Lower Mechanical Pressure Pain Thresholds in Female Adolescents With Patellofemoral Pain Syndrome

Self-reported knee pain is highly prevalent among adolescents. Cross-sectional studies show that 19% to 31% of adolescents report knee pain of different etiologies. As much as 50% of the nonspecific anterior knee pain among adolescents may be attributed to patellofemoral pain syndrome (PFPS). The prevalence of PFPS among high school students does not appear to be equally distributed across both genders, with females having a higher prevalence than males. PFPS is a broad definition of pain felt anteriorly around the patella, which increases during prolonged sitting, squatting, kneeling, and stair climbing.

Although the exact origin of patellofemoral pain is unknown, it is proposed to be secondary to excessive patellofemoral joint stress caused by abnormal patellar tracking. Tissue injury may lead to sensitization of peripheral nociceptors, hence increasing perceived pain. Continued peripheral nociceptive input over a long period, especially with high pain levels, is associated with reduced pressure pain threshold (PPT) both locally (localized hyperalgesia) and remotely from the site of reported pain (distal hyperalgesia). However, it is not known if symptom duration or pain intensity is associated with PPTs in adolescent females with PFPS or if this association may be confounded by quality of life, as previously shown among females with chronic nonmalignant pain.

Pressure algometry provides measurement of PPT both at the location of pain (localized hyperalgesia) and at areas remote from the pain site (distal hyperalgesia). A decrease in PPT is thought to be a result of altered central processing of the nociceptive information. Identification of distal hyperalgesia is clinically important and has been associated with poorer recovery in patients with acute whiplash injury, as well as increased pain after total knee replacement.

STUDY DESIGN: Cross-sectional study.
OBJECTIVES: To compare pressure pain thresholds (PPTs) between adolescent females diagnosed with patellofemoral pain syndrome (PFPS) and gender- and age-matched controls without musculoskeletal pain.
BACKGROUND: PFPS is prevalent among adolescents and may be associated with reduced PPT both locally and remotely from the site of reported pain. This may indicate altered central processing of nociceptive information. However, this has never been investigated in adolescents with PFPS.
METHODS: Adolescents with PFPS and a comparison group without musculoskeletal pain were recruited from a population-based cohort of students from 4 upper secondary schools, aged 15 to 19 years. All 2846 students within that age range were invited to answer an online questionnaire regarding musculoskeletal pain. The students who reported knee pain were contacted by telephone and offered a clinical examination by an experienced rheumatologist, who made a diagnosis. PPTs were measured at 4 sites around the knee and 1 site on the tibialis anterior in the 57 female adolescents diagnosed with PFPS and in 22 female adolescents without musculoskeletal pain.
RESULTS: Adolescents with PFPS, compared to controls, had significantly lower PPTs (26%-37% [100-178 kPa]) at each of the 4 sites around the knee, suggesting localized hyperalgesia. On the tibialis anterior, adolescents with PFPS had a 33% (159 kPa) lower PPT (distal hyperalgesia) compared with controls.
CONCLUSION: These findings suggest that adolescent females with PFPS have localized and distal hyperalgesia. These findings may have implications for treating PFPS, as both peripheral and central mechanisms may be driving the pain. Registered at clinicaltrials.gov (NCT01438762). J Orthop Sports Phys Ther 2013;43(6):414-421. Epub 18 March 2013 doi:10.2519/jospt.2013.4383
KEY WORDS: adolescents, anterior knee pain, hyperalgesia, pressure pain thresholds

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[RESEARCH REPORT]
The aims of this study were (1) to compare PPTs in female adolescents with PFPS with those in female adolescents without musculoskeletal pain, (2) to investigate if symptom duration, pain intensity, and quality of life are associated with PPTs, and (3) to describe self-reported pain localization and pain distribution in adolescents with PFPS. We hypothesized that adolescents with PFPS would have lower PPTs (suggesting hyperalgesia) around the patella and at sites remote from the area of self-reported knee pain, and that longer symptom duration, higher pain intensity, and lower quality of life would be associated with lower PPTs.

**METHODS**

**THIS WAS A CROSS-SECTIONAL STUDY**

that compared female adolescents diagnosed with PFPS to a gender- and age-matched comparison group without musculoskeletal pain. The study was approved by the local ethics committee in the North Denmark Region (N-20110020).

**Recruitment**

Both groups were recruited from a population-based cohort (the Adolescent Pain in Aalborg 2011 cohort) and consisted of adolescents, 15 to 19 years of age, from 4 Danish upper secondary schools. All 2846 adolescents (hereafter referred to as the cohort) were invited to answer an online questionnaire with specific questions about musculoskeletal pain and general questions about physical activity. The adolescents who reported knee pain were contacted by telephone and offered a clinical examination by an experienced rheumatologist if they fulfilled all the following criteria: pain for more than 6 weeks; pain provoked by at least 2 of the following activities: prolonged sitting or kneeling, squatting, running, hopping, or stair walking; tenderness on palpation of the posterior surface of the patella; and pain intensity in the previous week of at least 30 mm on a 100-mm visual analog scale. Exclusion criteria were as follows: concomitant injury or pain from the hip, lumbar spine, or other knee structures; previous knee surgery; patellofemoral instability; knee joint effusion; use of physiotherapy for treating knee pain within the previous year; currently undergoing medical treatment; or daily or weekly use of anti-inflammatory drugs.

Adolescent females without musculoskeletal pain were randomly recruited from the same cohort. The inclusion criteria for these adolescents were no current self-reported musculoskeletal pain, no self-reported prior surgery in the lower extremity, and no self-reported neurological or other medical conditions.

**Measures**

All measurements were performed by the same rater. PPTs were measured with a handheld pressure algometer (Algometer Type II; Somedic AB, Hörby, Sweden) at 3 sites around the patella, 1 site on the patella, and 1 site on the tibialis anterior. The probe (1 cm²) was placed perpendicular to the skin. Pressure was applied at a rate of 30 kPa/s, and adolescents were instructed to indicate when the sensation changed from a sensation of pressure to the first sensation of pain. Measurements were done with the adolescents resting in a reclining position and the knee flexed to approximately 20°, with a small pillow beneath the knee. PPT was measured twice at each site, and the average was calculated.

The 4 test sites in the patellar region and the site on the tibialis anterior were first located and marked. The 4 test sites on the knee were located based on bony landmarks (3 cm medial to the midpoint of the medial edge of the patella, 2 cm proximal to the superior edge of the patella, 3 cm lateral to the midpoint of the lateral edge of the patella, and at the center of the patella). The site on the muscle belly of the tibialis anterior was located 5 cm distal to the tibial tuberosity.

The reliability of PPT measurements performed on young adults has previously been investigated and found to be acceptable for sites around the hand and head (intraclass correlation coefficients ranging from 0.69 to 0.88). In adults with knee osteoarthritis, reliability was found to be good, with intraclass correlation coefficients between 0.83 and 0.86.

In addition to PPT, the following clinical measures were used: (1) the Knee Injury and Osteoarthritis Outcome Score (KOOS), (2) worst pain intensity last week and pain at rest, as measured on a 10-cm visual analog scale, (3) symptom duration (months), (4) most painful knee (right/left), and (5) unilateral or bilateral pain (yes/no).

**Pain Localization**

A modified version of the Knee Pain Map was used to describe pain location and pain distribution. The Knee Pain Map is an interviewer-administered survey that instructs patients to point to the area of pain. The participants sat on an examination table with the knees flexed over the edge of the table and pointed to, or covered, the area(s) that hurt. The interviewer identified and recorded the areas of pain on a drawing of the knee. Following the survey, the same researcher interpreted all the drawings. Based on the drawings, pain localization was classified as retropatellar, peripatellar, or a combination of both retropatellar and peripatellar. In addition, if the pain originated from a region 2 finger widths in size or smaller, it was defined as localized knee pain. If the pain originated from an area more than 2 but less than 4 finger widths in size, it was defined as regional knee pain. If the adolescents with PFPS felt the pain originating from an area larger than this or said that they felt the pain all around and on the patella, the pain was defined as diffuse knee pain. If the adolescents with PFPS reported more...
than 4 local areas of pain or more than 2 regions of pain in the knee, the pain was classified as diffuse.

**Sample Size**
The sample size was based on detecting a difference between groups of at least 25% on the PPT measurements. This difference was based on PPT data from a study comparing patients with knee osteoarthritis and subjects without knee pain. Using a common standard deviation of 80 kPa, a power of 80%, and an alpha level of .05, at least 18 adolescents were needed in each group to detect a 25% difference between groups.

**Statistical Analysis**
All demographic data and KOOS results were visually inspected using a Q-Q plot. The KOOS subscales among pain-free adolescents were nonnormally distributed, and between-group comparison was performed using a Mann-Whitney U test. All calculations were performed using Stata Version 11 (StataCorp, College Station, TX). If normally distributed, the data were reported as mean ± SD; if nonnormally distributed, they were presented as median and interquartile range.

A repeated-measures analysis of variance was used to test the difference in PPTs between adolescents with PFPS and adolescents without musculoskeletal pain. Group (healthy, PFPS) was included as the between-subject factor and PPT site as the within-subject factor. For adolescents with bilateral knee pain, only the data from the most painful knee were used in the analysis. The assumption of sphericity was not fulfilled in the repeated-measures analysis of variance; therefore, the Greenhouse-Geisser correction was applied to all tests. In cases of significant interactions, multiple pairwise tests with Bonferroni correction for multiple comparisons were performed.

A multivariate analysis was used to test the association between symptom duration, KOOS quality of life subscale (KOOS QoL), KOOS pain subscale (KOOS pain), and the average PPT of the 4 sites at the knee and the PPT on the tibialis anterior. The sample size allowed for 3 explanatory variables in the analysis. Variables with a P value of less than .20 in the univariate analysis were included in the preliminary multivariate analysis. In the multivariate analysis, a P value of less than .05 was considered statistically significant. Construction of the multivariate analysis followed the construction proposed by Hosmer et al. Variables in the final model with a P value above .05 were only kept in the model if their removal caused more than a 10% change in the estimate of the other variables. Goodness of fit of the model is
Among adolescents with PFPS, a repeated-measures analysis of variance was used to test the differences in PPTs between those with local, regional, or diffuse pain distribution. Pain distribution was the between-subject factor and PPT site was the within-subject factor. The same was done with pain localization (retropatellar, peripatellar, or a combination of both retropatellar and peripatellar) as the between-subject factor and PPT site as the within-subject factor. In cases of significant interactions, multiple pairwise tests with Bonferroni correction for multiple comparisons were performed.

### Results

#### Participants

Females with PFPS were recruited from a population-based cohort that contained a total of 153 adolescents with PFPS. A total of 82 female adolescents with PFPS were contacted. Sixty agreed to be examined, but 3 of these failed to show up on the day of testing.

One hundred eighty-seven randomly selected adolescents without musculoskeletal pain were contacted. Eighty-seven did not answer the phone. Sixty-six were not available at the time of the PPT measurements. A total of 24 agreed to participate, but 2 did not show up for the examinations. Thus, the comparison group consisted of 22 female adolescents without musculoskeletal pain.

Demographic data indicated that the female adolescents without musculoskeletal pain were similar to the adolescents with PFPS in age, height, weight, and body mass index (Table 1). The female adolescents with PFPS had significantly more pain, symptoms, and functional limitations and reduced quality of life as measured by the 5 KOOS subscales (Table 1).

Adolescents with PFPS had symptoms lasting, on average, 34 months. The majority had bilateral pain with a peripatellar pain localization and a diffuse pain distribution (Table 2).

#### Between-Group Comparison

There was a significant interaction between PPT site and group (F(12,236) = 3.1, P = .03). Pairwise multiple comparisons using Bonferroni correction showed that PPTs were significantly lower for adolescents with PFPS for all 5 sites (P < .002) (Table 3).

#### Correlation Analyses Within the PFPS Group

The univariate analysis showed that symptom duration was significantly associated with PPT on the knee (an average of the 4 sites on the knee) as well as on the tibialis anterior (Table 4 and 5). With the univariate model, the associations between PPT and KOOS QoL and KOOS pain were not significant (P > .05) but were included in the multivariate analysis model because the P value was below .20. The multivariate model indicated that longer symptom duration was significantly associated with a higher PPT on and around the knee and a higher PPT on the tibialis anterior. The multivariate analyses also showed that KOOS QoL and KOOS pain were not significantly associated with PPT; however, removing these variables caused more than a 10% change in the association between symptom duration and PPT. Goodness of fit showed that symptom duration, KOOS QoL, and KOOS pain only explained

### Table 3

<table>
<thead>
<tr>
<th>Sites</th>
<th>Healthy (n = 22)*</th>
<th>PFPS (n = 57)*</th>
<th>Difference†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 cm medial to the midpoint on the medial edge of the patella</td>
<td>385.3 ± 119.6</td>
<td>284.5 ± 125.5</td>
<td>100.8 (38.8, 162.7)</td>
<td>.002</td>
</tr>
<tr>
<td>2 cm proximal to the superior edge of the patella</td>
<td>472.7 ± 167.8</td>
<td>311.2 ± 145.1</td>
<td>161.5 (85.7, 237.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>3 cm lateral to the midpoint on the lateral edge of the patella</td>
<td>454.3 ± 147.3</td>
<td>300.9 ± 125.3</td>
<td>153.4 (87.6, 219.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Center of patella</td>
<td>484.2 ± 134.7</td>
<td>306.2 ± 122.9</td>
<td>178.0 (114.9, 241.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Muscle belly of tibialis anterior, 5 cm distal to the tibial tuberosity</td>
<td>476.0 ± 165.8</td>
<td>317.4 ± 191.1</td>
<td>158.6 (78.2, 239.1)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

**Abbreviation:** PFPS, patellofemoral pain syndrome.

*Values are mean ± SD kPa.†Values are mean (95% confidence interval) kPa. Positive values indicate lower pressure pain threshold for the group with PFPS.

### Table 4

<table>
<thead>
<tr>
<th>Duration of symptoms, mo</th>
<th>Crude Coefficient*</th>
<th>P Value</th>
<th>Adjusted Coefficient†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.61</td>
<td>.04</td>
<td>1.84 (0.32, 3.36)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>KOOS QoL</td>
<td>2.03</td>
<td>.07</td>
<td>1.95 (-0.36, 4.26)</td>
<td>.10</td>
</tr>
<tr>
<td>KOOS pain</td>
<td>2.22</td>
<td>.11</td>
<td>1.45 (-1.33, 4.23)</td>
<td>.30</td>
</tr>
</tbody>
</table>

**Abbreviations:** KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, quality of life subscale.

*Crude coefficient shows the result from the univariate linear regression analysis.†Values in parentheses are 95% confidence interval. Adjusted coefficients show the results from the multivariate analysis.
13.6% of the variance for the average PPT measured around the knee and 16.9% of the variance for PPT measured over the tibialis anterior.

There was a significant interaction between pain distribution and PPT site ($F_{2,510.2} = 2.3, P = .048$). Pairwise multiple comparisons showed that those with regional knee pain had a significantly lower PPT lateral to the patella ($-103.7$ kPa; 95% confidence interval: $-204.2$, $-3.3$) and on the center of the patella ($-105.1$ kPa; 95% confidence interval: $-203.8$, $-6.4$) compared with those who had local knee pain (Table 6).

There was no significant effect of pain localization ($F_{2,510.4} = 0.79, P = .46$) or PPT site on PPT ($F_{2,510.4} = 1.05, P = .37$) and no interaction between pain localization and site ($F_{2,510.4} = 0.62, P = .70$) (Table 7).

**DISCUSSION**

This study showed that female adolescents diagnosed with PFPS had lower PPTs compared with those without musculoskeletal pain, indicating both localized and distal hyperalgesia. Contrary to our hypothesis, the analysis showed an association between a longer symptom duration and higher PPT.

As hypothesized, we observed a lower PPT on all 4 sites around the knee and on the tibialis anterior. These findings are consistent with previous studies of PPT performed on individuals with osteoarthritic knee pain. Assuming that the main PFPS-related tissue pathologies are at the knee, the lower PPT in that region confirms localized hyperalgesia, which has been postulated as one of the underlying reasons for chronic pain conditions like PFPS. The distal hyperalgesia observed at the tibialis anterior could reflect a loss of descending inhibitory processes. Such impairment may lower the excitation threshold of spinal cord neurons to joint nociceptive input, increasing the receptive fields of neurons and ongoing discharges, and affect all segments along the neuroaxis. However, distal hyperalgesia among females with PFPS could also reflect central mechanisms responsible for lowering PPT.

Local pain may develop to cover a larger area of hyperalgesia as time and severity increase. We found that female adolescents who reported regional knee pain had a significantly lower PPT (approximately 100 kPa) lateral to the patella and on the center of the patella compared with those who reported localized knee pain. This could reflect that where pain covers a larger area of the knee, there is an associated increase in localized hyperalgesia. However, as there was no additional decrease in PPT among those with diffuse knee pain, an alternative interpretation is that the variation in PPT between local and regional pain distribution may represent 2 different underlying causes of PFPS.

Compared with controls, adolescents with PFPS had significantly lower PPTs at each of the 4 sites around the knee (26%-37% [100-178 kPa]) and lower PPTs on the tibialis anterior (33% [159 kPa]). Similarly, studies on the older population with advanced knee osteoarthritis have found an approximately 25% lower PPT compared with controls. The large difference between groups may be attributed to the severity of PFPS, as indicated by the low KOOS scores. The KOOS subscores in the present study’s sample of adolescents with PFPS resemble those of elderly patients (mean age, 71.3 years) 6 months after total knee replacement, whereas the KOOS pain and KOOS symptoms scores resemble those of younger female patients (mean age, 25 years) waiting for primary anterior cruciate ligament reconstruction. The low KOOS QoL among adolescents with PFPS may indicate increased anxiety and distress. Increased anxiety has previously been shown to lower pain thresholds. This could mean that the difference between groups could be greater than expected because of a potential higher degree of anxiety among adolescents with PFPS.

Contrary to our hypothesis, symptom duration was positively associated with PPT, indicating that adolescents with the longest symptom duration had higher PPTs. Earlier studies on older patients showed that a long symptom duration was associated with lower PPT. The time needed for patients to develop hyperalgesia may depend on the condition. At least 5 years of symptoms are needed for rheumatoid arthritis, whereas central sensitization may occur within the first month after injury in subjects with whiplash. The etiology and pain onset (traumatic or nontraumatic) could be the reasons why we did not observe the lowest PPT among those with the longest symptom duration. Previous research on adolescents failed to show an association between symptom duration and PPT. This could mean that pain development during adolescence may follow a different path than pain development during adulthood.

<table>
<thead>
<tr>
<th>TABLE 5</th>
<th>Univariate and Multivariate Linear Regression Analysis Between the Pressure Pain Threshold on the Tibialis Anterior and 3 Explanatory Variables</th>
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<tbody>
<tr>
<td></td>
<td>Crude Coefficient</td>
</tr>
<tr>
<td>Duration of symptoms, mo</td>
<td>2.37</td>
</tr>
<tr>
<td>KOOS QoL</td>
<td>2.11</td>
</tr>
<tr>
<td>KOOS pain</td>
<td>2.67</td>
</tr>
</tbody>
</table>

*Crude coefficient shows the result of the univariate linear regression analysis.
†Values in parentheses are 95% confidence interval. Adjusted coefficients show the results from the multivariate analysis.
Earlier research has reported an association between pain severity and PPT among older adult patients with knee osteoarthritis, as well as several other pain conditions. The results of the present study do not conflict with these previous findings; the multivariate analysis showed a trend toward higher PPT with higher KOOS QoL and KOOS pain scores, indicating more normal PPTs in those with less pain and better quality of life. However, the poor fit of the model showed that symptom duration, KOOS QoL, and KOOS pain only explained a small percentage of the overall variation in PPT, indicating a strong influence of other, unknown factors.

### Strengths and Limitations

The strength of our study is that all the participants were recruited from a large, well-defined, population-based cohort. Recruitment of a population-based sample suggests that our data may be generalizable to the female adolescent population. However, our sample may not be generalizable to female adolescents currently under medical treatment, as we excluded those from the sample. Even though we excluded female adolescents who were currently under medical treatment, the baseline demographics of worst pain last week and symptom duration showed that our sample of female adolescents with PFPS was comparable to previous patient-based studies in slightly older patients of mixed genders.

The investigation of the association between symptom duration and localized
and distal hyperalgesia may be limited, as the PFPS in the current study represented a chronic pain condition, defined as PFPS more than 3 months in duration. None of the adolescents had a symptom duration less than 3 months, even though 1 of our inclusion criteria was pain for more than 6 weeks. Likewise, the 5 KOOS subscales showed that this sample of adolescents with PFPS most likely represented the severe spectrum of cases.

To obtain spatial information, PPT was assessed at 4 sites around the knee and 1 site on the tibialis anterior. Due to the limited time available for each examination, it was unfortunately not possible to measure PPT from the upper extremity. This would have allowed us to investigate whether the distal hyperalgesia was generalized.

Clinical Implications

During exercise and physiotherapy interventions in PFPS, we should take into consideration facilitated pain reactions due to hyperalgesia, as patients may experience more pain than expected. Within the area of musculoskeletal pain, clinicians often underestimate pain that may result from sensitization.22

CONCLUSION

The current study showed lower PPTs in a population-based sample of female adolescents diagnosed with PFPS. Lower thresholds were found around the knee as an indicator for localized hyperalgesia and remote from the knee as an indicator for distal hyperalgesia, as seen in other conditions like knee osteoarthritis. PPTs were poorly correlated with self-reported pain and duration of symptoms, indicating the necessity for future studies to include both self-reporting and pressure pain testing to further elucidate the nature of pain in adolescents with PFPS.

KEY POINTS

- Findings: Female adolescents diagnosed with PFPS have lower mechanical PPTs compared with female adolescents without musculoskeletal pain, which suggests both localized and distal hyperalgesia.
- Rathleff MS, Roos EM, Olesen JL, Rasmussen S. Early intervention for adolescents with patellofemoral pain syndrome – a pragmatic cluster randomised controlled trial. BMC Mus-