DOES PAIN IN ONE KNEE AFFECT MEASUREMENT OF ISOMETRIC MUSCLE STRENGTH IN THE CONTRALATERAL LIMP? – DATA FROM THE OSTEOARTHRITIS INITIATIVE (OAI)

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Purpose: Muscle strength is an important prerequisite for adequate lower limb function and quality of life. Lack of thigh muscle strength is thought to play a potential role in the onset and progression of symptomatic knee OA, and is currently recommended for treatment of knee OA by the OARSI therapeutic guidelines. Force generated by the lower limb can be measured objectively to test unilateral muscle strength, whereas most other functional performance tests rely on both limbs. However, it is currently unclear to what extent measurement of knee extensor and flexor strength is independent of the pain status of the contralateral knee. The purpose of this study therefore was to determine whether pain in one knee affects the measurement of isometric muscle strength in the contralateral limb.

Methods: We used data from the Osteoarthritis Initiative (OAI), to explore whether isometric thigh muscle strength differs between the asymptomatic (pain-free) knee of participants with a non-acceptable symptom status in the contralateral knee (cases), and matched knees of participants without pain in either knee (controls). Of the 4796 OAI participants, 3078 had bilateral measurement of isometric muscle strength, full demographic information available at 2-year follow-up, and did not have end-stage radiographic (KLG4) knee OA. Of these, 312 fulfilled our case definition of unilateral pain: a) one knee with a numerical rating scale (NRS) pain intensity value ≥4 (i.e. greater than the patient acceptable symptoms state [PASS]) and either frequent pain (≥2) or infrequent pain (≥1) during the past 12 months; b) the contralateral knee with an NRS intensity value of 0–1, either no pain (≥0) or infrequent pain (≥1) during the past 12 months, and a WOMAC score of 0–1. 1027 of the 3078 participants fulfilled the control definition of bilateral pain-free knees, i.e. both knees had an NRS intensity value of 0–1, either no (0) or infrequent (≥1) pain during the past 12 months (≥0 or 1), and a WOMAC score of 0–1. Of the 312 participants with unilateral pain, 224 could be matched to a control with the same sex and race (White/African American), and with similar age (±5y), body height (±5cm), BMI (±3kg/m²) and radiographic knee OA status (KLG 0/1 or 2/3). The maximal force [N] obtained from three matched bilaterally pain-free controls (Table 1). The maximum strength also was significantly lower (77%, p = 0.02) in cases than in controls, whereas the difference in the physical activity score of the elderly (PASE: −7.5%, p = 0.12) did not attain statistical significance (Table 1). As a reference, the extensor strength in the painful limbs of the cases (312 ± 12 N) was significantly (p = 0.0001) lower than that of the pain-free limb in the same participant (−5.9% = −19.8 N [95% CI: −28.5; −11.2]), and the same applied for flexor strength (123 ± 52.8 N; difference −3.9% = −5.0 N [95% CI: −9.0; −1.0]; p = 0.01). The results suggest that isometric strength measurement in a limb with an asymptomatic knee is not independent of the pain status of the contralateral knee. Effects from the contralateral knee may be conveyed by central nervous system inhibition, or from a reduction in training status and general physical activity. Although the effect appears relatively small for the given conditions (i.e. the contra-lateral knee having an NRS≥4), it is almost as large as the difference between painful and the painless limbs in cases with unilateral non-acceptable knee pain.

MECHANICAL PAIN THRESHOLD PREDICTS RESPONSE TO INTRA-ARTICULAR STEROID THERAPY IN SYMPTOMATIC KNEE OSTEOARTHRITIS

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Purpose: Qualitative Sensory Testing (QST) is a non-invasive test battery that assesses sensory perception of pressure, mechanical and vibration stimuli. Pressure pain thresholds assessed at a pain free control site prior to surgery have been shown to predict pain levels one year after total knee replacement in patients with knee osteoarthritis (OA). However, to our knowledge there are no data looking at associations between QST measures and response to pharmacological interventions. The aim of this study was to determine whether, in patients with symptomatic knee OA, baseline QST measures predicted response to treatment with intra-articular steroid therapy and whether response was associated with change in any of the QST measures.

Methods: 32 men and women with symptomatic knee OA participating in an uncontrolled open label clinical trial of intra-articular steroid therapy completed QST assessments at the injected and contralateral knees at baseline prior to intra-articular injection of depomedrone (80 mg) with repeat assessments after an interval of between 5 and 15 days following the injection. Subjects were also asked to complete the pain subscale of the Knee Injury and Osteoarthritis Outcome Score (0–100 scale, worst to best) at baseline and at the follow-up assessment. The QST assessments performed at both knees included: mechanical detection threshold (0.25–512 mN von Frey filaments), mechanical pain threshold and mechanical pain sensitivity (8–512 mN punctate probes), dynamic mechanical allodynia (brush and cotton bud), vibration detection (64 Hz tuning fork), pressure pain (0–10kg/cm² algometer) and wind-up (256 mN punctate probe). Patientes also had a tender point examination (0–18 sites). Subjects were characterised as treatment responders or treatment non-responders at the follow up visit using the OARSI-OMERACT criteria. Wilcoxon rank-sum tests were used to determine differences between responders and non-responders in QST measures at baseline and in changes in the QST measures following intervention. Within person changes in QST measures were assessed using the Wilcoxon matched-pairs signed-rank test.

Results: 11 men and 21 women (mean age 62.8 years, SD 10.2 years) with symptomatic knee OA underwent QST assessments at the injected and contralateral knees. Twenty one (65.6%) participants were classified as treatment responders at follow-up. Compared to non-responders, treatment responders had significantly lower mean baseline mechanical pain thresholds at the injected knee (73.4, SD = 74.6 vs 147.6, SD = 112.6; p = 0.022) with values for the control knee also approaching significance (78.5, SD = 64.2 vs 123.5, SD = 68.6; p = 0.054), indicating higher sensitivity to mechanical pain among the responders. None of the other baseline QST assessments, however, differed by responder.

Table 1

<table>
<thead>
<tr>
<th>Case (Mean ± SD)</th>
<th>Control (Mean ± SD)</th>
<th>Difference (95% Confid. Int.)</th>
<th>Paired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extensor strength [N]</td>
<td>333 ± 108</td>
<td>351 ± 146</td>
<td>-18.2 (-35.7/-0.7)</td>
</tr>
<tr>
<td>Flexor strength [N]</td>
<td>128 ± 52.4</td>
<td>139 ± 74.1</td>
<td>-10.7 (-19.9/-1.6)</td>
</tr>
<tr>
<td>PASE-score (0–361)</td>
<td>148 ± 69.2</td>
<td>158 ± 83.0</td>
<td>-11.8 (-24.6/1.0)</td>
</tr>
<tr>
<td>Age [years]</td>
<td>63.9 ± 8.9</td>
<td>63.8 ± 8.8</td>
<td>0.1 (-0.1/0.3)</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>28.1 ± 4.2</td>
<td>28.1 ± 4.2</td>
<td>0.0 (-0.1/0.1)</td>
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</table>
status. There was no overall within person change in any of the QST measures following intervention. Among responders, there was a small decrease in within person change in mechanical detection threshold (−25.1, SD = 69.1), indicating increased sensitivity, while in non-responders there was a small increase indicating decreased sensitivity (22.4, SD = 61.8) with a significant difference between responders and non-responders (p = 0.04). There was no other significant within person change in any of the QST measures by responder status.

**Conclusions:** In this small interventional study, patients with higher sensitivity to mechanical pain were more likely to respond to intra-articular steroid therapy.

734 CHRONIC PAIN IN PATIENTS WITH THE HYPERMOBILITY TYPE OF EHLERS–DANLOS SYNDROME: EVIDENCE FOR GENERALIZED HYPERALGESIA

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**Purpose:** The Ehlers–Danlos Syndrome (EDS) is one of the most prevalent heritable connective tissue disorders. Generalized severe joint hypermobility, which is frequently associated with joint dislocations, chronic joint and limb pain, and premature osteoarthritis, are the dominant clinical manifestations of the hypermobility type of EDS (EDS-HT). Chronic widespread pain is highly present in this patient group, but up to now, evidence for generalized hyperalgesia is lacking. Several studies in chronic pain disorders examined whether central hyperexcitability could be existent by using algometry.

Therefore, the primary objective of the study was to investigate whether pressure pain thresholds (PPTs) at both symptomatic and asymptomatic body areas differ in EDS-HT patients compared to healthy subjects. In addition, we examined the type of chronic pain EDS-HT patients experience.

**Methods:** Twenty-three women with EDS-HT and 23 gender- and age-matched healthy controls participated. All subjects marked on Margolis Pain Diagram where they felt pain lasting longer than 24 hours in the past 4 weeks. Then, they completed several questionnaires assessing pain cognitions (Pain Catastrophizing Scale, Pain Vigilance and Awareness Questionnaire, Hospital Anxiety and Depression Scale), fatigue (Checklist Individual Strength subscale fatigue), disability (Health Assessment Questionnaire), and general health status (Short Form Health Survey-36), in order to take the possible influence of these factors on PPTs into account. Patients also completed the Pain Detect Questionnaire regarding the severity, course, quality and nature of the pain they experienced. Thereupon, a blinded researcher assessed PPTs at 14 body locations on the trunk and extremities. The pressure was gradually increased at a rate of 1 kg/s until the subject indicated that the pain level has been reached. The threshold was determined as the mean of the 2 last values out of the 3 consecutive measurements. This method has been found to be efficient and reliable in the exploration of pathophysiological mechanisms involved in pain. PPTs were compared for the 2 complete groups. In addition, PPTs of patients and controls who did not report pain in a respective zone were compared.

**Results:** The EDS-HT patient group demonstrated significantly lower PPTs compared to the control group for all zones. The mean (SD) PPT was 2.9 (1.62) kg/cm² in the EDS-HT patients and 5.2 (1.88) kg/cm² in the controls (p < 0.001). Also at asymptomatic (pain-free) zones, EDS-HT patients systematically showed significantly lower pain thresholds compared to the healthy subjects. No confounding factors responsible for the observed differences could be revealed.

According to the Margolis Pain Diagram, EDS-HT patients experienced pain on an average of 31% (±17.8) of their body surface, compared to 1% (±2.4) in the control subjects. Furthermore, approximately 40% of the patients presented with a nociceptive pain pattern, whereas in about 80% a predominantly neuropathic pain component was likely present.

**Conclusion:** This study shows that several forms of pain coexist in EDS-HT which are likely the result of different pain-triggering mechanisms. The widespread pain lacking local distinction together with the lower PPTs in body zones outside and remote to the symptomatic zone provide evidence for the existence of generalized secondary hyperalgesia in patients with EDS-HT, which may represent the involvement of a sensitized central nervous system as an important mechanism in the chronic pain problems of this challenging patient group.

735 PREDICTIVE VALIDITY OF THE PAIN BELIEF SCREENING INSTRUMENT FOR ESTIMATING PAIN RESPONSIVENESS TO THERAPY

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**Purpose:** To assess the predictive validity of the Pain Belief Screening Instrument (PBSI) for predicting clinically meaningful change in patient-perceived pain following conservative non-drug therapy; and to establish a cut-off value that distinguishes patients at risk of not achieving meaningful pain reduction following intervention (exercise therapy and/or manual therapy).

**Methods:** We used data from 308 patients in two randomized clinical trials (RCTs) of people with hip or knee osteoarthritis (OA), at baseline and 6-month follow-up. Pain was assessed using a numeric pain rating scale (NPRS) in one RCT and a visual analog scale (VAS) in the second RCT. From recent literature we considered the minimum clinically important difference (MCID) to be 2 points on a 0–10 scale. To determine the baseline association between baseline PBSI and clinically important change in pain at 6-month follow-up we used a three-phase approach: first using development data set, then an establishment dataset and subsequently a validation dataset, we estimated area under the curve (AUC) and parsimonious cut-point, using receiver operating characteristics (ROC) analyses, and predicted change in pain using linear regression.

**Results:** The data sets included 90 patients with hip OA in the development set, 116 patients with knee OA in the establishment set and 102 patients with hip OA in the validation set. The cut point on the PBSI (0–40 scale) was 27, 27 and 26 in the development, establishment and validation sets, respectively. The AUC for PBSI was .70, .70 and .65 in the development, establishment and validation sets, respectively. There was no overall within person change in any of the QST measures by responder status. There was no other significant within person change in any of the QST measures by responder status.

**Conclusions:** The PBSI demonstrated some predictive validity for estimating 6-month pain responsiveness to therapy, however the mean magnitude of difference in pain, between patients scoring above versus below these ROC-derived cut-points, did not reach the minimum clinically important difference, and the AUC values indicated only moderate accuracy. Despite a high level of consistency among the three datasets, the lack of clinically important difference in pain outcome suggests that this information is unlikely to be useful for targeting therapy, however it may be useful for statistically adjusting for variables associated with outcome in clinical research.

736 ENDGENOUS PAIN MODULATION IN THE EHLERS–DANLOS SYNDROME, HYPERMOBILITY TYPE

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**Purpose:** The Ehlers–Danlos Syndrome (EDS) is the most prevalent heritable connective tissue disorder. More than 90% of individuals are classified as having the hypermobility type (EDS-HT). Patients typically demonstrate generalized severe joint hypermobility, which is frequently associated with recurrent joint dislocations and premature osteoarthritis. Although pain is the number one complaint in EDS-HT, causing severe disability in daily life, the underlying pain mechanisms and the nature of pain are unknown. Therefore, this study aims to assess the nature of pain (nociceptive / neuropathic / dysfunctional pain) and the endogenous pain modulation in EDS-HT.