Larger pain extent is associated with greater pain intensity and disability but not with general health status or psychosocial features in patients with cervical radiculopathy

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Abstract
Pain as a result of cervical radiculopathy (CR) can be widespread, nondermatomal and individually specific, but the association between pain extent and other clinical features has never been explored. The objective of this study is to investigate whether pain extent relates to clinical variables including pain intensity in addition to health indicators including disability, general health, depression, somatic anxiety, coping strategies or self-efficacy.

An observational cohort study was conducted. Participants were recruited from 4 hospital spinal centres in Sweden. Pain extent was quantified from the pain drawings of 190 individuals with cervical disc disease, verified with magnetic resonance imaging (MRI) and compatible with clinical findings (examined by a neurosurgeon), that show cervical nerve root compression. Pain extent was evaluated in relation to neck pain, arm pain, and headache intensity. Multiple linear regression analysis were then used to verify whether pain extent was associated with other health indicators including disability, health-related quality of life, depression, somatic anxiety, coping strategies and self-efficacy.

Pain extent was directly related to neck, arm and headache pain intensity (all $P < .01$). Multiple linear regression revealed that pain extent was significantly associated only to the level of perceived disability ($P < .01$).

Increased pain extent in people with CR is associated with higher headache, neck and arm pain intensity, and disability but not measures of general health, depression, somatic anxiety, coping strategies or self-efficacy.

Abbreviations: CR = cervical radiculopathy, CSQ = Coping Strategy Questionnaire, DRAM = Distress and Risk Assessment Method, Modified Zung = Modified ZUNG Depression Index, MRI = magnetic resonance imaging, MSPQ = Modified Somatic Perception Questionnaire, NDI = Neck Disability Index, PD = pain drawing, VAS = visual analogue scale, WAI = work ability index, ZUNG = Self-rating Depression Scale.

Keywords: cervical, chronic pain, pain drawing, radiculopathy, widespread pain
### 1. Introduction

Cervical Radiculopathy (CR) is a disorder of the cervical nerve root often as a result of degenerative changes within the cervical spine causing either direct mechanical and/or chemical irritation and/or denervation of nerves. The incidence and prevalence of CR is estimated at 0.832 to 1.79 per 1000 person-years and 1.21 to 5.8 per 1000 respectively. Clinical manifestations of CR typically include pain within cervical and/or scapular region that radiates into arm which is accompanied by varying degrees of sensory, motor and reflex disturbances. 

Traditionally, the spatial distribution of symptoms experienced by people with CR was thought to correspond to the root innervated by the pathological nerve root; nevertheless, clinical observations suggest otherwise. Murphy et al (2009) used pain drawings (PD) to investigate whether cervical radicular pain follows the specific dermatomal pattern and found that in 69.7% of cases the distribution of pain was non-dermatomal. This study was however retrospective in nature with risk of selection bias and lack of standardisation for PD instruction. Inclusion criteria also lacked clarity and it is unknown if imaging and electrophysiological findings had to correspond with subjects’ symptoms. However, similar findings were reported for people with sciatica. Technological advances also brought changes in how PD are acquired (i.e., from pen and paper to stylus pen and tablet) and analyzed (i.e., from visual inspection to machine learning approaches). The utility of PD have therefore expanded from differentiation of organic vs non-organic pain to prediction of postoperative success, illustration of pain in human experimental studies, psychological screening, outcome measure in clinical trials and subgrouping of musculoskeletal conditions. Noticeably, the relationship between pain extent (i.e., percentage of area shaded for the PD relative to the total body area) and other variables (i.e., pain intensity, disability, quantitative sensory measurements, age, depression, anxiety, kinesiophobia) has been an intense area of research over the past decade for various musculoskeletal disorders. PD forms a routine part of clinical assessment and if associations exists between PD and other variables for example, psychological features, it may prompt the clinician to conduct further assessments and/or provision of treatment that otherwise would not usually be conducted. Previous studies have shown larger pain extent is associated with pain intensity and disability in people with chronic neck pain, whiplash associated disorders, spinal stenosis and chronic low back pain whereas this association was not evident for carpal tunnel syndrome, hip osteoarthritis, greater trochanteric pain syndrome and migraine. Differences observed might be secondary to unique pain pathophysiology (i.e., nociceptive, neuropathic, nociplastic dominant) highlighting that factors associated with larger pain extent are likely disorder specific.

Many people with CR experience pain outside of the affected dermatome, yet it is unknown whether these extended symptoms are related to distinct clinical variables identifiable using established and valid questionnaires. Thus, the objective of this study was to investigate whether pain extent relates to clinical variables including pain intensity in addition to health indicators including disability, general health, depression, somatic anxiety, coping strategies or self-efficacy.

### 2. Methods

#### 2.1. Study design

An observational cohort study was conducted in 4 spinal centre in Sweden between 2009 and 2012. This was a secondary analysis of baseline data from a randomized control trial registered at www.clinicaltrials.gov (NCT01547611) and therefore sample size was not calculated priori specifically for the present study. This study was approved by the regional ethical review board (Dnr-M126-08) and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies (Supplementary file 1, http://links.lww.com/MD/P811).

#### 2.2. Participants

Patients with single level CR scheduled for surgery were recruited to participate in a prospective, randomized clinical trial designed to compare 2 postoperative rehabilitation interventions. Inclusion criteria were age 18 to 70 years, evidence of cervical radiculopathy reported for a minimum of 2 months, and concordant nerve root compression visualized on magnetic resonance imaging (MRI). Potential participants were examined by a neurosurgeon and exclusion criteria were previous cervical surgery, a previous fracture or luxation of the cervical spine, myelopathy, malignancy or spinal tumor, systemic disease, diagnosed or suspected fibromyalgia or generalized myofascial pain, persistent or recurrent severe back pain, diagnosed psychiatric disorders, alcohol or drug addiction, and lack of familiarity with the Swedish language. All participants received verbal and written information about the study and informed written consent was obtained.

#### 2.3. Questionnaires

Participants completed multiple patient-reported measures and underwent a clinical examination on the day before surgery by one of 4 trained physiotherapists; 1 at each of the 4 hospitals. Patients also completed a generic questionnaire which detailed their sex, age, employment status, and physical activity levels.

##### 2.3.1. Pain intensity.

Pain intensity was measured using a visual analogue scale (VAS) anchored by 0=no pain, and 100=worst imaginable pain. Patients were asked to complete a VAS for their average (over the last month) neck pain intensity, arm pain intensity and headache intensity.

##### 2.3.2. Disability.

The Swedish version of the Neck Disability Index (NDI) was used to assess neck related disability specifically related to neck pain. The NDI consists of 10 items grading neck disability from 0 (no activity limitations) to 5 (major activity limitations) with a total maximum score of 50 points which is then expressed as a percentage (0%–100%) with a higher score representing a higher level of disability. The NDI is widely used, and is a reliable (intraclass correlation coefficient up to 0.98) and valid measurement of disability in neck pain disorders. The Swedish version of the NDI also demonstrates good validity, sensitivity and test-retest reliability.

##### 2.3.3. Psychosocial factors.

Three subscales of the Swedish version of the Coping Strategy Questionnaire (CSQ) were used to assess the patient’s current use of coping strategies. The
internal consistency and test-retest reliability of the Swedish CSQ were previously reported to be high and low to high respectively.[29] The CSQ includes the pain catastrophizing subscale which evaluates the use of negative thinking as a reaction to pain; a subscale which assess the patient’s belief in their control over pain and a subscale which evaluates their perceived ability to decrease their pain. The total score was retained for further analysis.

Distress and Risk Assessment Method (DRAM)[30] is made up of 2 questionnaires that is, Modified ZUNG Depression Index (Modified Zung) and Modified Somatic Perception Questionnaire (MSPQ) and it is used as a psychological status screening tool for patients with pain. Depression was evaluated with Modified Zung, which included 23 items and scores of 0 to 69; higher scores were indicative of depressed moods.

Self-Rating Depression Scale. 0 to 69 modified score
Self-Rating Depression Scale. 20 to 80, original scale
ZUNG Self Rating Depression Scale Index 0.25 to 1

Somatic anxiety was evaluated with the MSPQ, which included 22 items and scores of 0 to 39; higher scores were indicative of a higher level of somatic anxiety. Both Modified Zung and MSPQ have been tested previously in a Swedish population.[31,32]

2.3.4. General health. Health-related quality of life was quantified using the EuroQol Five Dimension Scale (EQ-5D, 243 possible health states converted to a single index value – 0.594 to 1, where 1 is perfect health) and EuroQol VAS (0–100 representing worst to best imaginable health state respectively).[33]

2.3.5. Lifestyle habits. Patients were also asked to report their daily physical activity and weekly habits of exercise, sports, and open-air activities during the preceding 12 months. Answers to these questions were combined and interpreted on the basis of a 4-point scale (1 = inactivity to 4 = high activity).[14]

2.3.6. Work ability index. Work ability index (WAI) is a self-administered questionnaire that measures individuals’ perceived ability to perform at work and identifies necessary action that prevents declining capacity and early retirement. It covers 7 items including current work ability compared with the lifetime best, work ability in relation to the demands of the job, number of current diseases diagnosed, estimated work impairment due to diseases, sick leave during the past year (12 months), own prognosis of work ability 2 years from now and mental resources. Each item are scored differently with the final score ranging from minimum of 7 to maximum of 49 and separated into 4 categories that is, 7 to 27 indicating poor work ability and to restore work ability; 28 to 36 indicating moderate work ability and to improve work ability; 37 to 43 indicating good work ability and to support work ability and 44 to 49 indicating very good work ability and to support work ability.[35] The WAI was shown to have acceptable predictive validity within a Swedish population in a previous study.[14]

2.3.7. Pain drawings. All participants were instructed to complete a pain drawing by shading their pain on 2 body charts; one showing a frontal view of the body and the other, the dorsal view. Body charts were printed on paper (A4 size) and patients were asked to shade each part of the body, regardless of the quality and intensity of the pain, using a pencil.

All pain drawings were then digitized using scanner and imported into an image analysis software (Inkscape version 0.48). The imported body charts were superimposed by 2 operators with a transparent digital body chart of the same size and features. Pain drawings were then encircled and copied on to the digital body charts using the region of interest tool function. The procedure for digitalizing pain drawings was described previously and its reliability was confirmed.[37,38]

Pain extent and pain location was computed using Matlab as described previously.[16] The software generates the number of shaded pixels from the pain drawing and exports this data which is defined as pain extent. Only pixels colored inside the perimeter of the body chart were considered. The pain extent was reported for each subject as the sum of the pixels in the frontal and dorsal body chart, expressed as a percentage of the total body chart area (i.e., a total of 381151 pixels, ventral: 191823 pixels, dorsal: 189328). Pain frequency maps were generated which consisted of all of the pain drawings superimposed and analyzed simultaneously solely for the purpose of illustrating where pain is most commonly perceived across the entire cohort. This was performed for both the dorsal and ventral body charts.

2.4. Statistical analysis

Descriptive statistics were used to describe the participant characteristics, their symptom characteristics and their overall health status considering pain, work, disability, general health and psychological factors. Pain frequency maps and the pain location analysis were also generated for descriptive purposes only to illustrate the most common painful regions across the entire sample.

The variables considered were divided into 3 groups:
- Clinical variables: namely EQ-5D, NDI, ZSDS (3 versions: original scale, modified score, index), MSPQ, SES, DRAM, CSQ, and the WAI.
- Pain extent variable: the variable of interest. Initial analysis revealed that pain extent data did not show a normal distribution and rather followed a Log-normal distribution. Therefore, a logarithmic transformation was performed on the pain extent data.
- Control variables: namely gender, age, work status (No work, Part-time work, Full time work), physical exercise in the past 12 months (“physical exercise”: None at all, Once or twice a week, Several times a week, daily/almost daily), CR level involved, and VAS for neck pain, arm pain and headache. To obtain more robust results for the “Physical exercise” variable we collapsed together the categories “None at all” and “Once or twice a week”; the new category is “At most once or twice a week”.

Multiple linear regression analysis was used to verify whether pain extent was significantly associated with the clinical variables (i.e., the dependent variables of the regression models) when accounting for sex, age, working situation, physical exercise habits over the past 12 months, vertebral level involved and neck, arm and headache intensity (i.e., the independent control variables). To obtain robust estimates of the standard errors we used the Huber-White sandwich estimators.

Before fitting the regression models, we explored the relations between pain extent and the control variables in order to avoid the use of strongly related variables as covariates in the models. The relations between pain extent and the categorical variables were examined using independent one-way analysis of variance. The relations between pain extent and the continuous independent variables were explored using 2 statistical instruments,
namely the Pearson correlation coefficient and the Spearman correlation coefficient. The latter was used to verify if there were nonlinear relations.

Data were analyzed with SPSS Version 22.0 (IBM Corp., Armonk, NY). Statistical significance was set at \( P < .05 \).

3. Results

A total of 201 patients were recruited however, 11 participants were excluded since their pain drawings could not be processed (poor shading of the pain area). Thus, the final sample included 190 patients. Table 1 presents the characteristics of the sample and their symptom characteristics including their general health and psychosocial status. The sample was composed of 53% men, and across the entire sample the mean age was 50 years (min = 22 years, max = 70 years, SD = 8.3 years). Exactly half of the patients were in full time work, 19% part-time work, whilst 31% were not working. The vast majority of the patients (73%) practiced physical exercise several times a week in the preceding 12 months (43% daily or almost daily), while only 4% did not exercise at all.

The mean value of their current neck pain intensity on the VAS was 56 (min = 0, max = 100, SD = 24.5), while for arm pain intensity the mean value was 50.2 (min = 0, max = 100, SD = 28.0) and for headache 24.6 (min = 0, max = 100, SD = 29.1).

Figure 1 illustrates the pain frequency maps for the full sample of participants included in the study. Table 2 presents the relations between pain extent and the categorical independent variables. Statistically significant differences between categories were only found for work status. Pain extent was significantly larger for those that do not work (6.7%) compared to those with part-time work (5.2%) or full time work (4.5%). Table 3 presents the correlation coefficients between pain extent and the continuous independent variables considered. The results for the Pearson correlation coefficient and the Spearman correlation coefficient were approximately the same, which indicates their robustness. Pain extent was directly related to neck, arm and headache pain intensity. Although statistically significant these relations are rather weak, with absolute values approximately ranging from 0.2 to 0.35. Pain extent was not related to age.

In only 2 patients, the C7/T1 level was implicated and therefore the C7/T1 variable was excluded from the regression models. The regression models were used to verify whether pain extent has a statistically significant association with the dependent variables’ scores when accounting for gender, age, socioeconomic status, working situation, physical exercise habits, nerve root involved and neck, arm and headache intensity. Table 4 illustrates the results of the first 5 models considered, namely the EuroQol Five Dimension Scale model, the NDI model and the 3 ZUNG depression models (ZSDS models). The ZSDS

1. model relies on the original ZUNG self-rating depression scale, the ZSDS
2. on the modified score and the ZSDS
3. on the self-rating depression scale index.

Pain extent was significantly associated only to the NDI \( (P < .01) \). Table 5 shows the result of the last 4 models considered, namely the MSPQ model, the DRAM model, the CSQ model and the WAI model. Pain extent was not significantly associated to any of these dependent variables.

4. Discussion

The present study is the first to investigate the association between pain extent and clinical and psychological variables in people with cervical radiculopathy. The cervical segment most affected within this cohort was C5 to C7 which resonates well with another surgical cohort of 1420 consecutive cases in the US.[39] Demographic data (i.e., age, gender) also showed similarities[39] however, baseline pain intensity was less severe within the present cohort.

Observation of the pain frequency maps revealed that the most common area of pain were the mid and lower neck region, trapezius and superior-anterior shoulder followed by anterolateral upper arm and forearm. Pain was also reported more frequently on the right upper extremity compared to the left. Cranial, torso and lower extremity pain were less frequently reported although such widespread pain was reported by a minority of individuals. Although all participants had to have MRI confirmed CR, other sources of pain were not excluded (i.e., facet joint referral, discogenic referral, muscular referral) and thus the pain frequency maps do not purely reflect the pain experienced from CR alone. The main finding of this study is that larger pain extent is associated with higher headache, neck and arm pain intensity, and higher disability but not general health, depression, somatic anxiety, coping strategies or self-efficacy in people with CR.

The association between pain extent and pain intensity is in alignment with most existing studies albeit in different cohorts.[11,16-18,40-42] The association between pain extent and pain intensity might be mediated by central sensitisation as repeated prolonged peripheral nociceptive afferents causes central wind-up together with hyperalgesic and allodynic responses.[43,44] Evi-
dence of an association between pain extent and mechanical hyperalgesia assessed via the pressure pain threshold has been demonstrated in hip osteoarthritis[20] and knee osteoarthritis[40] although not in fibromyalgia,[41] carpal tunnel syndrome,[19] greater trochanteric pain syndrome[21] and migraine.[22] No studies have assessed for an association between pain extent and physical measures of allodynia via the dynamic mechanical allodynia test, although Willett et al (2020) [20] showed an association between pain extent and Pain DETECT which includes a question assessing allodynia.

Within our cohort, the source of pain is likely of multiple origins that is, localized and/or referred nociceptive from muscles and joints, neuropathic from nerve structures and nociplastic driven predominately by the central nervous system. Individuals whose presentation is dominantly neuropathic are likely to report higher pain intensity and higher spread of symptoms compared to individuals whose presentation is largely nociceptive but with some neuropathic symptoms given the presence of CR. Individuals with neuropathic back pain report higher pain intensity compared to those with nociceptive pain (mean NRS 6.88 versus 4.62 respectively)[45] and similarly, people with CR report higher pain intensity compared to those with neck pain of nociceptive origin (mean NRS 6.5 versus 4.4 respectively).[46,47] Secondary to the nature of neuropathic and nociplastic pain, individuals whose presentation is dominated by these pain mechanisms are more likely to report larger pain extent compared to those with nociception dominant pain patterns.

The current study also revealed an association with larger pain extent and greater disability in patients with CR. According to previous reports, the relationship between pain extent and disability varies depending on the population examined and thus far 7 studies reported a significant association between pain extent and disability [11,16–18,42,48,49] while 7 did not.[16,19–22,40,41] Interestingly, 4 out of 5 studies which examined patients with spinal pain (i.e., neck pain, whiplash, spinal stenosis and low back related leg pain) did show an association.[11,16–18]

One may assume that the studies which found a nonsignificant association between pain extent and disability also reported a nonsignificant association between pain extent and pain intensity, given that it is often assumed that lower pain intensity implies a lower level of disability.[50] This however might not necessarily hold true; a systematic review and meta-analysis of mediation studies in low back pain and neck pain revealed that self-efficacy, psychological distress and fear are the main mediator/driver for a simultaneous increase in pain and disability meaning that individuals who have higher self-efficacy could have high pain intensity but with less disability.[51]

This is the first study to investigate the association between pain extent and work status. Pain extent was significantly larger for those that do not work (6.7%) compared to those with part-
time work (5.2%) or full time work (4.5%). The finding of this study seems coherent with the wider literature since a systematic review of 25 studies revealed that the presence of radicular pain predicts longer sick leave in acute low back pain.[52] In addition, the presence of multisite pain at baseline was predictive of an individual to be allocated into a higher absenteeism trajectory in a both a blue collar dominant cohort (Hallman et al., 2019a) and general working class.[54] However, many other factors are associated with absenteeism due to musculoskeletal disorders such as the level of pain intensity and disability,[52,53,55,56] degree of self-efficacy,[52,55,57] occupation,[58] physical activity level[59] and return-to-work coordination offered by employer.[55]

The present study demonstrated that general health, depression, somatic anxiety, coping strategies and self-efficacy had no association with pain extent. This is in contrast with a whiplash cohort where pain extent was associated with depression and self-efficacy.[17] This might be related to the questionnaire used where Falla et al (2016) used the Hospital Anxiety and Depression scale. However, previous reports have indicated only 38% of individuals with CR scored above the cut-off point for the presence of depression using Hospital Anxiety and Depression scale.[60] Nonsignificant associations between pain extent and psychological factors may also relate to the expectation of recovery as all participants were pending operative management within this cohort, thus potentially reducing psychological burden.

To date, 2 published systematic reviews have examined the association between pain extent and psychological variables...
interpretation of pain is complex\cite{62} and it remains unclear whether individual psychological traits determine a specific pain experience or whether psychological behavior are proportionally related to the degree of nociceptive input.\cite{63} The result of this study and the current cumulative evidence therefore recommend the use of pain drawings as a psychological screening tool in clinical settings. On the contrary, based on the demonstrated relationship with pain intensity and disability, the use of pain drawings could be considered as a low cost and easy tool which could be used to monitor the clinical course of CR.

### 4.1. Strengths and limitations

The standardized procedure of PD acquisition, scanning and analysis removes overestimation error often seen in pain drawing grid systems\cite{64} and allowed pain frequency maps to be generated which is a strength of this study. Selection bias was partially controlled by sampling from 4 separate spine centres. However, the results of this study should not be extrapolated to populations outside of surgical setting and to individuals who has multi-level CR as all participant were eligible for surgical management and had single level CR respectively. In addition, only individuals with nerve root compression visualized on MRI were included while it had been recognized that radiculopathy can be chemically induced via leakage of nucleus pulposus material into nerve root region.\cite{65}

Therefore, the results of this study do not consider individuals who suffers from chemically induced CR. CR can result in sensory, motor and reflex changes in addition to pain and these additional features were not considered in this study. In addition, and as noted earlier, although all participants had to have MRI confirmed CR, other sources of pain were not excluded (i.e., facet joint referral, discogenic referral, muscular referral) and thus the pain frequency maps and pain extent data may not uniquely reflect the pain experienced from CR alone. Subjective and objective markers of neuropathic pain were also not assessed which might have provided useful findings. A 2D unisexed body template was used in this study and it has been suggested that the area of pain drawn on 2D body template is typically larger than on a 3D template.\cite{66}

Additionally, participants have reported preference towards sex specific templates\cite{67} and the use of 3D body templates as it enables more accurate localization of pain.
5. Conclusion

This is the first study to provide evidence that increased pain extent in people with CR is associated with higher headache, neck and arm pain intensity, and disability but not measures of general health, depression, somatic anxiety, coping strategies or self-efficacy. Within a clinical context, pain drawings have the potential to be used to screen for disability with subsequent targeted interventions. Future research should investigate the prognostic utility of pain extent on conservative and surgical outcomes for people with CR.

Author contributions

Conceptualization: Kwun Lam, Marco Barbero, Deborah Falla.
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Formal analysis: Emiliano Soldini.
Funding acquisition: Anneli Peolsson, Åsa Dedering.
Investigation: Anneli Peolsson, Håkan Löfgren, Johanna Wibault, Åsa Dedering, Birgitta Öberg, Peter Zsigmond, Marco Barbero, Deborah Falla.

Methodology: Anneli Peolsson, Emiliano Soldini, Håkan Löfgren, Johanna Wibault, Åsa Dedering, Birgitta Öberg, Peter Zsigmond, Marco Barbero, Deborah Falla.
Software: Marco Barbero.
Supervision: Deborah Falla.
Writing – original draft: Kwun Lam, Deborah Falla.
Writing – review & editing: Anneli Peolsson, Emiliano Soldini, Håkan Löfgren, Johanna Wibault, Åsa Dedering, Birgitta Öberg, Peter Zsigmond, Marco Barbero.

References


Table 5
Result of the multiple linear regression model. Coefficient (standard error). Pain extent was the independent variable of interest.

<table>
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<th>DRAM</th>
<th>CSQ</th>
<th>WAI</th>
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<td>0.713</td>
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<td>(0.418)</td>
<td>(0.0737)</td>
<td>(0.678)</td>
<td>(0.610)</td>
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<td>(0.699)</td>
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<td>(0.769)</td>
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<tr>
<td>VAS Headache</td>
<td>0.0707***</td>
<td>0.0134**</td>
<td>0.0334</td>
<td>−0.0391*</td>
</tr>
<tr>
<td>(0.0133)</td>
<td>(0.0023)</td>
<td>(0.0247)</td>
<td>(0.0197)</td>
<td></td>
</tr>
<tr>
<td>Adjusted R²</td>
<td>0.2389</td>
<td>0.2784</td>
<td>0.1287</td>
<td>0.3627</td>
</tr>
<tr>
<td>(2.737)</td>
<td>(0.533)</td>
<td>(5.296)</td>
<td>(5.278)</td>
<td></td>
</tr>
</tbody>
</table>

*** P < .001.
** P < .01.
* P < .05.
CSQ = Coping Strategies Questionnaire, DRAM = Distress and Risk Assessment Method, MSPQ = Modified Somatic Perception Questionnaire, VAS = Visual Analogue Scale, WAI = Work Ability Index.


