ABSTRACT
Carpal Tunnel Syndrome is the most common compressive neuropathy in the general population, and it may lead to disabling symptoms and significant functional limitation. This systematic review covered Pubmed, Medline, Embase, Cochrane, CINAHL, LILACS, and SCIELO databases, with no time or language delimitations. The PICO strategy defined the search strategy with keywords extracted from the Medical Subjects Headings, and the quality of the studies was evaluated by the Agency for Healthcare Research and Quality (AHRQ) scale. Overall, 857 studies were identified, of which only 10 fulfilled the inclusion criteria. Despite the good results shown, a noticeable heterogeneity was observed among the studies included, associated with methodological discrepancy and to limited sample size in a few of them. Four studies showed no correlation between electrophysiological findings and clinical symptoms and signs, whereas three could demonstrate such association and other three studies had equivocal results. Other studies are necessary, with better methodological standards and more homogeneous and precise evaluations, so as to improve the level of scientific evidence.

Keywords: Carpal Tunnel Syndrome, Median Neuropathy, Electromyography, Electrodiagnosis, Neural Conduction, Signals and Symptoms

RESUMO
A síndrome do Túnel do Carpo é a neuropatia compressiva mais frequente na população geral que pode levar a sintomas incapacitantes e significativa limitação funcional. Uma revisão sistemática foi realizada nas bases de dados Pubmed, Medline, Embase, Cochrane, CINAHL, LILACS e SCIELO, sem delimitação de tempo ou idioma. Utilizou-se da estratégia PICO para a pesquisa, palavras-chave extraídas dos Descritores de Ciências da Saúde (Decs) e a qualidade dos estudos foi avaliada através da escala Agency for Healthcare Research and Quality (AHRQ). Identificaram-se 857 estudos dos quais, somente 10 obedeceram aos critérios de inclusão. Apesar dos bons resultados apresentados, verificou-se uma expressiva heterogeneidade existente entre os estudos incluídos, associado à discrepância metodológica, e um limitado tamanho amostral em alguns deles. São necessários estudos com melhor padrão metodológico, bem como avaliações mais homogêneas e precisas, a fim de melhorar o nível de evidência científica.

Palavras-chave: Síndrome do Túnel Carpal, Neuropatia Mediana, Eletromiografia, Eletrodiagnóstico, Condução Nervosa
INTRODUCTION

Carpal Tunnel Syndrome (CTS) is the most common compressive neuropathy, present in 3 to 16% of the general population, depending on the diagnostic method and used criteria.1,2 Thus, its correct diagnosis, treatment, and follow-up may offer significant health benefits to the population.3

According to the American Academy of Orthopedic Surgeons, CTS is a symptomatic compressive neuropathy of the median nerve in the carpal tunnel, characterized by an increased internal pressure in the carpal tunnel and neural dysfunction.4 It may present with other associated physiopathological factors such as mechanic compression and neural ischemia.4,5 It is more prevalent in women (3:1) between the ages of 45-65 years,6-8 and is associated with a series of clinical conditions such as obesity, pregnancy, diabetes, rheumatoid arthritis, hypothyroidism,9 or occupational factors (repetitive movements, vibrations, and lasting positions in extension and ulnar deviation of the wrist).9

CTS diagnosis involves the association of clinical symptoms and signs as well as the use of nerve conduction studies (NCS) with a sensitivity of 84% and specificity of 95%.10-13 The most prevalent symptoms are pain and paresthesia, which can afflict the hand diffusely, as well as the specific innervation region of the median nerve.5,6

Also, patients may wake up at night due to their symptoms and show weakness and thenar atrophy as clinical signs.5,6 Conversely, patients with clinical criteria and negative findings in NCS may represent as much as 10% of the cases. Therefore, according to with the American Academy Neurology (AAN), the use of the ultrasound image can also contribute to the diagnosis of CTS, once it may show structural anomalies in the wrist.10 Pain in CTS is one of the most prominent symptoms and may have, as a physiopathological element, neuropathic mechanisms related to a neural lesion and have nociceptive mechanisms compatible with the subjacent musculoskeletal change.11,12

Other conditions are possible causes of the similar CTS symptoms such as plexopathies, polyneuropathies, radiculopathies, osteoarticular injuries, cortical lesions, and compressions of the median nerve itself in other places, and these must be considered in a differential diagnosis.5,6 Thus clinical features are not entirely reliable and require the importance of NCS as a confirmatory resource.5,6 Besides, clinical characteristics of CTS are quite variable and difficult to interpret, being associated with psychosocial factors which may promote divergences between the clinical and electrophysiological diagnoses, as well as therapeutic inefficacy.17-22

Although the current literature recommends the combined use of clinical and NCS to establish CTS diagnosis, there are still conflicting results about the relationship between the severity of the electrophysiological findings and the clinical manifestations shown in CTS.13-29 Structured questionnaires to assess functioning and pain in multidimensional approaches have been used with progressive frequency to describe the impact of this condition on people’s lives, however they also seem to be poorly related to NCS severity. Therefore, to study the diagnostic methods it is essential to understand its symptomatology better and to implement the right therapy.24-30

OBJECTIVE

The aim of this text is to systematically review the scientific evidence on the correlation between the clinical-functional aspects with the electrophysiological severity in patients with CTS.

METHOD

This study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) recommendations for systematic reviews.31

Inclusion criteria for the studies

The inclusion and exclusion criteria are defined below, based on the question that guides the review, considering that there were no limitations on the period or language of the publications.

Types of studies

This review analyzed published studies of controlled randomized clinical trials, quasi-randomized controlled clinical trials, controlled clinical trials, diagnostic studies of accuracy, cohort studies, case-control studies, descriptive studies, case series, and case studies.

Characteristics of the population

The participants were adults aged between 18 and 65 years, with a clinical and electrophysiological diagnosis of CTS, with no previous surgical intervention.

Types of interventions

To be included this review, subjects should undergo at least to two stages of evaluation carried out by different blinded investigators.

• First stage: NCS performed or supervised by a medical specialist. Both upper limbs had to be examined and median nerve conduction tests confirmed CTS following the recommendation of the American Association of Electrodagnostic Medicine (AAEM).12 Padua’s electrophysiological classification32 or numerical variables (following the values for latency and amplitude in the NCS defined the electrophysiological severity of CTS.

• Second stage: clinical evaluation guided by the American Academy of Neurology criteria for CTS, followed by the application of questionnaires and various tests to estimate the clinical severity and functional state.

Outcome

The studies should correlate the clinical severity and functional state with the electrophysiological grades in patients with CTS.

Method and search strategy to identify the studies and eligibility

The following databases were used to identify likely eligible studies in October of 2013, without restriction on publication period or language, in the:

• Pubmed / Medline
• Embase
• Cochrane
• CINAHL
• LILACS
• SCIELO
• Thesis and Dissertations from the Universidade de São Paulo (USP) and the Universidade Federal de São Paulo (UNIFESP).

The search strategy was based on ques-
A correlation between clinical severity and functional state with nerve conduction studies findings in patients with carpal tunnel syndrome: a systematic review

RESULTS

The initial search identified 857 articles, 24 of which were excluded due to duplication, and 780 that were excluded during the analysis of titles and abstracts. Of the 53 remaining studies, only 10 studies23,34,35,36,38,39 met the inclusion criteria of the present review, after being thoroughly read, resulting in three case-control studies and seven cross-sectional observational studies. During the full reading, 43 studies were excluded: two of them scored less than 50 after the methodological quality analysis using the AHRQ scale, 38 studies analyzed the diagnostic correlation between the variables rather than the correlation of severity (object of this review), one study made a neurophysiological analysis with different electrophysiological studies (NCS and evoked potential associated), and two articles studied patients who had previously undergone surgery (Figure 1).

Despite the concern in selecting more homogeneous studies in relation to the type of severity measurements, the studies showed significant heterogeneity and methodological discrepancies (Chart 1).

Overall, the studies included 1184 subjects in the specified age range, the two case-control studies recruited 39 subject without CTS. Six articles included men and women in their studies23,34,35,36,40,42 and four included only women.34,35,37,39 All 10 studies used categorical scales based on electrophysiological findings: four studies used the electrophysiological classification by Pădua32 with five levels,36,37,40,41 five studies used a categorical classification with three levels (light, moderate, and severe),23,34,35,38,39 and one study used a categorical classification with six levels.42

In four studies, the evaluation of clinical and functional severity used the Boston Carpal Tunnel Questionnaire (BCTQ), the visual analogue scale (VAS), and a detailed physical exam with specific tests, including the fine motor ability test, the thumb abduction strength, the pinch grip strength, and the degree of thenar atrophy,34,35,40,42 while in four other articles, only the BCTQ and VAS were used.33,36,38 in the remaining studies, the researchers used their own clinical and functional questionnaires.39,42

Methodological limitations included the absence of controlled and randomized clinical trials, quasi-randomized or controlled trials, as well as the fact that three of the 10 articles contained less than 100 subjects.
<table>
<thead>
<tr>
<th>Author; Year; Journal Type of study</th>
<th>Population of the study (age, gender, inclusion and exclusion criteria)</th>
<th>Defined Diagnostic Criteria (clinical and ENMG severity used)</th>
<th>Interventions (Scales for clinical and ENMG severity used)</th>
<th>Outcomes / Results</th>
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<tr>
<td>1 - De la Llave-Rincón; 2011; American Journal of Physical Medicine &amp; Rehabilitation</td>
<td>66 women with Electrophysiological and clinical CTS (cases) and 20 healthy women (control).</td>
<td>Clinical CTS criteria: Pain and pares- thesis in the distribution of the median nerve. More intense symptoms of night, positive Tinel’s sign, positive Phalen’s sign, or self-perceived pinch grip deficit. Symptoms for at least six months, either unilateral or bilateral.</td>
<td>Electrodiagnostic criteria for CTS: sensor y and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>* The deficits relative to the fine motor ability and pinch grip strength are similar in patients with minimum, moderate, or severe CTS. Therefore, the clinical severity, verified in objective clinical tests, of pinch grip strength and fine motor ability are not associated with electrodiagnostic severity.</td>
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<td>Cross-sectional study</td>
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<tr>
<td>2 - De la Llave-Rincón; 2011; American Journal of Pain</td>
<td>72 women with Electrophysiological and clinical CTS and 19 healthy women.</td>
<td>Clinical CTS criteria: Pain and pares- thesis in the distribution of the median nerve. More intense symptoms of night, positive Tinel’s sign, positive Phalen’s sign, or self-perceived pinch grip deficit. Symptoms for at least six months, either unilateral or bilateral.</td>
<td>Electrodiagnostic criteria for CTS: sensor y and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>* There were no significant differences in the pain intensity parameters and score in the BCTQ for patients with minimum, moderate, and severe CTS.</td>
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<td>Case-control study</td>
<td>* Exclusion: score of &gt; 8 in the Beck Depression Inventory</td>
<td>Electrodiagnostic criteria for CTS: sensor y and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>Electrodiagnostic Criterio for CTS: sensor y and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>* There were no significant differences between the sensory alterations verified and the severity in the NCS.</td>
</tr>
<tr>
<td>3 - Chan L; 2007; Archives of Physical Medicine &amp; Rehabilitation</td>
<td>215 adults with Electrophysiological and clinical CTS</td>
<td>Clinical criteria: patients with symp- toms of pain and paresthesia in at least 2 fingers innervated by the median nerve and “classic,” “probable,” or “possible” CTS, according to the hand diagram by Kartz.</td>
<td>Electrodiagnostic criteria: (1) distal motor latency of the median nerve greater or equal to 4.4 ms, (2) positive Babinski sign, (3) palm-wrist test, with difference of latency median / ulnar greater than 0.3 ms, (4) difference in latency of the median and ulnar ner- ves, with capture of the fourth finger, greater than 0.4 ms, (5) combined sensory index greater than 1.0 ms.</td>
<td>Electrodiagnostic Criterio for CTS: divided into 3 groups according to the number of impairments: 1) sensory alteration; 2) motor alteration; 3) sensory and motor alterations.</td>
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<td>Cross-sectional study</td>
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<td>Clinical CTS criteria: patients with symp- toms of pain and paresthesia in at least 2 fingers innervated by the median nerve and “classic,” “probable,” or “possible” CTS, according to the hand diagram by Kartz.</td>
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<td>4 - Zanette G; 2007; J Peripher Nerv Syst</td>
<td>112 patients (175 hands)</td>
<td>Electrodiagnostic criteria: standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>Electrodiagnostic criteria: standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>* The Electrophysiological severity and the damage measurements of the median ner- ve were inversely correlated with the severe- ity of proximal pain (forearm, elbow, arm, shoulder) in some patients.</td>
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<td>Cross-sectional study</td>
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<td>Clinical CTS criteria: Pain and pares- thesis in the distribution of the median nerve. Symptoms worsen at night, positive Tinel’s sign, positive Phalen’s sign, or self-perceived pinch grip deficit.</td>
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<tr>
<td>5 - De la Llave-Rincón A.; 2012; Rev Neurol</td>
<td>92 women with CTS</td>
<td>Electrodiagnostic criteria for CTS: stan- dardized directives from the American Association of Electrodagnostic Medicine</td>
<td>Electrodiagnostic criteria for CTS: standardized directives from the American Association of Electrodagnostic Medicine</td>
<td>* There is no correlation between the inten- sity of pain and the scores in the disability questionnaire (BCTQ) with the Electrophysio- logical severity.</td>
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<tr>
<td>Cross-sectional study</td>
<td></td>
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<td></td>
<td>* Pain is reported as regular, repetitive, and disturbing in women with severe CTS.</td>
</tr>
<tr>
<td>6 - Modi CS; 2010; Orthopaedics and Traumatology: Surgery and Research</td>
<td>111 patients (165 hands)</td>
<td>Clinical CTS criteria: criteria from the American Academy</td>
<td>Clinical CTS criteria: criteria from the American Academy</td>
<td>* Mean motor latencies were greater in pa- tients who presented pain as the main and most frequent symptom.</td>
</tr>
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</table>
### Cross-sectional observational study

**Electrodiagnostic criteria:** standard directives from the American Association of Electrodiagnostic Medicine

**Clinical criteria:** Paresthesia and/or nocturnal/alarm pain in the distribution of the median nerve, paresthesia, and dropping things. Objective criteria such as positive Phalen or Tinel, sensory deficit of the median nerve (hypoesthesia in the fingers), and/or motor deficits (test of thumb abduction and opposition and atrophy of the thenar musculature)

**Clinical Scales:** Scale produced by the author himself - Light CTS: Isolated subjective symptoms and normal physical exam - Moderate CTS: Objective sensory deficit (hypoesthesia) in the distribution of the median nerve, with no motor deficits - Severe CTS: sensory and motor deficits, objective symptoms (weakness in abduction or opposition of thumb) in the distribution of the median nerve with or without thenar atrophy

**Electrophysiological Scale:** classification proposed by Stevens et al. into 3 groups: light, moderate, severe

**Electrophysiological criteria:**

- Sensitivity fascicle compression
  - Motor latency (m/s): light: 3.8 – 4.4; moderate: 4.5 – 4.9; severe: > 5

- Motor fascicle compression
  - Motor latency (m/s): light: 3.8 – 4.4; moderate: 4.5 – 4.9; severe: > 5

*The frequency with which the patients experience pain (pain as the main and most frequent symptom) is associated with the severity of motor fascicle compression of the median nerve, regardless of sensory involvement.*

*A positive correlation was found between the clinical scale and the Electrophysiological scale, confirming also that this correlation increased as the clinical graduation became more severe.*

### Cross-sectional observational study

**Electrodiagnostic criteria:** according to standardized directives from the American Association of Electrodiagnostic Medicine

**Clinical criteria:** criteria recommended by the American Academy of Neurology

**Clinical Scales:** VAS, BCTQ, Katz hand diagram, tactile hypoaesthesia, strength of abduction of the thumb recorded with the 5-point scale according to the Medical Research Council

**Electrophysiological Scale:** Classification by Pâdua et al.

*Statistically significant correlation between the neurophysiological compromising (total score) and the severity of the objective measurements of the injury to the median nerve (tactile hypoaesthesia and paresthesia in the abduction of the thumb).*

*Absence of correlation between the degree of neurophysiological compromising and the scores of subjective complaints.*

### Case-control study

**Clinical criteria:** criteria recommended by the American Academy of Neurology

**Clinical Scales:** VAS, BCTQ (evaluating separately the questions that involve weakness in the hand and lack of manual dexterity), tactile hypoaesthesia, strength of abduction of the thumb recorded with the 5-point scale according to the Medical Research Council

**Electrophysiological Scale:** 1 = minimum, 2 = light, 3 = moderate, 4 = severe, and 5 = extreme, according to Pâdua et al.

*Lack of hand dexterity was related to the severity of the clinical and Electrophysiological symptoms, when compared to the two other groups (1 – stocking and gloving distribution, 2 – distribution of the ulnar nerve).*

*Weakness in the hands related to the severity of sensory symptoms (pain, numbness, and tingling), but does not correlate with the degree of neurophysiological compromising of the median nerve;* (OR: 1.01 / CI 95% 0.68–1.47 / P: 0.99)

### Prospective study

**Electrodiagnostic criteria:** Sensory and motor conductions of the ulnar nerves were normal and the studies on the neural conduction of the median nerve were altered according to our abnormality values: 1) palm-wrist sensory velocity < 50.0 m/s; 2) sensory conduction velocity < 50.0 m/s; 3) initial distal motor latency > 4.0 ms.

**Electrophysiological criteria:** Developed by the author himself – Minimum (Grade 1): Light (Grade 2), Moderate (Grade 3), Moderate (Grade 4), Severe (Grade 5), Extreme (Grade 6)

**Clinical Scale:** their own scale, following the epidemiological classification scale for CTS

*The report of a classic CTS story, the presence of primary symptoms (nocturnal pain, paresthesia, and numbness) and the presence of sensitive and motor deficits in the physical exam are more frequent, the greater the severity of the CTS.*

*The report of a classic CTS story and the presence of all the symptoms analyzed had a significant positive correlation (p<0.01) with the grades of the Electrophysiological scale.*

*Significant positive correlation between the CTS Electrophysiological scale and the presence of Tinel’s sign (p<0.05), tactile hypoaesthesia in the second finger, weakness in the abduction of the thumb, and hypotrophy of the thenar eminence (p<0.01).
DISCUSSION

Despite the broad search strategies used in this review, the final number of articles selected was small. Even with the vast literature covering the diagnostic correlation between CTS identified using clinical signs and NCS findings, few studies tried to correlate the severity of clinical parameters with the electrophysiological severity, even though there were controversial results and limitations concerning this issue.

Of the 53 studies initially selected, only 10 could be included according to the inclusion criteria and methodological evaluation. The most frequent methodological limitation concerned the lack of reasoning for small samples. In various studies, blinding the investigators during the application of the assessment tools was not reported. Another limiting aspect is that few studies cared to control psychosocial factors such as depression and catastrophizing, once these factors may introduce divergences between the clinical and electrophysiological findings, as well as therapeutic inefficacy.

Four out of 10 studies correlated clinical and electrophysiological severity, using the following clinical scales: the Boston Carpal Tunnel Questionnaire (BCTQ), the Visual Analogue Scale for pain (VAS) and a detailed physical examination, with specific tests, evaluating pinch grip strength, thumb abduction, fine motor ability, and sensitivity. Of those four studies, two did not show any correlation between the electrophysiological severity and the scores of the subjective complaints presented by the patients. As a counterpart, the other two articles showed a positive correlation with objective measurements during the physical examination.

Tactile hyposthesia and reduced strength to abduct the thumb positively correlate with reduced neuroconduction velocities. Also, hands with a distribution of the symptoms in the median nerve territory showed greater electrophysiological severity and more objective alterations in the physical examination, when compared to the other two groups with a non-classic symptom distribution (1 – stocking and gloving distribution, 2 – distribution of the ulnar nerve).

When the motor conduction of the median nerve was analyzed, the lack of manual dexterity correlated with the electrophysiological severity. There was also a strong correlation between the intensity of motor symptoms and the intensity of pain, suggesting a possible contribution of the pain to the occurrence of weakness and lack of manual dexterity in CTS patients, favoring the hypothesis that this altered motor control could be a consequence of pain. This could induce a reorganization of the motor strategies in the central nervous system either by diminishing the agonist activity of the muscle order limiting the velocity and force used during the action. Motor control deficits may perpetuate chronic pain, because fear or avoidance and are considered maladaptive processes that generate disabilities. Besides, it is known that small fibers, which are mainly disordered in early CTS, are not routinely studied in NCS, thus such association is less likely to be found in this stage of the disease.

However, NCS are still the gold standard for the diagnosis of this condition. Four other studies coherently failed to correlate the neurophysiological severity scales with subjective clinical scales (analog scale for pain and the BCTQ). However, when the analysis used quantitative measures of latency and amplitude in the NCS, one of the studies succeeded to show this association. In CTS patients who presented pain as their main symptom, the average motor latencies of the median nerve were prolonged.

A significant correlation was demonstrated between the frequency of pain and the increase in the severity of damage to the motor fascicle of the median nerve, regardless of any sensory involvement. This fact could be explained by irritation of the nervi nervorum, and by the structural and functional alterations present in the denervated muscles, once they may reduce muscle strength and overload the spared muscle fibers, leading to the genesis of myofascial trigger points, for example.

The McGill Pain Questionnaire shows significant differences in the quality of pain in patients with light, moderate, and severe CTS. Pain is the most usual, repetitive, and disturbing symptom in women with severe CTS. Lack of correlation between electrophysiological findings and symptoms may be associated with alternative diagnoses like other neurological entrapments, myofascial pain syndrome and inflammatory conditions, which can mimic the clinical presentation of CTS.

Finally, two studies used clinical and electrophysiological non validated scales, produced by the authors themselves, and showed a correlation between the clinical and neurophysiological severities. Reporting of the classic CTS story, the presence of primary symptoms (pain, paresthesia, and numbness), and sensory or motor deficits in the physical examination are more frequent and predominant when the electrophysiological severity is greater. It is noteworthy, however, that at the extreme level of neurophysiological severity (grade 6), the CTS patients may present a lower frequency of pain and paresthesia. This may be explained by the reduction in the number of sensory fibers surviving within the fibrotic nerve fascicle, which would result in fewer pain or paresthesia crises and a higher prevalence of sensory and motor alterations.

CONCLUSION

Carpal Tunnel Syndrome is the most prevalent compressive neuropathy in the general population, and it can lead to disabling symptoms and functional limitations. It presents mixed pathophysiological mechanisms that, when not identified properly, can lead to therapeutic inefficacy. The consequences of this may be disabilities, psychosocial problems, decrease in the quality of life, and a reduction in the capacity for work. This review could demonstrate that some clinical findings from physical examination or standardized questionnaires could be correlated with NCS severity, but the presence of studies which failed to demonstrate this correlation keep the issue still as an unsolved question. The large heterogeneity and methodological discrepancies in the selected studies call for larger and more controlled studies in the issue.

DECLARATION OF INTEREST

The authors report no conflicts of interest.

REFERENCES

A correlation between clinical severity and functional state with nerve conduction studies findings in patients with carpal tunnel syndrome: a systematic review