



Treatment outcome in carpal tunnel syndrome: Does distribution of sensory symptoms matter?



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ABSTRACT

Background: Patients with complaints of carpal tunnel syndrome (CTS) with signs and symptoms not exclusively confined to the median nerve territory, but otherwise fulfilling the clinical criteria may erroneously be withheld from therapy.

Methods: One hundred and twenty one patients who fulfilled the clinical criteria for the diagnosis of CTS with signs and symptoms restricted to the median nerve territory (group A) and 91 patients without this restriction (group B) were included in a prospective cohort study. All patients fulfilled electrodiagnostic criteria of CTS. Outcome was determined after 7 to 9 months by means of Symptom Severity Score (SSS) and Functional Status Score (FSS) according to Levine and a patient satisfaction questionnaire.

Results: Response rates were 81.8% (group A) and 82.4% (group B). All patients in group B had sensory symptoms involving digit 5. There were no significant differences in improvement of SSS, FSS and patient satisfaction scores between groups after treatment.

Conclusion: CTS patients with characteristic sensory signs and symptoms not exclusively restricted to the median nerve innervated area should be treated in the same manner as patients with CTS symptoms restricted to the median nerve innervated area and should therefore not be withheld from surgical treatment.

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1. Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy [1,2]. Diagnosis is based on clinical signs and symptoms that typically show existence of nocturnal acroparesthesia in the area innervated by the median nerve. If CTS signs and symptoms are typical, these may easily and reliably lead to a definite diagnosis on clinical grounds exclusively. However, it is well known that a substantial number of CTS patients report signs and symptoms in the whole hand, which may eventually lead to uncertainty of the diagnosis of CTS. This may discourage the performance of an operative decompression of the median nerve or other types of intervention. Contrary to most other surgeons in the Netherlands, some surgeons do not require electrodiagnostic confirmation prior to operation in the case of a definite clinical diagnosis of CTS [3,4]. However, in patients with complaints outside the anatomical median nerve territory, hesitation may arise even if they fulfill electrodiagnostic criteria for CTS. As a consequence, this may exclude patients from proven effective operative therapy. The present study was conducted to determine whether CTS patients with signs and

symptoms not solely confined to the median nerve innervated area, which in addition were electrodiagnostically confirmed, benefit from treatment to the same extent as patients who do fit classic clinical CTS criteria.

2. Materials and methods

2.1. Patients

In this prospective cohort study, patients with complaints suggestive of CTS were referred to our outpatient clinic by their general practitioner. Patients were included if they fulfilled clinical criteria for CTS as well as electrodiagnostic criteria. Patients were divided into two groups according to strict clinical criteria having a typical, 'classic' CTS (group A, CCTS) or less typical, 'non-classic' CTS (group B, NCTS). Criteria were adapted from Witt et al., who distinguished patients with 'definite' and 'possible' CTS [5]. Patients with paresthesia and/or pain in the median nerve innervated area and 2 or more major criteria (Table 1) were defined as having classic CTS. Patients with paresthesia and/or pain in the median nerve innervated area and the fifth finger and 1 major or 2 minor criteria were categorized as non-classic CTS. Involvement of the fifth finger was indicated by history and confirmed in the Katz diagram [6]. Patients with sensory symptoms outside the classic

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Table 1
Major and minor criteria in diagnosing CTS.

<i>Major criteria</i>
1) Nocturnal paresthesia
2) Positive Flick sign
3) Aggravation by driving, holding a book or telephone
<i>Minor criteria</i>
1) Subjective weakness
2) Clumsiness of the hand
3) Positive Tinel or Phalen sign

Flick sign: paresthesia relieved by shaking the hand or holding it in a dependent position.

median nerve innervated area were thus classified as 'non-classic' CTS patients. When both hands were affected, the hand with the most severe complaints was included. Other exclusion criteria were age under 18, a significant language barrier, mental disorder, clinical signs of polyneuropathy, a history of wrist trauma or surgery, pregnancy, severe thenar atrophy, alcoholism, arthritis or arthrosis of the wrist, known diabetes mellitus, rheumatoid arthritis or thyroid dysfunction, HNLP (Hereditary Neuropathy with Liability to Pressure Palsies), other known causes of the complaints and a bifid median nerve on ultrasound imaging. Patients filled in a Symptom Severity Score (SSS) and Functional Status Score (FSS) according to Levine [7] before treatment and 7 (90% of the scores) or ultimately 9 months (some responded after a second call) after treatment. This is a validated patient-reported outcome measure for studies involving CTS [8]. Patients also received a multiple choice questionnaire to indicate their satisfaction with treatment result. The study was approved by the regional medical ethics committee. Written informed consent was obtained from each patient prior to inclusion. Electrodiagnostic reference values were collected in the same laboratory by examining 47 asymptomatic volunteers.

2.2. Clinical testing

All patients were clinically examined by experienced examiners. A complete neurological examination was performed. Tinel and Phalen signs were tested, and sensory examination was performed with a monofilament (10 g) and two-point discrimination. Motor function was tested according to MRC (Medical Research Council) as well as grip strength with a Martin vigorimeter [9]. Thenar atrophy was classified as absent, mild or severe. Patients with severe thenar atrophy were excluded from this study.

2.3. Electrodiagnostic testing

All patients underwent electrodiagnostic tests performed with standardized techniques according to the AANEM summary statement [10] and by an experienced neurophysiologist who was blinded for clinical data. Electrodiagnostic studies were performed on the same day for each subject. All tests were performed with a Viking myograph type IV (Nicolet Biomedical, Madison, WI, USA). We used earlier developed reference values that were obtained in the same laboratory by means of the same procedure as applied in the present study. Skin temperature was maintained at 31 °C or more during the test procedure. It was measured at the recording site by means of an infrared thermometer (62 Mini IR thermometer, Fluke Biomedical, Cleveland OH, USA) before and after performing the tests. Three different kinds of sensory nerve conduction studies were performed in each individual, as well as one motor nerve conduction study. Difference between onset latencies of the median nerve and ipsilateral ulnar nerve were recorded from the fourth finger over the same distance. Conduction velocity of the ulnar nerve should be at least 50 m/s. A difference in onset latency of more than 0.4 ms or the absence of the median sensory nerve action potential (SNAP) is considered to be consistent with CTS. SNAPs from median and radial nerves were recorded from the first finger after stimulation of the

median and radial nerve at the wrist, with the same conduction distance. A difference in onset latency of more than 0.6 ms or absence of the median SNAP is considered to be consistent with CTS. Segmental sensory conduction studies across the wrist recorded SNAPs from digits 2 and 3 after stimulation of the median nerve at the palm and at the wrist. Absence of SNAPs or a difference in conduction velocity between the palm-to-digit and palm-to-wrist greater than 10 m/s is considered to be consistent with CTS. Median motor nerve conduction studies were performed by stimulating the median nerve at the wrist and at the cubital fossa. A distal motor latency of more than 4.0 ms is considered to be consistent with CTS. For an EDX result to be consistent with CTS, at least 2 tests had to be abnormal.

2.4. Statistical analysis

Data concerning clinical variables and nerve conduction studies were processed using Microsoft Office Excel and Access and all statistical analyses were performed using SPSS Statistics 17.0. Comparison between patients and controls was performed with a t-test for continuous variables or a χ^2 test for categorical variables, as appropriate, and, in case of non-nominal distribution, the Mann–Whitney U test. $P < 0.05$ was considered to be statistically significant.

2.5. Treatment

Patients who fulfilled clinical criteria for group A or B and who had EDX corresponding with CTS criteria were informed about the study objectives. We discussed the different treatment options with patients: conservative treatment with a wrist splint during the night, local corticosteroid injection (methylprednisolone 40 mg) at the carpal tunnel or surgical decompression of the median nerve at the carpal tunnel. Patients were informed on treatment options according to the Dutch Consensus Guideline [11] for diagnosis and treatment of carpal tunnel syndrome. They were explained that on the long-term, surgical treatment could be expected to have the best treatment results [11–14]. Surgery was performed by experienced neurosurgeons under local anesthesia with an open surgical procedure.

2.6. Follow-up

The neurosurgeon performed the follow-up for removal of stitches and control of wound healing of the surgically treated patients 1 and 4 weeks after the operation. Six months after treatment all patients were sent the Symptom Severity Score and Functional Severity Score according to Levine [7]. We also sent a multiple choice questionnaire in which patients were asked to indicate the effect of treatment (no complaints, rarely any, occasional complaints, often, situation unchanged or deterioration). For the purpose of statistical analysis, we divided these options into four categories: 1) full recovery, 2) partial recovery, 3) no recovery at all, and 4) deterioration.

3. Results

3.1. Patients

Two hundred and twenty eight patients who initially met the inclusion criteria were selected: 131 patients with clinical 'classic' CTS (group A) and 97 patients with clinical 'non-classic' CTS (group B). Sixteen patients with a bifid median nerve on US were excluded, 10 in group A and 6 in group B. Clinical features of the patients are presented in Table 2. In group B, all patients presented with sensory symptoms or signs in median nerve sensory territory and in digit 5. There was a significantly higher percentage of women in group B (72.7% vs. 86.8%, $P = 0.013$). No statistically significant differences were found in age, duration of symptoms, BMI, weakness or atrophy of the abductor pollicis brevis muscle, sensory loss or occurrence of Tinel or Phalen

Table 2
Clinical features of CTS patients.

	N ^a	A N = 121	N ^a	B N = 91	P
Sex female	121	88 (72.7%)	91	79 (86.8%)	0.013
Age (mean ± SD, years)	121	50.59 ± 13.21	91	52.20 ± 13.78	n.s.
Range	121	18–86	91	23–85	
Median duration of symptoms (months)	120	12.00	91	12.00	
Mean duration of symptoms (months)	120	34.78 ± 55.31	91	37.68 ± 57.93	n.s.
Wrist included right	121	67 (55.4%)	91	61 (67.0%)	n.s.
BMI	121	27.63 ± 5.08	90	27.52 ± 4.78	n.s.
Atrophy of abductor pollicis brevis muscle	116	33 (28.4%)	90	27 (30.0%)	n.s.
Weakness					
APB muscle	119	41 (34.5%)	89	25 (28.1%)	n.s.
Opponens pollicis muscle	119	7 (5.9%)	89	3 (3.4%)	n.s.
Disturbed sensibility					
Two-point discrimination	120	78 (65.0%)	91	55 (60.4%)	n.s.
Monofilament	119	49 (41.2%)	89	43 (48.3%)	n.s.
Phalen positive	121	91 (75.2%)	91	78 (85.7%)	n.s.
Tinel positive	121	78 (64.5%)	91	56 (61.5%)	n.s.

A: CTS patients with clinical signs and symptoms restricted to the median nerve innervated area.

B: CTS patients with signs and symptoms not restricted to the median nerve innervated area.

^a Numbers due to missing values.

sign between groups. Symptom Severity Score on inclusion was not significantly different between groups, and Functional Severity Score was significantly higher in group B on inclusion and follow-up. This reflects mainly the surgically treated patients, since the conservatively treated group was significantly smaller than the surgically treated group.

3.2. Electrodiagnostic tests

All patients fulfilled electrodiagnostic criteria for CTS. Details are summarized in Table 3. Nerve conduction velocity in the palm to wrist segment in digit 3 in group A ($P = 0.001$) was significantly lower than that in group B and mean onset latency difference in digit 1 was significantly lower in group B (1.26 vs. 1.45 ms, $P = 0.036$). Other EDX test results showed no significant differences between groups. Fig. 1 shows electrophysiologic severity according to Padua et al. [15] in group A versus B patients.

3.3. Outcome

In group A, 99 out of 121 patients completed a follow-up. In group B, 80 out of 91 patients returned questionnaires. See Table 4A and B for

results of SSS and FSS and Figs. 2 and 3 for distribution of outcome according to the patient satisfaction questionnaire. In the whole group SSS at follow-up was significantly higher in group B (NCTS, $P = 0.035$) as compared to group A (CCTS), but the difference between inclusion and follow-up was not. FSS was significantly higher at inclusion and at follow-up in group B patients treated with surgery ($P = 0.007$ and $P = 0.013$ respectively) compared to group A patients. No difference was seen in improvement of FSS between groups A and B at inclusion and at follow-up. Only a small number of patients were treated non-surgically. Out of all patients, 19 were treated conservatively and 153 were treated surgically. Of conservatively treated patients, only 3 received local corticosteroid injection at the carpal tunnel. Improvement in the non-surgically treated patients was significantly lower ($P = 0.000$, Mann–Whitney U). Full recovery was reported by 60.6% of patients in group A (CCTS) after 7 to 9 months of follow-up, vs. 48.0% in group B (NCTS, $P = 0.222$, Fig. 2).

4. Discussion

The diagnostic hallmarks of CTS are the symptoms reported by patients during history-taking, which may vary considerably. Classic

Table 3
Electrodiagnostic test results in CTS patients.

	N ^a	A N = 121 Mean ± SD	N ^a	B N = 91 Mean ± SD	P
Digit 4 mean latency difference (ms)	60	1.70 ± 0.78	51	1.44 ± 0.69	n.s.
Unrecordable	61	50.4%	40	44.0%	n.s.
Digit 1 mean latency difference (ms)	81	1.45 ± 0.60	71	1.26 ± 0.54	0.036
Unrecordable	39	32.2%	19	20.9%	n.s.
Digit 2 mean NCV dig 2–palm (m/s)	98	47.50 ± 7.81	78	48.74 ± 7.69	n.s.
Unrecordable	22	18.2%	13	14.3%	n.s.
Mean NCV palm–wrist (m/s)	90	30.36 ± 7.32	77	32.46 ± 7.68	n.s.
Digit 3 mean NCV dig 3–palm (m/s)	96	46.29 ± 6.72	75	47.21 ± 7.45	n.s.
Unrecordable	24	19.8%	16	17.6%	n.s.
Mean NCV palm–wrist (m/s)	89	29.00 ± 7.44	73	32.86 ± 7.22	0.001
DML mean (ms)	116	5.69 ± 1.79	91	5.27 ± 1.59	n.s.
Median CMAP APB unrecordable	5	4.1%	0	0	n.s.

A: CTS patients with clinical signs and symptoms restricted to the median nerve innervated area.

B: CTS patients with signs and symptoms not restricted to the median nerve innervated area.

SNAP: sensory nerve action potential.

NCV: nerve conduction velocity.

DML: distal motor latency.

CMAP: compound muscle action potential.

APB: abductor pollicis brevis muscle.

^a Number of patients may vary due to missing values or unrecordable SNAPs or CMAPs.

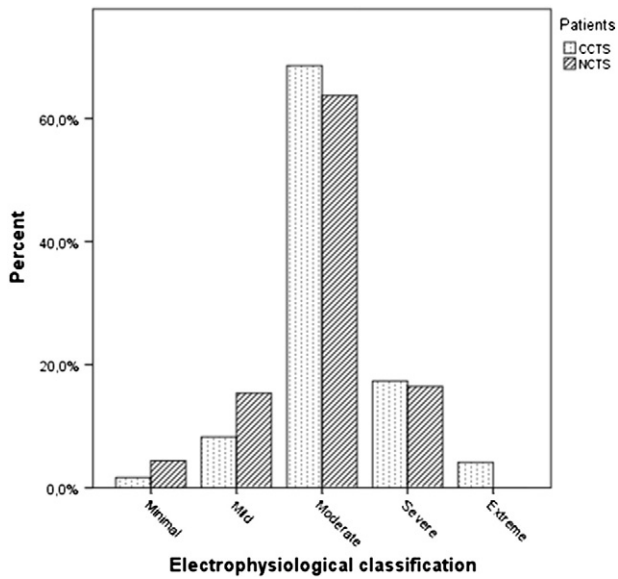


Fig. 1. Groups A and B versus electrophysiological severity according to Padua et al. [15].

symptoms of CTS typically include sensory symptoms in the territory of the median nerve. However, it is generally known among clinicians that patients often report symptoms outside the median nerve territory. Typical CTS complaints like nocturnal paresthesia or aggravation by driving or holding a telephone were often also present in group B in the present study. However, because of our strict clinical criteria, these patients were categorized as having ‘non-classic’ CTS, because of the presence of symptoms in digit 5. Therefore, in the present study, ‘non-classic’ CTS corresponds with CTS patients with sensory symptoms in median nerve distribution and digit 5. In most cases patients undergo

Table 4
Outcome SSS and FSS.

	N ^a	A Mean ± SD	N ^a	B Mean ± SD	P
A: Symptom Severity Score					
Surgery					
At inclusion	89	2.87 ± 0.65	64	3.08 ± 0.71	n.s.
At follow-up	89	1.50 ± 0.69	64	1.71 ± 0.77	n.s.
Difference	89	1.36 ± 0.82	64	1.37 ± 0.98	n.s.
Conservative					
At inclusion	8	2.41 ± 0.80	11	2.65 ± 0.69	n.s.
At follow-up	8	2.14 ± 0.83	11	2.31 ± 0.83	n.s.
Difference	8	0.28 ± 0.38	11	0.35 ± 0.93	n.s.
Total					
At inclusion	97	2.83 ± 0.67	75	3.02 ± 0.72	n.s.
At follow-up	97	1.55 ± 0.72	75	1.80 ± 0.80	0.035
Difference	97	1.27 ± 0.85	75	1.22 ± 1.03	n.s.
B: Functional Severity Score					
Surgery					
At inclusion	86	2.16 ± 0.70	61	2.48 ± 0.68	0.007
At follow-up	86	1.47 ± 0.64	61	1.78 ± 0.77	0.013
Difference	86	0.68 ± 0.84	61	0.70 ± 0.93	n.s.
Conservative					
At inclusion	8	2.00 ± 0.69	11	2.19 ± 0.79	n.s.
At follow-up	8	1.65 ± 0.65	11	2.03 ± 0.86	n.s.
Difference	8	0.35 ± 0.41	11	0.16 ± 0.63	n.s.
Total					
At inclusion	94	2.15 ± 0.70	72	2.43 ± 0.70	0.009
At follow-up	94	1.49 ± 0.64	72	1.82 ± 0.79	0.005
Difference	94	0.66 ± 0.82	72	0.62 ± 0.91	n.s.

A: CTS patients with clinical signs and symptoms restricted to the median nerve innervated area.

B: CTS patients with signs and symptoms not restricted to the median nerve innervated area.

^a Number of patients varies due to missing values.

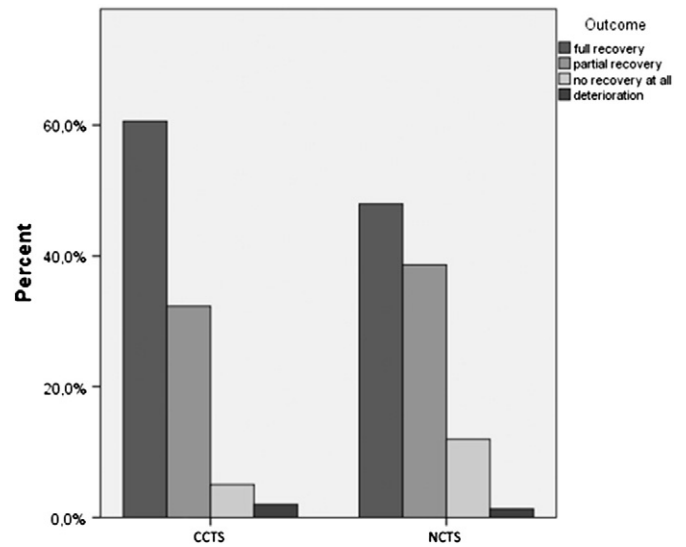


Fig. 2. Outcome all patients. CCTS: group A, CTS patients with clinical signs and symptoms restricted to the median nerve innervated area. N = 99, 22 lost to follow-up, response rate: 81.8%. NCTS: group B, CTS patients with signs and symptoms not restricted to the median nerve innervated area. N = 75, 16 lost to follow-up, response rate: 82.4%.

EDX to confirm the diagnosis, however there is no generally accepted gold standard. Studies of CTS patients frequently mention symptoms involving ulnar nerve territory or whole hand distributions of complaints [16–18]. In the study by Clark et al. [17], sensory disturbance in the little finger was mentioned in 39% of patients, and 11% mentioned occurrence of pain in this finger. Stevens et al. [16] found that in a group of 100 electrodiagnostically confirmed CTS patients, paresthesia of the little finger was present in 56.6% of hands. In 2.5% of hands, the little finger was even the most affected finger in this study. This was not the case in the population in the current study. Gupta et al. found that symptoms confined to the median nerve distribution only were present in 33% of affected hands, while in 40% of hands, sensory symptoms were present in the whole hand [19]. Improvement after therapeutic intervention may indirectly be interpreted as a confirmation of the clinical diagnosis. In the present study, no significant difference in outcome was found in patients with ‘classic’ and ‘non-classic’

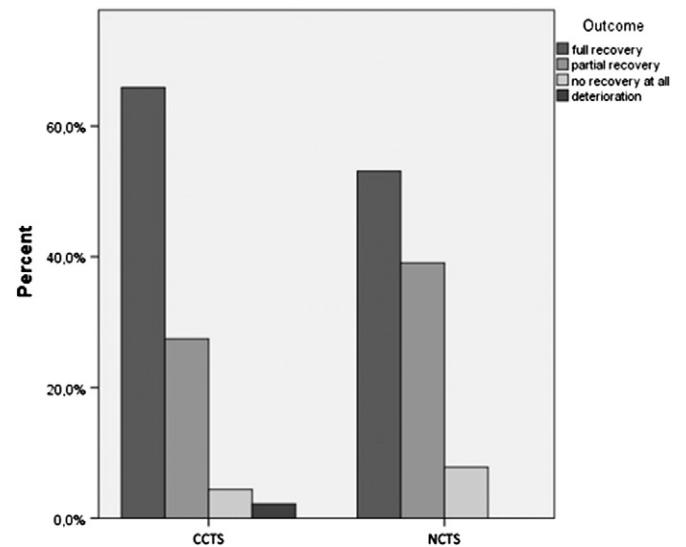


Fig. 3. Outcome of patients' surgical treatment. CCTS: group A: CTS patients with clinical signs and symptoms restricted to the median nerve innervated area. N = 91. NCTS: group B: CTS patients with signs and symptoms not restricted to the median nerve innervated area. N = 64.

sensory distribution of complaints after 7 to 9 months of follow-up. EDX was not significantly different between groups, except for 2 out of 5 tests, which showed a lower nerve conduction velocity across the carpal tunnel in digit 3 and higher latency difference between median and radial SNAPs in digit 1 in patients with ‘classic’ CTS. This suggests that median nerve dysfunction is more severe in patients with CTS symptoms restricted to the median nerve area, in accordance with Caliandro et al., who found that the likelihood of median nerve distribution increases with more severe neurophysiologic abnormalities [18].

The mechanisms that cause extra-median spread of symptoms in CTS patients are not known and are subject to discussion. Some authors suggest that abnormal activation of cortical sensory areas beyond the median nerve area can be responsible for GLOVE distribution [18,20,21]. Zanette et al. found that extra-median spread of sensory symptoms is associated with higher levels of pain and paresthesia [20]. Contrary to our results, they found significantly higher scores on SSS (numbness and tingling sensations) in CTS patients with a glove distribution in comparison to a median nerve distribution, and no significant difference in FSS between groups. In the present study, FSS at inclusion and at follow-up was significantly higher in patients with symptoms extending the median nerve innervated area. Remarkably, in the study by Zanette, tactile hypesthesia was significantly more present in patients with median nerve distribution. They hypothesized that central nervous system mechanisms of plasticity may be an explanation for the spread of symptoms in CTS. Others found that enlargement of cortical hand presentation is correlated with the inability of patients to correctly identify the involved hand districts [21]. Not all patients in the present study had objective sensory loss by means of decreased two-point discrimination and/or monofilament testing. Some patients reporting sensory disturbances in digit 5 had no sensory loss in this digit on examination. This could reflect the result of a central process rather than a peripheral one.

Another possible explanation for extra-median spread of sensory symptoms is involvement of ulnar nerve fibers. Many studies concern ulnar nerve conduction in patients with CTS without finding a clear explanation for the presence of minimal changes in ulnar nerve conduction in CTS patients [22–23]. Ginanneschi found significant changes in ulnar nerve conduction in CTS, even in the early stages [23]. They hypothesize that damage to ulnar fibers by compression in Guyon's canal as a consequence of high pressure in the carpal tunnel is the cause. In the present study, all patients in group B had sensory symptoms in the median nerve territory and digit 5. Patients with symptoms primarily in ulnar nerve territory or symptoms suspected for ulnaropathy were not included. This is also supported by the fact that no significant differences were found in outcome measures between these groups. It would be interesting to know whether patients with the clinical diagnosis of CTS according to our criteria in groups A and B benefit from operative therapy, regardless of the outcome of electrodiagnostic test results. As in the Netherlands most surgeons require preoperative electrodiagnostic confirmation, we chose to include only CTS patients who fulfilled electrodiagnostic criteria as well. We found no statistically significant differences in outcome after surgical or conservative treatment between both patient groups. This observation means that in daily clinical practice, CTS patients with sensory symptoms also involving the fifth finger have equal chances of positive results of treatment as patients with classic median nerve distribution. As was expected, the majority of patients who underwent operative treatment had full or partial recovery of complaints. Comparison of surgical and non-surgical treatment of CTS was not the main subject of this study. Patients treated conservatively showed a significantly smaller improvement on follow-up than surgically treated patients, however, the group of patients that was treated conservatively was very small. Our study has some limitations. We included patients suspected to have CTS referred by their general practitioner, therefore selection bias cannot be excluded. However, this reflects daily clinical practice in the Netherlands, where patients can only visit an outpatient

clinic by referral by their general practitioner. Patients with polyneuropathy or diabetes mellitus, more likely to present with atypical CTS complaints, were excluded from this study. More patients were treated surgically in group A than in group B. There might be a bias in the fact that we made a distinction between the groups and presented to the patients the results from the literature for surgery in ‘classic’ CTS; maybe some patients declined from surgery for that reason, which might explain the difference. In addition, patients were allowed to make their own decision on the treatment option, which might give some bias, however no statistically significant differences occurred between the groups of patients studied in this regard. Follow-up was done with a questionnaire sent by mail, which inherently means that response rate was not maximal. However, we tried to increase response rate by telephoning patients who did not respond initially. With response rates over 80% we managed to restrict this limitation. As a consequence, follow-up varies between 7 and 9 months after treatment. To compare the effect of surgical and non-surgical treatment in CTS patients with sensory symptoms restricted to the median nerve area and CTS patients without this restriction, a randomized controlled study is needed.

In conclusion, no statistically significant differences in outcome were found between CTS patients with symptoms confined to the median nerve territory and patients with extramedian spread of complaints who had been clinically defined and electrodiagnostically confirmed as CTS patients. Patients with characteristic CTS complaints, but sensory symptoms involving digit 5, seem not atypical at all and represent a significant amount of CTS patients. Therefore clinically defined and electrodiagnostically confirmed CTS patients with extramedian spread of symptoms should not be withheld from surgical treatment. Our suggestion is to refrain from terms as classic or non-classic CTS.

Disclosure

There is no conflict of interests.

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