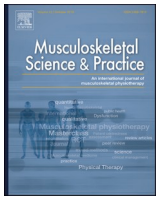
Musculoskeletal Science and Practice 69 (2024) 102897

Contents lists available at ScienceDirect

Musculoskeletal Science and Practice

journal homepage: www.elsevier.com/locate/msksp



Original article

Diagnostic accuracy of the upper limb neurodynamic test 1 using neurodynamic sequencing in diagnosis of carpal tunnel syndrome

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ARTICLE INFO

Keywords:
Accuracy
Carpal tunnel syndrome
Diagnosis
Median nerve
Neurodynamics
Validity

ABSTRACT

Background: The upper limb neurodynamic test 1 is used in the diagnosis of median nerve neuropathies such as carpal tunnel syndrome but its diagnostic validity remains limited. Neurodynamic sequencing has been suggested to increase the specificity of the neurodynamic tests, however, to date, information on the diagnostic accuracy of this variation in neurodynamic testing is required.

Objectives: The aim of this study was to analyze the diagnostic validity of the local sequence of ULNT1 (LS-ULNT1) (*i.e. a sequence that begins at the joint where the problem is (wrist) and progressively moves joints further away from it*), in the diagnosis of CTS. A secondary aim was to describe the location of sensory responses to this modified neurodynamic test sequence.

Design: A prospective diagnostic accuracy study was designed.

Method: Nerve conduction studies were used as the gold standard. The LS-ULNT1 was performed in 58 consecutive patients (17 men, 44 women) with suspected CTS.

Results: Sensitivity of the LS-ULNT1 was 65.7% (CI 48.0–80.9%) and the specificity was 95.7% (CI 78.1–99.9%). The positive and negative likelihood ratios were >5 and < 0.5, respectively, indicating the ability of the test to generate small but sometimes important changes in post-test probability.

Conclusions: The overall results of this study showed that the LS-ULNT1 could be useful in confirming the diagnosis of CTS. The test demonstrated high specificity and the +LR indicated the ability of the test to generate changes in posttest probability, especially with a positive LS-ULNT1 result.

1. Introduction

Carpal tunnel syndrome is the most prevalent entrapment neuropathy in the body (Ibrahim et al., 2012; Keith et al., 2009). Clinical presentation of CTS includes tingling, pain or numbness in the distal distribution of the median nerve, and reduction in grip strength and function of the affected hand)(Dilley et al., 2003; Keith et al., 2009) and it affects women more than men (Aroori and Spence, 2008; Atroshi et al., 1999).

Nerve conduction studies (NCS) are considered the reference standard in the diagnosis of CTS (Werner and Andary, 2011) but in clinical environments where NCS are not available, clinical tests such as neurodynamic tests (NDTs) have been recommended for the diagnosis of neuropathic pain conditions, including CTS (Keith et al., 2009; Nee et al., 2012). However, information about the diagnostic validity and reliability of NDTs remains limited (Bueno-Gracia et al., 2015; Trillos et al., 2018; C Vanti et al., 2011; Carla Vanti et al., 2011; Wainner et al., 2005). This limited diagnostic validity could be related to two key aspects: first, a. vague diagnostic criteria for a positive (abnormal) neurodynamic test (Bueno-Gracia et al., 2015; Nee et al., 2012) and, b. the lack of the test's ability to specifically produce a change in the mechanosensitivity of the median nerve at the wrist. Nee et al. (2012) proposed that at least two premises should be fulfilled to consider a test positive (abnormal) to make the diagnostic criteria more clearly defined: 1.

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https://doi.org/10.1016/j.msksp.2023.102897
Received 13 June 2023; Received in revised form 4 December 2023; Accepted 11 December 2023
Available online 15 December 2023

reproduction of the patient's symptoms during the NDTs and 2. a change in those symptoms by the structural differentiation (SD). Using these criteria, Bueno et al. (Bueno-Gracia et al., 2015) obtained higher validity for the ULNT1 in the diagnosis of CTS patients than previous studies (Vanti et al., 2012; Wainner et al., 2005). However, the imprecision in the confidence intervals and the larger number of false negatives limited the interpretation of their data and the validity of the ULNT1 is still limited in the detection of CTS.

Neurodynamic sequencing is when the order of joint movements during a neurodynamic test is varied (Butler, 1991; Shacklock, 1989). A working hypothesis is that different sequences of movements may be used to vary the concentration of force in nerves, thus making test more specifically emphasized. With the straight leg raise, Shacklock (Shacklock, 1989) found a greater prevalence of distally-located responses (calf area) was associated with ankle dorsiflexion being performed first; whereas, when dorsiflexion was performed last, the responses were located more proximally in the thigh. With the ULNT1, Zorn et al. (1995) found that wrist extension performed first was associated with a lower prevalence of proximally-located responses (arm and shoulder) than if the wrist was moved last.

In a cadaver study on biomechanical responses of the ulnar nerve at the elbow during the ulnar neurodynamic test, nerve strain was greater when the elbow flexion was performed first (Tsai, 1995). However, Nee et al. (2010) found that varying the sequence of the wrist, elbow, shoulder and neck movements during ULNT1 did not vary the strain in the median nerve near the wrist, likely because final nerve position was the same on account of the ROM of each of the movements being the same between sequences. They did however find that the median nerve near the wrist underwent strain for longer when wrist extension was the first movement because the nerve was loaded earlier. Suffices to say that the mechanics are not fully understood and the in-vivo studies that show a relationship in reported responses with sequencing are what this study is based on, particularly since testing for CTS is heavily based on reported responses.

The aim of this study was to analyze the diagnostic validity of the local sequence of ULNT1 (LS-ULNT1) (*i.e. a sequence that begins at the joint where the problem is (wrist) and progressively moves joints further away from it*), in the diagnosis of CTS. A secondary aim was to describe the location of sensory responses to this modified neurodynamic test sequence.

2. Materials and methods

2.1. Study design

A prospective diagnostic accuracy study was designed in which clinical testing occurred in a state of diagnostic uncertainty. The study followed the 2015 STARD reporting standards. The LS-ULNT1 was used as the index test and the NCS as the reference standard for the diagnosis of CTS. The study was conducted in accordance with the Ethical principles and the Helsinki Declaration on research involving human subjects. Local ethics committee approved the protocol of this study.

2.2. Participants

Participants were recruited from consecutive patients with suspected CTS referred to a Neurophysiology Department and were invited to voluntarily participate in the study. Patients were informed about the study and they gave their consent for participation before inclusion. Inclusion criteria were: patients aged >18 years with suspected CTS and referred by their physicians for NCS. Exclusion criteria for the participation were: any ROM limitation of the upper limbs that prevented LS-ULNT1 testing, inability to lie supine and any psychological factors that in the view of the investigators prevented participation or any physical contraindications for physical therapy (e.g. infection, tumours or fractures). Patients with suspected bilateral CTS were included in the study but the validity analysis was only performed on the most affected side. Fig. 1 is the flow chart of the study according to the 2015 STARD (Standards for Reporting of Diagnostic Accuracy) reporting guidelines (Bossuyt et al., 2004).

As the diagnosis of CTS is based mainly on clinical presentation and NCS, and physical tests to detect it are used as confirmation of the pathology, the sample size calculation was performed based on a very high expected specificity. Based on a specificity of 0.95, a prevalence of 50%, a z-score of 1.96, a marginal error of 0.20 and an attrition rate of 10%, a sample size of approximately 56 patients was required.

2.3. Reference standard

The NCS was performed by an experienced neurophysiologist by using routine motor and sensory studies. Contact surface electrodes (stickers type) were used for the exploration of the motor branch and sensory branches of the median nerve. Motor responses were elicited orthodromically by supramaximal stimulation at the wrist and antecubital fossa and recorded from the abductor pollicis brevis. Sensory responses were elicited antidromically by applying supramaximal stimulation at the palm, wrist and elbow and recorded from the index finger. The conduction from the wrist to the palm was calculated by subtracting the finger-palm latency to the wrist-finger latency. Latencies and conduction velocities were measured in milliseconds and meters per second, respectively. Entrapment of the median nerve in the carpal canal was determined by a slowing of sensory conduction velocity from wrist to palm (SCV-WP). SCV-WP was considered "abnormal" with values below 40 m/s (Yılmaz et al., 2017). All NCS were performed in a warm room (22°C-25 °C).

2.4. Index test

Approximately 30 min after the NCS was performed, a single physiotherapist >10 years of experience in neurodynamics evaluated the LS-ULNT1 on each participant. Participants were initially screened by another researcher who collected demographic data (height, weight, gender and arm dominance) and determined eligibility to participate, based on inclusion and exclusion criteria. All evaluators were blind to the patient history and NCS result. Participants who met the selection criteria were subsequently provided with an explanation of the study procedures and instructions regarding the information they should provide during the LS-ULNT1.

The LS-ULNT1 was performed following the sequence of movements described by Shacklock (2005): fingers and wrist extension, forearm supination, elbow extension and shoulder abduction (Fig. 2). The starting position for the test was also standardized. Participants were positioned supine without a pillow (thus avoiding any initial neural tension resulting from a flexed cervical spine), their arms along-side their bodies and lower limbs straight. The LS-ULNT1 was performed slow, and subjects were instructed to indicate the point of first appearance of symptoms (P1). Then, structural differentiation was completed. Structural differentiation movements consisted of the release of wrist extension in case of proximal symptoms (symptoms above the elbow) or the release of shoulder abduction in case of distal symptoms (symptoms below the elbow). If symptoms changed with SD, the response was classified as a "neurodynamic response". And when symptoms did not change with SD the response was classified as a "musculoskeletal response".

If the LS-ULNT1 produced symptoms at the wrist or hand, which is a common response for ULNT1, but did not reproduce the participant's clinical symptoms, the neurodynamic tests was classified as negative. Based on the Nee et al. (2012) recommendations, NDTs were considered positive if symptoms were reproduced and changed during SD.

Once the LS-ULNT1 and the structural differentiation manoeuvre were performed, characteristics of the response were recorded. Participants were asked to indicate the distribution of the sensory responses. A

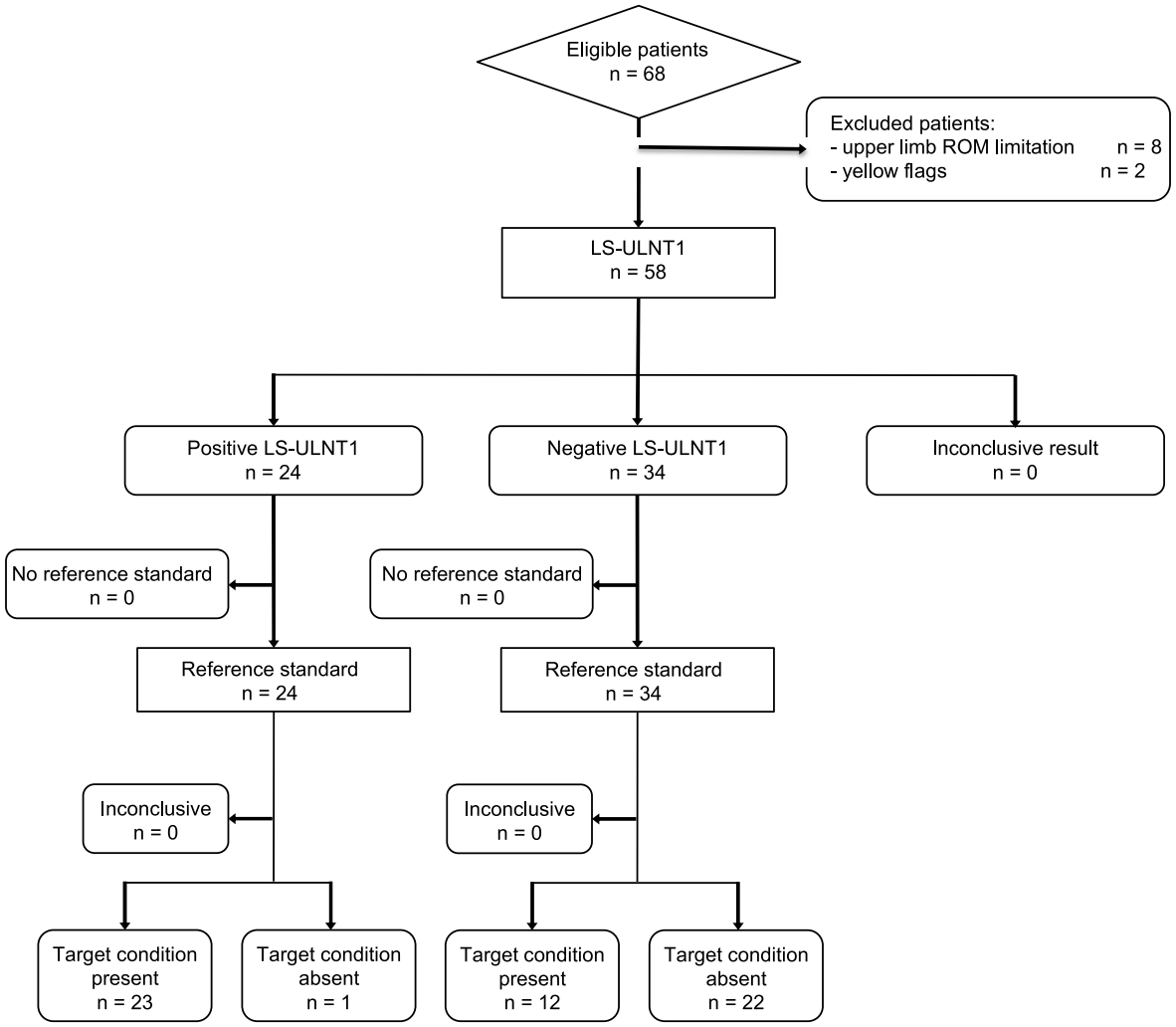

Fig. 1. Flow chart of the study profile according to the Standards for Reporting of Diagnostic Accuracy recommendations.

body chart depicting the left and right upper limb and divided in 6 areas (hand, wrist, forearm, elbow, arm/shoulder and neck) was used to document the distribution of sensory responses and each individual was asked to mark the location of his or her perceived sensory responses.

2.5. Statistical analysis

All data were recorded in an electronic database and analyzed in SPSS version 19.0 for Macintosh. Descriptive statistics were calculated for demographic variables and symptoms characteristics. In order to estimate diagnostic accuracy, sensitivity and specificity with 95% confidence intervals was calculated. A two-by-two contingency table for LS-ULNT1 results and CTS diagnosis was developed and likelihood ratios (LR) were also calculated. The + LR was calculated as sensitivity/(1-specificity) and the –LR was calculated as (1-sensitivity)/specificity (Altman, 2000). Because the LRs were not near 1 the Taylor method was used to calculate the 95% confidence intervals for both values LRs (Beecham and Weir, 2017). According to Jaeschke et al. (1994), the diagnostic accuracy of the LS-ULNT1 was considered satisfactory with +LR > 2 or –LR<0.50. Finally, a nomogram was performed to graphically represent the change in the posttest probability of a positive or negative LS-ULNT1 result. To establish the prevalence of the pathology, the prevalence found in the study sample itself was used. That is, the percentage of patients who obtained a positive result in the NCS.

3. Results

3.1. Sample characteristics

Sixty-eight participants were initially enrolled in the study but ten were excluded, leaving 58 remaining participants (42 women and 16 men). The mean age was 54.39 ± 14.51. Bilateral symptoms were reported in 65.5% of the participants and 96.8% reported chronic symptoms lasting more than 3 months. Table 1 shows the baseline characteristics of the participants.

3.2. NCS results

Thirty-five of the 58 evaluated limbs demonstrated abnormal NCSs findings and were diagnosed of CTS. NCS parameters are shown in detail in Table 2.

3.3. LS-ULNT1 results

LS-ULNT1 demonstrated a sensitivity of 65.7% (CI 48.0–80.9%), a specificity of 95.7% (CI 78.1–99.9%) with a +LR of 15.1 (CI 2.2–104.3) and a –LR of 0.36 (CI 0.22–0.57). Fig. 3 shows a likelihood ration nomogram adapted from Fagan (Fagan, 1975). The pre-test probability of CTS in our sample was placed at 60.3%. The positive likelihood ratio of 15 for the LS-ULNT1 is indicated along with the corresponding post-test probability of 96% (CI 77–99%) (blue line). The negative

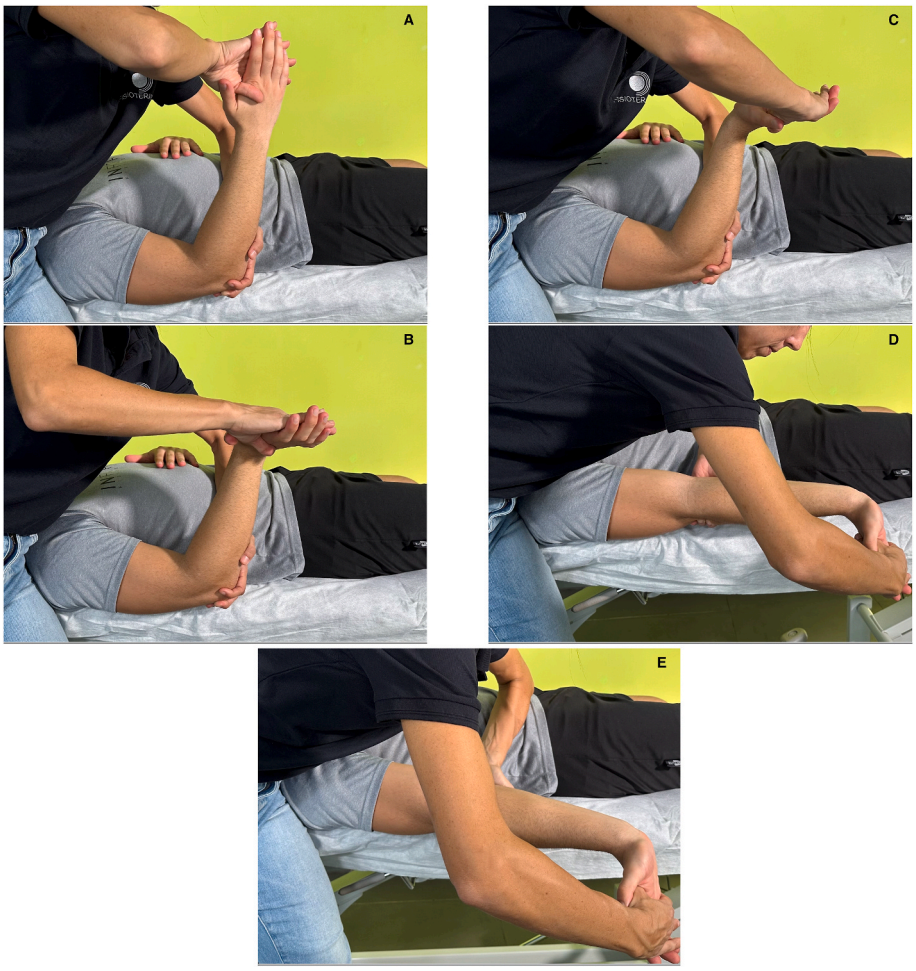

Fig. 2. Sequence of movements of the LS-ULNT1. A: starting position; B: wrist extension; C: forearm supination; D: elbow extension; E: shoulder abduction.

Table 1
Mean ± SD and percentages of descriptive information for participants.

Characteristics	Cases (n = 58)	CTS (n = 35)	Non CTS (n = 23)
Gender (female)	70.7%	74.3%	65.2%
Mean age (years)	54.6 ± 14.8	57.9 ± 13.9	49.4 ± 14.9
Bilateral involvement		63.6%	52.6%
Duration of symptoms >3 months	98.3%	100%	95.7%
Presence of night pain	60.3%	60%	60.9%
Principal symptom	60.3% pain 39.7% numbness	60% pain 40% numbness	60.9% pain 39.1% numbness

Table 2
Mean ± SD of descriptive NCS results.

NCS parameter	CTS (n = 35)	Non CTS (n = 23)
Distal motor latency (APB) (ms)	4.9 ± 1.7	3.2 ± 0.3
Motor amplitude (APB) (mV)	9.4 ± 4.3	13.3 ± 3.8
Median motor velocity (m/s)	39.4 ± 4.3	56.3 ± 3.8
Median sensory conduction velocity (digit II) (13 cm) (m/sec)	35.5 ± 12.2	57.5 ± 4.1
Sensory amplitude (μV)	9.9 ± 6.7	21.7 ± 9.2

Abbreviations: APB, abductor pollicis brevis; NCS, Nerve Conduction Study; CTS, Carpal Tunnel Syndrome; m/sec, meters per second; ms, milliseconds.

likelihood ratio of 0.36 for the LS-ULNT1 is indicated, along with the corresponding post-test probability of 35% (CI 25–46%) (red line).

The LS-ULNT1 produced a neurodynamic response in 48 patients (82.8%) and a musculoskeletal response in 10 patients (17.2%). Sensory responses were principally located in the distal upper extremity. Percentages for each individual sensory location are shown in Fig. 4. The test reproduced the patients' clinical symptoms and was considered positive in 24 patients (41.4%).

4. Discussion

The present study analyzed the validity of the LS-ULNT1 in the diagnosis of CTS using NCS as the reference standard. The study was performed in a situation of diagnostic uncertainty and a specific sequence of the ULNT1 was used, that is, the LS-ULNT1 (wrist first) which is hypothesized to be more specific for the median nerve at the wrist compared to the standard ULNT1 (Butler, 2000; Shacklock, 2005). Also, a more rigid definition of what constitutes a positive neurodynamic test was used and compared to previous studies (Trillos et al., 2018; C Vanti et al., 2011; Wainner et al., 2005). Findings were that LS-ULNT1 showed a sensitivity of 65.7% and a specificity of 95.7%. According to Jaeschke et al. (1994), both the +LR and the -LR demonstrated a satisfactory diagnostic accuracy, being the +LR > 5 and the -LR<0.5. The clinical interpretation of these results would be that LS-ULNT1 is capable of generating small but sometimes important changes in post-test probability (Jaeschke et al., 1994). Specifically, based on the sensitivity and specificity values, the test would have a greater capacity to detect cases with CTS than those without CTS. And

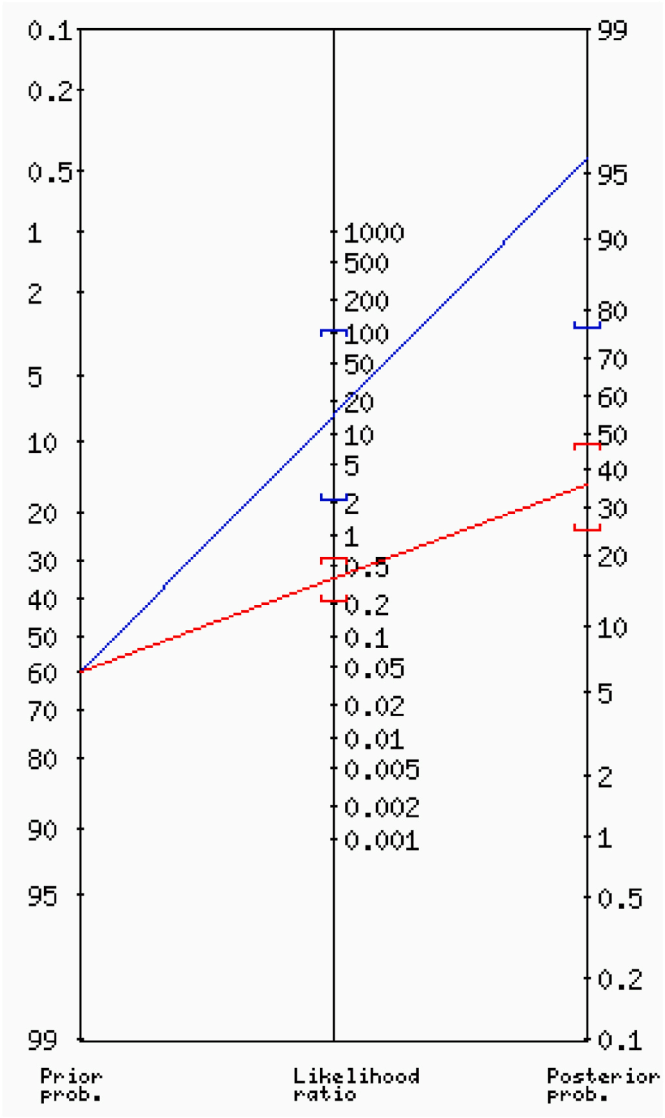

Fig. 3. Likelihood ratio nomogram adapted from Fagan (Fagan, 1975). The pretest probability of CTS in our sample is placed at 60.34%. The positive likelihood ratio of 15 for the LS-ULNT1 is indicated along with the corresponding post-test probability of 96% (blue line). The negative likelihood ratio of 0.36 for the LS-ULNT1 is indicated, along with the corresponding post-test probability of 35% (red line). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

based on the LRs, since the +LR obtained a greater value than the -LR, a positive test result would indicate a high probability that the patient had CTS.

The validity results obtained in this study are slightly higher than those obtained in previous studies and this is the first study that shows that a neurodynamic test is useful in the detection of CTS. Previous studies on the validity of the ULNT1 in the diagnosis of CTS (Trillos et al., 2018; C Vanti et al., 2011; Wainner et al., 2005) had obtained higher sensitivity values compared to our study but with very low specificity values, making the overall validity of the test low and determining that the test was not useful in the diagnosis of CTS. The commonality between these studies was less clear diagnostic criteria, making the sensitivity very high at the cost of specificity. To solve this problem, Nee et al. proposed incorporating structural differentiation and reproduction of symptoms as criteria for a positive test. Following this recommendation, Bueno et al. (Bueno-Gracia et al., 2015) obtained improved validity of the ULNT1 in the detection of CTS, with a lower sensitivity than previous studies but a much higher specificity. Even showing better sensitivity and specificity values, and higher dOR value in a recent meta-analysis on the validity of CTS diagnostic tests (De Arenas-Arroyo et al., 2022), the wide confidence intervals did not allow us to conclude that the ULNT1 was a useful test for the diagnosis of CTS.

In the present study, in addition to maintaining the diagnostic criteria proposed by Nee et al., neurodynamic sequencing was incorporated in order to make the test more specific for the median nerve at the wrist. According to Shacklock (1989), first moving the joints closest to the affected area might facilitate symptom reproduction in patients whose problem is less irritable, thus helping in the diagnosis.

While it is true that neurodynamic sequencing has been shown to produce different responses to neurodynamic testing in healthy subjects (Shacklock, 1989; Zorn et al., 1995), the mechanism underlying neurodynamic sequencing is still unknown. Studies in cadavers have shown that the tension experienced in different parts of the nerve with two sequences of ULNT1 was the same when reaching the same end position of the test (Nee et al., 2010). However, what is observed when neurodynamic sequencing is applied to living subjects is that the subjects never reach the same final position, because the symptoms appear earlier. In the present study, symptoms appeared very early in shoulder abduction, with the wrist, fingers, and elbow extended. This is a different position to the final position obtained in previous studies using the standard ULNT1 sequence, where shoulder abduction was 90-110° and maximum elbow extension was not reached (Lohkamp and Small, 2011). Regarding the location of symptoms, most of the patients reported symptoms in the distal part of the upper limb (hand, wrist, and forearm), suggesting an effect of the LS-ULNT1 in the distal part of the median nerve. To date, there are no studies that have measured and compared the amount of stress generated in the median nerve in these final positions between two different neurodynamic test sequences in living subjects.

Although the results obtained in this study show greater validity of the neurodynamic tests for the diagnosis of CTS compared to previous studies, the validity is still lower compared to other orthopedic tests for the diagnosis of CTS (De Arenas-Arroyo et al., 2022), making neurodynamic tests not the test of choice for the diagnosis of this syndrome. Indeed, CTS is a clinical diagnosis, that is aided by nerve conduction tests, and single tests, as neurodynamic tests could be helpful to confirm the diagnosis but are not powerful enough to diagnose it validly. On the other hand, there is an increasing body of evidence that heightened nerve mechanosensitive can be present or absent in patients with CTS (De Arenas-Arroyo et al., 2022) and the neurodynamic tests are not likely diagnostic of a condition, but rather of a mechanism (heightened nerve mechanosensitivity).

Some authors (Stalioraitis et al., 2014; Van Hoof et al., 2012) propose incorporating asymmetry in some of the test response variables between the affected and healthy limb as a diagnostic criterion for neurodynamic tests. According to these authors, the greater the number of asymmetric variables (range of motion, location of symptoms, type of symptoms …) the greater the evidence of increased nerve mechanosensitivity in the affected limb. Perhaps, the incorporation of these aspects as diagnostic criteria when classifying the neurodynamic test as positive could be useful to increase its validity.

4.1. Study limitations

This study has some limitations. First, a very rigid definition of what constitutes a neurodynamic test was used. That is, only those tests in which there was a change in the symptoms with the structural differentiation maneuver and the patients reported that they were their own symptoms were considered positive. This definition includes a high component of subjectivity to consider the test positive, since a positive or negative response depends on the patient reporting their symptoms. Although asymmetries between extremities are less useful in pathologies that tend to be bilateral, such as CTS, they could be used as diagnostic

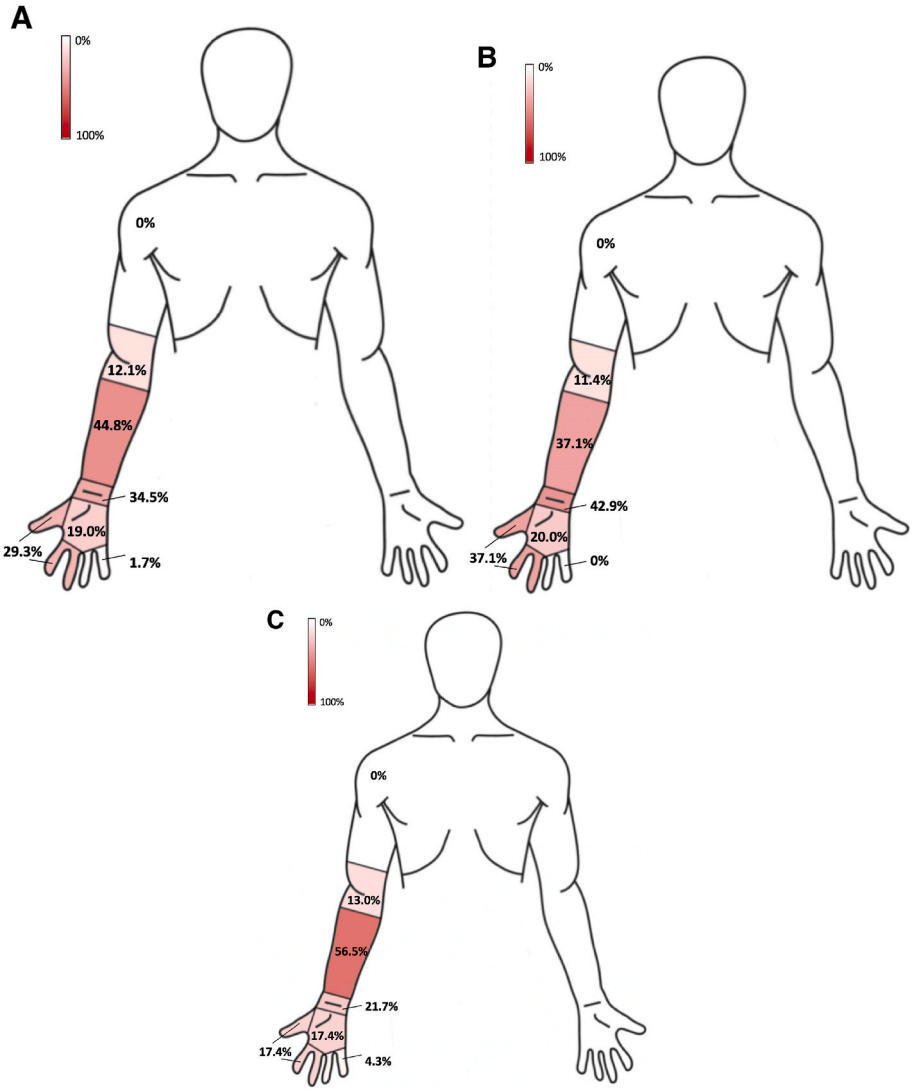

Fig. 4. Sensory responses distribution during the LS-ULNT1 in A: Overall; B: CTS patients; C: Non-CTS patients.

criteria in a sample of subjects with unilateral CTS to determine their usefulness in the diagnostic validity of CTS. Second, while de examiner reliability for ULNTs has been established for identifying a "positive" test, examiner reliability for applying the LS-ULNT1 was not determined in the present study. Third, only the LS-ULNT1 was performed and analyzed in the present study. It would have been helpful to have also performed the ULNT1 and LS-ULNT1 and compared the results to provide a direct comparison of the diagnostic validity of different sequences of the median nerve neurodynamic test. All these aspects should e taken into account in future studies on the diagnostic validity of neurodynamic tests. Third, the study collected some demographic variables and some characteristics of the symptoms of the sample. However, it would have been interesting to also collect the level of self-reported disability of CTS symptoms as additional information on the sample. Finally, findings need to be interpreted with some caution given the wide 95% Cis.

5. Conclusions

The overall results of this study showed that the LS-ULNT1 could be useful in confirming the diagnosis of CTS. The test demonstrated high specificity and the +LR indicated the ability of the test to generate changes in posttest probability, especially with a positive LS-ULNT1 result.

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