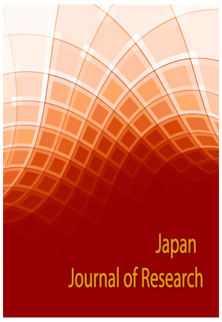

Study of Carpal Tunnel Syndrome Using Electroneurography and Ultrasound in a Spanish Cohort

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Carpal; electroneurography; syndrome; tunnel; ultrasound.

Abbreviations

AANEM: American Association of Neuromuscular and Electrodiagnostic Medicine; AMP: amplitude; BMI: body mass index; CTS: carpal tunnel syndrome; CSA: cross-sectional area; CSAc: carpal cross-sectional area; CSAf: forearm cross-sectional area; CV: conduction velocity; DML: distal motor latency; ENG: electroneurography; US: ultrasound

Abstract

Introduction: *Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. Its diagnosis is clinically supported by the electroneurography (ENG). The use of ultrasound (US) has increased in recent years. Our objectives are: to describe the ENG and US findings in patients with suspected CTS, based on age, sex and anthropometric data; and to study the correlation of both tests based on the severity of CTS.*

Material and methods: *prospective study of patients with suspected CTS who undergo ENG and US. ENG examination: antidromic sensory median at 3rd and 4th finger; distal motor of median. US: cross-sectional area (CSA) prior to or within the tunnel (higher values). Inclusion criteria: patients aged 18 to 85 years. Exclusion criteria: previous trauma or previous surgery for CTS or forearm, carpus or hand. Statistical study with the SPSS 29.0 program.*

Results: *400 nerves from 266 patients (52.59 ± 12.09 years) were studied, 183 women and 83 men. According to the ENG, 129 did not have CTS, 61 were incipient, 113 mild, 19 moderate and 75 severe. The mean CSA was 8.37 ± 1.21 mm² in non-CTS, 10.09 ± 1.45 mm² in early, 11.33 ± 1.87 mm² in mild, 14.63 ± 1.92 mm² in moderate and 15.46 ± 3.33 mm² in severe CTS, with a significance of $p<0.01$ (95% CI) in the ANOVA test. The highest and inverse correlation appears between the conduction velocities (CV) at the 4th finger with CSA (-0.816) and CV at the 3rd finger with CSA (-0.800), which coincides with the most sensitive ENG values for the diagnosis of CTS.*

Discussion: *CSA is an appropriate test as a complement to ENG in the diagnosis of CTS. However, it has limitations when establishing the cut-off point between normality and neuropathy, as well as when classifying based on severity.*

Introduction

Carpal tunnel syndrome (CTS) is the most common neuropathy in humans. It is characterized by compression of the median nerve at the level of the carpus, causing paresthesia in the fingers dependent on the nerve. It is more common in women, between the fifth and sixth decades of life, and with a preference for the dominant hand, although it can also be bilateral. In Western countries, it is estimated to have a prevalence of 10% of the total population. In most cases, its cause is idiopathic, and pathophysiologically it is characterized by compression of the median nerve as it passes through the carpal tunnel, which it passes through accompanied by nine flexor tendons [1].

The symptoms will depend on the degree of nerve involvement. The form of presentation is sinuous and quite stereotyped. Patients report, in mild stages, tingling in the middle finger and the medial edge of the ring finger, predominantly at night, when they are at rest, and in the absence of other external stimuli. Physical examination may show signs of Tinnel or Phalen [1,2]. Gradually, the tingling increases and spreads to the thumb and index fingers, and pain may appear in the wrist and a sensation of electric shocks that ascend to the elbow. This is accompanied by a loss of strength, which can be seen when grasping objects, buttoning up a shirt, etc. We are now talking about moderate stages. Finally, and paradoxically, the sensory discomfort disappears. The patient no longer reports tingling or pain, and if they do feel it, it is less intense. On the other hand, greater weakness and even muscle atrophy will appear in the thenar eminence. These are now severe cases. This is the characteristic clinical evolution of idiopathic CTS, and the majority. The diagnosis is essentially clinical, supported by complementary tests.

The reference test in the diagnosis of CTS is electroneurography (ENG) [1-5]. It

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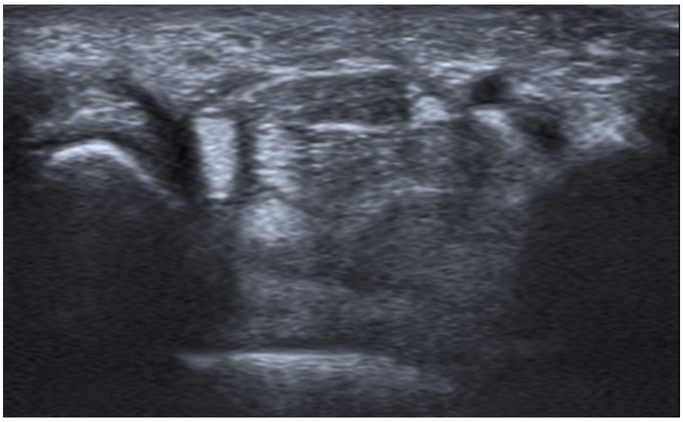

Figure 1. *CSA in a moderate CTS.*

allows studying the functionality of the nerve and making the differential diagnosis with a polyneuropathy or with a cervical radiculopathy. To date, it is the one with the greatest sensitivity and the greatest capacity to classify this neuropathy as mild, moderate or severe. As for the drawbacks, it can be uncomfortable for the patient, and its availability is not adequate in all health areas equally.

However, in recent years there have been multiple attempts to protocolize ultrasound (US) in this use, and dozens of studies have been carried out trying to find out which of the two tests has the greatest diagnostic performance in CTS [6-9]. Within US, several variables have been studied such as the cross-sectional area (CSA) of the median nerve at its entrance into the carpus, the thickness of the flexor retinaculum, or the height of the carpal tunnel in the axial plane (Figure 1). The most widespread and protocolized is the CSA of the median nerve at its entrance into the carpal tunnel, at the height of the pisiform bone. In essence, US allows studying the morphology of the nerve and its adjacent structures. It is harmless, comfortable for the patient, fast and inexpensive. However, it presents difficulties in establishing cut-off points between normality and neuropathy [8,9], as well as in establishing the severity of the latter. This makes it difficult to establish the surgical indication only with this examination. Even in the absence of clinical symptoms, it is not very specific.

Our objectives are: to describe the ENG and CSA findings in patients with suspected CTS, based on age, sex and anthropometric data; and to study the correlation of both tests based on the severity of CTS.

Material and methods

Prospective, descriptive, case series study, in which the quantitative values of ENG and US are analyzed, and associations between both and with age, sex and body mass index (BMI) are studied. The study has been approved by the Ethics Committee of the HM Foundation.

Inclusion criteria: patients aged 18 to 85 years with suspected CTS who have attended the Clinical Neurophysiology service of HM La Esperanza for ENG, between April and December 2023.

Exclusion criteria: patients with previous CTS or forearm, carpus or hand surgeries; previous significant trauma or fractures in the forearm, carpus or hand; underlying neuromuscular diseases, diabetes mellitus, acromegaly or rheumatoid arthritis.

ENG studies performed: antidromic sensory ENG of the middle to 3rd and 4th fingers; Antidromic sensory ENG from the ulnar nerve to the 4th and 5th fingers; in both, conduction velocities (CV) and peak-to-peak amplitudes (AMP) were studied. Motor ENG from the median nerve from the wrist and elbow; motor ENG from the ulnar nerve from the wrist; in both, distal latencies and amplitudes were studied. Natus KeyPoint equipment was used. The nerves examined were categorized into 4 groups: controls, on the one hand, and incipient, mild, moderate and severe cases on the other, based on the severity according to the ENG results. The recommendations of the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) are followed for this classification, but modified for the staging of severity [3,5]:

- **Incipient:** CV to the 4th lower finger or up to 49 m/s, with no difference of 0.5 ms with the 4th ulnar finger.
- **Mild:** CV at 4th < 49 m/s and difference equal to or greater than 0.5 ms in relation to the 4th ulnar finger. Distal motor latency (DML) < 4.2 ms.
- **Moderate:** CV at 3rd and 4th fingers up to 40 m/s or less and DML equal to or greater than 4.2 m/s.
- **Severe:** CV at 3rd and 4th fingers < 35 m/s, drop in the AMP at 3rd and 4th fingers and DML > 4.2 m/s.

US studies performed: transverse sections from the middle third of the forearm to the distal exit of the carpal tunnel. Longitudinal sections in the same region [5,10,11]. The presence of anatomical variants such as bifid or trifid nerves and persistent median artery has been assessed [11]. A Toshiba Aplio 400 device was used with a 12 MHz linear probe. The wrists were examined in the supine position and in the neutral position after the ENG examination. A clinical neurophysiologist performed the ENG and US scans. Subsequently, a musculoskeletal radiologist reviewed the images of each nerve, in a blinded manner, to avoid confirmation bias.

Statistical analysis was performed using the SPSS 29.0 program. Means and standard deviations were calculated for quantitative variables. The t-Student test was used to compare the means of two groups, while the ANOVA test was used to compare the means of three or more groups. The Kruskall-Wallis test was also used for an independent variable. Finally, the Spearman Rho test was used to calculate correlations between variables with a non-normal distribution.

Result

The study sample consisted of 400 median nerves from 266 patients, 183 women and 83 men. The mean age of the sample was 52.59 ± 12.09 years. The distribution of anthropometric data (age, sex, hand, height, weight and BMI and their relationship with the degree of involvement) are shown in Table 1.

According to the ENG examination, 270 nerves were cases and 130 controls. The controls had a mean CV at the 4th finger of 56.56 ± 3.66 m/s, and an CSAc of 8.37 ± 1.21 mm^2. The cases were divided into 4 groups based on the degree of involvement. Group 1 is made up of the incipient ones, with 61 nerves, which present signs of focal demyelination through the carpus, without criteria of neuropathy, and have presented a mean CV to the 4th finger of 49.24 ± 1.82 m/s and an CSAc of 10.09 ± 1.45 mm^2.

Group 2 is made up of the mild ones, with 113 nerves, and presents a mean CV to the 4th finger of 43.86 ± 2.71 m/s and a mean CSAc of 11.33 ± 1.87 mm^2. Group 3, the moderate ones, with 19 nerves, presents a mean CV to the 4th finger of 36.36 ±

Table 1. *Data of the sample under study.*

	Controls (129)	Cases (271)	Total (400)	p
Age (years)	47,31 ± 11,23	55,10 ± 11,68	52,59 ± 12,09	<0.001
Women (n // %)	97 // 75.1%	177 // 65.3%	274 // 68.5%	0.047
Men (n // %)	32 // 34.8%	94 // 34.7%	126 // 31.5%	0.047
Height (cm)	165,56 ± 9,66	164,48 ± 8,82	164,83 ± 9,10	0.270
Weight (kg)	71,69 ± 16,44	76,62 ± 15,88	75,03 ± 16,20	0.004
BMC	26,08 ± 4,89	28,06 ± 4,81	27,42 ± 4,92	<0.001
Hand R/L	64/65	151/120	215/185	0.252
Dominant yes / no	67/60	154/115	221/175	0.401
CSA carpal (mm^2)	8,37 ± 1,21	12,43 ± 3,16	11,12 ± 3,29	<0.001
CSA forearm (mm^2)	4,96 ± 0,88	5,31 ± 0,87	5,20 ± 0,88	<0.001
CSAc/CSAf	1,74 ± 0,34	2,40 ± 0,72	2,19 ± 0,70	<0.001

Table 2. *Correlations between ENG and US variables*

Rho de Spearman	CV 3º	AMP 3	CV 4º	AMP 4º	DML	Motor AMP
CSAc	-0.800	-0.559	-0.816	-0.598	0.740	-0.222
CSAf	-0.139	-0.023	-0.117	-0.017	0.106	-0.055
CSAc/CSAf	-0.625	-0.473	-0.660	-0.524	0.592	-0.166

3.16 m/s and an CSAc of 14.63 ± 1.92 mm^2. Group 4, the severe ones, with 75 nerves, presents a mean CV at the 4th finger of 25.09 ± 13.74 m/s and an CSAc of 15.46 ± 3.33 mm^2.

Neither height nor the fact of having a dominant hand, or a specific hand, right or left, have shown a statistically significant relationship with having CTS or not. The same has not happened with sex, which is more frequent in women, weight and BMI, which do have a statistically significant relationship with the presence of CTS.

In Figure 2 we can see the number of nerves classified according to their CSA and as cases or controls based on the results of the ENG. From 9 mm^2 there is a drastic drop in the controls, which points to that figure as the cut-off point for normality.

In Figure 3, in the box diagram, we can see the distribution of the mean CSA of the nerves grouped according to their degree of affectation. It can be seen that there is some overlap between the edges of the boxes, especially in severe cases, which may present greater variability, which will be influenced by the time of evolution of the CTS.

Finally, the correlations between the quantitative variables of the ENG and those of the ultrasound have been studied. The results are detailed in Table 2. The highest correlation, and inverse, appears between the mean CV at the 4th finger with CSAc (-0.816) and the mean CV at the 3rd finger with CSAc (-0.800), which coincides with the most sensitive ENG values for the diagnosis of STC, such as the CV at the 4th and 3rd fingers respectively. Another interesting fact is that the correlations between ENG and US values have been stronger with the CSAc than with the CSAc/CSAf ratio.

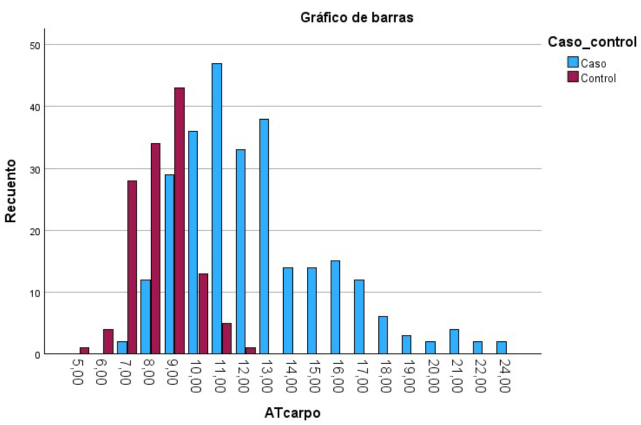

Figure 2. *CSA distribution based on cases or controls.*

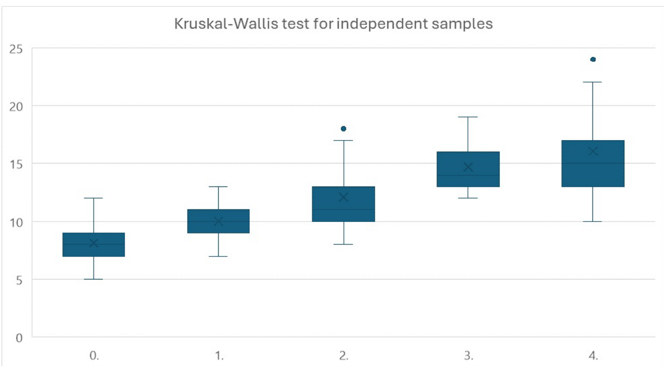

Figure 3. *Average of CSA as a function of severity according to ENG*

Discussion

Our study sample coincides on several points collected to date in other research and is one of those with the largest sample size in the Spanish population to date. On the one hand, there has been a statistically significant association between female sex and the presence of CTS, just as there is also a significant association between age, obesity or high BMI and CTS [1,2,12]. This last fact has already been included in several publications [12]. On the contrary, there has been no relationship with either height or type of hand, which suggests that the pathophysiology of CTS is independent of whether the hand is right or left or dominant or non-dominant. However, Tahmaz M et al., in a study in 2020, found a positive relationship between hand volume and CSA [13].

The study of the CSA of the median nerve in the carpus by US has been shown to be a reliable tool for the study of CTS, since its correlation with ENG is adequate (greater than ± 0.70). Both the CSA in the carpus (CSAc) and forearm (CSAf), as well as their quotient, have presented statistically significant associations, which coincides with the great majority of published studies [4,6-9,13,14]. However, ultrasound has presented two limitations: on the one hand, at the cut-off point, as can be seen in the bar graph (Figure 1) where there is significant overlap up to 9-10 mm^2. The other obstacle lies in the staging of CTS, based only on the CSAc, as can be seen in the box diagram (Figure 2). Nerves in a serious state according to ENG can present CSAc of 10 mm^2 or up to 24 mm^2, which has been the maximum in this sample. This disparity for severe cases coincides with what has already been reported in the literature, and will depend, to a large extent, on the time of evolution of CTS. In a complete sensory and motor axonotmesis, there will be a loss of intraneural volume and a progressive decrease in CSAc [2].

On the other hand, the highest correlations, and inverse ones (greater than 0.70 are significant) reside between the conduction velocities to the 4th and 3rd fingers, with the CSA of the median nerve in the carpus. The US value most sensitive to changes in ENG will be CSAc and it is the first to be assessed, although there have been attempts to protocolize the CSAc/CSAf ratio [4,8,14]. In addition, from the point of view of the expertise of the ultrasound examination it is simpler.

For these two reasons, US has limitations to replace ENG as the only test for the diagnosis and staging of CTS. However, it can be a good complement, since it will allow us to assess the morphology of the nerve throughout its course, and its relationship with the adjacent structures [5,7,11].

Aside from these findings, we must not forget that the diagnosis of CTS is fundamentally clinical, and that therapeutic decision-making must be based on the rational use of information obtained from the clinical history, physical examination and complementary tests such as ENG and US.

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