Pain is Associated to Clinical, Psychological, Physical, and Neurophysiological Variables in Women With Carpal Tunnel Syndrome

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Objectives: To investigate potential relationships of clinical (age, function, side of pain, years with pain), physical (cervical range of motion, pinch grip force), psychological (depression), and neurophysiological (pressure and thermal pain thresholds) outcomes and hand pain intensity in carpal tunnel syndrome (CTS).

Methods: Two hundred and forty-four (n = 224) women with CTS were recruited. Demographic data, duration of the symptoms, function and severity of the disease, pain intensity, depression, cervical range of motion, pinch tip grip force, heat/cold pain thresholds (HPT/CPT), and pressure pain thresholds (PPT) were collected. Correlation and regression analysis were performed to determine the association among those variables and to determine the proportions of explained variance in hand pain intensity.

Results: Significant negative correlations existed between the intensity of pain and PPTs over the radial nerve, C5/C6 zygapophyseal joint, carpal tunnel and tibialis anterior muscle, HPT over the carpal tunnel, cervical extension and lateral-flexion, and thumb-middle, fourth, and little finger pinch tip forces. Significant positive correlations between the intensity of hand pain with function and depression were also observed. Stepwise regression analyses revealed that function, thumb-middle finger pinch, thumb-little finger pinch, depression, PPT radial nerve, PPT carpal tunnel, and HPT carpal tunnel were significant predictors of intensity of hand pain ($R^2 = 0.364$; R^2 adjusted = 0.343; $F = 16.87$; $P < 0.001$).

Conclusion: This study showed that 36.5% of the variance of pain intensity was associated to clinical (function), neurophysiological (localized PPT and HPT), psychological (depression), and physical (finger pinch tip force) outcomes in women with chronic CTS.

Key Words: carpal tunnel syndrome, pain, depression, function, cervical spine, pressure pain

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Carpal tunnel syndrome (CTS) is a pain disorder of the upper extremity mainly characterized by compression of the median nerve at the carpal tunnel. Women are most often affected reporting an annual incidence of approximately 139 per 100,000 females compared with 67 cases per 100,000 in males.[1] Dale et al[2] have recently reported an overall annual incidence rate of 2.3 cases per 100 people in a working population. A recent study found a prevalence ranging from 6.3% to 11.7%; however, this study also showed that the prevalence rate of CTS varies depending on the criteria included.[3] The societal burden of CTS is substantial and it was calculated that the income loss per patient with CTS over a period of 6 years was $45,000 to $89,000 compared with healthy people.[4] In addition, a recent survey found that carpal tunnel release showed the highest utilization rate of surgical procedures performed in the United States for the upper extremity.[5]

Pain and paresthesia within the median nerve–related areas are the most common symptoms experienced by patients with CTS.[6] Pain is mainly determined by the activity of peripheral nociceptors of the nerve supporting a role of the sensitization mechanisms in this condition.[7] In fact, several studies have demonstrated the presence of widespread pressure pain hypersensitivity and thermal pain hyperalgesia in individuals with CTS as a sign of central and peripheral sensitization mechanisms.[8–10] In addition, there is also evidence reporting the presence of fine motor deficits[11,12] and restricted cervical range of motion (CROM)[13,14] in individuals with CTS. Current results support the hypothesis that CTS is a multidimensional condition where several clinical, physical, and neurophysiological aspects act at the same time.

A better understanding of the potential influence of clinical, physical, and neurophysiological impairments on the intensity of hand pain in patients with CTS can assist clinicians in determining adequate therapeutic programs for this group of patients. Few studies have investigated the predictors variables associated with hand pain intensity in CTS. Nunez et al[15] observed that only psychological variables, that is, misinterpretation of nociception and depression, were associated and accounted for 39% of the variation in pain intensity in CTS. Similarly, Vranceanu et al[16] also reported that depression was the only predictor accounting for a 25% of the variance in pain intensity after minor hand surgery in a population with different hand pain conditions, including CTS. These 2 studies support the role of depression as potential predictor of pain intensity in patients with CTS. However, they did not collect other physical or neurophysiological outcomes which could also be associated with the intensity of pain in this population. Therefore, the

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purpose of our study was to investigate the relationship of clinical (age, function, side of pain, years with symptoms), physical (CROM, pinch grip force), neurophysiological (pressure pain threshold [PPT] and thermal pain thresholds), and psychological (depression) outcomes to pain intensity in women with electrodiagnostic and clinical diagnosis of CTS.

METHODS

Participants

Consecutive women diagnosed with CTS from January 2013 to December 2014 by a neurophysiologist with 10 years of clinical experience were screened for eligibility criteria. CTS was diagnosed based on both clinical and electrophysiological findings.[17] To be eligible, they had to exhibit all the following clinical signs: pain and paresthesia in the median nerve distribution, increasing symptoms during the night, positive Tinel sign, and positive Phalen sign. Symptoms had to have persisted for at least 12 months In addition, the electrodiagnostic examination had to reveal deficits of sensory and motor median nerve conduction according to international guidelines of American Association of Electrodiagnosis, American Academy of Neurology, and the American Physical Medicine and Rehabilitation Academy.[18,19] A median nerve sensory conduction velocity of <40 m/s and a median nerve distal motor latency of >4.20 ms were considered abnormal. Patients were classified as minimal, moderate, or severe CTS.[20]

Patients were also excluded if they exhibited any of the following criteria: (1) any sensory/motor deficit in ulnar or radial nerve was present; (2) older than 65 years of age; (3) previous surgery or steroid injections; (4) multiple diagnoses on the upper extremity (eg, cervical radiculopathy); (5) history of neck, shoulder, or upper extremity trauma; (6) history of a systemic disease causing CTS (eg, diabetes mellitus, or thyroid disease); (7) history of musculoskeletal medical condition (eg, rheumatoid arthritis or fibromyalgia); (8) pregnancy; or (9) male sex.

All participants signed an informed consent before their inclusion in the study. The local human research committee (HUFA-12/14) approved the study project.

Clinical Outcomes

The clinical history included questions regarding the location of the symptoms, aggravating and relieving factors, intensity, duration, and previous treatments. The main outcome in the current study was the intensity of hand pain. An 11-point Numerical Pain Rating Scale (0: no pain, 10: maximum pain) was used to determine the patients' current level of hand pain, and the worst and lowest level of pain experienced in the preceding week.[21] The mean value of the 3 scores was used in the analysis. The mean value of the 3 scores was used in the analysis as the main outcome.

The Spanish version[22] of the Boston Carpal Tunnel Questionnaire (BCTQ)[23] was used to assess function and severity of the disease. This questionnaire evaluates 2 main domains: (1) the functional status scale assesses ability to perform 8 common hand-related tasks; and (2) the symptom severity scale includes 11 items assessing pain severity, numbness, and weakness at night and during the day. Each question is answered on a 5-point scale (1: no complaint; 5: severe complaint). Higher scores indicate greater severity. The BCTQ has been shown to be valid, reliable, and responsive for individuals with CTS.[24]

TABLE 1. Clinical, Psychological, Physical and Neurophysiological Data for the Total Sample (n = 224)

Age (y)	45.6 ± 9.0 (44.4-4 6.8)
Years since beginning pain	3.6 ± 3.1 (3.1-4.0)
Intensity of hand pain (mean score, NPRS, 0-10)	4.8 ± 2.2 (4.5-5.1)
Pressure pain thresholds over median nerve (kPa)	193.6 ± 55.3 (186.1-201.1)
Pressure pain thresholds over ulnar nerve (kPa)	290.8 ± 76.7 (279.9-300.8)
Pressure pain thresholds over radial nerve (kPa)	226.7 ± 65.0 (216.5-233.9)
Pressure pain thresholds over C5/C6 joint (kPa)	169.9 ± 51.2 (162.8-176.7)
Pressure pain thresholds over carpal tunnel (kPa)	344.0 ± 97.7 (329.0-355.4)
Pressure pain thresholds over tibialis anterior (kPa)	327.9 ± 86.6 (316.6-340.1)
Cervical range of motion in flexion (deg.)	47.5 ± 7.9 (46.4-48.6)
Cervical range of motion in extension (deg.)	58.8 ± 10.3 (57.4-60.3)
Cervical range of motion in lateral-flexion (deg.)	37.4 ± 8.8 (36.2-38.6)
Cervical range of motion in rotation (deg.)	74.1 ± 5.3 (67.4-81.2)
Heat pain thresholds over the carpal tunnel (deg.)	40.0 ± 2.9 (39.5-40.3)
Cold pain thresholds over the carpal tunnel (deg.)	19.7 ± 7.1 (18.8-20.7)
Heat pain thresholds over the thenar eminence (deg.)	40.2 ± 3.1 (39.8-40.6)
Cold pain thresholds over the thenar eminence (deg.)	19.3 ± 6.6 (18.3-20.2)
Pinch grip force thumb-index finger (lbs)	4.2 ± 1.8 (3.9-4.4)
Pinch grip force thumb-middle finger (lbs)	3.9 ± 2.3 (3.6-4.2)
Pinch grip force thumb-fourth finger (lbs)	2.3 ± 1.5 (2.1-2.5)
Pinch grip force thumb-little finger (lbs)	1.1 ± 0.8 (1.0-1.2)
Function status scale carpal tunnel syndrome (1-5)	2.4 ± 0.8 (2.3-2.5)
Severity status scale carpal tunnel syndrome (1-5)	2.9 ± 2.2 (2.6-3.2)
Beck Depression Inventory (BDI-II, 0-21)	4.5 ± 2.9 (4.1-4.9)

NPRS indicates Numerical Pain Rating Scale.

Psychological Outcomes

Participants completed the Beck Depression Inventory (BDI-II) for reporting their level of depressive symptoms. The BDI-II is 21-item self-report questionnaire assessing affective, cognitive, and somatic symptoms of depression.[25] The BDI-II can be easily adapted in most clinical conditions for detecting major depression.[26]

Neurophysiological Outcomes

PPTs, the minimal amount of pressure where a sense of pressure first changes to pain,[27] were bilaterally assessed with an electronic algometer (Somedic AB, Farsta, Sweden) over the peripheral nerve trunks of the upper extremity, that is, median, radial, and ulnar nerves, the articular pillar of C5-C6 zygapophyseal joint, carpal tunnel, and tibialis anterior muscle. These points have been reported to exhibit mechanical hypersensitivity in women with CTS as sign of

TABLE 2. Pearson Product-Moment Correlation Matrix for Each Study Variable

Variables	1	2	3	4	5	6	7	8	9	10	11
Intensity of hand pain											
Age	NS										
Years with pain	NS	NS									
PPT median nerve	NS	NS	NS								
PPT ulnar nerve	NS	NS	NS	0.596**							
PPT radial nerve	−0.239**	NS	NS	0.620**	0.605**						
PPT C5/C6 joint	−0.163*	NS	NS	0.610**	0.542**	0.591**					
PPT carpal tunnel	−0.200**	NS	NS	0.557**	0.519**	0.628**	0.572**				
PPT tibial anterior	−0.183**	NS	NS	0.595**	0.541**	0.505**	0.566**	0.620**			
Cervical flexion	NS	−0.191**	NS	NS	0.146*	NS	NS	NS	0.212**		
Cervical extension	−0.140*	NS	NS	NS	NS	NS	NS	0.167*	0.213**	0.287**	
Cervical lateral-flexion	−0.135*	−0.235**	NS	NS	NS	NS	NS	NS	0.228**	0.374**	0.242**
Cervical rotation	NS	NS	NS	NS	NS	NS	NS	NS	NS	0.132*	0.140*
HPT carpal tunnel	−0.210**	NS	NS	NS	NS	NS	NS	0.263**	0.153*	NS	NS
CPT carpal tunnel	NS	NS	NS	−0.214**	−0.160*	−0.151*	−0.194**	−0.204**	−0.199**	NS	NS
HPT thenar eminence	NS	NS	NS	0.162*	NS	0.151*	NS	0.238**	0.228**	NS	NS
CPT thenar eminence	NS	NS	NS	NS	−0.212**	−0.220**	−0.201**	−0.257**	−0.233**	NS	NS
Middle finger pinch	−0.285**	−0.149*	NS	0.196**	NS	NS	0.169*	NS	NS	NS	NS
Fourth finger pinch	−0.232**	−0.122	NS	NS	NS	NS	NS	NS	NS	NS	NS
Index finger pinch	NS	−0.134*	NS	NS	NS	NS	0.139*	NS	NSNS	NS	NS
Little finger pinch	−0.144*	NS	NS	0.159*	NS	NS	NS	NS	0.148*	0.135*	NS
Function subscale	0.446**	NS	0.184**	−0.231**	−0.222**	−0.220**	−0.302**	−0.285**	−0.258**	−0.205**	NS
Severity subscale	NS	NS	NS	NS	NS	NS	−0.150*	−0.157*	NS	NS	NS
BDI-II	0.316**	NS	NS	−0.214**	−0.256**	−0.231**	−0.320**	−0.176**	−0.259**	−0.117	NS

central sensitization.[8] The mean of 3 trials was calculated for each point and the mean of both sides was used for the analysis. A 30-second resting period was allowed between trials. The reliability of pressure algometry has been found to be high (intra-class correlation coefficient = 0.91; 95% confidence interval, 0.82-0.97).[28]

Thermal pain thresholds were bilaterally tested with a Thermotest System (Somedic AB) over the carpal tunnel and the thenar eminence. Participants were instructed to press a hand-controlled switch when the sensation changes from heat/cold to heat/cold pain (heat/cold pain thresholds [HPT/CPT]). The mean of 3 trials at each point was calculated and the mean of both sides was used for the main analysis. A rest of 5 seconds occurred between trials.

Physical Outcomes

A CROM device (Performance Attainment Associate, St. Paul, MN) was used to determine CROM. CROM was recorded in a single direction (flexion, extension, lateral-flexion toward or away from the side of the CTS, and rotation toward or away from the side of the CTS). Two measurements were recorded for each cervical motion and the mean was used in the analysis. Since no side-to-side differences were observed in CROM mean of both lateral-flexions and rotations were used in the analysis. The intratester reliability of the CROM device ranges from 0.87 to 0.96, showing a SE of measurement from 2.3 to 4.1 degrees.[29,30]

Pinch tip grip force (lbs) between the thumb with the index, middle, or little finger was measured with a pinch grip dynamometer (Psymptec, Spain). The digital display was visible for the patients to obtain a feedback. The tip pincer was performed with the thumb below and the other finger on top. The mean of 3 trials with each finger was calculated and the mean of both sides was again used for the analysis. A rest of 10 seconds occurred between trials. The interexaminer reliability for tip grip assessment ranges from 0.82 to 0.93.[31]

Statistical Analysis

Means, SDs, and confidence intervals were calculated to describe the sample. The Kolmogorov-Smirnov test revealed that all quantitative data exhibited a normal distribution. To determine the relationship between the dependent measure (the intensity of hand pain) and the independent variables, several Pearson product-moment correlation coefficients were firstly assessed. The following independent variables were included in the analysis: age, duration of the symptoms, PPT over the median, nerve and ulnar nerves, PPT over C5-C6 zygapophyseal joint, carpal tunnel and tibialis anterior, HPT and CPT over the carpal tunnel and thenar eminence, depression (BDI-II), function and severity of the disease (BCTQ), CROM (flexion, extension, lateral-flexion, and rotation), and pinch tip with the index, middle, and little fingers. The same statistical analysis was used to check for multicollinearity and shared variance between the measures.

TABLE 2. *Continued*

12	13	14	15	16	17	18	19	20	21	22	23
NS											
NS	NS										
NS	NS	−0.453**									
NS	NS	0.487**	−0.536**								
NS	NS	−0.475**	0.535**	−0.575**							
NS	NS	NS	NS	NS	NS						
NS	NS	NS	NS	NS	NS	0.416**					
NS	NS	NS	NS	NS	NS	0.488**	0.489**				
0.185**	NS	NS	NS	0.212**	NS	0.403**	0.520**	0.368**			
−0.259**	NS	−0.158*	NS	−0.151*	NS	−0.241**	−0.230**	−0.194**	−0.193**		
NS	NS	NS	NS	NS	NS	NS	−0.135*	NS	NS	0.147*	
−0.170*	NS	NS	NS	NS	NS	−0.190**	−0.158*	−0.133*	−0.137*	0.402**	NS

*$P < 0.05$.
**$P < 0.01$.
BDI-II indicates Beck Depression Inventory; CPT, cold pain threshold; HPT, heat pain threshold; NS: nonsignificant; PPT, pressure pain threshold.

A regression model was used to assess the independent variables that contributed significantly to the variance in the intensity of hand pain. To examine the proportions of explained variance in hand pain intensity a hierarchical regression analysis was used. To analyze the contribution of function, index and middle finger pinch tip, depression, PPT over the radial nerve, and PPT and HPT over carpal tunnel were entered into the regression model in 7 steps. Hand function was entered into the model at the first step, followed by thumb-middle finger pinch grip force (step 2), thumb-index finger pinch grip force (step 3), depression (step 4), PPT over the radial nerve (step 5), and PPT over carpal tunnel (step 6). Finally, HPT over the carpal tunnel was added in the seventh step. Changes in R^2 were reported after each step of the regression model to determine the association of the additional variables. Finally, variables that significantly contributed to the intensity of hand pain were selected for inclusion into parsimonious final regression models. The significance criterion of the critical F value for entry into the regression equation was set at $P < 0.05$. $P < 0.05$ was considered significant in all tests.

RESULTS

Three hundred (n = 300) consecutive patients with CTS between January 2013 and December 2014 were screened for possible eligibility criteria. Of these, 224 women presenting with CTS satisfied all the eligibility criteria and agreed to participate. The reasons for exclusion were as follows: previous hand surgery (n = 20), steroid injections (n = 18), diabetes (n = 12), previous whiplash (n = 9), pregnancy (n = 9), and age above 65 (n = 8). Eighty-four (38%) had unilateral symptoms (59 right side, 25 left side), and the remaining 140 (62%) showed bilateral symptoms. Sixty-six patients (29%) had minimal CTS, 75 (34%) had moderate CTS, and the remaining 83 (37%) presented severe CTS. Demographic data and mean outcome measure scores are listed in Table 1.

Correlation Analysis

Significant negative correlations existed between the intensity of hand pain and PPT over the radial nerve ($r = -0.239$; $P = 0.004$), C5/C6 joint ($r = -0.163$; $P = 0.14$), carpal tunnel ($r = -0.200$; $P = 0.003$), and tibialis anterior muscle ($r = -0.183$; $P = 0.006$): the higher the pain intensity, the lower the PPT, that is, the greater the widespread pressure pain hypersensitivity. Pain intensity was also negatively correlated with cervical extension ($r = -0.140$; $P = 0.037$) and lateral-flexion ($r = -0.135$; $P = 0.044$); range of motion, middle finger ($r = -0.285$; $P < 0.001$), fourth finger ($r = -0.232$; $P < 0.001$), and little finger ($r = -0.144$; $P = 0.006$) pinch tip forces; and HPT over the carpal tunnel ($r = -0.210$; $P = 0.035$).

Again, the higher the pain intensity, the more restricted CROM, the lower the pinch tips force or the lower the HPT (the higher the heat pain hypersensitivity).

Significant positive correlations between the intensity of hand pain with function ($r = 0.446$; $P < 0.001$) and depression ($r = 0.316$; $P < 0.001$) were also observed: the higher the pain intensity, the higher depression level, or the worse the functional status. In addition, significant correlations existed among the independent variables ($r = -0.133 < r < 0.62$; Table 2, 5), but none were considered to be multicollinear (defined as $r > 0.80$); therefore, each variable was included in the regression analyses.

Regression Analyses

Table 3 shows the alternate hierarchical regression analysis conducted in this study. Function subscale of the BCTQ questionnaire, thumb-middle finger pinch force, and thumb-little finger pinch contributed approximately 27% ($P < 0.001$) of the variance in the intensity of hand pain. Depression and PPT over the radial nerve contributed an additional 2% in each one ($P < 0.001$); PPT over the carpal tunnel contributed an additional 4% ($P < 0.001$); and HPT over the carpal tunnel contributed an additional 2% ($P < 0.001$).

Stepwise regression analyses revealed that function scale, thumb-middle finger pinch, thumb-little finger pinch, depression, PPT radial nerve, PPT carpal tunnel, and HPT carpal tunnel were significant predictors of the intensity of hand pain, and when combined, they explained 36.5% of the variance of hand pain intensity ($R^2 = 0.364$; R^2 adjusted = 0.343; $F = 16.87$; $P < 0.001$) (Table 4).

DISCUSSION

The objective of our study was to determine the potential clinical, psychological, physical, and neurophysiological variables associated in the intensity of hand pain in a cohort of women with CTS. We found significant low to moderate associations between pain intensity and function, depression, PPT, HPT, CROM, and finger pinch tip forces. In addition, results from the regression analyses showed that function, thumb-middle and thumb-little finger pinch tip force, depression, PPT over radial nerve and carpal tunnel, and HPT carpal tunnel were significant predictors of pain intensity in women with chronic CTS.

We found that function was the first predictor of the intensity of hand pain in patients with CTS, which seems expected as pain influences functional outcomes. In fact, this association was observed in a sample of women with CTS exhibiting moderate levels of pain and function supporting that it maybe not necessary to report higher levels of pain to find a repercussion in functional activities. Our results agree with those previously reported by Seventer et al[32] who identified that pain intensity was correlated with self-reported outcomes of function in individuals with neuropathic pain. Similarly, the intensity of the pain was a risk factor of poor outcome in individuals with low back pain[33] and sciatica.[34] Current and previous results suggest that the intensity of pain is consistently identified as a predictor of worse function in a variety of populations including CTS. In fact, several studies have demonstrated that proper management of pain improves self-reported function in individuals with chronic pain.[35,36]

The analysis also identified that pinch tip grip forces between the thumb-middle and thumb-little fingers were predictive of hand pain intensity. This is also an expected result as patients with CTS reduce manual ability and tip grip force because of the pain resulting in adaptive tip grip forces during manual activities.[37] A potential physiological mechanism may be related to the fact that the thumb musculature involved in the pinch tip, that is, opponens pollicis muscle, is mainly innervated by the median nerve, whereas musculature involved in middle and little fingers tip also receives some branches from the median nerve.[38] These results support the theory that median nerve entrapment can also affect function from related nerves, such as the ulnar nerve, independently that no electromyography signs of ulnar nerve involvement were permitted in our study.

Depression is a psychological factor clearly associated with pain[39]; therefore, it is not surprising that we identified depression as a contributor to the intensity of hand pain in women with CTS. In fact, depression is linked to the

TABLE 3. Model Summary for the Alternate Hierarchical Regression Analysis With the Intensity of Hand Pain as the Dependent Variable

Models	R^2	Adjusted R^2	F	P
1*	0.235	0.231	65.11	< 0.001
2†	0.267	0.260	38.33	< 0.001
3‡	0.282	0.272	27.47	< 0.001
4§	0.296	0.283	22.01	< 0.001
5‖	0.311	0.294	18.77	< 0.001
6¶	0.346	0.327	18.27	< 0.001
7#	0.364	0.343	16.87	< 0.001

*Predictors: constant, function subscale of the BCTS questionnaire.
†Predictors: constant, function subscale, thumb-middle finger pinch.
‡Predictors: constant, function subscale, thumb-middle finger pinch, thumb-little finger pinch.
§Predictors: constant, function subscale, thumb-middle finger pinch, thumb-little finger pinch, depression.
‖Predictors: constant, function subscale, thumb-middle finger pinch, thumb-little finger pinch, depression, PPT radial nerve.
¶Predictors: constant, function subscale, thumb-middle finger pinch, thumb-little finger pinch, depression, PPT radial nerve, PPT carpal tunnel.
#Predictors: constant, function subscale, thumb-middle finger pinch, thumb-little finger pinch, depression, PPT radial nerve, PPT carpal tunnel, HPT carpal tunnel.
BCTS indicates Boston carpal tunnel syndrome; HPT, heat pain threshold; NS: nonsignificant; PPT, pressure pain threshold.

TABLE 4. Summary of Stepwise Regression Analyses to Determine Predictors of Hand Pain Intensity ($R^2 = 36.4\%$)

Independent Variables	*B*	SE *B*	β	*t*
Step 1				
Function subscale	1.440	0.178	0.485	8.060
Step 2				
Function subscale	1.290	1.820	0.436	7.130
Thumb-middle finger pinch	−1.780	0.059	−1.840	−3.010
Step 3				
Function subscale	1.326	0.181	0.446	7.340
Thumb-middle finger pinch	−0.242	0.066	−0.249	−3.668
Thumb-little finger pinch	0.171	0.080	0.142	2.121
Step 4				
Function subscale	1.166	0.195	0.392	5.974
Thumb-middle finger pinch	−0.234	0.065	−0.241	−3.570
Thumb-little finger pinch	0.175	0.080	0.145	2.191
Depression (BDI-II)	0.101	0.049	0.134	2.079
Step 5				
Function subscale	1.207	0.195	0.406	6.205
Thumb-middle finger pinch	−0.228	0.065	−0.236	−3.513
Thumb-little finger pinch	0.167	0.079	0.139	2.112
Depression (BDI-II)	0.121	0.049	0.159	2.451
PPT radial nerve	0.004	0.002	0.125	2.097
Step 6				
Function subscale	1.076	0.194	0.362	5.545
Thumb-middle finger pinch	−0.215	0.064	−0.222	−3.377
Thumb-little finger pinch	0.145	0.078	0.121	1.869
Depression (BDI-II)	0.129	0.048	0.171	2.687
PPT radial nerve	0.010	0.003	0.275	3.738
PPT carpal tunnel	−0.006	0.002	−0.247	−3.341
Step 7				
Function subscale	1.136	0.193	0.383	5.876
Thumb-middle finger pinch	−0.190	0.064	−0.196	−2.982
Thumb-little finger pinch	0.137	0.077	0.114	1.789
Depression (BDI-II)	0.128	0.048	0.169	2.697
PPT radial nerve	0.010	0.003	0.299	4.072
PPT carpal tunnel	−0.007	0.002	−0.293	−3.877
HPT carpal tunnel	0.109	0.045	0.143	2.425

$R^2 = 0.235$ for step 1; $R^2 = 0.267$ for step 2; $R^2 = 0.282$ for step 3; $R^2 = 0.296$ for step 4; $R^2 = 0.311$for step 5; $R^2 = 0.346$ for step 6; $R^2 = 0.364$ for step 7; $P < 0.001$.

BDI-II indicates Beck Depression Inventory; HPT, heat pain threshold; PPT, pressure pain threshold.

intensity of pain in several chronic pain conditions, including those involving the upper extremity.[40] Our results are consistent with those previously reported by Nunez et al[15] and Vranceanu et al[16] where depression was associated with pain in different chronic hand conditions including CTS. This is an interesting finding as the level of depression in our sample size was small. In fact, depression levels in the current study were minimal. It is possible that the role of depression in pain would be higher in those patients with higher levels of depression. Although pain and depression are associated, the direction of this relationship seems to be bidirectional, pain may induce depression, but depression can also perpetuate and/or potential pain symptoms. Perhaps proper management of depressive symptoms in CTS may reduce, not only chronicity, but also induce an improvement in hand pain–related disability. Future clinical trials should examine the effects of depression management on the clinical and physical outcomes of patients with chronic CTS as it has been previously reported that depressive symptoms resolved over physical therapy treatment in around 40% of patients with work-related musculoskeletal pain injuries.[41]

We found that PPT over the radial nerve and the carpal tunnel also contributed to the variance of hand pain intensity suggesting the relevance of pressure hyperalgesia in CTS. In addition, heat pain hyperalgesia over the carpal tunnel was another factor associated with intensity of hand pain. These results would support a role of peripheral sensitization over the carpal tunnel as a potential relevant factor for self-perceived hand pain intensity in women with CTS. In fact, it has been previously demonstrated that the sensitization mechanisms observed in this condition are present from the beginning.[42] Current findings are similar to those found by a previous study analyzing the predictive validity of both pressure and thermal pain hypersensitivity for identifying women with CTS who were likely to have a quick positive response for physical therapy treatment.[43] Current results support a potential role of peripheral sensitization mechanisms over the carpal tunnel as a prognosis factor for pain in women with CTS.

Our results indicate that the intensity of pain is related to clinical, psychological, physical, and neurophysiological variables in women with CTS. These results have potential clinical implications as proper management of individuals with CTS should include therapeutic interventions targeting physical impairments, that is, manual therapies; psychological disturbances, that is, cognitive behavior; and mechanical hypersensitivity, that is, neuromodulatory pain approaches.

There are a number of limitations that should be recognized. First, we used a cross-sectional design; therefore,

cause and effect relationships between those variables associated with the intensity of hand pain cannot be inferred. Second, as all patients were of the outpatient neurological population, extrapolation of current results to the general population with CTS should be considered with caution at this stage. Third, we included women with CTS; therefore, we do not know if the current results would be similar in men with this pain condition. Finally, other potential variables, for example, sleep disturbances, fear to movement or anxiety, were not included which could give a broader vision of the biopsychosocial model approach.

CONCLUSIONS

This study showed that function, thumb-middle and thumb-little finger pinch tip, depression, PPT radial nerve, PPT carpal tunnel, and HPT carpal tunnel explained 36.5% of the variability of the intensity of hand pain in women with CTS. These results provide preliminary evidence that CTS-related pain exhibit a combination of clinical (function), neurophysiological (localized PPT and HPT), psychological (depression), and physical (finger pinch tips) factors which may be crucial for proper management of patients with CTS. Future longitudinal studies will help to determine the clinical implications of these findings.

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