Clinical, Physical, and Neurophysiological Impairments Associated With Decreased Function in Women With Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is a disorder characterized by compression of the median nerve at the carpal tunnel, often as a result of repetitive activities. The clinical presentation of CTS includes motor and sensory deficits in the median nerve distribution and numbness, which may be worse during the night. Women are most often afflicted with CTS, with a reported annual incidence of 139 per 100,000 females, compared to 67 cases per 100,000 males. CTS can result in considerable pain, loss of function, and disability. The societal burden of CTS is substantial, and it has been reported that individuals with CTS exhibit loss in productivity and monetary income. Although CTS is primarily considered a peripheral neuropathy, increasing evidence is showing that musculoskeletal disorders and sensitization mechanisms are related in this condition. Previous studies have demonstrated the presence of widespread pressure pain hypersensitivity.
sitivity in individuals with CTS as a sign of central sensitization. In fact, the magnitude of widespread pressure hypersensitivity is not significantly different between minimal, moderate, or severe CTS, suggesting that this may be a common feature in this condition. Further, it has been demonstrated that subjects with signs and symptoms of CTS exhibit increased sensitivity (temporal summation), suggesting the presence of a central mechanism and that changes in sensitivity are directly correlated with clinical outcomes.

There is recent scientific evidence suggesting the presence of physical impairments in this population. For instance, it has been reported that women with unilateral moderate CTS exhibit bilateral deficits in fine motor control and pinch tip grip force compared to healthy women. In fact, these deficits seem to be similar in individuals with minimal, moderate, or severe CTS. Deficiencies in sensory and motor processes often result in alteration in force adaptations, which can lead to the inability to adequately perform functional activities with the upper limb.

Patients with CTS exhibit physical and psychological impairments before surgical intervention. It has been reported that women with CTS exhibit restricted cervical range of motion (ROM) in flexion, extension, and lateral flexion compared to healthy people. In fact, based on electrodiagnosis, restricted cervical ROM seems to be a common feature of CTS, independent of the severity. Whether restricted cervical ROM is a consequence or a causative/promoting factor of the pain in women with CTS is not clear. Although a recent systematic review found that neck pain is a factor related to decreased function of the hand, the contribution of decreased cervical ROM to CTS-related disability and function has not been investigated.

Because some clinical (pain) and physical (cervical ROM) outcomes are potentially modifiable risk factors, a better understanding of the interactions between clinical, physical, and neurophysiological impairments associated with self-reported function in women with CTS may assist clinicians in determining adequate therapeutic programs for this group of patients. Therefore, the purpose of the current study was to examine the relationship of clinical, physical (cervical ROM, pinch grip force), and neurophysiological (pressure pain thresholds [PPTs]) factors to self-reported function and disability in women with electrodiagnosis and clinical diagnosis of CTS.

METHODS

Participants

A cross-sectional design was used in this study. Consecutive women diagnosed with CTS from January 2011 to December 2012 by a neurophysiologist with 10 years of clinical experience were screened for eligibility. They were diagnosed based on both electrophysiological and clinical findings. To be eligible, the women had to exhibit at least 4 of 5 of the following clinical signs: pain and paresthesia in the median nerve distribution (with no symptoms outside the median nerve territory), greater symptoms during the night, positive Tinel sign, positive Phalen sign, or self-perceived hand-strength deficit. Symptoms had to have persisted for at least 3 months.

Additionally, the electrodiagnostic examination had to reveal deficits of sensory and motor median nerve conduction according to standardized guidelines of the American Association of Electrodagnostic Medicine, American Academy of Neurology, and the American Academy of Physical Medicine and Rehabilitation. A median nerve sensory conduction velocity of less than 40 m/s and a median nerve distal motor latency of greater than 4.20 milliseconds were considered abnormal. Participants were classified as having minimal (abnormal segmental/comparative tests only), moderate (abnormal median nerve sensory velocity conduction and distal motor latency), or severe (absence of median nerve sensory response and abnormal distal motor latency) CTS.

Individuals were also excluded from the study if they (1) had any sensory/motor deficit related to the ulnar or radial nerve; (2) were over 65 years of age; (3) had previous surgical intervention or steroid injections; (4) had multiple diagnoses of the upper extremity (eg, cervical radiculopathy); (5) had a history of neck, shoulder, or upper-limb trauma (whiplash); (6) had a history of systemic disease causing CTS (eg, diabetes mellitus or thyroid disease); (7) had a history of musculoskeletal medical conditions (eg, rheumatoid arthritis, fibromyalgia); (8) were pregnant; or (9) were of male gender. All subjects read and signed a consent form prior to enrollment, and the study was approved by the Ethics Board of the Universidad Rey Juan Carlos.

Clinical Outcomes

The clinical history included questions regarding the onset, nature, and location of the symptoms, and the aggravating and relieving factors. An 11-point numeric pain rating scale, where 0 indicated no pain and 10 maximum pain, was used to assess the patient’s current level of hand pain, and the highest and lowest level of hand pain experienced in the preceding week. The mean value of the 3 scores was used in the analysis. For women with unilateral CTS, side was classified as affected or unaffected. In those with bilateral symptoms, the most painful side reported by the patient was considered the affected side and the least painful side the unaffected side.

The Spanish version of the Boston Carpal Tunnel Questionnaire was used to assess function and the severity of the disease. This questionnaire evaluates these 2 domains with the functional status subscale, which assesses the ability to perform 8 common hand-related tasks, and the symptom severity subscale, which includes 11 items assessing pain severity, numbness, and weakness at night and during the day. Each question
is answered on a 5-point scale, with 1 as no complaint and 5 as severe complaint, higher scores indicating greater severity. The Boston Carpal Tunnel Questionnaire has been shown to be valid, reliable, and responsive in individuals with CTS.\textsuperscript{24} The main outcome in the current study was the score of the functional status subscale of this questionnaire.

Patients also completed the Beck Depression Inventory, a 21-item self-report questionnaire assessing affective, cognitive, and somatic symptoms of depression.\textsuperscript{4} The Beck Depression Inventory has been shown to exhibit good internal consistency and adequate divergent validity.\textsuperscript{17}

Physical Outcomes

The CROM device (Performance Attainment Associates, Lindstrom, MN) was used to measure cervical ROM. Cervical ROM was recorded in a single direction (flexion, extension, lateral flexion toward or away from the side of CTS, and rotation toward or away from the side of CTS). For patients with unilateral symptoms, sides were classified as affected or unaffected, whereas in those with bilateral symptoms, the most painful side was considered the affected side and the less painful side the unaffected side. Two measurements were recorded for each motion, and the mean was used in the statistical analysis.\textsuperscript{13,21} Several studies have reported an intratester reliability of the CROM device ranging from 0.87 to 0.96, and standard errors of measurement ranging from 2.3° to 4.1°.\textsuperscript{3,31}

Pinch grip force between the tip of the thumb and the tip of the index or the little finger was measured with a pinch grip dynamometer (Psymtec, Madrid, Spain). The patients were asked to watch the screen for visual feedback.\textsuperscript{13,39} They performed the pinch with the thumb below and either the index or little finger on top of the pinch grip dynamometer. The mean of 3 trials with each finger was calculated and used for the analysis. A rest of 10 seconds occurred between trials. Schreuders et al\textsuperscript{35} reported excellent interexaminer reliability (intraclass correlation coefficient [ICC] = 0.82-0.93) for finger pinch grip force assessment with the same instrument.

Neurophysiological Outcomes

PPT, the minimal amount of pressure at which the sense of pressure changes to pain,\textsuperscript{26} was assessed over the articular pillar of the C5-6 zygapophyseal joint, carpal tunnel, and tibialis anterior muscle with an electronic algometer (Somedic AB, Hörby, Sweden). The assessed locations have been reported to exhibit mechanical pain hypersensitivity as a sign of central sensitization in individuals with CTS.\textsuperscript{15,17,18} The mean of 3 trials was calculated and used for the analysis. A 30-second rest was allowed between each measure. The reliability of pressure algometry has been found to be high (ICC = 0.91; 95% confidence interval: 0.82, 0.97) in healthy subjects.\textsuperscript{13} More recently, Walton et al\textsuperscript{36} found that PPT assessed over the cervical spine also exhibited excellent intrarater reliability (ICC = 0.94-0.97) and good to excellent interrater reliability (ICC = 0.79-0.9) in subjects with acute neck pain. To our knowledge, no study has yet determined the reliability of PPT measured with the same algometer over the points included in the current study in patients with CTS. Nevertheless, previous studies have found high reliability (ICC = 0.89-0.92) of PPT assessments over these specific points in women with CTS.\textsuperscript{15,18}

To avoid assessment variability, the physical and neurophysiological outcomes from all participants in the study were examined by the same physical therapist, who had 10 years of experience in CTS.

Statistical Analysis

Means, standard deviations, and confidence intervals were calculated to describe the sample. The Kolmogorov-Smirnov test revealed that all data exhibited a normal distribution ($P$.05). To determine the relationships between the dependent measure (the score on the functional status subscale) and the independent variables, several Pearson product-moment correlation coefficients were calculated. The following independent variables were included in the analysis: index and little finger pinch grip force; severity of depression (Beck Depression Inventory); cervical ROM (flexion and lateral flexion); PPT over the C5-6 joint, carpal tunnel, and tibialis anterior; intensity of pain (numeric pain rating scale); and duration of the symptoms. The same statistical analyses were used to check for multicollinearity and shared variance between the measures.

Independent variables that contributed significantly to the variance in the score on the functional status subscale were assessed with a regression model. To examine the proportions of explained variance in the score on the functional status subscale, a hierarchical regression analysis was used. To analyze the unique contribution of pain intensity, depression, and finger pinch grip force to the score on the functional status subscale beyond PPT, independent variables were entered into the regression model in 4 steps: (1) pain intensity, (2) depression, (3) pinch grip force, and (4) cervical lateral flexion away from the side of the symptoms. Changes in $R^2$ were reported after each step of the regression model to determine the association of the additional variables. Last, variables that significantly contributed to the score on the functional status subscale were selected for inclusion into the parsimonious final regression model. The significance criterion of the critical F value for entry into the regression equation was set at $P$.05, which was considered significant in all tests.

RESULTS

Two hundred fifty consecutive patients with CTS between January 2011 and September 2012 were screened for eligibility criteria. Of these, 154 women presenting with CTS satisfied all the eligibility criteria and agreed...
to participate. The reasons for exclusion were as follows: previous surgery (n = 21), previous steroid injections (n = 16), fibromyalgia (n = 12), whiplash injury (n = 15), pregnancy (n = 10), diabetes (n = 8), and age greater than 65 years (n = 14). Demographic data are listed in Table 1, and mean outcome measure scores are summarized in Table 2.

**Correlation Analysis**

There were significant positive correlations between functional status subscale score and pain intensity \( (r = 0.36, P < .001) \), depression severity \( (r = 0.32, P < .001) \), and duration of symptoms \( (r = 0.23, P = .005) \), with higher pain intensity, more severe depression, and longer symptom duration being associated with higher functional status subscale score (worse function). There were significant negative correlations between functional status subscale score and pinch grip force of the index finger \( (r = -0.25, P = .002) \) and little finger \( (r = -0.28, P < .001) \), with lower pinch grip force being associated with a higher functional status subscale score (worse function). In addition, cervical ROM in flexion \( (r = -0.22, P = .003) \) and lateral flexion away from the CTS side \( (r = -0.24, P = .002) \) and toward the CTS side \( (r = -0.16, P = .045) \) were negatively correlated with functional status subscale scores, with more restricted cervical ROM in these directions being associated with higher functional status subscale score (worse function). Finally, there were significant negative correlations between functional status subscale score and PPT at C5-6 \( (r = -0.34, P < .001) \), carpal tunnel \( (r = -0.35, P < .001) \), and tibialis anterior muscle \( (r = -0.26, P < .001) \), with lower PPT (greater pressure pain hypersensitivity) being associated with higher functional status subscale score (worse function).

There were also significant correlations among the independent variables \( (r \text{ values between } -0.43 \text{ and } 0.59) \) (Table 3), with no multicollinearity (defined as \( r > 0.80 \)); therefore, each variable was included in the regression analyses.

**Regression Analyses**

Table 4 shows the hierarchical regression analyses conducted in this study. PPT over the C5-6 zygapophyseal joint, PPT over the carpal tunnel, and pain intensity contributed approximately 26% \( (P < .001) \) of the variance in the score on the functional status subscale. The pinch grip force between the thumb and little finger contributed an additional 6% \( (P < .001) \), depression severity an additional 3% \( (P < .001) \), and cervical lateral flexion ROM away from the side of the CTS symptoms an additional 3% \( (P < .001) \), after accounting for PPT and pain intensity.

Stepwise regression analyses revealed that pain intensity, finger pinch grip force between the thumb and little finger, depression severity, and cervical ROM in lateral flexion away from the side of the symptoms were significantly associated with the score on the functional status subscale and, when combined, explained 38.2% of the variance in functional status \( (R^2 = 0.411, \text{adjusted } R^2 = 0.382, F = 15.42, P < .001) \) (Table 5).

**DISCUSSION**

The objective of our study was to investigate the relationships between CTS-related function and disability and clinical, physical, and neurophysiological characteristics, including the intensity of pain, severity of depression, cervical ROM, finger pinch grip force, and PPT, in women with CTS. We found significant low to moderate positive associations between function...
and pain intensity, severity of depression, and duration of symptoms. We also found negative associations between function and finger pinch grip force, cervical ROM, and PPT. Overall, results from the regression analyses showed that pain intensity, PPT, finger pinch grip force between the thumb and little finger, severity of depression, and cervical ROM in lateral flexion away from the side of the CTS symptoms were significantly associated with function in women with chronic CTS. These findings suggest that some clinical (pain and depression), physical (finger pinch grip force and cervical mobility), and neurophysiological (PPT) outcomes have a relevant association with function in women with CTS (TABLE 6).

We found pain intensity and function in patients with CTS to be associated, which is consistent with previous findings in patients with other musculoskeletal pain conditions. For example, subjects in an elderly community with subjective reports of knee pain exhibited a 5-fold increase in the likelihood of exhibiting poor lower extremity function as compared to individuals without knee pain.13 van Seventer et al14 identified that pain was directly correlated with patient-reported outcomes of function in individuals with chronic neuropathic pain. It is clear that pain has consistently been associated with disability in a variety of populations with musculoskeletal disorders, including CTS.

It is noteworthy that pressure sensitivity over the C5–6 zygapophyseal joint and over the carpal tunnel contributed to approximately 26% of the variance in functional status. These findings are consistent with those of a previous study that examined the predictive validity of PPT in identifying individuals with CTS who were likely to have a favorable prognosis.25 The positive predictor of outcome in that previous study was PPT over the C5–6 joint, with a positive likelihood ratio of 4.2.27 This may be related to the association between upper extremity function and the cervical spine. Sterling31 also demonstrated that higher pressure and cold hypersensitivity were associated with poor outcomes in subjects with whiplash-associated disorders. We did not measure cold pain tolerance in the current study, which prevents us from making direct comparisons to the findings in patients with whiplash.

Age has been previously reported to be a predictor of function in patients with whiplash.26 However, other studies performed on patients with whiplash33,34 and neck pain35 did not find a link between age and disability. We also did not find age to be related to the CTS-related level of disability. One possible reason may be that we only included middle-aged women and excluded women older than 65 years. Future research should examine the predictive validity of age in determining functional levels in patients with CTS in a wide range of ages.

The regression analysis found finger pinch grip force of the thumb and little finger to be associated with hand function, but found no such association for the pinch grip force of the index and thumb. It is normal that pinch grip force between the thumb and any other finger is affected in CTS, because the opponens pollicis muscle is innervated by the median nerve. Further, the flexor digitorum profundus muscle, which is also involved in the thumb–little finger pinch grip force, while primarily innervated by the ulnar nerve, also receives some of its innervations through branches from the median nerve.27 Oh et al38 suggested that because the flexor digitorum profundus tendons expand to the index and little fingers, this muscle may be affected in lesions of the median or ulnar nerve. It is possible that patients might attempt to overcome the weakness associated with first-digit flexion by producing excessive forces that do not correlate with functional levels. Recently, Affifi et al examined the ability of patients with CTS to alter grip force when grasping objects of different textures. Patients successfully adapted their grip force in association with varying textures, but did so with excessive force. The authors concluded that patients might have used sensory information from the little digit to control the magnitude of the force produced. Our results may also reflect the altered function of the ulnar nerve that patients with CTS often exhibit; however, in the current study, we excluded patients with ulnar nerve elec-

### TABLE 2

**Physical and Neurophysiological Data for the Total Sample (n = 154)**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical ROM</td>
<td></td>
</tr>
<tr>
<td>Flexion, deg</td>
<td>46 ± 7 (45, 47)</td>
</tr>
<tr>
<td>Extension, deg</td>
<td>58 ± 10 (57, 60)</td>
</tr>
<tr>
<td>Lateral flexion away from the side of CTS, deg</td>
<td>36 ± 9 (34, 38)</td>
</tr>
<tr>
<td>Lateral flexion toward the side of CTS, deg</td>
<td>41 ± 11 (35, 46)</td>
</tr>
<tr>
<td>Rotation away from the side of CTS, deg</td>
<td>75 ± 10 (65, 84)</td>
</tr>
<tr>
<td>Rotation toward the side of CTS, deg</td>
<td>71 ± 16 (69, 73)</td>
</tr>
<tr>
<td>Pinch grip force</td>
<td></td>
</tr>
<tr>
<td>Thumb and index finger, kg</td>
<td>2.0 ± 1.0 (1.7, 2.4)</td>
</tr>
<tr>
<td>Thumb and little finger, kg</td>
<td>0.45 ± 0.4 (0.4, 0.5)</td>
</tr>
<tr>
<td>Pressure pain threshold</td>
<td></td>
</tr>
<tr>
<td>C5–6 zygapophyseal joint, kPa</td>
<td>175 ± 49 (167, 182)</td>
</tr>
<tr>
<td>Carpal tunnel, kPa</td>
<td>352 ± 86 (338, 366)</td>
</tr>
<tr>
<td>Tibialis anterior muscle, kPa</td>
<td>317 ± 73 (305, 329)</td>
</tr>
</tbody>
</table>

**Abbreviations:** CTS, carpal tunnel syndrome; ROM, range of motion.

*Values are mean ± SD (95% confidence interval).*
Depression itself is one of the most prevalent reasons for disability; therefore, it is not surprising that we identified depression as being associated with disability in women with CTS. Depression is also linked to disability in individuals with chronic low back pain.24 Similarly, a recent study23 examined the prevalence of depression and its association with outcomes in a sample of 8300 individuals with musculoskeletal complaints. The results indicated that depression consistently exhibited an impact on patient outcomes, including those with upper extremity pathologies.23 In another recent study,20 it was determined that depressive symptoms resolved over the course of physical therapy treatment in around 40% of patients with work-related musculoskeletal injuries and symptoms of depression. In addition, the resolution or improvement of depression was associated with long-term improvements in pain and disability.20 Our study suggests that depressive symptoms are associated with function and disability in women with CTS.

Cervical ROM restriction (in lateral flexion away from the affected side) was also identified as a variable associated with hand function. This finding may be related to the fact that CTS is a neuropathic condition and that cervical lateral flexion away from the affected side can potentially increase neural tension, resulting in an increase of symptoms.8 Potentially, treating the neural tension with mobilization of the nervous system may assist with restoring normal cervical ROM and improving patient symptoms. We have also recently identified that cervical ROM restriction in extension was associated with disability in individuals with chronic mechanical neck pain.42 Additionally, reduced cervical ROM has consistently been shown to be predictive of poor prognosis.79,30 Women with CTS in the current study showed chronic symptoms (averaging 3.5 years in duration).
TABLE 5

Summary of Stepwise Regression Analyses to Determine Predictors of the Functional Status Subscale

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>β</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>3.627</td>
<td>8.766</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pain intensity</td>
<td>0.098</td>
<td>3.734</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depression (BDI-II)</td>
<td>0.044</td>
<td>2.234</td>
<td>.027</td>
</tr>
<tr>
<td>Pinch grip force: thumb-little finger</td>
<td>-0.174</td>
<td>-2.843</td>
<td>.005</td>
</tr>
<tr>
<td>Cervical lateral flexion toward nonaffected side</td>
<td>-0.015</td>
<td>-2.743</td>
<td>.007</td>
</tr>
<tr>
<td>PPT over C5-6 joint</td>
<td>-0.003</td>
<td>-2.720</td>
<td>.007</td>
</tr>
<tr>
<td>PPT over carpal tunnel</td>
<td>-0.002</td>
<td>-3.291</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: BDI, Beck Depression Inventory; PPT, pressure pain threshold.

Values in parentheses are 95% confidence interval.

TABLE 6

Conceptual Overview of This Study

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measurement</th>
<th>Objective</th>
<th>Theorized Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain intensity</td>
<td>Numeric pain rating scale</td>
<td>Current, worst, and lowest level of hand pain</td>
<td>Supported</td>
</tr>
<tr>
<td>Depression</td>
<td>Beck Depression Inventory</td>
<td>Symptoms of depression</td>
<td>Supported</td>
</tr>
<tr>
<td>Physical</td>
<td>CROM device</td>
<td>Movement quantification</td>
<td>Refuted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Flexion-extension</td>
<td>Refuted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lateral flexion</td>
<td>Supported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rotation</td>
<td>Refuted</td>
</tr>
<tr>
<td>Finger pinch grip force</td>
<td>Pinch grip dynamometer</td>
<td>Pinch force</td>
<td>Refuted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thumb-index finger</td>
<td>Supported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thumb-little finger</td>
<td></td>
</tr>
<tr>
<td>Neurophysiological</td>
<td>Detect magnitude of widespread pressure pain hypersensitivity</td>
<td>Minimal amount of pressure where a sense of pressure changes to pain</td>
<td>Supported</td>
</tr>
<tr>
<td>Pressure pain threshold</td>
<td></td>
<td>• Articular pillar of C5-6</td>
<td>Supported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Zygopophyseal joint</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Carpal tunnel</td>
<td>Supported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tibialis anterior muscle</td>
<td>Refuted</td>
</tr>
</tbody>
</table>

CONCLUSION

This study showed that pain intensity, PPT, thumb-little finger pinch grip force, depression severity, and cervical lateral flexion ROM away from the side of the CTS symptoms explained 38.2% of the variability of self-reported function and disability in women with CTS. These results provide preliminary evidence that a combination of clinical, physical, and psychological factors, which may be crucial for the management of patients with CTS, is related to self-reported function. The identification of modifiable factors may allow for appropriate management strategies and potentially enhance the outcomes in this patient population. Future longitudinal studies will help to determine the clinical implications of these findings.

KEY POINTS

FINDINGS: This study revealed that pain intensity, PPT, thumb-little finger pinch grip force, depression severity, and cervical lateral flexion ROM away from the side of the pain symptoms were associated with self-reported function and disability in women with CTS.

IMPLICATIONS: The identification of clinical, physical, and neurophysiological variables associated with function and disability in this population may assist clinicians in determining more optimal therapeutic programs for this population.

CAUTION: The cross-sectional design of the study does not permit us to determine whether cause-and-effect relationships exist. Only middle-aged women with CTS were included in the study.
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