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Combined Median Score Increasing Sensitivity of Carpal Tunnel Syndrome Diagnosis

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Abstract

Carpal tunnel syndrome (CTS) is the most common of all focal neuropathies. Electrodiagnostic (EXD) of CTS has advanced to include Combined Sensory Indexes (CSI) improving the specificity and sensitivity of EXD by employing intra-hand comparative data. Ultrasound (US) is a popular tool for the assessment of CTS. Cross Sectional Area (CSA) is the most consistent US parameter, but as a single test, it has a similar false negative profile to EXD. This study describes a dual method of CTS interrogation by EXD and US with the results applied to a single numerical score; the Combined Median Score (CMS). This is the product of CSA of median nerve at Carpal Tunnel inlet and CSI. In a series of 100 suspected cases, standard EDX identified 89 positive cases, CSI identified 92 positives, CMS identified 95 positives. This new method of combining anatomical as well as physiological data in a numerical score increases the sensitivity of diagnosing the most common entrapment neuropathy, CTS.

Keywords

Carpal Tunnel Syndrome, Ultrasound, Median Nerve, Combined Sensory Index, Combined Median Score

1. Introduction

Carpal tunnel syndrome (CTS) is the most common and best studied of all focal neuropathies. The electrodiagnostic methodology for evaluating cases of carpal tunnel syndrome has advanced significantly over the past three decades. CTS accounts for 90% of all known entrapment neuropathies [1]. This syndrome is caused by the entrapment of the median nerve as it travels to the dumbbell shaped passage known as the Carpal Tunnel. The nerve travels through the bony and ligamentous structure in the company of nine flexor tendons; the inlet of the canal having the bony land mark of the pisiform bone, the outlet being identified

by the hook of the hamate bony land mark.

The clinical evaluation of Carpal Tunnel Syndrome involves a history of pain, tingling, numbness and relief with hand-shaking. An association of nocturnal awakenings is also common elements in the history. Some individuals with more advanced symptoms will complain of weakness in thumb abduction and occasional atrophy of the thenar eminence. Clinical examination historically has included the median nerve Compression Test, Tinels Test and Phalens Test to help identify the condition. A 2002 research paper confirmed that no "gold standard" clinical test with both high sensitivity and specificity to diagnose CTS existed. They suggested that the diagnosis of CTS should be made based on patient history, physician clinical evaluation and supported by Electrodiagnostic testing (EXD) [2].

CTS symptoms can also mimic other conditions such as a cervical radiculopathy, thoracic outlet syndrome or other focal neuropathies of the upper limb; hence, EXD is useful in excluding these conditions as well as confirming a focal neuropathy.

Descriptions of CTS first surfaced in the 1830's and were described independently by James Paget in 1854 and James Jackson Putman in 1880 [3]. George Phalen, an American hand Surgeon at the Cleveland Clinic, popularised the use of the term Carpal Tunnel Syndrome in 1950 [4].

The modern diagnosis of Carpal Tunnel Syndrome involves an electrodiagnostic evaluation of the median nerve assessing the effects of compression of the median nerve at the level of the carpal tunnel. The compressive injury results in abnormalities of the function to the sensory and motor components of the nerve. The nerve conduction study results usually identify conduction slowing and block at the level of the tunnel with changes in latencies and amplitudes. Classically, the findings are compared to standard laboratory normal and abnormalities are thus identified. What constitutes normal and when physiology becomes pathology has always been a controversial issue when diagnosing this common focal neuropathy. Most EXD laboratories have their own set of normal values for each nerve conduction study. Standard values for the assessment and recording of nerve conduction studies are available from many learned bodies [5] [6]. In these instances, early and mild cases of Carpal Tunnel Syndrome may show abnormalities only in the mixed transpalmar nerve conduction studies or in the sensory studies with the motor studies frequently showing normal readings.

It was reported in 1990's that up to 15% of all cases of Carpal Tunnel Syndrome were being missed due to a lack of sensitivity in the methodologies employed to assess this focal neuropathy. The state of the art was improved significantly by the introduction of intra-hand comparative data, where latency differences between median and non-median nerves were employed in addition to standard values to assess cases of CTS. In this protocol, the non-median nerves which did not pass through the carpal tunnel acted as controls for the median nerves that did. A variety of methods and protocols using this scheme were

identified [7]—the Robinson's index using a summary index being the most widely accepted [8]. This methodology improved the diagnostic return as the data was analyzed in both relative and absolute terms.

The Combined Sensory Index (CSI) maximised the sensitivity for detection of Carpal Tunnel Syndrome without reducing the specificity by using a single score derived from multiple sensory tests. The Robinson's Combined Sensory Index uses the sum of comparison of the sum of sensory latencies collected from three established sensory tests for the median nerve compared to 3 non-median nerves. It is based on the difference of distal latency between the radial and median sensory recording to the thumb, the ulnar and median transpalmar distal latency difference and the difference between the median sensory distal latency recording to the second digit and the ulnar recording to the fifth digit; each pair of tests being performed at similar distances. Should the Combined Sensory Index be above 1 ms, the test is considered to be positive. The Combined Sensory Index has a very high specificity with few false positives and a high sensitivity with very few false negatives and has excellent test reliability [8]. The upper limit of normal is set at 1 ms, CSIs of greater than 1ms are considered to be positive for CTS.

Despite this advances in EXD assessment of this common focal neuropathy the sensitivity of EXD testing for this condition continues to be of the order of 90%, with up to 10% of patients with CTS exhibiting normal nerve conduction studies.

Diagnostic ultrasound has also been used for the past 15 years to interrogate different aspects of neuromuscular disease. It has become a popular test in focal neuropathies as it examines the anatomical structure of the nerve and the location of the entrapment in comparison to nerve conduction studies which specifically look at the physiological function of the nerve. US can be helpful in assessing cases of Carpal Tunnel Syndrome. The classical triads of ultrasound findings in cases of CTS are:

1) Swelling of the median nerve in the proximal tunnel at the level of the pisiform bone.

2) Flattening of the nerve in the distal tunnel at the level of the hamate.

3) Bowing of the transverse ligament [9].

All 3 signs are present in only a minority of cases. The most predictive of the 3 signs is the swelling of the nerve at the canal inlet. A series examining 102 nerves showed swelling in a CTS group [10] with a Cross Sectional Area (CSA) of on average 0.13 cm^2, in comparison to a control group of non CTS individuals' average of 0.07 cm^2.

The specificity of this study of 102 US tests for CTS was 97% and the sensitivity 82%. Further research has confirmed the veracity of CSA enlargement with the degree of EXD abnormalities [11]. Hence measurement of the CSA of the median nerve can be informative in the evaluation of suspected cases of CTS. In this study a CSA of 0.10 cm^2 (10 mm^2) of the median nerve at the tunnel inlet was used as the upper limit of normal.

US examination can be done in a simple and timely fashion where the swollen median nerve can be visualized and measured by current modern EXD systems. Some of the current EXD systems incorporate US as part of the diagnostic system. This US component is a reliable additional diagnostic test for Carpal Tunnel Syndrome as it can clearly visualise the extent of swelling of the nerve as it enters the canal at the level of the pisiform bone.

The normal median nerve has a CSA at the level of the pisiform bone of between 0.6 and 0. 9 cm^2, the upper limit of normal being 0.99 cm^2, with readings of 0.10 cm^2 (10 mm^2) or greater considered to be abnormal. This was the upper limit employed in this study.

While ultrasound as a stand-alone test is a highly sensitive screening tool for CTS it cannot determine the severity of the disease [12]. CTS has been graded mild, moderate to severe depending on the number of abnormalities identified in EXD.

US as stand-alone test does not increase the pick-up rate of this common focal neuropathy. Mondeli and Filippou reported in 2008 a series of clinically diagnosed mild Carpal Tunnel Syndromes (CTS) that no anomalies were detected with either Nerve Conduction studies or US examination in 23.5% of cases. Of the 76.5% positive cases US did not detect more anomalies than NCS alone and vice versa [13]. It is however a useful adjunct investigation for suspected cases of CTS.

It is hypostasised that US, if used in combination with standard EXD testing, will provide additional sensitivity to the diagnosis of CTS.

This research paper examines a method where both the structure and function of the median nerve can be evaluated together in a single procedure using standard EXD techniques and US. The results are applied to a formula which provides a single numerical score; the Combined Median Index (CMS), in a similar way to the derivation of the CSI with the addition of US data of the CSA of the nerve. It is suggested that this protocol and method of data assessment will improve the diagnostic yield for CTS by using a combination of anatomical and physiological parameters.

2. Method

100 consecutive hands were referred to a Consultant Neurophysiologist at the Sports Surgery Clinic, Dublin by senior physicians and surgeons for assessment of possible CTS. A Natus Ultra Pro 100 S Neurophysiology EXD System was used to perform Nerve Conduction studies. The system incorporated a Vista Ultrasound unit and a Nautus MV linear array transduce ultrasound probe which was employed to assess the Cross Sectional Area of the median nerve at the carpal tunnel inlet. The pisiform bone was employed as the bony landmark for the inlet.

The 100 consecutive cases underwent a standard neurophysiology assessment for suspected cases of CTS. There were 67 females, 33 males with an age range of

21 years to 72 years and an average age of 52 years. Patients who were pregnant or suffered with thyroid disease, rheumatoid arthritis and Diabetes Mellitus were excluded.

The EXD testing involved 7 nerve conduction studies, namely a median motor nerve conduction study, median sensory nerve conduction study to digit 2, median trans-palmar mixed nerve conduction study, ulnar sensory study to digit 5 and ulnar trans-palmar mixed nerve study. A radial sensory study, and median sensory study to the thumb using a similar stimulation point were also performed. The test procedure followed the 2002 AEEM Practice parameters for diagnosis of CTS [5]. A Combined Sensory Index was also calculated using the Robinson methodology [7].

The US examination of the median nerve was performed using a Natus MV 12 high frequency ultrasound probe and the Vista software which was incorporated into the Natus Ultra Pro 100S system. Transverse images of the median nerve were obtained at the level of pisiform. The CSA of the median nerve was calculated using the 5 point automated measuring system embedded in the Vista software. This was measured in cm^2. The upper limit of normal was set at 0.99 cm^2.

Having calculated the CSI this number was multiplied by the CSA (in cm^2) of the median nerve at the level of the carpal tunnel inlet. The resultant calculation gave a numerical score called the Combined Median Score (CMS) which incorporated the physiological and anatomical findings into a single numerical score. See formula below.

Combined Median Score (CMS) Formula

$$\mathrm{CMS} = (A - B) + (C - D) + (E - F) \times Z$$

where:

A = distal latency of median sensory nerve conduction study to digit 2 stimulating at 14 cm.

B = distal latency of ulnar sensory nerve conduction study to digit 5 stimulating at 14 cm.

C = distal latency of median transpalmar nerve conduction study to palm stimulating at 8 cm.

D = distal latency of ulnar transpalmar nerve conduction study to palm stimulating at 8 cm.

E = distal latency of median sensory nerve conduction study to the thumb stimulating at 8 cm.

F = distal latency of radial sensory nerve conduction study to the 1st web space stimulating at 8 cm.

Z = Cross Sectional Area of the Median Nerve at the carpal tunnel inlet, using the pisiform bone asa surface anatomical landmark.

The cut off value between normal and abnormal in diagnosing CTS was similar to the Robinson Index where 1.0 or less is considered normal (see **Table 1**).

Table 1. Nerve conduction study results with CSI calculation and CMS calculation.

Nerve conduction Results	distal latency	Difference
Median Sensory [digit 2] distal latency	3.5 ms	
Ulnar Sensory [digit 5] distal latency	2.9 ms	0.6 ms
Median Sensory [thumb] distal latency	2.0 ms	
Radial Sensory [1st web space] distal latency	1.8 ms	0.2 ms
Median Transpalmar distal latency	2.2 ms	
Ulnar Transpalmar distal latency	2.1 ms	0.1 ms
Combined Sensory Index (CSI)	0.9 ms [Equivocal]	Normal < 1.0 ms
Median nerve circumference (Z)		1.3 cm^2
Combined Median Score (CMS) = 1.3 × 0.9 = 1.17 (1.2)		
CMS 1.2 [Positive]		

The example shows equivocal nerve conduction studies, with borderline distal latencies in absolute terms in the median sensory study to digit at 3.5 ms [n < 3.5 ms stimulating at 14 cm], and in the median transpalmar mixed nerve distal latency at 2.2 ms [n < 2.2 ms stimulating at 8 cm]. The CSI also shows a borderline score at 0.9 ms [n < 1.0 ms]. If the CSA of the median nerve at the Carpal Tunnel inlet is used as a multiplier of the CSI, the CMS that is generated in this example creates a positive result. Hence the CMS is useful in mild or borderline cases of CTS and may help to improve diagnostic sensitivity.

If the CSA of the nerve is normal [equal or less than 0.99 cm^2] then the product of the multiplication with the CSI will not increase the CMS. If the nerve is swollen then the product of the multiplication of the CSA and the CSI value will increase the CMS, which may then exceed the cut off of 1.0 yielding a positive result. The addition of US derived CSA of the median nerve at the carpal tunnel inlet improves the sensitivity of CTS evaluation by augmenting the nerves' physiological parameters with anatomical parameters.

3. Results

89 of the 100 hands referred for assessment met the criteria for diagnosis of CTS (Table 2) based on absolute values. In this group the nerve conduction studies showed slowing of either one or a combination of the median motor, sensory or transpalmar distal latencies thereby grading the focal neuropathy mild, moderate or severe depending on the number of positive tests.

89 of the hands had slowing in the median trans-palmar mixed nerve distal latency. 87 of the hands had slowing in the median sensory distal latencies. 42 of the hands had slowing in the median motor distal latencies. 12% of the median motor studies, 49% of the sensory studies and 29% of the trans-palmar studies showed an amplitude loss.

Application of the Robinson Index to the data increased the pick-up rate by 3 extra cases, improving the diagnostic yield to 92%.

Table 2. Sensitivity of nerve conduction studies, CSI and CMS in detecting CTS.

Motor distal latency > 4.2 ms	42%
Median Motor amplitude < 6.0 mV	12%
Median Sensory study to digit 2 distal latency > 3.5 ms	87%
Median sensory amplitude < 20 uV	45%
Median Transpalmar mixed nerve distal latency > 2.2 ms	89%
Median Transpalmar mixed nerve amplitude < 10 uV	29%
Combined sensory index > 1.0 ms	92%
Median Nerve CSA < 10 mm^2	18%
Median Nerve CSA > 10 mm^2	82%
Median Nerve CSA > 13 mm^2	14%

Of 89 hands that showed positive findings for CTS, the most sensitive NVS s were the median transpalmar distal latency [89%] and the median sensory distal latency [87%]. In 82% of cases the CSA of the median nerve showed evidence of swelling greater than 10 mm^2.

The US examination of the median nerve of the 100 consecutive hands identified a CSA of 0.10 cm^2 or more in 82 of the hands examined. 14 hands had a median nerve CSA of 1.4 cm^2 or greater. All 82 hands with a swollen median nerve showed slowing in one or a combination of median nerve conduction studies. 7 hands had positive nerve conduction studies for CTS but normal CSA of the median nerve at 0.9 cm^2 or less.

The CMS was then calculated and confirmed a further 3 cases where the numerical score was greater than 1.0; the new CMI score increasing the diagnostic rate to 95%.

4. Discussion

CTS continues to be the most common of all focal neuropathies. The pick-up rate for this condition which causes significant morbidity continues to be suboptimal in a clinical setting where there are reliable and available conservative and surgical solutions to the syndrome. Early detection of this condition will favourably impact on outcomes. Experienced clinicians have a higher index of suspicion for this condition which can present with a myriad of symptoms. There is endless debate as to which battery of EDX tests is the most accurate in detecting this condition. Even with the addition of the CSI, which significantly helped to maximize the sensitivity and specificity of EXD evaluation, a proportion of CTS cases continued to be missed with false negative rates ranging from 10% to 23.5% (2.13). With advances in technology US has become a valuable clinical tool in assessing the structure and function of neurological tissue. However, in the case of CTS, US is no more accurate in detecting cases of CTS than EXD. The incorporation of CSA evaluation with US into the standard EDX assessment appears to improve the sensitivity and specificity of evaluation of this neuropathy. This

paper suggests that clinical evaluation by an experienced clinician who identifies the possibility of CTS with evaluation of the nerve with both EDX tools and US may improve the accurate diagnosis of this challenging focal neuropathy. The clinical data is applied to a single numerical score.

In classical medical teaching interrogation of a suspected medical complaint is best achieved by a combination of clinical, anatomical and physiological evaluation. Atrial Fibrillation is an analogous example in cardiology, where the clinician picks up the initial symptoms of breathlessness and palpitations and an electrical physiological test by ECG will confirm the irregular rhythm and the absence of P waves, followed by an Ultrasound Examination of the hearts chambers by ECHO cardiograph to evaluate the structure of the heart, its chambers and vales and any decrees in the hearts pumping function, by evaluation of the ejection fraction. If the cardiac physician confined him or herself to only one of the testing parameters they reduce their chances of making an accurate diagnosis. The same is true of focal neuropathies and particularly of CTS.

In the past decade High Resolution Ultrasound (US) has become a useful adjunct diagnostic tool with a favourable cost in comparison to MRI and Neurography for obtaining anatomical information in patients with neuromuscular disease [14].

US can be a useful anatomical assessment in cases of suspected Carpal Tunnel Syndrome. Various anatomical measurements of the median nerve are possible with US. Ratios of CSA differences at the carpal tunnel inlet and outlet have been proposed [15], but this can be a technically difficult examination to replicate. A fundamental finding in all cases of nerve entrapment is that of swelling proximal to the entrapment site.

The CSA of the median nerve is usually increased proximal to the site of entrapment in cases of CTS due to swelling in the nerve caused by its compression. In these cases there is enlargement of the median nerve at the level of the Carpal Tunnel Inlet, which has the bony land mark of the pisiform bone. US at this site is considered to be a reliable diagnostic test for CTS as it can clearly identify swelling of the nerve as it enters the canal under the flexor retinaculum.

The normal median nerve has a CSA at the level of the pisiform bone of between 6 and 0.9 mm^2 (0.06 - 0.09 cm^2) the upper limit of normal being 9.9 mm^2 [16]. Readings greater are considered to be abnormal. In a recent study the mean inlet CSA was 8.7 mm^2 (0.87 cm^2) in healthy controls and 14.6 mm^2 (1.46 cm^2) CTS group ($P < 0.001$) [17] [18].

Ultrasound is a highly sensitive screening tool for CTS but it cannot determine the severity of the disease. This is best achieved by EXD. US can provide additional sensitivity to the diagnosis of CTS if used in combination with standard nerve conduction studies.

The current study confirms that the augmentation of the EDX for suspected cases of CTS with routine US of the median nerve at the canal inlet will increase the pickup rate for this condition. A calculation is made which marries the US

Table 3. Combined median score formula with selected examples. Formula $(a-b)+(c-d)+(e-f)\times z$.

NCS/Scores	a	b	c	d	e	f	CSI	z	CMS
Example 1	3.8	3.1	2.4	1.9	2.4	1.7	1.9	1.3	2.47
Example 2	4.8	3.3	3.1	1.9	2.4	1.6	3.5	1.3	4.55
Example 3	3.5	3.3	2.3	2.0	2.1	1.9	0.7	1.7	1.19
Example 4	3.6	3.0	2.3	1.8	2.3	1.6	1.8	0.8	1.44
Example 5	3.5	3.2	2.2	1.9	2.2	1.7	1.1	1.2	1.32
Example 6	3.6	3.1	2.2	1.8	2.3	1.8	1.4	1.2	1.68

6 clinical examples of the use of the CMS. In example 3 the Nerve Conduction Studies show borderline results but the CSI is positive. Despite the CSA of the median nerve being positive the CMS remains positive. In Example 5, the Nerve Conduction Studies and CSI are borderline but the CMS is positive.

Table 4. Detection rate of CTS in a cohort of 100 patients using absolute EXD values, comparative values using CSI and combined EXD and US values using CMS.

NCV Absolute terms	NCV Combined Sensory Index (CSI)	Combined Median Score (CMS)
89%	92%	95%

Of 100 patients referred for assessment of CTS 89% had a positive result based on standard laboratory values, 92% had a positive result based on the Combined Sensory Index. A single number index, combining the CSI and the Ultrasound derived CSA of the median nerve at the Carpal Tunnel inlet (CMS) increased the diagnostic yield to 95%.

and EXD data to give a combined score of physiology function and anatomical structure in a numerical score: the Combined Median Score (CMS). The mathematical calculations can be simply performed by a software package which records the numerical data and applies the formula.

This numerical score will be of diagnostic assistance in cases of borderline nerve conduction studies with a compelling clinical history and examination. Currently EXD evaluation of CTS has a sensitivity of 85% - 90% with approximately 10% - 15% of subjects with clinical CTS having normal Nerve Conduction Studies [19]. This CMS score will assist in identifying these borderline cases thus increasing the overall sensitivity of the examination (**Table 3**).

5. Conclusions

CTS is the most common encountered focal neuropathy. Despite great advances in the EXD techniques for the assessment of this condition, neurophysiological medicine still fails to recognise a significant number of cases, the majority of which are at the milder end of the spectrum. Some authors suggest that Ultrasound might become the prime method of diagnosing CTS, with ultrasound CSA evaluation of the median nerve at the carpal tunnel inlet a reliable and reproducible procedure. The research, however, indicates that despite US specificity and sensitivity in mild cases of CTS, it does not detect any more anomalies than EXD alone.

Mild cases are the sub set of CTS that are most frequently missed. They are a critical group as early detection will give an opportunity of resolving the complaint with conservative interventions, such as splinting, topical NSAIDS, steroid injections and alteration in provoking activities.

There is wide variation of sensitivities and specificities reported in the literature regarding the use of ultrasound as a screening or confirmatory tool in the diagnosis of CTS. It is suggested that the composite sensitivity and specificity of ultrasound for the diagnosis of CTS, using a sample size of 3131 wrists is 77.6% and 86.8% respectively. This is in comparison to EDX which reports a sensitivity and specificity of 80.2% and 78.7%, respectively [20]. Ultrasound will not replace electrodiagnostic testing as the most sensitive and specific test for the diagnosis of CTS. However, this paper proposes that combining the 2 test modalities together in a combined numerical index will increase the overall sensitivity for the diagnosis of this common condition.

This research suggests that US should be used in combination with Nerve Conduction studies and as part of the EXD work up for CTS assessment. By combining the physiological and anatomical data in a single numerical score, this method of assessment increases the diagnostic yield by 3%, thus improving the overall sensitivity of the investigation of CTS (**Table 4**). It is postulated that this 3% may relate to the part of the population with mild CTS patients which are being missed by current protocols, and hence this score may be valuable in assessing equivocal cases of CTS.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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