We suggest that different mechanisms underlie joint pain at rest and on movement in osteoarthritis and that separate assessment of these two features with a visual analogue scale (VAS) offers better information about the likely effect of a total knee replacement (TKR) on pain. The risk of persistent pain after TKR may relate to the degree of central sensitisation before surgery, which might be assessed by determining the pain threshold to an electrical stimulus created by a special tool, the Pain Matcher. Assessments were performed in 69 patients scheduled for TKR. At 18 months after operation, separate assessment of pain at rest and with movement was again carried out using a VAS in order to enable comparison of pre- and post-operative measurements. A less favourable outcome in terms of pain relief was observed for patients with a high pre-operative VAS score for pain at rest and a low pain threshold, both features which may reflect a central sensitisation mechanism.
approved the study. A power analysis was performed which demonstrated that 28 patients were required to show a strong relationship \( r = 0.50 \) with a level of significance of 5% and a power of 80% when using a two-tailed test. Our sample size of 69 patients also permitted an analysis of subgroups, although we did not do this. There were 34 men and 35 women, with a mean age of 68 years (40 to 80). The mean duration of knee pain was 8.5 years (1 to 25). No patient had a clinical history of drug abuse or was taking opioid drugs before surgery. For haemostatic reasons, non-steroidal anti-inflammatory drugs (NSAIDs) were withdrawn between three and 14 days prior to surgery, as is routine in our practice. All patients received a posterior cruciate ligament (PCL)-retaining TKR, the fixed-bearing PFC Sigma prosthesis (DePuy International Ltd; Johnson & Johnson, Leeds, United Kingdom). The patella was not resurfaced.

**Pre-operative assessments.** All patients were asked the day before surgery about the total duration of pain in the knee and its current intensity both at rest and with movement. Pain with movement was defined as pain during walking, whereas pain at rest included pain in any position (sitting, standing or lying down) while not moving the joint. Pre-operative pain was assessed using both a visual analogue scale (VAS), and an electrical stimulation device, the Pain Matcher. The Pain Matcher was used to determine the threshold for the first noticeable sensation for the stimulus and the threshold for pain.

The validity of a VAS for assessment of pain has been reported previously. In the present study, the ratings were recorded on a 100 mm horizontal line, where zero represented no pain and ten the worst imaginable. Patients were instructed to select a position on the line which corresponded to their level of pain. Measurements were recorded as whole numbers.

The Pain Matcher (Fig. 1) is an instrument for electrical stimulation and was used pre-operatively on all patients to assess not only the matched pain, i.e., the pain corresponding to the knee pain with movement, but also to determine the thresholds for sensation and pain. As a control group, 12 men and 12 women, all healthy and without pain, were tested for the same thresholds. The purpose of the Pain Matcher is to expose the patient to an electrical stimulus which matches the intensity, but not necessarily the nature, of the actual pain. This provides a numerical value to a level of pain without the influence of other factors. The Pain Matcher provides constant current stimulation, despite variable skin resistance, and is controlled by a microprocessor which provides rectangular pulses at a frequency of 10 Hz and an amplitude of 10 mA. Increasing the stimulus is achieved by successively raising the pulse width \( \mu \) from zero to a possible maximum of 396 \( \mu \) in increments of 4 \( \mu \) over a total of 99 steps. The electrical charge per second is extremely low and causes no tissue damage. The value reached (0 to 99) is directly related to the pulse width and is displayed on a liquid crystal screen.

The patients were instructed to grasp the electrodes of the Pain Matcher between the thumb and index finger of their right hand. The electrical stimulation was started by the patients who were told to press a button on the device at the first noticeable sensation, the sensation threshold. Subsequently, the device was started again and the patients were instructed to press the button when the perceived signal was painful, the pain threshold. The procedure was repeated a third time and the patients were asked to press the button when the intensity of pain was the same as that from their knee on movement, the matched pain.

**Outcome.** At 18 months after operation, a questionnaire was sent to all patients who were requested to estimate their pain at rest and with movement according to the same VAS scale as applied before surgery. No measurements with the Pain Matcher were made at follow-up, as this would have required many patients to travel extensively from distant regions of Sweden.

**Statistical analysis.** All variables were summarised using standard descriptive statistics such as mean, standard deviation (SD) and frequency. As several variables were positively skewed all statistical analyses were made using non-parametric methods, such as Kendall’s rank order correlation for relationships, Mann-Whitney U test for differences between genders, and the Wilcoxon signed rank test for intra-group differences, e.g. differences between pain at rest and with movement. A p-value of \( < 0.05 \) was regarded as significant.

The relationships between pre- and post-operative measurements of pain at rest and with movement at 18 months were studied in a stepwise (forward) logistic regression analysis (Table I). Eight variables were entered in the analysis. The logistic regression analysis yields odds ratios (OR). All variables were dichotomised according to a procedure denoted in Table I based on the median value for each variable. The criterion for inclusion in the regression equation was \( p = 0.05 \). Pain with movement measured by the Pain Matcher was omitted from the regression analysis because of a high drop-out rate (\( n = 17 \)) resulting from difficulties...
Relationships between pain measurements.

Pain Matcher.

Pre-operative visual analogue scale.

Results

The mean pre-operative knee pain at rest and with movement according to the VAS, as well as the sensation and pain thresholds, and matched pain with movement as measured by the Pain Matcher, are shown in Table II. As can be seen, approximately 23% (16 of 69) of patients had no pain at rest. Pain at rest was significantly less than that with movement (z = 7.03; Wilcoxon signed rank test, p < 0.001). All patients, except four, rated their pain on movement almost three times higher (2.90) on the VAS than their pain at rest. No significant gender difference was found in the pain ratings using the VAS.

Pain Matcher. The mean pain threshold was 2.4 (1.1 to 9.6) times higher than the sensation threshold, while the matched pain with movement was 1.42 (0.43 to 3.43) times higher than the pain threshold. Notably, nine of 52 patients (17%) rated their matched pain with movement as being lower than the pain threshold. In comparison with the control group, the patient group had a significantly higher sensation threshold (7.1 vs 4.5, z = 4.146, Mann-Whitney U test, p < 0.001) and a significantly lower pain threshold (16.4 vs 21.1, z = 2.50, Mann-Whitney U test, p = 0.012). Women had significantly lower sensation thresholds than men (6.4 vs 7.8, z = 2.38, Mann-Whitney U test, p = 0.017) and also lower pain thresholds (13.5 vs 19.4, z = 2.89, Mann-Whitney U test, p = 0.004). Their matched pain with movement was significantly lower than that for men (14.9 vs 26.2, z = 3.28, Mann-Whitney U test, p = 0.001).

Relationships between pain measurements. The correlations between the pain ratings, including the thresholds to sensation and pain, are presented in Table III. No significant correlation was found between pain at rest and pain with movement as assessed by VAS.

Significant but modest correlations were found between the sensation and pain thresholds on one hand and the matched pain with movement on the other. A low sensation threshold tended to be associated with a low pain threshold. Comparisons of pain with movement according to the VAS, and the matched pain with movement according to the Pain Matcher, showed no significant relationship (Kendall’s rank order correlation, p = 0.440; correlation coefficient, -0.08).

Outcome. At 18 months after operation, the rating by VAS was undertaken by 63 of the 69 patients (91%) for knee pain at rest and by 62 patients (90%) for knee pain with movement. There were 21 (34%) patients who had no pain at rest or with movement. There were 15 (24%) patients who still had pain at rest and 41 (66%) who had pain with movement. All 15 patients who had pain at rest also had pain with movement.

Prediction. Three of the pre-operative variables, pain at rest according to VAS (chi-squared test = -9.91, p = 0.015), and sensation and pain thresholds according to the Pain Matcher (chi-squared test = 4.00, p = 0.045, and chi-squared test, = 6.34, p = 0.012, respectively), were significantly related to pain at rest 18 months after operation. In the logistic regression analysis, only two of these variables contributed significantly and uniquely to prediction, namely pain at rest and pain threshold (Table IV); the greater the pain at rest and the lower the pain threshold pre-operatively the worse the outcome in terms of persistent pain at rest. Notably, pain with movement at 18 months was not related to any of the tested variables. Neither the age of the patient nor the duration of pain before surgery was significantly related to the outcome measures.

Discussion

The problem of persistent pain after TKR was addressed in a recent study by Elson and Brenkel18 showing that unexplained pain at six months was resolved within five years in ten of 18 patients. However, no pre-operative characteristics were assessed, nor was a distinction made between pain at rest and pain with movement. Our study suggests that patients reporting a high pre-operative score for knee pain at rest are at increased risk of persistent pain after TKR. Thus, a distinction between pain at rest and pain with movement in pre-operative planning appears to be of prognostic relevance. It also appears that the assessment of pain threshold to electrical stimulation by the Pain Matcher in patients with OA provides valuable predictive information. Notably, patients with a low pre-operative pain threshold benefit the least from TKR in terms of pain relief. Presumably, pain at rest and a low pain threshold reflect a central sensitisation mechanism.

It is widely recognised that the perception and assessment of pain are influenced by a variety of social, economic, cognitive and emotional factors. However, in routine clinical practice, a simpler approach for the assessment and prediction of pain relief after a given intervention is needed. Clinical research might also benefit from such an approach in order to allow a comparison of pre- and post-intervention characteristics. In the present study, the measurement threshold tended to be associated with a low pain threshold. Comparisons of pain with movement according to the VAS, and the matched pain with movement according to the Pain Matcher, showed no significant relationship (Kendall’s rank order correlation, p = 0.440; correlation coefficient, -0.08).

Outcome. At 18 months after operation, the rating by VAS was undertaken by 63 of the 69 patients (91%) for knee pain at rest and by 62 patients (90%) for knee pain with movement. There were 21 (34%) patients who had no pain at rest or with movement. There were 15 (24%) patients who still had pain at rest and 41 (66%) who had pain with movement. All 15 patients who had pain at rest also had pain with movement.

Prediction. Three of the pre-operative variables, pain at rest according to VAS (chi-squared test = -9.91, p = 0.015), and sensation and pain thresholds according to the Pain Matcher (chi-squared test = 4.00, p = 0.045, and chi-squared test, = 6.34, p = 0.012, respectively), were significantly related to pain at rest 18 months after operation. In the logistic regression analysis, only two of these variables contributed significantly and uniquely to prediction, namely pain at rest and pain threshold (Table IV); the greater the pain at rest and the lower the pain threshold pre-operatively the worse the outcome in terms of persisting pain at rest. Notably, pain with movement at 18 months was not related to any of the tested variables. Neither the age of the patient nor the duration of pain before surgery was significantly related to the outcome measures.

Discussion

The problem of persistent pain after TKR was addressed in a recent study by Elson and Brenkel18 showing that unexplained pain at six months was resolved within five years in ten of 18 patients. However, no pre-operative characteristics were assessed, nor was a distinction made between pain at rest and pain with movement. Our study suggests that patients reporting a high pre-operative score for knee pain at rest are at increased risk of persistent pain after TKR. Thus, a distinction between pain at rest and pain with movement in pre-operative planning appears to be of prognostic relevance. It also appears that the assessment of pain threshold to electrical stimulation by the Pain Matcher in patients with OA provides valuable predictive information. Notably, patients with a low pre-operative pain threshold benefit the least from TKR in terms of pain relief. Presumably, pain at rest and a low pain threshold reflect a central sensitisation mechanism.

It is widely recognised that the perception and assessment of pain are influenced by a variety of social, economic, cognitive and emotional factors. However, in routine clinical practice, a simpler approach for the assessment and prediction of pain relief after a given intervention is needed. Clinical research might also benefit from such an approach in order to allow a comparison of pre- and post-intervention characteristics. In the present study, the measurement
of pain was confined solely to its intensity. Given that the response on a VAS is affected by both intrinsic and extrinsic factors, it may be argued that comparison between individuals is questionable, whereas individual assessments, e.g. before and after intervention, are more reliable. We focused on two components of joint pain, that at rest and that with movement. Our purpose was twofold. First, to assess the predictive strength of each of the two components of pain according to VAS measures. Secondly, to test the usefulness of determining sensory thresholds by the Pain Matcher as additional predictors of outcome after TKR.

The predictive value of self-assessed pain at rest being associated with a poor outcome, as opposed to that with movement, would suggest that the underlying mechanisms may differ. The poor correlation between pain at rest and that with movement supports this notion. While pain with movement has mainly been associated with sensitisation of peripheral Aδ and C-fibres, pain at rest has been linked to sensitisation of nerve terminals in the dorsal horn and spinal cord neurones. Although it has been shown that a lowered pain threshold may return to normal after total joint replacement, there is also experimental support from animal studies for the persistence of central hypersensitivity after complete resolution of tissue damage. Persistent central hypersensitivity may explain the less favourable outcome noted in our study for patients with a high pre-operative VAS score for pain at rest. Similarly, a low pre-operative pain threshold to an electrical stimulus may be assumed to involve central sensitisation, and is associated with a poor outcome.

Table II. Pre-operative detection levels and pain thresholds in the 69 patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Range (SD)</th>
<th>Number of patients with no pain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual analogue scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain, at rest</td>
<td>2.4</td>
<td>0 to 7.0</td>
<td>(1.86) 16 (23)</td>
</tr>
<tr>
<td>Pain, with movement</td>
<td>7.1</td>
<td>3.0 to 10.0</td>
<td>(1.72) 0 (0)</td>
</tr>
<tr>
<td>Pain Matcher</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory threshold</td>
<td>7.1</td>
<td>3 to 19</td>
<td>(3.17) -</td>
</tr>
<tr>
<td>Pain threshold</td>
<td>16.4</td>
<td>5 to 78</td>
<td>(10.63) -</td>
</tr>
<tr>
<td>Pain, matched with movement</td>
<td>20.6</td>
<td>5 to 85</td>
<td>(12.47) -</td>
</tr>
</tbody>
</table>

Table III. Relationships between different aspects of pain and sensory characteristics as determined by the visual analogue scale (VAS) and Pain Matcher (Kendall’s rank order correlation coefficients)

<table>
<thead>
<tr>
<th>Variable</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain at rest</td>
<td>0.10</td>
<td>-0.08</td>
<td>-0.04</td>
<td>0.05</td>
</tr>
<tr>
<td>Pain with movement</td>
<td>-</td>
<td>-0.06</td>
<td>-0.13</td>
<td>-0.08</td>
</tr>
<tr>
<td>Pain Matcher</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensation threshold</td>
<td>-</td>
<td></td>
<td>0.42*</td>
<td>0.46*</td>
</tr>
<tr>
<td>Pain threshold</td>
<td>-</td>
<td></td>
<td>-</td>
<td>0.52*</td>
</tr>
<tr>
<td>Matched pain - with movement</td>
<td>-</td>
<td></td>
<td></td>
<td>-</td>
</tr>
</tbody>
</table>

* p < 0.001

Table IV. Odds ratios (OR) for variables predicting a poor outcome, i.e. a high score for pain at rest 18 months after operation

<table>
<thead>
<tr>
<th>Predictive variables</th>
<th>B</th>
<th>SE</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative pain at rest (VAS)§</td>
<td>1.87</td>
<td>0.72</td>
<td>0.009</td>
<td>6.48</td>
<td>1.32 to 31.96</td>
</tr>
<tr>
<td>Pre-operative pain threshold (Pain Matcher)</td>
<td>2.22</td>
<td>0.87</td>
<td>0.010</td>
<td>9.19</td>
<td>1.69 to 50.07</td>
</tr>
<tr>
<td>Constant (y-intercept)</td>
<td>-3.76</td>
<td>0.96</td>
<td>0.000</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* B, slope of the regression equation
† SE, standard error
‡ 95% CI, 95% confidence interval
§ VAS, visual analogue scale
with a less favourable outcome. Surprisingly, this mechanism seems to be independent of the duration of the painful condition.

It may be argued that the specific site of cartilage destruction within a joint might explain the presence of pain at rest and/or movement. Patellofemoral arthritis is exacerbated by climbing stairs or sitting with the knee flexed, whereas tibiofemoral arthritis is believed to cause pain when walking on level ground. In our study, we did not find any correlation between the radiological presence of patellofemoral arthritis and pain, either at rest or with movement. Moreover, patellofemoral arthritis was not found to be of any predictive value for joint pain at 18 months after operation even though the patella was not resurfaced.

The Pain Matcher used in the present study for matching pain and determining the detection level and pain threshold has been reported to be both reliable and reproducible. However, in this study we found it difficult for patients to match the pain created by the Pain Matcher with their knee pain. Some found the electrical impulse unpleasant and, therefore, stopped the test before experiencing pain. Others had problems in discriminating pain from unpleasantness. An indication of the difficulties in understanding the instructions was that as many as nine patients scored higher for pain threshold than for matched pain despite reporting considerable knee pain on the VAS scale. Also the disagreement between the matched and scored joint pain indicates that the matched pain, as determined by the Pain Matcher, is of questionable value. Nevertheless, our data suggest that the tool can offer meaningful measurements of thresholds for sensation and pain.

As in previous studies on patients with OA, we observed signs of disturbances in the sensory thresholds to electrical stimulation. Thus, our patients with OA of the knee exhibited a significantly higher sensation threshold and a significantly lower pain threshold compared with the normal controls. This agrees with the findings of Lund et al. The observed changes in sensory thresholds in OA supports the notion of a central sensitisation mechanism, probably induced primarily by nociceptive input which arises from diseased tissue.

Although many orthopaedic surgeons consider pain at rest a prerequisite for TKR, 23% of the patients in this study reported no pain pre-operatively at rest. Our data suggest that the results of TKR are good for the subgroup of patients who only have pain with movement. This seems to refute the concept that pain at rest should be a mandatory feature of those scheduled to undergo TKR. In this study, patients who had severe pre-operative pain with movement benefited the most, whereas those with a high score for pain at rest benefited the least.

It may in due course be shown that the degree of central sensitisation is an important determinant of the effect of surgical treatment, and therefore, of pre-operative prognostic value. Joint pain at rest and/or a low pain threshold may partly explain persistent pain at rest after prosthetic replacement because of central sensitisation. These findings suggest that numerical pain scores in OA should be applied separately to the different aspects of pain, i.e., pain at rest and pain with movement. The combined pre-operative findings of a high VAS score for pain at rest and a low pain threshold to an electrical stimulus does not preclude surgical treatment, but suggest that patients should be given proper information about an increased risk of persistent pain at rest after TKR.

We thank Gunnar Edman for invaluable help with statistics, also Stockholm Specialistvård AB and Stockholm Spine Centre for providing facilities for this study. The Karolinska Institutet and the Folksam research fund financially supported this study.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References


