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Clinical Study

Sonographic differences in carpal tunnel syndrome with normal and abnormal nerve conduction studies

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ABSTRACT

We evaluated the differences in sonographic parameters in carpal tunnel syndrome (CTS) patients with normal and mildly abnormal nerve conduction studies (NCS). This was a prospective cross-sectional study. We assessed 169 wrists (101 patients) with a clinical diagnosis of carpal tunnel syndrome (CTS), as well as 20 healthy controls (40 wrists). 49 wrists were classified as mild NCS-positive and 38 as NCS-negative based on our laboratory NCS normal values. The cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet and mid-forearm were measured and the wrist-to-forearm ratio (WFR) was calculated. 26% of the NCS-negative group had abnormal CSA. The CSA and WFR also differed significantly between the two groups. There was significant correlation between the sonographic and electrophysiologic variables. Ultrasound was diagnostic for CTS in a third of the NCS-negative wrists. Ultrasound may be useful in clinical CTS patients with normal or borderline NCS.

1. Introduction

Carpal tunnel syndrome (CTS) is the commonest entrapment neuropathy and is due to compression of the median nerve at the wrist [1]. There is still no gold standard for the diagnosis of CTS and a clinical diagnosis is usually reached on the basis of characteristic symptoms and signs, with confirmation by nerve conduction studies (NCS) [2]. However, NCS remains normal in 15% of patients with characteristic clinical features of CTS [3].

In the last few years, ultrasonography (US) has been shown to be a useful diagnostic tool in CTS [4–6]. Ultrasound is painless, non-invasive, and provides a view of the anatomy of the nerve, as well as of surrounding structures. There is currently Class A evidence showing that sonographic measurement of the median nerve cross-sectional area (CSA) may be used as a diagnostic test for CTS [7]. Furthermore, several studies have shown that the median nerve CSA at the wrist correlates well with clinical and electrophysiological severity [8–13].

A few studies have also reported on the diagnostic utility of ultrasound in clinical CTS patients in whom NCS are normal [14–16]. These patients often referred to as NCS-negative CTS patients have typical clinical features of CTS, including positive provocative testing, and yet electrodiagnostic testing for CTS may be normal. Some studies have reported sonographic abnormalities (diagnostic of CTS) in up to 50% of this population.

Most of the studies that have evaluated the sonographic characteristics of NCS-positive and NCS-negative CTS have included patients with varying grades of severity, ranging from mild lesions to severe (or sometimes complete) lesions. The inclusion of patients with severe lesions has the tendency to overstate the sonographic differences between these groups. A less biased approach will be to include only NCS-positive CTS patients with mild NCS abnormalities.

In this study, our aim was to explore potential differences between CTS patients with mild electrophysiological abnormalities and CTS patients who had completely normal NCS. Our aim was to determine if there were differences in the sonographic parameters between these two groups.

2. Methods

We examined 169 wrists from 101 consecutive patients referred to our Neurophysiology laboratory with a clinical diagnosis of CTS which met the American Academy of Neurology (AAN)/

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American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) clinical diagnostic criteria. These can be summarized as nocturnal and/or activity-related sensory symptoms, sensory deficits in the median nerve distribution, and weakness and/or atrophy of median-innervated thenar muscles [3]. Patients with peripheral neuropathy, traumatic nerve injury and previous wrist or CTS surgery as well as those less than 18 years of age were excluded from this study. The study was approved by the local research ethics committee and informed consent was obtained from all study participants.

A cohort of 20 age and gender-matched healthy controls (40 wrists) were also examined.

2.1. Nerve conduction studies

All studies were conducted with skin temperature maintained above 32°C. Orthodromic recording of the median nerve sensory nerve action potential (SNAP) was obtained following stimulation of the index finger with ring electrodes. The onset latency, peak amplitude, and sensory conduction velocity (SCV) were noted. The median nerve compound muscle action potential (CMAP) was recorded from the abductor pollicis brevis muscle following median nerve stimulation at the wrist. The distal motor latency (DML) and peak amplitude of the CMAP were also measured. Comparative sensory studies (orthodromic median and radial conduction with ring electrode stimulation from the thumb and recording from the wrist; orthodromic median and ulnar conduction with ring electrode stimulation from the 4th digit and recording from the wrist) and needle electromyography were performed when indicated.

The severity of CTS was graded as mild, moderate, or severe based on the following criteria [17]:

- Mild – prolonged median sensory distal latency. No evidence of axon loss.
- Moderate – prolonged median sensory and motor distal latency. No evidence of axon loss.
- Severe – Any of the aforementioned NCS abnormalities with evidence of axon loss as defined by either: (1) an absent or low-amplitude SNAP; (2) a low-amplitude or absent thenar CMAP; or (3) a needle EMG with fibrillation potentials or motor unit potential changes (large amplitude, long-duration motor unit potentials, or excessive polyphasia).

2.2. Ultrasonography

Sonographic examination of all the subjects was performed using a MyLabOne system with a 10–18 MHz probe (Whiteley Diagnostics, Esaote, Italy). The median nerve in the carpal tunnel and mid-forearm were imaged in both the transverse and longitudinal planes. The ultrasound probe was kept perpendicular to the nerve in order to maintain reproducibility of results. The median nerve cross-sectional area (CSA) was measured (in mm^2) at the carpal tunnel inlet (at the level of the pisiform bone) and mid-forearm (junction of the middle and distal third) by outlining the inner margin of the epineurium using the continuous trace method [7], and a wrist-forearm ratio (WFR) was then calculated [18]. (Fig. 1). For bifid nerves, both CSAs were recorded and averaged. Two separate CSA measurements were obtained at each site and the average value was used.

2.3. Data analysis

Statistical analyses were conducted using SPSS (version 22.0, SPSS Inc., Chicago, IL, USA). Normality of all continuous variables was tested using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Descriptive statistics (mean and standard deviation) were applied for data analysis. The Wilcoxon signed-rank test was used to test the differences between the means of the groups and statistical significance was defined as $p < 0.05$. Spearman coefficients were calculated to determine the correlation between ultrasonographic (median nerve CSA and WFR) and NCS parameters of CTS.

3. Results

Of the 169 wrists with a clinical diagnosis of CTS, 131 (77.5%) were confirmed to have CTS on NCS. The remaining 38 (22.5%) had negative NCS. 20 healthy controls (40 wrists) were also studied. Of the 131 NCS-positive wrists 49, 41 and 41 were classified as having mild, moderate and severe CTS respectively. We determined the optimal cut-off value for the detection of mild CTS using the median nerve CSA to be 11.4 mm^2 (sensitivity = 71%; specificity = 97.5%). For the WFR, the cut-off value for mild CTS was estimated to be 1.53 (sensitivity = 60%; specificity = 92.5%). Data obtained from mild NCS-positive patients was compared with the NCS-negative group. Two patients had complete lesions with no recordable sensory or motor potentials. The baseline characteristics are listed in Table 1.

The mean median nerve CSA was 13.2 ± 3.5 mm^2 for the mild NCS-positive group, 10.1 ± 2.4 mm^2 for NCS-negative wrists and 9.3 ± 1.2 mm^2 for the healthy controls. Similarly, the mean WFRs were 1.63 ± 0.38, 1.38 ± 0.30 and 1.19 ± 0.17 respectively. As shown in Figure 2, there was a significant difference between the median nerve CSA of the mild NCS-positive group, NCS-negative group and healthy controls. The WFR also differed significantly between all groups. There was a strong correlation between the CSA and WFR ($r = 0.726$, $p < 0.001$). In the mild NCS-positive group, 67% had enlarged CSA at the wrist compared with 26% of the NCS-negative wrists ($p < 0.0001$). Similarly, 57% of the mild NCS-positive group had abnormal WFR compared to 32% in the NCS-negative group ($p < 0.0001$).

As shown in Table 2, the following variables correlated well with the median nerve CSA at the carpal tunnel inlet: SCV ($r = -0.564$, $p < 0.0001$), SNAP amplitude ($r = -0.574$, $p < 0.0001$), DML ($r = 0.523$, $p < 0.0001$) and CMAP amplitude ($r = -0.216$, $p < 0.01$). Furthermore, the following variables were correlated with the WFR: SCV ($r = -0.552$, $p < 0.0001$) SNAP amplitude ($r = -0.465$, $p < 0.0001$) and DML ($r = 0.454$, $p < 0.0001$).

In the moderate and severe NCS-positive groups, the mean median nerve CSA was 14.0 ± 3.0 mm^2 and 18.2 ± 6.2 mm^2 respectively. Similarly, the mean WFR for both groups was 1.81 ± 0.33 and 2.23 ± 0.71 respectively. There was significant correlation between the sonographic parameters and electrophysiological severity ($r = 0.608$, $p < 0.0001$ for CSA, $r = 0.547$, $p < 0.0001$ for WFR). This further demonstrates the relationship between nerve structure and function, as well as the potential benefit of ultrasonography in assessing CTS severity.

Bifid median nerves were found in 16 wrists (10%) but there was no significant difference between NCS-positive group, NCS-negative group and healthy controls ($p = 0.63$). A persistent median artery was identified in two NCS-positive patients and one NCS-negative patient. Analysis of the data with and without these patients made no difference to the overall conclusions.

4. Discussion

This study has shown that there are significant sonographic differences between clinical CTS patients with normal NCS and those with mild NCS abnormalities. We have demonstrated that the CSA (and hence WFR) is smaller at the wrist in NCS-negative patients than in mild NCS-positive patients. The significance of these