Pain propagation in the carpal tunnel syndrome: a quantitative sensory testing

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ABSTRACT

Aim To determine the existence of damage to thin sensitive fibres (Aδ and C) by quantitative sensory testing (QST) in female patients with carpal tunnel syndrome (CTS), the existence of pain, and a connection with the innervation field of the nerve itself.

Methods Forty-two consecutive female patients with symptoms of CTS participated in the research. According to the clinical findings and electroneurography they were divided into group I of 22 women with confirmed CTS and group II of 20 women with non-confirmed disease. Using QST, the threshold of heat and cold, and the threshold of pain caused by heat and cold on the thenar, second, and third finger of the dominant hand in both groups was determined.

Results There was a statistically significant difference in group I for the threshold of heat and cold detection and the threshold of pain caused by heat and cold between the thenar and the fingers. In the group II, there was a statistically significant difference in the threshold of heat detection between the thenar and the fingers. There was a statistically significant difference between the groups in the threshold of heat and cold detection on the fingers and the threshold of pain induced by heat on the fingers.

Conclusion In the carpal tunnel syndrome, there was damage to thin Aδ and C fibers in the innervation field of the median nerve, which causes pain within the innervation field of the nerve, but also outside it, which can most likely be a consequence of brain plasticity and central sensitization.

Keywords: diagnosis, median nerve, thermosensing, unmyelinated nerve fibre

INTRODUCTION

Carpal tunnel syndrome (CTS) represents a compressive neuropathy of the median nerve at the level of the wrist that is characterized by physiological evidence of increased pressure in the carpal tunnel and reduction of the nerve’s function at that level along with consequent symptomatology. There are numerous risk factors for CTS (1–5). Females get it 4-5 times more often than males, whereas the disease peak is between 50 and 59, and after 80 years of age (6). The perimenopausal period is an important risk factor (7,8).

The basic symptom of CTS is paraesthesia of the innervation field of the median nerve, on the palmar side of the first three and a half fingers, and middle and distal joints of the same fingers on the dorsal side (9). In detecting the expansion of the paraesthesia and sensibility changes, it should be kept in mind that the cutaneous palmar branch of the median nerve starts from the anterior lateral side of the nerve in the distal segment of the forearm, between 4 and 10 centimetres proximal from the hand flexor crease. Then it travels in the space between the tendons of palmaris longus and flexor carpi radialis, piercing the forearm fascia at 1.9 cm proximal from the hand flexor crease. Then it travels in the space between the tendons of palmaris longus and flexor carpi radialis, piercing the forearm fascia at 1.9 cm proximal from the joint bend and continues superficially into the palm giving a sensory innervation of the thenar. This is important to us because it separates paresthesias in CTS from dermatomal type of changes (10).

In 1% of cases, the patients state the existence of pain. Usually, it spreads to a part of the hand that does not
belong to the innervation field of the median nerve, as well as accidently even though there is no other disease that affects peripheral nerves. The presence of spreading of the symptom includes mechanisms of sensibilization and neuroplasticity (11).

Although the provocative tests, primarily the Phalen’s test, which shows the highest sensitivity, and combined sensitivity and specificity (12), are a good tool in confirming the CTS’s existence. The electroneurography (ENG) test as a golden standard should give the final judgment (13). On the other hand, the guidebooks (14) provide limited support to ENG in establishing the diagnosis. The ENG shows only the damage of thick myelinated Aδ fibers (which can explain one part of symptoms but not all). To assess the damage of thin myelinated Aδ and unmyelinated C nerve fibres, the quantitative sensory testing (QST) is applicable (15,16).

The damage to Aδ fibres is connected to the occurrence of paroxysmal pain, evoked pain, and paraesthesia/dysesthesia, which confirms their involvement in CTS (17). It is believed that this abnormal activity includes high-frequency ectopic discharges along Aδ fibres and central sensitization at the level of the dorsal horns of the spinal cord. Therefore, it is usually considered that central sensitization is the main mechanism of the sensory symptoms of CTS (18).

Fibers responsible for the transfer of pain are Aδ and C thin fibres, and it is necessary to apply quantitative sensory (QST) testing (19) to prove their damage. There is a relatively small number of research focusing on Aδ and C fibres after establishing the diagnosis of CTS, clinically or electrophysiologically. In patients with CTS, first researches on the QST sensory testing found significantly increased thresholds in the fingers innervated with the median nerve compared to the little finger of the same hand and fingers of the opposite hand where the CTS findings were not confirmed (20). Some researches on the type of affected fibres, issues of pain propagation in CTS, and central sensitization, has emerged (17,21,22) and explained the well-known discrepancy between CTS symptoms and electrodiagnostic findings.

In Bosnia and Herzegovina (B&H) we did not find researches on QST on any nerve. If proximal propagation of pain exists among patients with CTS, QST can perform, because ENG or clinical examination cannot explain the pain propagation.

The aim of this study was to determine the damage of thin sensory fibres (Aδ and C) by QST in female patients with symptoms of CTS, the existence of pain and its spreading inside and outside of the innervation field of the median nerve. In order to exclude the existence of physiological decrease of detection of thermal sensation and pain threshold caused by thermal sensations on a part of the median nerve distal from the carpal tunnel, two groups of female patients (with and without symptoms of CTS) were compared.

## Patients and Methods

### Patients and Study Design

The research was conducted at the Institute for Physical Medicine, Rehabilitation, and Orthopaedic Surgery “Dr Miroslav Zotović” in Banja Luka, B&H, in the period between December 2023 and February 2024.

This research involved 42 consecutive female patients aged 35 to 75 years of life, who came to the Cabinet for Electromyoneurography with symptoms suspecting CTS. Females get CTS 4-5 times more often than males (6), therefore, only women were selected and gender bias was excluded.

Due to the representation of both unilateral and bilateral electrophysiologically proven CTS, the research was conducted only on the dominant hand in both groups. The patients were divided into two groups: group I consisting of 22 women with confirmed CTS based on symptoms, clinical examination, and neurophysiological evaluation, and group II of 20 women with the exclusion of the disease.

Exclusion criteria were: the presence of diseases that may lead to consequential transitory or permanent damage of the peripheral nervous system, some other primary disease of the peripheral nervous system was verified (mononeuropathies, focal neuropathies except CTS, radiculopathies, plexitis, polynuropathies), the presence of some orthopaedic or rheumatological disease that causes pain and functional limitation in the extremity, and local skin changes on the place of the application of electrodes in neurophysiological evaluation. All participants have signed the informed consent.

An approval of the Ethics Committee of the Institute for Physical Medicine, Rehabilitation, and Orthopaedic Surgery “Dr Miroslav Zotović” in Banja Luka, B&H was obtained (Number: 53-01-15488-1/23).

### Methods

Before neurophysiological evaluation, data were collected about the dominant extremity, the presence and propagation of paraesthesia and pain, subjective feeling of damaged coordination, and weakness of the thenar muscles and duration of symptoms. Afterwards, the clinical examination estimated the strength of thenar muscles and checked the presence of positive Phalen’s and Tinel signs.

To confirm the presence of CTS and to exclude other diseases of the peripheral nervous system and muscles, a complete electromyoneurographic evaluation (EMNG) was performed on both upper limbs (9). After EMNG,
the QST was performed too. The data were taken from the dominant extremity regardless of the presence of unilateral or bilateral CTS. Both examinations were performed by the same examiner.

For the QST examination, the TSA-II NeuroSEnsory Analyzer (Medoc Ltd., RamatYishai, Israel) was used. Thresholds were determined with the Method of Limits (19,23). Heat and cold stimuli were delivered through a 30x30 mm² thermode attached to the skin of the palmar surface of the thenar with constant pressure. To determine the warm detection threshold (WDT) and the cold detection threshold (CDT), the skin was allowed to adapt to a temperature of 32 ºC for 5 minutes and then cooled down or warmed up linearly at a slow rate (1 ºC/second) until warm and cold sensation was perceived, at which moment the subject stopped the stimulus by pressing a button on a patient-response unit. Tests with thermodes on the palmar side of the second and third finger were carried out in the same way. The QST was carried out by placing the thermode on the thenar, as well as on the 2nd and 3rd finger of the dominant hand, due to the existence of the cutaneous palmar branch of median nerve that innervates the skin of the thenar and separates before the carpal tunnel in order to estimate the damage to fibres of the median nerve innervation field before and after the carpal tunnel.

The pain threshold was measured in the same way by placing the thermode on the surface of the thenar, first by heat (HPT) and then cold stimuli (CPT). The patients were told to stop the further heating/cooling at the first pain sensation with heat or cold stimulation by pressing the button. Afterwards, the same procedure was repeated with thermodes on the palmar side of the second and third finger.

In order to ensure compliance with the appropriate safety guidelines, the unit automatically stops measurements when it reaches a temperature of 0 ºC or 50 ºC and returns to the starting temperature of 32 ºC to avoid skin irritation. Warm and cold stimulation were repeated 6 times each, and the mean of peak temperatures was considered the threshold. The stimulation by heat or cold in determining the pain threshold was repeated three times each and the average value represented the threshold of HPT or CPT. Testing was preceded by detailed instructions to patients and a demonstration test for each type of stimulus and performed in a designated, quiet room with no distractions (19,23).

**Statistical analysis**

For the comparison of QST variables between thenar and second and third finger paired-samples t-test was used, while comparisons between groups were done with independent samples t-test. Duration of CTS and QST variables were correlated with Pearson’s correlation coefficient. A p<0.05 was considered statistically significant.

**RESULTS**

Among the patients in group I threshold for WDT was higher, and threshold for CDT was lower on 2nd and 3rd finger compared to the patients in group II. HPT in group I was higher, while CPT was lower compared to group II (Table 1).

The comparison of values of investigated QST parameters between the thenar and 2nd and 3rd finger in each group reached high statistically significant difference in all parameters in group I, but in group II the difference was seen only in WDT (Table 2).

### Table 1. Quantitative sensory testing (QST) parameters in two groups of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group of patients</th>
<th>Mean (Min. - Max.) (±SD) (%)</th>
<th>p Value</th>
<th>CI 95% Lower</th>
<th>CI 95% Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>WDT, thenar</td>
<td>I</td>
<td>34.775 (33.90 - 37.11) (±0.796)</td>
<td>0.053</td>
<td>-0.007</td>
<td>0.941</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>34.308 (33.45 - 36.01) (±0.717)</td>
<td>0.216</td>
<td>-1.367</td>
<td>0.318</td>
</tr>
<tr>
<td>CDT, thenar</td>
<td>I</td>
<td>29.125 (23.25 - 30.35) (±1.597)</td>
<td>0.000</td>
<td>2.003</td>
<td>4.649</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>29.649 (26.48 - 30.71) (±1.007)</td>
<td>0.000</td>
<td>-2.722</td>
<td>-0.875</td>
</tr>
<tr>
<td>WDT, 2nd and 3rd finger</td>
<td>I</td>
<td>38.079 (34.03 - 42.88) (±2.833)</td>
<td>0.000</td>
<td>2.003</td>
<td>4.649</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>34.753 (33.63 - 37.90) (±1.004)</td>
<td>0.000</td>
<td>-2.722</td>
<td>-0.875</td>
</tr>
<tr>
<td>CDT, 2nd and 3rd finger</td>
<td>I</td>
<td>27.804 (23.65 - 30.06) (±1.986)</td>
<td>0.302</td>
<td>-3.021</td>
<td>0.962</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>29.603 (27.75 - 30.50) (±0.675)</td>
<td>0.302</td>
<td>-3.021</td>
<td>0.962</td>
</tr>
<tr>
<td>HPT, thenar</td>
<td>I</td>
<td>44.019 (36.20 - 47.17) (±3.172)</td>
<td>0.753</td>
<td>-5.055</td>
<td>3.684</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>45.048 (38.16 - 48.93) (±3.208)</td>
<td>0.753</td>
<td>-5.055</td>
<td>3.684</td>
</tr>
<tr>
<td>CPT, thenar</td>
<td>I</td>
<td>11.589 (4.26 - 27.13) (±6.437)</td>
<td>0.023</td>
<td>0.323</td>
<td>4.015</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>12.275 (3.00 - 24.33) (±7.568)</td>
<td>0.023</td>
<td>0.323</td>
<td>4.015</td>
</tr>
<tr>
<td>HPT, 2nd and 3rd finger</td>
<td>I</td>
<td>48.606 (43.20 - 50.00) (±1.979)</td>
<td>0.086</td>
<td>-7.614</td>
<td>0.537</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>46.437 (38.66 - 50.00) (±3.569)</td>
<td>0.086</td>
<td>-7.614</td>
<td>0.537</td>
</tr>
</tbody>
</table>

*Group I, 22 patients with carpal tunnel syndrome; Group II, 20 patients without carpal tunnel syndrome; CI, confidence interval; CDT, cold detection threshold; WDT, warm detection threshold; CPT, cold pain threshold; HPT, heat pain threshold
Values between the groups showed higher values for CDT (p=0.216), HPT (p=0.302), and CPT (p=0.753) on the thenar, CDT (p=0.000) and CPT (p=0.086) on the fingers of group II, whereas the values of WDT (p=0.053) on the thenar, WDT (p=0.000), and HPT (p=0.023) on the fingers were higher in the group I (Table 1).

Duration of the disease did not correlate with CDT (p=0.189), WDT (p=0.520), HPT (p=0.949), and CPT (p=0.677) on the 2nd and 3rd finger in the group with CTS.

Eleven (out of 22; 50 %) patients had no pain. The pain was localised in six (out of 22; 27.27%) patients with CTS at the level of hand or wrist, whereas the neurographic values of the ulnar and radial nerve were in order, and five (out of 22; 22.73%) patients reported pain spreading ascendingly to the elbow and shoulder. Such pain propagation can be seen among patients with radiculopathy C5-C8 (Th1). Therefore, we used electromyography to exclude such patients.

In our patients with CTS, the mean value of HPT was 44.02 °C on the thenar, and 48.60 °C on the fingers, whereas in the group without CTS, the threshold was 45.04 °C on the thenar and 46.43 °C on the fingers. There was a statistically significant difference in HPT on fingers between the groups (p=0.023) (Table 1), as well as between the thenar and fingers in the group with CTS (p=0.000) (Table 2). In our patients with CTS, the average mean value of CPT was 11.58 °C on the thenar, and 7.6 °C on the fingers, whereas in the group without CTS, the threshold was 12.27 °C on the thenar and 11.14 °C on the fingers. There was a statistically significant difference in CPT between the thenar and fingers in the group with CTS (p=0.001) (Table 2).

**DISCUSSION**

Comparing data within two groups of patients, with and without CTS, a statistically significant difference in WDT and CDT, HPT, and CPT between values obtained on the thenar and the values from the fingers in the group with CTS was found; in the group without CTS, there was a difference only in WDT. Also, a statistically significant difference was found in WDT, CDT, and the threshold of HPT measured on the 2nd and 3rd finger between these two groups, whereas the experience threshold in the stated parameters in the group with CTS was higher with heat stimuli, i.e. lower with cold stimuli compared to the group without CTS. This is supported by literature data (22, 24) where no difference was found between the values of CPT between the groups on the fingers.

Reference values of the stated parameters of QST are still not defined (25), and there are more factors influencing the patient’s response during the examination. One of the factors is also the place of measuring the threshold of WDT, CDT, HPT, and CPT (26). Both, lower WDT and higher CDT are seen on the hand and foot in females, while males have higher HPT. The hand is more sensitive to cold and heat than the foot, i.e. the region of the thenar is more sensitive to heat than the dorsal and plantar side of the forearm, although that difference is clinically negligible; all those anatomic places are equally sensitive to cooling, whereas the interindividual variance is the lowest in thenar (26). The average values of WDT on the thenar in the group without CTS are confirmed by data from certain studies where the reference value was determined on a large number of samples (27). We took into consideration the values for the time of life above 40 years; the range of age in our research was somewhat narrower. We assume that this was affected by the number of examinees too. There are more factors influencing the patient’s response during the examination. One of the factors is also the place of measuring the threshold of WDT, CDT, HPT, and CPT (26). Both, lower WDT and higher CDT are seen on the hand and foot in females, while males have higher HPT. The hand is more sensitive to cold and heat than the foot, i.e. the region of the thenar is more sensitive to heat than the dorsal and plantar side of the forearm, although that difference is clinically negligible; all those anatomic places are equally sensitive to cooling, whereas the interindividual variance is the lowest in thenar (26). The average values of WDT on the thenar in the group without CTS are confirmed by data from certain studies where the reference value was determined on a large number of samples (27). We took into consideration the values for the time of life above 40 years; the range of age in our research was somewhat narrower. We assume that this was affected by the number of examinees too.

The values of CDT were also consistent with literature data (25, 27). Although there was a statistically significant difference in parameters of WDT on the thenar and fingers in the group without CTS, both values differed minimally, which is clinically negligible.

Fibers responsible for the transfer of cold are Aδ fibres (28). The study (21) states that only Aδ fibres are involved in CTS. In our group with CTS, a difference in CDT and CPT on the thenar and fingers was found, indicating the involvement of Aδ fibres. However, there was a difference between the findings of WDT and HPT on the thenar and fingers in the group with CTS, as

**Table 2. Comparison of quantitative sensory testing (QST) parameters between thenar and 2nd and 3rd finger within each group**

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Variable</th>
<th>Mean (±SD) (%)</th>
<th>CI 95%</th>
<th>Lower</th>
<th>Upper</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>WDT</td>
<td>-3.304 (±2.472)</td>
<td>95%</td>
<td>-4.400</td>
<td>-2.208</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CDT</td>
<td>1.321 (±1.852)</td>
<td></td>
<td>0.499</td>
<td>2.142</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>HPT</td>
<td>-4.587 (±2.388)</td>
<td></td>
<td>-5.646</td>
<td>-3.529</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>CPT</td>
<td>3.991 (±4.576)</td>
<td></td>
<td>1.962</td>
<td>6.020</td>
<td>0.001</td>
</tr>
<tr>
<td>II</td>
<td>WDT</td>
<td>-0.445 (±0.777)</td>
<td>95%</td>
<td>-0.809</td>
<td>-0.081</td>
<td>0.019</td>
</tr>
<tr>
<td></td>
<td>CDT</td>
<td>0.046 (±0.636)</td>
<td></td>
<td>-0.251</td>
<td>0.344</td>
<td>0.747</td>
</tr>
<tr>
<td></td>
<td>HPT</td>
<td>-1.389 (±2.986)</td>
<td></td>
<td>-2.786</td>
<td>0.009</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>CPT</td>
<td>1.138 (±6.059)</td>
<td></td>
<td>-1.698</td>
<td>3.975</td>
<td>0.411</td>
</tr>
</tbody>
</table>

*Group I, 22 patients with carpal tunnel syndrome; Group II, 20 patients without carpal tunnel syndrome; CI, confidence interval; WDT, warm detection threshold; CDT, cold detection threshold; HPT, heat pain threshold; CPT, cold pain threshold.

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well as on the fingers between the group with and without CTS, indicating damage to both Aδ fibres and C fibres in the CTS group, but only in the innervation field of that part of the median nerve that is compressed in the carpal tunnel. Some studies reported changes in the threshold of heat detection on the affected hand in CTS [21], while others could not identify a significant thermal hypoesthesia [29].

Some patients with CTS have a localized pain sensation or with ascending propagation, without the existence of any correlation between the severity of the sensitive symptoms, including pain, and the severity of neurophysiological changes [30]. The expansion of symptoms outside of the innervation field of the median nerve in CTS can be even up to 70%, while the proximal expansion of pain is found in up to 40% of patients [21].

Pain sensation on heat and cold is transferred across Aδ and C fibres [31]. TRPV 2 tunnels are activated by high temperature and threshold of 52 °C, for which the Aδ fibres [32] are responsible. The threshold of our heat stimulation was up to 50 °C, after which the device switched off the automatic operation for security reasons. When the temperature of the stimulus increases (< 2.0 °C/s), the responses of the pain threshold can be based on the activation of C fibres [33]. In our work, it was 1.0 °C/s, which indicates that the response was by the C fibres. Pain sensation appears at a temperature of around 45 °C [34]. Using the limit method, the cutaneous threshold of thermal pain was 45.9±4.2 °C [35] on the hand. In our examinees with CTS, the average value of HPT was 44.02 °C on the thenar, and 48.60 °C on the fingers, whereas in the group without CTS, the threshold was 45.04 °C on the thenar and 46.43 °C on the fingers.

Literature data indicate that the pain threshold in thermic testing in patients with CTS was significantly higher compared to the healthy ones [36]. The values of HPT in healthy persons are in the range 37.8 °C-46.26 °C, in which the result of the measurement on the thenar for both groups with the similar range of min and max values falls in too [25,26,37,38]. Hyposensitivity was observed in some studies [22], especially for HPT in patients with CTS compared to the control group, which again indicates central sensitization.

The values of CPT in researches ranged from 20.7 °C to 26.3 °C, taking into consideration the hand [26,37], although certain papers [26] state the value of 9.8 °C (range of 1.2-24.5 °C), whereas the thenar is less sensitive to the cold. CPT values on the thenar in our work were significantly lower comparing to most other studies, 12.27 °C (3 °C-24.33 °C) in the group without CTS, and 11.58 °C (4.26 °C-27.13 °C) in the group with CTS. The values of CPT. The reason might be related to anthropometric characteristics, and climate factors, i.e. customs and mentality of the population. The assumption is that the work on a larger population would change the results more significantly.

In our work, there was no difference in CPT on the thenar between the two groups, but not even on the fingers. The reason may be the difference in density of the peripheral innervation, because of activation of “silent” nociceptors [39]. The potential explanation for the spread and increase of HPT, but not CPT, could be different central processing of the heat and cold stimuli. A certain subset of thalamic neurons reacts exclusively to harmful heat stimuli, while others react to harmful cold stimuli [40]. Furthermore, higher temperature differences are needed for the cold stimuli to provoke a similar perception to harmful heat stimuli. Also, it is believed that the receptors that mediate the harmful heat stimuli are located more superficially in the skin compared to the receptors for the harmful cold, which are positioned more deeply [41].

In conclusion, the patients with CTS, which was confirmed by neurophysiological diagnostics, have damaged thin Aδ and C fibres, which provide the basis for the development of pain within the innervation field of the nerve, but also outside it. Previous studies on the carpal tunnel syndrome and pain have not involved anatomical specificities of the innervation field and the damaged part of the nerve. This was the starting point for determining the area of pain propagation and the innervation field of the median nerve. At the same time, it is the basis for further upgrade in research of the relationship between pain and carpal tunnel syndrome in the area of peripheral and central sensitization.

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**TRANSPARENCY DECLARATION**

Conflict of interests: None to declare.

**REFERENCES**


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