Review Article

Carpal tunnel syndrome – Part I (anatomy, physiology, etiology and diagnosis)\textsuperscript{☆,☆☆}

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ABSTRACT

Carpal tunnel syndrome (CTS) is defined by compression of the median nerve in the wrist. It is the commonest of the compressive syndromes and its most frequent cause is idiopathic. Even though spontaneous regression is possible, the general rule is that the symptoms will worsen. The diagnosis is primarily clinical, from the symptoms and provocative tests. Eletroneuromyographic examination may be recommended before the operation or in cases of occupational illnesses.

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Síndrome do túnel do carpo – Parte I (anatomia, fisiologia, etiologia e diagnóstico)

RESUMO

A síndrome do túnel do carpo (STC) é definida pela compressão do nervo mediano no punho. É a mais frequente das síndromes compressivas e a causa mais frequente é a idiopática. Ainda que as regressões espontâneas sejam possíveis, o agravamento dos sintomas é a regra. O diagnóstico é, acima de tudo, clínico pelos sintomas e testes provocativos. Um exame eletroneuromiográfico pode ser recomendado no pré-operatório ou em caso de doença laboral.

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Introduction

Carpal tunnel syndrome (CTS) is the most frequent of the compressive syndromes and is defined by compression and/or traction of the median nerve at wrist level. Its first description is attributed to Paget, who reported on a case of compression of the median nerve consequent to a fracture of the distal radius. In 1913, Marie and Foix published the anatomical and histopathological description of an hourglass-shaped lesion of the median nerve with neuroma, proximal to the flexor retinaculum. In the 1950s, studies by Phalen established the principles of CTS.

The estimated prevalence of CTS among the population is between 4% and 5%, particularly affecting individuals between 40 and 60 years of age. In 2008, 127,269 individuals aged 20 years and over were operated to treat CTS in metropolitan France, representing an incidence of 2.7/1000 (females: 3.6/1000; males: 1.7/1000). There were two peak frequencies: the first and higher of them between 45 and 59 years of age (75% female); and the second between 75 and 84 years (64% female).

Anatomical variations

Anatomical variations may explain the variations in symptoms and give rise to risks of iatrogenic injuries.

Anatomical variations in the nerves

A bifid median nerve caused by high division is observed in 1–3.3% of the cases and may be associated with persistence of the median artery or with an accessory branch of the superficial flexor of the third finger. In cases of a bifid median nerve, the radial portion is the most important one.

Variations of the motor branch of the median nerve

Lanz found five types of starting points and paths of the thenar branch: the extraligamentous form, which is the most frequent type (46%); the subligamentous form (31%) and the transligamentous form (23%). Kozen found that 4% of the cases had two motor branches that crossed the flexor retinaculum. The nerve bundles destined for the thenar branch are located radially to the median nerve in 60% of the cases, anteriorly in 20% and centrally in 18%. Sometimes, the thenar branch passes through a tunnel before entering the thenar muscles. These variations may explain the variable motor impact in cases of severe compression of the median nerve.

Variations of the palmar cutaneous branch of the median nerve

The palmar cutaneous branch usually begins 4–7 cm above the wrist crease and follows along beside the median nerve for 1.6–2.5 cm. It then enters a tunnel formed by the fascia at the medial edge of the FCR and emerges 0.8 cm above the wrist flexion crease, to innervate the skin of the thenar eminence. The palmar cutaneous branch may cross the transverse ligament of the carpus or may go to the ulnar side of the median nerve.

Intratunnel positioning of the ulnar nerve

It is extremely rare to find the ulnar nerve inside the tunnel. This abnormality presents the combined symptoms of the median and ulnar nerves.

Areas of the hand innervated by the median nerve

The area sensitized by the median nerve comprises the palmar face of the three radial fingers and the radial half of the ring finger; and on the dorsal face, the last two phalanxes of the first three fingers and the radial half of the fourth finger. The more proximal the palmar cutaneous branch is, above the anterior ligament, the better this explains the lack of participation in the symptoms of the thenar zone. In relation to the motor plane, the median nerve classically innervates the opposition muscles (short adductor of the thumb, opponens pollicis muscle and superficial bundle of the short flexor of the thumb) and the first two lumbral muscles. There are anastomoses with the sensory ulnar nerve on the palmar face (Berretini) and on the dorsal or motor face (Martin and Grüber in the forearm and Riche and Cannieu in the hand).
Berretini’s palmar sensory anastomosis
This anastomosis, which is found in 67–92% of the cases, is situated below the superficial palmar arch and is responsible for the variations in the sensitized area at the level of the ulnar edge of the third and fourth fingers and the radial edge of the fifth finger, between the median and ulnar nerves. In certain cases, this anastomosis is immediately distal to the flexor retinaculum.

Riche and Cannieu’s motor anastomosis
This anastomosis, which is observed very frequently (77% to 100%), is responsible for the distribution of the innervation of the thenar muscles between the median and ulnar nerves and takes on a variety of forms:

- The most classical form is a communicating branch between the thenar branch of the median nerve and the deep branch of the ulnar nerve.
- Anastomosis at the level of the adductor muscle of the thumb.
- Anastomosis between the thenar branch and the deep branch of the ulnar nerve at the level of the first lumbrical muscle.
- Anastomosis between a collateral nerve of the thumb and the deep branch of the ulnar nerve.
- It should be noted that the innervation of the lumbrical muscles is superimposed on that of the deep flexors of the fingers.

Martin-Grüber and Marinacci’s median ulnar anastomosis in the forearm
Anastomoses of the median nerve to the ulnar nerve in the forearm were described by Martin and Grüber. Their incidence ranges from 5 to 40%. The anastomosis comes from the median nerve or anterior interosseous nerve, or is situated between the branches that reinnervate the flexor of the fingers. This anastomosis coexists most frequently with an anastomosis in the hand and contains fibers that innervate the deep flexors of the fingers and the intrinsic muscles. There is controversy regarding the participation of sensory fibers. Inverse anastomoses from the ulnar nerve to the median nerve are very rare and are situated in the distal part of the forearm.

Leibovic and Hastings’ anastomoses
Type I (60%): anastomosis of the median nerve with the ulnar nerve that continues into the hand due to innervation of the muscles that are normally innervated solely by the median nerve (la) or with some muscles innervated by the ulnar nerve (lb).

Type II (35%): anastomosis of the median nerve with the ulnar nerve that continues into the hand to innervate the muscles that are normally innervated by the ulnar nerve.

Type III (3%): anastomosis of the ulnar nerve with the median nerve that continues into the hand due to innervation of the muscles that are normally innervated by the median nerve.

Type IV (1%): anastomosis of the ulnar nerve with the median nerve that continues into the hand due to innervation of the muscles that are normally innervated by the median nerve.

Vascular variations
Persistence of the artery of the median nerve
This leftover from the embryonic stage is observed in 1–16% of the cases. According to Kleinert et al., who found it in 3.4% of their cases, it participated significantly in the superficial palmar arch in 0.5% of the cases. A bifid median nerve may be found together with this. The complication produced is thrombosis, which gives rise to acute CTS.

The ulnar artery is in a superficial position, under the fascia and above the muscle.

Muscle and tendon variations
Long palmar muscle
There is a variation of the long palmar muscle with an intratunnel tendon, called the deep long palmar muscle, which is inserted in the deep face of the palmar aponeurosis and may give rise to constriction of the median nerve. The long palmar muscle may also be in an inverse position, with intratunnel muscle bodies, and this is called an inverse long palmar muscle.

Superficial flexor of the fingers
Extension of the muscle body in the carpal tunnel is the most frequent variation: 46% in women and 7.8% in men. An accessory muscle body or an anastomosis with the long palmar muscle has been described in association with CTS.

Lumbrical muscles
Extension of the intratunnel insertion or abnormal insertion over the superficial flexor of the index finger may be observed, but it remains unproven whether these occurrences might be responsible for compression of the median nerve.

Physiopathology and etiology
Ultrastructural nerve anomalies and clinical correlations
From a physiopathological point of view, compressive syndromes combine the phenomena of compression and tension. Anatomically, there are two sites of median nerve compression: one at the level of the proximal limit of the carpal tunnel, caused by wrist flexion because of changes in thickness and stiffness of the forearm fascia and in the proximal portion of the flexor retinaculum; and the second at the level of the narrowest portion, close to the hamate hook.

Nerve compression and traction may sequentially create problems relating to intraneurial blood microcirculation, lesions at the level of the myelin sheath and at axonal level, and changes to the supporting connective tissue. Lundborg proposed the following clinical-anatomical classification:

Early stage – Initial, characterized by intermittent symptoms that only occur at night. In idiopathic CTS, many factors can originate increased nocturnal intratunnel pressure:
• Redistribution of fluids to the upper limbs, when in a supine position;
• Lack of a muscle pump mechanism that might contribute toward drainage of interstitial fluids in the carpal tunnel;
• Tendency to keep the wrist in a flexed position, thereby increasing the intratunnel pressure;
• Increased arterial pressure during the second half of the night.

If the pressure exceeds 40–50 mmHg, this will interfere with the venous return of the intraneural microcirculation and cause diminished intraneural oxygen supply and venous stasis, with permeability problems originating from the endoneurial edema. An increase in pressure of 30 mmHg for 2 h leads to progressive weakening of the slow and fast axonal transportation. This is correct when the patient repositions his wrist and makes finger movements, thereby enabling drainage of the edema. After the compression has been relieved, there is a rapid improvement in the symptoms.

Intermediary stage – The symptoms are both nocturnal and diurnal. Abnormalities of the microcirculation are constantly present, with epineural and intrafascicular interstitial edema, which causes increased endoneurial fluid pressure. This interstitial edema causes absence of cell flow and thickening of the connective envelope, notably in relation to the epineurium. Destruction of the myelin sheath and nodes of Ranvier also occurs, based on saltatory conduction of inflows to the surface of the myelinated nerve fibers. After the compression has been relieved, rapid improvement of the symptoms occurs through reestablishment of the intraneural microcirculation. Unlike the restoration, repair of the myelin sheath requires weeks to months and causes intermittent symptoms and persistent electrophysiological abnormalities.

Advanced stage – Symptoms are constantly present, especially signs of sensory or motor deficit, translated as disruption of a greater or lesser number of axons (axonotmesis). Wallerian degeneration exists at the level of the disrupted axons. The connective envelopes form the site for reactive fibrous thickening. After release of the nerve, the recovery depends on nerve regeneration, which takes several months and may be incomplete. The significance of the recovery will depend on the patient’s potential for axonal regeneration, particularly with regard to age, the existence of polyneuropathy and the severity of the compression.

In reality, even with compression of all the nerve fibers within the same nerve, they will not be at the same stage of injury. It has been demonstrated that the peripheral nerve fibers in the region of the nerve trunk are affected before the more central fibers and, likewise, the myelinated fibers in relation to the smaller fibers and the sensory fibers in relation to the motor fibers.

In chronic CTS cases, worsening may occur over a period of months or years.

Associated pathological conditions

Polyneuropathy
All forms of polyneuropathy, including those relating to diabetes mellitus, promote CTS with structural and functional alterations of the median nerve, which makes the nerve more sensitive to all compressive phenomena.

Hereditary neuropathy with hypersensitivity to pressure is a hereditary sensory-motor form of neuropathy that is focal and recurrent. The first symptoms only rarely appear before the age of 20 years. It is characterized by occurrences of crises with paralysis and paresthesia in well-defined areas of the nerve trunk. These crises, which are generally secondary to mild trauma or prolonged compression, often regress. Recurrence is frequent. Paralysis may become definitively established. At the electrophysiological level, this condition is characterized by myelinopathy with stretching of the distal motor latency. Biopsies of the nerve show zones of focal thickening of myelin in the form of sausages (tomacula). Hereditary neuropathy with hypersensitivity to pressure is inherited as a dominant autosomal genetic lesion in 80% of the cases, through a deletion of chromosome 17. The treatment is symptomatic.

Nerve compression syndrome: “double constriction syndrome”
The concept of double compression of the nerve is attributed to Upton and MacComas and is based on the fact that proximal compression on the path of a nerve makes it more susceptible than if the compression was located more distally, because of cumulative effects on anterograde axonal transportation. Likewise, this can occur in cases of distal compression, due to alterations of the retrograde axonal transportation (“inverted double constriction syndrome”). This may occur in practice in cases of association between proximal compression of the nerve route at the vertebral level (or thoracic outlet syndrome) and distal CTS. Careful clinical examination, aided by an electrophysiological study, will determine where the compression site is (proximal or distal), i.e. the main agent responsible for the symptoms, thus guiding the treatment. Treatment applied to the main compression site is generally sufficient for such patients. Compression of the nerve layer should be borne in mind if the results are incomplete or there is therapeutic failure in the medical or surgical treatment.

Etiologies
In the great majority of cases, CTS is called idiopathic. Secondary CTS may be related to abnormalities of the container or content. Furthermore, dynamic CTS is frequently found under pathological conditions relating to manual work.

Idiopathic carpal tunnel syndrome
Idiopathic CTS occurs more frequently in females (65–80%) and between the ages of 40 and 60 years; 50–60% of the cases are bilateral. The bilateral characteristic increases in frequency with the duration of symptoms. Idiopathic CTS is correlated with hypertrophy of the synovial membrane of the flexor tendons caused by degeneration of the connective tissue, with vascular sclerosis, edema and collagen fragmentation. From meta-analyses conducted in 2002 and 2008, it was demonstrated that sex, age and genetic and anthropometric factors (size of the carpal tunnel) were
the most important predisposing factors. Repetitive manual activities and exposure to vibrations and cold temperatures were the least important. Other factors involved were obesity and smoking.

**Secondary carpal tunnel syndrome**

**Abnormalities of the container**

Any condition that modifies the walls of the carpal tunnel may cause compression of the median nerve.

- Abnormalities of the shape or position of the carpal bones: dislocation or subluxation of the carpus;\(^ {28,29}\)
- Abnormalities of the shape of the distal extremity of the radius: fractures (translation of more than 35%)\(^ {30}\) or skewed consolidation of the distal radius; osteosynthesis material on the anterior face of the radius;\(^ {31}\)
- Joint abnormalities: wrist arthrosis,\(^ {32}\) inflammatory arthritis\(^ {33}\) (due to synovial hypertrophy, bone deformation and/or carpal shortening), infectious arthritis,\(^ {34,35}\) rhizarthrosis\(^ {36}\) or villonodular synovitis;\(^ {37}\)
- Acromegaly.\(^ {38}\)

**Abnormalities of content**

- Tenosynovial hypertrophy;
- Inflammatory tenosynovitis: inflammatory rheumatism,\(^ {33}\) lupus and infection;
- Metabolic tenosynovitis: diabetes mellitus\(^ {31}\) (abnormality of collagen turnover), primary or secondary amyloidosis (chronic hemodialysis with deposition of beta-2-microglobulin),\(^ {39}\) gout\(^ {40}\) and chondrocalcinosis;\(^ {41}\)
- Abnormalities of fluid distribution: pregnancy,\(^ {42,43}\) in 0.34% to 25% of the cases, especially in the third trimester, with frequent signs of deficit in 37–85% of the cases; hypothyroidism,\(^ {44}\) and chronic kidney failure (arteriovenous fistula).\(^ {39}\)
- Abnormal or supernumerary muscle: deep palmar muscle,\(^ {45}\) intratunnel position of the muscle body of the superficial flexor\(^ {46}\) or proximal extension of the muscle body of the lumbrical muscles;\(^ {47}\)
- Persistent arterial hypertrophy of the median nerve;\(^ {48}\)
- Intratunnel tumor: lipoma, synovial cyst, synovial sarcoma or neural tumor (schwannoma, neurofibroma or lipofibroma);
- Hematoma: hemophilia,\(^ {49}\) anticoagulant accident\(^ {50}\) or trauma;\(^ {51}\)
- Obesity.\(^ {52}\)

**Dynamic carpal tunnel syndrome**

The pressure inside the carpal tunnel increases during wrist extension and flexion.\(^ {53}\) Repetitive extension and flexion movements of the wrist, along with flexion of the fingers and supination of the forearm, have been implicated in this increase.\(^ {54}\) Incursions of muscle bodies from the superficial and deep flexors of the fingers, when the wrist and fingers are extended, have been found in 50% of the cases.\(^ {55}\) This particular movement can be seen in occupational pathological conditions.\(^ {56}\)

**CTS and working on computers**

No increase in the prevalence of CTS in cases of working on computers for more than 15 h per week has been observed. A tendency toward increased prevalence has been demonstrated in cases of working on computers for more than 20 h per week.\(^ {57}\)

**Exposure to vibration**

Exposure to vibration is one of the lesser predisposing factors.\(^ {27,54}\) The ultrastructural consequences comprise microcirculatory compression problems and intraneural edema following injury of the myelin and axons.

**Acute carpal tunnel syndrome**

**Etiologies:**

- Trauma: displacement due to fracturing of the distal radius or dislocation of the wrist;
- Infection;
- Hemorrhage due to overdose of anticoagulant or in cases of hemophilia;
- High-pressure injection;
- Acute thrombosis of the artery of the median nerve;
- Burns.

**Diagnosis**

The clinical approach toward patients with acroparesthesia of the hand consists of five stages:

- Discuss the diagnosis from the consultation office, challenge tests, analyses on possible associated pathological conditions and differential diagnosis;
- Determine the etiology;
- Evaluate the severity of compression through discriminative sensitivity analysis on the Weber test and analysis on the strength of the thenar muscles innervated by the median nerve;
- Judge whether it is appropriate to perform complementary examinations, starting with electroneuromyography (ENMG);
- Propose treatment adapted to the severity of the condition, etiology, location and activity context.

It should be noted first of all that there is no gold standard for a positive diagnosis of CTS.

**Challenge tests**

The median nerve is accessible in front of the wrist flexion crease and behind the long palmar tendon or in the middle of the wrist.

- Tinel sign: the test is positive if the patient perceives paresthesia during manual percussion on the palmar face of the wrist at the level of the median nerve. The sensitivity is between 26 and 79% and the specificity is between 40 and 100%.\(^ {58}\)
The earliest and most sensitive electrical abnormality is a decrease in the sensory conduction velocity (possibly identified through the centimeter measurement method) between the palm of the hand and the fingers and wrist. A median transtunnel velocity <45 m/s in pathological cases can be accepted, versus normal values ≥50 m/s.63,64

This examination is operator-dependent. The skin temperature and age have an influence on the results. ENMG may be positive in 0–46% of asymptomatic subjects and negative in 16–24% of patients with a clinical diagnosis of CTS.65–68 Serror69 evaluated ENMG in cases in which the motor distal latency alone was studied and found sensitivity of 54% but specificity of 97.5%. ENMG does not provide supplementary evidence in diagnosing CTS in relation to the clinical evaluation, when the clinical diagnosis seems evident.70 Anatomical variations of the Martin–Gruber and Riche–Cannieu types may disturb the interpretation of the ENMG analysis of stimulation-detection.

The working group of the French National Agency for Healthcare Accreditation and Evaluation (ANAES)71 concluded the following:

- ENMG is situated after clinical examination;
- ENMG is not indispensable for diagnosing typical forms;
- ENMG is unnecessary before corticoid infiltration;
- ENMG is recommended in cases of doubt. It aids in making differential diagnoses;
- ENMG is recommended before making surgical decisions;
- ENMG is requested in recognizing occupational diseases.

Images

Wrist radiographs and incidence of CTS

In a study on 300 patients (477 cases),72 radiographic abnormalities were found in 33% of the cases, and 18.6% of the patients had lesions that could be involved in the appearance of CTS. None of these etiologies modified CTS treatment. In two cases out of the 477, the abnormalities required specific treatment. It was concluded that systematic radiographic examinations made insufficient contribution to be justified.

Radiographs of the wrist (face, lateral and carpal tunnel views) are useful in the following situations:73

- To explain the clinical examination;
- To explain the anamnasis.

Echography

Echography is operator and material-dependent. In the initial forms, the median nerve may conserve normal morphology. However, a median nerve of normal appearance does not rule out CTS. Echography may help in making an etiological diagnosis for morphological analysis of the content. The area of the median nerve is determined better on ultrasound at the level of the distal radius or the pisiform bone, which is considered to be the site of the proximal carpal tunnel and the expected location for maximum edema of the nerve. If an elliptical shape is assumed, the area of the nerve in the proximal carpal tunnel should not be greater than 10 mm.74
Magnetic resonance imaging (MRI)
MRI is rarely indicated, but may be useful for etiological diagnoses in the following situations:

- For examining secondary synovial pathological conditions;
- As part of diagnosing CTS in children or young adults, with the aim of detecting intratunnel muscle abnormalities, particularly in cases of CTS occurring through exertion or intratunnel tumors.

Final remarks
Detailed anatomical knowledge is fundamentally important for medical practice, given that anatomical variations, when unknown, may give rise to severe complications in surgical procedures. Clinical comprehension of a disease is only attained when its physiopathology and etiology are known; from this knowledge, possible treatments can be analyzed. Thus, although CTS is mostly idiopathic, other causes need to be determined in order to progress with adequate prevention and treatment. Another difficulty in clarifying this syndrome is the absence of any gold standard for confirmation. Hence, the diagnosis is primarily clinical and most of the tests that can be applied for evaluating its severity vary in sensitivity and specificity. Nonetheless, such tests are of great value for ruling out other possible pathological conditions.

Conflicts of interest
The authors declare no conflicts of interest.

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