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TITLE

Ultrasonography and Nerve Conduction Study in patients with carpal tunnel syndrome, comparison between the two techniques before and after median nerve decompression surgery: observational study.

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Abstract

Purpose: Traditional evaluation of suspected carpal tunnel syndrome (CTS) involves a thorough history, physical examination, and nerve conduction velocity studies (NCS). The aim of the study is to evaluate whether ultrasound (US) is a valid alternative to the emg as a routine pre-operative examination, to evaluate patients with STC, comparing some us values with NCS findings pre and postopertively

Methods: Only patients with symptoms, clinical examination, and NCS findings consistent with CTS were included in the study, according to the inclusion criteria.

Four ultrasonographic variables were considered in treated patients: 1) CSPA (cross sectional pisiform area); 2) S-P dt: the largest diameter of the nerve in the same point; 3) Prox Area: the section area approximately 4 cm proximal to the pisiform; 4) Prox DT: the largest diameter in the same point.

Each of these values was measured pre and postoperatively (three months after surgery)

As for the emgraphic variables, the VCS and the SAP were taken into consideration, that is sensitive variables.

The NCS and the ultrasound values are compared

In this preliminary phase of the study, 25 patients were recruited.

Results: A significant correlation was found between "CSPA" and "SAP" before and after surgery, As if the CSPA could be a reliable parameter for the diagnostic evaluations of these patients, as well as for any postoperative or post-therapeutic evaluation.

Conclusions: Our results indicate that high-resolution ultrasound is informative in the evaluation of CTS and shows enlargement of the median nerve at the distal wrist crease in symptomatic patients. Therefore it is a reliable modality for imaging the wrist in patients with CTS. In addition ultrasound is well tolerated and safe.

The extended role of US in STC diagnosis awaits further definition, these are preliminary findings to be confirmed by further studies with larger sample size

Introduction

Compression of median nerve at the level of wrist causes the most common form of peripheral nerve entrapment neuropathy, known as Carpal Tunnel Syndrome (CTS).

The hallmark of classic CTS is pain or paresthesia (numbness and tingling) in a distribution that includes the median nerve territory, with involvement of the first three digits and the radial half of the fourth digit. The symptoms of CTS are typically worse at night and often in awaken patients from sleep. Some patients react to these symptoms by shaking or wringing their hands or by placing them under warm running water. Bilateral CTS is common at first presentation, affecting up to 65% of patients. The diagnosis is suspected when the characteristic symptoms and signs are present.

Provocative manoeuvres for CTS include the Phalen, Tinel, manual carpal compression and hand elevation tests. However, the sensitivity and specificity of these provocative tests is moderate at the best.

Considering the high incidence and prevalence reported for CTS and the considerable national healthcare costs associated, it is of paramount importance to define the most accurate and appropriate diagnostic approach.

Traditional evaluation of suspected carpal tunnel syndrome (CTS) involves a thorough history, physical examination (PE), and nerve conduction velocity studies (NCS), that is electromyography (EMG), the latter being a standard part of the evaluation for CTS. They are useful to support the diagnosis of CTS, to assess severity and to rule out other abnormalities.

The diagnosis is primarily dependent on results from the NCS. The main utility of EMG is to exclude other conditions, such as polyneuropathy, plexopathy, and radiculopathy. Although physiologic information is obtained based on nerve conduction studies (NCS), it has a specificity of 95% and a low sensitivity that ranges from 49% to 86%.

Imaging studies are not routinely employed in the evaluation for possible CTS. Several studies using sonography have shown that sonographic evaluation of median nerve, even if not routinely employed in CTS, provides further spatial information that can give assistance in determining aetiology, treatment planning and post-operative follow up. Nevertheless, few and not conclusive studies have focused on the potential advantages of ultrasound (US) as compared to NCS⁴. Considering lower costs, shorter examination time, less discomfort, wide availability and non-invasiveness of US modalities, it is important to better investigate and assess the value of sonography.

Aim of this study is to compare the EMG parameters with some selected ultrasound parameters in patients with STC, before and after the surgery, in order to evaluate if the US can be considered a reliable test, in addiction or alternative to EMG, in the preoperative evaluation of these patients, also in the perspective to replace the EMG in a not distant future.

Material and Methods

The study protocol was approved by Lazio 2 ethics committee. The study was conducted at the Plastic Surgery Division of the Policlinico Casilino, sited in Rome, between October 2016 and June 2018.

Phase 1: Patients' recruitment and Preoperative assessment

Each patient accessing in our clinics was interviewed by the same research staff member.

Only patients with symptoms, clinical examination, and NCS findings consistent with CTS were included in the study, according to the inclusion criteria.

Children, women with pregnancy-related CTS, patients with hereditary CTS (amyloidosis), renal failure patients with arteriovenous shunts in the arm, and patients with prior CTS surgery (on that hand) or if there was a known history of other systemic neurologic disorders were excluded from the study.

The diagnostic criteria of CTS included clinical history, symptoms and evidence of slowing of distal median nerve conduction. The clinical diagnosis of CTS was based on signs and symptoms of median nerve distribution, such as: (i) paresthesia, pain, swelling, weakness or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position or repetitive action of the hand or wrist that is mitigated by

a change in posture or by shaking of the hand; (ii) sensory deficits in the median nerve- innervated regions of the hand; (iii) motor deficit or hypotrophy of the median nerve-innervated thenar muscles; and (iv) positive provocative clinical tests (positive Phalen's maneuver and/or Tinel's sign). Anthropometric and demographic data, including age, height, body mass index (BMI), sex, occupation, ae well as medication history, hand dominance and underlying disorders associated with CTS, such as diabetes mellitus, rheumatoid arthritis, pregnancy, acromegaly or hypothyroidism, were collected.

Electrodiagnostic and ultrasonographyc evaluation were performed in patients who were suspected of having CTS. Four ultrasonographic variables were considered in treated patients: 1) CSPA (cross sectional pisiform area): that is the section area of the median nerve at the scaphopisiform level;

2) S-P dt: the largest diameter of the nerve in the same point; 3) ProxArea: the section area approximately 4 cm proximal to the pisiform; 4)Prox DT: the largest diameter in the same point.

Each of these values was measured pre and postoperatively

As for the emgraphic variables, the VCS and the SAP were taken into consideration, that is sensitive variables, considering that not all patients have motor alterations that is advanced stages of the disease.: In this preliminary phase of the study, 25 patients were recruited.

The study protocol was discussed in detail with patients and written informed consent was obtained in all patients.

Nerve conduction studies

Bio-electrical signals have been sampled in a quiet room with controlled temperature (24°), through a Medelec Synergy electromyographic device, Oxford Instruments Medical Ltd Manor Way, Old Woking, Surrey, GU22 9JU, UK, installed on a Personal Computer.

Patients underwent examination in semi-orthostatic position. Percutaneous electrodes Arbo Kendall all Q-trace, have been applied, connected to a pre-amplifier DIN 5 channel through cables with alligator clips endings. All samplings started after percutaneous earth electrode application.

Conduction studies of the median and ulnar nerves have been conducted according international standard protocols (Kimura J. Electrodiagnosis. In Diseases of Nerve and Muscle: Principles and Practice. 3rd ed. Philadelphia, PA: Davis; 2001. pp. 131–68; 180, 412-3. Buschbacher RM. Median nerve motor conduction to the abductor pollicis brevis. Am J Phys Med Rehabil. 1999;78 (6 Suppl):S1–8. Oh S. Anatomical and physiological basis for electromyography studies. In: Clinical electromyography nerve conduction studies. 3rd Edition. Philadelphia, PA, USA: Lippincott Williams & Wilkins, 2003. p. 3-13).

Compound Muscle Amplitude Potentials (cMAPs) were obtained within a 3 Hz–10 KHz frequency range; pre-amplifier gain has been adjusted to a monitor voltage division of 2 mV, and monitor time division was set at 10 msec. Sensitive Amplitude Potentials (SAPs) were obtained in a 20 Hz–2 Khz frequency range, pre-amplifier gain has been adjusted to a monitor voltage division of 20 μ V, monitor time division was 5 msec.

To evaluate motor median nerve axons we applied a couple of electrodes on the skin overlying the abductor brevis muscle, the recording cathode (+) on the muscle firepoint (most prominent portion), and the referring anode (-) on his distally sinewy insertion at the first phalanx. To evaluate ulnar nerve motor axons, the couple of percutaneous electrodes were set to overlie the fifth finger's adductor muscle, the recording cathode (+) on the muscle firepoint, and the referring anode (-) on its distally sinewy insertion at the fifth phalanx.

According to a standard antidromic sensory nerve study, sensitive median nerve axons have been tested by an cathode on the skin surface of the basis of the third finger referring to a distally placed anode at 4 cm of distance. Likewise, sensitive ulnar nerve axons were tested by an cathode on the skin surface of the basis of the fifth finger referring to a distally placed anode at 4 cm of distance.

Trunk nerve stimulation has been employed through a stimulator couple of percutaneous electrodes, standard inter-electrode distance of 3 cm and cathode-versus-anode conventional sampling method. Stimulus was a 70 mA constant current, depolarizing square-wave of manually adjusted 1-300 V and 0.1-0.2 msec width (respectively for SAP and cMAP sampling). Stimulus voltage has been manually adjusted to achieve the ceiling amplitude responses of cMAP and SAP. Trace-to-trace average until a maximum of 10 samples for each final record has been developed to determine the final SAP signal. To obtain the distal cMAP, from both median and ulnar nerves, the distal stimulus has been administered 7 cm along the course of the nerve trunk from the recording cathode. To achieve SAPs, the distance between cathodes has been set to 14 cm. Proximal stimuli to estimate Motor Conduction Velocity (MCV) have been provided, respectively, close to the course of the brachial artery on the volar skin surface of the elbow for the median nerve and just under the olecranon process for the ulnar nerve.

Bio-electrical signals have been processed through an analogic-digital conversion by computer. The onset and amplitude of cMAPs and SAPs

have been recognized off-line and manually revisited by well-trained operators. Digital values from the sampled data have been transferred in databases and tables, the latter offering an easier way to analyse study data.

Ultrasonography

Ultrasound of the wrist was performed by a 10/5 MHz linear array transducer. Patients were seated on a chair with the arms on the table positioning their palms up and their hands in neutral position.

The exam started performing a sagittal view of the median nerve to have an overview of its course positioning the probe at the midline between the radius and ulna with the center at the distal wrist crease.

This scan was helpful to obtain an axial cross-sectional view; it was supposed to consider the nerve length 5 cm proximal and 2 cm distal to the wrist crease. The nerve was scanned along its course and the maximum and minimum diameters were obtained. Median nerve was identified in a position anterior to the flexor tendons.

Although the area of the median nerve was calculated drawing a region of interest along the profile of the axial section of that nerve at the level of the distal wrist crease and at its proximal portion (5 cm from the wrist creae); the pisiform bone provided a consistent internal landmark. We observed that the maximum nerve area was calculated in various levels but distal measurement at pisiform level was obtained in all patients.

The median nerve area and diameters samplings were obtained three times for each level moving the probe in different angulations to reach the best perpendicular plan to the nerve; the smallest measurements were chosen. The area was calculated tracing along the inside of the echogenic surface of the median nerve.

All the measurements were obtained on magnified images because of the small dimensions of the examined structures.

We also classified the echogenicity of the nerve in ipo-anechoic, ipoechoic, isoechoic and iperechoic by referencing to the surrounding tendons.

Phase 2: Surgery

Selected patients performed EMG and US after clinical evaluation. Approximately two months after the visit, they underwent median nerve decompression surgery. Surgery was performed by the same operator and with the same technique.

Patients were placed in supine decubitus with the affected arm abducted 90 degrees on a table. Surgery was performed under local anesthesia and in ischemia by tourniquet. Mepivacaine was used with 2% adrenaline as

a local anesthetic, and infiltration occurred on the wrist flexion fold between the FRC tendon and the palmaris longus tendon and after a few minutes along the proximal palmar line at the axis of the iv finger, for about 2 cm.

After the skin incision, the transverse ligament was identified and dissected throughout its thickness, visualizing the median nerve through the sandmiller retractors.

Distally, the nerve was released until the adipose tissue appeared, proximally up to the antibrachial fascia.

At the end of the intervention the ischemic band was released and a good haemostasis was ensured, then the suture was carried out with Nylon 4/0 and a dressing with elastic-compression band up to the wrist.

After one week patients were re-evaluated and the dressing lightened. Stitches were removed after two weeks.

Phase 3: Postoperative assessment

Three months after the surgery, patients underwent a new clinical, neurological and ultrasound evaluation.

The neurological and ultrasound evaluation were performed with the same methods described above, by the same staff members.

Statistical analysis

Variation among pre- and post- surgery variables was explored through a permutation paired test (an approximation of the exact conditional distribution with 100.000 Monte Carlo samples). Linear correlation between ECO (CSPA; S-P dt; Prox Area; Prox dt) and EMG (VCS; SAP) variables was calculated by using Perason's correlation both in pre- and post- surgery. Univariate distributions were showed by using a gaussian Kernel Density Estimation (KDE) plot [Venables, W. N. and Ripley, B. D. (2002) Modern Applied Statistics with S. New York: Springer], with bandwidths chosen according to Sheather–Jones method [Sheather, S. J. and Jones, M. C. (1991) A reliable data-based bandwidth selection method for kernel density estimation. Journal of the Royal Statistical Society B 53, 683–690].

In order to estimate the values related to SAP and VCS two different multiple linear regression models were applied, using as regressors all the ECO variables and their iterations. To this end, a backward selection, starting from the full model including all of the iterations, was applied according to minimum Akaike Information Criterion (AIC) value. Anyway, in consideration of the small sample size, when appropriate a conservative approach was adopted by including in the model also regressors with an estimated coefficient corresponding to a p-value

<0.10. All analysis were performed by using RStudio (version 0.98.945, RStudio Inc., Boston, MA, USA) for the software R (3.3.2–2016-10-31, R Foundation for Statistical Computing, Vienna, Austria). Significance was set when p-value <0.05.

Results

Table 1 summarizes the comparison between US variables before and after surgery. A statistical significative decreasing was reported for CSPA (Δ : -8.40; p-value: <0.0001), S-P dt (Δ : -0.60; p-value: 0.0320), Prox Area (Δ : -2.32; p-value: <0.0001), while no statistical difference was highlighted for Prox dt (Δ : -0.26; p-value: 0.3278).

Variable	N	PRE°, mean (sd)	POST°, mean (sd)	Delta (Δ)	p-value
CSPA	25	13.36 (2.23)	4.96 (2.05)	-8.40	<0.0001
S-P dt	25	4.16 (1.19)	3.56 (1.03)	-0.60	0.0320
Prox Area	25	7.16 (2.58)	4.48 (1.99)	-2.32	<0.0001
Prox dt	23	3.30 (0.90)	3.04 (1.01)	-0.26	0.3278

Table 1. Comparison of ECO variables before and after surgery.

° PRE: before surgery, POST: after surgery.

In **Table 2** is reported the comparison for EMG variables. A clear significant increasing was documented for both the considered variables: VCS (Δ : +34.54; p-value: <0.0001), SAP (Δ : +23.89; p-value: <0.0001).

Variable	Ν	PRE°, mean (sd)	POST°, mean	Delta	p-value
			(sd)	(Δ)	
VCS	25	10.00 (10.00)	44.54 (8.59)	+34.54	<0.0001
SAP	25	5.12 (4.54)	29.01 (11.83)	+23.89	<0.0001

Table 2. Comparison of EMG variables before and after surgery.

° PRE: before surgery, POST: after surgery.

A significant correlation (Table 3) was found between "CSPA" and

"SAP" before surgery (r: -0.58; p-value: 0.0024) and after surgery (r:

0.41; p-value: **0.041**), only.

	Ν	VCS	p-value	SAP	p-value	
-pre°						
CSPA	25	-0.21	0.3135	-0.58	0.002	
S-P dt	25	0.11	0.5871	-0.24	0.257	
Prox Area	25	-0.09	0.6543	0.30	0.139	
Prox dt	23	-0.11	0.5016	0.41	0.053	
-post°						
CSPA	25	0.12	0.5519	0.41	0.041	
S-P dt	25	0.03	0.8965	0.01	0.972	
Prox area	25	0.05	0.8035	0.01	0.970	
Prox dt	23	-0.16	0.4679	-0.04	0.872	

Table 3. Pearson's (r) correlation between ECO and EMG diagnostic parameters.

° PRE: before surgery, POST: after surgery.

Figure 1 shows the univariate KDE distributions for "CSPA" (a) and "SAP" (b) and the bivariate (c) empirical distribution of the observed values for "CSPA" and "SAP", before and after surgery. The univariate analyses clearly depict the shifting of the two distributions between before and after surgery ("CSPA" decreases while "SAP" increases). The bivariate analysis (b) highlights the negative correlation before surgery (Pearson's r: -0.58) and the positive correlation after surgery (Pearson's r: 0.41) between "CSPA" and "SAP" (as reported in **Table 3**).

Figure 1. Univariate KDE distributions for "CSPA" (a) and "SAP" (b) and their bivariate (c) empirical distribution.



Legend: lines in Figure 1.c are related to correlations before (dashed) and after (solid) surgery.

Table 4 reports the estimated parameters of the multiple linear regression model for VCS using US variables as regressors. After stepwise selection of all the possible combinations of independent variables, the resulting model (p-value: <0.0001) showed an excellent fitting (adjusted Rsquared: 79.78%). Furthermore, no statistical association was found between VCS and Prox Area.

Coefficients		Estimations	p-value
α_0 (intercept)	561.300	0.0119	
α_1 (CSPA)		-35.725	0.0190
α_2 (S-P dt)		-130.342	0.0313
α_4 (Prox dt)		-154.599	0.0082
α ₅ (Pre/Post, ref.: "Pre")		-323.850	0.0297
α_{25} (S-P dt, Pre/Post)		86.869	0.0364
α_{12} (CSPA), S-P dt)		8.450	0.0421
α_{45} (Prox dt, Pre/Post)		100.925	0.0111
α_{14} (CSPA), Prox dt)		9.870	0.0140
α_{24} (S-P dt, Prox dt)		36.938	0.0217
α_{245} (S-P dt, Prox dt, Pre/Po	-24.712	0.0265	
α_{124} (CSPA), S-P dt, Prox dt)		-2.371	0.0341
Regression's p-value: < Ac		ljysted R-squa	red:
0.0001 79		.78%	

Table 4. Multiple regression linear model for VCS variable.

In Figure 2 is depicted the goodness of fitness of multiple linear regression model for VCS variable. The distance between the fitted and the observed values was dramatically small as already reported in Table 4 (adjusted R^2 : 79.78%).

Figure 2. Deviation of values estimated by the multiple linear regression model from observed VCS values.



Table 5 reports the estimated parameters of the multiple linear regression model for SAP using US variables as regressors. After stepwise selection of all the possible combinations of independent variables, the resulting model (p-value: <0.0001) showed an excellent fitting (adjusted R-

squared: 79.50%). This model followed a conservative approach by including also regressors with an estimated coefficient corresponding to a p-value <0.10.

Coefficients	Estimations	p-value
β_0 (intercept)	-745.547	0.0601
β_1 (CSPA)	57.781	0.0475
β_2 (S-P dt)	194.033	0.0397
β ₃ (Prox Area)	86.985	0.0168
β_4 (Prox dt)	215.170	0.0761
β ₅ (Pre/Post, ref.: "Pre")	975.729	0.0195
β ₁₅ (CSPA, Pre/Post)	-146.366	0.0022
β ₂₅ (S-P dt, Pre/Post)	-293.247	0.0066
β_{12} (CSPA, S-P dt)	-15.224	0.0491
β_{13} (CSPA, Prox Area)	-6.876	0.0374
β_{23} (S-P dt, Prox Area)	-22.205	0.0088
β ₄₅ (Prox dt, Pre/Post)	-294.045	0.0236
β_{14} (CSPA, Prox dt)	-16.214	0.0548
β_{24} (S-P dt, Prox dt)	-54.327	0.0453
β_{34} (Prox Area, Prox dt)	-23.200	0.0299
β ₁₂₅ (CSPA, S-P dt, Pre/Post)	55.357	0.0011
β ₁₃₅ (CSPA, Prox Area, Pre/Post)	-4.751	0.0222
β_{123} (CSPA, S-P dt, Prox Area)	1.775	0.0362

Tabella 5. Multiple linear regression model for SAP.

β ₁₄₅ (CSPA, Prox dt, Pre/Post)	45.988	0.0020	
β ₂₄₅ (S-P dt, Prox dt, Pre/Post)	88.168	0.0072	
β_{234} (S-P dt, Prox Area, Prox dt)		5.934	0.0164
β_{1245} (CSPA, S-P dt, DT Prox, Pre/Post:"Pre	")	4.177	0.0583
β ₁₂₄₅ (CSPA, S-P dt, Prox dt, Pre/Post:"Post"	")	-13.156	0.0052
β ₁₃₄₅ (CSPA, Prox Area, Prox dt,		1.811	0.0640
Pre/Post:"Pre")			
β ₁₃₄₅ (CSPA, Prox Area, Prox dt,		3.461	0.0104
Pre/Post:"Post")			
β_{1234} (CSPA, S-P dt, Prox Area, Prox dt)		-0.468	0.0657
Regression's p-value: < 0.0001	Adjy	ysted R-squared	d:
	79.5	0%	

Figure 3 depicts the goodness of fitness of multiple linear regression model for SAP. The distance between fitted and the observed values was dramatically small for this model, also, as reported in Table 5 (adjusted R^2 : 79.50%).

Figure 3. Deviation of values estimated by the multiple linear regression model from observed SAP values.



DISCUSSION

The study evaluate whether ultrasound is a valid alternative to the emg as a routine pre-operative examination, to evaluate patients with STC, before they undergo surgery for decompression of median nerve.

The study was performed at the U.O. of Plastic Surgery of the Casilino hospital, located in Rome.

25 patients were recruited in this first observational phase of the study, each of them underwent clinical evaluation; preoperative ultrasound and EMG; surgery; postoperative ultrasound and emg 3 months post-op.

Accurate diagnosis of CTS and its differentiation from other causes of hand morbidity is essential, particularly if the patient is a candidate for surgery. Currently, ultrasonography is a reliable method for the diagnosis of CTS. In comparison with NCS, ultrasonography does not evaluate the physiologic condition of the median nerve but may show swallowing and flattening of the median nerve. Many authors believe that ultrasonography can be an alternative method in comparison with NCS for the primary evaluation of CTS in daily practice, or propose the use of both.

Buchberger et al. were the first researchers who assessed the cross sectional area of the median nerve using a high resolution ultrasonography machine with a 7 MHz transducer to confirm previously reported magnetic resonance imaging of the carpal tunnel. Compression of the median nerve in the canal may increase diagnostic yield of the ultrasound.

The ultrasonographic measurement used in CTS diagnosis is the CSA of the nerve at various levels of the carpal canal, the flattening ratio, the swelling ratio and the increased palmar bowing of the flexor retinaculum. The sensitivity and specificity of ultrasonographic measures vary widely among studies. Many authors demonstrated that the increase in CSA at the tunnel inlet had the highest sensitivity and specificity; moreover, the measurement at this level was easier to perform. There was also disagreement about the exact localization of tunnel inlet.

Most authors considered the proximal edge of the flexor retinaculum, approximately at the level of the distal radioulnar joint, as the tunnel inlet, while others considered the pisiform bone and tubercle of the navicular bone as the landmarks. The sensitivity of the CSAs ranged from 48% to 89% and the CSA cutoff at which the value was considered abnormal varied from 9 to 15 mm

These discrepancies result from many factors: selection criteria of patients and controls, gold standard for diagnosis of CTS, electrodiagnostic methods, levels of CSA measurement and

ultrasonographic cut-off values.

Wong et al. measured cross-sectional areas of the median nerve at three different levels: immediately proximal to the carpal tunnel inlet, at the carpal tunnel inlet and at the carpal tunnel outlet. Using a classification and regression tree, they determined optimal threshold values for each of these levels and suggested diagnostic algorithms based on a combination of fixed cut-offs at two levels of the median nerve that differed for the left and right hands.

Some studies considered that differing demographic and biometric features, such as older age, male gender, body mass index and handedness, may contribute to the range of normal values. However, the debate still remains; another study found no significant association between biometric characteristics of subjects and median nerve CSA at wrist and forearm in their well-matched case controls. Thus, it can be said that the range of normal values for median nerve CSA in the literature more likely reflects variations in study design and ultrasonographic technique.

For this reason, as well as for the small sample, this study doesn't want consider the value of CSA, but to evaluate the correlation between this,

among ultrasound parameters, and the NCS, before and after surgery.

In this study we talk about CSPA (cross sectional pisiform area) to indicate the cross sectional area at the pisiform bone, so as to objectively identify the location of the point of the median nerve that is measured to evaluate the area.

There are several existing studies on ultrasound evaluation of patients with STC, all these studies fundamentally correlate these parameters with the same parameters in normal patients

To our knowledge to date this is the only study that evaluates the affected patients with NCS and ultrasound both pre and postoperatively

EMG represents the gold standard instrumental examination to evaluate patients with STC, and is now a fundamental preoperative examination to justify median nerve decompression surgery, even for medicolegal purposes.

In this study, NCS were compared with some ultrasound parameters belonging to patients with STC, before and after the median nerve decompression surgery, in order to evaluate if the ultrasound could be considered in the future a reliable test as the EMG and one day replace the latter in the evaluation of these patients. Studies in the literature have so far evaluated the ultrasound values of patients affected by CTS and compared with those of healthy patients. This study deals with the subject in a different way.

We evaluated the ultrasound values of affected patients and put them in relation to the NCS. We did this both before and after median nerve decompression surgery.

We did this to understand if the trend in ultrasound values mirrored that of NCS in the few treated patients.

Table 1 evaluates mean values of the ultrasound variables, before and after nerve decompression.

A significant reduction of the cross-sectional pisiform area (CSPA); pisiform dt; prox area variables is observed.

These data indicate that there is a reduction of these values given by the removal of the inflammatory-compressive component on the nerve. The same thing occurs for the average US parameters (SAP and VCS), as shown in table 2. For both, a significant increase in values is observed. Table 3 represents the heart of the study. The NCS and the ultrasound values are compared.

It is observed that there is a correlation only between the trend of CSPA value and the SAP, both before and after surgery

The CSPA values and the SAP in particular have a significant correlation both before and after surgery, and their average trend is therefore comparable in the treated patients. As if the CSPA could be a reliable parameter for the diagnostic evaluations of these patients, as well as for any postoperative or post-therapeutic evaluation.

Figure 1 shows the univariate KDE distributions for "CSPA" (a) and "SAP" (b) and the bivariate (c) empirical distribution of the observed values for "CSPA" and "SAP", before and after surgery. The univariate analyses clearly depict the shifting of the two distributions between before and after surgery ("CSPA" decreases while "SAP" increases). The bivariate analysis (b) highlights the negative correlation before surgery (Pearson's r: -0.58) and the positive correlation after surgery (Pearson's r: 0.41) between "Area SP" and "SAP" (as reported in **Table 3**).

Table 5 reports the estimated parameters of the multiple regression model for SAP using ECO variables as regressors. After stepwise selection of all the possible combinations of independent variables, the resulting model (p-value: <0.0001) showed an excellent fitting (adjusted Rsquared: 79.50%). This model followed a conservative approach by

including also regressors with an estimated coefficient corresponding to a p-value<0.10.

In patients with CTS, anatomical evaluation of the carpal tunnel is a strong plus in diagnosis and management. Chronic focal compression of the median nerve can lead to alteration in its morphology and cause demyelination by mechanical stress, deforming the myelin lamellae. Ischaemia can account for the intermittent paraesthesia that can occur at night or with wrist flexion [39]. Imaging techniques were unimportant in the assessment of CTS until recently.

Sonography measures a different parameter (structural pathologic abnormalities of nerve swelling) from that (physiological malfunctions of the median nerve) measured at an electrodiagnostic study. It is possible that some patients who have CTS that is detectable at sonography may have swelling of the median nerve that is not severe enough to cause impairment in conduction. Therefore one must understand the limitations of an electro- diagnostic study concerning its sensitivity and specificity.

Considering the small number of treated patients, an ultrasound (cutoff) value of the CSPA has not been established within the study, beyond which to speak of STC. This can be done through a multi-center study

that evaluates thousands of patients.

The objective of the study is another, to underline the tendency to the correlation between CSPA and sap, the two most significant parameters. the CSPA could therefore be considered as the US parameter to be evaluated in the diagnosis of these patients.

Moreover this is a parameter that is clearly identifiable from an anatomical point of view

Although the data in this study suggest that US is effective in the diagnosis of CTS, the extended role of US in that diagnosis awaits further definition. In the past, the electrodiagnostic study has had other roles in the treatment of CTS. Grading systems for the severity of CTS that are based on elec- trodiagnostic study results have been devised. In addition, electrodiagnostic study results can be used to identify other conditions that mimic CTS, such as cervical radiculopathy, poly- neuropathy, or other median nerve en- trapment syndromes. Whether sonography plays a role as a predictor of treatment response or a role in the differentiation of CTS from conditions that simulate CTS remains unknown.

Moreover sonography is an operator-dependent test, and appropriate experience is required to ensure reliability and repro- ducibility. With

appropriate training of operators, however, this issue can be resolved readily.

In conclusion, high-frequency US examination of the median nerve and measurement of its cross-sectional area should be strongly considered as a new, alternative diagnostic modality for the evaluation of CTS. It offers high diagnostic accuracy, as indicated by high correlation with the present standard EMG as well as patient-oriented measures. In contrast to these two tools, US provides information about the possible causes of CTS and hence has a therapeutic impact regarding the management of the patients. US provides a reliable method for following the response to therapy.

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