Ultrasonography for the diagnosis of carpal tunnel syndrome: correlation of clinical symptoms, cross-sectional areas and electroneuromyography

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Abstract
This study evaluates the usefulness of ultrasonography in diagnosing carpal tunnel syndrome (CTS). The cross-sectional area of the median nerve was measured at the forearm and its entry into the carpal tunnel and compared with clinical symptoms and electroneuromyography. A total of 124 patients were examined, 77 patients with clinically confirmed CTS and 47 controls. A significant correlation was found between the ultrasonography cross-sectional area values at entry points into the carpal tunnel and electroneuromyography. The highest sensitivity (87%) and specificity (91%) for different cut-off values (8.5–12.5 mm²) of the cross-sectional area was for 11.5 mm². The use of ultrasonography may provide a quick and reliable differential diagnostic tool for the primary diagnosis of CTS in patients with classical symptoms.

Level of evidence: II

Keywords
Carpal tunnel syndrome, ultrasound, hand surgery, ENMG, Tetron’s test, cross-sectional area

Introduction
The lack of a gold standard remains problematic for the diagnosis of carpal tunnel syndrome (CTS). Traditionally, CTS is diagnosed by nerve-conduction studies (Sonoo et al., 2018; Torres-Costoso et al., 2018); however, there are variations in the cut-off points used for determining what constitutes abnormalities. Nerve conduction studies can also produce both false-negative and false-positive results (Fowler et al., 2019; Torres-Costoso et al., 2018); furthermore, the studies can be time consuming, expensive and painful. Several clinical diagnostic tests and criteria have been described to evaluate these symptoms in CTS (Amirfeyz et al., 2011; Hsu et al., 2015; McCabe, 2010). The American Association of Surgery has recommended a validated diagnostic tool for CTS known as CTS-6, including numbness and tingling in the median nerve distribution, nocturnal numbness, weakness, atrophy of the thenar musculature, positive Tinel’s sign, positive Phalen’s test and loss of 2-point discrimination (Surgeons, 2016). As the number of positive findings on the tool increases, the probability of having a true diagnosis of CTS increases (Graham, 2008). However, on the basis of recent studies, physical tests alone cannot be regarded as reliable screening methods for CTS (Dale et al., 2011; Izadi et al., 2018) even with the CTS-6 criteria, as clinical accuracy is not always 100% and additional diagnostic criteria are recommended (Surgeons, 2016).
Ultrasonography has been proposed as an alternative method for diagnosing CTS (Roll et al., 2011). In CTS, nerve compression results in a localized circulatory disturbance with collapse of the blood–nerve barrier (Sugimoto et al., 1994) resulting in increased endoneurial fluid pressure, with resultant nerve swelling and further impairing of the local blood flow. In CTS, therefore, swelling of the nerve at the carpal tunnel, as shown by ultrasonography, is recognized as a sign of compression within the tunnel (Roll et al., 2011). The quality of ultrasonography (US) images has markedly improved in the past decade due to emergence of ultrahigh-frequency transducers. In addition, high-quality US devices have become significantly cheaper, which makes it possible to acquire and use these devices in routine hand surgery practice. Despite this, there are ongoing debates about the best location to measure the median nerve and the thresholds for confirming the diagnosis of CTS (Ng et al., 2018; Pan et al., 2016; Torres-Costoso et al., 2018). Such information may be helpful in establishing the use of ultrasonography in a routine outpatient clinic visit. The aim of this study was to evaluate the diagnostic accuracy of ultrasonography in diagnosing CTS and its correlation with other modalities, such as clinical examination and electroneuromyography.

Methods

This prospective study was approved by the institutional review board. Written informed consent was obtained from all participants. A total of 124 consecutive patients (247 wrists) who presented with symptoms of CTS and other hand conditions, like cubital tunnel syndrome, masses (ganglions, cysts, tumours) or tendinitis, were examined between April 2018 and May 2018. Patient age, sex, height, weight, disease history and smoking status were recorded. Symptoms indicating CTS, including numbness, nocturnal paraesthesia, shaking of hands, dropping of items and positive Tetro’s test (thumbs over carpal tunnel and holding pressure and flexion for 30 seconds), were recorded (Tetro et al., 1998). Patients were given one point for each symptom present and a score of two or more points indicated clinical CTS. Seventy-seven patients had clinically confirmed CTS and 47 patients were nonsymptomatic for CTS but had other hand problems. The baseline characteristics of the cohorts are presented in Table 1. Only one hand per patient was used for analyses in patients with bilateral symptoms and this was the right hand except where the only symptoms were in the left hand. The duration of clinical history was over 1 year in 62 cases (range 4 months to 25 years).

Ultrasonography assessment of the median nerve

An ultrasound device (Samsung Medison Co. Ltd, Seoul, South Korea) with LA 3-14 MHz AD linear HD transducer was used. The patients were seated in a comfortable position, facing the examiner with their hands resting on a firm surface and fingers semi-flexed. The patients extended their forearms on a flat surface in the supine position with their fingers semi-extended. The cross-sectional area of the median nerve was measured at the following two levels: 10–12 cm proximal of the wrist crease diameter (Figure 1(a)), and just proximal to the entry into the carpal tunnel where the nerve had the largest diameter (Figure 1(b)). The ultrasound traced the outline of the nerve by measuring the cross-sectional area, perpendicular to the course of the nerve just at the hyperechoic epineurial boundary of the nerve. In case of a bifid nerve, both areas were measured together as one.

| Table 1. Demographic data of the clinical CTS patients and control patients in 124 patients. |
|-----------------------------------------------|
| Clinical CTS | Control group | p-value |
|----------------|--------------|---------|
| Patients [number] | 77 | 47 | |
| Gender (women/men) | 53/24 | 33/14 | 0.506 |
| Age [years] | 59 [29–87] | 48 [19–80] | 0 |
| Weight [kg] | 86 [50–145] | 79 [58–112] | 0.169 |
| Height [cm] | 168 [151–189] | 168 [154–187] | 0.486 |
| Body mass index | 30 [20–51] | 28 [20–41] | 0.178 |
| Diabetes | 13 | 2 | 0.027 |
| Hypothyroidism | 14 | 2 | 0.018 |

CTS: carpal tunnel syndrome.
An experienced hand surgeon (MR) of Level 3 experience according to Tang and Giddins (2016) and who have received training in ultrasonography examination measured the cross-sectional area of consecutive patients for a 2-month period in the outpatient department. The results were then compared with the findings of clinical symptoms and the electroneurography results.

Nerve conduction studies were available in 82 patients, these were taken alternatively before or after the clinic visit, and all results correlated with the US measurements. The following parameters were measured for the diagnosis and grading of CTS: distal motor latency (DML), motor conduction velocity (MCV), amplitude of the compound muscle action potential (CMAP) and of the sensory nerve action potential (SNAP), and the sensory wrist-to-digit and palm-to-wrist conduction velocities (SCV). Diagnosis of (at least mild) CTS was made if DML was >4 ms, if any of the SCVs were <50 m/s, or both, with significant differences (>10 m/s) between corresponding ulnar SCV. From electroneurography reports, data were collected on MCV (ms), DML (ms), CMAP (palm–wrist) and CMAP (elbow–wrist), SCV (m/s), SNAP (\mu V), palm to wrist SCV and temperature for linear analysis.

### Statistical analysis

An independent \( t \)-test was used to compare age, weight, height, BMI and inlet cross-sectional area and wrist-to-forearm values between the clinical CTS and the control groups. Linear regression analysis was used to evaluate the correlation between clinical symptoms measurements and weight, height, age (under or over 65 years), cross-sectional area and nerve conduction studies. The cut-off values with the highest sensitivity and specificity for the cross-sectional area and wrist-to-forearm ratio were determined by receiver operating characteristic (ROC) analysis. A chi-squared test was used to examine the relationships between the results of clinical, ultrasonography and electroneuromyography results.

### Results

There were no statistical differences in patient demographics when comparing age or sex in the clinically confirmed CTS patients. A greater proportion of patients in the CTS group had diabetes and hypothyroidism (Table 1). There were two patients diagnosed with bifid median nerve by ultrasonography. The mean cross-sectional area in clinically confirmed CTS patients was significantly higher as compared with the control group (Table 2). A significantly higher wrist-forearm ratio of the median nerve was also observed for the CTS group than for the control group (Table 2).

In ROC analysis, a cross-sectional area cut-off value of 11.5 mm\(^2\) yielded a sensitivity of 87% and a specificity of 91% (Figure 2). There were four false positive patients with inlet cross-sectional area over 11.5 mm\(^2\) and only one symptom for CTS and these were therefore recorded as control patients. Three of these had positive electroneuromyography studies. There were ten false negative patients having more than one symptom of CTS, even though their cross-sectional area was under 11.5 mm\(^2\). Of these, five were over 75 years old with symptoms over 2 years of duration. Six of these ten had positive electroneuromyography studies and one had a ganglion in the carpal tunnel area. The relation between clinically diagnosed CTS and ultrasound confirmed CTS, as well as clinically diagnosed CTS and electroneuromyography confirmed CTS was statistically significant (Table 3).

### Discussion

In this study, a statistically significant correlation was observed between clinically diagnosed CTS and the
cross-sectional areas of the nerve at its entry into the carpal tunnel and at the forearm level. We also found a statistically significant correlation between clinically diagnosed CTS and electroneuromyography diagnosed CTS. This is consistent with previous studies suggesting that ultrasonography might be a useful tool in diagnosing CTS (Fowler et al., 2014; Moschovos et al., 2019).

Many attempts have been made to find new additional sonographic parameters to characterize the median nerve in patients with CTS. Sensitivity in scanning might be increased if the tunnel outlet measurements were also included (Csillik et al., 2016). In our study, the entry area and wrist-to-forearm ratio measurements were analysed, as these were easily measured during the outpatient clinic visit. The wrist-to-forearm ratio did not increase sensitivity or specificity compared with the inlet area measurement according to the ROC analysis.

There is some overlap in distributions between normal or pathological cross-sectional area values. Normal measurements from the inlet area are between 8 and 14 mm² (Pan et al., 2016); this variation is possibly due to issues of resolution, machine settings, patient size and individual examination technique. In most studies, the set cut-off value of cross-sectional area is 9 to 11 mm² (Tai et al., 2012). In our study, the mean cross-sectional area of control groups was 9.6 mm². In one study it was noted that the lower cut-off point for inlet cross-sectional area made it more sensitive for CTS diagnosis. Sensitivity reached 99% when the cut-off point was set as low as 10 mm². However, the low cut-off point of 10 mm² resulted in a low specificity value (71%), which increased the number of false positives (Fu et al., 2015). In our study, the best cut-off was over 11 mm²; at a cut-off point of 11.5 mm, only ten false-negative and four false-positive findings were observed.

Although electrodiagnostic testing is largely considered the reference standard for confirmation of a clinical diagnosis of CTS, false-negative results can still result as electroneuromyography tests only larger fibres. If there is no myelin deficiency, the electroneuromyography results may remain negative, for example, in mild compression or if the compression is posture dependent. In our study, we were able to find a good correlation between the diagnosis of CTS by neurophysiological studies and clinical symptoms (Table 3), in contrast to a recent study which suggested that electroneuromyography has a low specificity for CTS diagnosis (Wang et al., 2018).

In our study, there were five wrists in elderly patients over the age of 75 that showed severe disease in electroneuromyography but no signs of nerve enlargement in ultrasonography. According to one study, elderly patients with long-lasting CTS may have minimally enlarged or even normal median nerve cross-sectional area and may be poor candidates for any kind of therapy (Miwa and Miwa, 2011). All five patients in our series had symptoms longer

| Variable          | Clinical CTS $n = 77$ | Controls $n = 47$ | $p$-value |
|-------------------|-----------------------|-------------------|-----------|
| Inlet CSA         | 15.0 (6.0–28.0)       | 9.6 (6.0–19.0)    | <0.001    |
| Forearm           | 7.5 (6.0–10.0)        | 7.0 (5.0–10.0)    | 0.183     |
| Wrist–forearm ratio | 2.0 (1.0–3.8)          | 1.4 (1.0–2.4)    | <0.001    |

CTS: carpal tunnel syndrome; CSA: cross-sectional area.
than 2 years and, in these cases, generalized nerve atrophy might have led to decreased nerve swelling over time. We recommend that ultrasonography results in elderly patients be interpreted with caution and priority be given to clinical examination and electroneuromyography for the diagnosis of CTS.

In some hand surgery centres, including our own tertiary clinic, every patient with suspected CTS undergoes electroneuromyography tests before invasive treatment (Sonoo et al., 2018). However, there is widespread consensus among hand surgeons that such tests are not necessary for all CTS patients to confirm diagnosis (Fowler, 2017; McCabe, 2010; Zyluk and Szlosser, 2013; Zyluk et al., 2014). If confirmation is desired, ultrasonography can be performed instead, as it is rapid and painless. Additionally, space-occupying lesions, such as ganglia, neural tumours and tenosynovitis, can be additionally diagnosed with US and not with electroneuromyography.

We believe that the use of ultrasonography requires a short learning curve for any hand surgeon to acquire sufficient proficiency in order to achieve reliable cross-sectional area measurements. Learning the technique of wrist ultrasonography may take some time, but as the anatomy of CTS is very familiar to hand surgeons, this is a skill that can be learned with relative ease, especially with current ultrasonography equipment.

This study has several limitations. None of the tests in the patients were blinded, although the electroneuromyography results were analysed only after the US measurements had been performed, thus minimizing the degree of bias. In conclusion, our study indicates that ultrasonography is a credible alternative test to the nerve conduction test in the diagnosis of CTS with characteristic symptoms in the hands of a hand surgeon. Our study may provide information on the future selection of patients that are suitable for electroneuromyography examination. Further studies on the correlation between disease severity, ultrasonography findings and postoperative satisfaction are required.

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