Life satisfaction in patients with chronic pain – relation to pain intensity, disability, and psychological factors

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Aims: To investigate pain intensity, posttraumatic stress, depression, anxiety, disability, and life satisfaction in patients with injury-related chronic pain and to analyze differences in these variables regarding gender.

Methods: Questionnaires addressing pain intensity (visual analogue scale [VAS]), anxiety and depression (hospital anxiety and depression [HAD] scale), posttraumatic stress (impact of event scale), disability (disability rating index, and life satisfaction [LiSat-11]) were answered by 160 patients at assessment at the Pain Rehabilitation Clinic at the Umeå University Hospital (Umeå, Sweden).

Results: High level of pain intensity was scored on the VAS (mean value 64.5 ± 21.1 mm) together with high levels of anxiety, depression, and posttraumatic stress. Activity limitations in everyday life and decreased life satisfaction were reported, especially on the items physical health and psychological health. A multivariate logistic regression model showed a statistically significant association between low scores on the overall life satisfaction on LiSat-11 and high scores on HAD-depression (odds ratio = 1.141, confidence interval 1.014–1.285). Few gender differences were found.

Conclusion: These findings highlight the value of a broad screening in patients with injury-related chronic pain with respect to the relationship of life satisfaction with pain intensity, anxiety, depression, posttraumatic stress, and disability. In addition, these findings support the biopsychosocial approach to assess and treat these patients optimally.

Keywords: whiplash injuries, depression, quality of life

Introduction

The definition of pain according to the International Association of the Study of Pain (IASP) is: “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is always a subjective experience that is related to emotional and psychological experiences.”

IASP defines chronic pain as pain that persist beyond the normal tissue healing time (usually with duration of more than three months). Chronic pain is a common condition in Sweden and in other European countries that is affected by physical, psychological, emotional, and social factors and constitutes a major health problem in Western countries because of the number of people affected and the increasing economical costs. However, persons with chronic pain constitute a heterogeneous group with different backgrounds and causes of pain that may also influence the clinical characteristics.

Injuries, especially traffic injuries, are a common cause of chronic pain. Whiplash injuries are probably the most common injury by a traffic-related accident. The incidence of whiplash injuries varies from 1.0 to 3.2 per 1000 per year. A significant proportion
of patients with whiplash injuries may suffer from chronic symptoms (whiplash associated disorder), with the dominating complaints being neck pain and headache.

The persistence of chronic pain after traffic accidents may be related to psychological factors such as anxiety, depression, and posttraumatic stress. In the group of patients with traffic injury-related problems, 10%-30% are reported to suffer from severe posttraumatic stress symptoms and the diagnosis of posttraumatic stress disorder. Posttraumatic stress is characterized by three major symptom clusters: re-experiencing symptoms, avoidance symptoms, and arousal symptoms. Since chronic pain and posttraumatic stress may co-occur, it has been suggested that there are factors in common that maintain both conditions.

In most persons with chronic pain, the pain condition has consequences on the level of activity in everyday life both during work and leisure. Moreover, there is a considerably difference between individuals with similar pain condition regarding perceived pain and disability. Chronic pain may also affect satisfaction with life. In a previous study by Silvemark et al, patients with chronic pain were shown to report significantly lower life satisfaction in comparison with a reference group without pain.

Chronic pain is more common in women than in men. During the last few years there has been a growing interest in the importance of gender; in rehabilitation of patients with chronic pain, some studies have reported gender differences with respect to various pain related items, although others have found no differences in outcome between men and women.

In rehabilitation practice at the Pain Rehabilitation Clinic at the University Hospital (Umeå, Sweden), interdisciplinary assessment and rehabilitation are provided for patients with chronic pain. Since life satisfaction seems to be of importance for the chronic pain situation and has been proposed to be studied further in chronic pain patients, it was considered important to address this issue in these patients.

Therefore, the aim of this study was to investigate the perceived life satisfaction and the pain-related characteristics (pain intensity, posttraumatic stress, and disability) in patients with injury-related chronic pain. Additionally, the study aimed to analyze differences in these variables with regards to gender.

Materials and methods

Patients
Participating subjects were 160 consecutive patients (collected from September 2005 to November 2007), 104 women and 57 men, aged 17-62 years (36 ± 10) diagnosed with chronic musculoskeletal pain caused by an injury and referred from regional general practitioners to the Pain Rehabilitation Clinic at the Umeå University Hospital (Umeå, Sweden). The patients in this study are the same as those contributing to a companion study. Out of all the participants, 68% suffered from pain caused by whiplash injuries, and 32% reported that their pain was caused by other accidents, such as falls and assaults. None of these patients had problems related to other causes of pain. The time between injury and assessment at the Pain Rehabilitation Clinic was 5.2 ± 5.7 years.

Procedure
A set of questionnaires was sent to the participants before an assessment at the clinic by an interdisciplinary team that consisted of a physician (specialist in rehabilitation medicine), a physiotherapist, a social worker, and (if needed) a psychologist and occupational therapist. Information about each participant’s trauma history was collected from hospital records.

Questionnaires
The visual analogue scale (VAS)
Pain intensity was rated by the VAS. The scale consists of a 100 mm straight line with defined endpoints (“no pain” and “worst pain imaginable”) on which the patients were asked to mark their experienced pain (results in mm) at the actual time (“VAS now”). The VAS is considered to have a high degree of reliability and validity.

The impact of event scale (IES)
The IES is a widely used self-report scale. It is a valid measure of posttraumatic stress reactions and has been suggested as a screening tool for posttraumatic stress. The IES comprises 15 statements: seven questions regarding intrusive symptoms, and eight addressing avoidance symptoms. The patients answer the questionnaire regarding their symptoms during the previous week. A total score can vary from 0 to 75. The total IES scale includes the intrusion and the avoidance subscales.

The hospital anxiety and depression (HAD) scale
The HAD scale is an instrument that measures anxiety and depression, which is developed and validated on nonpsychiatric medical patients. The questionnaire comprises 14 items divided into two parts, for rating of depression and anxiety. Each item has a 4-response category range from 0 to 3. The scale ranges from 0 to 21 for both depression and anxiety.
The cutoff level for possible cases of anxiety disorder and depression is a score ≥8 on each subscale.

The life satisfaction checklist (LiSat-11)

With the LiSat-11, patients self-report their levels of satisfaction on eleven items: one item addresses life as a whole, and ten other items address vocation, economy, leisure, contacts, sexual life, activities of daily living, family life, partner, somatic health, and psychological health.24 Levels of satisfaction are estimated on a 6-point response Likert scale: 1 = very dissatisfied, 2 = dissatisfied, 3 = rather dissatisfied, 4 = rather satisfied, 5 = satisfied, 6 = very satisfied. Higher scores indicate higher levels of life satisfaction; a total score can be calculated (range: 11–66). In accordance with previous studies using the LiSat-11,24,25 for comparison purposes, the scale was dichotomized into either satisfied 5–6 or dissatisfied 1–4 in this study.

The disability rating index (DRI)

For the assessment of activity limitations in everyday life, the DRI score26 was used. The DRI, a self-administered instrument, covers twelve daily physical activities. The patients indicate on a 100-mm VAS their ability to perform these daily physical activities from 0 (“without difficulty”) to 100 (“not at all”). The distance is measured in millimeters, and an index is obtained. Patients are asked how they manage the following activities: (1) dressing, (2) outdoor walks, (3) climbing stairs, (4) sitting for a long time, (5) standing bent over a sink, (6) carrying a bag, (7) making a bed, (8) running, (9) light work, (10) heavy work, (11) lifting heavy objects, and (12) participating in exercise/sports. The twelve items are divided into three sections: 1–4, common basic activities; 5–8, more demanding daily physical activities; 9–12, work-related or more vigorous activities. The DRI has proven to be both reliable and validated.26

Statistics

All statistical analysis was performed with SPSS Statistics (IBM Corporation, Somers, NY) software, version 17.0 for Windows. Data are reported as means ± standard deviations unless indicated otherwise. Comparisons of populations were made using the Mann–Whitney U-test and chi-square test when data was categorical. Spearman’s correlation coefficient was calculated for the analysis of bivariate correlations. Multivariate logistic regression was performed to test associations between the dependent variable, the overall life satisfaction (1 = nonsatisfied, 0 = satisfied), and the following variables: VAS, IES, and DRI. The results of the logistic regression analysis are presented as odds ratios (ORs). The reliability of the OR is expressed as 95% confidence interval (CI). Statistical significance level was set at 0.05, two sided.

The study was approved by the ethics committee of Umeå University.

Results

Pain intensity, depression, anxiety, posttraumatic stress, and disability

Table 1 shows pain intensity on the VAS, the scores of anxiety and depression on the HAD scale, and the scores of life satisfaction on the LiSat-11. Pain intensity on the VAS rated by all patients was 64.5 mm (standard deviation 21.1 mm). All patients rated VAS higher than 10 mm and a majority (78.5%) rated VAS higher than 50 mm. The cutoff level of the HAD (>8) was rated by 45.8% on the HAD-anxiety scale and by 47.1% on the HAD-depression scale. Moderate to severe stress response (total IES score of ≥26)26 was reported by 48.1% of the patients.

Women reported higher scores than men on the VAS, the HAD, the IES, and the DRI scores, but the difference was only significant on the DRI subscale “carrying” (P = 0.023).

Life satisfaction

Table 2 shows the distribution of patients satisfied (score 5–6) with the eleven items on the LiSat-11. The frequency of women who were satisfied with contacts with friends (42.4%) was significantly higher than men (25.9%) (P = 0.031). Only 6.6% of all participants were satisfied with their somatic health, (5.1% women and 9.3% men). The women’s scores were lower than the men’s scores, but the difference was not statistically significant (P > 0.05). More men (40.7%) than women (28.9%) were satisfied with their psychological health.

The global domain “life as a whole” and the domains “physical health” and “psychological health” were analyzed separately. Patients who were satisfied were compared with the nonsatisfied group with respect to total scores of VAS, IES, HAD, and DRI. In the domain “life as a whole,” the nonsatisfied patients reported statistically significant higher scores on VAS (P = 0.035), HAD-anxiety (P = 0.015), HAD-depression (P < 0.001), and DRI (P = 0.011) in comparison with patients who were satisfied. On the domain “psychological health” the nonsatisfied patients reported significantly higher scores than the satisfied patients on IES (P = 0.002), HAD-anxiety (P = 0.001), and HAD-depression.
No significant differences were found between satisfied and nonsatisfied patients regarding physical health.

**Correlations**

Correlation between the scores of three LiSat-11 items – life as a whole, physical health, and psychological health – and the scores of VAS, IES, HAD, and DRI were analyzed.

“Life as a whole” was significantly negatively correlated to VAS ($r = -0.216, P = 0.008$), HAD-anxiety ($r = -0.278, P = 0.001$), HAD-depression ($r = -0.380, P < 0.001$), IES ($r = -0.179, P = 0.026$), and DRI ($r = -0.287, P < 0.001$).

Physical health was significantly negatively correlated to VAS ($r = -0.236, P = 0.003$), HAD-anxiety ($r = -0.203, P = 0.013$), HAD-depression ($r = -0.222, P = 0.006$), IES ($r = -0.233, P = 0.004$), and DRI ($r = -0.384, P < 0.001$).

Psychological health was significantly negatively correlated to HAD-anxiety ($r = -0.351, P < 0.001$), HAD-depression ($r = -0.314, P < 0.001$), IES ($r = -0.328, P < 0.001$), and DRI ($r = -0.179, P = 0.027$).

**Table 1** Questionnaire response for the total group

<table>
<thead>
<tr>
<th>LiSat-11 item</th>
<th>All participants (n = 160)</th>
<th>Women (n = 103)</th>
<th>Men (n = 57)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity (VAS)</td>
<td>64.5 (21.1)</td>
<td>66.5 (20.4)</td>
<td>60.8 (21.9)</td>
<td>0.176</td>
</tr>
<tr>
<td>Impact of event scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>24.1 (15.5)</td>
<td>24.5 (16.1)</td>
<td>23.2 (14.7)</td>
<td>0.632</td>
</tr>
<tr>
<td>Intrusion subscale</td>
<td>12.3 (8.3)</td>
<td>12.3 (7.9)</td>
<td>12.2 (8.8)</td>
<td>0.705</td>
</tr>
<tr>
<td>Avoidance subscale</td>
<td>11.7 (9.4)</td>
<td>12.2 (10.2)</td>
<td>10.8 (7.2)</td>
<td>0.667</td>
</tr>
<tr>
<td>Hospital anxiety</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>7.5 (4.4)</td>
<td>7.3 (4.4)</td>
<td>7.8 (4.4)</td>
<td>0.532</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.4 (4.4)</td>
<td>7.5 (4.6)</td>
<td>7.4 (4.1)</td>
<td>0.974</td>
</tr>
<tr>
<td>Disability rating index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dressing</td>
<td>11.7 (19.6)</td>
<td>11.1 (18.6)</td>
<td>12.7 (21.2)</td>
<td>0.747</td>
</tr>
<tr>
<td>Walking</td>
<td>25.6 (27.5)</td>
<td>26.9 (27.5)</td>
<td>23.2 (27.5)</td>
<td>0.350</td>
</tr>
<tr>
<td>Climbing stairs</td>
<td>25.2 (27.4)</td>
<td>27.5 (28.6)</td>
<td>21.1 (24.9)</td>
<td>0.187</td>
</tr>
<tr>
<td>Sitting</td>
<td>52.1 (30.6)</td>
<td>54.4 (29.7)</td>
<td>48.1 (31.9)</td>
<td>0.249</td>
</tr>
<tr>
<td>Standing</td>
<td>51.6 (33.5)</td>
<td>52.5 (31.8)</td>
<td>49.8 (36.6)</td>
<td>0.831</td>
</tr>
<tr>
<td>Carrying</td>
<td>56.9 (31.2)</td>
<td>61.3 (29.7)</td>
<td>49.2 (32.4)</td>
<td>0.023</td>
</tr>
<tr>
<td>Making a bed</td>
<td>37.9 (31.0)</td>
<td>40.9 (31.5)</td>
<td>32.7 (29.8)</td>
<td>0.093</td>
</tr>
<tr>
<td>Running</td>
<td>63.7 (34.5)</td>
<td>65.6 (32.6)</td>
<td>60.3 (37.6)</td>
<td>0.502</td>
</tr>
<tr>
<td>Light work</td>
<td>41.6 (30.1)</td>
<td>42.2 (29.4)</td>
<td>40.7 (31.5)</td>
<td>0.592</td>
</tr>
<tr>
<td>Heavy work</td>
<td>76.7 (28.2)</td>
<td>78.4 (25.7)</td>
<td>73.7 (32.3)</td>
<td>0.938</td>
</tr>
<tr>
<td>Lifting</td>
<td>78.5 (28.5)</td>
<td>81.3 (24.7)</td>
<td>73.1 (33.9)</td>
<td>0.273</td>
</tr>
<tr>
<td>Sports</td>
<td>52.9 (33.0)</td>
<td>54.3 (32.7)</td>
<td>50.4 (33.7)</td>
<td>0.422</td>
</tr>
<tr>
<td>DRI index</td>
<td>47.7 (21.2)</td>
<td>49.6 (20.3)</td>
<td>44.5 (22.6)</td>
<td>0.340</td>
</tr>
</tbody>
</table>

Note: All values are means, with standard deviations in parentheses.

Abbreviations: DRI, disability rating index; VAS, visual analogue scale.

**Table 2** Self-reported levels (%) of satisfaction with life as a whole and with ten different life domains; LiSat-11

<table>
<thead>
<tr>
<th>LiSat-11 item</th>
<th>All participants (n = 160)</th>
<th>Women (n = 103)</th>
<th>Men (n = 57)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life as a whole</td>
<td>28.1%</td>
<td>25.3%</td>
<td>33.3%</td>
<td>0.288</td>
</tr>
<tr>
<td>Vocation</td>
<td>24.8%</td>
<td>25.3%</td>
<td>24.1%</td>
<td>0.872</td>
</tr>
<tr>
<td>Economy</td>
<td>20.3%</td>
<td>18.2%</td>
<td>24.1%</td>
<td>0.386</td>
</tr>
<tr>
<td>Leisure</td>
<td>20.3%</td>
<td>20.2%</td>
<td>20.4%</td>
<td>0.980</td>
</tr>
<tr>
<td>Contacts</td>
<td>36.6%</td>
<td>42.4%</td>
<td>25.9%</td>
<td>0.031</td>
</tr>
<tr>
<td>Sexual life</td>
<td>37.0%</td>
<td>42.4%</td>
<td>27.8%</td>
<td>0.055</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>57.0%</td>
<td>56.7%</td>
<td>57.4%</td>
<td>0.933</td>
</tr>
<tr>
<td>Family life</td>
<td>64.6%</td>
<td>66.3%</td>
<td>61.4%</td>
<td>0.579</td>
</tr>
<tr>
<td>Partner</td>
<td>66.4%</td>
<td>68.8%</td>
<td>61.9%</td>
<td>0.417</td>
</tr>
<tr>
<td>Somatic health</td>
<td>6.6%</td>
<td>5.1%</td>
<td>9.3%</td>
<td>0.314</td>
</tr>
<tr>
<td>Psychological health</td>
<td>33.1%</td>
<td>28.9%</td>
<td>40.7%</td>
<td>0.126</td>
</tr>
</tbody>
</table>

Abbreviation: LiSat-11, 11-item life satisfaction questionnaire.
Bivariate logistic regression

Logistic regression was used to investigate factors that could be associated with life satisfaction. The global item “life as a whole” was chosen as a dependent variable and coded as a binary variable (1 = unsatisfied, 0 = satisfied). A multivariate forward stepwise logistic regression was performed with the following independent variables: age, gender, pain intensity, anxiety, depression, posttraumatic stress, and disability (Table 3). A statistically significant association was only found between “unsatisfied with life as a whole” and HAD-depression (OR = 1.141, CI 1.014–1.285).

Discussion

The present study shows that patients with injury-related chronic pain who had been referred to a specialist rehabilitation clinic reported high levels of pain intensity, anxiety, depression, and posttraumatic stress, with activity limitations in everyday life and decreased life satisfaction.

Pain intensity rated on the VAS was high; all patients rated the VAS-scores higher than 10 mm, a value that has been considered symptomatic, and in the majority (78.5%), the reported VAS scores were 50 mm or higher. Moreover, patients also rated their level of depression and anxiety, and more than 40% were identified as having possible depression or anxiety disorder according to the HAD scores. These results may reflect that the participants suffered from severe symptoms and that they were in need of the specialist assessment.

Posttraumatic stress reactions are commonly reported after traffic accidents, specifically after whiplash injuries. Despite the fact that posttraumatic stress decreases with time, the frequency of patients with moderate to severe stress response (48%) was clearly higher in the present study than previous studies that documented patients both in the acute phase (13%) and 5 years after whiplash injuries (15%).

In a study of acute whiplash patients, Sterling et al found that high IES scores post trauma persisted into the chronic stage of the injury, especially in persons with high disability. Since the IES scores in their study at 6 months (IES 23 ± 13) were only slightly lower than the values seen in the present study, the results of this present study may indicate that high posttraumatic stress scores may last for several years in persons with severe symptoms after an accident.

Although some previous studies have reported on pain and posttraumatic stress together with psychological factors such as anxiety and depression after traffic injuries, few studies have focused on the consequences of the experienced disability on quality of life.

In the present study, the mean value of DRI was in the same range as previously reported in patients with chronic pain from the same department. The ratings of life satisfaction in the present study were low and clearly lower on all the eleven items on the LiSat-11 than those of a large population-based Swedish reference group of 2600 individuals described by Fugl-Meyer et al and of persons with whiplash injuries 5 years after the trauma. However, in the present study, the patient group with chronic pain was a selected group of patients referred to the Pain Rehabilitation Clinic, and the ratings of satisfaction with somatic and psychological health were surprisingly low. Only 6.6% were satisfied with their somatic health and 33.1% were satisfied with their psychological health.

Moreover, a clear relationship between not being satisfied with “life as whole” and high values of pain, anxiety, depression, posttraumatic stress, and disability was shown in the present patient population.

However, since depression was the only single factor in a multivariate logistic regression model that was associated with low level of the overall life satisfaction, this relationship should be taken into consideration in the management of persons with injuries related to chronic pain. Previous studies have shown that depression is common among chronic pain patients and has been found to increase the risk for pain intensity, reduce activity levels, deteriorated social and occupational functioning, and lower life satisfaction. It is well known that chronic pain can trigger depressive symptoms and that depression in turn increases the adverse effects of pain. These two conditions work in a negatively synergic way: the depression reinforces the chronic pain and the chronic pain promotes depressive symptoms, and together this can manifest in less physical activity and less life satisfaction.

In the present study, few differences between genders regarding pain and symptoms were found. Women reported

### Table 3 Bivariate logistic regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.374</td>
<td>1.437</td>
<td>0.646–3.195</td>
</tr>
<tr>
<td>Gender</td>
<td>0.231</td>
<td>1.642</td>
<td>0.730–3.693</td>
</tr>
<tr>
<td>DRI</td>
<td>0.052</td>
<td>1.019</td>
<td>1.000–1.039</td>
</tr>
<tr>
<td>IES</td>
<td>0.545</td>
<td>1.008</td>
<td>0.982–1.035</td>
</tr>
<tr>
<td>VAS</td>
<td>0.384</td>
<td>0.992</td>
<td>0.974–1.010</td>
</tr>
<tr>
<td>HAD-anxiety</td>
<td>0.956</td>
<td>1.004</td>
<td>0.885–1.138</td>
</tr>
<tr>
<td>HAD-depression</td>
<td>0.029</td>
<td>1.141</td>
<td>1.014–1.285</td>
</tr>
</tbody>
</table>

*Note:* Dependent variable: global LiSat-11 item “life as a whole” (1 = unsatisfied, 0 = satisfied).

*Abbreviations:* CI, confidence interval; DRI, disability rating index; HAD, hospital anxiety and depression scale; IES, impact of event scale; OR, odds ratio; VAS, visual analogue scale.
slightly nonsignificantly higher scores on pain intensity, anxiety, depression, and posttraumatic stress than men. Women reported also higher scores on most disability items than men, yet a significant difference was found only on the item “carrying.” Although some studies have reported more women than men to suffer from chronic pain and pain-related symptoms, the results of the present study are in line with the studies that have failed to show any gender differences. The inconsistent findings may be due to differences in study populations, but the findings do indicate the importance of adequate rehabilitation, regardless of gender.

Some limitations of this study should be noted. Since patients were referred to a specialist clinic for pain rehabilitation, they probably represent a selected group of patients with chronic pain with severe consequences and high complexity. As this study was carried out in a clinical setting, there was a lack of blinding, there was no comparable control group, and there was no possibility of randomizing the patients.

Some objections may also be raised concerning the findings of this study. Although patients referred their chronic pain condition and other symptoms to their previous injury, there was a lack of the pre-injury characteristics. This may have affected the results. Chronic pain is influenced by different physical and emotional factors that have consequences on disability/activity and affect life satisfaction. Therefore, there were several multiple comparisons made to study the relationship between these factors and the LiSat-11 findings of this study. Moreover, since the study population is small, the generalizability of the study is limited.

However, this study has implications for clinicians; since the results highlight the importance of assessment of life satisfaction in patients with injury-related chronic pain. Furthermore, this study emphasizes the value of a broad screening in patients with chronic pain with respect to the relation of pain intensity and the different categories of nonpain symptoms (anxiety, depression, and posttraumatic stress), disability, and life satisfaction and supports the biopsychosocial approach of these patients to optimize the assessment and treatment.

However, this study shows that life satisfaction was low in patients with injury-related chronic pain, especially satisfaction with somatic and psychological health on the LiSat-11 instrument. Since this instrument has been found to harmonize well, the difference between patients’ subjective reality and needs or desires has been suggested as an outcome measure in pain rehabilitation. This could be a valuable method included in a broad screening of chronic pain patients.

Disclosure
The author reports no conflicts of interest in this work.

References

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