**Supplementary text 1: Description of used questionnaires and scoring systems**

A set of questionnaires assessing the presence of pain, pain intensity and characteristics, severity of neuropathy and disability, and psychological impact of pain were completed during the appointment (usually in the intervals between blood withdrawal, clinical and electrophysiological examination, and QST testing).

**Modified Toronto Clinical Neuropathy Score (mTCNS)** [7] is a screening tool for diabetic peripheral neuropathy, and correlates with the severity of diabetic neuropathy. It uses a simplified neurological examination assessing peripheral sensory perception and the presence of neuropathy symptoms. In contrast to the original Toronto Clinical Neuropathy Score (TCNS) that contained also reflex scores, the mTCNS consists of two subscores only: symptom score and sensory test score. Each of the following neuropathy symptoms - pain, numbness, tingling and weakness in the feet, the presence of similar upper limb symptoms, and the presence of unsteadiness on ambulation (ataxia) is graded as absent (0), present but no interference with sense of well-being or activities of daily living (1), present, interferes with sense of well-being but not with activities of daily living (2), and present and interferes with both sense of well-being and activities of daily living (3). The values of the symptoms score ranges between 0 and 18 points. Sensory testing is performed on the lower extremities for the following: pinprick sensation, temperature discrimination, proprioception, light touch, and vibration, and rated as normal (0), reduced at the toes only (1), reduced to a level above the toes, but only up to the ankles (2), and reduced to a level above the ankles and/or absent at the toes. The sensory tests score values range between 0-15), and the mTCNS sum-score is the sum of both subscores (range 0-33).

Similarly, The Inflammatory Neuropathy Cause and Treatment (INCAT) **Overall Disability Sum Score** (ODSS) [26], originally designed as a measure of disability in dysimmune neuropathies, was used to quantify disability in DSPN. It consists of arm and leg grades classifying severity of neuropathic symptoms and signs and their impact on disability between grade 0 (normal) and 5 (severe symptoms and signs in both arms preventing all purposeful movements) in the arms, and between 0 (walking is not affected) and 7 (restricted to wheelchair or bed most of the day, preventing all purposeful movements of the legs). The ODSS sum score is thus calculate as a sum of Arm and Leg grades (range 0-12).

**Neuropathic Pain Symptom Inventory** **(NPSI)** [6,31,36] is a self-administered questionnaire designed to evaluate neuropathic pain symptoms. The NPSI was completed for pain in feet and hands. It evaluates the presence and severity of 12 different neuropathic pain descriptors, each on an 11 point scale where 0 indicates no symptoms and 10 indicates maximal symptoms experienced (with the exception of Q4 and Q7 items graded on a 5-point categorical scales):

Q1: burning

Q2: squeezing (jaw wise)

Q3: pressure

Q4: spontaneous pain duration

Q5: electrifying

Q6: stabbing

Q7: number of attacks

Q8: evoked pain upon rubbing

Q9: evoked pain upon pressure

Q10: evoked pain upon cold

Q11: pins and needles

Q12: tingling

In addition, 5 subscales are calculated (values in a range 0-10):

* Burning = Q1
* Pressing (deep) spontaneous pain = (Q2+Q3/2)
* Paroxysmal pain = (Q5+Q6/2)
* Evoked pain = (Q8+Q9+Q10/3)
* Paresthesia/dysesthesia = (Q11+Q12/2)

Finally, a total NPSI score is a sum of Q1+Q2+Q3+Q5+Q6+Q8+Q9+Q10+Q11+Q12 (values in a range 0-100).

**Graded Chronic Pain Scale (GCPS)** [45] is another questionnaire used to evaluate pain intensity and its impact on everyday life activities based on the following 7 questions:

1. Current (immediate) pain: 0 = no pain, 10 = pain as bad as it could be
2. Worst pain during last 6 months: 0 = no pain, 10 = pain as bad as it could be
3. Average pain during last 6 months: 0 = no pain, 10 = pain as bad as it could be
4. Disability days (number of days in the past 6 months in which the subject has been kept from his/her usual activities (work school or housework) because of pain: 0-6 days = 0, 7-14 days = 1, 15-30 days = 2, >31 days = 4
5. Daily activities (how much has the pain interfered with daily activities) (0 = no interference, 10 = unable to carry on any activities)
6. Social activities (how much has the pain changed ability to take part in recreational social and family activities) (0 = no interference, 10 = unable to carry on any activities)
7. Work activities (how much has the pain changed your ability to work (including housework) (0 = no interference, 10 = unable to carry on any activities)

**Characteristic pain intensity** was calculated as a sum of responses to questions (1+2+3)/3 x 10 (range 0-100)

**GCPS disability score** was calculate as a sum of responses to questions (5+6+7)/3 x 10 (range 0-100)

Disability points = points for disability days + points for disability score (disability score 0-29=0, disability score 30-49 = 1, disability score 50-69 = 2, disability score >70 = 3)

**GCPS grades**:

0 = no pain problems for the prior 6 months

I = charactersitic pain intensity < 50, disability points < 3

II = charactersitic pain intensity > 50, disability points < 3

III = disability points 3-4

IV = disability points 5-6

**Pain Catastrophizing Scale (PCS)** [27] assessed the cognitive process by which pain is appraised in terms of threat and negative consequences. It consists of 13 descriptions of thoughts and feelings related to pain. Study participants were asked to indicate the degree to which they experience these on a 5-point rating scale from 0 (not at all) to 4 (always). A high total score indicates a high level of pain catastrophizing. Catastrophizing is defined as a maladaptive response to pain and is characterized by an experience of heightened pain intensity and difficulty in disengaging from pain; it is an important predictor of pain severity, and of how people cope with pain, and appears to predict future disability better than do other variables. PCS comprises 3 dimensions: rumination, magnification, and helplessness. Rumination subscore (sum of items 8-11) refers to the patients’ preoccupation with pain; magnification subscore (sum of items 6,7,13) expresses the exaggerated cognitions of pain as a threat; and hopelessness subscore (items 1-5+12) is patients’ feelings that they are unable to influence their pain.

**Beck Depression Inventory (BDI) II** is a 21-question [multiple-choice](https://en.wikipedia.org/wiki/Multiple_choice) [self-report inventory](https://en.wikipedia.org/wiki/Self-report_inventory) for the measuring the severity of [depression](https://en.wikipedia.org/wiki/Clinical_depression). It is composed of items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, [weight loss](https://en.wikipedia.org/wiki/Weight_loss), and lack of interest in sex. Every item is scored from 0 to 3 and the sum-score ranges between 0-63.

**State-Trait Anxiety Inventory version Y (STAI Y)** [35] comprised of two separate 20-item self-report scales that measure both state (S-Anxiety) and trait (T-Anxiety) anxiety. Every item is a statement that is evaluated by a responder using 4-grade scale:

1 = not at all

2 = somewhat

3 = moderately so

4 = very much so

As a result, STAI S and STAI T subscores are calculated (range 20-80 each) and higher STAI scores suggest higher levels of anxiety.

**Supplementary Table 1 – Results of additional laboratory parameters**

| **Laboratory parameter** | **Moderate/severe pain(NRS ≥ 4)** | **Mild pain (NRS 1-3)** | **Painless** **(NRS 0)** | **P** |
| --- | --- | --- | --- | --- |
|  | N = 106 | N = 52 | N = 74 |  |
| Folate level (nmol/l) | 17.2 (6.6; 36.1) | 25.4 (11.6; 39.2) | 15.3 (4.6; 38.1) | 0.120 |
| B12 level (pmol/l) | 263 (148; 822) | 291 (150; 1065) | 282 (149; 509) | 0.762 |
| fT4 (pmol/l) | 15.7 (12.1; 20.9) | 15.3 (12.6; 21.9) | 15.4 (12.4; 21.9) | 0.540 |
| TSH (mU/l) | 2.5 (0.8; 5.7)a | 2.4 (0.7; 6.2) | 2.5 (1.0; 4.7) | 0.864 |
| Bilirubin (µmol/l) | 8.3 (3.4; 21.6) | 9.4 (4.8; 23.2) | 8.0 (3.7; 18.7) | 0.230 |
| ALT (µkat/l) | 0.45 (0.19; 0.98) | 0.42 (0.29; 1.01) | 0.42 (0.21; 0.89) | 0.709 |
| AST (µkal/l) | 0.42 (0.30; 0.79) | 0.46 (0.31; 0.78) | 0.41 (0.27; 0.72) | 0.476 |
| Leukocytes (109/l) | 7.0 (4.1; 10.5) | 6.8 (4.9; 10.0) | 6.8 (4.2; 10.8) | 0.821 |
| Erytrocytes (1012/l) | 4.8 (3.9; 5.5) | 4.8 (4.0; 5.5) | 4.9 (4.0; 5.7) | 0.232 |
| Haemoglobin (g/l) | 144.0 (112.0; 164.0)a | 1431.0 (121.0; 163.0)a | 147.0 (117.0; 171.0)b | 0.109 |
| Trombocytes (109/l) | 214.0 (130.0; 338.0) | 209.0 (144.0; 441.0) | 216.0 (144.0; 342.0) | 0.961 |

Continuous parameters are summarized as median (5th–95th percentile range).

P-value represents the comparison of patients with different levels of pain (Kruskal-Wallis test for continuous variables); post-hoc tests: a, b, c – same letters marking values of categories within given row denote mutually statistically not different groups.

NRS – numerical rating scale, fT4 – free thyroxine ,TSH – thyroid stimulating hormone , ALT – alanine aminotransferase, AST – aspartate aminotransferase

**Supplementary Table 2 – Summary of analgesic use**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Moderate/severe pain(NRS ≥ 4)** | **Mild pain (NRS 1-3)** | **Painless** **(NRS 0)** | P |
| Number of participants | 106 | 52 | 74 |  |
| Participants reported analgesic drug use | 64 (60.4%)a | 29 (55.8%)a | 15 (20.3%)b | **<0.001** |
| Participants reported use of analgesic drug specific for treatment of neuropathic pain | 49 (46.2%)a | 21 (40.4%)a | 6 (8.1%)b | **<0.001** |
| Gabapentinoids  |  |  |  |  |
| Pregabalin | 21 (19.8%)a | 2 (3.8%)b | 2 (2.7%)b | **<0.001** |
| Gabapentin | 15 (14.2%)a | 13 (25.0%)a | 2 (2.7%)b | **<0.001** |
| Antidepressants |  |  |  |  |
| Tricyclics (amitriptyline) | 10 (9.4%) | 3 (5.8%) | 2 (2.7%) | 0.173 |
| SNRI (duloxetine, venlafaxine) | 8 (7.5%)a | 2 (3.8%)ab | 0 (0.0%)b | **0.033** |
| Tramadol | 8 (7.5%) | 2 (3.8%) | 6 (8.1%) | 0.709 |
| Opioids | 6 (5.7%) | 0 (0.0%) | 2 (2.7%) | 0.205 |
| NSAIDs | 23 (21.7%) | 7 (13.5%) | 11 (14.9%) | 0.366 |
| Clonazepam | 7 (6.6%) | 3 (5.8%) | 0 (0.0%) | 0.056 |

NeuP – neuropathic pain, NRS – numerical rating scale**,** SNRI – serotonin-norepinephrine reuptake inhibitors, NSAIDs – non-steroidal anti-inflammatory drugs

**Supplementary table 3.** Clinical sensory, motor and autonomic symptoms and/or signs

| **Parameters** |  | **Moderate/severe pain(NRS ≥ 4)** | **Mild pain (NRS 1-3)** | **Painless (NRS 0)** | **P** |
| --- | --- | --- | --- | --- | --- |
|  |  | N = 106 | N = 52 | N = 74 |  |
| Sensory examination in feet |  |  |  |  |  |
| Hypoesthesia (touch) | Abnormal | 61 (57.5%)b | 16 (30.8%)a | 18 (24.3%)a | **< 0.001** |
| Hypoalgesia (toothpicks, neurotips) | Abnormal | 61 (57.5%)b | 16 (30.8%)a | 16 (21.6%)a | **< 0.001** |
| Hyperesthesia (touch) | Abnormal | 4 (3.8%) | 2 (3.8%) | 1 (1.4%) | 0.689 |
| Hyperalgesia (toothpick, pressure) | Abnormal | 16 (15.1%) | 6 (11.5%) | 9 (12.2%) | 0.771 |
| Cold hypoesthesia (tip therm) | Abnormal | 80 (75.5%)a | 33 (63.5%)ab | 39 (52.7%)b | **0.006** |
| Cold hyperesthesia (tip therm) | Abnormal | 2 (1.9%) | 2 (3.8%) | 1 (1.4%) | 0.716 |
| Warm hypoesthesia (tip therm) | Abnormal | 51 (48.1%)a | 17 (32.7%)ab | 20 (27.0%)b | **0.011** |
| Warm hyperesthesia (tip therm) | Abnormal | 2 (1.9%) | 0 (0.0%) | 0 (0.0%) | 0.707 |
| Vibration sense, big toe (X/8) right |  | 4.1 ± 3.1a | 5.1 ± 2.6ab | 5.4 ± 2.4b | **0.028** |
| Vibration sense, big toe (X/8) left |  | 4.2 ± 3.1a | 4.8 ± 2.9ab | 5.7 ± 2.1b | **0.006** |
| MRC (0-5) | Hand finger spreading right | 4.9 ± 0.3 | 5.0 ± 0.0 | 5.0 ± 0.0 | 0.090 |
|  | Hand finger spreading left | 4.9 ± 0.4 | 5.0 ± 0.0 | 5.0 ± 0.0 | 0.090 |
|  | Foot extension right | 4.7 ± 0.6b | 4.9 ± 0.3a | 5.0 ± 0.3a | **< 0.001** |
|  | Foot extension left | 4.8 ± 0.6b | 5.0 ± 0.2a | 5.0 ± 0.3a | **< 0.001** |
|  | Foot flexion right | 4.8 ± 0.4b | 5.0 ± 0.3a | 5.0 ± 0.0a | **< 0.001** |
|  | Foot flexion left | 4.8 ± 0.4b | 5.0 ± 0.3a | 5.0 ± 0.0a | **< 0.001** |
|  | Big toe extension right | 4.7 ± 0.6b | 4.9 ± 0.3a | 5.0 ± 0.1a | **< 0.001** |
|  | Big toe extension left | 4.6 ± 0.8b | 4.9 ± 0.3a | 4.9 ± 0.3a | **< 0.001** |
|  | Big toe flexion right | 4.7 ± 0.7b | 5.0 ± 0.3a | 5.0 ± 0.0a | **< 0.001** |
|  | Big toe flexion left | 4.6 ± 0.8b | 4.9 ± 0.4a | 5.0 ± 0.2a | **< 0.001** |
| MRC – Arm sum-score (R+L: 0-60) | 59.8 ± 1.0a | 60.0 ± 0.0ab | 60.0 ± 0.0b | **0.049** |
| MRC – Leg sum-score (R+L: 0-60) | 57.5 ± 4.7b | 59.5 ± 2.1a | 59.8 ± 0.9a | **< 0.001** |
| MRC – Final sum-score (arm + leg: 0-120) | 117.4 ± 5.0b | 119.5 ± 2.1a | 119.8 ± 0.9a | **< 0.001** |
| Skin color changes in sitting position | Yes | 49 (46.2%) | 17 (32.7%) | 26 (35.1%) | 0.174 |
| Sexual dysfunction | Yes | 15 (14.2%) | 4 (7.7%) | 7 (9.5%) | 0.490 |
| Voiding problems | Yes | 30 (28.3%) | 10 (19.2%) | 11 (14.9%) | 0.096 |
| Sweating | Normal | 85 (80.2%) | 40 (76.9%) | 66 (89.2%) | 0.406 |
|  | Hyperhidrosis | 15 (14.2%) | 9 (17.3%) | 6 (8.1%) |
|  | Hypohidrosis | 6 (5.7%) | 3 (5.8%) | 2 (2.7%) |

Continuous parameters are summarized as mean ± standard deviation (SD). Categorical parameters are expressed as absolute and relative frequencies.
P-value represents the comparison of patients with different levels of pain (Kruskal-Wallis test for continuous variables and Fisher’s exact test for categorical variables); post-hoc tests: a, b, c – same letters marking values of categories within given row denote mutually statistically not different groups.

NRS – numerical rating scale, MRC – medical research council

**Supplementary Table 4.** Quantitative sensory testing

| **Parameters** |  | **Moderate/severe pain(NRS ≥ 4)** | **Mild pain** **(NRS 1-3)** | **Painless (NRS 0)** | **P** |
| --- | --- | --- | --- | --- | --- |
|  | N = 106 | N = 52 | N = 74 |  |
| **QST parameters - foot** |  |  |  |  |  |
| CDT (Z-score) |  | -2.0 (-3.3; 0.2)a | -1.5 (-3.3; 0.1)b | -1.0 (-3.3; 0.7)c | **< 0.001** |
| CDT | Normal | 52 (49.1%) | 36 (69.2%)a | 59 (79.7%)a | **< 0.001** |
|  | Abnormal (loss: <-2) | 54 (50.9%) | 16 (30.8%) | 15 (20.3%) |
| WDT (Z-score) |  | -1.8 (-2.7; 0.1)a | -1.6 (-2.5; 0.1)b | -1.2 (-1.9; 0.7)c | **< 0.001** |
| WDT | Normal | 70 (66.0%)a | 45 (86.5%)b | 72 (97.3%)c | **< 0.001** |
|  | Abnormal (loss: <-2) | 36 (34.0%) | 7 (13.5%) | 2 (2.7%) |
| TSL (Z-score) |  | -1.7 (-3.1; 0.0)a | -1.4 (-2.5; 0.2)b | -0.9 (-2.3; 0.6)c | **< 0.001** |
| TSL | Normal | 58 (54.7%)b | 41 (78.8%)a | 68 (91.9%)a | **< 0.001** |
|  | Abnormal (loss: <-2) | 48 (45.3%) | 11 (21.2%) | 6 (8.1%) |
| CPT (Z-score) |  | -0.7 (-1.2; 1.4)a | -0.4 (-1.1; 1.5)ab | 0.0 (-1.1; 1.6)b | **0.002** |
| CPT | Normal | 105 (99.1%) | 52 (100.0%) | 73 (98.6%) | 0.999 |
|  | Abnormal gain (>2) | 2 (1.9%) | 0 (0.0%) | 1 (1.4%) |
|  | Abnormal loss (<-2) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |  |
| HPT (Z-score) |  | -1.5 (-2.0; -0.2)a | -1.5 (-2.0; 1.2)a | -1.2 (-2.0; 2.5)b | **< 0.001** |
| HPT | Normal | 82 (77.4%) | 44 (84.6%) | 64 (86.5%) | 0.280 |
|  | Abnormal gain (>2) | 2 (1.9%) | 2 (3.8%) | 5 (6.8%) |
|  | Abnormal loss (<-2) | 22 (20.8%) | 6 (11.5%) | 5 (6.8%) |  |
| PPT (Z-score) |  | -1.6 (-3.7; 0.9) | -1.8 (-4.1; 1.6) | -1.6 (-3.6; 1.1) | 0.461 |
| PPT | Normal | 68 (64.2%) | 28 (53.8%) | 40 (54.1%) | 0.297 |
|  | Abnormal gain (>2) | 1 (0.9%) | 1 (1.9%) | 1 (1.4%) |
|  | Abnormal loss (<-2) | 37 (34.9%) | 23 (44.2%) | 33 (44.6%) |  |
| MPT (Z-score) |  | -0.4 (-3.2; 2.9)a | -0.1 (-3.2; 3.6)ab | 0.4 (-3.2; 3.0)b | **0.040** |
| MPT | Normal | 60 (56.6%) | 32 (61.5%) | 47 (63.5%) | 0.645 |
|  | Abnormal gain (>2) | 13 (12.3%) | 10 (19.2%) | 9 (12.2%) |
|  | Abnormal loss (<-2) | 35 (33.0%) | 10 (19.2%) | 18 (24.3%) |  |
| MPS (Z-score) |  | -0.8 (-4.2; 3.2)a | -0.8 (-4.0; 2.2)ab | 0.2 (-4.0; 3.5)b | **0.028** |
| MPS | Normal | 50 (47.2%) | 33 (63.5%) | 42 (56.8%) | 0.132 |
|  | Abnormal gain (>2) | 12 (11.3%) | 7 (13.5%) | 8 (10.8%) |
|  | Abnormal loss (<-2) | 44 (41.5%) | 12 (23.1%) | 24 (32.4%) |  |
| WUR (Z-score) |  | 0.0 (-1.6; 3.7) | 0.3 (-1.5; 2.5) | 0.1 (-1.5; 2.8) | 0.643 |
| WUR | Normal | 93 (88.6%) | 46 (88.5%) | 64 (87.7%) | 0.999 |
|  | Abnormal (gain: >2) | 12 (11.4%) | 6 (11.5%) | 9 (12.3%) |
| MDT (Z-score) |  | -0.1 (-4.2; 1.9)a | 0.7 (-2.6; 1.9)b | 1.0 (-2.3; 2.0)b | **< 0.001** |
| MDT | Normal | 90 (84.9%) | 48 (92.3%) | 69 (93.2%) | 0.186 |
|  | Abnormal (loss: <-2) | 16 (15.1%) | 4 (7.7%) | 5 (6.8%) |
| VDT (Z-score) |  | -1.1 (-6.5; 1.0) | -0.5 (-6.5; 1.4) | -0.5 (-5.9; 1.4) | 0.093 |
| VDT | Normal | 69 (65.1%) | 38 (74.5%) | 58 (80.6%) | 0.077 |
|  | Abnormal (loss: <-2) | 37 (34.9%) | 13 (25.5%) | 14 (19.4%) |
| DMA | Normal (absent) | 98 (92.5%) | 48 (92.3%) | 74 (100.0%) | 0.052 |
|  | Abnormal (present) | 8 (7.5%) | 4 (7.7%) | 0 (0.0%) |
| PHS | Normal (absent) | 49 (46.2%)a | 32 (62.7%)b | 46 (63.9%)b | **0.036** |
|  | Abnormal (present) | 57 (53.8%) | 19 (37.3%) | 26 (36.1%) |  |
| QST summary\* | Normal (no abnormities) | 5(4.7%) | 3 (5.8%) | 8 (10.8%) | 0.265 |
|  | Abnormal (at least one abnormity) | 101(95.3%) | 49 (94.2%) | 66 (89.2%) |  |
| QST summary† | Normal (no abnormities) | 20 (18.9%)a | 12 (23.1%)a | 28 (37.8%)b | **0.015** |
|  | Abnormal (at least one abnormity) | 86 (81.1%) | 40 (76.9%) | 46 (62.2%) |  |
| Sensory profiles  | Irritable nociceptor profile | 13 (12.3%)a | 10 (19.2%)b | 8 (10.8%)c | **< 0.001** |
|  | Deafferentation profile | 61 (57.5%) | 24 (46.2%) | 20 (27.0%) |
|  | Other | 32 (30.2%) | 18 (32.6%) | 46 (62.2%) |

Continuous parameters are summarized as median (5th–95th percentile range). Categorical parameters are expressed as absolute and relative frequencies.
P-value represents the comparison of patients with different levels of pain (Kruskal-Wallis test for continuous variables and Fisher’s exact test for categorical variables); post-hoc tests: a, b, c – same letters marking values of categories within given row denote mutually statistically not different groups.

\*Hypoesthesia to thermal or mechanical stimuli (i.e. loss of detection in CDT, WDT, TSL, MDT and VDT) and/or hyper- or hypoalgesia to thermal or mechanical stimuli (i.e. both gain or loss of function in HPT, CPT, MPT, MPS, DMA or PPT) and/or gain in WUR or PHS were taken into account in definition of abnormity.

†According to Maier et al.(2010), hypoesthesia to thermal or mechanical stimuli (i.e. loss of detection in CDT, WDT, MDT and VDT) and/or hyperalgesia to thermal or mechanical stimuli (i.e. gain of function in HPT, CPT, MPT, MPS, DMA or PPT) were taken into account in definition of abnormity.

NRS – numerical rating scale, QST – quantitative sensory testing, CDT – cold detection threshold, WDT – warm detection threshold, TSL – thermal sensory limen, CPT – cold pain threshold, HPT – heat pain threshold, PPT – pressure pain threshold, MPT – mechanical pain threshold, MPS – mechanical pain sensitivity, WUR – wind-up ratio, MDT – mechanical detection threshold, VDT – vibration detection threshold, DMA – dynamic mechanical allodynia, PHS – paradoxical heat sensation

**Supplementary table 5.** Correlation between quantitative sensory testing z-scores, and clinical scores

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | CDT | WDT | TSL | CPT | HPT | PPT | MPT | MPS | WUR | MDT | VDT |
| mMRC motor sum score | **0.251\*\*** | **0.248\*\*** | **0.265\*\*** | **0.161\*** | 0.116 | 0.031 | 0.124 | 0.128 | 0.053 | 0.053 | 0.053 |
| mTCNS symptoms | **-0.381\*\*** | **-0.391\*\*** | **-0.429\*\*** | **-0.301\*\*** | **-0.247\*\*** | -0.049 | **-0.141\*** | **-0.220\*\*** | -0.063 | -0.063 | -0.063 |
| mTCNS sensory tests | **-0.375\*\*** | **-0.326\*\*** | **-0.357\*\*** | **-0.294\*\*** | **-0.162\*** | **-0.232\*\*** | **-0.303\*\*** | **-0.324\*\*** | **-0.182\*\*** | **-0.182\*** | **-0.182\*** |
| mTCNS sum score | **-0.439\*\*** | **-0.416\*\*** | **-0.458\*\*** | **-0.359\*\*** | **-0.245\*\*** | **-0.150\*** | **-0.253\*\*** | **-0.298\*\*** | **-0.145\*** | **-0.145\*\*** | **-0.145\*\*** |
| ODSS sum score | **-0.405\*\*** | **-0.307\*\*** | **-0.375\*\*** | **-0.312\*\*** | **-0.208\*\*** | -0.099 | **-0.153\*** | **-0.226\*\*** | -0.017 | -0.017 | -0.017 |

Spearman correlation

\*P<0.05

\*\*P<0.01

mMRC – modified Medical research council, ODSS - overall disability sum score, mTCNS – modified Toronto clinical neuropathy score, CDT – cold detection threshold, WDT – warm detection threshold, TSL – thermal sensory limen, CPT – cold pain threshold, HPT – heat pain threshold, PPT – pressure pain threshold, MPT – mechanical pain threshold, MPS – mechanical pain sensitivity, WUR – wind-up ratio, MDT – mechanical detection threshold, VDT – vibration detection threshold, DMA – dynamic mechanical allodynia, PHS – paradoxical heat sensation

**Supplementary table 6.** Nerve conduction studies

| **Nerve conduction parameters** |  | **Moderate/severe pain(NRS ≥ 4)** | **Mild pain (NRS 1-3)** | **Painless (NRS 0)** | **P** |
| --- | --- | --- | --- | --- | --- |
|  | N = 106 | N = 52 | N = 74 |  |
| N. suralis SNAP [µV] |  | 3.0 (1.3; 10.0) | 3.4 (1.1; 15.1) | 3.4 (1.5; 12.6) | 0.566 |
| N. suralis SNAP  | Abnormal (< 4 µV) | 79 (74.5%) | 37 (71.2%) | 47 (63.5%) | 0.279 |
| N. suralis SCV [m/s] |  | 43.0 (35.9; 54.5) | 43.8 (32.2; 52.3) | 43.6 (35.2; 52.1) | 0.892 |
| N. suralis SCV  | Abnormal (<37 m/s) | 8 (9.6%) | 6 (14.6%) | 5 (7.7%) | 0.574 |
| N.radialis superficialis SNAP [µV] |  | 4.6 (1.9; 12.1) | 5.9 (1.4; 11.7) | 4.8 (1.9; 12.3) | 0.284 |
| N.radialis superficialis SCV [m/s]  |  | 48.0 (40.2; 57.0) | 48.0 (35.4; 61.9) | 48.9 (37.8; 56.8) | 0.734 |
| N. tibialis CMAP [mV] |  | 4.2 (0.3; 14.0) | 5.6 (0.3; 14.0) | 4.8 (0.8; 14.7) | 0.293 |
| N. tibialis CMAP  | Abnormal (<2,5 mV) | 41 (38.7%) | 14 (26.9%) | 18 (24.3%) | 0.097 |
| N. tibialis DML [ms] |  | 4.4 (3.5; 6.3) | 4.5 (3.8; 6.2) | 4.4 (3.4; 6.3) | 0.070 |
| N. tibialis DML  | Abnormal (>5.0 ms) | 36 (34.0%) | 18 (34.6%) | 15 (20.3%) | 0.097 |
| N tibialis MCV [m/s] |  | 40.9 (33.1; 49.7) | 40.6 (32.7; 48.7) | 41.1 (32.4; 48.7) | 0.994 |
| N tibialis MCV  | Abnormal (<40 m/s) | 44 (44.4%) | 24 (47.1%) | 30 (40.5%) | 0.766 |
| N. tibialis F-wave: latency [ms] |  | 58.9 (46.9; 71.3) | 59.2 (47.2; 70.7) | 58.5 (49.4; 69.6) | 0.916 |
| N. tibialis F-wave: latency  | Abnormal | 82 (77.4%) | 34 (65.4%) | 47 (63.5%) | 0.090 |
| N. peroneus CMAP [mV] |  | 2.3 (0.7; 7.3) | 2.6 (0.3; 5.4) | 2.7 (0.4; 7.7) | 0.943 |
| N. peroneus CMAP  | Abnormal (<4.0 mV) | 83 (79.0%) | 41 (78.8%) | 53 (71.6%) | 0.469 |
| N. peroneus DML [ms] |  | 4.7 (3.6; 6.5) | 5.1 (3.8; 6.7) | 5.0 (4.0; 7.0) | 0.057 |
| N. peroneus DML  | Abnormal (>5.0 ms) | 49 (46.7%) | 27 (51.9%) | 36 (48.6%) | 0.835 |
| N. peroneus MCV [m/s] |  | 41.5 (34.3; 49.3) | 40.0 (29.3; 49.9) | 42.2 (31.3; 50.3) | 0.223 |
| N. peroneus MCV  | Abnormal (<40 m/s) | 35 (37.2%) | 24 (47.1%) | 23 (31.5%) | 0.220 |
| N. peroneus F-wave: latency [ms] |  | 55.9 (46.5; 69.3) | 55.9 (45.7; 67.8) | 55.8 (47.4; 64.4) | 0.955 |
| N. peroneus F-wave: latency  | Abnormal | 71 (71.0%) | 30 (57.7%) | 44 (62.0%) | 0.211 |
| N. ulnaris distal amplitude [mV] |  | 9.0 (4.7; 12.5) | 9.8 (6.4; 12.9) | 9.5 (5.3; 13.7) | 0.103 |
| N. ulnaris distal amplitude  | Abnormal (<4.0 mV) | 5 (4.7%) | 0 (0.0%) | 3 (4.1%) | 0.296 |
| N. ulnaris DML [ms] |  | 3.3 (2.7; 4.2) | 3.4 (2.7; 4.0) | 3.3 (2.8; 4.2) | 0.679 |
| N. ulnaris DML  | Abnormal (>3.4 ms) | 43 (40.6%) | 23 (44.2%) | 30 (41.1%) | 0.925 |
| N. ulnaris MCV [m/s] |  | 54.5 (46.7; 64.7) | 55.8 (44.5; 65.0) | 55.4 (44.3; 64.3) | 0.779 |
| N. ulnaris MCV  | Abnormal (<45 m/s) | 3 (2.8%) | 3 (5.8%) | 4 (5.5%) | 0.536 |
| N. ulnaris F-wave: latency [ms] |  | 29.3 (25.4; 35.4) | 29.9 (25.0; 34.5) | 30.1 (25.6; 36.7) | 0.685 |
| N. ulnaris F-wave: latency | Abnormal | 37 (34.9%) | 17 (32.7%) | 22 (30.1%) | 0.801 |
| Nerve conduction study | Abnormal | 99 (93.4%) | 52 (100.0%) | 74 (100.0%) | **0.021** |

Continuous parameters are summarized as median (5th–95th percentile range). Categorical parameters are expressed as absolute and relative frequencies.
P-value represents the comparison of patients with different levels of pain (Kruskal-Wallis test for continuous variables and Fisher’s exact test for categorical variables); post-hoc tests: a, b, c – same letters marking values of categories within given row denote mutually statistically not different groups.

NRS – numerical rating scale, SNAP – sensory nerve action potential, µV – microvolts, SCV – sensory conduction velocity, m/s – meters per second, CMAP – compound muscle action potentials, dML – distal motor latency, MCV – motor conduction velocity

**Supplementary** **Table 7.** Comparison of patient characteristics according to level of DSPN pain (DSPN with moderate/severe pain (NRS >4) vs. painless DSPN) in groups with balanced distribution of mTCNS sensory test score by propensity score matching

| **Parameters** |  | **Moderate/severe pain(NRS ≥ 4)** | **Painless (NRS = 0)** | **P** |
| --- | --- | --- | --- | --- |
|  | N = 48 | N = 48 |  |
| Age (years) |  | 65.1 (41.0; 79.4) | 63.7 (28.9; 80.1) | 0.593 |
| Gender | Women | 26 (54.2 %) | 9 (18.8 %) | **0.001** |
|  | Men | 22 (45.8 %) | 39 (81.3 %) |
| Type of diabetes | Type 1 | 10 (20.8 %) | 19 (39.6 %) | 0.074 |
|  | Type 2 | 38 (79.2 %) | 29 (60.4 %) |
| Duration of diabetes (years) |  | 11.0 (1.0; 29.0) | 15.0 (1.0; 27.0) | 0.099 |
| mTCNS - symptom score | Score of symptoms (0-18) | 8.4 ± 4.4 | 0.9 ± 2.1 | **< 0.001** |
| mTCNS - sensory test score | Score of sensory tests (0-15) | 4.3 ± 3.9 | 3.3 ± 3.8 | 0.112 |
| mTCNS sum-score (0-33) | Sum score (0-33) | 12.5 ± 6.9 | 4.2 ± 5.0 | **< 0.001** |
| PCS sum-score |  | 15.9 ± 9.9 | 2.1 ± 5.1 | **< 0.001** |
| Other chronic pain(NRS >= 4, > 3 months) | No | 19 (39.6 %) | 26 (54.2 %) | 0.220 |
| Yes | 29 (60.4 %) | 22 (45.8 %) |

Continuous parameters are summarized as median (5th–95th percentile range) or mean ± standard deviation (SD). Categorical parameters are expressed as absolute and relative frequencies.
P-value represents the comparison of patients with different levels of pain (Mann-Whitney U test for continuous variables and Fisher’s exact test for categorical variables).

DSPN – diabetic symmetrical sensory-motor polyneuropathy, NRS – numerical rating scale, mTCNS – modified Toronto clinical rating scale