



# Carpal tunnel syndrome: clinical features, diagnosis, and management

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Carpal tunnel syndrome is the most common peripheral nerve entrapment syndrome worldwide. The clinical symptoms and physical examination findings in patients with this syndrome are recognised widely and various treatments exist, including non-surgical and surgical options. Despite these advantages, there is a paucity of evidence about the best approaches for assessment of carpal tunnel syndrome and to guide treatment decisions. More objective methods for assessment, including electrodiagnostic testing and nerve imaging, provide additional information about the extent of axonal involvement and structural change, but their exact benefit to patients is unknown. Although the best means of integrating clinical, functional, and anatomical information for selecting treatment choices has not yet been identified, patients can be diagnosed quickly and respond well to treatment. The high prevalence of carpal tunnel syndrome, its effects on quality of life, and the cost that disease burden generates to health systems make it important to identify the research priorities that will be resolved in clinical trials.

## Introduction

Entrapment neuropathies are the most frequent mononeuropathies encountered in clinical practice. In these neuropathies, the nerve is damaged at sites where it passes through narrow, restricted spaces.<sup>1</sup> Although entrapment neuropathies affect only a small portion of the nerve, they can have substantial physical, psychological, and economic (eg, loss of earnings) consequences.<sup>2-4</sup> The exact cause of these neuropathies is largely unknown and a multifactorial origin is presumed; in such cases, the entrapment syndromes are defined as idiopathic.

Carpal tunnel syndrome is the most common and widely studied nerve entrapment syndrome.<sup>5</sup> It is caused by compression of the median nerve at the wrist as it passes through a space-limited osteofibrous canal. This canal, known as the carpal tunnel, contains the wrist bones, transverse carpal ligament, median nerve, and digital flexor tendons. Oedema, tendon inflammation, hormonal changes, and manual activity can contribute to increased nerve compression and sometimes cause pain, as in the case of tendon inflammation. In more severe cases, weakness of median nerve innervated muscles can occur, resulting in hand weakness.

The diagnosis and treatment of carpal tunnel syndrome has been approached from different perspectives and with different methods. This variation has occurred because of the high incidence of the syndrome, its tendency to be symptomatic even in mild cases, the availability of sensitive electrophysiological measures, the development of patient-centred measures and novel nerve imaging techniques, and the availability of several therapies ranging from non-surgical to surgical management. In this Review, we will present up-to-date information about carpal tunnel syndrome, focusing on the most common and controversial clinical topics.

## Epidemiology

The reported prevalence and incidence of carpal tunnel syndrome vary widely according to the diagnostic criteria used in different studies. Overall, it is thought that,

clinically, one in ten people develop carpal tunnel syndrome at some point.<sup>6</sup> The use of clinical criteria in diagnosis results in a higher estimate than does the use of electrophysiological criteria (table 1). Even when clinical presentation alone is used to define carpal tunnel syndrome, the choice of broad (history or Phalen's test) or strict (sensory or motor deficits) criteria leads to variability in the prevalence findings.<sup>7-9</sup>

Carpal tunnel syndrome has been reported to affect mostly women (with mean age of diagnosis about 50 years), but these data are based on patients who self-referred to a neurophysiological laboratory or clinic and so are intrinsically biased.<sup>10,11</sup> Results of a postal survey of 3000 individuals randomly selected from the general population register of southern Sweden showed that the prevalence of carpal tunnel syndrome was similar in men and women (male:female ratio 1:1.4). However, prevalence was highest in older women; by age 65–74 years, the prevalence in women was almost four times higher than in men (5.1% vs 1.3%, respectively).<sup>7</sup>

## Risk factors and causes

Suspected risk factors of carpal tunnel syndrome include diabetes mellitus, menopause, hypothyroidism, obesity, arthritis, and pregnancy.<sup>12-15</sup> Because hypothyroidism,<sup>12</sup> menopause,<sup>8,13</sup> and pregnancy<sup>13</sup> are risk factors, there is a strong suspicion that hormonal changes might be causative; however, no evidence exists to support this hypothesis.

Recent research provides evidence in support of established risk factors for carpal tunnel syndrome. A comprehensive meta-analysis<sup>12</sup> focusing on the relation between hypothyroidism and carpal tunnel syndrome showed a modest association, but the investigators concluded that confounding factors (eg, rheumatoid arthritis and overweight) and publication bias might account for part of the increased risk. Pregnancy probably increases the risk of carpal tunnel syndrome by a combination of oedema and hormonal alterations; epidemiological data show that the incidence of

*Lancet Neurol* 2016; 15: 1273–84

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Study	Factor assessed	Prevalence (%) or incidence (per 100 000 person-years)
Atroshi et al (1999) <sup>7</sup>	Population prevalence of pain, numbness, or tingling in the median nerve distribution area	14.4%
Atroshi et al (1999) <sup>7</sup>	Prevalence of median nerve neuropathy	4.9%
Atroshi et al (1999) <sup>7</sup>	Prevalence of clinically and electrophysiologically confirmed carpal tunnel syndrome	2.7%
Mondelli et al (2002) <sup>8</sup>	Standardised incidence	276
Bland et al (2003) <sup>9</sup>	Incidence corrected to the WHO European standard population	180; 120.5 for women and 60.0 for men in east Kent, UK, 61.5 for women and 35.0 for men in Huddersfield, UK

**Table 1: Prevalence and incidence of carpal tunnel syndrome**

pregnancy-related carpal tunnel syndrome is high (7–43% when diagnosed electrophysiologically, and 31–62% when diagnosed on the basis of history and clinical examination findings only). Acute onset with striking symptoms and motor weakness is not infrequent,<sup>16</sup> and symptoms often persist after delivery.<sup>13</sup> Onset of symptoms in the first trimester is associated with impaired quality of life during pregnancy and after delivery, and long-term persistence of symptoms.<sup>13</sup> Strict monitoring is recommended because treatment before delivery can avoid post-partum difficulties in treatment.<sup>13</sup>

Strong evidence supports both type 1 and type 2 diabetes mellitus as risk factors for carpal tunnel syndrome (pooled odds ratio for the association between diabetes and carpal tunnel syndrome or carpal tunnel release 1.97).<sup>14</sup> Similarly, being overweight increases the risk of carpal tunnel syndrome by 1.5 times and obesity increases the risk by two times.<sup>15</sup> However, no evidence exists for a specific mechanism by which diabetes or obesity increase the risk of carpal tunnel syndrome.

The association between computer (keyboard or mouse) use and carpal tunnel syndrome is still controversial. Available evidence suggests that at most, excessive computer use is a minor risk factor, probably resulting from the mechanical stress of the nerve caused by contact with overused surrounding tendons. However, findings from two recent meta-analyses did not show an association between modest computer use and carpal tunnel syndrome, although some work circumstances might be associated with the syndrome.<sup>17,18</sup> So-called occupational carpal tunnel syndrome is beyond the scope of this Review.

Tobacco smoking is a suspected risk factor for development of carpal tunnel syndrome and, over the years, cross-sectional studies have reported an association between current smoking and the syndrome,<sup>19</sup> but investigators of a recent comprehensive meta-analysis<sup>20</sup> reported that there is insufficient evidence to prove an association.

Although suspected because of wrist bone and joint deformity impacting the carpal tunnel space, the association between osteoarthritis and carpal tunnel syndrome is unproven. Results of a randomised controlled trial in a large sample of 192 men and 176 women older than 65 years showed that the prevalence of carpal tunnel

syndrome is similar in patients with and without radiographic findings of basal joint arthritis of the thumb.<sup>21</sup>

### Clinical features

The importance of the clinical presentation of carpal tunnel syndrome is demonstrated by the fact that the long-accepted gold standard for diagnosis is a comprehensive and accurate clinical history, along with the exclusion of other possible causes. The syndrome is characterised first by intermittent, nocturnal paraesthesias and dysaesthesias that increase in frequency and occur during waking hours.<sup>22</sup> Subsequently, loss of sensation develops along with weakness and thenar muscle atrophy later in the disease course, which result from extensive axonal degeneration.<sup>22</sup> This sequence of symptoms is quite typical, rarely occurring in disorders other than carpal tunnel syndrome.

Carpal tunnel syndrome is usually characterised by symptoms in the hand that, in severe cases, can spread proximally to the forearm, upper arm, and sometimes shoulder. When patients with carpal tunnel syndrome are asked specifically where their pain and sensory symptoms are, they usually report that the proximal symptoms are characterised by pain and not by numbness, tingling, or other sensory abnormalities. For many years, sensory diagnostic criteria in the literature were limited to symptoms occurring in the median nerve territory of the hand. Yet, in clinical practice, broader sensory criteria were used, not limiting symptoms to the first three digits but rather including the entire palmar surface. This frequently observed pattern of sensory abnormalities might be secondary to a peripheral or central nervous system mechanism (simultaneous ulnar involvement or central sensitisation, respectively), or both.<sup>23–26</sup> Evidence suggests that symptoms being limited to the first three digits might indicate more severe median nerve involvement (ie, distribution of the symptoms in the area innervated by the median nerve is associated with more severe changes in nerve conduction velocity).<sup>27</sup> Hence, the symptom distribution must be defined as precisely as possible and strongly considered when deciding the treatment strategy and determining prognosis.<sup>23</sup> However, assessment of sensory function is not useful unless performed carefully with specific tools (eg, monofilament or static two-point discrimination).

Although pain is a common symptom in patients presenting with carpal tunnel syndrome in clinical practice, it is not widely studied and is often considered only one of a wide range of symptoms. Pain is not always present, but is an important symptom, and must not be confused with neuropathic sensory abnormalities (eg, paraesthesias, numbness, or tingling) that might also be reported. The presence of chronic pain can modify the cortical hand somatotopy differently from paraesthesias.<sup>24</sup> In a multicentre study of 1123 patients with carpal tunnel syndrome, pain was present in 52% of cases.<sup>22</sup>

Tinel's sign and Phalen's manoeuvre are popular diagnostic tests for carpal tunnel syndrome. Results are deemed positive when symptoms are evoked by percussion of the median nerve at the wrist or by forced compressive wrist posture for 1 min, respectively.<sup>28</sup> Although these tests are widely used because of ease of performance, their sensitivity and specificity are widely debated. Sensitivity ranges from 42% to 85% for Phalen's manoeuvre and from 38% to 100% for Tinel's test; specificity ranges from 54% to 98% and from 55% to 100%, respectively.<sup>28</sup>

The strength of the abductor pollicis brevis muscle can provide useful information about functional impairment caused by carpal tunnel syndrome, but assessment by clinical examination alone is not reliably quantifiable.<sup>29</sup> Hand dynamometry might be a better method than clinical examination, but is not commonly used in clinical practice because of limitations of time and of the need for specialist equipment.<sup>30</sup> Additionally, hand dynamometry requires standardisation and age-adjusted and sex-adjusted normative values to provide meaningful results.<sup>30,31</sup> The best method for assessing hand muscle strength after carpal tunnel surgery is still a matter of debate.<sup>31</sup>

## Diagnosis

If we were to ask physicians what test should be used to diagnose carpal tunnel syndrome, the answer would vary widely, depending on their specialty and clinical experience. As previously mentioned, in both clinical and research settings, clinical assessment is considered the gold standard and, in absence of motor and sensory deficits, taking an accurate history is crucial. Controversies exist regarding the need for confirmatory testing and the role of nerve conduction studies, electromyography, and nerve ultrasonography in treatment decision making. Most of these questions have no definite answer or, more precisely, there is a paucity of evidence to support any particular conclusion.

Electrophysiological assessment (ie, nerve conduction studies) is very sensitive<sup>11</sup> in examining median nerve dysfunction caused by damage to the nerve; these tests can define the degree of demyelination and axonal loss that has occurred.<sup>11</sup> For this reason, when diagnosing carpal tunnel syndrome, it is useful to assess nerve function and quantify the nerve damage, because the

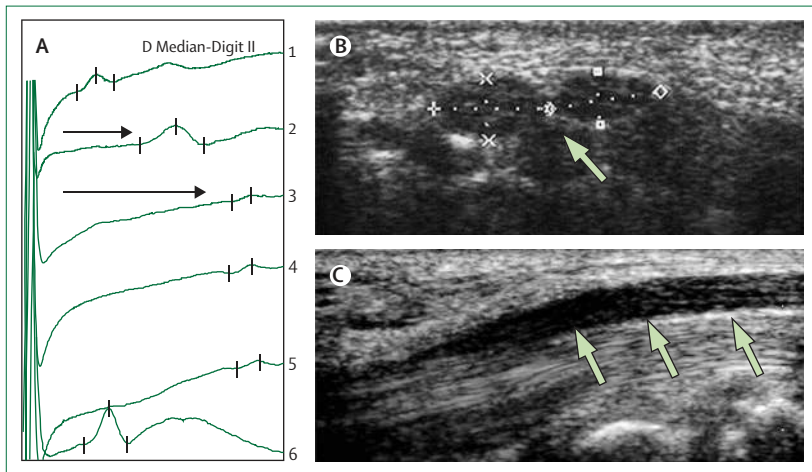
findings could have implications for prognosis. Sensory and motor nerve conduction studies that assess the ability of the nerve to conduct an electrical stimulus are commonly used, whereas needle electromyography is not particularly useful in most patients.<sup>11</sup> Current practice guidelines consider needle electromyography to be an optional test, better suited to exclude concurrent causes of the patient's symptoms (eg, cervical radiculopathy), than for improving diagnostic sensitivity.<sup>11</sup> Needle electromyography can document axonal loss, but this information can often be inferred by assessing abductor pollicis brevis atrophy on clinical examination.<sup>32,33</sup> A decrease in conduction velocity of sensory fibres in the digital segments of the nerve can be detected earlier than in motor fibres or the nerve as a whole.<sup>11</sup> The reasons for earlier involvement of the sensory fibres are unknown.<sup>11</sup>

Since entrapment of the median nerve causes focal slowing of nerve conduction velocity in cases of mild demyelination, the following conditions might reduce the sensitivity of electrophysiological testing: averaging of nerve conduction slowing along the wrist–finger segment (the short length of the involved nerve segment results in an overall normal conduction velocity); inter-individual variability of nerve conduction velocity; and inter-nerve variability that limits the possibility to assess normality or abnormality by comparing different nerves in the same patient. Moreover, since bilateral carpal tunnel syndrome is common, side-to-side electrophysiological (or imaging) comparisons do not increase diagnostic sensitivity.

Extensive work by three US scientific societies (the American Academy of Neurology, the American Association of Electrodiagnostic Medicine [now known as the AANEM], and the American Academy of Physical Medicine and Rehabilitation) have provided physicians with recommendations for electrophysiological testing. These recommendations suggest performing median sensory and motor nerve conduction studies across the wrist and, if these tests are normal, performing comparative, segmental, or comparative and segmental tests, which have been shown to have high sensitivity and specificity (80–90% and >95%, respectively; figure 1).<sup>34</sup> When clinical signs are present, but no electrophysiological abnormalities, then the disease is functionally mild, although there might be severe symptoms.

Validated patient-centred measures (eg, the Boston Carpal Tunnel Syndrome Questionnaire [BCTQ]) are able to quantify symptoms and disability.<sup>22</sup> Level of disability is correlated with both clinical findings and nerve conduction findings.<sup>22</sup>

Recent technical advances, including the development of affordable high-frequency probes, have allowed ultrasonography to reach the resolution required (<1 mm) to be useful in the diagnosis of carpal tunnel syndrome. Ultrasonography is now capable of faithfully reproducing nerves (fascicles, epineurium, and perineurium), and surrounding structures (figure 1). Morphological changes



**Figure 1: Electrophysiological and ultrasound features of carpal tunnel syndrome**  
 (A) Nerve conduction study. 1=radial nerve, first digit to wrist, normal latency of sensory response. 2=median nerve, first digit to wrist, delayed latency of sensory response (small arrow). 3=median nerve, third digit to wrist, very delayed latency and reduced amplitude of sensory response (long arrow). 4 and 5=repeated stimulation to check the reproducibility of sensory response in 3. 6=ulnar nerve, fifth digit to wrist, with normal latency of sensory response. (B) Transverse ultrasound image of bifid median nerve (arrow). (C) Longitudinal ultrasound image of median nerve (arrows). The delayed median nerve sensory response (ie, decreased nerve conduction velocity) indicated involvement of the median nerve but with atypical presentation: much more severe involvement of the third digit compared with the first digit. Ultrasound findings explained the non-uniform involvement, demonstrating a bifid median nerve.

of the median nerve are expected in carpal tunnel syndrome, as the compression of the surrounding non-rigid structures alters its shape. This effect results in a reduction of nerve volume at the site of compression and increased size proximal (and sometimes distal) to the compression. Traditionally, the clinical diagnosis of carpal tunnel syndrome was confirmed with electrophysiological demonstration of decreased focal nerve conduction velocity at the site of entrapment. Now, ultrasonography can show an increased cross-sectional area of the nerve just before it is flattened at the site of compression. A recent meta-analysis<sup>35</sup> concluded that the technique has a sensitivity of 77.6% and a specificity of 86.8% for diagnosis of carpal tunnel syndrome, when clinical presentation is used as the gold standard. Moreover, evidence-based guidelines state that ultrasound measurement of the median nerve cross-sectional area at the wrist probably adds value to electrodiagnosis and might be used as a complementary diagnostic test, which should be considered in screening for structural abnormalities at the wrist (figure 1).<sup>36</sup> Despite promising diagnostic sensitivity and the potential for other applications in the assessment of nerve function, it is not clear whether ultrasonography is a potential alternative to electrophysiology. Methodological discrepancies among a plethora of studies restrict the ability to identify specific diagnostic thresholds for each approach and the two approaches have not been exhaustively tested in a head-to-head study.<sup>37</sup>

An emerging technique for nerve imaging is now available: MRI tractography. This technique can provide

details on morphological damage and inflammation, with early studies showing that fractional anisotropy and the apparent diffusion coefficient agree with the results of nerve conduction studies.<sup>38,39</sup> Although providing excellent imaging capabilities, use of the technique is limited by cost and, as with ultrasonography, research must prove that its added clinical value justifies the cost.

### Differential diagnosis

Few disorders have to be considered in the differential diagnosis of carpal tunnel syndrome. Besides history, neurological assessment, and nerve conduction studies can help to distinguish between carpal tunnel syndrome and these other disorders. Cervical radiculopathy is the primary disorder that might be confused with carpal tunnel syndrome. Cervical radiculopathy is usually characterised by pain in the neck with radiation (often with positive sensory symptoms [eg, paraesthesia or dysaesthesia], sometimes exacerbated by rotation, flexion, or extension of the head) to the upper limb often with typical dermatomal distribution. Reduced or abolished deep tendon reflexes are typical of radiculopathy. Needle electromyography and cervical spine imaging can also be useful in differentiating cervical radiculopathy from carpal tunnel syndrome, if the clinical presentation and history are atypical. Other diseases that must be considered in the differential diagnosis of carpal tunnel syndrome are polyneuropathies, in which symptoms usually affect distal regions of lower limbs, and osteoarthritis, in which pain is the main symptom, and paraesthesias and other neuropathic symptoms are not usually present.

### Non-surgical treatment

Various non-surgical treatments are available for the management of carpal tunnel syndrome (table 2). The first-line management approach should include education of the patient.<sup>40</sup> Changes in habits (eg, limitation of wrist movement and reduction of heavy work activities) should be considered as a first-line approach and the use of ergonomically friendly work tools can be useful in reducing median nerve stress. However, there is little adequate evidence about the success of this approach. For example, the effectiveness of ergonomic keyboards in the treatment of carpal tunnel syndrome is unknown.<sup>41,42</sup> Apart from these interventions, patients should be informed about the standard surgical and non-surgical strategies for treating carpal tunnel syndrome.<sup>40</sup>

### Laser therapy

Low-level or low-power laser therapy, which exposes tissue to low levels of red and near-infrared light (referred to as low level because of the use of light at energy densities lower than that used in other forms of laser for surgical procedures), is one of the non-surgical options for treatment of carpal tunnel syndrome. Different

	Study type	Evidence for use	Comments and recommendations
Patient education	1 systematic review	A guideline reports the usefulness of education <sup>40</sup>	Low cost, high efficacy, and non-invasive; recommended as first-line therapy
Ergonomic tools	2 meta-analyses	Unknown effectiveness <sup>41,42</sup>	These tools might reduce median nerve oedema
Laser therapy	6 RCTs	More effective than placebo, even at 3 months, in some RCTs, <sup>43,44</sup> but other trials did not show laser therapy to be more effective than placebo <sup>45,46</sup> or than TENS, <sup>47</sup> and can have similar effectiveness to magnetic field therapies <sup>48</sup>	Laser therapy seems to be useful for the treatment of carpal tunnel syndrome, but further studies are needed
Local corticosteroid	13 RCTs	Corticosteroid injection was more effective than placebo in an RCT; <sup>49</sup> other RCTs showed that palmar needle insertion was better than wrist needle insertion <sup>50</sup> and ultrasound guidance was very useful; <sup>51-54</sup> phonophoresis seemed to be an effective method of non-invasive corticosteroid administration in two RCTs; <sup>55,56</sup> corticosteroid injection seemed more effective than non-steroidal anti-inflammatory drugs in several RCTs; <sup>57-60</sup> one RCT <sup>61</sup> showed that corticosteroid injection had similar effectiveness to extracorporeal shock wave therapy	Corticosteroid injection, using palmar needle insertion and ultrasound guidance, seems to be useful for the treatment of carpal tunnel syndrome
Palmitoylethanolamide	1 RCT	More effective than placebo in an RCT <sup>62</sup>	Further studies are needed
Gabapentin	1 RCT	No more effective than placebo in an RCT <sup>63</sup>	Further studies are needed
Local lidocaine injection	1 RCT	A single RCT showed symptom reduction and electrophysiological improvement <sup>64</sup>	Further studies are needed
Therapeutic ultrasound	3 RCTs; 2 meta-analyses	RCTs and meta-analyses did not show increased efficacy compared with placebo or other non-surgical therapies, <sup>65-68</sup> but therapeutic ultrasound seemed better than paraffin therapy in an RCT <sup>69</sup>	There is no clear evidence regarding therapeutic ultrasound in the treatment of carpal tunnel syndrome
Splints	4 RCTs; 1 meta-analysis	This technique might reduce oedema <sup>70</sup> and was effective when used for 8 weeks in an RCT; <sup>71</sup> but sufficient evidence does not exist, even when investigated in combination with muscle stretching in a meta-analysis and RCTs <sup>72-74</sup>	Use of splints seems to be useful, but further studies are needed
Musculoskeletal manipulation	2 RCTs; 1 meta-analysis	Madenci massage seems to be more effective than splints, <sup>75</sup> but a meta-analysis concluded that there is limited evidence; <sup>76</sup> tendon gliding exercises seem to be better than median nerve gliding exercises <sup>77</sup>	Massage, exercise, and mobilisation of the wrist joint seem to be useful, but further studies are needed
Linseed oil	1 RCT	A single RCT showed improvements (BCTQ and median nerve conduction velocity) <sup>78</sup>	Further studies are needed
Acupuncture	2 RCTs; 1 systematic review	No differences compared with placebo, <sup>79</sup> but better than prednisolone; <sup>80</sup> however, a systematic review did not demonstrate clear benefit <sup>81</sup>	Encouraging, but not convincing, results regarding acupuncture benefits
<i>Eremostachys laciniata</i> ointment	1 RCT	A single RCT showed improvements in pain and function <sup>82</sup>	Further studies are needed
Interferential current therapy	1 RCT	Improvement in function, symptom severity, and electrophysiological measures compared with TENS and splint use <sup>83</sup>	Further studies are needed
Local microwave hyperthermia	1 RCT	Improvement in pain and function compared with sham therapy <sup>84</sup>	Further studies are needed

RCT=randomised controlled trial. TENS=transcutaneous electrical nerve stimulation.

**Table 2: Non-surgical treatments for carpal tunnel syndrome**

methods of laser therapy exist, so this term encompasses several approaches. Laser therapy is able to improve function, symptoms, and electrophysiological measures in the short term; results of a randomised controlled study showed that laser treatment is more effective than placebo, especially if it is used in patients with mild to moderate disease.<sup>43</sup> In another study, use of the gallium-aluminium-arsenide laser with wrist splint showed higher efficacy than placebo laser therapy with wrist splint, especially in improvement of hand grip strength, even up to 3 months after treatment.<sup>44</sup> Not all studies are in agreement, however; results of another randomised trial<sup>45</sup> showed that laser therapy was no more effective than placebo (in terms of visual analogue scale, grip strength, symptoms severity and functional scores, and median nerve cross-sectional area) in patients with carpal tunnel syndrome; only sensory nerve conduction was improved with laser treatment.

Several studies have compared laser therapy with other non-surgical treatments. In a randomised controlled trial comparing laser therapy with fascial manipulation,

laser therapy provided transient, short-term pain relief, whereas fascial manipulation showed an improvement in pain (by visual analogue scale) and function (by BCTQ), over a longer time period (>3 months).<sup>46</sup> In another study, high-intensity laser therapy was compared with transcutaneous electrical nerve stimulation (TENS), which stimulates large-diameter A sensory fibres; findings showed that laser therapy was more effective than TENS, in terms of pain, paraesthesia, median nerve sensory conduction velocity, and distal motor latency.<sup>47</sup> In a study comparing low-level laser therapy with magnetic field therapies, the effectiveness of the techniques in reducing pain was shown to be similar.<sup>48</sup>

### Pharmacotherapy

Local corticosteroid injections are commonly used to treat carpal tunnel syndrome. The rationale for the use of this treatment is the ability of corticosteroids to reduce oedema, improving the spatial relation between the carpal tunnel and the median nerve and tendons. In a randomised trial of 111 patients,<sup>49</sup> methylprednisolone

(80 mg or 40 mg) injection into the carpal tunnel was more effective than placebo, reducing symptoms severity and rate of surgery at 1 year. However, the effectiveness of corticosteroid injections for halting disease progression was limited, because in this study three-quarters of patients had surgery within 1 year. The preferred site for local corticosteroid injection has been assessed; in a comparison of distal (palmar) needle insertion with proximal (wrist) needle insertion, the palmar approach proved less painful only from the perspective of patients (pain measured by visual analogue scale); no difference was observed in objective measures, such as nerve conduction findings.<sup>50</sup> Furthermore, corticosteroid injection with the use of ultrasound guidance is better than blind administration and reduces the time to symptom resolution, even if it is more expensive.<sup>51–54</sup>

Regarding non-invasive methods of local corticosteroid administration, a comparison of phonophoresis and iontophoresis of dexamethasone sodium phosphate showed that phonophoresis was more effective in improving symptoms and hand function.<sup>55</sup> Phonophoresis with dexamethasone combined with splint use has been shown to provide better symptom relief than iontophoresis with dexamethasone combined with splint use or splint use alone.<sup>56</sup>

Corticosteroid therapy has been compared with other drugs. By use of phonophoresis for local administration, corticosteroids led to greater reductions in nerve dimensions than did non-steroidal anti-inflammatory drugs and splint use alone in patients with carpal tunnel syndrome.<sup>57</sup> Triamcinolone acetonide injection and procaine hydrochloride injection were more effective than placebo, and the effectiveness of procaine hydrochloride was similar to that of triamcinolone acetonide.<sup>58,59</sup> A comparison between 17- $\alpha$ -hydroxyprogesterone caproate and corticosteroid showed that both treatments were efficacious, but only patients treated with 17- $\alpha$ -hydroxyprogesterone caproate continued to have symptom relief after 3 months.<sup>60</sup> Corticosteroid injection has also been compared with extracorporeal shock wave therapy, which uses acoustic waves to produce transient pressure increases in tissues with no damaging effects. No difference in symptoms or electrophysiological outcomes was seen between the two treatments.<sup>61</sup>

Non-steroidal drugs have been assessed as an alternative treatment for carpal tunnel syndrome. Palmitoylethanolamide, a nuclear factor agonist, improved median nerve motor latency, reduced the proportion of patients with positive Tinel's sign, and reduced symptoms of discomfort compared with placebo; however, further studies are needed to substantiate these results.<sup>62</sup> Gabapentin was no more effective than placebo in reducing pain, numbness, paraesthesia, weakness or clumsiness, or nocturnal awakening in a randomised controlled trial.<sup>63</sup> Repetitive local injection of lidocaine resulted in symptom reduction and electrophysiological improvement compared with single injection.<sup>64</sup>

### Therapeutic ultrasound

Therapeutic ultrasound is a treatment approach based on the hypothesis that mechanical waves interacting with the tissues of the carpal tunnel (including the median nerve) will reduce inflammation. No clear evidence about the effectiveness of therapeutic ultrasound exists, but the reported results are similar to those obtained with placebo and other non-surgical therapies (splint, exercises, oral pharmacotherapy).<sup>65–68</sup> However, findings from a randomised trial<sup>69</sup> suggest that ultrasound therapy is more effective than paraffin therapy, a deep heat treatment that ameliorates local blood flow.

### Musculoskeletal manipulation and splinting

Musculoskeletal manipulation is widely used. This approach includes massage, exercise, and mobilisation of the wrist joint. Another important non-surgical approach is the use of devices such as splints. These methods are designed to reduce the mechanical stress due to the contact between the median nerve and the surrounding tissues of the carpal tunnel. The possible mechanism of splinting and gliding exercises is oedema reduction.<sup>70</sup> The use of a splint for 8 weeks combined with a formal education programme, improved hand function and reduced symptom severity compared with no intervention.<sup>71</sup> However, a meta-analysis has shown that sufficient evidence does not yet exist to confirm the clinical usefulness of splints, its efficacy in comparison with other treatments, or the efficacy of nocturnal splints.<sup>72</sup> A combination of splints and lumbrical stretches was shown to be more effective than splints and general stretches in terms of symptom severity and functional score, but further studies of this combination are needed.<sup>73</sup> Although the use of stretches and splints might temporarily improve muscle deficits, residual strength impairments can remain 4 weeks later.<sup>74</sup> The Madenci massage technique (30–60 s cycles of effleurage, friction, petrissage, shaking, and repeated effleurage), has been shown to be more effective than use of splints alone in a single study.<sup>75</sup> However, little evidence exists about the effectiveness of exercise and mobilisation of carpal tunnel structures.<sup>76</sup> A combination of tendon gliding exercises (moving hand flexor tendons through five different finger positions: straight, hook, fist, table top, and straight fist) and splint and paraffin therapy (defined as “conventional treatment”) might be better than conventional treatments alone or in combination with median nerve gliding exercises (grasp, finger extension, wrist extension, thumb extension, forearm supination, and soft stretch of the thumb by contralateral hand).<sup>77</sup>

### Complementary therapies

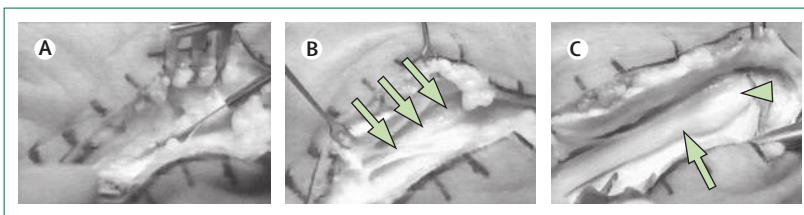
Other non-surgical treatments have been assessed in patients with carpal tunnel syndrome. Linseed oil might provide mild or moderate improvement in symptoms severity and functional scores and median nerve conduction velocity, as assessed in a randomised trial.<sup>78</sup>

Acupuncture was not better than placebo for treatment of carpal tunnel syndrome, but it has been shown to improve electrophysiological measures and reduce symptom severity compared with prednisolone.<sup>79,80</sup> The effect of acupuncture was assessed in a systematic review that showed encouraging, but not convincing, results.<sup>81</sup> *Eremostachys laciniata* ointment, an extract of a plant in the Lamiaceae family used in Persian traditional medicine as an anti-inflammatory and analgesic, was compared with placebo ointment (splints were used in both groups). Treatment with *E laciniata* ointment resulted in improvements in pain perception and palmar prehension, but further studies are needed to confirm these findings and to understand the long-term effects of this treatment.<sup>82</sup> Interferential current therapy (ie, a low frequency electrical stimulation of nerves) resulted in improvement in function, symptom severity, and electrophysiological measures compared with TENS and splint use.<sup>83</sup> Local microwave hyperthermia, a type of thermotherapy used in different musculoskeletal diseases, was more effective than sham therapy (treatment simulation with warm water, with microwave generator on stand-by) at providing short-term improvements in pain and function in patients with carpal tunnel syndrome.<sup>84</sup>

### Surgical treatment

Surgical treatment, consisting of release of carpal tunnel content by transection of the transverse carpal ligament, is considered the most effective treatment to alter the relation between content (the median nerve and tendons) and container (the carpal tunnel; figure 2).

Surgical decompression can be done by a traditional open technique (long longitudinal wrist incision and direct visualisation of transverse carpal ligament); by a minimally invasive approach (short wrist incision); or by an endoscopic technique. Studies have shown that, in terms of long-term functional outcome, there is no significant difference between open and endoscopic release.<sup>85–91</sup> However, some other differences exist. The endoscopic technique shows a shorter postoperative recovery period, reduced scar tenderness, and allows earlier return to work than the open technique.<sup>85–91</sup> However, endoscopic release is more expensive<sup>92</sup> and is associated with higher rates of transient and nerve damage.<sup>86</sup> Findings from a meta-analysis<sup>88</sup> suggest that endoscopic release is associated with fewer minor complications (such as scar pain and infection) compared with open carpal tunnel release, with similar rates of major complications (mainly complex regional pain syndrome).<sup>88</sup> Differences in outcome might be dependent on the expertise of the performing surgeon.<sup>92</sup> In one study,<sup>87</sup> the two techniques were compared in patients with bilateral carpal tunnel syndrome; each patient received both techniques, one in each hand. Although there were no differences between techniques in terms of functional outcomes, patients preferred the endoscopic approach, as shown by significantly higher overall satisfaction scores.



**Figure 2: Open carpal tunnel release**

(A) Subcutaneous layer dissection. (B) Transverse carpal ligament partially released (arrows). (C) Median nerve (triangle) showing the site of previous nerve compression (arrow).

Different open carpal tunnel release techniques are available (limited open release with direct vision and tunnelling technique or standard open carpal tunnel release,<sup>93</sup> or open-field surgical release followed or not by a longitudinal epineurotomy) and have shown similar effectiveness.<sup>94</sup> Z-type lengthening of the transverse carpal ligament results in significant improvement in function and satisfaction score compared with a standard open technique.<sup>95</sup> Minimally invasive techniques, compared with the standard open approach, seem to provide better outcomes (fewer complications; higher patient satisfaction; improvement in symptoms, results of Tinell's, Phalen's, and compression tests, electrodiagnostic assessment, grasp strength assessment, and time to recover ability to perform personal tasks).<sup>91,96,97</sup> A meta-analysis<sup>98</sup> showed that the minimally invasive approach versus open carpal tunnel release allowed an early return to work. Further investigations are needed to recommend the best approach.

Surgical complications of carpal tunnel release are reported to occur in 1–25% of patients.<sup>99</sup> The incidence of serious complications consisting of structural damage to nerves, arteries, or tendons is no more than 0·5% (0·49% for open carpal tunnel release and 0·19% for endoscopic methods).<sup>100</sup> One potential severe complication of carpal tunnel operations is complex regional pain syndrome, which presents as hand pain, increased sweating, and vasomotor instability. Complex regional pain syndrome complicates recovery, delays return to work, causes deterioration of health-related quality of life, and increases the probability of poor outcomes and litigation. Its incidence after carpal tunnel release varies from 2·1% to 5%. Early diagnosis and treatment of complex regional pain syndrome is essential for optimising patient outcomes.<sup>101,102</sup> Other complications of carpal tunnel release are scar tenderness, pillar pain (tenderness close to the ligament release), transient neuropraxia, and reoperation (with little difference between open and endoscopic carpal tunnel release).<sup>86</sup>

Regarding the postsurgical phase, there is limited low-quality evidence for the benefit of postoperative rehabilitation interventions.<sup>103</sup> In patients requiring repeat carpal tunnel release after failure to improve, decompression with the use of vascularised flap coverage seems to have a higher success rate than simple repeat

decompression (although it is more complex and time consuming).<sup>99,104</sup> Regarding timing, the authors of a meta-analysis<sup>99</sup> reported a small sample of patients in whom recurrent symptoms began from 3 months to 4 years after surgery and the mean time between first and revision surgery was 31 months.<sup>99</sup>

Long-acting intraoperative local anaesthesia (ropivacaine) has been shown to provide longer duration of postoperative analgesia than short-acting local anaesthesia (lidocaine); however, it might also result in a poorer first night's sleep after surgery.<sup>105</sup> Local anaesthesia is also associated with less severe postoperative pain compared with general anaesthesia.<sup>106</sup> No association between anaesthetic technique and incidence of complex regional pain syndrome has been recorded.<sup>102</sup>

### Surgical versus non-surgical treatment

As previously described, the literature shows that both non-surgical therapies and surgical intervention have clinical benefit in carpal tunnel syndrome.<sup>107–109</sup> In a randomised trial comparing local corticosteroid injection with surgical decompression, both treatments were similarly effective at alleviating symptoms, with corticosteroids being more effective in short-term follow-up (3 months), and surgical release having additional benefit for symptom resolution in the long term (2-year follow-up).<sup>108</sup> There is evidence that clinical outcomes significantly improve after decompressive surgery and several non-surgical treatments (eg, splints and low-level laser therapy), but decompressive surgery shows a higher long-term effectiveness.<sup>109</sup> Surgery is also more effective than non-surgical treatment at improving electrophysiological measures.<sup>107</sup> Furthermore, a systematic review reported in 2011 that surgical carpal tunnel release is two times more likely to result in normal nerve conduction findings and resolution of symptoms after 6 and 12 months than non-surgical treatment.<sup>109</sup>

### Conclusion and future directions

Although carpal tunnel syndrome is a well studied nerve entrapment syndrome, several important questions remain unanswered. Is confirmation by diagnostic testing necessary? Does clinical assessment provide enough information to guide the choice of treatment? Is electrophysiology needed? Is ultrasonography a potential alternative to nerve conduction studies?

The roles of electrophysiology and ultrasonography in diagnosis are well known, but their roles in management and treatment decision making are unclear. Until ultrasonography and electrophysiology can be done with a simple device simultaneously, the advantages and disadvantages of each technique should be considered (eg, ultrasonography is non-invasive but does not provide functional information, whereas electrophysiology provides functional data but does not allow visualisation of the nerve and surroundings). The pathway for assessment of carpal tunnel syndrome is still a matter of debate. In the

absence of evidence, we believe that general practitioners should be the first point of contact for patients. Neurologists and neurophysiologists have training in the specialty care of patients with carpal tunnel syndrome and are more likely to have experience managing a range of severities. They often have access to more resources that allow a comprehensive diagnostic approach (clinical, electrodiagnostic, and ultrasonographic). However, there are, of course, fewer specialists than general practitioners.

Until a single diagnostic method is able to accurately diagnose carpal tunnel syndrome, guide therapy, and assess prognosis, we believe that a comprehensive diagnostic investigation is needed. However, the economics of health care require careful consideration before recommending such investigations.

Regarding management of carpal tunnel syndrome, both surgical and non-surgical interventions can be beneficial. Surgical treatment has been shown to have longer lasting effects, with patients reporting reduced symptoms and improved function 6 and 12 months after surgery. Patients undergoing surgical release are twice as likely to have normal post-treatment nerve conduction findings, but also have risks of surgical complications. The different surgical techniques have been compared, but it is not clear whether one surgical treatment is more effective or safer than another. In view of the treatment differences and the potential for surgical adverse events, initial non-surgical management is supported by evidence, with surgical release then being considered for patients with severe or persistent symptoms. Further studies of non-surgical approaches are also needed, particularly for pharmacotherapy.

Researchers should examine when and for whom non-surgical care is an effective choice. Although carpal tunnel syndrome is very common, only a few randomised controlled trials addressing these issues have been done. A crucial part of developing any high-quality clinical trial is the use of validated outcome measures.<sup>110</sup> Different perspectives in methods of assessment of carpal tunnel syndrome provide different results that vary in consistency, but are all useful. Patient-centred measures (eg, BCTQ) are crucial for quantifying symptoms and disability, whereas the functional (electrodiagnostic) and morphological (ultrasound) measures are essential for assessing nerve involvement and progression. We believe that all these outcome measures should be included in clinical trials. A unique composite outcome measure, assessing the clinically meaningful change, could be used to provide high-quality evidence and allow proper comparison in meta-analysis.

With regard to outcomes of treatment, crucial questions remain. What is more important in the treatment of carpal tunnel syndrome: palliation of symptoms or modification of the course of the disease so that axonal degeneration is avoided? Should we measure patient satisfaction with treatment or should we measure effect on objective measures of nerve function? These



### Search strategy and selection criteria

We searched PubMed, Cochrane, Embase, Web of Science, and Google Scholar for articles published in English between Jan 1, 2011, and Aug 1, 2016, using “carpal tunnel syndrome” as MeSH term in PubMed. We filtered the search for “randomised controlled trial”, “meta-analysis”, and “systematic review”. 119 articles were identified. After excluding inappropriate papers, we selected 79 articles (20 meta-analyses, 52 randomised controlled trials, and seven systematic reviews). Because of the paucity of evidence-based data for epidemiology, clinical features, and risk factors of carpal tunnel syndrome, we did not exclude any article types. Moreover, because most studies on epidemiology and clinical features were published before 2011, we extended the search for this topic from Jan 1, 1996, to Aug 1, 2016. We then selected those papers that were most relevant to this Review on the base of the size of the studied cohort and the number of Scopus citations. We attempted to avoid referencing review articles if possible.

topics deserve attention. We believe that treatment goals change depending on the affected individual and how the disorder affects daily life. For example, in an old patient with thenar atrophy and striking sensory symptoms, the preferred aim might be to reduce symptoms. In a young patient, preserving hand function might be essential for maintenance of current lifestyle.

The introduction of a stricter concept of outcome measures must be associated with proper use of statistical tests. Carpal tunnel syndrome requires an often overlooked specific methodological and statistical approach because it is frequently bilateral, preventing the use of an inpatient contralateral control.<sup>111,112</sup>

The academic literature is full of assertions about short-term, mid-term, or long-term outcomes, but there is no set definition of these terms. We recommend that a multidisciplinary group establish and define common data elements for future studies of carpal tunnel syndrome, as advocated for other disorders by the US National Institutes of Health.<sup>113</sup>

Carpal tunnel syndrome is often defined as idiopathic, but this definition can be misleading. A debate should be started on the topic of idiopathic carpal tunnel syndrome, and its risk factors, causes, and associated disorders. Finally, although challenging, neurobiological research should be attempted to allow a better understanding of the disease and how to prevent it.

### Contributors

LP designed the Review, did the literature search, and contributed to the writing of the Review, production of the figures, and the final editing of the Review. DC contributed to the literature search, the writing of the Review, and editing of the figures. CE contributed to the literature search and the writing of the Review. IP, CP, and PC contributed to the literature search. CL contributed to the literature search and editing of the Review. LDH-W contributed to the literature search, the writing of the Review, language editing, and drafting of revisions.

### Declaration of interests

We declare no competing interests.

### Acknowledgments

We thank Chiara Cambise and Filippo Maria del Tedesco for their support in writing this Review.

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