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ELECTRODIAGNOSTIC TESTS TO CONFIRM CLINICALLY SUSPECTED CARPAL TUNNEL SYNDOME.

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Submitted in fulfilment of the requirements in respect of the Master's Degree MMED in the Department of Neurology in the Faculty of Health Sciences at the University of the Free State.

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Declaration of Authorship:

"I, DL Nkoana-Erasmus, declare that the coursework Master's Degree mini-dissertation that I herewith submit in a publishable manuscript format for the Master's Degree qualification in clinical neurology at the University of the Free State is my independent work, and that I have not previously submitted it for a qualification at another institution of higher education."

Acknowledgement and dedication:

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Table of contents:

Abstract:

Background:

Compression of the median nerve at the wrist is the most common entrapment neuropathy. Patients present with sensory symptoms in the median nerve distribution, pain in the hand, wrist or forearm and weakness of thumb opposition or abduction in severe cases.

The value of nerve conduction studies (NCS) in the diagnosis of carpal tunnel syndrome (CTS) is not clear. There are contradicting results from different reports, other reports citing the importance of electrodiagnostic (EDX) test in the diagnosis of CTS while other reports did not establish that link.

In the Free State Province, patients with CTS are mainly managed by orthopaedic surgeons. Only a small proportion of patients are managed by neurosurgeons at Universitas Academic Hospital.

The diagnosis is primarily made on clinical grounds. Conservative measures are tried first, but patients who do not respond to these, undergo carpal tunnel release surgery (CTRS).

Objectives:

The aim was to determine which EDX tests best correlate with the clinical diagnosis and severity of CTS.

The objective was to establish EDX guidelines to be used in the neurology electrophysiology unit when diagnosing CTS.

Method:

A cross sectional analytic study.

Patients with a diagnosis of CTS based on clinical signs and symptoms were recruited into the study from January 2019 to October 2019. They were requested to complete the Boston questionnaire (BQ) which assesses symptoms severity and functional capacity.

Nine NC parameters were then tested and results compared with those from the BQ to determine whether they correlate.

EDX severity score for CTS was assessed and was compared to the two components of the BQ.

Results:

Eighty-three percent of hands had severe to very severe symptoms on Boston 1 however, only 37.5% had severe to very severe functional impairment on Boston 2.

Weighted kappa of 0.19 indicating no agreement between Boston 1 and 2, severe symptoms is not associated with an increase in functional impairment.

No statistically significant correlation was found between EDX severity score, symptoms and functional status with a *p value* of 0.44 and 0.77 respectively.

Conclusion:

- There was no linear relationship between symptom severity and functional impairment; the majority of patients reported severe symptoms but no disability.
- Clinical and EDX tests showed a weak positive correlation which is statistically insignificant.
- Symptomatology rather than functional impairment was more indicative of severity of CTS.
- No correlation was found between EDX tests, Boston 1 and Boston 2.
- We were unable to answer with confidence the question of whether NCS is always necessary and feel that a follow-up post-op study will provide useful insights.

Keywords:

1. Boston questionnaire.
2. Carpal tunnel syndrome.
3. Electrodiagnostic tests.
4. Electrophysiological studies.
5. Median nerve neuropathy.
6. Nerve conduction studies.
7. Phalen’s test.
8. Tinel’s sign.

List of abbreviation:

1. CTRS: carpal tunnel release surgery.
2. CTS: carpal tunnel syndrome.
3. D1MRLC: digit 1 median versus radial nerve sensory latency comparison.
4. D2MULC: digit 2 median versus ulnar nerve sensory latency comparison.
5. EDX: electrodiagnostic.
6. MMA: Median nerve motor amplitude.
7. MMCV: Median nerve motor conduction velocity.
8. MML: Median nerve motor onset latency.
9. EDX severity score: Electrodiagnostic severity score.
10. MSA: Median nerve sensory amplitude.
11. MSCV: Median nerve sensory conduction velocity.
12. MSPL: Median nerve sensory peak latency.
13. MSSS: Median nerve segmental sensory study.
14. MUPSCS: Median/Ulnar nerve palmar sensory comparison study.
15. NC: nerve conduction.
16. NCS: nerve conduction study/studies.
17. UMA: Ulnar nerve motor amplitude.
18. UMCV: Ulnar nerve motor conduction velocity.
19. UML: Ulnar nerve motor onset latency.
20. USA: Ulnar nerve sensory amplitude.
21. USCV: Ulnar nerve sensory conduction velocity.
22. USPL: Ulnar nerve sensory peak latency.

List of appendices:

Chapter 1

Background:

Carpal tunnel syndrome is caused by compression of the median nerve as it passes through the carpal tunnel (CT) in the wrist [1]. Associated sensory changes in the hand, along the median nerve distribution can include pain, loss of sensation and paraesthesia [1, 2, and 3].

Patients with CTS are often referred to neurology for electrodiagnostic (EDX) tests to establish whether the diagnosis is correct, to exclude other differential causes of their symptoms and to determine how severe the median nerve has been damaged.

Carpal bones and the transverse carpal ligament (TCL) at the wrist form the CT. The floor of the tunnel is formed by the carpal bones, while the ligament forms the roof of the tunnel [2, 3]. Structures that pass through the tunnel include the median nerve and nine tendons from muscles of the forearm; this makes the median nerve easily susceptible to damage by conditions that cause an increase in carpal tunnel pressure (CTP) [4].

CTP in normal subjects is measured to be between 2-10mmHg [4]. This is high in patients with CTS as a result of abnormally thickened connective tissue in the tunnel and the overlying restrictive TCL [4].

In 2015, Aboong noted in his review article that flexion and extension of the wrist increases CT pressure eight to ten times the normal limit respectively [4]. He explained that, compression of the nerve results in ischaemia and subsequent segmental demyelination [4]. This is followed by axonal loss in severe cases [4].

Several conditions are associated with CTS, but in the majority of cases the cause is not known. In idiopathic CTS repetitive activity of the wrist, which occurs in certain occupation and hobbies have a high incidence of CTS. Preston et al observed that “in most cases, oedema, vascular sclerosis and fibrosis are seen, which are consistent with repeated stress to connective tissue” [1]. Rheumatoid arthritis, diabetes mellitus, hypothyroidism, amyloidosis, acromegaly and pregnancy are among the common conditions associated with CTS [2].

The incidence and prevalence of CTS varies between different studies, but the prevalence is higher in females compared to males. The National Institute of Neurological Disorder and Stroke, states that "women are three times more likely than men to develop carpal tunnel syndrome" [5].

Porras et al graded the level of manual activity as low, medium and high activity. An example of low manual activity was associated with being a housewife, medium manual activity with being a cleaner or a typist and high manual activity with the use of heavy machinery like operating drilling machines used in road construction [6]. Yoon et al recruited 30 patients in their study with CTS. Twenty-eight were females and 16 out of the 28 were housewives [7]. However, they did not elaborate further on the type of house chores they did or their hobbies and whether that could have contributed to the development of CTS in those patients. Regardless, this supported the notion that repeated activity of the hand increased the risk of developing CTS [6].

The association between obesity and CTS is well established, with a high body mass index (BMI) increasing the incidence of CTS 2.5 times compared to slimmer individuals. A study that was done in Islamabad, Pakistan between March and August 2016 looked at the prevalence of obesity in CTS patients at their neurophysiology unit [8]. They had 112 patients enrolled in their study, 38 patients were obese [8]. The importance of documenting the BMI of patients with CTS is that obesity is a modifiable risk factor and with appropriate lifestyle changes, CTS can be managed without surgery.

In several studies, it has been reported that CTS is one of the commonest entrapment neuropathies [4, 5, and 9] and it often occurs in both hands, even in patients who have symptoms in one hand. Padua et al reported that CTS is bilateral in most cases and in the majority, unilateral CTS will become bilateral [3]. This indicates the importance of proper diagnosis and urgent management of CTS. When the patient presents with CTS in one hand, subclinical CTS in the other hand may be detected electrophysiologically.

The importance of EDX tests cannot be overlooked when planning appropriate management for this condition. Naidu et al emphasised the importance of EDX testing in the diagnosis of CTS. They stated that "nerve conduction studies are of established value in the diagnosis of CTS" [10].

Most electrophysiology units in the public and private sectors do not have standardised guidelines with regard to EDX testing and diagnosis of CTS. In facilities where electrophysiological services are not available for pre-surgical NCS to be done, the diagnosis is made solely on clinical findings, which is based on the presenting symptoms and signs observed during physical examination.

Clinical Symptoms and signs highly suggestive of CTS include:

1. Numbness and paraesthesia on the volar aspect of the thumb, index, middle finger and the lateral half of the ring finger [1, 2 and 8].
2. Nocturnal pain or paraesthesia that radiates first into the hands, then up the forearm and arm at times and usually awakens the patient from sleep [1, 2] .
3. Atrophy of the thenar muscle [1, 2].
4. Weakness of thumb abduction and opposition [1, 2].
5. Positive provocative test for CTS (Tinel's sign and Phalen's test) [1]

Tinel's sign is elicited by tapping the middle of the wrist over the median nerve. The test is positive when a patient reports paraesthesia in the hand, which radiates into the fingers supplied by the median nerve [1]. Phalen's test is performed by flexing the wrists with the dorsum of the hands held together, while the elbows are flexed. The test is positive when paraesthesia develops in 30 seconds to 2 minutes, along the distribution of the median nerve [1].

Ultrasound of the wrist is another investigation that can be utilised in the diagnosis of CTS but it has not been used routinely. A review article by McDonagh et al published in August 2015 suggested that ultrasound could be used as an alternative to EDX tests to diagnose CTS [11]. The cross sectional area (CSA) of the median nerve is measured and swelling of the nerve is assessed. Karadag et al noted the advantages of using ultrasound in the diagnosis of CTS, which included the fact that ultrasound imaging of the median nerve is well tolerated, is cheaper and quicker to do than EDX tests [12]. Another advantage is that ultrasound guided corticosteroid injection into the carpal tunnel can be done at the same time [12]. The cut off points of the CSA of the median nerve was 10-13mm² for mild symptoms, 13-15mm² for moderate symptoms and > 15mm² for severe symptoms [12]. The sensitivity and specificity of

ultrasound diagnosis of CTS was 89% and 83% respectively when measuring the median nerve CSA [13]. According to McDonagh et al, the sensitivity and specificity of EDX in the diagnosis of CTS was 85% and > 95% respectively [11]. EDX abnormalities have therefore been shown to be more specific than ultrasound.

Another advantage of ultrasonography over NCS in the diagnosis of CTS is that other structural pathology at the wrist like cysts can be visualised directly.

The Primary Care Rheumatology Society proposed clinical criteria that can assist when evaluating a patient with suspected CTS [13]. It is made up of eight questions that the patient must answer regarding their symptoms and an algorithm that the clinician follows based on the answers given by the patient.

Questions to be asked to a patient presenting with hand or wrist symptoms[13]

1. Do you have numbness or tingling in your wrist, hand or fingers?
2. Do your symptoms spare your little finger?
3. Are the symptoms worse at night?
4. Do the symptoms wake you up at night?
5. Have you noticed you hand is weak, for example, have you found yourself dropping things?
6. Do you find shaking your hand, holding your hand or running it under warm water improves your symptoms?
7. Re the symptoms made worse by activities such as driving, holding a telephone, using vibrating stools, or typing?
8. Have splints or injection helped with your pain if you have had it in the past?

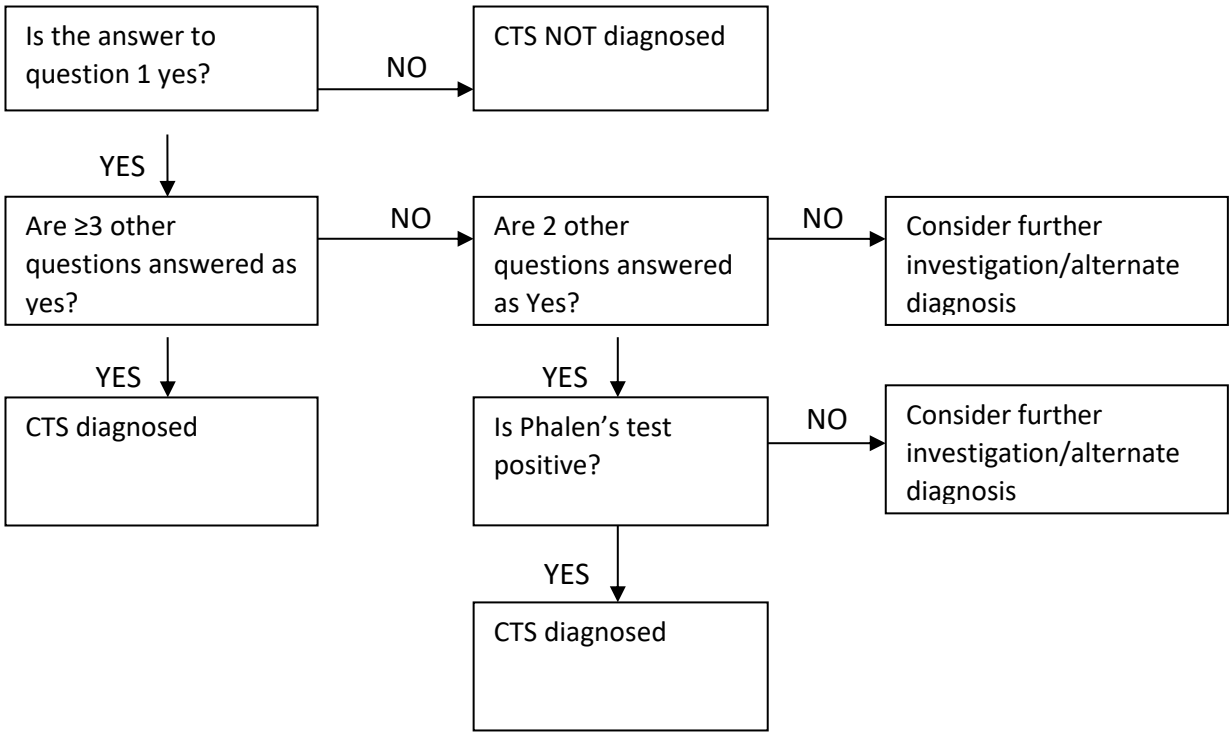


Figure 1: Algorithm for the diagnosis of carpal tunnel syndrome from the primary care rheumatology Society, Burton et al [13]

The Boston and DASH questionnaires have been used in several studies to assess the clinical severity of CTS, both test have been validated and were found to be equivalent in determining the severity of CTS [14]. The Boston questionnaire, which will be used in this study, is made up of two parts: 1. Symptom severity and 2. Functional capacity score. This questionnaire gives a subjective report of the severity of individual symptoms and whether this affects daily activities.

Patients are usually requested to grade their pain using the visual analogue scale. Pain is scored between 1-10, with a score of 1 being minimal and 10 indicating extreme and intolerable pain.

Nerve conduction studies that are routinely done are the Median nerve sensory amplitude (MSA), Median nerve sensory peak onset latency (MSPL), Median nerve motor amplitude (MMA), Median nerve motor onset latency (MML) and Median/Ulnar palmar sensory comparison (MUPSCS).

Other studies that compare the median nerve to ulnar and radial nerve studies are done for detection of more extensive neuropathy. There are other NCS parameters that could be tested in CTS if the above tests do not show any abnormalities, to confirm the diagnosis in a symptomatic patient.

These specific tests according to Preston et al are more sensitive in diagnosing CTS but the tests might remain abnormal even after decompression surgery unlike the median motor distal onset latency, sensory peak onset latency and sensory amplitude which usually recover after surgery [1]. This correlates with findings by Naidu et al who demonstrated a significant improvement of the median sensory amplitude and distal motor latency after surgery compared to poor recovery of the median motor amplitude [10]. These more specific tests include median versus ulnar or median versus radial sensory comparison, but they are most important when co-existing ulnar or radial neuropathy is present [1]. While these additional tests are usually not required to confirm or refute the presence of CTS, they will be routinely performed for all cases in this study.

Yoon et al categorised the EDX severity of CTS into mild, moderate and severe (Table 1) [7]. They also included features of denervation demonstrated on electromyography in their classification. Needle examination of the muscle will not be included as a diagnostic parameter in this study, because it is invasive and is usually indicated when there is marked muscle atrophy and weakness, making it necessary to exclude other neurological conditions.

CHARACTERISTIC	MILD	MODERATE	SEVERE
Motor latency, msec	4.5-5.0	5.0-7.0	>7.0 or negative
Sensory amplitude, µV	<20 µV	<20 µV	<20 µV or negative
Sensory latency, msec	3.0-4.0	4.0-6.0	>6.0 or negative
Denervation	Negative	Negative	Positive

Table 1: EDX Classification of severity of CTS, Yoon et al [7]

When doing NCS the hand should be warmed to a temperature ≥ 32˚C. Cold hand temperature impairs nerve conduction by slowing conduction velocity and prolonging latencies [16]. Cold temperature also increases both motor and sensory nerve amplitude [16]. The hands should be cleaned with skin preparation to remove dead skin which can also affect conduction especially of sensory studies.

Preston et al in the 3rd edition of "Electromyography and Neuromuscular Disorders: Clinical Correlations" illustrate how different NCS parameters are to be properly tested and they also provide normal values for each test [1]. Images shown below are from our electrophysiology unit. These tests include the following:

1. Median nerve motor study (MMS) to determine:-

a) Median nerve motor onset latency (MML).
b) Median nerve motor amplitude (MMA).
   - The abductor pollicis brevis (APB) muscle is recorded. G1, the active electrode is placed on the muscle belly and G2, the reference electrode is placed on the metacarpophalangeal joint.

- Stimulation is at the wrist, 7 cm from G1 between the tendon of the flexor carpi radialis and palmaris longus distally and on the antecubital fossa over the brachial pulse proximally. The distance between the distal and proximal site is measured.

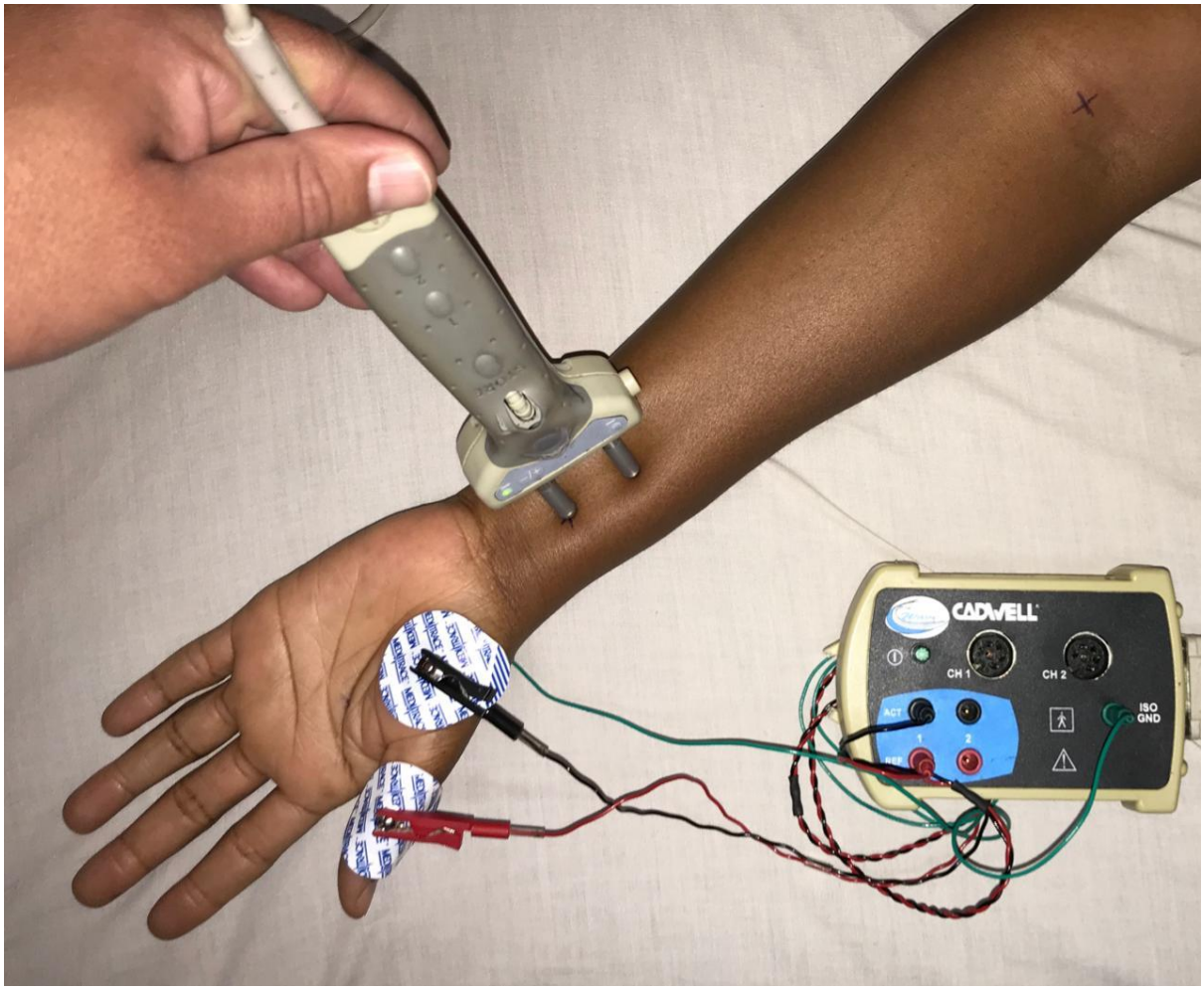


Figure 2: Median nerve motor studies, recording abductor pollicis brevis (APB). Marking on the cubital fossa is the site for proximal stimulation.

2. Median nerve sensory study to determine:-

a) Median nerve sensory peak onset latency (MSPL).
b) Median nerve sensory amplitude (MSA).
   - Using ring electrodes, G1 is placed on the metacarpophalangeal joint of the index finger and G2 is placed on the distal interphalangeal joint.
   - Stimulation is at 13 cm on the wrist between the tendon of the flexor carpi radialis and palmaris longus.

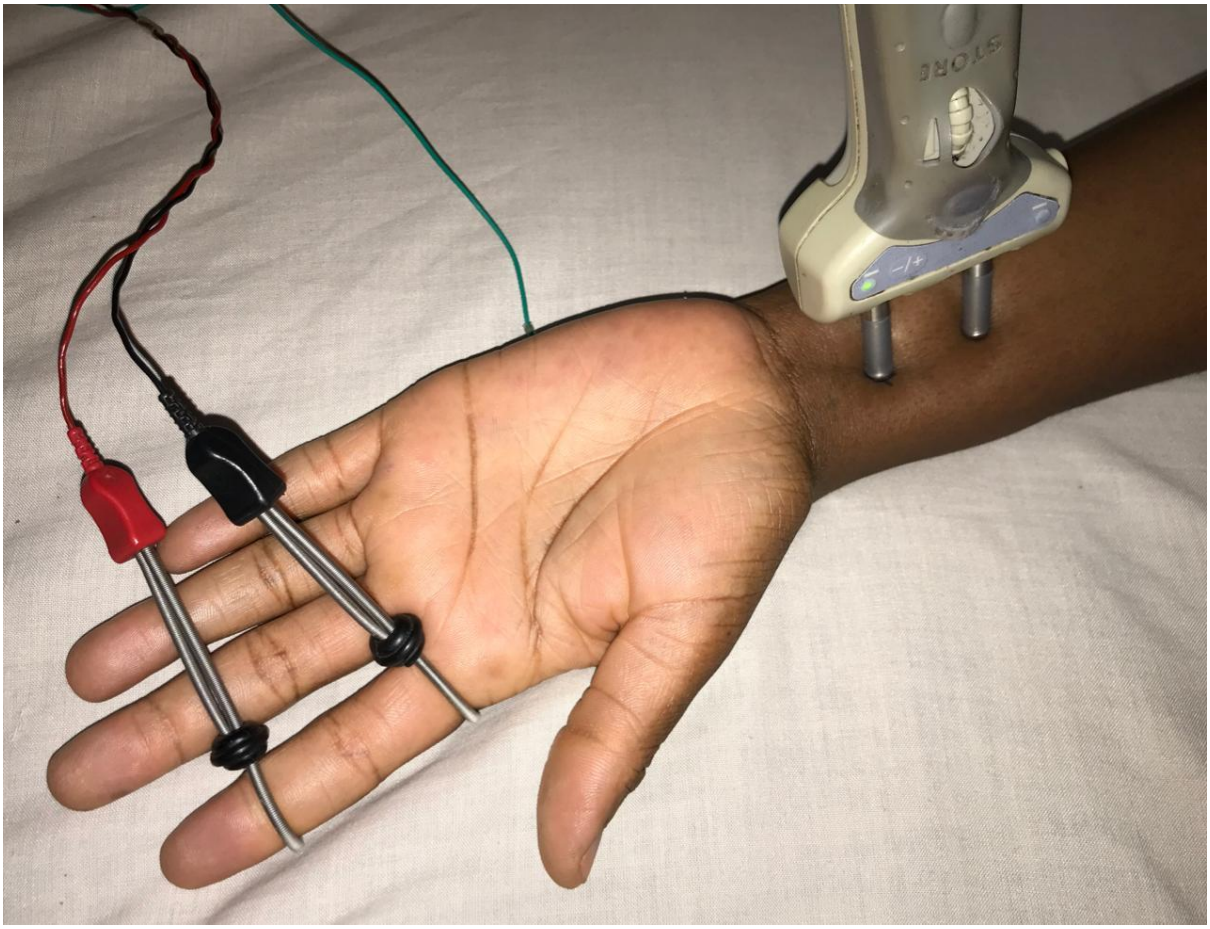


Figure 3: Median nerve sensory study, recording with ring electrode.

3. Median/Ulnar nerve palmar sensory comparison study (mixed).

- The recording electrode G1 is placed on the middle of the wrist between flexor carpi radialis and palmaris longus for median nerve and adjacent to flexor carpi ulnaris tendon for ulnar nerve.
- G2 is placed 4 cm proximal to G1.
- Stimulation of the median nerve on the palm 8 cm from G1, between the web space of the index and middle finger. For ulnar nerve stimulation is done on the palm between the web space of the ring and the 5^{th} finger.

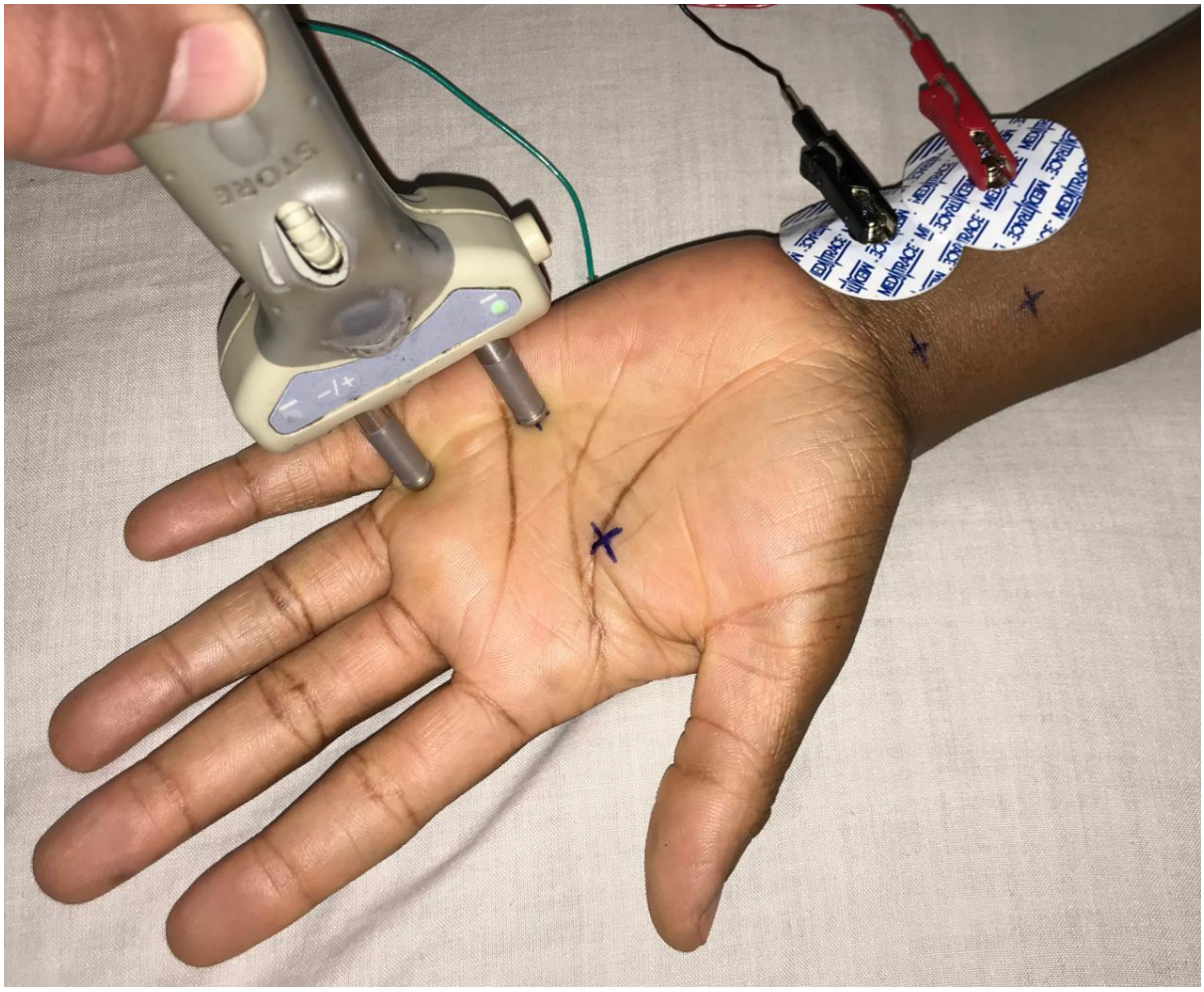


Figure 4: Median/Ulnar nerve palmar sensory comparison study: Stimulation over the ulnar nerve. Markings indicate where the recording electrodes will be placed on the wrist and stimulation site on the palm for the median nerve.

4. Median nerve second lumbrical and ulnar first dorsal interosseous distal motor latency study.

- The recording electrode G1 is place slightly lateral on the third metacarpal bone and G2 is place distally on the metacarpophalangeal joint of the 2nd digit.
- Both the median and ulnar nerves are stimulated 8 cm from G1 on the wrist using the same anatomical sites as above.
- In CTS, Median motor latency is prolonged compared to ulnar motor latency; latency difference of ≥0.5 ms is abnormal.

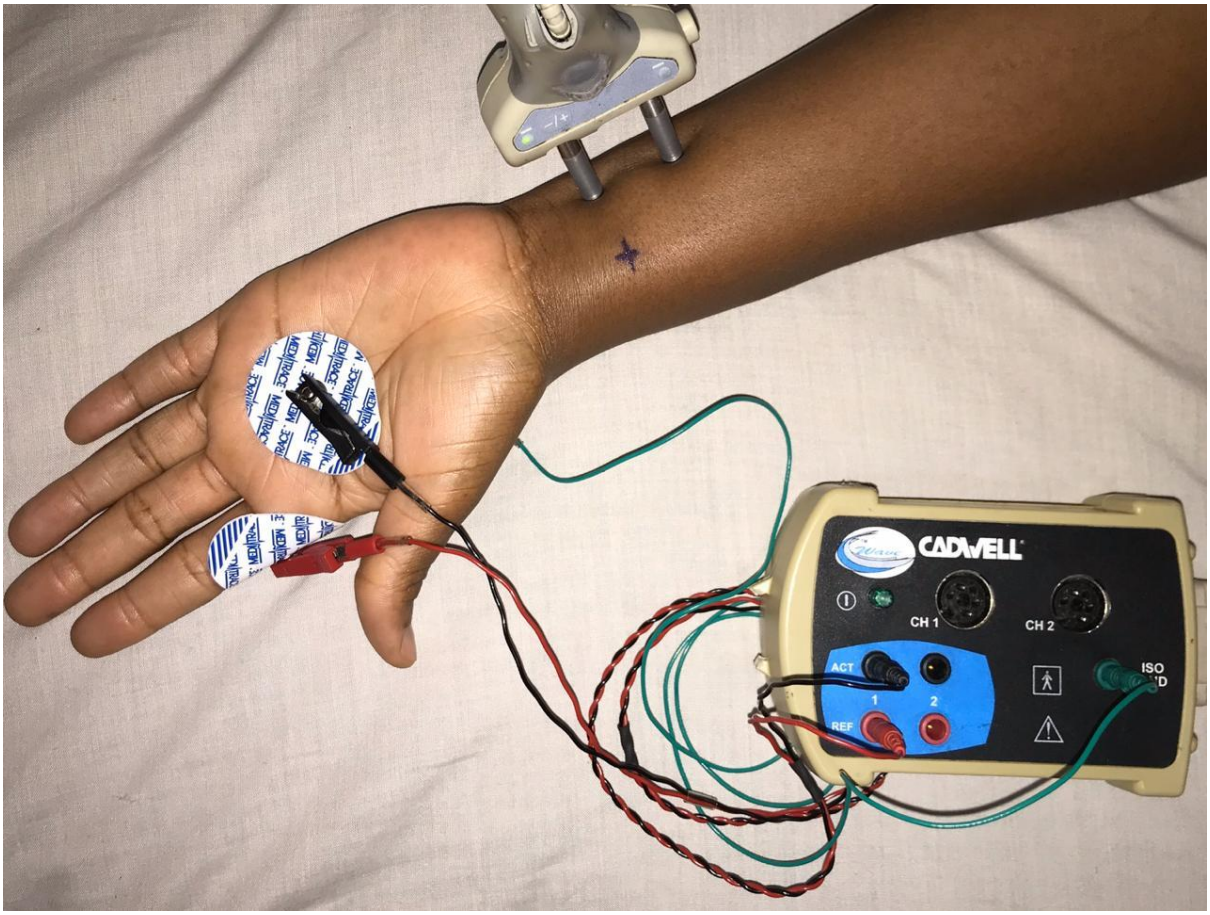


Figure 5: Median 2nd lumbrical and ulnar 1st dorsal interosseous motor latency study: stimulating over the ulnar nerve. Markings indicate stimulation site for median nerve.

5. Median segmental sensory study (Median sensory palmar study).

- Recording ring electrodes were placed on the middle finger, with G1 over the proximal interphalangeal joint and G2 over the distal interphalangeal joint.
- The first stimulation site is on the wrist 14 cm from G1 and the second stimulation point is 7 cm on the palm from G1.
- Palm/wrist sensory action potential (SNAP) amplitude ratio > 1.6 indicates conduction block.

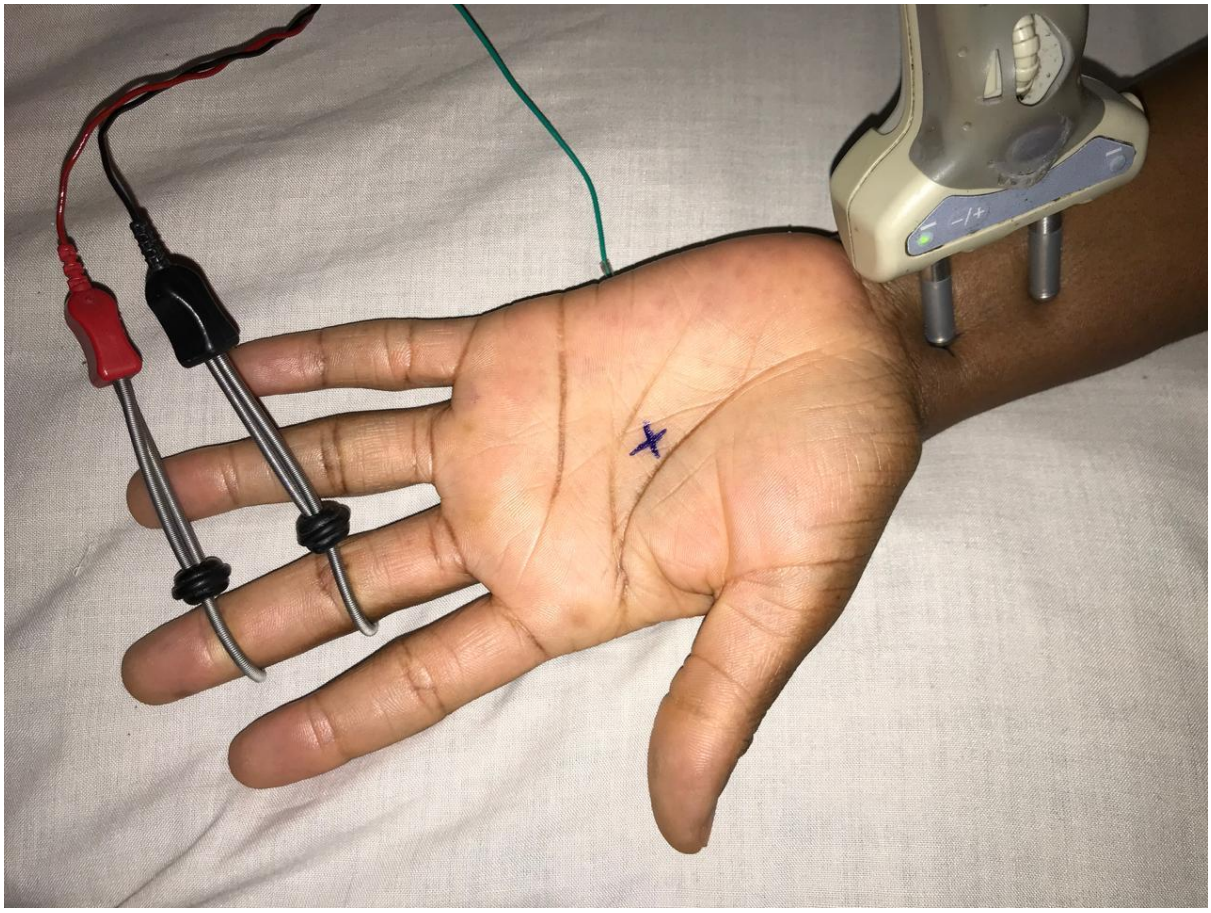


Figure 6: Median nerve segmental sensory study, the marking on the palm indicates the 2nd stimulation point.

6. Digit 4 Median versus Ulnar sensory latency comparison.
    - Recording digit 4 with ring electrodes, G1 is placed on the metacarpophalangeal joint and G2 is placed 4 cm distally on the distal interphalangeal joint.
    - Stimulating on the wrist 13cm over the median nerve and ulnar nerve.
    - Median nerve sensory peak latency is prolonged in CTS and when compared to the ulnar peak onset latency the difference will be ≥0.5 ms.

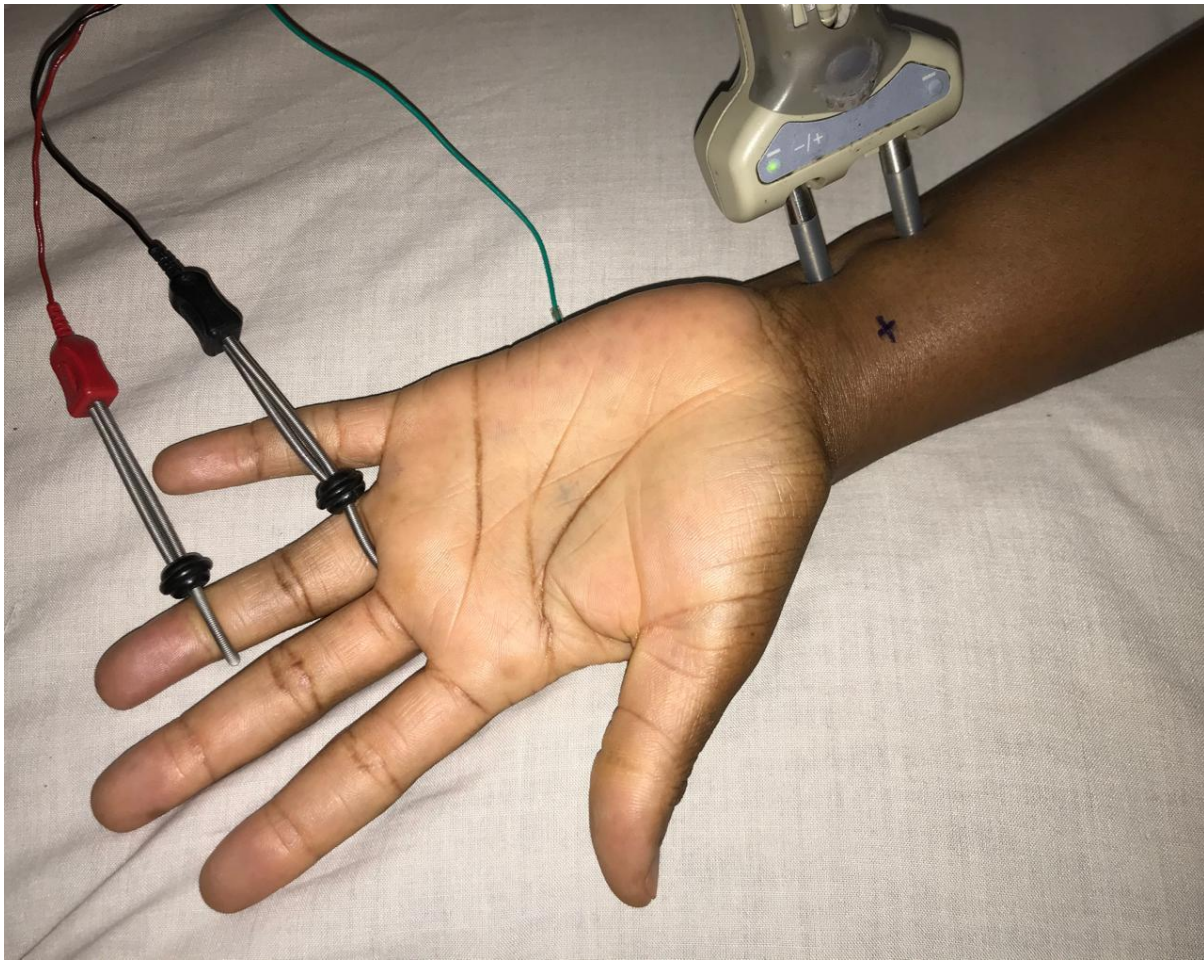
- 

Figure 6: Digit 4 median versus ulnar sensory latency comparison, the marking on the wrist is the stimulation point for median nerve.

7. Digit 1 Median versus Radial sensory latency comparison study.
    - Recording digit 1 using ring electrodes, G1 was placed on the metacarpophalangeal joint and G2 on the distal interphalangeal joint.
    - Stimulation is 12 cm for both the median nerve at the wrist and radial nerve on the lateral forearm over the radial bone.
    - The difference between the median and radial digit 1 latencies of ≥ 0.5 ms is abnormal.

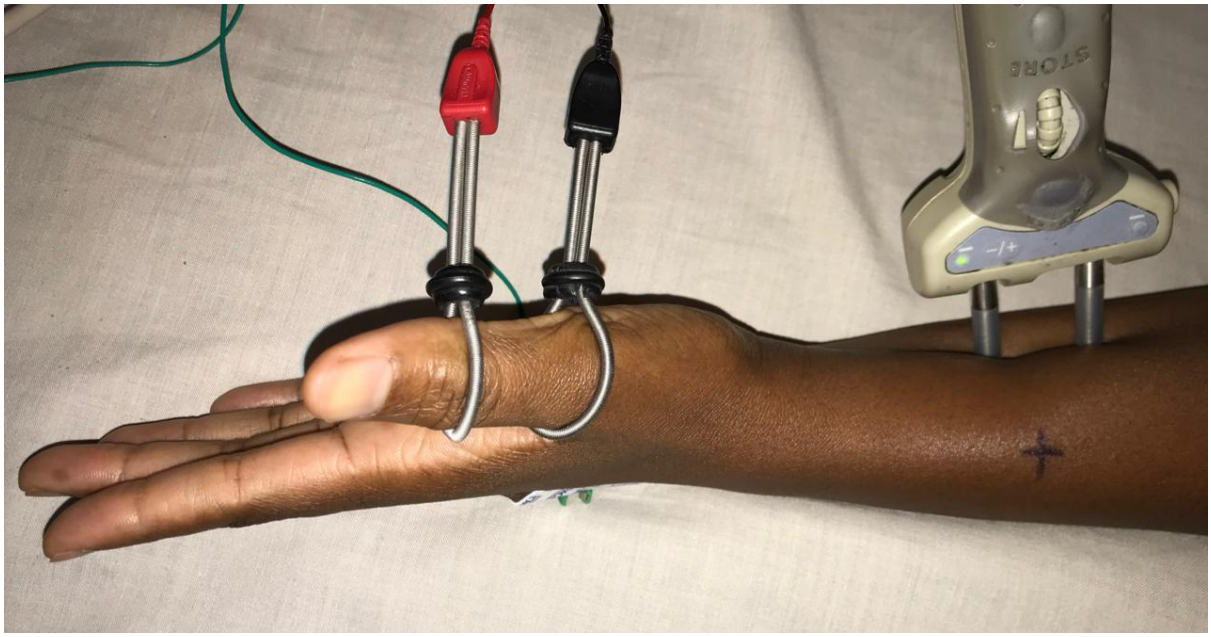


Figure 7: Digit 1 median versus radial nerve sensory latency comparison, the marking on the forearm indicates where the radial nerve will be stimulated.

Tables with normal reference values for median and ulnar motor and sensory NCS [1]:

Motor study

Nerve	Record	Amplitude (mV)	Conduction Velocity (m/s)	Distal Latency (ms)	Distal distance (cm)
Median motor	Abductor pollicis brevis	≥4.0	≥49	≤4.4	7
Ulnar motor	Abductor digiti minimi	≥6.0	≥49	≤3.3	7

Table 2: Reference values for motor conduction studies. **Preston et al [1]**

Antidromic Sensory

Nerve	Record	Amplitude (µV)	Conduction Velocity (m/s)	Distal Latency (ms)	Distal distance (cm)
Median sensory	Digit 2	**≥20**	**≥50**	**≤3.5**	**13**
Ulnar sensory	Digit 1	≥17 or ≥10 in adults older than 60 years.	≥50	≤3.1	11

Table 3: Normal reference values for sensory conduction studies. Preston et al [1]

The correlation between clinically diagnosed CTS and EDX studies is still not clear, even though the value of EDX tests was already emphasised by Naidu et al [10]. There are conflicting reports from other studies. In Suraj A Mulley's article that was published in 2017 titled "CTS with equivocal electrophysiological findings: Additional testing may improve diagnostic sensitivity", he commented that the diagnostic sensitivity of electrodiagnostic testing is relative when tested in mild and early CTS, but compared to moderate and severe cases the diagnosis can be made easily [16] . He further noted that the current practice is to start with median nerve sensory studies, followed by comparison of sensory studies to adjacent nerves in the same hand, mainly the ulnar nerve.

He looked at 85 patients who were diagnosed with CTS. The patients had pre-surgical NCS and they had repeat tests six months post surgery. He could not establish a statistically significant relationship between the patient's subjective impairment and the EDX test. However post-surgical NCS did show a significant improvement of sensory nerve conduction velocity (SNCV).

When doing nerve conduction studies for CTS, it makes sense to start first with sensory studies because sensory nerve fibres are damaged early. Motor fibres become damaged only in severe cases.

A study conducted in 2004 by Tuncali and colleagues, looked at 31 hands surgically treated for CTS. They documented the severity of clinical signs and EDX test and compared that with intra-operative findings of the median nerve which they graded to be between 1-3 based on the presence of oedema, vascularisation and fibrosis [17] . They found a high statistical correlation between clinical severity and intra-operative findings with a p-value of ≤0.01 but could not demonstrate any correlation between EDX and the pathological features of the median nerve as graded intra-operatively [17].

The American Academy of Orthopaedic Surgery (AAOS) in May 2007 published guidelines to be used by clinicians in the management of patients with CTS [19]. The aims of the recommendation are to improve patient care and guide decision making processes [18]. With regard to EDX, their recommendations are as follows:-

Recommendation 3: Nerve conduction velocity studies is divided into a, b and c.

3.1a: The physician may obtain EDX tests to differentiate among diagnoses.

3.1b: The EDX test may be obtained in the presence of thenar atrophy and/or persistent numbness.

3.1c: Obtain electrodiagnostic tests if clinical and/or provocative tests are positive and surgical management is being considered.

They further recommended that when a physician orders EDX tests they should use guidelines for the diagnosis of CTS from the following bodies: American Academy of Neurology/American Association of Neuromuscular and Electrodiagnostic Medicine/American Academy of Physical Medicine and Rehabilitation [19], which are as follows:

a. Sensory NCV studies to the median nerve with distal latency compared to the ulnar and radial nerves.
b. Median motor nerve conduction in most patients.
c. Needle EMG at the discretion of the physician.

A review article by Mohammed H Alanazy looked at the approach and pitfalls in clinical and electrophysiological evaluation of CTS [15]. He stated that "Failure to capture electrodiagnostic abnormalities especially in mild CTS (false-negative) is less hazardous than the false diagnosis of a normal subject with CTS (false-positive)". False positive results may influence treatment decisions and subject the patient to an unwarranted intervention. He recommended that a minimum of two tests that demonstrates prolonged median nerve latencies are required to minimize the incidence of false positive results. He further advised that incidental nerve slowing at the wrist in asymptomatic workers, diabetics or in those with demyelinating neuropathy should be reported as median neuropathy at the wrist rather than CTS [15]. In such instances, comparison studies showing slowing of the median nerve relative to the ulnar or radial nerve are important in providing internal control for confounding factors, including age, gender, weight, height, hand size, temperature and the presence of a coexistent polyneuropathy. That is because the median nerve is the only nerve passing through the

carpal tunnel and any abnormality demonstrated on NCS is most likely as a result of compression at the wrist and not as a results of those other confounding factors. He approximated that 10-15% of patients with CTS diagnosed on clinical grounds have normal NCS [15].

In 2003 Kikas assessed conduction studies of the second lumbrical muscle (2L) and mixed nerve segmental studies in CTS. He stated that focal demyelination of the median nerve is located 2-3cm distal to the proximal edge of the transverse ligament which corresponds to the distal crease of the wrist [19]. He proposed that the segmental studies are the best nerve conduction parameters to determine slowing of conduction velocity in the distal segment of the median nerve across the carpal tunnel. He also stated that the 2L conduction study is particularly useful "when the abductor pollicis brevis (APB) is completely denervated and the motor response to the APB is unobtainable" [19].
This shows that conduction of the 2L will only be abnormal in severe cases and that early CTS can be missed when other parameters are not tested first.

In one of the earliest research conducted by G.J. Carroll in New Zealand and published in 1986, he compared the median and radial nerve sensory latencies in patients diagnosed clinically with CTS [20]. Median sensory nerve action potential confirmed CTS in 79 of symptomatic hands (49.1%). Of the remaining hands additional comparison of the distal sensory latencies (DSLs) for the median and radial nerve increased the EDX yield to 59.6%.

Electrodiagnostic studies in the diagnosis of CTS remains a controversial issue with conflicting reports from various studies.

Research question

Could the diagnosis of CTS be made confidently based on the presenting symptoms and clinical signs alone without NCS confirming the diagnosis?

Aims:

To determine which electrophysiological tests are most appropriate and best correlate with the clinical diagnosis and severity of carpal tunnel syndrome.

Objective:

To establish electrodiagnostic guidelines for the diagnosis of Carpal Tunnel Syndrome at Universitas Academic Hospital, electrophysiology clinic.

Hypothesis:

We hypothesise that NCT are invaluable tests needed in the diagnosis of CTS and that they are relevant in the initial work up of patients with clinically suspected CTS.

We further hypothesise that EDX test will be found to be statistically significant and correlate with clinical severity of CTS.

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Chapter 2

Electrodiagnostic tests to confirm clinically suspected carpal tunnel syndrome

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Keywords: Electrodiagnostic tests, nerve conduction studies, carpal tunnel syndrome, Boston questionnaire, median neuropathy

Abbreviated title: Nerve conduction tests in carpal tunnel syndrome

Abstract:

Background:

Carpal tunnel syndrome is defined as median nerve neuropathy at the wrist, caused by compression of the nerve in the carpal tunnel (CT). The diagnosis is clinical with electrophysiological confirmation when available.

In this study, we investigated the relationship between clinical diagnostic criteria and electrophysiological testing to evaluate the need for the latter.

Objectives: To determine which electrodiagnostic (EDX) tests best correlate with clinical diagnosis and severity of CTS.

Method:

Participants with a clinical diagnosis of CTS were recruited for EDX tests. The study was conducted over a 10 month period, from the beginning of January 2019 to the end of October 2019 at Universitas Academic Hospital, electrophysiology unit.

Data was collected by means of an evaluation sheet, which captured participant's demographic details and presence or absence of clinical signs suggestive of CTS. The investigators assisted participants to complete the Boston questionnaire (BQ) which assesses symptom severity and functional capacity. Pain intensity was scored using a visual analogue scale.

Nine nerve conduction (NC) measures of the median nerve conduction were tested. Ulnar and radial nerve studies were done for comparison.

Results:

Thirty-two participants were recruited into the study. Sixteen participants had bilateral hand symptoms, making a total study sample of 48 hands. The majority of participants were female and white. Median age was 50 years. Thirteen participants had rheumatoid arthritis, seven had thyroid disease and another seven had diabetes mellitus. Fifty-six percent of participants had a BMI in the obese range.

Thirty-four hands had sensory loss on the median nerve distribution, fourteen had thenar muscle atrophy, 31 had a positive Phalen's test and only 22 hands had thumb abduction weakness. Eighty-three percent of hands had severe to very severe symptoms on Boston 1, however only 37.5% had severe to very severe functional impairment on Boston 2.

Six NC parameters demonstrated abnormality of median nerve conduction across the wrist in 60% of the hands, but only two NC parameters had a pickup rate of > 70%. The correlation of EDX test with BQ was statistically insignificant with p-values of 0.44 for symptom severity and 0.77 for functional capacity. Weak correlation was also found between the two parts of the BQ.

Conclusion:

Symptoms rather than functional capacity are more indicative of severity of CTS when assessed with the BQ. Electrodiagnostic tests poorly correlate with the clinical diagnosis of CTS, even in those nerve conduction parameters that demonstrated conduction abnormality within the median nerve.

Title: Electrodiagnostic tests to confirm clinically suspected carpal tunnel syndrome.

Introduction:

Carpal tunnel syndrome (CTS) is a compressive neuropathy of the median nerve [1, 2]; the nerve is compressed as it passes through the carpal tunnel (CT) at the wrist. Associated sensory changes in the hand, along the median nerve distribution can include pain, loss of sensation and paraesthesia [1, 2,]. In most cases, both hands are affected [3]. Compression of the median nerve, subsequently results in ischaemia and segmental demyelination of the nerve [4]. Only in severe cases does it cause axonal nerve damage [4]. In most cases, the cause of CTS is not known, but certain conditions are associated with an increased risk of developing CTS. Rheumatoid arthritis, Diabetes mellitus, thyroid disease, amyloidosis, acromegaly and pregnancy are among the most common conditions associated with CTS [5]. Obesity is a modifiable risk factor in the development of CTS [6].

Non-pharmacological management of CTS includes wrist splinting and avoidance of activities that requires excessive hand movement, especially at the wrist. Pharmacological treatment includes paracetamol, non-steroidal anti-inflammatory drugs and corticosteroid injection into the carpal tunnel, if other measures are ineffective [7]. Surgical treatment is considered a last option and is indicated mainly for severe cases. Most electrophysiology units in the public and private sectors do not have standardised guidelines with regard to electrodiagnostic testing for the diagnosis of CTS. The value of electrodiagnostic (EDX) tests in the diagnosis of CTS is an ongoing debate, with some reports stressing their importance and others failing to establish a correlation between clinical severity and nerve conduction studies (NCS).

Patients with CTS in the Free State Province are mainly managed at the orthopaedic hand unit, at Pelonomi secondary hospital and at Universitas academic hospital. A few other cases are seen at the neurosurgical department in both hospitals.

Aims and objectives:

The aim of the study was to determine which EDX tests are most appropriate and best correlates with the clinical diagnosis and severity of carpal tunnel syndrome. It was also to determine whether CTS can be diagnosed solely on clinical grounds. This was done by comparing symptom severity and functional capacity to EDX tests.

The objective is to develop an EDX protocol, which can be adopted at Universitas Academic Hospital electrophysiology unit, when evaluating patients with suspected CTS.

Research method and design

Study design:

This was a cross sectional analytic study that recruited participants with a clinical diagnosis of CTS from the orthopaedic hand unit.

The intended study sample size was 36-40 hands. Pelonomi secondary hospital orthopaedic hand clinic, which was the main unit where the participants were referred from, evaluates about three new patients per week (sometimes more) with possible CTS. Some of the patients have symptoms in both hands. We were therefore expecting a sample size of 36 to 40 hands in a period of three months.

Setting:

The study was conducted at Universitas Academic Hospital, electrophysiological unit, in Bloemfontein, Free State Province of South Africa.

Participant:

Participants from the orthopaedic hand unit who met the criteria for CTS based on clinical signs and symptoms were included in the study. These participants were being considered for carpal tunnel release surgery (CTRS).

Inclusion criteria:

Participants older than the age of 18 years, diagnosed with CTS and who consented to take part in the research study were included.

Participants were required to have one of more of the following signs and symptoms suggestive of CTS:

1. Numbness and paraesthesia on the volar aspect of the thumb, index, middle finger and the lateral half of the ring finger [1, 8].
2. Nocturnal pain or paraesthesia that radiates first into the hands, then up the forearm and arm at times and usually awaken the patient from sleep [1, 8].
3. Atrophy of the thenar muscle [8].
4. Weakness of thumb abduction and opposition [8].
5. Positive provocative test for CTS (Tinel and Phalen's test) [3, 8].

Exclusion criteria:

Individuals with previous surgery to the same hand, proximal median nerve pathology, nerve root pathology, brachial plexopathy and peripheral neuropathy, which might obscure electrophysiological parameters, were excluded from the study. In such instances, abnormal studies may be indicative of other peripheral nerve disorders and not necessarily as a result of median nerve compression at the wrist.

Data collection:

Participants completed the evaluation sheet, which included demographic information and the Boston questionnaire, with the assistance of the investigators. The demographic data included: age, gender, residential area, occupation, hobbies, co-morbidities, body mass index and documentation of the symptomatic hand.

The principal investigator performed a clinical assessment on all participants and specifically documented if there was any weakness of thumb abduction or opposition, sensory loss on the fingers supplied by median nerve, thenar muscle atrophy and whether provocative tests (Tinel or Phalen's test) were positive.

Participants completed the Boston Questionnaire parts 1 and 2, which subjectively assesses symptom severity and functional capacity respectively [9]. They also graded their pain intensity by completing the visual analogue scale (VAS) [9].

In preparation before proceeding with nerve conduction tests, the hands were first warmed to 32˚C using warm water or a heater. Cold temperature of the hands can interfere with nerve conduction parameters [8, 10]. The skin was then cleaned with skin prep to remove dead skin that might slow sensory conduction of the nerves and cause greater impedance.

Pre-surgical NCS were done to confirm the diagnosis and comparisons were made with Boston questionnaire parts 1 and 2. Electrodiagnostic severity grading of CTS was also determined by using reference from Yoon et al [11]. The grading system was modified by excluding features of denervation, since electromyography with needle examination was not done.

Nine nerve conduction parameters were tested. The method used was from the 3rd edition of 'Electromyography and Neuromuscular Disorders' by Preston DC and Shapiro BE [8].

1. Median nerve motor study (MMS) to determine:

a) Median nerve motor onset latency (MML).
b) Median nerve motor amplitude (MMA).
   - The abductor pollicis brevis (APB) muscle is recorded. G1, the active electrode is placed on the muscle belly and G2, the reference electrode is placed on the metacarpophalangeal joint.
   - Stimulation is at the wrist, 7 cm from G1 between the tendon of the flexor carpi radialis and palmaris longus distally and on the antecubital fossa over the brachial pulse proximally. The distance between the distal and proximal site is measured.

2. Median nerve sensory study to determine:

a) Median nerve sensory peak onset latency (MSPL).
b) Median nerve sensory amplitude (MSA).
   - Using ring electrodes, G1 is placed on the metacarpophalangeal joint of the index finger and G2 is placed on the distal interphalangeal joint.
   - Stimulation is at 13 cm on the wrist, between the tendons of the flexor carpi radialis and palmaris longus.

3. Median –versus –Ulnar nerve palmar sensory comparison study (mixed):

- The recording electrode G1 is placed in the middle of the wrist, between flexor carpi radialis and palmaris longus for median nerve and adjacent to flexor carpi ulnaris tendon for ulnar nerve.
- G2 is placed 4 cm proximal to G1.
- Stimulation of the median nerve on the palm 8 cm from G1, between the web space the index and middle finger. For ulnar nerve, stimulation is done on the palm between the web space of the ring and the 5^{th} finger.

4. Median second lumbrical and ulnar nerve first interosseous distal motor latency study:

- The recording electrode G1 is place slightly lateral on the third metacarpal bone and distally G2 is place on the metacarpophalangeal joint of the 2^{nd} digit.
- Both median and ulnar nerves are stimulated 8cm from G1 on the wrist using the same anatomical sites as above.
- In CTS, median motor latency is prolonged compared to ulnar motor latency and latency difference of ≥0.5 ms is abnormal.

5. Median nerve segmental sensory study (Median nerve sensory palmar study):

- Recording ring electrodes were placed on the middle finger, with G1 over the proximal Interphalangeal joint and G2 over the distal interphalangeal joint.
- The first stimulation site is 14 cm on the wrist from G1 and the second stimulation site is on the 7cm from G1.
- Palm/wrist sensory action potential (SNAP) amplitude ratio > 1.6 indicates conduction block.

6. Digit 4 Median versus Ulnar nerve sensory latency comparison:

- Recording digit 4 with ring electrodes, G1 is placed on the metacarpophalangeal joint and G2 is placed 4 cm on the distal interphalangeal joint.
- Stimulating on the wrist 13 cm over the median nerve and ulnar nerve.
- Median nerve sensory peak latency is prolonged in CTS and when compared to the ulnar peak onset latency the difference will be ≥0.5 ms.

7. Digit 1 Median versus Radial nerve sensory latency comparison study:

- Recording digit 1 using ring electrodes, G1 was placed on the metacarpophalangeal joint and G2 on the distal interphalangeal joint.
- Stimulation is 12 cm for both median nerve at the wrist and radial nerve on the lateral forearm over the radial bone.
- The difference between median and radial nerve sensory latencies of ≥ 0.5 ms abnormal.

Tables with normal reference values for median and ulnar motor and sensory nerve conduction studies [8]:

Motor nerve studies:

Nerve	Record	Amplitude (mV)	Conduction Velocity (m/s)	Distal Latency (ms)	Distal distance (cm)
Median motor	Abductor pollicis brevis	≥4.0	≥49	≤4.4	7
Ulnar motor	Abductor digiti minimi	≥6.0	≥49	≤3.3	7

Table 1: Reference values for motor conduction studies. Preston et al [8]

Antidromic Sensory nerve studies:

Nerve	Record	Amplitude (µV)	Conduction Velocity (m/s)	Distal Latency (ms)	Distal distance(cm)
Median sensory	Digit 2	≥20	≥50	≤3.5	13
Ulnar sensory	Digit 1	≥17 or ≥ 10 in adults older than 60 years.	≥50	≤3.1	11

Table 2: Reference values for sensory conduction studies. Preston et al [8]

Data analysis:

Collected data was entered into an excel spreadsheet and was analysed by the Department of Biostatistics of the University of the Free State. Results were summarised by frequencies and percentages (categorical variables) and by means, standard deviations or percentiles (numerical variables). Ninety-five percent confidence intervals were calculated for main outcomes. Associations were evaluated by correlations for numerical variables and risk measures for categorical variables. For hypothesis testing, kappa test and Fisher's exact score were used.

Boston 1 and 2 were compared, to see if there is an association between symptom severity and functional capacity.

Boston 1 and 2 were each compared to individual nerve conduction parameters, to determine which electrodiagnostic test best correlate with subjective severity of symptoms and functional state reported by the patients.

Pain intensity as documented on the VAS was also compared to both Boston 1 and 2 parts of the questionnaire, to see if the severity scores recorded corresponded.

Demographic data which included gender, age, race, co-morbidities, body mass index, occupation and hobbies were analysed and reported as frequency and percentages.

We compared the patients EDX severity score to their specific occupation and hobbies, to see if we could establish a link between certain activities and severity grades of CTS on electrophysiological test.

Ethical consideration:

Ethical approval to conduct the study was obtained from the University of the Free State health sciences ethics committee and the Free State department of health granted special permission. Ethics approval number: UFS-HDS2018/1188/2901.

Participants who agreed to take part in the study were included and all signed an informed written consent. None of the patients withdrew their consent due to physical discomfort during testing.

Participants' details were kept strictly confidential and only the investigators had access to their personal information. Coding was done for all the patients so that identifying information was only known to the principal investigator.

Results:

Thirty-two participants were recruited into the study; sixteen of them had symptoms in both hands, making a total study sample of 48 hands with CTS. All the participants came from the Free State Province and the majority of them were from the Bloemfontein area. Sixty-nine percent of the study population were white people, 22% were black people and 9% were people of mixed ancestry.

Twenty-four participants (75%) were females. This is in keeping with population based incidence reports that female are more affected than males [12].

Gender	• Male/Female = 8:24
Age	• Median age 50yrs (range 29-71)
Race	• White people 22 (69%) • Black people 7 (22%) • People with mixed ancestry 3 (9%)
Occupation	• Unemployed 9 (28%) • Pensioners 2 (6%) • Employed 16 (50%) • Not captured 5 (16%)

Table 3: Demographic data.

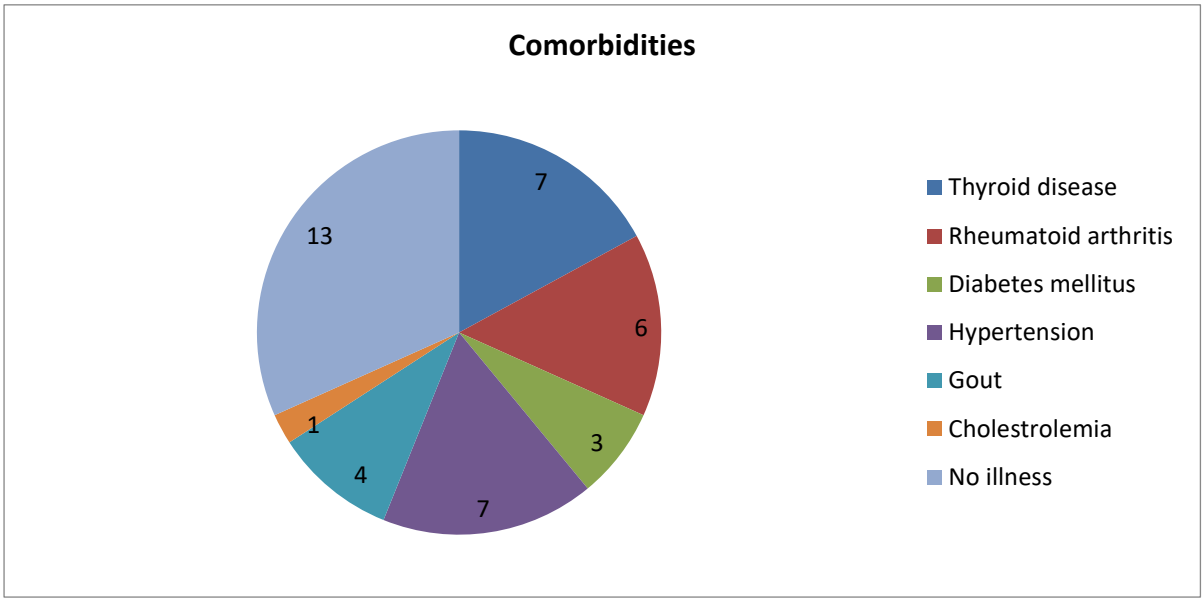


***Figure 1*: Thirty-two participants with pre-existing medical conditions, some with more than one illness. The numbers indicates how frequent each condition occurred amongst the study group. Thirteen patients did not report any pre-existing medical condition.**

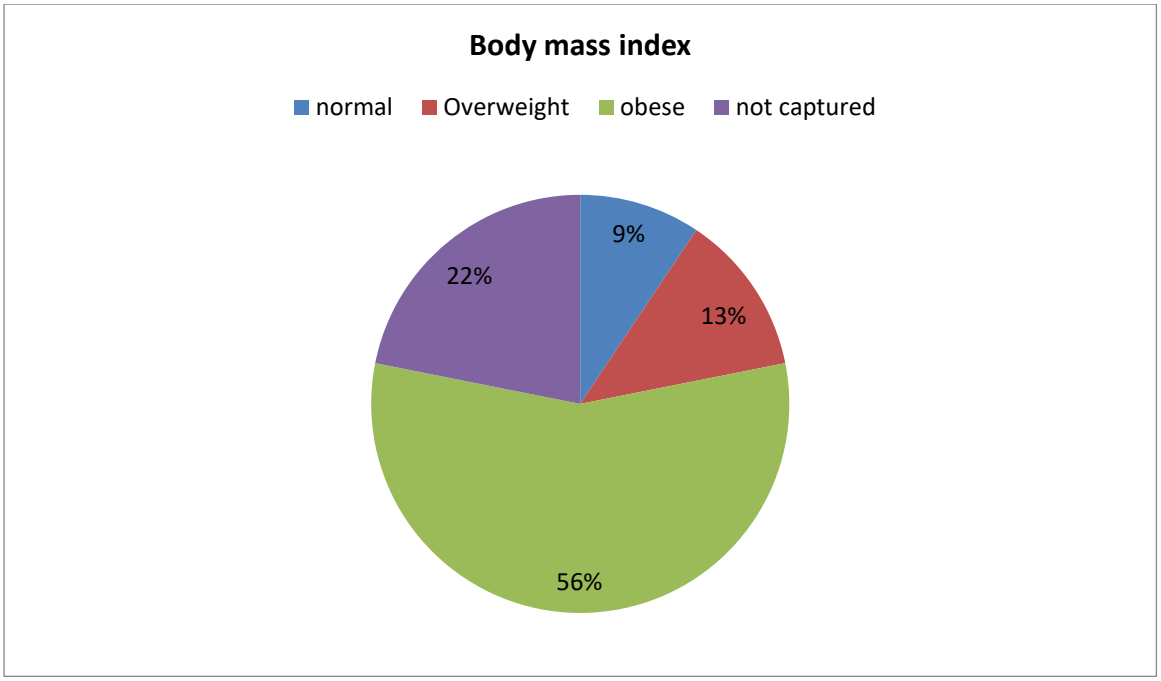
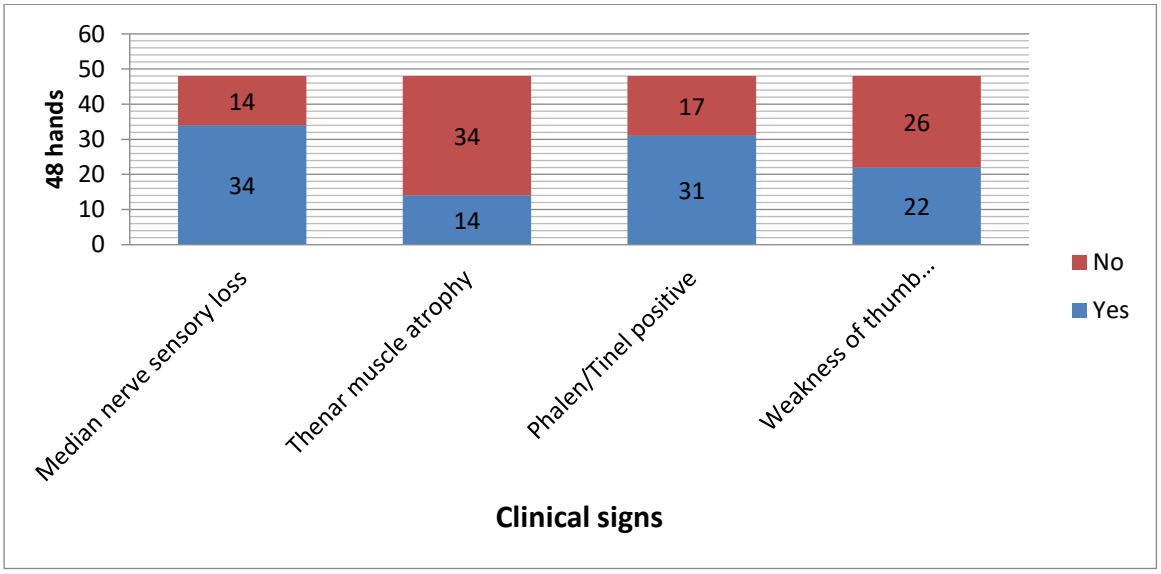


Figure 2: Body mass index of the 32 patients, normal weight (3), overweight(4), obese(18), not captured(7).



Graph 1: The number of hands with positive clinical signs on physical examination, including weakness of thumb abduction and opposition.

Electrodiagnostic severity grading did not correlate with clinical symptoms and functional capacity, with zero correlation for Boston 1 and 0.11 for Boston 2. The Fishers exact test was noted to be 0.0003 and 0.0002 for the two parts of the questionnaire to EDX tests, indicating very poor correlation between the two.

Pain score was assessed by the Visual Analogue Scale and was compared to Boston 1 and 2. Pain severity increased as symptom severity worsened, as assessed by Boston 1. In contrast, severe pain intensity did not correlate with functional capacity which was assessed by part 2 (even in those patients who reported severe pain, there was no associated impairment in functional capabilities). An association between pain intensity and BQ could not be established, with weak positive correlation of 0.24 for Boston 1 and a very weak correlation of 0.13 for Boston 2.

Eighty-three percent of hands had severe to very severe symptoms on Boston 1, however only 37.5% had severe to very severe functional impairment on Boston 2. There was no linear relationship between symptom severity and functional impairment, even though the majority of the patients reported severe symptoms that did not affect their activities of daily living. A weighted kappa of 0.19 indicated no agreement between Boston parts 1 and 2.

Different nerve conduction parameters were tested, the percentage of hands with abnormal tests and their association with symptoms and functional status as recorded on the two parts of the Boston questionnaire was determined by using Fisher's exact score. Results were given as probability values. (Table 4)

Of the nine nerve conduction parameters tested, only six recorded conduction abnormalities of the median nerve across the wrist in more than 60% of the hands. Those were median sensory amplitude (69%), median 2^{nd} lumbrical- Ulnar 1^{st} dorsal interosseous (67%), digit4 median-ulnar sensory latency comparison (64%) and 60% Median motor onset latency.

Of the six nerve conduction parameters, there were only two that were able to confirm CTS in more than 70% of the study sample viz. median nerve sensory peak onset latency (75%) and median-ulnar palmar comparison (73%). (Table2)

Median nerve motor amplitude, median segmental sensory study and digit1 median-radial sensory latency comparison failed to demonstrate impairment of median nerve conduction across the wrist compared to other test, percentage of abnormalities picked up was 14%, 37% and 42% respectively. (Table 2)

NCS parameter	Percentage of abnormality	Symptom severity	Functional limitation
	NCS	Correlation with NCS given as p-value	
Median sensory peak onset latency (MSPL)	75%	0.4	0.47
Median-ulnar palmar comparison (MUSPC)	73	0.8	0.26
Median sensory amplitude (MSA)	69%	0.7	0.21
Median 2nd Lumbrical-ulnar 1st dorsal interosseous motor latency difference (M2U1LC)	67%	0.6	0.08
Digit4 median-ulnar sensory latency comparison (D4SLC)	64%	0.6	0.7
Median motor onset latency (MML)	60%	1.0	0.16
Digit1 median-radial sensory latency comparison (D1SLC)	42%	0.3	0.78
Median sensory segmental study (MSSS)	37%	0.08	0.77
Median motor amplitude (MMA)	14%	0.36	0.47

Table 4: Nerve conduction parameters and percentages of abnormalities are given and were correlated with symptoms severity and functional limitation. Results are given as P-values.

Comparison of electrophysiological severity of CTS to symptoms severity (Boston 1) and Functional capacity (Boston 2)				
		Percent	Boston1	Boston 2
EDX Severity of CTS	Mild	31.25%	4%	35.42%
	moderate	39.58%	12.50%	27.08%
	Severe	27.08%	83.34%	37.40%
P-value			*0.44*	*0.77*

Table 5: Ninety-five percent of participants reported moderate-severe symptoms on Boston 1, but only 64% had moderate-severe limitation in daily functional activities as recorded by Boston 2. 66% had moderate-severe CTS on electrodiagnostic severity grading. This indicates weak correlation between EDX tests and Boston questionnaire, with p-values of 0.44 and 0.77 for symptoms severity and functional capacity respectively.

	Occupation	Hand	Hobby	EDX severity of CTS
1.	Cashier	R L	None	Moderate Normal
2.	Unemployed	R	Watching TV	Mild
3.	Unemployed	L	None	Mild
4.	Factory worker	R L	Watching TV	Severe Moderate
5.	Pensioner	R	Needle work	Mild
6.	Pensioner	R	None	Severe
7.	Domestic worker	R L	Domestic worker	Mild Mild
8.	Pensioner	L	Needle work	Moderate
9.	General worker	R L	None	Moderate-severe Moderate
10.	Not specified	R	None	Mild
11.	Housewife	R	None	Mild
12.	Housewife	L	Reading	Mild
13.	Artist	R	None	Mild-moderate
14.	Housewife	L	None	Moderate-severe
15.	Housewife	R	None	Mild
16.	Pensioner	R	None	Severe
17.	Not known	R	Reading	Mild
18.	Unemployed	R L	Needle work	Mild Mild
19.	Pensioner	R	Needle work	Mild
20.	Admin clerk	R L	None	Mild Moderate
21.	Housewife	R L	None	Moderate Moderate
22.	Typist	R L	Knitting	Mild Severe
23.	Care taker	L	Reading	Severe
24.	Mechanic	R L	Oval truck racing	Mild Severe
25.	Mining	R L	Golf	Severe Severe
26.	Housewife	R L	Knitting	Moderate Mild

27.	Scrap work	R L	Repairs computers	Moderate Mild
28.	Truck driver	R	None	Mild
29.	Panel beater	R L	Fishing	Mild Mild
30.	Hair dresser	R L	None	Severe Mild
31.	Machine operator	R	None	Mild
32.	Mechanic	R L	Gun shooting	Mild Mild

Table 6: Comparing the type of work and hobbies with EDX severity of CTS.

Discussion:

Symptom severity and functional capacity are both subjective reports from the participants and do not correlate with each other. The majority of the participants reported severe symptoms but only a few had functional impairment, which could be because sensory symptoms occur at night whereas activities during the day that increase pressure on the median nerve are functionally limiting. According to Aboonq flexion and extension of the wrist increases the pressure eight to ten times the normal limit respectively [4].

Phalen's test and Tinel sign were positive in 31 (64.5 %) of the 48 hands. These are provocative tests that increase pressure on the median nerve across the carpal tunnel and result in sensory symptoms in the median nerve distribution [8]. A wide range of different results have been observed in other studies. Padua et al reported positive Phalen's test as high as 75% of the 266 hands with CTS in their study [3]. While Ali et al reported lower percentages of positive Phalen's and Tinel's test of 48.8 % and 59.1% respectively [13].

Thirty-four participants had sensory loss in the median nerve distribution, with sparing of the 5^{th} finger and lateral half of the 4^{th} finger. Only 14 hands had atrophy of the thenar muscle and 22 demonstrated weakness of thumb abduction. Thenar muscle atrophy and weakness of thumb abduction or opposition only occurs in severe cases when there is axonal damage. The findings were in keeping with what Aboong et al referred to in their study that, compression of the median nerve results in ischaemia and segmental demyelination of the nerve across the CT, including axonal loss in severe cases [4]. Only when axonal loss is severe with subsequent atrophy of the muscles supplied by the median nerve, will there be associated motor weakness.

Sixty-nine percent of the patients were above the ideal body mass index of 18.5-25 kg/m². Thirteen participants from the 32 did not have chronic illnesses. Thyroid disease, diabetes mellitus, rheumatoid arthritis and gout which are conditions most associated with CTS [5] were documented in several of our patients. This indicates that CTS is common in certain medical conditions.

There was poor correlation between symptom severity (p value <0.44), functional capacity (p value 0.77) and EDX test. Our findings are in agreement with a statement made by Alanazy in his review article that "EDX grading scale is an objective measure for the severity of the median neuropathy at the wrist and does not measure the subjective severity of the clinical symptoms

(which is based on patient report)" [10]. The results were also similar to that of Porras and colleagues who did not find statistically significant relationship between the patient's subjective impairment and EDX tests [14].

Limitations of the study: There was incomplete demographic data on some of the participants but this was accounted for in the analysis. Occupation and body mass index was not always recorded. The study sample was small and follow-up nerve conduction were not done due to time constraints.

Conclusion and Recommendation:

The hypothesis that EDX tests are invaluable tests, required to confirm CTS was not supported by a statistically significant correlation of symptoms severity and functional capacity with EDX tests. Our findings were not similar to those of Lhan and colleagues, who found a statistically significant correlation between the Boston questionnaire, VAS and EDX [15].

The value of EDX studies cannot be overlooked when the clinical diagnosis of CTS is not clear and in those patients with other neuropathies who are suspected to have concurrent CTS. We were unable to answer with confidence the question of whether NCS is always necessary and feel that a follow-up EDX test post carpal tunnel release surgery will provide useful insights.

Even though Porras et al could not establish a statistically significant relationship between EDX and subjective impairment reported by those who participated in their study, they were able to demonstrate a significant relationship between clinical improvement as well as improvement in the sensory nerve conduction velocity after surgery [14].

The neurology department at Universitas Hospital is expected to do NCS for patients referred to the unit for various neuromuscular disorders, including CT.

Based on the findings of this study, we propose the following NCS parameters to be tested first in all patients with a clinical diagnosis of CTS seen in the unit. These comprise tests that demonstrated median nerve conduction abnormalities in more than 60% of the study sample and are therefore most useful:

A. Median nerve sensory studies, specifically the median sensory peak onset latency and median nerve sensory amplitude.
B. Median-ulnar palmar sensory comparison study.
C. Median 2nd lumbrical and 1st dorsal interosseous motor latency study.
D. Digit 4 median versus ulnar sensory latency comparison.
E. Median nerve motor studies, specifically the median motor onset latency.

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Authorship contribution:

DL Nkoana-Erasmus and A Moodley were responsible for conceptualisation, data analysis, write-up and review of the document. DL Nkoana-Erasmus was responsible for data collection.

Conflicts of interests:

The authors declare no conflict of interest. The study is required for MMed qualification.

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Appendices:

14 September 2018

For attention: Health Sciences Research Ethics Committee, UFS

Title of project:

Electrophysiological Outcomes of Carpal Tunnel Release for Carpal Tunnel Syndrome

Researcher:

Dr DL Nkoana-Erasmus, Dept of Neurology

I hereby confirm that I gave inputs in the protocol and approve the revised protocol.

Yours faithfully

G Joubert

Boston Carpal Tunnel Syndrome Questionnaire (BCTQ)

(一) Symptom severity scale (11 items)

	1	2	3	4	5
1. How severe is the hand or wrist pain that you have at night?	Normal	Slight	Medium	Severe	Very serious
2. How often did hand or wrist pain wake you up during a typical night in the past two weeks?	Normal	Once	2 to 3 times	4 to 5 times	More than 5 times
3. Do you typically have pain in your hand or wrist during the daytime?	No pain	Slight	Medium	Severe	Very serious
4. How often do you have hand or wrist pain during daytime?	Normal	1-2 times / day	3-5 times / day	More than 5 times	Continued
5. How long on average does an episode of pain last during the daytime?	Normal	< 10minutes	10~60 Continued	> 60minutes	Continued
6. Do you have numbness (loss of sensation) in your hand?	Normal	Slight	Medium	Severe	Very serious
7. Do you have weakness in your hand or wrist?	Normal	Slight	Medium	Severe	Very serious
8. Do you have tingling sensations in your hand?	Normal	Slight	Medium	Severe	Very serious
9. How severe is numbness (loss of sensation) or tingling at night?	Normal	Slight	Medium	Severe	Very serious
10. How often did hand numbness or tingling wake you up during a typical night during the past two weeks?	Normal	Once	2 to 3 times	4 to 5 times	More than 5 times
11. Do you have difficulty with the grasping and use of small objects such as keys or pens?	Without difficulty	Little difficulty	Moderately difficulty	Very difficulty	Very difficult

(二) Functional status scale (8 items)：

	No difficulty	Little difficulty	Moderate difficulty	Intense difficulty	Cannot perform the activity at all due to hands and wrists symptoms
Writing	1	2	3	4	5
Buttoning of clothes	1	2	3	4	5
Holding a book while reading	1	2	3	4	5
Gripping of a telephone handle	1	2	3	4	5
Opening of jars	1	2	3	4	5
Household chores	1	2	3	4	5
Carrying of grocery basket	1	2	3	4	5
Bathing and dressing	1	2	3	4	5

Protocol:

Electrodiagnostic test to confirm clinically suspected Carpal Tunnel Syndrome

Researcher: Dr DL Nkoana-Erasmus

Supervisor: Prof A Moodley

Clinical Technologist Neurophysiology: Mrs JE Le Roux

Clinical technologist (Supervised practice neurophysiologist): Mr MG Klopper

Introduction:

Carpal tunnel syndrome (CTS) is caused by compression of the median nerve at the wrist [1] and presents commonly with sensory symptoms of paresthesia, numbness and pain in the median nerve distribution [1, 2-3].

Patients with CTS are often referred to neurology for electrodiagnostic studies (EDX) to confirm the diagnosis, grade the severity of the disease and excluded other possible causes.

The carpal tunnel (CT) at the wrist is formed by the transverse carpal ligament (TCL) and the carpal bones; the ligament forms the roof of the tunnel while the carpal bones form the floor and walls of the tunnel [2, 3]. Nine muscle tendons and the median nerve pass through the tunnel, thus the median nerve is easily damaged by any condition that results in increased carpal tunnel pressure (CTP) [4].

CTP in normal subjects is measured to be between 8-10mmHg [4]. This is high in patients with CTS as a result of abnormally thickened connective tissue in the tunnel and the TCL as well [4]. According to Aboonq flexion and extension of the wrist increases the pressure eight to ten times the normal limit respectively [4].

Compression of the median nerve results in ischaemia and segmental demyelination of the nerve across the CT as well as axonal loss in severe cases [4].

There are several conditions associated with CTS but in the majority of cases the cause is not known. In idiopathic CTS repetitive activity of the wrist, certain occupations and hobbies have high incidence of people with CTS. Preston et al observed that 'in most cases, oedema, vascular sclerosis and fibrosis are seen which are findings consistent with repeated stress to connective tissue' [1].

Rheumatoid arthritis, diabetes mellitus, hypothyroidism, amyloidosis, acromegaly and pregnancy are among the common conditions associated with CTS [2].

CTS is known to be the most common entrapment neuropathy as noted by several studies [4,5,6] and it is often bilateral even in patients who present with symptoms in one hand only[3] .

Padau et al report that CTS is bilateral in almost all cases and that most cases of unilateral CTS will probably become bilateral [7]. This indicates the importance of proper diagnosis and urgent management of CTS.

The importance of EDX cannot be overlooked when planning appropriate management for this condition. The importance of nerve conduction studies was also emphasised by Naidu et al who stated in their study that "Nerve conduction studies are of established value in the diagnosis of CTS" [8].

Most electrophysiology units in public and private sectors do not have standardised guidelines with regard to electrodiagnostic testing and diagnosis of CTS.

The orthopaedic hand unit at Pelonomi regional hospital provides services for the whole of the Free State Province, neighbouring provinces and Lesotho. Patients diagnosed with CTS at Pelonomi hospital do not get nerve conduction studies before carpal tunnel release (CTR) surgery in most cases and are operated based on clinical symptoms and signs suggestive of CTS.

Pre-surgery EDX would assist in determining which NCS parameters have a high sensitivity in diagnosing CTS in clinically suspected, cases that will help develop standardised guidelines to be used in our clinic.

Clinical Symptoms and signs highly suggestive of CTS include:

1) Numbness and paresthesia on the medial side of the thumb, index, middle finger and the lateral half of the ring finger [1, 2, 8].
2) Nocturnal pain or paresthesia that radiates first into the hands then up the forearm and arm at times and usually awaken the patient from sleep. [1,2]
3) Atrophy of the thenar muscle.[1,2]
4) Weakness of thumb abduction and opposition.[1,2]
5) Positive provocative test for CTS (Tinel and Phalen's test) [10]

Treatment options for carpal tunnel can be surgical decompression of the nerve or non-surgical options including wrist splinting and steroid injection into the carpal tunnel [8].

Open CTR is used by the neurosurgeons at Universitas academic hospital and it is the gold standard procedure for decompression of the median nerve but there are other technique like the endoscopic procedure and the limited incision carpal tunnel release.

CTS is treatable with good outcomes when diagnosed and managed appropriately, hence confirmation of the diagnosis beyond clinical suspicion, with nerve conduction tests should be done routinely and is expected to be done as standard workup.

The following parameters on nerve conduction studies are commonly tested: [1]

1. Median motor and sensory onset latencies.
2. Median motor and sensory conduction velocity.
3. Median motor and sensory amplitude.
4. Ulnar motor and sensory peak latency.
5. Ulnar motor and sensory amplitude.
6. Ulnar motor and sensory conduction velocity.

The ulnar and radial nerve studies are done for comparison and to detect more extensive neuropathy. There are more specific parameters that are tested in symptomatic patients with CTS, to confirm the diagnosis if the above tests do not show any abnormalities.

These specific tests according to Preston et al are more sensitive in diagnosing CTS but the tests might remain abnormal even after decompression surgery unlike the median motor distal onset latency, sensory peak onset latency and sensory amplitude which usually recover after surgery [1.]. These correlate with findings by Naidu et al who demonstrated a significant improvement of the median sensory amplitude and distal motor latency before and after surgery compared to the poor recovery of the median motor amplitude [8]. Those specific tests include median versus ulnar or median versus radial comparison tests, but the two studies are most important when co-existing ulnar or radial neuropathy is present [1]. While these additional tests are not routinely required to confirm or refute the presence of CTS they will be routinely performed for all cases in this study.

Objective

To establish electrodiagnostic guidelines for diagnosis of Carpal Tunnel Syndrome at Universitas Academic Hospital, electrophysiology clinic.

Primary aims

1. To determine which electrophysiological tests are most appropriate and best correlate with the clinical diagnosis and severity of carpal tunnel syndrome.
2. To develop guidelines for the diagnosis of CTS at Universitas Academic Hospital electrophysiology laboratory.

NCS are commonly done to confirm and assess the severity of CTS. In most units worldwide it's standard procedure. Where the tests are not available or surgeons opt to operate without electrophysiological confirmation, results are based on clinical parameters. Even in units where NCS are routinely done, the tests chosen are technician dependent and may not necessarily reflect the most informative and clinically relevant or clinically correlated tests. By establishing standard testing protocols for CTS the aim will be to avoid technician bias. The added benefit will be the adoption of objective and standardised tests.

Methodology

Cross Sectional Analytic Study

Patients with a clinical diagnosis of carpal tunnel syndrome who are scheduled to be operated on will have nerve conduction studies before surgery.

After detailed explanation of the study to the patient, informed consent will be obtained for participation.

Eligible patients will be requested to complete the Boston questionnaire [11] before surgical procedure. The Boston and DASH questionnaires have been validated to assess objectively the symptoms and severity of the disease in CTS and have been found to be equivalent [11]. The Boston questionnaire will be used in this study, the researcher will assist the patients to understand the questionnaire and explain any medical terminology which they don't understand. The Boston questionnaire will be completed by the principal investigator in conjunction with the participant. Translation of the questionnaire into Sesotho and Afrikaans can be difficult and the essence lost in translation.

Visual analogue scale will be used to assess the severity of pain associated with the patient's CTS.

NCS will be performed on the patient according to standard testing procedures as described under measurements below.

Sample participants

Sample participants will include patients clinically diagnosed with carpal tunnel syndrome from Pelonomi hand clinic and Neurosurgery department. Both departments are referral centres in Free-state province and also receive patients from Lesotho and other provinces like Northern Cape. These patients are referred to the neurophysiology department at Universitas hospital for confirmation of diagnosis and preoperative baseline testing.

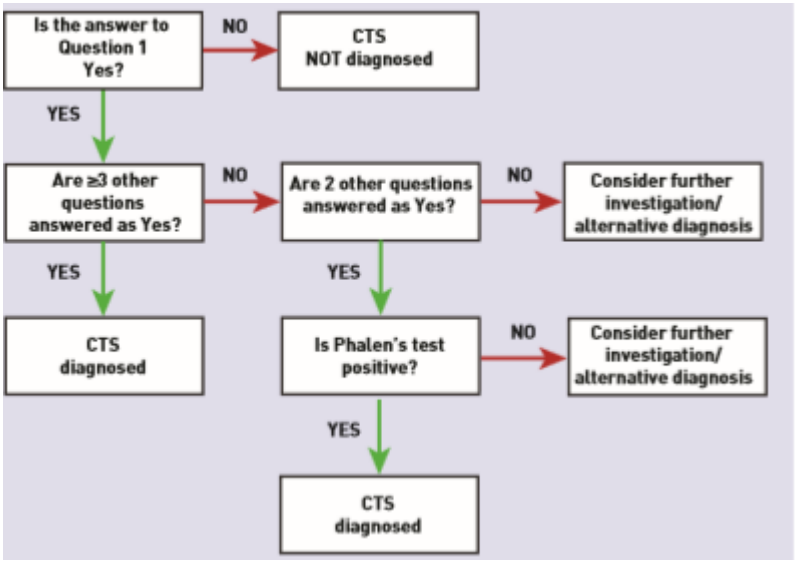
Those patients who meet the clinical criteria for CTS will then be recruited in the study for NCT.

The criteria to clinically diagnose CTS from the Primary Care Rheumatology Society will be used [13]. It includes 8 questions that the patient must answer regarding their symptoms and an algorithm that the clinician then follows based on the answers given by the patient.

Refer to Box1 and Figure1 for the questions and algorithm respectively [13].

Box 1. Questions to be asked to a patient presenting with hand or wrist symptoms

1. Do you have numbness or tingling in your wrist, hand, or fingers?
2. Do your symptoms spare your little finger?
3. Are the symptoms worse at night?
4. Do the symptoms wake you up at night?
5. Have you noticed your hand is weak; for example, have you found yourself dropping things?
6. Do you find shaking your hand, holding your hand or running it under warm water improves your symptoms?
7. Are the symptoms made worse by activities such as driving, holding a telephone, using vibrating tools, or typing?
8. Have splints or injections helped with your pain if you have had it in the past?



An agreement has been reached with the orthopaedics department for referrals to be made directly with the principal investigator.

A minimum of 36 hands with a diagnosis of carpal tunnel syndrome will be looked at. Pelonomi hand clinic, which will be the main unit where the patients will be referred from, evaluates about 3 new patients per week (at times more) with possible CTS, some of whom have symptoms in both hands.

We are therefore expecting a sample size of 36 to 40 hands in a period of three months. The initial assessment and studies done on the patients will be part of their standard workup. Transport to Universitas Hospital will therefore be by standard hospital transport or patient's funds.

Methods for conducting measurements:

First the patient's hands should be warmed to 32 degree Celsius using warm water since cold temperature of the hands can interfere with nerve conduction parameters. The skin is

then cleaned with skin prep to remove dead skin that might slow sensory conduction. This causes no discomfort to the patient.

Electrodes are placed on the area to be measured and connected to an amplifier which is connected to the monitor (computer screen). A small hand held transducer is used to stimulate the nerve and the tracing will be displayed on the screen. The voltage applied is very low, in microvolts (μV) for sensory studies and millivolts (mV) for motor study, unlike megavolts used in household appliances. One of the electrodes applied to patient's skin is an earth electrode that diverts unwanted voltage away from the patient.

The voltage applied to the skin is extremely small and has no detrimental effects to the patient. The patient might experience a little sting at the site of stimulation for each study. They adapt to this sting very rapidly. Where patients experience too much discomfort, they will be excluded from the test and study. The referring physician will then be informed and further management decided by him. The patient's ongoing care will not be prejudiced by exclusion from the study.

The following will be measured:

1. Median –versus –Ulnar nerve comparison studies (Palmar mixed)
    - Palmar stimulation of the median and ulnar sensory nerves
2. Median nerve motor study:
    - Recording at the abductor pollicis brevis muscle and stimulation of the median nerve at the wrist and cubital fossa.

3. Median nerve sensory studies:
    - Recording electrodes will be placed on the index finger and the nerve will be stimulated at the wrist.

4. Ulnar nerve motor study:
    - Recording electrodes will be placed on the abductor digiti minimi muscle and the ulnar nerve will be stimulated at the wrist, elbow and above the elbow.
5. Ulnar nerve sensory study:
    - A recording ring electrode will be placed on the fifth finger and stimulation will be at the wrist.

6. Median second lumbrical and ulnar nerve first interosseous distal motor latencies studies:
    - In normal subjects the difference should be less than 0.5ms.
    - Recording electrodes will be placed midway on the third metacarpal bone and on the distal interphalangeal joint of the index finger.

7. Median segmental nerve sensory study (Median sensory palmar study).
    - Recording ring electrodes will be placed on the middle finger.
    - Median nerve stimulation 14cm on the wrist and on the palm 7 cm from the wrist stimulation site.

- The palmar /wrist sensory nerve action potential (SNAP) amplitude ratio should be less than 1.6.
- Slowing of >10 m/s across the wrist is considered abnormal.

8. Digit 4 Median and Ulnar nerve sensory latencies comparison.
    - Recording digit 4.
    - Stimulating on the wrist, over the median nerve and ulnar nerve respectively.
    - Stimulating the same distance at 13cm.
9. Median and Radial nerve sensory latencies comparison study.
    - Recording digit 1.
    - Stimulating median nerve at the wrist and superficial radial sensory nerve at the forearm.
    - Stimulating identical distance of 12cm.

Reference values for the above tests are displayed in Appendix E

Yoon at el classified the severity of CTS based on the Median nerve electrodiagnostic findings as mild, moderate and severe, as displayed on Table 1[12]. They also included features of denervation in their classification which will not be included as a diagnostic parameter because needle electromyography will not be done in this study.

Table 1

CHARACTERISTIC	MILD	MODERATE	SEVERE
Motor latency, Msec	4.5-5.0	5.0-7.0	>7.0 or negative
Sensory amplitude, µV	<20µV	<20µV	<20µv
Sensory latency, msec	3.0-4.0	4.0-6.0	>6.0 or negative

Inclusion and exclusion criteria:

Those who are referred for NCS for CTS and consent to take part in the study will be included. Male and female participants of 18 years and older will be included, as CTS usually does not occur in children.

Patients who will be excluded from the study are those with previous hand surgery to the same hand, proximal median nerve pathology, nerve root pathology, brachial plexopathy and peripheral neuropathy, which might obscure electrophysiological testing for the study. In such instances, abnormal studies may be indicative of other peripheral nerve disorders and not CTS.

Data analysis:

Data collected will be entered into excel data sheet. Results will be summarised by frequencies and percentages (categorical variables) and means, standard deviations or percentiles (numerical variables). 95% confidence intervals will be calculated for main outcomes. Changes over time will be summarised similarly and analysed using 95% confidence intervals for means, medians or percentages with appropriate paired hypothesis testing. Associations will be evaluated by correlations for numerical variables and risk measures for categorical variables, with appropriate hypothesis testing.

Time Schedule

Submission to HSREC	17 August 2018
Submission to FSDoH	17 October 2018
Data collection nine months (First 3 months for the pre-op NCS and the following 3 months for post-op NCS)	01 November 2018 - 01 August 2019
Data analysis two months	02 August 2019 - 30 September 2019
Reporting 1 month	01 October 2019 - 31 October 2019

*HSREC (Health science research ethics committee)

* FSDoH (Free-state department of health)

The study is expected to take 9-12 months as it is dependent on the flow of patients from referral centres.

Study method summarised	Tests
Recruitment and 2 – 4 weeks pre surgery	1. Information leaflet 2. Consent form 3. Evaluation Sheet (Demographics, clinical data and VAS) 4. Boston Questionnaire 5. Tests: 5.1 Median –versus –Ulnar comparison studies (Palmar mixed) 5.2 Median motor study 5.3 Median sensory studies

	5.4 Ulnar motor study. 5.5 Ulnar sensory study. 5.6 Median Second lumbrical and ulnar first interosseous distal motor latencies studies. 5.7 Median segmental sensory study (Median sensory palmar study). 5.8 Digit 4 Median and Ulnar sensory latencies comparison. 5.8 Median and Radial sensory latencies comparison studies.

Ethical aspects

Permission will be requested first from HSREC and FSDoH before commencing with the research.

There is no financial gain for the researcher. Benefit would be realised by the establishment of a standardised electrophysiological guideline which can be used for our patients.

Patients will be coded to ensure confidentiality. On recruitment each patient will be given a code which will be derived from their demographic data which will be kept privately away from other data. All subsequent data will only contain the patient's code. Considering that the study can be done separately for each upper limb, as CTS can be unilateral or bilateral, each hand will be coded separately. For example coding number 18P1A; 18 for the year, P1 patient number 1. A or B for the right and left hand respectively.

There will be a separate sheet with the patient's name and code that will be kept in a safe at the Department of Neurology.

Results will be made available to the patient immediately after the test as these results have to be sent to the referring physician as is routinely done. Additional study tests will also be included as this may impact on the final diagnosis.

Patients who are willing to participate in the study will have to first read the information leaflets and sign the consent form if they understand and agree to participate in the study.

No conflict of interest exists for this study by the principal investigator and co-investigators.

Limitations**:**

Inter-investigator variability will be minimised by the researcher and two technologists doing all the tests. The researcher and the technologists will be using the same documented technique including electrode placement and stimulus intensity parameters, when doing the tests. The technologists and the principal investigator will be guided initially by Professor Moodley to ensure that they master the technique at first and apply selected techniques.

During the test the principal researcher will always be available, working together with one of the clinical technologists.

The role of the technologist is to provide professionalism and technical skills as they are formally trained in the performance of NCS. This will limit inter-observer variability.

Pilot study:

Five participants will be selected for the pilot study. Only pre-operative nerve conduction studies will be done and their data will only be included in the final analysis if there are no problems encountered with the technique.

Budget:

The budget is for approximately 30 – 40 patients.

Adult digital scale with height	R3261.00
ECG stickers R20 each, 3 stickers per patient per visit (40) , total 120 stickers	R2400
Skin prep x1	R450
Ear buds x 2 packets	R80
Stationary	R1500
Non contact thermometer	R810
Fuel R450 per month for the first three months going to Pelonomi hospital hand unit to recruit patients.	R1350
	Total R7451

Sponsorship:

The Postgraduate office has approved funding for the study.

References:

1. Preston DC, Shapiro BE. Median Neuropathy at the Wrist. In: Electromyography and Neuromuscular Disorders, Clinical-Electrophysiologic Correlations. London. Elsevier, 2013; p. 267-288.

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9. Borisch N, Haussmann P. Neurophysiological recovery after open carpal tunnel decompression: Comparison of simple decompression and decompression with epineurotomy. J Hand Surg Am. 2003; 28B (5):450-454

10. Rotman MB, Enkvetchakul B V, Megerian JT, et al. Time course and predictors of median nerve conduction after carpal tunnel release. J Hand Surg Am. 2004; 29A:367-372.

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12. Yoon ES, Kwon HK, Lee HJ, et al. The outcome of the nonoperated contralateral hand in carpal tunnel syndrome. Ann Plast Surg. 2001.

13. Burton C, Chesterton LS, Davenport G. Diagnosing and managing carpal tunnel syndrome in primary care. Br J Gen Pract. 2014; 47:20-24.

EVALUATION SHEET:

DEMOGRAPHIC DETAILS:

Code number	
Date and time	
Referring department	
Sex	
Age	
Body weight	
Height	
Body mass index	
Hand Dominance	
Hobbies	
Residence	
Occupation	

Current complaints:

History of current complaints:

Surgical history:

	Yes	No
Have you ever had any neck operation before?		
Have you had surgery to the same wrist previously?		
Did you ever have any injury to the neck, shoulder, arm or hand?		

If you answered yes to any of the above, please elaborate:

Medical history:

Were you ever diagnosed with any of the following conditions?

	Yes	No
Diabetes mellitus		
Thyroid disease		
Amyloidosis		
Sarcoidosis		
Rheumatoid arthritis		
Peripheral neuropathy		
Acromegaly		
Gout		
Other:		

If you answered yes to any of the above, please elaborate:

CLINICAL SIGNS:

RIGHT HAND	Yes	No
Atrophy of the intrinsic hand muscle (Thenar muscle)		
Phalen's test		
Tinel's sign		
Loss of sensation on the 1^{st},2^{nd},3^{rd} finger		
Loss of sensation on the lateral half of the ring finger		
Weakness of thumb opposition		
Weakness of thumb abduction		

LEFT HAND	Yes	No
Atrophy of the intrinsic hand muscle (Thenar muscle)		
Phalen's test		
Tinel's sign		
Loss of sensation on the 1^{st},2^{nd},3^{rd} finger		
Loss of sensation on the lateral half of the ring finger		
Weakness of thumb opposition		
Weakness of thumb abduction		

Information leaflet and consent form:

My name is Dr DL Nkoana-Erasmus and I am a registrar (doctor training to become a specialist) in the department of Neurology at Universitas Academic Hospital.

I would like to invite you to participate in a research study that will be conducted at Universitas hospital neurology department from the beginning of November 2018. The study is expected to take one year to complete, but your participation will take three months only.

The aim of the study is to determine which nerve conduction test is most appropriate and best matches with your diagnosis of carpal tunnel syndrome.

We also want to know which of the nerve studies recovers the most after operation so that the same tests can be used in the future to make the correct diagnosis when the same condition is suspected in other patients.

Carpal tunnel syndrome means that one of the nerves that supply the hands is pressed tightly and is damaged as it passes through the wrist to the hand muscles and skin. That leads to the hand becoming weak and losing feeling.

The information obtained will help establish guidelines to be used with regard to the diagnosis and follow- up after operation for patients with carpal tunnel syndrome.

WHAT IS THE TEST AND WHY IS IT NECESSARY?

Nerve conduction studies for carpal tunnel syndrome are tests done to confirm the diagnosis and to measure the severity of carpal tunnel syndrome. It is also used determine the success of the operation.

HOW IS IT DONE?

The nerve is stimulated by applying a very low current to the skin above the nerve and recording the response on the computer. This is experienced as a slight sting or discomfort at the testing point.

The study will include routine tests for carpal tunnel syndrome for which you were referred for but will also include a few additional tests. If you at any point feel that these additional tests are unbearable, they will be stopped immediately.

The skin is first cleaned to remove excess oil on the skin that might interfere with conduction and thus give false information.

The first nerve conduction study will be done before the operation and the second one will be done after the operation.

You will receive a certain amount of the money for transport and refreshments when you come for the second nerve conduction test.

POSSIBLE COMPLICATIONS

The test is safe. Only mild discomfort is felt when the nerve is stimulated, but you will get used to it quickly.

If it becomes too painful and unbearable for you inform the doctor or the technologist.

You are free to stop the test at any time if you want to and that will not influence your management further on.

IS THE INFORMATION KEPT SAFE?

Please note by completing this form means you are agreeing to voluntarily participate in this research study. You will remain anonymous and the information you give will be treated with confidentially at all times.

Feel free to contact me on the following details at any time, if you need more information about the study and the tests that will be performed.

Dr DL Nkoana-Erasmus

Cell phone number: 083 544 0393

Email address: nkoanaerasmus@gmail.com

Once you have read and understood the above, please sign below**.**

Name and surname:

Signature:

Date and time:

Witness 1:

Witness 2:

Signature of the doctor:

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UFS·UV
HEALTH SCIENCES
GESONDHEIDSWETENSKAPPE

Health Sciences Research Ethics Committee

12-Feb-2020

Dear **Dr Dikeledi Nkosana-Erasmus**

Ethics Number: UFS-HSD2018/1188/2901

Ethics Clearance: **New title (Electrodiagnostic test to confirm clinically Suspected Carpal Tunnel Syndrome)**

Principal Investigator: **Dr Dikeledi Nkosana-Erasmus**

Department: **Neurology Department (Bloemfontein Campus)**

SUBSEQUENT SUBMISSION APPROVED

With reference to your recent submission for ethical clearance from the Health Sciences Research Ethics Committee. I am pleased to inform you on behalf of the HSREC that you have been granted ethical clearance for your request as stipulated below:

1. Changed the title from to "Electrophysiological Outcomes of Carpal Tunnel Release for Carpal Tunnel Syndrome" to"Electrodiagnostic test to confirm clinically Suspected Carpal Tunnel Syndrome".
2. Removed secondary aims because they had to do with post-op NCS.
3. Research methodology
4. Budget now less
5. Clinical criteria used by Rheumatology 6. Removed anything that had to do with post-op NCS.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this request for ethical clearance and we wish you continued success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
T: +27 (0)51 401 7795/7794 | E: ethicsfhs@ufs.ac.za
IRB 0001992; REC 230408-011; IORG 0010096; FWA 00027947
Block D, Dean's Division, Room D104 | P.O. Box/Posbus 339 (Internal Post Box G40) | Bloemfontein 9300 | South Africa
www.ufs.ac.za

http://operativeneurosurgery.com/doku.php?id=visual_analog_scale

Patient Code:

Date:

Please rate the severity of your pain based on the above scale. Ring the number that closely resembles your pain

health
Department of Health
FREE STATE PROVINCE

26 November 2018

Dr. D Nkoana-Erasmus
Dept. of Neurology
UFS

Dear Dr D Nkoana-Erasmus

Subject: Electrophysiological Outcomes of Carpal Tunnel Release for Carpal Tunnel Syndrome.

- Please ensure that you read the whole document. Permission is hereby granted for the above – mentioned research on the following conditions:
- Participation in the study must be voluntary
- A written consent by each participant must be obtained.
- Serious Adverse events to be reported to the Free State department of health and/ or termination of the study
- Ascertain that your data collection exercise neither interferes with the day to day running of Unversitas Hospital nor the performance of duties by the respondents or health care workers.
- Confidentiality of information will be ensured and please do not obtain information regarding the identity of the participants.
- **Research results and a complete report should be made available to the Free State Department of Health on completion of the study (a hard copy plus a soft copy).**
- Progress report must be presented not later than one year after approval of the project to the Ethics Committee of the University of Free State and to Free State Department of Health.
- Any amendments, extension or other modifications to the protocol or investigators must be submitted to the Ethics Committee of the University of Free State and to Free State Department of Health.
- **Conditions stated in your Ethical Approval letter should be adhered to and a final copy of the Ethics Clearance Certificate should be submitted to** sbheelats@fshealth.gov.za or lithekom@fshealth.gov.za **before you commence with the study**
- No financial liability will be placed on the Free State Department of Health
- Please discuss your study with the institution manager/CEOs on commencement for logistical arrangements
- Department of Health to be fully indemnified from any harm that participants and staff experiences in the study
- Researchers will be required to enter in to a formal agreement with the Free State department of health regulating and formalizing the research relationship (document will follow)
- You are required to present your study findings/results at the Free State Provincial health research day

Trust you find the above in order.
Kind Regards

UFS·UV

Department of Neurology

20 January 2020

The chairperson
HSREC
UFS

Amended protocol for Dr Nkoana Erasmus' study: Electrodiagnostic tests to confirm clinically Suspected Carpal Tunnel Syndrome (CTS)

Kindly note that Dr D Nkoana Erasmus has amended her research protocol as follows:

1. Changed the title.
2. Removed secondary aims because they had to do with post-op NCS.
3. Research methodology
4. Budget now less
5. Clinical criteria used by Rheumatology
6. Removed anything that had to do with post-op NCS.

She has revised her protocol to address pre-operative electrophysiological findings in Carpal tunnel syndrome and has cancelled the post-operative findings reflected in the secondary aims of the study. I fully support her changes, as this will allow her to complete her study this year prior to her sitting the final college exam.

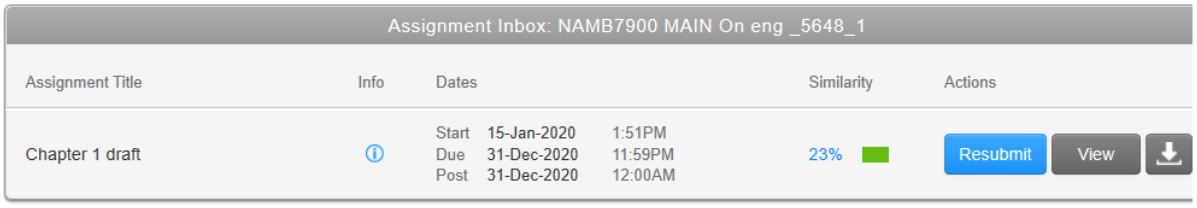
The study is still beneficial, as it will provide essential information on the guidelines required for electrophysiological testing of CTS in South Africa.

Yours sincerely

Prof A Moodley
HOD: Neurology

Turnitin Plagiarism Search engine:

Chapter 1:



Assignment Inbox: NAMB7900 MAIN On eng _5648_1

Assignment Title	Info	Dates	Similarity	Actions
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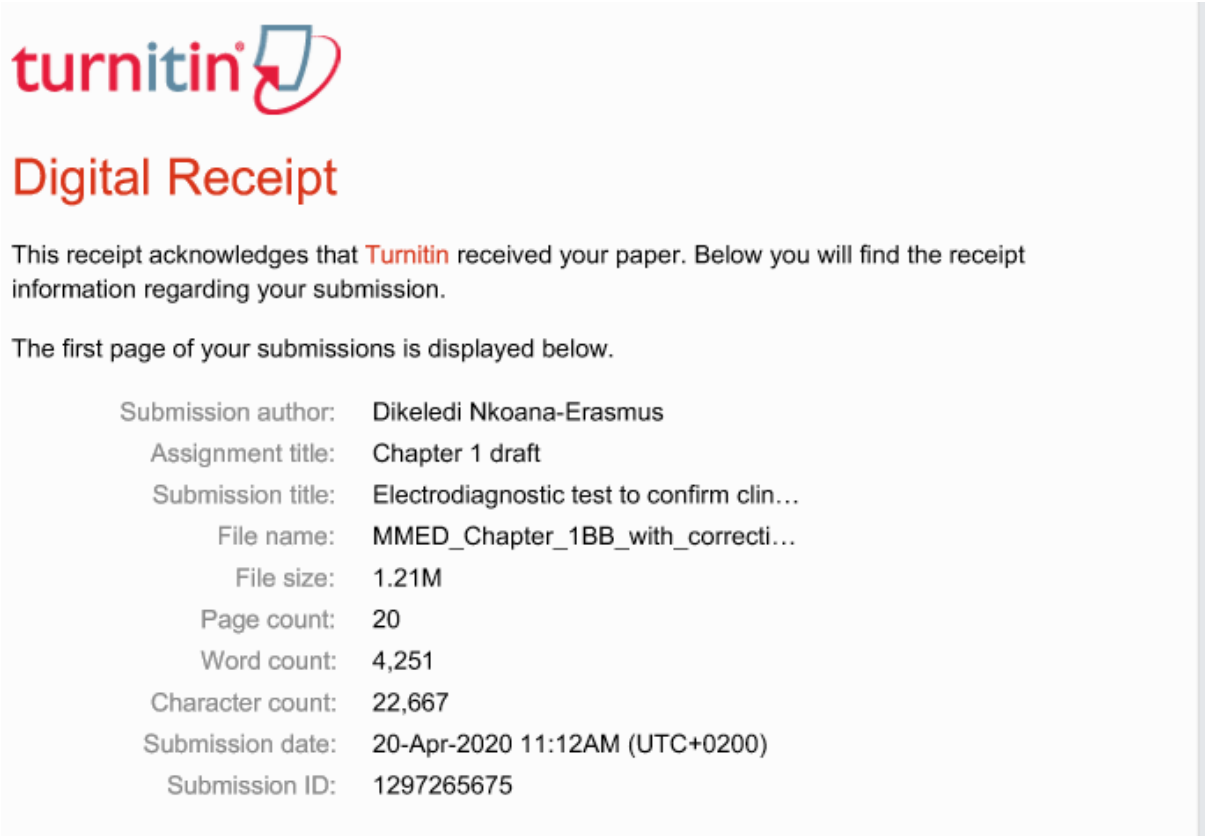

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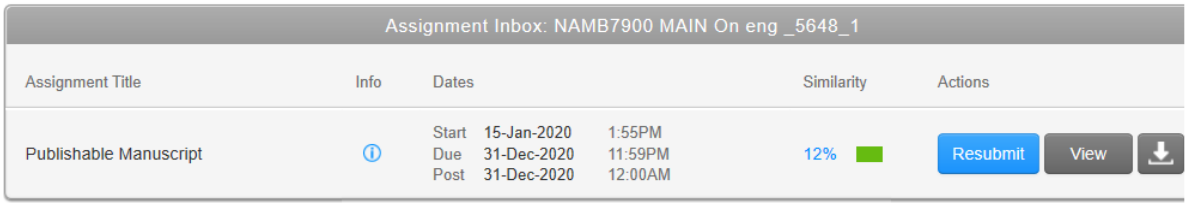
File name:	MMED_Chapter_1BB_with_correcti…
File size:	1.21M
Page count:	20
Word count:	4,251
Character count:	22,667
Submission date:	20-Apr-2020 11:12AM (UTC+0200)
Submission ID:	1297265675

Chapter 2:



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Submission title:	Electrodiagnostic test to confirm clin…
File name:	MMED_Chapter_2_with_corrections…
File size:	85.92K
Page count:	21
Word count:	4,706
Character count:	25,699
Submission date:	20-Apr-2020 11:14AM (UTC+0200)
Submission ID:	1297271964

SAMJ: South African Medical Journal

General article format/layout

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres are denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

**NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'

- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease

indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.

- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.