Carpal tunnel syndrome
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INTRODUCTION

Carpal tunnel syndrome (CTS) is characterized by a compression of the median nerve in the carpal tunnel. It is a common pathology affecting an estimated 10% of the population according to the American Academy of Neurology (AAN 1993a,b, Olney 2001). It is considered the most common nerve compression disorder of the arm, with reported prevalence rates of 3.8% (95% CI, 3.1–4.6%) for women and 2.7% (95% CI, 2.1–3.4%) for men (Atroshi et al 1999). Bland et al (2003) found an annual incidence of 139.4 cases per 100,000 females and 67.2 cases per 100,000 males, with a female:Male ratio of 2.1. Bongers et al (2007) have recently reported an incidence rate of CTS of 1.8/1000 (95% CI, 1.7–2.0). In females the incidence was 2.8 (95% CI, 2.6–3.1) and in males 0.9 (95% CI, 0.8–1.0) showing a female:Male ratio of 3:1 (Bongers et al 2007). Further, this study showed that in 2001 the incidence of CTS was calculated to be 1.5 times higher than in 1987 (this difference disappeared after subdividing patients by age and sex) (Bongers et al 2007). It has been estimated that in the USA around one million people require care for CTS, around 200,000 surgical interventions are needed and that the social costs are in the millions of dollars range (Tanaka et al 1995).

Analysis of the literature raises the difficulty of accurately estimating the incidence and prevalence of CTS due to the fact that it is a very common pathology and, as we discuss below, can be associated with manual work. This last controversial association means that incidence and prevalence of CTS are often calculated in a specific work-population. Moreover, another confounding factor could be the method used to diagnose CTS, as Atroshi et al’s (1999) study, the combination of clinical and neurophysiological evaluations contributed to diagnosing CTS in 1 in 5 symptomatic subjects in the general population.

ANATOMY

In the carpal tunnel the median nerve is surrounded by bones on three sides with the transverse carpal ligament on the top. The nerve lies within the nine flexor tendons of the hand, and supplies function, feeling and movement to first digit of the hand and one-half of the ring finger (Fig 28.1).
The median branches for finger and wrist flexors originate in the forearm, while motor branches, that control the thumb flexor and adductor muscles, and sensory branches, that provide over half the hand with the sense of touch, usually originate at the end of the tunnel. Compression of the nerve can be due to a decrease in the size of the canal, an increase of the size of tendons, or both. For further information, readers are referred to Heidelberg (1989).

**PATHO-BIOMECHANISM OF CARPAL TUNNEL SYNDROME**

In most cases CTS is idiopathic (Sternbach 1999) but sometimes it is associated with trauma, pregnancy, hypothyroidism, multiple myeloma, amyloidosis, rheumatoid arthritis, or acromegaly (Stevens et al 1992). As discussed above, in this pathology the changes occurring in the carpal tunnel are responsible for the median compression. For example:

- Rheumatoid arthritis causes inflammation of the flexor tendons determining median nerve compression.
- Pregnancy and hypothyroidism cause fluid retention in tissues, which swells the tenosynovium (we discuss the role of pregnancy in more detail later in this chapter).
- Acromegaly causes the compression of the nerve because of the abnormal growth of bones around the hand and wrist.
- Tumours (usually benign), such as a ganglion or a lipoma, can protrude into the carpal tunnel, reducing the amount of space. This is exceedingly rare (<1%). Carpal tunnel tumours can mimic CTS (Padua et al 2006) and in these cases the use of ultrasound evaluation has been crucial. This topic will be discussed below (Granata et al 2008).
- Obesity also increases the risk of CTS; a BMI > 29 (obese individuals) increases the risk by 2.5 compared to a BMI < 20 (slender individuals) (Werner et al 1994).
- Double crush syndrome is a speculative and debated theory which postulates that when there is compression or irritation of nerve branches contributing to the median nerve in the neck or anywhere above the wrist, this increases the liability of the nerve to compression in the wrist. Pierre-Jerome & Bekkelund (2005) reported that patients with CTS experienced a higher incidence of narrowing of the cervical foramen when compared to controls. These authors hypothesized that the compromised neural foramen could potentially lead to nerve compression and possibly a double crush syndrome in patients with CTS. However, there is little evidence that this syndrome really exists in CTS (Wilbourn & Gilliatt 1997, Russell 2008).
- There is a great number of traumas can cause CTS (Colles’ fracture, dislocation of one of the carpal bones of the wrist, haematoma forming inside the wrist, etc.).
- The role of manual activities and CTS is still a matter of debate. A number of authors found that there is strong relation between hand positions and increased pressure on the carpal tunnel (Keir et al 1998, Luchetti et al 1998) and strongly supports the hypothesis that forceful use of the hands, repetitive use of the hands, and hand-arm vibration may cause or contribute to CTS. But other studies do not support the relationship between manual activity and CTS (Chiang et al 1993, Moore & Garg 1994). Despite researchers’ efforts, the debate is still far from concluded.

Readers are referred to other texts for a greater understanding of these mechanisms (Werner 2006, Van Rijn et al 2009).

**SENSITIZATION MECHANISMS IN CARPAL TUNNEL SYNDROME**

Although the aetiology of CTS is not completely understood, there is some evidence involving the whole nociceptive system. Previous studies have investigated the function of nociceptive thermo-receptive fibres in CTS patients. Different studies found elevated thermal pain thresholds in the fingers and the palm within the affected hand in patients (Arendt-Nielsen et al 1991, Westerman & Delaney 1991, Goadsby & Burke 1994). Lang et al (1995) suggested that pain intensity in CTS depends on alterations of peripheral and central nervous function.

More recent studies reported that 45% of CTS patients also reported spreading proximal symptoms, which might be related to central nervous system mechanisms (Zannete et al 2006, 2007). Chow et al (2005) found that neck pain was present in 14% of patients with CTS. Tucker et al...
(2007) found bilateral generalized increase in vibration thresholds in patients with CTS which suggests a generalized disturbance of somato-sensory functions rather than the existence of an isolated peripheral neuropathy. In fact, two image studies have shown cortical remapping in the primary somato-sensory cortex (S1) in patients with CTS supporting a possible role of central mechanisms in CTS (Tecchio et al 2002, Napadow et al 2006).

Additionally, recent clinical studies also support the presence of peripheral and central sensitization mechanisms in patients with moderate CTS. Fernández-de-las-Peñas et al (2009a) found bilateral widespread decrease in pressure pain thresholds in patients with unilateral CTS (clinically and neurophysiological) when compared to healthy controls. This study reported bilateral lower pressure pain thresholds (PPT) over the median, radial and ulnar nerve, the carpal tunnel, the C5–C6 zygapophyseal joint and the tibialis anterior muscle. A significant decrease in PPT over C5–C6 zygapophysseal joint may represent the existence of segmental sensitization of the nociceptive system in CTS, whereas a bilateral decrease in PPT over the tibialis anterior muscle indicate multi-segmental sensory sensitization or sensitization of the central nervous system in patients with CTS (Fernández-de-las-Peñas et al 2009a). De-la-Llave Rincon et al (2009) reported that patients with unilateral CTS also show a bilaterally thermal hyperalgesia (lower heat pain thresholds and reduced cold pain threshold), but not hypoaesthesia (normal thermal detection threshold) as compared to healthy subjects. Again, bilateral changes in patients with unilateral diagnosis (clinical and neurophysiological) of CTS reflect central sensitization mechanisms. These clinical findings are supported by animal studies where peripheral neural pathology in one local area can cause widespread effects, including effects in apparently uninvolved limbs (Koltzenburg et al 1999, Kleinschnitz et al 2005).

A recent study investigating impairments in fine motor control and ability skills also showed bilateral deficits in fine motor control ability and pinch grip force in unilateral CTS (Fernández-de-las-Peñas et al 2009b). The authors of this study hypothesized that bilateral motor control impairment and pinch grip force deficit can reflect a reorganization of the motor control strategy of the central nervous system as a consequence of the pain in CTS, which was supported by Tamburin et al (2008).

Finally, these studies also showed that bilateral sensory and motor deficits were associated to the intensity and duration of pain symptoms, supporting a role of the peripheral drive to initiate and maintain central widespread sensitization (De-la-Llave-Rincón et al 2009, Fernández-de-las-Peñas et al 2009a,b). Gracely et al (1992) proposed a model of neuropathic pain in which ongoing nociceptive afferent input from a peripheral nociceptive focus dynamically maintains altered central processing. In such instances, it can be suggested the painful condition, that is the ischaemia of the nervi nervorum (Watkins & Maier 2004) (the nerves innervating the connective tissue layers of the nerve itself) sensitized by the compression of the median nerve in the carpal tunnel (Hall & Elvey 1999), may as such act as a trigger for gradual sensitization of nociceptive pathways in CTS patients. New studies should investigate the role of these sensitization mechanisms in the evolution of CTS.

**Clinical examination**

The gold standard for the diagnosis of CTS is considered the clinical picture, according to the AAN (1993a,b) diagnostic criteria: paraesthesia, pain, swelling, weakness or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position, repetitive action of the hand or wrist that is mitigated by changing posture or by shaking of the hand, sensory deficits in the median innervated region of the hand and motor deficit or hypotrophy of the median innervated thenar muscles. Wainner et al (2005) developed a clinical prediction rule for the diagnosis of CTS. The rule identified consisted of 1 question (shaking hands for symptom relief), wrist-ratio index > 0.67, symptom severity scale score > 1.9, reduced median sensory field of digit 1, and age > 45 years (LR = 18.3).

Recent studies have evidenced the relationship between the distribution of sensory symptoms and the severity of CTS, according to the neurophysiological classification. Patients with lower severity of pathology complain of sensory symptoms with a glove distribution, while patients with higher severity of pathology complain of sensory symptoms with the ‘classical’ median distribution (Callandro et al 2006).

The patient history is extremely important for the differential diagnosis, especially as CTS can be secondary to endocrinial and metabolic pathologies; therapy for the primary pathology can remit the CTS. For clinical examination, in addition it is possible to use a historic and objective scale (Hi-Ob) of CTS that includes two measures (Giannini et al 2002). The first has clinical history and objective sub-scores: (1) nocturnal paraesthesia only; (2) nocturnal and diurnal paraesthesia; (3) sensory deficit; (4) hypotrophy or motor deficit of the median innervated thenar muscles; (5) plegia of median thenar eminence muscles. The second evaluates, by patient-oriented measurement, the presence or absence of pain with a forced-choice answer (‘yes’ or ‘no’). Therefore, the Hi-Ob score is composed of a number (Hi-Ob) with or without the pain variable (Giannini et al 2002).

The physical examination includes the Phalen test (Fig 28.2), performed by a prolonged (1-minute) passive forced flexion of the wrist; the Tinel test that consists...
of a percussion of the median nerve trophism of the thenar eminence; motor function of the median innervated muscles; and sensory function (cotton wool is used as a standard material for skin stimulation).

**Questionnaires**

As doctors want to help patients, the assessment of patients’ perspective is also useful in the comprehensive evaluation of CTS. The most common used questionnaire is the Boston Carpal Tunnel Questionnaire (BCTQ) (Levine et al 1993). The BCTQ evaluates two domains of CTS: ‘symptoms’ (SYMPT = patient-oriented symptom) assessed on an 11-step scale; and ‘functional status’ (FUNCT = patient-oriented function) assessed on a 8-step scale. Each item includes five possible responses, and the score for each section (SYMPT or FUNCT) is calculated as the mean of the responses to the individual items. The use of this questionnaire in several multi-centric studies on CTS showed interesting results; while function has a linear significant correlation when assessed both by physicians and patients, symptoms do not have a clear linear correlation (Padua et al 2002). Patients with mild-to-moderate CTS seemed to function well, although severe symptoms may be reported by the patient. However, when nerve impairment becomes severe, the patient’s hand function is extremely impaired although symptoms may be milder. The data show that the patient’s point of view is reliable (Padua et al 2002).

**Electrodiagnostic evaluation**

Electrodiagnostic evaluation is very important to define the impairment of the median nerve. It is now accepted that, in order to increase the sensitivity of conventional nerve conduction studies (sensory digit-wrist and motor wrist-thennar), segmentary and/or comparative tests should be used (see below) as stated in AAN and AAEM recommendations (AAN 1993a,b). When the standard tests yield normal results (‘standard negative’ hands), the following studies increase the electrodiagnostic sensitivity:

1. Segmental motor or sensory conduction tests in palmar-wrist segment.
2. Comparative studies (median-ulnar or median radial)
3. Segmental/comparative studies (as disto-proximal ratio)

A study conducted on CTS patients showed that the sensitivity of standard tests can reach 83.5%, comparative/segmental tests can disclose abnormal findings in a further 11.4% of cases, providing CTS electro-diagnosis in about 7 of 10 ‘standard negative’ cases. The overall sensitivity of protocol thus reaches 94.9% (Padua et al 1999). The severity of neurophysiologic CTS impairment can be assessed and scored according to a published neurophysiologic classification (Padua et al 1997a,b).

**ULTRASOUND ASSESSMENT**

Thanks to the advances in technology (refinement of high-frequency broadband linear-array transducers, and sensitive colour and power Doppler technology), the low cost, the wide availability, and the ease of use, ultrasound (US) has recently been applied to the study of tendons and nerves. In tendon and nerve imaging, US can assess a great number of pathologies such as dislocations, degenerative changes, extrinsic or intrinsic focal compression. Moreover US can support clinical and electrophysiological testing and in most cases, a focused US examination can be performed more rapidly and efficiently than MR imaging (Martinoli et al 2002).

From a technical point of view, although tendons and nerves share similar characteristics (dimensions, tubular conformation, and striated appearance) US can easily differentiate them. Tendons have a fibrillar pattern of parallel hyperechoic lines in the longitudinal plane because of collagen bundles and endotendineum septa with a hyperechoic round to ovoid image containing bright dots (Fornage & Rifkin 1988, Martinoli et al 1993); nerves have a fascicular pattern due to hypoechoic parallel linear, the neuronal fascicles, separated by hyperechoic bands (the interfascicular epineurium) (Graif et al 1991, Silvestri et al 1995). On transverse scans, nerves assume a honeycomb-like appearance with hypoechoic dots surrounded by a hyperechoic background (Fig 28.3).

Ultrasound has been mainly tested in the evaluation of CTS because of the complementary perspective it provides (Beekman & Visser 2003, Hobson-Webb & Padua 2009, Karadag et al 2010, Smith et al 2009). CTS can be assessed by using the following measures: cross-sectional area (CSA), swelling ratio, retinacular bowing, retinacular thickness, flattening ratio. Several studies have shown that the most useful diagnostic criterion is the CSA, which is the area of median nerve calculated at the wrist, both by using the ellipse formula or by manual tracing; the best cut off value is CSA of ≥ 9.875 mm² at the pisiform level (Wang et al 2008).
Moreover, more sensitive tests have been developed in order to obtain the best sensitivity and specificity. For example, the wrist-to-forearm ratio (WFR) of median nerve area can be considered more sensitive than measure of median nerve area at the wrist alone (Hobson-Webb et al 2008). The sensitivity of the combination of US and neurophysiology is higher than that of neurophysiology or US alone. US is hence a useful complementary tool for CTS assessment, with a positive correlation between US findings and conventional measures of CTS severity (clinical, neurophysiological and patient-oriented) (Padua et al 2008).

In conclusion, there is increasing evidence that US is a useful complement in a neurophysiology laboratory, it greatly increases the diagnostic power and therapeutic work-up of patients with mononeuropathies (Padua et al 2007) and the morphological evaluation of nerves helps in avoiding severe misdiagnoses (e.g. a median nerve tumour that may mimic CTS), especially in cases with atypical neurophysiological findings (Padua & Martinoli 2008).

**PROGNOSIS**

**Prognosis of untreated carpal tunnel syndrome**

The knowledge of evolution of untreated CTS is very important in order to administer the best therapeutic approach. Only a few studies have evaluated this topic (Padua et al 1998, 2001, Resende et al 2003, Ortiz-Corredor et al 2008) and all authors agreed that many patients improved spontaneously. When the evolution is analyzed according to the initial picture, it is observed that CTS hands with initial low severity tend to get worse while CTS hands with initial high severe impairment tend to improve (this is observed in all CTS measurements, either patient-oriented or neurophysiologic).

Moreover, the factor that is most predictive of untreated CTS evolution is the duration of symptoms. In particular, a long duration of symptoms is a negative prognostic factor according to all patient-oriented measurements. Conversely a long duration of symptoms is not significantly associated with a bad neurophysiological or clinical examination outcome. With regard to the positive prognostic value of hand stress at the baseline, note that this value is probably due to the interruption of the stress. In this sense it is interesting to note that in the entrapment syndrome the ‘natural history’ can be influenced by the physicians with an explanation of the patho-physiology of CTS. If doctors, while giving the patients the diagnosis, also provide practical information about the hand positions to be avoided, they can alter the natural course of the pathology.

**Therapy**

With regard to the conservative options of CTS therapy a review by Piazzini et al (2007), including 33 randomized controlled trials, showed that there is a strong evidence (level 1) on efficacy of local and oral steroids; moderate evidence (level 2) that vitamin B6 is ineffective and that splints are effective, and limited or conflicting evidence that NSAIDs, diuretics, yoga, laser and ultrasound are effective whereas exercise therapy and botulinum...
toxin B injection are ineffective. A recent systematic review focused on neural mobilization interventions for the management of CTS included six studies and found weak to strong effects of neural gliding exercises with benefits seen across different outcome measures (Medina McKeon & Yancosek 2008). Nevertheless, these authors proposed that the benefit of neural gliding may be best identified within a specific subpopulation of CTS patients. It is possible that neural gliding may be more effective in a population with less advanced CTS. A clinical prediction rule identifying CTS patients who will benefit from neural mobilization interventions is urgently needed.

Regarding the surgical approach, a Cochrane review of 2003 concluded that surgical treatment relieves symptoms significantly better than splinting but further research is needed to discover whether this conclusion applies to people with mild symptoms and whether surgical treatment is better than steroid injection (Verdugo et al 2003).

Analyzing the factors that influence the surgical results in different populations, a number of studies have been performed, e.g. the results of surgical decompression were similar in men and women (Mondelli et al 2004a). On the other hand elderly patients showed less improvement with respect to younger patients, presumably due to greater preoperative damage and less repair capacity of the compressed nerve, but this aspect was not a contraindication for surgical release in elderly patients (Mondelli et al 2004b). Also the presence of comorbidity has been investigated, e.g. patients with diabetes have the same probability of positive surgical outcome as patients with idiopathic CTS (Mondelli et al 2004a).

In the same trend, the analysis of cost-effectiveness of non-surgical versus surgical treatment showed that surgery, rather than non-surgical care, should be considered as the initial form of treatment when patients are diagnosed with CTS (confirmed by nerve conduction studies), as this provides symptom resolution with a favourable cost analysis (Pomerance et al 2009).

**CARPAL TUNNEL SYNDROME AND PREGNANCY**

Because CTS is frequent during pregnancy (PRCTS) it can be considered a distinct entity. Studies have shown that PRCTS does not disappear after delivery (it may improve but on the contrary it may remain and the prolonged compression may result in median nerve defect) so CTS symptoms must be accurately assessed in pregnant women, and when present they must be monitored either clinically or neuro-physiologically (the role of ultrasound in PRCTS is not well known and must be assessed as it could be a non-invasive monitoring tool).

In cases of early appearance (before the last trimester) the median compression must be well assessed as it may result in acute or disabling CTS and improvement is less frequent. In case of severe CTS with early onset the surgical decompression during pregnancy may prevent nerve damage and a negative psychological influence after delivery.

Appearance of CTS symptoms in the last trimester is the more usual condition and has a higher probability of improvement after delivery; but around half of women may complain of CTS symptoms for a long time post partum, so clinical and neurophysiological monitoring is suggested. Note that despite improvement of symptoms, the distal sensory conduction velocity of the median nerve improved but remained delayed in 84% of women long after delivery (Mondelli et al 2007).

Apart from acute CTS, which may be an emergency (with the need for rapid surgical decompression), the first line in approaching PRCTS should be conservative therapy. But in absence of improvement and the presence of severe neurophysiological CTS (disappearance of sensory or motor responses) or disabling symptoms, surgical decompression before delivery must be considered in order to prevent not only nerve damage but also deterioration of quality of life due to difficulty and anxiety in handling the baby.

**CONCLUSION**

Although CTS has been defined as "complex issues with a 'simple' condition" (Olney 2001), and this is confirmed by the high number of publications concerning all aspects of CTS, in recent years efforts have been conducted to improve knowledge of this condition. Tools imported from other fields, such as ultrasound, have been commonly accepted in improving the diagnostic sensibility, although the gold standard remains the clinical picture. The natural history of the pathology shows that some untreated CTS patients can improve, but this is probably due to the doctor explaining to the patient how to avoid wrong hand postures and thus reducing the stresses on the hand. Conservative therapies have been used and were demonstrated to be effective, but surgical decompression, also used in elderly or diabetic patients, remains the definite cure and is efficient from the cost effectiveness point of view.

The opinion of the authors concerning surgical decompression, based on clinical experience and on unpublished data on the natural history of CTS, is that surgery is suggested in severe cases (either neuro-physiologically or clinically) with duration of symptoms longer than 1 year and in patients over 50 years old. A brief period of conservative therapy can be tried in cases of acute CTS, but any case in which we suspect an acute CTS that is not secondary to a particularly stressing event – a very rare but very severe condition – urgent decompression must be considered together with a comprehensive assessment of a possible primary subclinical cause.
REFERENCES


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