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A Novel Method of Diagnosing Autonomic Dysfunction in Carpal Tunnel Syndrome: Measuring Skin Capacitance

Inji Ibrahim[(A,B,D,E,F)], Wasim Sardar Khan[(A,B,D,E,F)], Sujay Dheerendra[(A,B,D,E,F)], Peter Smitham[(A,B,D,E,F)], Nicholas Goddard[(A,B,D,E,F)]

University College London Institute of Orthopaedics and Musculoskeletal Science, Royal National Orthopaedic Hospital, Stanmore, Middlesex, London

SUMMARY

Background. Carpal Tunnel Syndrome (CTS) is normally diagnosed via its sensory and motor manifestations. The associated autonomic dysfunction has not been exploited to its full potential as a diagnostic tool due to the difficulties in quantifying it. We aim to demonstrate that autonomic dysfunction of CTS can be quantified by measuring skin capacitance.

Material and methods. Fifty-one patients with clinical signs and electrophysiological evidence of CTS in 89 hands were recruited. Skin capacitance was measured using Corneometer CM825 (C&K Electronic, GmbH) from the palmar aspect of the distal phalanx of the index and little finger of the affected hand. Healthy gender- and age-matched individuals were recruited as controls.

Results. The mean ratio of hydration of the index to the little finger was 0.82. The mean difference was 10.98 arbitrary units. The control group consisted of 151 subjects (80 Male & 71 Female) and 302 hands with an average age of 40.1 years (18-81 years). The mean ratio of hydration of the index to the little finger was 0.87. The mean difference was 8.67 arbitrary units. The measurement ratios (index to little finger skin hydration) between the two groups was compared directly and gave a significant mean difference of 0.05 arbitrary units.

Conclusions. 1. Statistically significant differences in skin capacitance between CTS patients and controls have been demonstrated and quantified using a rapid and simple method. 2. This can be used in clinic to reduce the reliance on Nerve Conduction Studies for diagnosing CTS.

Key words: carpal tunnel syndrome, autonomic dysfunction, corneometer, nerve conduction studies

BACKGROUND

Carpal Tunnel Syndrome (CTS) accounts for 90% of all entrapment neuropathies [1]. Diagnosis is via a combination of a detailed history, clinical examination, and nerve conduction studies (NCS). Although CTS is a clinical diagnosis, NCS is often considered to be the gold standard for investigations because it is an objective test that provides information on the physiological health of the median nerve across the carpal tunnel [2]. Prolonged motor and sensory latencies of the median nerve, and reduced sensory and motor conduction velocities are acceptable diagnostic criteria [3]. However, false negative and false positives still occur [4] possibly due to lack of standardised diagnostic criteria, resulting in 16-34% of clinically defined CTS being missed [5]. Moreover, blanket referrals for NCS are expensive and inefficient [6], as studies have reported that NCS do not change the probability of diagnosing CTS [7]. NCS may not detect transient or mild CTS, as more permanent physiological changes that cause median nerve slowing may not yet be present. Finally, patients describe NCS as uncomfortable; Jarvik et al. reported that 76% of patients described NCS as unpleasant [8].

Physiological changes in sensory and motor functions in CTS have been reported [9] but few studies have investigated the sympathetic skin response (SSR) of the hand to evaluate autonomic function [10-13]. The SSR is a transient change in the electrical skin potential evoked by internal or external stimuli [14]. The polysynaptic reflex arc of the SSR includes large myelinated afferent sensory fibres and efferent sympathetic preganglionic and postganglionic unmyelinated fibres, with sweat glands as effectors [15,16]. CTS patients have an absent or reduced SSR compared to controls indicating a reduction of sweat glands' function [10-13]. The use of autonomic dysfunction as a potential diagnostic tool has been previously reported in the context of thermal imaging [17-19]. Changes in NCS appear late in CTS [20], hence patients with clinical signs and symptoms of CTS may have normal (negative) NCS. Thermography is able to detect mild CTS because the sympathetic branches of the median nerve are so sensitive to damage that even a minor compression is picked up [21]. Earlier diagnosis may change treatment options or lead to earlier surgery. Conservative treatment such as splints and non-steroidal anti-inflammatory medications may be prescribed earlier, which has been shown to successfully reverse mild CTS, therefore eliminating the need for surgery [22]. This justifies using autonomic dysfunction in the diagnosis of CTS and in other conditions involving autonomic dysfunction.

We aim to demonstrate that autonomic dysfunction of CTS can be quantified by measuring skin moisture of the stratum corneum of the finger tips using skin capacitance measurements. Patient satisfaction will be increased by the pain- and electricity-free method of diagnosis. To our knowledge, no previous studies have investigated this method. We hope to demonstrate that measuring capacitance is an effective and sensitive method of diagnosing CTS. It can potentially be used in clinical practice as a quicker, cheaper, non-invasive alternative to NCS. This will reduce the time from referral to operation, costs and workload of neurophysiologists by reducing the reliance on NCS.

MATERIALS AND METHODS

Corneometer CM825 (C& K Electronic, GmbH) was used to measure skin capacitance from the palmar aspect of the distal phalanx of the digit. The readings between 0 and 130 in arbitrary units were stored in the Multiple Probe Adaptor programme. Measurements were used to calculate the moisture content ratio of the index to little finger. Multiple measurements were taken on four individuals at 11 different time points over one week to ensure that no significant differences in the measurement values from the same skin areas existed over different time points.

The inclusion criteria for the study were: patients aged 18 or above who could speak and read English, had no other upper limb neuropathy, had not sustained an upper limb fracture in the past six months, and had no psychiatric illness. Patients with clinical signs and symptoms of CTS, and electrophysiological evidence of CTS confirmed by NCS were recruited from the orthopaedic clinic and day surgery unit prior to median nerve decompression surgery from March to April 2011 following local ethical committee approval. Age- and sex-matched healthy individuals with no signs and symptoms of CTS were recruited as controls. An information sheet was given to the subjects who met the inclusion criteria, and the procedure explained before obtaining verbal and written consent. Controls were clinically tested for CTS using Phalen's and Tinel's tests.

There were 51 patients (15 Males and 36 Females) in the CTS group with 89 affected hands. The mean age was 57.63 years (range 33-85 years). In the control group there were 151 healthy patients and volunteers (80 Males and 71 Females) with 302 hands. The mean age was 40.1 years (range 18-81 years).

Skin capacitance was measured from the palmar aspect of the distal phalanx of the index and little finger from both hands. The cleaned probe head was

placed vertically on the test area. Single measurements were taken under constant conditions avoiding direct lamp or sunlight, after at least a 20 minute rest. The temperature (°C) and air humidity (relative humidity %) of the room were measured by a sensor, and stored with the hydration measurement value. The data was analysed in IBM SPSS Statistics programme version 19.

RESULTS

On validating the corneometer, the mean values for the 11 measurements of each finger tip for each person were measured. Moving from the thumb to the little finger in each hand, the moisture content increased linearly. The left hand gave higher readings on each finger tip than the right hand. Multiple measurements on the same finger tip did not produce a significantly large range of readings and the standard error bars were small.

The mean ratio of hydration of the index to the little finger of the affected hand in the CTS group was 0.82 (95% CI 0.77-0.87; SD 0.24). There was a significant difference between the index and little finger measurements in the affected hands ($p<0.001$ paired t-test), and the mean difference was 10.98. The mean ratio of hydration of the index to the little finger in the control group was 0.87 (95% CI 0.86-0.89; SD 0.14). There was a significant difference between the index and little finger measurements in each hand, ($p<0.001$ paired t-test), and the mean difference was 8.67. The SD (0.14) was smaller than the SD for the CTS group (0.24) by 0.1 arbitrary units of skin moisture, indicating a slightly tighter range of values. Difference in means of measurement ratios (index to little finger skin hydration) between the two groups was compared directly. This gave a significant mean difference of 0.05 ($p=0.038$, independent t-test).

Table 1 summarises the output from the generalized linear model analysis. Using restructured data (one ratio per person, combined as the average of the left and right hand ratio) it appears that neither gender ($p=0.362$), temperature ($p=0.189$) nor humidity ($p=0.125$) are significantly associated with the combined ratio. A ratio for diagnosis of CTS using the Corneometer CM825 was taken as 0-0.82 inclusive (mean hydration ratio for CTS group) and we calculated the sensitivity and specificity of this device from the following data. Table 2 shows that sensitivity and specificity were calculated as 46.08% and 57.39% respectively.

DISCUSSION

Several reasons may explain the unexpected statistically significant difference between index and little finger measurements in controls. Firstly, several of them may have asymptomatic median nerve neuropathy (AMNN) and yet met the inclusion criteria. Approximately 15% of the general population has AMNN [23]. AMNN may be explained by the insidious onset of a pathophysiological abnormality that may not result in complete ischemia of the nerve and the resulting paraesthesia. In the preliminary studies, the thumb and index fingers had the least amount of moisture compared to other fingers. This is more profound in the right hand, which was the dominant hand for the subjects on which validation measurements were taken. Several participants in the control group were diabetic, and diabetic patients have higher tendency to develop CTS due to a lower threshold for nerve damage [24].

Despite the significant difference in skin capacitance between the index and little finger in the control group, it is smaller than the mean difference in the CTS group (by 2.31 arbitrary units). Further-

Tab. 1. Generalized Linear Model – Tests of Model Effects showing the significance of association of each variable with the combined ratio

Source	Type III		
	Wald Chi-Square	Df	Significance
(Intercept)	23.428	1	0.000
Gender	.831	1	0.362
Temp	1.726	1	0.189
Humidity	2.356	1	0.125

Tab. 2. Data from which Sensitivity and Specificity were calculated

		Corneometer CM825 (CON)		
		CON Positive	CON Negative	
Nerve Conduction Studies (NCS)	NCS Positive	47 True Positives NCS + CON +	55 False Negatives NCS + CON -	102
	NCS Absent Assume Negative	150 False Positives NCS assume normal CON +	202 True Negatives NCS assume normal CON -	352
		197	257	454

more, the difference in means of the measurement ratios (index to little finger skin hydration) between the two groups gave a statistically significant mean difference of 0.05 (p=0.038). Thus, the significant difference in skin capacitance in the control group does not undermine the principle of using this method to diagnose CTS, and further work is needed to produce more robust results by ensuring that AMNN is eliminated from the control group by subjecting controls to NCS studies or a more thorough clinical and questionnaire evaluation. Furthermore, a larger number of controls should be tested to increase the statistical confidence of whether the capacitance difference is real or artificial. All controls should be measured at a time when activity does not affect measurements. The effect of activity on measurements could be further determined by taking measurements at rest and then after writing for a defined amount of time.

The estimated sensitivity and specificity of the corneometer were calculated to be 46.08% and 57.39% respectively. This seems low when compared to the sensitivity of NCS. However, reported NCS sensitivity ranges from 49% to 84%. It should be noted that the sensitivity and specificity of NCS cannot be determined with absolute certainty because a diagnosis of CTS cannot be made with absolute certainty without a 'gold standard'. The lack of a reliable 'gold standard' and the use of reference standards that are variable from study to study give dissimilar results [2]. The data generated in our study to calculate the sensitivity and specificity for skin capacitance was based on several assumptions that reflect the worst case scenario.

A cost-analysis comparing the corneometer and NCS revealed that in the long term, the Corneometer CM825 is a cheaper diagnostic tool. One Corneometer costs $8,510, whilst NCS cost $200-300 each [25, 26]. When assuming an average cost of $250 per NCS, 34 NCS would pay for the cost of one corneometer. This does not take into account neurophysiologists' time and cost, which add to the cost of NCS further, nor the time and cost of the person performing the corneometer test. Ideally, the clinician would perform this test in clinic, thereby not incurring extra costs allowing the corneometer test to remain a significantly cheaper option than NCS.

Kumar et al. reported the modified 'biro test' as a method of quantifying autonomic dysfunction: sliding a biro over the palmar skin of the index and little finger to determine the level of friction present [27]. Easy movement at a low angle indicates less friction/less sweating/sympathetic denervation and easy movement only at a high angle indicates high friction/high sweating/normal sympathetic innervations. This study reported that a difference less or equal to 5 degrees in the critical angle between the index and little fingers of the same hand would have a sensitivity of 69% and specificity of 86% in detecting CTS [27]. Although this method seems better at quantifying autonomic dysfunction than the corneometer due to the higher sensitivity and specificity; and because there were no statistical differences in the critical angle in controls, this method is not as reliable as the corneometer due to the possibility of observer error when determining the critical angle. Observer error was reduced in the reported study by using the same observer for all measurements, but this is not possible to replicate in clinic, and hence observer error in clinic is inevitable leading to a low inter-rater reliability. The corneometer gives an objective measurement that cannot be influenced by the person taking measurements, and hence has a higher inter-rater reliability in clinic than the biro test.

CONCLUSIONS

1. This study demonstrates that there is potential in exploiting the differences in skin capacitance as a diagnostic tool, which is supported by the statistically significant difference between the two groups (p=0.038). 2. We recommend further studies using NCS data for controls to ensure that CTS patients are not being matched to individuals that may have AMNN as well as a more detailed health economic impact evaluation.

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Adres do korespondencji / Address for correspondence
Wasim S Khan, Clinical Lecturer, Institute of Orthopaedics and Musculoskeletal Sciences,
Royal National Orthopaedic Hospital, Stanmore, Middlesex, HA7 4LP.
Telephone: +44 (0) 7791 025554, e-mail: wasimkhan@doctors.org.uk

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