosseous pressure is thought to be the result of systemic increases in bone water content (i.e., venous stasis) [7], and/or focal accumulation of extracellular fluid within the trabeculae (i.e., bone marrow lesions) [8]. Given that mechanical nociceptors are sensitive to pressure, intraosseous hypertension could create a noxious environment for the highly-innervated subchondral bone [6].

To date, it is unknown whether persons with PFP exhibit elevated bone water content. Such information is relevant as the presence of elevated bone water content could explain the tendency of persons with PFP to exhibit increased symptoms following a bout of repetitive loading (i.e., running). Using a chemical-shift-encoded water-fat magnetic resonance imaging (MRI) protocol [9,10], the purpose of this preliminary study was to compare patella water content between female runners with and without PFP. We hypothesized that the PFP group would demonstrate elevated patella water content when compared to the control group. Information obtained from this investigation may provide 1) potential insight into the cause of patellofemoral symptoms in runners, and 2) the feasibility of measuring water content in bone marrow in this population.

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Table 1
Subject characteristics (mean ± standard deviation).

<table>
<thead>
<tr>
<th></th>
<th>Patellofemoral pain group (n = 10)</th>
<th>Control group (n = 10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>25.1 ± 4.7</td>
<td>25.8 ± 6.1</td>
<td>0.78</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>0.97</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59.7 ± 9.3</td>
<td>59.8 ± 7.1</td>
<td>0.45</td>
</tr>
<tr>
<td>Activity level, MET.min/week</td>
<td>2168.0 ± 960.1</td>
<td>19440 ± 859.0</td>
<td>0.39</td>
</tr>
<tr>
<td>Distance of running, miles/week</td>
<td>15.9 ± 6.3</td>
<td>15.5 ± 6.9</td>
<td>0.88</td>
</tr>
<tr>
<td>Anterior Knee Pain Scale*</td>
<td>89.0 ± 5.7</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms, months</td>
<td>57.6 ± 28.8</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

* A score of 100 on the Anterior knee Pain Scale indicates no anterior knee pain or disability.

2. Materials and methods

2.1. Subjects

Twenty female subjects were recruited for this study (10 with a diagnosis of PFP and 10 pain-free controls; Table 1). The data presented here for subjects in the PFP group have been reported in a previous publication [11]. All subjects were recreational runners who ran at least 6 miles per week. Individuals with PFP were admitted to the study if their pain originated from behind the patella (i.e., retropatellar pain), and reported an insidious onset of symptoms of at least 3 months in duration. All subjects in the PFP group reported symptoms with running. Prior to participation, all subjects were informed of the nature of the study and signed a human subjects’ consent form approved by the Health Sciences Institutional Review Board of the University of Southern California.

Subjects were screened through physical examination to rule out concomitant sources of pain. This process included palpation of the soft tissues around the patellofemoral joint to identify the location of pain. If the source of pain was localized to the quadriceps tendon, patellar tendon, patella bursa, patella fat pad, tibio-femoral joint, or the lateral and medial joint line, the subject was disqualified from the study. Persons with PFP also were excluded from participation if they reported having any of the following: 1) history of knee surgery, 2) history of traumatic patellar dislocation, or 3) implanted biological devices that could interact with the magnetic field.

Subjects in the control group were age, height, weight, and activity matched (<10% difference) to those in the PFP group. Subjects’ physical activity levels were determined based on the World Health Organization’s Global Physical Activity Questionnaire. This questionnaire has been reported to provide a valid and reliable estimate of physical activity [12]. Subject selection for the control group was based on the same criteria as the experimental group except that these subjects had no history of PFP.

2.2. Image acquisition

Prior to the MRI assessment, subjects were asked to refrain from sport or vigorous activity for 1 day. In addition, subjects refrained from weight-bearing for 1 hour prior to imaging. This was accomplished by having subjects sit in a chair, and was done to control for potential load-induced increases in bone water content [13]. For subjects in the PFP group, imaging was performed on the symptomatic side. For subjects with bilateral pain, the more painful side was evaluated. The limb evaluated in the control subjects was matched to that of their counterpart in the PFP group.

MRI scanning was performed on a 3.0 Tesla General Electric scanner (Excite HD, GE Healthcare, Milwaukee, WI, USA) with an 8-element knee coil. An investigational version of GE Healthcare’s water-fat MRI technique (i.e., IDEAL) was utilized [10]. Briefly, this form of MRI technique exploits the differences in resonance frequency (e.g. chemical-shift) to accurately separate on a voxel-wise basis the component signals of protons from unbound free water and fat from the underlying tissue. A subsequent water fraction map can then be computed for quantitative analysis. The quantitative accuracy of the IDEAL method in measuring water and fat fractions has recently been validated in the bone marrow against MR spectroscopy [14]. Current literature has also demonstrated that the IDEAL technique provides a strong reproducibility in fat fraction estimation [15].

A 3-dimensional multi-echo spoiled-gradient-echo pulse sequence that incorporated signal relaxation compensation (e.g. T1, T2*) [16,17] and a 6-peak fat spectrum in the IDEAL reconstruction algorithm [17] was utilized in this study. The scan parameters were: TR = 20.2 ms, 1st TE = 1.68 ms, echo spacing = 0.98 ms, 6 echoes, echo train length = 2, flip angle = 5°, slice thickness = 2 mm, FOV = 160 × 160 mm, matrix = 224 × 224, BW = ±125 kHz, scan time = 9 minutes 50 seconds. Each subject was positioned supine with full knee extension during the MRI examination.

2.3. Image analysis

Since the IDEAL technique was originally designed to measure organ steatosis, the default reconstruction software provided by GE Healthcare automatically returned individual series of water-only, fat-only, and fat fraction maps (fat/[fat + water]x100%) (Fig. 1). For purposes of this study, we performed additional post-processing analysis using ImageJ software (National Institutes of Health, Bethesda, MD, USA). First, the subchondral bone region on the fat fraction maps (defined as the bright region under articular cartilage) was manually contoured on all image slices containing the patella (Fig. 1 C). A single region of interest was then identified on each image slice.

The average fat fraction of each region of interest was obtained by averaging the signal intensities of all voxels within the region of interest. The water fraction of each region of interest was then

Fig. 1. Default output of IDEAL water-fat MRI: (A) water-only image; (B) fat-only image; (C) fat fraction map. A region of interest was contoured on the fat fraction map (dashed line), and the average water fraction of the region of interest was calculated as 100-far fraction (%).
computed by simply subtracting the fat fraction from 100%. Next, Eq. (1) was used to compute the total percent water content of all images measured [11].

\[
\text{Water Content (\%)} = \frac{\sum_{n=1}^{n} \text{Water Fraction}(n) \times \text{Area Measured}(n)}{\sum_{n=1}^{n} \text{Area Measured}(n)}
\]

, where \(n\) is number of images.

We further evaluated the patella water content with respect to the lateral and medial aspects of the patella. As the images were obtained in sagittal plane, an indirect approach was utilized (Fig. 2). First, the median ridge of the patella was located on the reformatted axial plane image. Once the median ridge was identified, all sagittal plane images located lateral to the median ridge were used to evaluate the water content within this region. Similarly, all sagittal plane slices located medial to the median ridge were used to estimate the water content of the medial aspect of the patella. Eq. (1) was used to compute the percent water content of all images measured within the lateral and medial aspects of the patella.

2.4. Statistical analysis

Independent t tests were used to compare total patella water content, lateral patella water content, and medial patella water content between the PFP and control groups. All statistical analysis was performed on SPSS 18.0 statistical software (International Business Machines Corp., Armonk, NY, USA) using a significance level of 0.05.

3. Results

Representative water fraction maps for a subject with PFP and a control subject are presented in Fig. 3. When compared with the control group, subjects with PFP exhibited significantly greater total patella water content (15.4 ± 3.5 vs. 10.3 ± 2.1%; \(P = 0.001\)). In addition, the PFP group also exhibited greater water content within lateral aspect of the patella (17.2 ± 4.2 vs. 11.5 ± 2.4%; \(P = 0.002\)), as well as medial aspect of the patella (13.2 ± 2.7 vs. 8.4 ± 2.3%; \(P < 0.001\)) (Fig. 4).

4. Discussion

The purpose of the current study was to test the hypothesis that recreational runners with PFP would exhibit elevated patella water content when compared to pain-free controls. Our data support this hypothesis in that the PFP group demonstrated significantly higher total patella water content compared to those without PFP. On average, the difference in water content for the entire patella was 50% higher in the PFP group. When the medial and lateral aspects of the patella were considered separately, similar increases of patella water content were observed.

Our study is the first to evaluate patella water content in persons with PFP. Although normal values for patella water content have not been previously established, it has been reported that the water content in the healthy calcaneus is approximately 10% in persons.
between 20 to 30 years of age [18]. This value is consistent with the observed patella water content of the control group (10.3%). In contrast, the average percentage of patella water content in persons in the PFP group (15.5%) is similar to what has been reported in persons with advanced tibio-femoral arthritis using magnetic resonance spectroscopy (14.3%) [5]. Our finding of elevated patella water content in the PFP group is suggestive of subchondral bone edema in this young, active population.

Intraosseous hypertension resulting from venous engorgement has been hypothesized to be a possible mechanism of pain in persons with advanced patellofemoral osteoarthritis [6,7]. More specifically, it has been suggested that increased arterial blood flow combined with increased resistance to venous outflow are factors responsible for intramedullary hypertension in degenerated bones [7]. Barton and colleagues [19] have reported that the complex intraosseous nerve network within the patella is accompanied by intraosseous capillaries. Furthermore, Wojtys et al. [20] have demonstrated abnormal erosion channels at the bone–cartilage interface in degenerated patella (i.e., tidemark region), a region in which there is a close spatial relationship between substance P (a neural transmitter enhancing capillary system in the patella, it has been suggested that patella hypertension may be a possible pain mechanism in persons who have patellofemoral joint osteoarthritis [7]. Given our finding of a systemic increase in bone water content in female runners with PFP, it is conceivable that such an increase in patella water content may contribute to the propensity for retropatellar pain during running.

In this study, we used a chemical-shift-encoded water-fat MRI protocol to evaluate the feasibility of assessing patella water content. The technique appears to have adequate sensitivity in differentiating between persons with PFP and those without symptoms. We propose that bone water content derived from water-fat MRI protocols may be useful as a biomarker for the early detection of bone abnormalities in this population. Due to limited funding and MRI scan time, only 10 PFP and 10 control subjects were involved in this preliminary study. Future large-scale clinical studies are necessary to assess bone water fraction in persons with and without symptoms. In addition, validation studies that compare IDEAL MRI against other traditional pulse sequences (e.g., T2 FSE) [21] in this cohort are also needed.

With respect to the findings of the current study, there are 2 limitations. First, only young, active females were evaluated. As such, caution should be taken when generalizing our results to all persons with PFP. Second, as this study was aimed to determine the influence of excessive patellofemoral joint loading on patella water content, only persons with retropatellar symptoms were studied. The proposed mechanism of pain described above may not be applicable to patients who have peripatellar or infrapatellar pain. Future work that evaluates bone water content in other PFP populations (e.g., males or persons with different origins of pain) will provide further informative insights into the mechanism(s) of PFP.

5. Conclusion

On average, the PFP group exhibited 50% greater patella water content when compared with pain-free controls. The higher patella water content observed in this study is suggestive of venous engorgement and elevated extracellular fluid. Such an increase in extracellular fluid may contribute to increases in intraosseous pressure and patellofemoral symptoms.

Acknowledgments

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