

# Acupuncture and electroacupuncture in the treatment of carpal tunnel syndrome: Systematic review

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**Introduction** Carpal tunnel syndrome (CTS) is the most diagnosed compression neuropathy of the upper limb. In mild and moderate cases, the treatment is extensive and controversial, whereas severe cases receive surgical intervention.

**Objective** To analyze the scientific evidence on the effectiveness of treatment of CTS using acupuncture and electroacupuncture.

**Methods** The PRISMA declaration was followed. A literature search was performed using the following databases: Clinical Evidence BMJ, NICE, Cochrane Library, PubMed, PEDro, Science Direct, SciELO, Google Scholar. The search strategy used the terms "*acupuncture*", "*electroacupuncture*" "*carpal tunnel syndrome*". The inclusion criteria limited studies to English publications. The risk of bias was assessed for each study using the Cochrane scale. The level of evidence and the level of recommendation was determined using the SIGN scale. **Results** The search retrieved 698 articles in total. After applying the inclusion and exclusion criteria, 21 articles were included. The level of evidence of all the articles was neutral, with a tendency towards low bias. The articles included revealed symptomatic and neurophysiological improvements, both peripheral as well as central, due to the cerebral response that occurs associated with the function of the median nerve. **Conclusion** Acupuncture and electroacupuncture are a therapeutic option for mild to

moderate CTS with a medium level of scientific evidence, tending towards a high level,

and with a medium level of recommendation.

### **Keywords**

- magnetic resonance
- median nerve
- neurography
- neuronal plasticity
- ► pain

## Introduction

Carpal tunnel syndrome (CTS) is a neuropathy caused by the compression and traction of the median nerve in the carpal tunnel, delimited by the carpal bones and the transverse carpal ligament.<sup>1</sup> The clinical symptoms of CTS are syndromic, including paresthesia and nocturnal pain, normally related with poor positioning of the radius.<sup>2</sup> This syndrome is very common (4–5% of the general population), especially in people between 40–60 years old. Furthermore, it is more frequent in women (9.2%) than in men (6%).<sup>2–4</sup>

received November 1, 2019 accepted November 22, 2019 DOI https://doi.org/ 10.1055/s-0040-1701432. ISSN 2386-4591. The carpal tunnel is an osteofibrous outlet between the flexor retinaculum and the carpal bones. The roof of this tunnel is the fibrose carpal ligament, located deep in the intermediate region of the flexor retinaculum. In this space, nine tendons are found with their sheath and the median nerve. The nerve enters the tunnel in the midline or slightly radial to the same.<sup>5</sup> The median nerve has sensory branches to supply the three radial digits and the radial half of the fourth finger, as well as the palmar cutaneous sensory branches, which innervate the skin of the palm,<sup>6</sup> and the recurrent thenar branch. The sensitive area of the median

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nerve comprises the palmar aspect of the three radial fingers, and the radial half of the fourth finger, the dorsal aspect of the last two phalanges of the three first fingers, and the external half of the fourth finger. The motor branch passes by the distal aspect of the ligament, although in 20% of cases it is transligamentary, and because of this anatomic variant, an isolated compression exits at the level of the ligamentous outlet. The motor branch innervates the abductor pollicis brevis and the first lumbrical muscles.

Anatomically, two points of compression exist for the median nerve, one at the proximal border of the carpal tunnel, caused by wrist flexion and due to the change of thickness and stiffness between the forearm fascia and the proximal portion of the flexor retinaculum, and a second in the narrowest portion of the tunnel, at the level of the hook of the hamate. Pathological changes are thought to occur in the ligaments that surround the nerves, including alterations in the quantity and flexibility of the connective tissue as the source of the increase in pressure. This increase in pressure of the carpal tunnel causes the ischemic compression of the median nerve.<sup>7</sup> In CTS, the nocturnal increase in pressure at the level of the tunnel may be due to several factors, such as the redistribution of fluids of the upper limbs in supine position, the lack of muscle pumping mechanisms which contribute towards draining the interstitial liquid in the carpal tunnel, the tendency to place the wrist in flexion, increasing pressure within the canal, an increased blood pressure during the second half of the night, and a drop in the level of cortisol.<sup>8</sup>

Median nerve entrapment can cause disorders of intraneural microcirculation, and injuries to the myelin sheath and the axon (altered function and dysfunction or damage from the point of compression in the distal direction).<sup>6</sup> Additionally, there may be decomposition of the hematoencephalic barrier of the median nerve, formed by perineural cells and endothelial cells of endoneural capillaries.<sup>5</sup> Together, these events can provoke an increased pressure of the endoneural liquid and the development of an intrafascicular edema,<sup>9</sup> provoking an early impairment of the perineural and endoneural microcirculation, with fibrosis and secondary axonal demyelination. Demyelination is responsible for blocking the nerve transmission (neuropraxia) recorded under electromyography, and, if the compression persists, it can lead to Wallerian degeneration.<sup>1</sup> The rapid development of edema with epineural predominance leads to the inflammation of the nerve, limiting its ability to slide during movements. In response to this injury, there is an increased density of fibroblasts, of the size of the collagen fibers, an increase of type-III collagen, and vascular proliferation in the subsynovial connective tissue.<sup>10</sup> This scar tissue is formed around the median nerve,<sup>11</sup> which, in turn, contributes to the nerve entrapment.

Treatment of CTS may be conservative or surgical. Conservative treatment may be active or passive. Passive treatments are based on the use of a wrist splint and infiltration of corticosteroids. Immobilization of the wrist in a neutral position of 0° of extension can provide symptom relief.<sup>12</sup> Furthermore, infiltration with corticosteroids is indicated in patients with mild to moderate clinical symptoms, offering a marked relief mainly for pain.<sup>13,14</sup> Active treatments are applied to patients with mild and moderate symptoms, and they include physical therapy, thermotherapy, electro-therapy, ultrasound therapy, laser, magnetotherapy, and manual techniques of mobilization of the carpal bones.

Acupuncture is reported to modulate the immune response and decrease inflammatory mediators (IL1,2 and FNT) which induce inducible cyclooxygenase (COX2). COX2 has an antiinflammatory effect as it decreases the synthesis of prostaglandins.<sup>15</sup> Furthermore, endogenous opioid activation has been suggested.<sup>16</sup> In addition, electroacupuncture can develop a powerful inhibitory effect upon hyperalgesia in the short term, as well as an anti-inflammatory effect. It appears that the effects of electroacupuncture on hyperalgesia and inflammation can involve both the endocrine system and the nervous system.<sup>17,18</sup> From the endocrine point of view, the participation of the suprarenal system has been suggested, therefore, producing an anti-inflammatory effect.<sup>19,20</sup> In addition, at the spinal level, electroacupuncture inhibits the expression of Fos (transcription factor)<sup>19,20</sup> as well as inducing an increased expression of opioid receptors mu and delta.<sup>21,22</sup>

In the treatment of CTS, acupuncture is an easily accessed resource, with a low cost and without secondary effects, especially compared to more conventional treatments, such as infiltration of corticosteroids or surgical intervention. Thus, the aim of this systematic review was to evaluate the published evidence on the use of acupuncture for the treatment of CTS, and to assess the effectiveness of this treatment approach to therefore validate its use.

## Methods

This systematic review has followed the criteria of the PRISMA declaration.

Selection criteria. The search was limited to:

- Case series, case studies, clinical trials, case-control studies, randomized controlled trials.
- Publications in English.
- Subjects with a medical diagnosis of carpal tunnel syndrome.
- Studies in which the intervention/therapy is acupuncture in carpal tunnel syndrome.

Studies which did not fulfill the previously described requisites were excluded, together with systematic reviews, as the aims of these were different to that of the present review.

**Search strategy.** A literature search was performed in the following databases: Cochrane Library, PubMed, Clinical Evidence BMJ, NICE, PEDro, Science Direct, SciELO, and Google Scholar. The last search was performed on April 21, 2019.

The search strategy used was based on the terms "*acupuncture*" and "*electroacupuncture*" and "*carpal tunnel syndrome*" as the key word related to CTS, to locate articles within the objectives of the review. Subsequently, the articles were selected according to eligibility criteria. Finally, systematic reviews were excluded. In all of the databases, the following terms were used: (*acupuncture*[MeSH Terms] OR acupuncture[All Fields] OR acupuncture therapy[MeSH Terms] OR (acupuncture[All Fields] AND therapy[All Fields]) OR acupuncture therapy[All Fields]) AND (carpal tunnel syndrome[MeSH Terms] OR (carpal[All Fields] AND tunnel [All Fields] AND syndrome[All Fields]) OR carpal tunnel syndrome[All Fields]) AND (electroacupuncture[MeSH Terms] OR electroacupuncture[All Fields]) AND (carpal tunnel syndrome[MeSH Terms] OR (carpal[All Fields]) AND tunnel [All Fields] AND syndrome[All Fields]) OR carpal tunnel syndrome[MeSH Terms] OR (carpal[All Fields] AND tunnel [All Fields] AND syndrome[All Fields]) OR carpal tunnel syndrome[All Fields]).

**Study selection.** After performing the database search and downloading the total results, firstly, the title and abstract of all articles were read to exclude the articles which failed to fulfill the previously described eligibility criteria. Thereafter, records which were duplicated among the different databases were removed. The resulting articles were then read in-depth, to determine whether they fulfilled the eligibility criteria and to further screen those to be used for the data analysis. Subsequently, the selected studies were analytically read for data collection. A results table was created to determine the inclusion and exclusion criteria according to the specified eligibility criteria.

**Risk of bias of individual studies.** – **Table 1** displays the risk of bias of each study, using the bias risk scale by Cochrane.

**Level of evidence and degree of recommendation.** The level of evidence and the degree of recommendation of each individual study is shown in **-Table 2**, based on the scale proposed by the Scottish Intercollegiate Guidelines Network (SIGN).

**Synthesis of the results.** To unify the results of the selected studies for the performance of the systematic review, a table was created, (**Table 3**) featuring the study results, based on eight items: author and year, design, subjects and stage of illness, intervention, duration or follow-up, outcome measures, relevant findings, conclusions or commentaries. The results were then analyzed and interpreted as presented in the discussion.

## Results

The aim of this review was to demonstrate the scientific evidence of the effects of acupuncture and electroacupuncture on the evolution and treatment of CTS.

Eight databases were consulted in this review, retrieving 698 articles, of which 20 were from the Clinical Evidence BMJ search engine, 45 were from NICE, 3 were retrieved from the Cochrane Library, 59 were from PubMed, 25 were from PEDro, 437 were from Science Direct, 1 was from SciELO, and, 108 were retrieved from Google Scholar.

Article	ltem 1	ltem 2	Item 3	ltem 4	Item 5	ltem 6	ltem 7
Schulman et al, 2008 <sup>23</sup>	(-)	(-)	(-)	(-)	(-)	(+)	(-)
Shokunbi, 2014 <sup>24</sup>	(-)	(-)	(-)	(-)	(-)	(-)	(-)
Napadow et al, 2004 <sup>25</sup>	(-)	(-)	(-)	(+)	(+)	(+)	(+)
Zailaa, 2010 <sup>26</sup>	(+)	(+)	(-)	(+)	(+)	(+)	(+)
Ding and Shen, 2013 <sup>27</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Wong et al, 2016 <sup>28</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Dimitrova et al, 2019 <sup>29</sup>	(+)	(+)	(-)	(+)	(+)	(+)	(-)
Chen et al, 2017 <sup>30</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Ural and Öztürk, 2017 <sup>31</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Maeda et al, 2017. <sup>32</sup>	(-)	(-)	(-)	(+)	(+)	(+)	(+)
Hadianfard et al, 2015 <sup>33</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Maeda et al, 2013a <sup>34</sup>	(+)	(+)	(-)	(+)	(-)	(+)	(-)
Ho et al, 2014 <sup>35</sup>	(-)	(-)	(-)	(+)	(+)	(+)	(-)
Maeda et al, 2013b <sup>36</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(-)
Khosrawi et al, 2012 <sup>37</sup>	(+)	(+)	(-)	(-)	(-)	(+)	(+)
Kumnerddee and Kaewtong, 2010 <sup>38</sup>	(+)	(+)	(-)	(-)	(+)	(+)	(+)
Yang et al, 2011 <sup>39</sup>	(+)	(+)	(-)	(-)	(-)	(+)	(-)
Yang et al, 2009 <sup>40</sup>	(+)	(+)	(-)	(-)	(-)	(+)	(-)
Napadow et al, 2007a <sup>41</sup>	(+)	(+)	(+)	(-)	(+)	(+)	(-)
Napadow et al., 2007b <sup>42</sup>	(+)	(+)	(+)	(-)	(+)	(+)	(-)
Yao et al, 2012 <sup>43</sup>	(+)	(+)	(-)	(+)	(+)	(-)	(-)

Table 1 Evaluation of risk of bias of individual studies. Analysis of risk of bias of the studies included, using the COCHRANE tool

Notes: (+), low bias; (-), high bias. Item 1: generation of the random sequence. Item 2: concealed allocation. Item 3: type of blinding of participants and researchers. Item 4: type of blinding of evaluators. Item 5: follow-up and conclusions. Item 6: selective report of results. Item 7: other biases.

Database	Reference	Number of patients	Level of evidence	Level of recommendation
Google Scholar	Schulman et al, 2008 <sup>23</sup>	17	3	D
	Shokunbi, 2014 <sup>24</sup>	3	3	D
	Napadow, et al, 2004 <sup>25</sup>	11	2+	С
	Zailaa, 2010 <sup>26</sup>	22	2++	В
	Ding and Shen, 2013 <sup>27</sup>	38	2–	С
ScienceDirect	Wong et al., 2016 <sup>28</sup>	181	2+	С
PubMed	Dimitrova et al, 2019 <sup>29</sup>	60	2++	В
	Chen et al, 2017 <sup>30</sup>	60	2+	С
	Ural and Öztürk, 2017 <sup>31</sup>	27	2+	С
	Maeda et al, 2017 <sup>32</sup>	80	2+	С
	Hadianfard et al, 2015 <sup>33</sup>	50	2+	С
	Maeda et al, 2013a <sup>34</sup>	67	2++	В
	Ho et al, 2014 <sup>35</sup>	26	2+	С
	Maeda et al, 2013b <sup>36</sup>	59	2++	В
	Khosrawi et al, 2012 <sup>37</sup>	72	2+	С
	Kumnerddee and Kaewtong, 2010 <sup>38</sup>	61	2+	С
	Yang et al, 2011 <sup>39</sup>	77	2+	С
	Yang et al, 2009 <sup>40</sup>	77	2+	С
	Napadow et al, 2007 <sup>41</sup>	25	2++	В
	Napadow et al, 2006 <sup>42</sup>	25	2++	В
	Yao et al, 2012 <sup>43</sup>	41	2+	С

#### Table 2 Level of evidence

Legend: 1++ (meta-analysis of high quality, systematic review of clinical trials or high quality clinical trials with very low risk of bias), 1+ (well performed meta-analyses, systematic reviews of clinical trials or well performed clinical trials with a low risk of bias), 1- (meta-analysis, systematic reviews of clinical trials or clinical trials with a high risk of bias), 2++ (high quality systematic reviews of cohort studies or of cases and controls. Cohort studies or of cases and controls with a very low risk of bias and a high probability of establishing a causal relationship), 2+ (cohort or case and control studies which are well performed with low risk of bias and with a moderate probability of establishing a causal relation), 2- (cohort or case and control studies with a high risk of bias and a significant risk for a non-causal relation), 3 (non-analytic studies, such as case reports and case series), 4 (expert opinion), A (at least one meta-analysis, systematic review or clinical trial classified as 1+ and directly applicable to the target population of the guide; or a volume of scientific evidence comprised of studies classified as 1+ and with large consistence among them), B (a volume of scientific evidence extrapolated from studies classified as 1+ or 1+), C (a volume of scientific evidence comprised of studies classified as 2++, directly applicable to the target population of the guide and which demonstrate a great consistency among them; or scientific evidence extrapolated from studies classified as 2++, P (level 3 or 4 scientific evidence; or scientific evidence extrapolated from studies classified as 2++), P (recommended practice based on clinical experience and consensus of the research team).

As shown on **► Figure 1**, in a first analysis, 622 articles were discarded by their title and abstract, failing to fulfill the inclusion criteria for this review, because of different aims or treatments. Of the 76 remaining studies, 39 were discarded (34 were duplicated in several databases, and 5 were discarded as these were systematic reviews). Of the 37 remaining articles selected, after an in-depth reading, 16 papers were discarded for the following reasons: 7 performed the study together with other therapies or drugs, 5 because of stimulation of the acupuncture point or the needle with other techniques that do not concern this study (laser, moxibustion, acupressure, cupping therapy), 3 did not fulfill the study aims because of performing other analyses, 1 performed the treatment by medical decision external to the study. Finally, 21 articles were selected for inclusion in this systematic review. The selected studies are analyzed in ► Table 3.

► Table 2 shows that the level of evidence is medium with a tendency to be high and the level of recommendation is medium. Regarding the individual bias of the articles gathered in this systematic review (►Table 1; ►Figure 2), in general, there is a risk of neutral bias, with a tendency for low bias. To a large extent, this validates the results obtained in this study.

Of the articles gathered in this review, over 95% report favorable changes in response to the intervention with acupuncture and electroacupuncture, showing improvements in CTS (-**Table 3**).<sup>23-42</sup> The only study introduced which did not show favorable changes was the study by Yao et al (-**Table 3**).<sup>43</sup> These authors found that the group receiving intervention with acupuncture improved at 3 months in an identical manner to the placebo group. Several studies<sup>27,28,32,36,43</sup> show that changes experienced by subjects via the application of acupuncture and electroacupuncture are maintained during long

<b>Table 3</b> Analysis of results, key concepts and brief description of the arti-
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Author, year	Type of study	Number (N) of subjects and stage of evolu- tion	Intervention	Duration of follow-up	Outcome mea- sures	Relevant results	Conclusion
Schulman et al, 2008 <sup>23</sup>	Case series	N = 17. Nerve conduction im- pairment: mild, moderate and severe.	Needling for 20 minutes with electrical stimulation at 4 Hz.	(-)	Patient verbaliza- tion regarding the res- olution of symp- toms: complete, partial or without resolution.	Of 14 patients treated with acupuncture, 12 reported a partial or complete resolution of symptoms, and 2 did not obtain a resolution of symptoms.	Early intervention for CTS in patients with mild to mod- erate impairment provides better results than those of advanced cases.
Shokunbi 2014 <sup>24</sup>	Case study	3 subjects with over 3 months of evolution and refractory to other non-surgical treatments.	16 sessions of acupuncture lasting 30 minutes, twice a week during 8 weeks. Needling and ergonomic changes at work.	8 weeks.	SSS test at base- line and 8 weeks after.	SSS test: improve- ment. The symp- toms of waking up in the middle of the night were eliminated. Reduc- tion of the intensity of pain: 80% in 2 cases. Re- duction of 50% of: paresthesia, numbness, and weakness.	Acupuncture treatment with er- gonomic work- place changes improves the sub- jective symptoms of CTS.
Napadow et al, 2004 <sup>25</sup>	Case-control study	N = 11 subjects with positive mild to moder- ate CTS. Intervention group, N = 6; control group, N = 5.	5-week acu- puncture protocol.	Assessment before the session, at 2 weeks and after 5 weeks.	Nerve conduction somatosensory evoked potential, and functional magnetic reso- nance before, dur- ing and after treatment. Boston questionnaire. Physical exam Phalen test, Tinel sign, and grip strength.	Functional mag- netic resonance: activation of the postcentral gyrus of the con- tralateral fingers. For patients with CTS, activation af- ter 5 weeks of acu- puncture changed more for the 2nd and 3rd fingers than for the 5th finger. Boston questionnaire: de- creasing the mean severity of the neuropathic symp- toms of CTS.	CTS improved with acupuncture. Real acupuncture was superior to simulated acu- puncture in pe- ripheral and cerebral neuro- physiology. Func- tional magnetic resonance can be used to monitor the cortical acti- vation associated with a chronic neuropathy due to entrapment.
Zailaa, 2010 <sup>26</sup>	Case-control study	N = 22 subjects with documented history of CTS, assessed using magnetic resonance.	Application of a small dose of neutral liquid on acupuncture points.	The following six hours after the intervention with functional magnetic resonance assessment.	Structural images of the wrist in high resolution 4T of the median nerve. Grouped function- al magnetic resonance data, BOLD-contrast im- aging response.	All of the subjects reported a moder- ate sensation of electric tingling. Functional reso- nance; no signifi- cant BOLD- contrast imaging response was found to the stimulations on both points. Medi- an nerve without structural changes.	Statistically signif- icant reduction in the intensity of the signal and the inflammation within the median nerve after acupuncture.
Ding and Shen, 2013 <sup>27</sup>	Randomized controlled trial	N = 38 Inter- vention group: N = 19 Control group.	Group C: moxibustion performed on the Yangchi point. Group I: electric acu- puncture on the Yangchi point.	3 months.	VAS assessments, SSS before and af- ter treatment	VAS, SSS assess- ments: improve- ments compared to the same group before treatment in favor of the acu- puncture group. 3 months later: the VAS scores did not show differences between both groups; the SSS scores showed dif- ferences for the	Acupuncture improves pain, numbness and motor activity in patients with CTS.

(Continued)

Author, year	Type of study	Number (N) of subjects and stage of evolu- tion	Intervention	Duration of follow-up	Outcome mea- sures	Relevant results	Conclusion
						acupuncture group.	
Wong et al, 2016 <sup>28</sup>	Randomized controlled trial	N = 181. Elec- troacupuncture + nocturnal splinting: N = 90. Control group: N = 91; only nocturnal splinting.	Electroacu- puncture (10–20 mA, 20–40 Hz, continuous wave) on the affected side in 20-minute sessions dur- ing 17 weeks, with a total of 13 sessions.	17 weeks.	Boston question- naire; DASH ques- tionnaire. Pain intensity, strength, fingertip pinch measured with a dynamometer of therapeutic pinch; Sensation of pain; Semmes-Wein- stein monofila- ment examina- tion; Dexterity; Moberg pick-up test (modified by Dellon).	Boston and DASH questionnaires: improvement. For pain intensity: re- duction of pain. Dexterity, strength and sensation of pain: greater pro- portion of patients with improvement.	Electroacupunc- ture improves the symptoms of the disability function, dexterity and strength in a 17- week assessment, in combination with nocturnal splinting.
Dimitrova et al, 2019 <sup>29</sup>	Mechanical pilot study	N = 60. Mild to moderate CTS based on EMG. Group 1: manu- al acupuncture. Group 2: low frequency elec- troacupunc- ture. Group 3: high frequency elec- troacupunc- ture.	Needling on points of the pericardial nerve and heart associat- ed with the median and ul- nar nerves re- spectively. Two treatments: acupuncture on the median nerve-pericar- dium meridian and ulnar nerve-heart meridian, with one week in between.	2 weeks.	Assessment of sensory nerve conduction and qualitative senso- ry test (assess- ment of cold and vibration threshold); postin- tervention in the median and ulnar nerve compared to preintervention measures.	Group 1: improve- ment of the threshold for de- tection of cold in the median nerve, but not in the healthy ulnar nerve. Group 2: recovery of action potentials of the sensory median nerve. Group 3: improvement of the sensation of cold of the median nerve and vibration with increased conduction veloci- ty of the sensory and motor median nerves.	Acupuncture has a specific effect on the me- dian and ulnar nerves of the forearm, which can be measured with a nerve conduction test and quantitative sensory test.
Chen et al, 2017 <sup>30</sup>	Case-control study	N = 60 subjects with mild to moderate CTS. Control group: N = 30; Case group: N = 30.	Case group: needling on the contralat- eral side and then needling on the affect- ed side. Con- trol group: acupuncture on the points of the affect- ed side. 10- day treat- ment, with acupuncture once a day for 30 minutes.	10 days.	3 sessions. Electrophysiology of the median nerve. CTS ques- tionnaire by Lev- ine. Wrist assessment classi- fied by the patients.	Effectiveness of 90% in the observation group, and of 70% in the control group. The velocity of the sensory conduc- tion and the am- plitude of the median nerve in- creased in both groups.	The combined treatment with the technique of homo and contra- lateral acupunc- ture achieves therapeutic effects in cases of mild to moderate CTS, which are superior to those of the regular needling technique.
Ural and Öztürk, 2017 <sup>31</sup>	Case-control study	N = 27 women diagnosed with CTS by EMG. Control group: treatment with nocturnal splinting. Case group: treat- ment with nocturnal splinting plus acupuncture.	Acupuncture was per- formed during 10 sessions lasting 25 minutes each; 2 or 3 sessions per week.	4 weeks	Visual scale for the severity of the symptoms. Dur- uoz Hand Index and DASH ques- tionnaire for hand function and dis- ability. Electro- physiology: mus- cle action potential, speed of motor and sensory nerve conduction.	All of the param- eters improved in both groups. The diameter of the median nerve de- creased in the acu- puncture group. The changes were greater in the acu- puncture group than in the control group.	The diameter of the median nerve decreased after treatment with acupuncture, as well as the severity of the symptoms, the functions of the hand and the electromyograph- ic measurements, which were more significant in the

Author, year	Type of study	Number (N) of subjects and stage of evolu- tion	Intervention	Duration of follow-up	Outcome mea- sures	Relevant results	Conclusion
					distal motor la- tency. Ultrasound: diam- eter of the median nerve.		acupuncture group.
Maeda et al, 2017 <sup>32</sup>	Randomized clinical trial	N = 80: group of real local electroacupunc- ture on the af- fected hand; group of real electroacupunc- ture distal in the ankle contrale- sional to the af- fected hand; and group of simulated elec- troacupuncture with a non-pen- etrating sham needle.	The 3 groups underwent 16 sessions of electroacu- puncture dur- ing 8 weeks.	3 months.	Boston question- naire: scoring of pain and pares- thesia at the be- ginning of the study, after treat- ment, and during the 3 months of follow-up. Deter- mination of the sensory latency of the nerve. Func- tional magnetic resonance of the somatosensory cortex at the be- ginning of the study and after therapy.	The three groups displayed an im- provement in the severity of symp- toms. Neurophysi- ology: real local and distal electro- acupuncture was superior to simu- lated electroacu- puncture. The greatest improve- ment in the dis- tance of cortical separation oc- curred between digits 2 and 3 in real elec- troacupuncture at 3 months of follow- up.	Acupuncture on local sites versus distal sites can improve the func- tion of the median nerve at the wrist by somatotopic neuroplasticity, different at the level of the prima- ry somatosensory cortex after therapy.
Hadianfard et al, 2015 <sup>33</sup>	Case-control study	N = 50 subjects with mild to moderate CTS. Ibuprofen group, N = 25. Acupuncture group, N = 25.	Both groups were submit- ted to noctur- nal splinting. Acupuncture group: 8 ses- sions for 20 minutes twice a week during 4 weeks. The Ibuprofen group received 400 mg of ibu- profen 3 times a day during 10 days.	1 month	VAS score, Boston questionnaire, BCQT FUNCT and BCQT SYMPT. Electrophysiology at the beginning and end of the treatment.	Significant improve- ments in both groups with greater significance in the acupuncture group. The scores on the BCTQ, FUNCT, global SYMPT, VAS, and electrophysio- logical findings were superior in the acu- puncture group compared with the ibuprofen group.	Acupuncture could be an effective treat- ment for CTS.
Maeda et al, 2013a <sup>34</sup>	Case-control study	N = 67. CTS group, N = 37; group of healthy sub- jects N = 30.	Electroacu- puncture at 2 Hz on the affected wrist and dominant hand in healthy sub- jects. Distal acupuncture on the contra- lateral leg in relation to the most affected hand with CTS or dominant in healthy subjects.	(-)	Data of structural image via weight- ed pulse sequence of multiple captures.	The brain response in both groups and acupuncture points included the activation of the contralesional so- matosensory cor- tex. Difference be- tween points of local and distal acupuncture for healthy subjects, but not for subjects with CTS. No correlation was found between distal acupuncture points for any of the groups.	The brain re- sponse to electro- acupuncture dif- fers among subjects with CTS and healthy sub- jects for the local stimulation of the acupuncture point.
Ho et al, 2014 <sup>35</sup>	Case-control study	N = 26. Acu- puncture group, $N = 15$ ; electroacupunc- ture group, N = 11.	24 sessions of acupuncture for 15 minutes during 6 weeks.	6 weeks.	Short clinical questionnaire by LO and Chiang; electrophysiologi- cal	Improved scores for symptoms after treatment with electroacupunc- ture.	Electroacupunc- ture can improve symptoms.

(Continued)

Author, year	Type of study	Number (N) of subjects and stage of evolu- tion	Intervention	Duration of follow-up	Outcome mea- sures	Relevant results	Conclusion
					assessment; Tinel sign.		
Khosrawi et al, 2012 <sup>36</sup>	Case-control study	N = 72. Control group (N = 32): nocturnal splinting, vita- mins B1 and B6; Case group (N = 32): acupuncture.	Control group: inter- vention with nocturnal splinting, vitamin B1 and B6 and simulated acupuncture during 5 weeks. Case group: 8 ses- sions of acu- puncture and nocturnal splinting during 4 weeks.	4 weeks.	Global score of clinical symptoms; SSS; electrophysi- ology.	Case group: im- provement in the SSS and electrophysiology.	Acupuncture improves the symptoms of CTS.
Kumnerddee et al, 2010 <sup>38</sup>	Randomized clinical trial	N = 61 subjects with mild to moderate CTS. Acupuncture group; noctur- nal splinting group.	Acupuncture group: 10 sessions of electroacu- puncture twice a week; nocturnal splinting group: neutral wrist splint worn each night.	5 weeks.	BCTQ, SSS, FSS, VAS.	VAS score: de- creased in the acupuncture group compared with the nocturnal splint- ing. There were no differences in the SSS and FSS be- tween the groups.	Electroacupunc- ture reduced pain more than noctur- nal splinting in cases of mild and moderate CTS.
Yang et al, 2011 <sup>39</sup>	Randomized controlled trial	N = 77. Mild to moderate idio- pathic CTS con- firmed with electrophysiolo- gy. Prednisone group, n = 39; acupuncture group, n = 38.	Prednisone group: 2 weeks with 20 mg of prednisone a day followed by 2 weeks of 10 mg of prednisone a day during 4 weeks; acu- puncture group: 8 ses- sions during 4 weeks.	13 months.	Follow-up at 7 and 13 months using the assessment of global symptoms, SSS, repeated nerve conduction tests.	Acupuncture group compared to the prednisone group: improve- ment in SSS, distal motor latencies and distal sensory latencies. A significant corre- lation was observed between the SSS changed from month 13 to the baseline and all of the electrophys- iological param- eters, except the amplitude of the composed muscle action potential	Treatment with acupuncture in the short term improves mild to moderate idio- pathic CTS in the long term.
Yang et al, 2009 <sup>40</sup>	Randomized controlled trial	N = 77. Patients with mild to moderate idio- pathic CTS di- agnosed with studies of nerve conduction. Acupuncture group: N = 38; prednisone group: N = 39.	Acupuncture group: 8 sessions during 4 weeks. Prednisone group: 20 mg a day during 2 weeks, and 10 mg a day during the 2 following weeks.	4 weeks.	SSS questionnaire on weeks 2 and 4. Neurophysiology at the end of the study.	SSS: a high per- centage of improvement in both groups; how- ever, without dif- ferences between both groups. The acupuncture group compared to the prednisone group: decrease in distal motor latency in week 4.	Treatment with acupuncture in the short term is as effective as prednisone in the short term for the treatment of mild to moderate CTS.
Napadow et al, 2007a <sup>41</sup>	Case-control study	N = 25. CTS group: $N = 13$ ; Group of	Electroacu- puncture dur- ing	5 weeks.	Functional mag- netic resonance.	Real acupuncture activates the hypo- thalamus and	Patients with chronic pain respond to

Author, year	Type of study	Number (N) of subjects and stage of evolu- tion	Intervention	Duration of follow-up	Outcome mea- sures	Relevant results	Conclusion
		healthy subjects: N = 12.	10 minutes at 2 Hz. Treat- ment 3 times ar week dur- ing 3 weeks and 2 times a week during the last 2 weeks. Elec- troacupunc- ture in patients with CTS in the affected hand. Electro- acupuncture in the domi- nant hand in healthy subjects.			deactivates the amygdala. Acu- puncture inversely activates the hypo- thalamus and the amygdala. The hy- pothalamus re- sponse was positively correlat- ed with the level of adapted cortical plasticity in patients with CTS.	acupuncture in a different way compared to healthy subjects via the limbic sys- tem, which includes the hypothalamus and the amygdala.
Napadow et al, 2007b <sup>42</sup>	Case-control study	N = 25. CTS group: N = 13; group of healthy sub- jects: N = 12.	Sensory stim- ulation during the imaging test. Electroa- cupuncture at 2 Hz during 10 minutes, 3 times a week, for the first three weeks, and twice a week during the remaining 2 weeks.	5 weeks	Functional magnet- ic resonance. Electro- physiology of the ulnar and median nerve. Grip strength, sen- sory threshold test- ing with Semmes- Weisntein monofil- ament examination and Phalen and Tinel tests. CTS test BCTQ.	Acupuncture im- proved all of the subjective and ob- jective measures. Upon functional magnetic reso- nance, it was observed that acu- puncture activated the corti- cal areas of the median nerve, but decreased the acti- vation in the con- tralateral precen- tral and postcentral gyrus, in the prefrontal parietal cortex and the inferior dorso- lateral cortex.	Electroacupunc- ture provokes a stimulus of so- matosensory conditioning.
Yao et al, 2012 <sup>43</sup>	Randomized controlled trial	N = 41. Acu- puncture group: N = 21; simulated acu- puncture (pla- cebo): N = 20.	Noctural splints for both groups. 6 weekly ses- sions of 20 minutes of acupuncture on the affect- ed and con- tralateral side.	3 months	Symptoms and function domains of the self-assess- ment scale of the carpal tunnel CTSAQ. Pinch strength. Com- bined sensory index.	Acupuncture group and placebo group: improve- ment in symptom domain 3 months after the last treatment.	Acupuncture is not a better treat- ment than simu- lated acupuncture when used with the splint for patients with mild to mod- erate CTS.

Abbreviations: BCTQ, Boston carpal tunnel syndrome questionnaire; BCQT FUNCT, functional status score; BCQT SYMPT, and symptom severity score; BOLD, blood-oxygen-level-dependent; CTS, carpal tunnel syndrome; CTSAQ, carpal tunnel syndrome assessment questionnaire; DASH, Disabilities of the Arm Shoulder and Hand questionnaire; EMG, electromyography; FSS, Functional Status Scale; FUNCT, functional status; SSS, Symptom Severity Scale; SYMPT, symptom severity; VAS, Visual Analog Scale. Note: (-), not available.

periods of time after acupuncture, registering benefits up to 12 weeks later.

From the methodological point of view, over 50% of the studies showed improvements that were proven with electrophysiology (**-Table 3**).<sup>25,26,29–37,39,40,42</sup> Hadianfard et al (**-Table 3**).<sup>33</sup> compared treatment with acupuncture and another with ibuprofen, obtaining a decrease of DSL (*distal sensory latency*) in the acupuncture group, whereas

DML (*distal motor latency*) significantly decreased in both groups. Similarly, Yang et al (**-Table 3**)<sup>40</sup> also compared acupuncture treatment with treatment using prednisone and in the group with acupuncture, a decrease in distal motor latency was obtained. Occasionally, electrophysiological studies of nerve conduction were combined with other imaging studies, for example the study by Napadow et al. (**-Table 3**)<sup>25,42</sup> combined electrophysiological methods



Fig. 1 Study selection process. This figure represents the study selection process, including the selection criteria and reasons for exclusion.



**Fig. 2** Graph of risk of bias. Review of the arguments of the authors of the studies included in this systematic review on each item of risk of bias, presented as percentages. Item 1: Generation of the random sequence. Item 2: Concealed allocation. Item 3: Type of blinding of participants and researchers. Item 4: Type of blinding of evaluators. Item 5: Follow-up and exclusions. Item 6: Selective report of results. Item 7: other biases.

(nerve conduction) with functional magnetic resonance, obtaining improved neruophysiological results, both peripheral as well as cerebral after treatment with acupuncture.

Over 25% of the articles included in this review performed a cerebral assessment using functional magnetic resonance, finding changes which underline the interaction of the effect of acupuncture and electroacupuncture in the improvement of symptoms of patients with CTS (**-Table 3**).<sup>25,32,34,36,41,42</sup> In addition, most of these studies also described differences regarding the group of real-simulated acupuncture, localdistal points, symptomatic-asymptomatic side, as well as changes in control subjects at the level of the brain (**-Table 3**).<sup>25,32,34,36,41,42</sup> For example, Maeda et al (**-Table 3**).<sup>32,34</sup> performed a functional magnetic resonance during the intervention, showing that local electroacupuncture produced an activation of brain areas related with pain modulation, both directly and indirectly, and, however, simulated electroacupuncture did not show any response.<sup>32</sup>

## Discussion

Most articles gathered in this review reveal favorable changes in response to acupuncture and electroacupuncture in CTS. Several studies report that the changes experienced by subjects via the application of acupuncture and elecroacupuncture are maintained during long periods of time after receiving acupuncture.

The maintained improvement of symptoms after real acupuncture found in the present systematic review is in line with the results of previous clinical trials<sup>43</sup> that relate this effect with the plasticity of the primary somatosensory cortex (S1).

Moreover, the reduction of the symptoms of CTS has been found to persist during months after the cessation of therapy with acupuncture.<sup>39</sup> These improvements are shown in studies measuring the latency of nerve conduction and cerebral neuroplasticity. It is known that intraneural blood flow is controlled by the sympathetic system;<sup>44</sup> therefore, it has been proposed that acupuncture may be able to modulate the blood flow of the vasa nervorum of the median nerve via antidromic vasodilation after stimulation of the dorsal spinal roots. Furthermore, using neuroimaging techniques, the S1 has been shown to be a part of the cerebral regions that regulate the outflow of the sympathetic system,<sup>45</sup> providing feedback to the process. A recent study in patients with chronic pain found an increased connectivity of the S1 and the cortex of the anterior/middle insula that was associated with reduced cardiovagal modulation.<sup>46</sup> On the peripheral level, this vascular effect could be mediated by the calcitonin gene-related peptide (CGRP).47,48 Ultrasound has been used to explore the vascularization of the median nerve trapped in the CTS,49,50 observing hypervascularization. This particular vascular situation has been interpreted as a compensatory response to ischemia within the tunnel. This compensation can be due to the decrease in the peripheral afferent, which triggers an increased central processing; therefore, the brain tries to compensate the slower signaling in the periphery by amplifying the signal in regions of somatosensory cerebral processing. A greater activation of the S1 cortex has been described and visualized using magnetic resonance<sup>51</sup> functional or contralateral electrophysiological amplification<sup>52</sup> after stimulation of the side affected by CTS, which confirms this hypothesis. In addition, it is known that the activity of the S1 cortex reflects discriminatory sensory information, such as the intensity of the sensation.53,54

In several of the assessed studies simulated acupuncture was performed as a placebo in the control group. This indeed is a controversial subject. A previous systematic review affirmed that the evidence of the benefits of acupuncture in the treatment of CTS was unsatisfactory due to the poor method-ological quality of the study.<sup>55</sup> In other words, simulated

procedures are not physiologically inert.<sup>56,57</sup> Indeed, simulated acupuncture has been observed to reduce aversive symptoms more easily than a placebo pill.<sup>58</sup> Interestingly, analgesia can be obtained with both real and simulated electroacupuncture. The brain mechanisms that support this analgesia can differ substantially. One study by Maeda et al,<sup>36</sup> for example, described that the brain response in the combined-acupuncture group was more intense than that of the simulatedacupuncture group. The authors described an activity in specific brain regions in response to combined electroacupuncture that may be related to the reduction of pain. One study<sup>59</sup> also found that this cerebral response is also proposed as an objective marker to discriminate simulated acupuncture from real acupuncture in a more reliable manner than the subjective pain reports made by the patients.

The physiological mechanism of the action of electroacupuncture on CTS pain has also been proposed to occur via the central nervous system.<sup>60,61</sup> Several studies<sup>62,63</sup> demonstrate that electroacupuncture induces a large cerebral response in healthy adults. The study by Maeda et al<sup>36</sup> demonstrated that electroacupuncture was able to deactivate brain areas of the network in limbic mode in patients with CTS and in healthy subjects on a subthreshold level. Thus, this study by Maeda et al<sup>36</sup> differs from previous publications on this subject, possibly because different intensities were used, activation thresholds.

The reduction of pain after real combined electroacupuncture has been related with the activation of the supplementary motor area (SMA). The SMA is a cortical region that modulates the communication between the somatosensory and motor systems, and it has been found to be activated by painful stimulation, as seen on functional magnetic resonance,<sup>64</sup> and it also contributes to pain control.<sup>65</sup> A greater activation after combined electroacupuncture can reflect a greater transfer of somatosensory entrances induced by electroacupuncture to the motor system,<sup>66</sup> promoting a more normalized sensorimotor communication, compared with the sporadic input of diffuse paresthesia. Therefore, electroacupuncture, either local or distal, can also reduce pain by providing a regulated somatosensory entrance to the brain. Therefore, studies<sup>66,67</sup> involving magnetic resonance have demonstrated that treatment with acupuncture can alter the brain activity and regulate the activity of the limbic system in patients with CTS.

## Conclusions

The studies featured in the present systematic review have a medium to high level of evidence, with a neutral to low risk of bias, which, together, largely validate the present work. Most studies evaluated nerve conduction and functional magnetic resonance imaging, demonstrating beneficial effects of acupuncture and electroacupuncture in the evolution of CTS. Thus, acupuncture and electroacupuncture are treatment options for CTS that may provide clinical and neurophysiological improvements (peripheral and cerebral) that may be superior to those obtained through treatment merely based on the use of nocturnal splints and nonsteroidal anti-inflammatory drugs (NSAIDs). **Conflict of Interests** 

The authors have no conflict interests to declare.

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