



(REVIEW ARTICLE)



Diagnosis of carpal tunnel syndrome in perspective of clinical features, neurophysiological studies and high resolution ultrasound

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Abstract

Carpal tunnel syndrome (CTS) is compression of median nerve during its course through the carpal tunnel in the hand. CTS is the most common mononeuropathy diagnosed in neurological clinics. CTS can cause pain, psychological distress, decreased performance at work, absentia from work and financial loss. The diagnosis is mainly based on high degree of clinical suspicion with positive clinical symptoms and signs and must be confirmed with either neurophysiological testing or high resolution ultrasonography. Neurophysiological studies had been the gold standard in diagnosis and grading CTS and for excluding it from other neuromuscular disorder. High resolution ultrasound is being increasingly utilized to diagnose CTS as it can show the pathology of CTS such as swelling and inflammation of median nerve and bowing of flexor retinaculum indicating compressive median neuropathy at the carpal tunnel. It is noninvasive, painless and cheaper but the measurements are operator dependent. Neurophysiological studies have well defined criteria for grading. The use of combined ultrasound and neurophysiological study show greater sensitivity and specificity than the individual procedures and can provide greater clarity to avoid false positive and false negative results. High resolution ultrasonography can help in evaluation of persistence of symptoms even after surgical release and to detect anatomical variations. Early diagnosis and grading is critical in following the appropriate treatment strategy. Clinical features, neurophysiological studies and ultrasound are valuable tools in the identification and assessment of CTS whenever each is used individually or as complementary to each other.

Keywords: Carpal Tunnel Syndrome; Clinical Features; Neurophysiological Study; Ultrasound

1. Introduction

Neurological abnormality in any condition provides a challenge for our normal day to day activities. Even the mildest of neurological affliction makes a person unable to perform to his or her fullest capacity causing depression, disability, dependency, lack of ability to do skillful work, absentia from work, and may ultimately develop desolate life with a considerable financial loss on the individual and the society. Diagnosing the disease early in its course and identifying the factors causing it may greatly help in its prevention and produce better treatment outcome. A major component of these neurological disorders is entrapment mononeuropathies involving a single nerve entrapped or compressed along its anatomical pathway. The most common entrapment neuropathy is Carpal tunnel syndrome (CTS) due to compression of median nerve in its anatomical course at the wrist. The estimated prevalence of clinically and electrophysiologically confirmed CTS in the general population is found to be 2.7 % [1] and an incidence of 491 and 258 per 100,000 person-years for women and men respectively [2] with high preponderance in females. CTS is observed more in working population with a prevalence of 7.8% in United States [3]. The cost of treatment by surgical release operation for CTS can be anywhere from \$2149 to \$9927 per patient, accounting to \$2 billion for 500000 release operations every year in United States alone [4, 5]. Cumulated loss of earnings over a period of 6 years was found to be \$45,000 - \$89,000 per CTS patient in a study on United States claimants of workers compensation insurance [6]. This highlights the importance of an in-depth analysis on causative factors, prevention, early diagnosis and treatment so as to minimize the misery of pain, the disability, permanent damage to nerve and the financial burden. Furthermore it

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effects the outcome of treatment as has been observed by surgical treatment showed improvement in 100% of mild CTS cases compared to 84% in cases of moderate CTS [7]

Carpal tunnel is an osteofibrous canal formed by the flexor retinaculum or transverse carpal ligament attached to the arch of the carpal bones at the hamate and pisiform medially and scaphoid and trapezoid carpal bones at the lateral or radial aspect of wrist between the carpal bones and the flexor retinaculum on the palmar aspect of hand just distal to the wrist. The transverse carpal ligament is 1-3mm in thickness and 3-5 cm wide. It allows the passage of 9 tendons that is 4 tendons of flexor digitorum profundus, 4 tendons of flexor digitorum superficialis and tendon of flexor pollicis longus [8] and the tendon of flexor carpi radialis traverse through a separate fascial compartment between the two laminae of transverse carpal ligament. The median nerve while passing through the forearm supplies the muscles of anterior compartment except the flexor carpi ulnaris and the medial part of flexor digitorum profundus. It passes between the tendons of flexor digitorum superficialis and flexor digitorum profundus to lie superficially at the wrist. Just proximal to the distal wrist crease it enters the carpal tunnel lying superficial to the tendons of flexor pollicis longus and flexor digitorum superficialis on the palmar aspect of hand. Studies reveal a wrist ratio (ratio between the wrist depth at distal flexor wrist crease to the wrist width measured at distal crease) higher than 0.69 or a more square shaped wrist increases the likelihood of CTS by 3- 8%. [9, 10, 11]

Before entering the carpal tunnel it gives of the palmar cutaneous branch for sensory supply to skin over the surface of the thenar eminence. Inside the carpal tunnel, the digital cutaneous branch and the recurrent branch of median nerve arise just distal to the carpal tunnel. The digital cutaneous branch supplies the skin over the lateral 3 and half fingers on the palmar surface and the similar digits upto the distal to the proximal interphalangeal joint on the dorsal surface of hand which relate to the distribution of sensory symptoms of carpal tunnel syndrome. It also supplies the first two lumbricals going to the 2 and 3 digits. The recurrent branch of median nerve supplies the muscles of the thenar eminence- opponens pollicis, abductor pollicis brevis, and superficial part of flexor pollicis brevis. Carpal tunnel syndrome can cause weakness in these muscles leading to hand weakness, hand clumsiness and impaired pinch precision [12, 13]. It has observed that median motor function starts getting affected in the mild stage of CTS itself [13] as opposed popular belief that sensory only is affected in early stages.

Carpal tunnel syndrome occurs due to compression of median nerve as it passes under the flexor retinaculum through the carpal tunnel. The pressure in carpal tunnel in CTS patients have been found to be higher than controls specially in the midsection of the tunnel which increases several fold with dynamic changes, more with extreme flexion than extension of wrist [15,16] The carpal tunnel pressure as well as the median intraneuronal pressure decreases significantly with release operation of transverse flexor retinaculum [17,18,19] with alleviation of symptoms in most of the cases unless permanent damage to the nerve has occurred.

Most of the cases are idiopathic with no true identifiable cause but it has been established that there are certain risk factors which increases the likelihood of CTS such as increase in repetitive movement of hand at the wrist e.g.: assembly line workers, increased exposure to vibrations at the wrist as an occupational hazard, hormonal abnormalities like hypothyroidism, acromegaly, in use of aromatase inhibitors in hormone dependent breast cancer treatment. [20], collagen disorders like rheumatoid arthritis, metabolic disorders like diabetes mellitus and chronic renal insufficiency, fluid retention as in pregnancy, fractures or trauma to wrist, osteoarthritis of wrist [21] and obesity

The peak age of CTS was found to be 45-60yrs [24]. The compression of the median nerve occurs mostly as a result of hypertrophy or edema of synovial sheaths of flexor tendons leading to elevated carpal tunnel pressures causing increase in mechanical contact pressure between the carpal tunnel structures, producing edema of the median nerve followed by ischemic changes in the nerve with decreased perineural blood flow in mild cases, associated with loss of myelin sheath in moderate cases and in severe cases cause damage to the nerve axon itself [22, 23,24].

2. Clinical signs and symptoms

The clinical features (Table 1) include,

2.1. Gender

Females are more likely to develop CTS than males with a prevalence rate of 9.2% in females and 6% in males [25] But a study has observed when job profiles are same then the likelihood of CTS in males or females is almost equal [26] though females are more likely to present earlier with milder symptoms compared to males [27] who may seek help in more advanced severity.

2.2. Age

Peak incidence of CTS was found to be between 45-60 and only 10% were found to be below 31 years of age[28,29] in both sexes though the no. of cases were much higher in females.

2.3. Occupation

Prevalence in blue collar workers was double that in white collar workers [30]

2.4. Clinical symptoms

The clinical symptoms of CTS are 1. Sensory symptoms pain numbness paresthesia nocturnal symptoms, 2. Motor symptoms, 3. Autonomic symptoms

2.4.1. Sensory symptoms

The sensory symptoms are first to be manifested in a case of CTS following the initial pathology of demyelination of the nerve. These include numbness, tingling, pain, decreased sensation in any or all fingers innervated by median nerve that is thumb, index finger or the middle finger. It is unlikely to be CTS if it is ring finger or little fingers which are supplied by ulnar nerve. The Katz hand diagram (Fig 1) shows a sensitivity of 80% and specificity of 90% with the classic and probable presentation of numbness, tingling pain and paresthesia [31]. Nocturnal pain, pain provoked by extreme positions of hand and repetitive movements favors CTS and history of pain getting relieved by shaking the hand that is Flick sign or changing the position of hand adds to diagnosis.

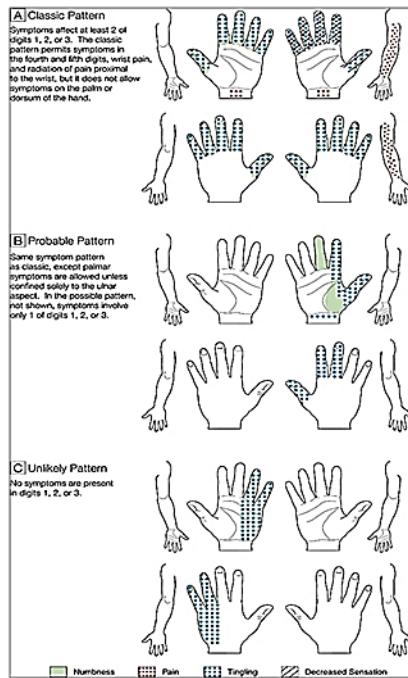


Figure 1 Katz Hand Diagram For sensory symptoms of CTS [31]

2.4.2. Motor symptoms

Motor symptoms include weakness and atrophy of thenar eminence that is the muscles of abductor pollicis brevis, opponens pollicis and flexor pollicis brevis observed as hand weakness and hand clumsiness may be observed in moderate to severe CTS and may also be correlated with fibrillations and fasciculation in these muscles by Electromyography (EMG). EMG is also a useful tool to exclude other neuromuscular disorders with similar presentation as CTS.

2.4.3. Autonomic symptoms

Autonomic symptoms like swelling color changes, sweating and skin temperature with significant alteration in sympathetic skin response have been observed to increase with increasing severity of electrophysiological findings

observed as significant difference between median and ulnar SSR response but studies cannot give definitive clinical association with mild CTS [32, 33,34]

2.5. Clinical tests

For CTS have been found to have low validity and must be confirmed with electrophysiological studies [35]. Provocative tests such as

2.5.1. Phalen's test

Ask the subject to bring the two hands together and perform extreme flexion of about for about 30 seconds. It can reproduce the symptoms

2.5.2. Tinel's percussion test

Tap on the median nerve at the wrist reproduces symptoms.

2.5.3. Manual carpal compression test

Applying pressure over the carpal tunnel for about 30 seconds reproduces the symptoms.

Table 1 Clinical signs and symptoms of Carpal Tunnel Syndrome

Symptoms and signs	Findings indicative of CTS
Age	40-60 years
Gender	Female > males
Risk Factors	Obesity, Diabetes mellitus, hypothyroidism, rheumatoid arthritis, Chronic Renal failure, pregnancy
Occupation	More in occupation involving repeated hand movements or vibrations
Sensory symptoms	Pain Paresthesia Numbness Classic or Probable pattern of Katz Hand Diagram Flicks sign
Motor symptoms	Hand Clumsiness Weakness of Thumb Atrophy of Thenar Muscles
Autonomic symptoms	Swelling or Feeling of Tightness in Hand Temperature change Difference in skin color Difference in sympathetic skin response of median to ulnar nerve
Provocative tests	Phalen's test Tinel sign Manual Carpal Compression test

3. Electro diagnostic testing

Though CTS is mainly a clinical diagnosis, Electro diagnostic testing is important to confirm the diagnosis, grade its severity and rule out any other disease such as peripheral neuropathy, radiculopathy, plexopathy or any other neuromuscular disorders mimicking it. The tests performed (Table 2) are the following

3.1. Median sensory nerve action potential over first to fourth finger

Antidromic conduction studies are better to use as the amplitude of response is higher than that of orthodromic technique. The 2nd digit is most often used for sensory testing. Put the reference (red) electrode over the distal interphalangeal joint and the active (black) electrode 3cm proximal to the red electrode on the 2nd digits. Stimulate the median nerve at the wrist between 13cm proximal to the active (black) electrode. A response showing onset distal latency of less than 3.5m and amplitude of > 20mV is taken as normal. If the response is abnormal, compare it with sensory response of either ulnar or radial nerve of the same limb. An abnormal response of other nerves excludes CTS. Mild CTS causes delayed peak latency beyond 3.7ms. Moderate to severe CTS is shows prolonged distal latency along with decreased amplitude which may be associated with increased median motor nerve latency. Severe CTS may show absent sensory response with increased latency and decreased amplitude of median motor nerve.

3.2. Median compound muscle nerve action potential over the Abductor pollicis brevis muscle

Put the active electrode (black) on the belly of the APB muscle and the reference electrode on the tendon (red). Stimulate 8cms proximal to active electrode over the median nerve at the wrist. A distal latency of <4.4ms and amplitude of >4mV is taken as normal.

3.3. Comparison between sensory latency median and ulnar nerves recorded from 2nd and 5th digit respectively

Keep the reference and active electrodes over the 2nd digit and stimulate 14 cm proximal to active electrode over the wrist. Compare its latency with that of ulnar nerve stimulated at the wrist with recording electrodes at the 5th digit. A difference of more than 0.5ms between their peak latencies indicates CTS.

3.4. Comparative test with ulnar nerve over ring finger

Place the recording electrodes on the ring finger on proximal and distal interphalangeal joints 3cm apart and stimulate the median nerve 13 cm proximal to active electrode at the wrist and the ulnar nerve 13cm proximal over ulnar nerve at wrist. Normal value is 0.4m or less. An increase in latency of median nerve by 0.5ms or more than ulnar latency indicates CTS.

3.5. Comparative test with radial nerve over the thumb

Place the recording electrodes over the thumb and stimulate the median nerve and the radial nerve over their respective location at the wrist 10 cm proximal to the active electrode. Normal value is 0.5m or less. An increased in median wrist distal latency by >0.5ms than that of radial nerve indicates CTS.

3.6. Comparison between lumbrical and introsseus motor response by stimulating median and ulnar nerves respectively

The red electrode is placed over the proximal interphalangeal joint, the active (black) electrode between the midpoints of 2nd and 3rd metacarpals with the ground (green) electrode on the dorsum. Stimulate the motor median nerve and the motor ulnar nerve at their respective wrist locations at a distance of 10cm from the active electrode. CMAP are recorded from 2nd second lumbrical for median nerve and interosseous for ulnar nerve muscles. A difference of >0.4ms is taken as CTS [36]. Even in cases of severe CTS with absent sensory and motor response this technique can be used to localize the lesion [37].

3.7. Median-ulnar palmar mixed comparison orthodromic study

Place the recording electrodes over the median and ulnar nerves at the wrist at their respective locations. Stimulate at the palm between midpoints of 2nd and 3rd metacarpals for median nerve and midpoints between 4th and 5th metacarpals for ulnar nerve, both 8 cm distal to the recording electrodes. Normal value 0.3ms and less. A difference of latency of 0.4ms or more [38, 39] indicates CTS.

3.8. Comparison of distal latency between Palm and wrist stimulation

The electrodes are placed over 2nd digit for antidromic median sensory SNAP recording and stimulation is 7cm proximal over the palm and 14cm proximal to active electrode at the wrist over the median nerve. Proximal amplitude less than 50% of distal response amplitude indicates conduction block and neuropraxia at the carpal tunnel [38].

3.9. Inchng technique

The electrodes are placed over the second digit for antidromic SNAP and 7-8 segmental stimulations are done starting from 10cms proximal to the active electrode at the wrist. Each consecutive stimulation is done with a decrement of 1 cm towards the active electrode. An increase in distal latency of >0.5 ms across the carpal tunnel is diagnostic of CTS. [41] It also distinguishes it from diabetic neuropathy [42]. Segmental tests over the course of median nerve: the segmental studies are more sensitive than the comparative tests [41] for CTS.

Table 2 Nerve Conduction Studies and EMG In Carpal Tunnel Syndrome

Electrodiagnostic Test	Electrodiagnostic test and Site of recording	Response indicative of CTS
Median sensory Nerve Action Potential(SNAP)	Over 1st to 4th finger	Onset latency >3.5 ms and Amplitude < 20 mV with normal response of other nerves of the same hand
Median Compound Muscle action Potential (CMAP)	Over Abductor Pollicis Longus	Distal latency > 4.4 ms and Amplitude < 4 mV
Segmental tests	Comparison of amplitude of median SNAP between stimulation at wrist and stimulation at palm	Proximal amplitude less than 50% of distal response amplitude
	Inching technique	increase in distal latency of >0.5 ms across the carpal tunnel
Comparative Tests	Comparison between the Median SNAP at 2nd digit with Ulnar SNAP at 5th digit	Increased latency by > 0.5 ms of Median than Ulnar
	Comparison between distal latencies of the Median and Ulnar SNAP recorded over the 4th digit	Increased latency by > 0.5 ms of Median than Ulnar
	Comparison between distal latencies of the Median and Radial SNAP recorded over the 1st digit	Increased latency by > 0.5 ms of Median than Radial
	Comparison between the Lumbrical and Introssei motor response	Increased latency by > 0.5 ms of median lumbrical than Ulnar introssei
	Comparison between the Median and Ulnar Palmar mixed Orthodromic Study	Increased latency by > 0.4 ms of median than Ulnar
Electromyography	Of Abductor Pollicis Brevis	Presence of Fasciculation and Fibrillation

Neurophysiological Grading of carpal tunnel syndrome based on Blands classification [43] is given in (Table 3).

3.10 Combined sensory index

The combined sensory index (CSI) is sum of median-radial latency difference+ median-ulnar latency difference+ median ulnar palmar orthodromic latency difference better than considering only median sensory distal latency[44,45] in detecting CTS in early stage. A CSI of more than 1 is taken as early CTS in cases where sensory distal latency of SNAP and motor CMAP are within normal range. A comparison of distal latency between palm and wrist stimulation as a single test showed the highest likelihood ratio [46]

Table 3 Neurophysiological Grading of carpal tunnel syndrome based on Blands classification [43]

Grade of Carpal Tunnel syndrome	Neurophysiological finding
Grade 0 –normal	No abnormality detected neurophysiologically
Grade 1 – very mild	Detected in sensitive segmental and comparative
Grade 2 – mild	Increased sensory latency of > 3.5ms or decreased sensory conduction velocity < 40m/s with normal motor response of median nerve
Grade 3 - moderate	Increased sensory latency with decreased amplitude, increased motor latency of > 4.5 ms
Grade 4 – severe	Motor latency > 4.5ms with absent sensory response
Grade 5 – very severe	Motor latency > 6.5 ms
Grade 6 – extremely severe	Decreased CMAP amplitude < 0.2mV

4. High resolution ultrasound

High resolution Ultrasound is an easy, noninvasive, cheaper and painless procedure for confirming CTS done by an experienced and skillful radiologist. The shape, crossectional area (CSA) and echogenicity are considered. Decreased echogenicity with increased crossectional area indicates median nerve edema. A hyperechoic median nerve may be a sign of demyelination and fibrosis. A compression in carpal tunnel will show hourglass figure of median nerve with increased CSA proximally and distally and compression in the middle of flexor retinaculum. Ultrasonography is highly useful for evaluation of postoperative carpal tunnel syndrome which might show fibrosis and adhesions over the flexor retinaculum. High resolution ultrasound is used also to exclude abnormality of palmar cutaneous nerve which may be a cause of persistence of symptoms. Ultrasound studies have shown there is swelling of the nerve proximal to the carpal tunnel observed as increased proximal cross sectional area (CSA) of more than 9-11mm³ [47,48,49] with CSA of >11.4 mm³ in Electrodiagnostic mild CTS[47] which may be lesser that is >9.4 mm³ in clinically positive CTS with normal nerve conduction study [50]. The ultrasonographic parameters (Table 4) considered for CTS are

4.1. Proximal cross sectional area (CSA) of median nerve

The CSA is measured at opening or entry of median nerve into the carpal tunnel between the pisiform and the scaphoid bones. Hypoechoic median nerve with CSA equal to or more than 9-11square mm has been taken as CTS. A cut off area of >10square millimeter of proximal median nerve has a sensitivity, specificity and accuracy of 85%, 92% and 89.3% [51].

4.2. Distal cross sectional area and its ratio with the proximal CSA

Measurement of median CSA distally at the exit of carpal tunnel between the trapezium and the hamate bones: An inlet to outlet ratio of 1.14 [52] or above indicates CTS.

4.3. Ratio of median CSA at the wrist and the forearm

Ratio of more than > 1.4 is diagnostic of CTS. A difference in CSA of more than 2.1 ± 0.5 square millimeter indicates CTS with a sensitivity and specificity of 99% and 100% [53,54].

4.4. Palmar bowing of flexor retinaculum

Palmar bowing of flexor retinaculum of more than 2 square mm outside the line connecting pisiform with scaphoid indicates likelihood of CTS.

Table 4 Ultrasonography Criteria for Diagnosis of Carpal Tunnel Syndrome

Ultrasonographic test	Ultrasonographic Findings indicative of CTS
Proximal Cross Section Area (entry/inlet of carpal tunnel)	Cross sectional area (CSA) equal to or more than 9-11 square mm
Proximal to Distal Cross Section Area ratio (inlet to outlet ratio)	inlet to outlet CSA ratio of 1.14 or above
Wrist-Forearm Ratio	>1.4
Palmar Bowing of Flexor Retinaculum	>2 square millimeter

5. Conclusion

The diagnosis of CTS is mainly clinical but the role of neurophysiological studies and ultrasound is also crucial in confirming diagnosis, grading the severity and excluding other neuromuscular conditions as the etiology. The treatment strategy and the outcome depend heavily on the severity of the disease. In the present times with increased patient awareness and physician training, most of the CTS cases diagnosed are in mild stage but the chances of false negative or false positive increase with such borderline severity. It is utmost important in diagnosing such cases with accuracy to avoid unnecessary expenditure of money and time in false positive case or delaying treatment in false negative cases causing patient suffering and monetary loss. Neurophysiological testing had been the gold standard in diagnosis of CTS. Evaluation with neurophysiological testing along with ultrasound showed sensitivity of 86% and specificity of 83% which is higher than that of neurophysiological testing or ultrasound alone[55]. CTS with grade more than very mild are easier to diagnose with confirmation of diagnosis and severity with either neurophysiological testing or ultrasound before analyzing the treatment and outcome. Very mild cases can ideally have neuro-electrophysiological testing followed by ultrasound because of its high diagnostic accuracy [56] to avoid false negative or false positive tests.

Compliance with ethical standards

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