

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

Correlação entre gravidade clínica e estado funcional com achados eletroneuromiográficos, em pacientes com síndrome do túnel do carpo: uma revisão sistemática

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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

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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.¹⁻³ 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.^{5,6} It is more prevalent in women (3:1) between the ages of 45-65 years^{2,7} and is associated with a series of clinical conditions such as obesity, pregnancy, diabetes, rheumatoid arthritis, hypothyroidism,⁸ 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.^{5,6,14}

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.^{12,15}

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.^{5,6,16} 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.²³⁻²⁹ 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.^{14,15,30}

OBJECTIVE

The aim of this text is to systematically review the scientific evidence on the correlation between the clinic-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 Electrodiagnostic Medicine (AAEM).¹³ 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-

tions structured in the P.I.C.O. format ("Patient", "Intervention", "Control", "Outcome") using as descriptors: Carpal tunnel syndrome (Carpal Tunnel Syndromes OR Syndrome, Carpal Tunnel OR Syndromes, Carpal Tunnel OR Median Neuropathy, Carpal Tunnel OR Compression Neuropathy, Carpal Tunnel OR Entrapment Neuropathy, Carpal Tunnel) AND (nerve conduction OR Neural Conduction OR electrodiagnosis) AND signs and symptoms (neuropathic pain OR Neuralgia).

Two investigators performed the search in the databases independently rigorously following the search strategy and inclusion and exclusion criteria. Any disagreements occurring between the two investigators were solved by consensus and by the analysis of a senior investigator. First, a triage of the studies was carried out, evaluating the titles and abstracts identified in the search. When the title and abstract were not sufficiently clarifying, the article was thoroughly read to prevent the loss of any critical studies to the review.

Finally, the evaluator extracted data from each study with a standardized form for the following parameters: age and gender of the subjects, number of subjects included in the study, the electrophysiological and clinical diagnostic criteria used for CTS, types of interventions (classifications of electrophysiological and clinical severity), types of results measured, and the authors' conclusions about the outcomes of the interventions.

Evaluation of the methodological quality

The two reviewers used the scale for observational studies from the Agency for Healthcare Research and Quality (AHRQ), modified and validated by West et al.³³ to define methodological quality, and any discrepancies were examined by a third reviewer and by consensus. This instrument assess: study goal (2), population studied (8), comparability of the subjects (22), exposure or intervention (11), measurements of the results (20), statistical analysis (19), results (8), discussion (5), and support or sponsorship (5), totaling 100 points. Only articles with a score greater than 50 (scale of 0-100) were accepted.

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 studies^{23,34,35,36-42} 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 studies,^{23,36,38,40-42} 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 Pádua³² 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,^{34,35,40,41} while in four other articles, only the BCTQ and VAS were used;^{23,36-38} 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.

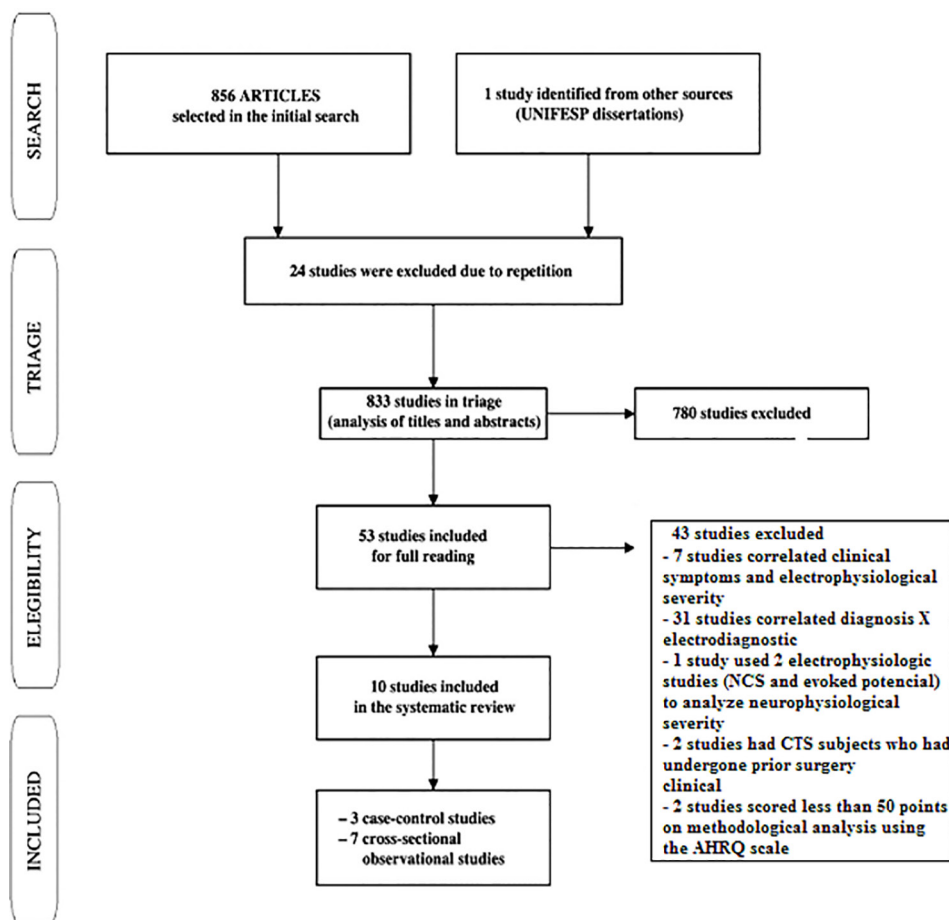


Figure 1. Study selection flowchart

Chart 1. Studies which correlate NCS findings and clinical severity in CTS

Author; Year; Journal Type of study	Population of the study (age, gender, inclusion and exclusion criteria)	Defined Diagnostic Criteria (clinical and NCS)	Interventions (Scales for clinical and ENMG severity used)	Outcomes / Results
1 - De la Llave-Rincón; 2011; American Journal of Physical Medicine & Rehabilitation ³⁴ Case-control study	66 women with Electrophysiological and clinical CTS (cases) and 20 healthy women (control).	Clinical CTS criteria: Pain and paresthesia in the distribution of the median nerve, more intense symptoms at 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. Electrodiagnostic criteria for CTS: sensory and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodiagnostic Medicine	Clinical Scales: VAS, Boston Carpal Tunnel Questionnaire (BCTQ), Purdue Pegboard Test, pinch grip strength with dynamometer Electrophysiological Scale: Minimum (only segmentary tests – abnormal comparative); Moderate (Abnormal velocity of sensory conduction to median nerve or distal motor latency); Severe (absence of sensory response from the median nerve and abnormal distal motor latency).	* 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. * There was no association between electrophysiological severity and the pain severity parameters (VAS) or BCTQ score
2- De la Llave-Rincón; 2011; Clinical Journal of Pain ³⁵ Case-control study	72 women with Electrophysiological and clinical CTS and 19 healthy women. * Exclusion: score of > 8 in the Beck Depression Inventory	Clinical CTS criteria: Pain and paresthesia in the distribution of the median nerve, more intense symptoms at 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. Electrodiagnostic criteria for CTS: sensory and motor conduction deficits in the median nerve according to the standardized directives from the American Association of Electrodiagnostic Medicine	Clinical Scales: VAS, Boston Carpal Tunnel Questionnaire (BCTQ), Pain threshold through pressure (evaluated bilaterally on the territories of the median, ulnar, radial, the C5 - C6, the carpal tunnel, and the tibialis anterior muscle), and pain threshold through the use of heat and cold (evaluated bilaterally on the carpal tunnel and on the thenar eminence) Electrophysiological Scale: Minimum (only segmentary tests – abnormal comparative); Moderate (Abnormal velocity of sensory conduction to median nerve or distal motor latency); Severe (absence of sensory response from the median nerve and abnormal distal motor latency).	* There were no significant differences in the pain intensity parameters and score in the BCTQ for patients with minimum, moderate, and severe CTS. * There were no significant differences between the sensory alterations verified and the severity in the NCS. * The pain threshold through pressure was significantly lower, bilaterally, in the median, ulnar, and radial nerves, in the carpal tunnel, in the C5 and C6, and in the tibialis anterior muscle for patients with minimum, moderate, or severe CTS in comparison with the healthy controls (p < 0.001). * The pain threshold through the use of heat and cold showed reduction in comparison with the controls (p < 0.001).
3 - Chan L; 2007; Archives of Physical Medicine & Rehabilitation ²³ Cross-sectional observational study	215 adults with Electrophysiological and clinical CTS	Clinical criteria: patients with symptoms 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 ⁴³ Electrodiagnostic criteria: (1) distal motor latency of the median nerve greater or equal to 4.4 ms, (2) positive Bactrian 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 nerves, with capture of the fourth finger, greater than 0.4 ms, (5) combined sensory index greater than 1.0 ms.	Clinical Scales: BCTQ, VAS, Pain Catastrophizing Scale (PCS), and SCL-90 Electrophysiological Scale: divided into 3 groups according to the number of impairments: 1) sensory alteration; 2) motor alteration; 3) sensory and motor alterations.	* No statistically significant correlation between Electrophysiological severity of CTS with the clinical parameters, even with the control of possibly confounding factors such as age, gender, BMI, duration of symptoms, catastrophizing, and depression.
4- Zanette G; 2007; J Peripher Nerv Syst ³⁶ Cross-sectional observational study	112 patients (175 hands)	Clinical criteria: criteria from the American Academy of Neurology. The negativity of Tinel and Phalen signs was not used as exclusion criteria Electrodiagnostic criteria: standardized directives from the American Association of Electrodiagnostic Medicine	Clinical Scales: BCTQ and VAS, Katz hand diagram, thumb abduction strength and sensitivity Electrophysiological Scale: 1 = minimum, 2 = light, 3 = moderate 4 = severe, and 5 = extreme ³¹	* None of the objective and electrophysiological variables correlated with the severity of sensory complaints restricted to the hand in patients with CTS. * The Electrophysiological severity and the damage measurements of the median nerve were inversely correlated with the severity of proximal pain (forearm, elbow, arm, shoulder) in some patients.
5- De la Llave-Rincon A; 2012; Rev Neuro ³⁷ Cross-sectional observational study	92 women with CTS	Clinical CTS criteria: Pain and paresthesia 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. Electrodiagnostic criteria for CTS: standardized directives from the American Association of Electrodiagnostic Medicine	Clinical Scales: VAS, McGill Pain Questionnaire, BCTQ Electrophysiological Scale: neurophysiological classification by Pádua et al. ³²	* There are great differences in the quality of pain in patients with light, moderate, and severe CTS. * There is no correlation between the intensity of pain and the scores in the disability questionnaire (BCTQ) with the Electrophysiological severity. * Pain is reported as regular, repetitive, and disturbing in women with severe CTS.
6- Modi CS; 2010; Orthopaedics and Traumatology: Surgery and Research ³⁸	111 patients (165 hands)	Clinical CTS criteria: criteria from the American Academy	Clinical Scales: VAS, BCTQ	* Mean motor latencies were greater in patients who presented pain as the main and most frequent symptom.

Cross-sectional observational study		Electrodiagnostic criteria: standardized directives from the American Association of Electrodiagnostic Medicine	Electrophysiological Scale: Sensitive fascicle compression velocity of the sensitive conduction (m/s): light: 31-49; moderate: < 30; severe = absent 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 gradation became more severe.
7- Sabry MM; 2009; Egyptian Journal of Neurology, Psychiatry and Neurosurgery ³⁹	65 women with CTS (110 hands)	Clinical CTS criteria: Paresthesia and/or nocturnal/diurnal 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	* A positive correlation was found between the clinical scale and the Electrophysiological scale, confirming also that this correlation increased as the clinical gradation became more severe.
Cross-sectional observational study		Electrodiagnostic criteria: standardized directives from the American Association of Electrodiagnostic Medicine	Electrophysiological Scale: classification proposed by Stevens et al. ⁴⁵ into 3 groups: light, moderate, severe	
8- Zanette G; 2006; Pain ⁴⁰	103 patients (165 hands)	Clinical criteria: criteria recommended by the American Academy of Neurology ⁴⁴	Clinical Scales: VAS, BCTQ, Katz hand diagram, tactile hypoesthesia, strength of abduction of the thumb recorded with the 5-point scale according to the Medical Research Council ⁴⁶	* Statistically significant correlation between the neurophysiological compromising (total score) and the severity of the objective measurements of the injury to the median nerve (tactile hypoesthesia and paresis in the abduction of the thumb).
Cross-sectional observational study		Electrodiagnostic criteria: according to standardized directives from the American Association of Electrodiagnostic Medicine	Electrophysiological Scale: Classification by Pádua et al. ³²	* Absence of correlation between the degree of neurophysiological compromising and the scores of subjective complaints. * Hands with distribution of symptoms in the median nerve territory had greater Electrophysiological severity and more severe objective alterations in the physical exams, when compared to the two other groups (1 – stocking and gloving distribution, 2 – distribution of the ulnar nerve).
9- Tamburin S; 2008; J Neurol ⁴¹	129 patients -113 hands presenting weakness	Clinical criteria: criteria recommended by the American Academy of Neurology ⁴⁴	Clinical Scales: VAS, BCTQ (evaluating separately the questions that involve weakness in the hand and lack of manual dexterity), tactile hypoesthesia, strength of abduction of the thumb recorded with the 5-point scale according to the Medical Research Council ⁴⁶	* Lack of hand dexterity was related to the severity of the clinical and Electrophysiological symptoms, when compared to the motor neuroconduction of the median nerve (OR: 1.68 / CI 95% 1.09–2.57 / P: 0.02)
Case-control study	- 98 hands presenting lack of manual dexterity	Electrodiagnostic criteria: standardized directives from the American Association of Electrodiagnostic Medicine	Electrophysiological Scale: 1 = minimum, 2 = light, 3 = moderate, 4 = severe, and 5 = extreme, according to Pádua et al. ³¹	* 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)
10- Carvalho F N; 2007; Acta Fisiatrica ⁴²	400 hands from 219 patients with CTS	Clinical criteria: criteria recommended by the American Academy of Neurology ⁴⁴	Clinical Scale: their own scale, following the epidemiological classification scale for CTS ⁴⁷	* 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.
Prospective study		Electrodiagnostic criteria: Sensory and motor conduction 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 Scale: Developed by the author himself – Minimum (Grade 1); Light (Grade 2), Moderate (Grade 3); Moderate (Grade 4), Severe (Grade 5), Extreme (Grade 6)	* 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 hypoesthesia 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.¹⁷⁻²²

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.^{34,35,40,41} Of those four studies, two did not show any correlation between the electrophysiological^{34,35} severity and the scores of the subjective complaints presented by the patients. As a counterpart, the other two articles showed a positive correlation^{40,41} with objective measurements during the physical examination.

Tactile hypoesthesia 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 severe objective alterations in the physical examinations, when compared to the two other groups with a non-classic symptom distribution (1 – stocking and gloving distribution, 2 – distribution of the ulnar nerve).⁴⁰

When the motor conduction of the median nerve was analyzed, the lack of manual dexterity correlated with the electrophysiological severity.⁴¹ 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,^{34,41} favoring the hypothesis that this altered motor control could be a consequence of pain.^{34,41,48} 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.^{34,41,48} Motor control deficits may perpetuate chronic pain, because fear or avoidance and are considered maladaptive processes that generate disabilities.³⁴ 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^{23,36-38} 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.³⁸ 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.³⁸

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.³⁷ 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^{39,42} 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.⁴² 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.⁴²

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 physiopathological 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

1. Atroshi I, Gummesson C, Johnsson R, Ornstein E, Ranstam J, Rosén I. Prevalence of carpal tunnel syndrome in a general population. *JAMA*. 1999;282(2):153-8. DOI: <http://dx.doi.org/10.1001/jama.282.2.153>
2. Bongers FJ, Schellevis FG, van den Bosch WJ, van der Zee J. Carpal tunnel syndrome in general practice (1987 and 2001): incidence and the role of occupational and non-occupational factors. *Br J Gen Pract*. 2007;57(534):36-9.
3. Alfonso C, Jann S, Massa R, Torreggiani A. Diagnosis, treatment and follow-up of the carpal tunnel syndrome: a review. *Neurol Sci*. 2010;31(3):243-52. DOI: <http://dx.doi.org/10.1007/s10072-009-0213-9>
4. American Academy of Orthopaedic Surgeons. Clinical practice guideline on the diagnosis of carpal tunnel syndrome. Rosemont: AAOS; 2007.

5. brahim I, Khan WS, Goddard N, Smitham P. Carpal tunnel syndrome: a review of the recent literature. *Open Orthop J.* 2012;6:69-76 DOI: <http://dx.doi.org/10.2174/1874325001206010069>
6. Aroori S, Spence RA. Carpal tunnel syndrome. *Ulster Med J.* 2008;77(1):6-17.
7. British Society for Surgery of the Hand. Guideline: carpal tunnel syndrome (CTS). London: BSSH; 2012.
8. Van Dijk MA, Reitsma JB, Fischer JC, Sanders GT. Indications for requesting laboratory tests for concurrent diseases in patients with carpal tunnel syndrome: a systematic review. *Clin Chem.* 2003;49(9):1437-44. DOI: <http://dx.doi.org/10.1373/49.9.1437>
9. Armstrong T, Dale AM, Franzblau A, Evanoff BA. Risk factors for carpal tunnel syndrome and median neuropathy in a working population. *J Occup Environ Med.* 2008;50(12):1355-64. DOI: <http://dx.doi.org/10.1097/JOM.0b013e3181845fb1>
10. Cartwright MS, Hobson-Webb LD, Boon AJ, Alter KE, Hunt CH, Flores VH, et al. Evidence-based guideline: neuromuscular ultrasound for the diagnosis of carpal tunnel syndrome. *Muscle Nerve.* 2012;46(2):287-93. DOI: <http://dx.doi.org/10.1002/mus.23389>
11. New York carpal tunnel syndrome medical treatment Guidelines. New York: Workers' Compensation Board; 2013.
12. Gürsoy AE, Kolukisa M, Yıldız GB, Kocaman G, Celebi A, Koçer A. Relationship between electrodiagnostic severity and neuropathic pain assessed by the LANSS pain scale in carpal tunnel syndrome. *Neuropsychiatr Dis Treat.* 2013;9:65-71. DOI: <http://dx.doi.org/10.2147/NDT.S38513>
13. American Association of Electrodiagnostic Medicine, American Academy of Neurology, and American Academy of Physical Medicine and Rehabilitation. Practice parameter for electrodiagnostic studies in carpal tunnel syndrome: summary statement. *Muscle Nerve.* 2002;25(6):918-22.
14. Nora DB, Becker J, Ehlers JA, Gomes I. Clinical features of 1039 patients with neurophysiological diagnosis of carpal tunnel syndrome. *Clin Neurol Neurosurg.* 2004;107(1):64-9. DOI: <http://dx.doi.org/10.1016/j.clineuro.2004.08.003>
15. Truini A, Padua L, Biasiotta A, Caliandro P, Pazzaglia C, Galeotti F, et al. Differential involvement of A-delta and A-beta fibres in neuropathic pain related to carpal tunnel syndrome. *Pain.* 2009;145(1-2):105-9.
16. Campos CC, Manzano GM, Castelo Filho A, Nóbrega JAM. Parestesia e/ou dor nas mãos e/ou punhos como motivo de encaminhamento para estudo eletroneuromiográfico. *Arq Neuropsiquiatr.* 2003;61(1):56-60. DOI: <http://dx.doi.org/10.1590/S0004-282X2003000100010>
17. Sardá Junior J, Nicholas MK, Pereira IA, Pimenta CAM, Asghari A, Cruz RM. Validação da Escala de Pensamentos Catastróficos sobre Dor. *Acta Fisiatr.* 2008;15(1):31-6.
18. Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine (Phila Pa 1976).* 2002;27(5):E109-20.
19. Keefe FJ, Rumble ME, Scipio CD, Giordano LA, Perri LM. Psychological aspects of persistent pain: current state of the science. *J Pain.* 2004;5(4):195-211. DOI: <http://dx.doi.org/10.1016/j.jpain.2004.02.576>
20. Sullivan MJ, Thorn B, Haythornthwaite JA, Keefe F, Martin M, Bradley LA, et al. Theoretical perspectives on the relation between catastrophizing and pain. *Clin J Pain.* 2001;17(1):52-64. DOI: <http://dx.doi.org/10.1097/00002508-200103000-00008>
21. Bair MJ, Wu J, Damush TM, Sutherland JM, Kroenke K. Association of depression and anxiety alone and in combination with chronic musculoskeletal pain in primary care patients. *Psychosom Med.* 2008;70(8):890-7. PMID: 18799425 DOI: <http://dx.doi.org/10.1097/PSY.0b013e318185c510>
22. Nunez F, Vranceanu AM, Ring D. Determinants of pain in patients with carpal tunnel syndrome. *Clin Orthop Relat Res.* 2010;468(12):3328-32. DOI: <http://dx.doi.org/10.1007/s11999-010-1551-x>
23. Chan L, Turner JA, Comstock BA, Levenson LM, Hollingworth W, Heagerty PJ, et al. The relationship between electrodiagnostic findings and patient symptoms and function in carpal tunnel syndrome. *Arch Phys Med Rehabil.* 2007;88(1):19-24. DOI: <http://dx.doi.org/10.1016/j.apmr.2006.10.013>
24. You H, Simmons Z, Freivalds A, Kothari MJ, Naidu SH. Relationships between clinical symptom severity scales and nerve conduction measures in carpal tunnel syndrome. *Muscle Nerve.* 1999;22(4):497-501. DOI: [http://dx.doi.org/10.1002/\(SICI\)1097-4598\(199904\)22:4<497::AID-MUS11>3.0.CO;2-T](http://dx.doi.org/10.1002/(SICI)1097-4598(199904)22:4<497::AID-MUS11>3.0.CO;2-T)
25. Dhong ES, Han SK, Lee BI, Kim WK. Correlation of electrodiagnostic findings with subjective symptoms in carpal tunnel syndrome. *Ann Plast Surg.* 2000;45(2):127-31. DOI: <http://dx.doi.org/10.1097/0000637-200045020-00005>
26. Schrijver HM, Gerritsen AA, Strijers RL, Uitdehaag BM, Scholten RJ, de Vet HC, et al. Correlating nerve conduction studies and clinical outcome measures on carpal tunnel syndrome: lessons from a randomized controlled trial. *J Clin Neurophysiol.* 2005;22(3):216-21.
27. Ansari NN, Adelmanesh F, Naghdi S, Mousavi S. The relationship between symptoms, clinical tests and nerve conduction study findings in carpal tunnel syndrome. *Electromyogr Clin Neurophysiol.* 2009;49(1):53-7.
28. Ortiz-Corredor F, Calambas N, Mendoza-Pulido C, Galeano J, Díaz-Ruiz J, Delgado O. Factor analysis of carpal tunnel syndrome questionnaire in relation to nerve conduction studies. *Clin Neurophysiol.* 2011;122(10):2067-70. DOI: <http://dx.doi.org/10.1016/j.clinph.2011.02.030>
29. Oncel C, Bir LS, Sanal E. The relationship between electrodiagnostic severity and Washington Neuropathic Pain Scale in patients with carpal tunnel syndrome. *Agri.* 2009;21(4):146-8.
30. Hayashida K, Eisenach JC. Multiplicative interactions to enhance gabapentin to treat neuropathic pain. *Eur J Pharmacol.* 2008;598(1-3):21-6.
31. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
32. Padua L, LoMonaco M, Gregori B, Valente EM, Padua R, Tonali P. Neurophysiological classification and sensitivity in 500 carpal tunnel syndrome hands. *Acta Neurol Scand.* 1997;96(4):211-7. DOI: <http://dx.doi.org/10.1111/j.1600-0404.1997.tb00271.x>
33. West S, King V, Carey TS, Lohr KN, McKoy N, Sutton SF, et al. Systems to rate the strength of scientific evidence. *Evid Rep Technol Assess (Summ).* 2002;(47):1-11.
34. De la Llave-Rincón AI, Fernández-de-Las-Peñas C, Pérez-de-Heredia-Torres M, Martínez-Pérez A, Valenza MC, Pareja JA. Bilateral deficits in fine motor control and pinch grip force are not associated with electrodiagnostic findings in women with carpal tunnel syndrome. *Am J Phys Med Rehabil.* 2011;90(6):443-51. DOI: <http://dx.doi.org/10.1097/PHM.0b013e31821a7170>
35. De la Llave-Rincón AI, Fernández-de-las-Peñas C, Laguarda-Val S, Alonso-Blanco C, Martínez-Pérez A, Arendt-Nielsen L, et al. Increased pain sensitivity is not associated with electrodiagnostic findings in women with carpal tunnel syndrome. *Clin J Pain.* 2011;27(9):747-54. DOI: <http://dx.doi.org/10.1097/AJP.0b013e31821c29d3>
36. Zanette G, Marani S, Tamburin S. Proximal pain in patients with carpal tunnel syndrome: a clinical-neurophysiological study. *J Peripher Nerv Syst.* 2007;12(2):91-7. DOI: <http://dx.doi.org/10.1111/j.1529-8027.2007.00127.x>
37. De la Llave-Rincón AI, Laguarda-Val S, Arroyo-Morales M, Martínez-Pérez A, Pareja JA, Fernández-de-Las-Peñas C. Characterisation of pain in patients with carpal tunnel syndrome according to electromyographic severity criteria. *Rev Neurol.* 2012;54(7):407-14.
38. Modi CS, Ho K, Hegde V, Boer R, Turner SM. Diagnosis of motor fascicle compression in carpal tunnel syndrome. *Orthop Traumatol Surg Res.* 2010;96(4):485-9. DOI: <http://dx.doi.org/10.1016/j.otsr.2010.01.009>
39. Sabry MM, Elkader GA, Fahmi MK, Abdel-Rehman A. Correlation of Nerve Conduction Studies to the Anthropometric Measurements of the Hand and to the Clinical Severity of Carpal Tunnel Syndrome. *Egypt J Neurol Psychiat Neurosurg.* 2009;46(1):67-77.
40. Zanette G, Marani S, Tamburin S. Extra-median spread of sensory symptoms in carpal tunnel syndrome suggests the presence of pain-related mechanisms. *Pain.* 2006;122(3):264-70. DOI: <http://dx.doi.org/10.1016/j.pain.2006.01.034>
41. Tamburin S, Cacciatori C, Marani S, Zanette G. Pain and motor function in carpal tunnel syndrome: a clinical, neurophysiological and psychophysical study. *J Neurol.* 2008;255(11):1636-43. DOI: <http://dx.doi.org/10.1007/s00415-008-0895-6>
42. Carvalho FN, Carneiro AP, Paulinelli RR, Carvalho TN. Classificação neurofisiológica da Síndrome do Túnel do Carpo. *Acta Fisiatr.* 2007;14(4):190-5.
43. Katz JN, Stirrat CR. A self-administered hand diagram for the diagnosis of carpal tunnel syndrome. *J Hand Surg Am.* 1990;15(2):360-3. DOI: [http://dx.doi.org/10.1016/0363-5023\(90\)90124-A](http://dx.doi.org/10.1016/0363-5023(90)90124-A)
44. Practice parameter for carpal tunnel syndrome (summary statement). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 1993;43(11):2406-9.
45. Stevens JC. AAEM minimonograph #26: the electrodiagnosis of carpal tunnel syndrome. *American Association of Electrodiagnostic Medicine. Muscle Nerve.* 1997;20(12):1477-86.
46. Memorandum No. 45 - Aids to the examination of the peripheral nervous system. London; H.M. Stationery Office; 1976.
47. Rempel D, Evanoff B, Amadio PC, de Krom M, Franklin G, Franzblau A, et al. Consensus criteria for the classification of carpal tunnel syndrome in epidemiologic studies. *Am J Public Health.* 1998;88(10):1447-51. DOI: <http://dx.doi.org/10.2105/AJPH.88.10.1447>
48. Sterling M, Jull G, Wright A. The effect of musculoskeletal pain on motor activity and control. *J Pain.* 2001;2(3):135-45.