Peripheral nerve damage : diagnosis and prediction of recovery

Datema, M.

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Sensation recovers less in the old than in the young patient after carpal tunnel release

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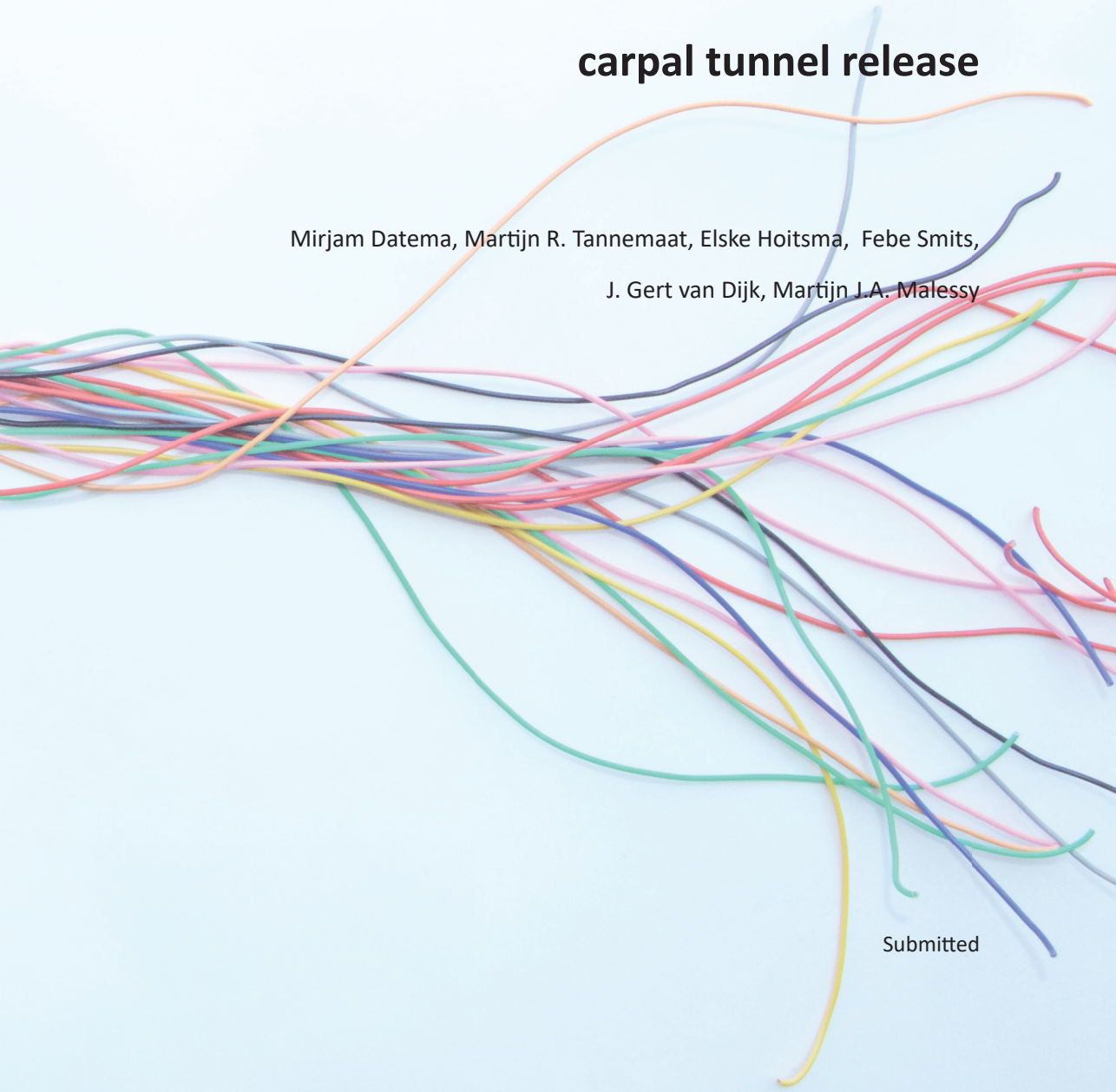

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ABSTRACT

Background: An increase in the proportion of the elderly among patients with an indication for carpal tunnel release (CTR) is to be expected with ageing of the population. This increases the importance of reports on the outcome of CTR in older patients. This could be different from younger patients for several reasons, such as age-related decrease of function and regenerative capacity of nerves.

Objective: To examine differences in symptom profile between older and younger patients with CTS before and after CTR.

Methods: Prospective study in a general hospital with data collection at baseline, three and 12 months after CTR on three outcome measures: 1) CTS symptoms (Boston Carpal Tunnel Questionnaire -BCTQ), 2) palmar pain and 3) patient satisfaction. We compared nerve conduction studies, the individual items of the BCTQ before and after CTR, and the other outcome parameters, between patients aged <70 and ≥70 years.

Results: We included 227 patients (75 patients ≥70). Older patients had more severe NCS abnormalities than younger patients ($p<0.001$). Before CTR, the symptom profile did not differ between the age groups, but one year after CTR the older group exhibited more residual numbness and paraesthesiae ($p<0.001$). Yet, patient satisfaction and the occurrence of postoperative palmar pain did not differ between the age groups.

Conclusion: One year after CTR, older patients reported more residual numbness and paraesthesiae than younger patients. However, we feel that older patients with CTS should be encouraged to undergo CTR just as much as younger patients, since they did not differ on reported satisfaction.

INTRODUCTION

Carpal tunnel syndrome (CTS) was generally described as a disorder typically occurring in middle-aged women. [1] A recent review from New Zealand however, found that the highest incidence of CTS concerned those who were 70-79 years of age.[2] The annual rate of CTS surgery, i.e. carpal tunnel release (CTR), in the United States increased remarkably in the previous decade in older patients. [3] An increase in the proportion of the elderly among patients with an indication for CTR is to be expected with ageing of the population. This increases the importance of reports on the outcome of CTR in older patients, but these were somewhat contradictory. Some studies reported less patient satisfaction or less recovery of symptoms and function in patients older than either 60 or 55 years compared with younger patients.[4,5] Most studies reported no age-related difference in outcome at all when comparing patients over and under age 70 or 80 years [6-9] and most authors conclude that older patients benefited from CTR, so CTR should not be denied based on age. [4,6,8-12] However, there are clinical differences between younger and older patients with CTS. Firstly, nerve conduction abnormalities occurred more often and were more severe in the elderly. [7,13,14] The rate of thenar wasting and weakness was higher in the elderly.[7,9,14,15] Secondly, the prevalence of comorbidity generally increases with age; conditions that affect joints or nerves may complicate CTS either by contributing to its severity (e.g through swelling) or by causing symptoms similar to those of CTS (eg, pain, paraesthesiae) Thirdly, the age-related decrease in functions of the peripheral nervous system may affect the perception of CTS symptoms in older patients (e.g., decreased sensibility).[16-18] Finally, the rate and magnitude of nerve regeneration are reduced with increasing age, which is likely to affect recovery of function after CTR.[17,19-21]

We previously performed a prospective study on the outcome of CTS.[22] This included age-related clinical differences before and after CTR. Multivariable analyses from this study had shown no direct relation between age and outcome of CTR, defined as the total score on the Boston Carpal Tunnel Questionnaire (BCTQ), patient satisfaction and the occurrence of palmar pain.[22] In this paper, we focussed on differences in clinical features and comorbidity between patients with CTS ≥70 years and <70 years, before and after surgery. Major complaints of patients with CTS for which they seek treatment are tingling sensations and numbness, so we were interested in the outcome of surgery in elderly, specifically related to these complaints.

METHODS

This study was part of a large prospective observational study in patients with CTS in the setting of the Alrijne hospital in Leiden, the Netherlands.[22] The study was approved by the medical ethics committee of Leiden University Medical Centre. All participants provided written informed consent. In short, all adult patients who underwent CTR from March 2012 to July 2014 were eligible. Baseline variables were sex, age, the presence of diabetes mellitus (assessed through the use of antidiabetic medication), the presence of joint disorders (arthritis or arthrosis as reported by patients), and alcohol intake (expressed in number of glasses per week). Patients filled out the first part of the BCTQ within two weeks prior to surgery, three months post-surgery with a two week margin and one year

post-surgery with a four week margin. The BCTQ is a validated questionnaire that includes 11 questions concerning severity, frequency and duration of pain and tingling at night and daytime, numbness and loss of dexterity.[23-25] Each question provides five response choices, from 1 (no symptoms) to 5 (most severe/often); the mean of 11 responses is calculated as the BCTQ score, ranging from 1 to 5. See appendix for the complete questionnaire. In addition, patients answered questionnaires on the presence and severity of pain at the scar and/or the proximal palm, resulting in a palmar pain score ranging from 0-9. (for details see Datema et al 2017[22]) Finally, to determine whether patients were satisfied with the results of surgery, we asked whether their symptoms had been relieved on a seven-point scale: 1) completely resolved, 2) improved considerably, 3) improved somewhat, 4) no change, 5) worsened somewhat, 6) worsened considerably and 7) symptoms have become much worse.

Nerve conduction studies (NCS) were performed preoperatively in all patients and comprised motor and sensory nerve conduction tests according to the CTS guidelines of the Dutch Society of Neurology.[26] Skin temperature had to be at least 30 °C. Open CTR was performed by one of three experienced neurosurgeons applying the same technique under local anaesthesia with xylocaine and epinephrine.[27]

Statistical analysis

Patients were considered 'older' from age 70 or older and patients <70 years were named 'younger'. Baseline data and outcome after one year were compared between older and younger patients with chi-square test for categorical data, Student's t-test for normally distributed continuous data and the Mann-Whitney U-test for not-normally distributed continuous data. Data from the assessment three months after surgery were not analysed as we previously showed that the outcome of CTR continued to improve from three months to one year post surgery.[22] We analysed a possible correlation between the sensory nerve conduction velocity (CV) of the ulnar nerve and age, and between the CV of median nerve and age, to see if we should correct for an age-related decline in CV. As this proved not the case, we selected the difference between the sensory CV of the ulnar and median nerve of the wrist-finger segment on the fourth finger as a marker for the severity of NCS abnormalities.[28] We formed four NCS severity categories: 1) CV difference <10 m/s, 2) CV difference ≥10 and <20 m/s, 3) CV difference ≥20 m/s, 4) absent sensory nerve action potential (SNAP) of the median nerve, but present ulnar SNAP. We also noted cases with absent median and ulnar SNAPs. The use of these categories enabled us to include cases with absent median nerve SNAPs.

The scores for each item of the BCTQ in both age groups were compared pre- and postoperatively using the Wilcoxon signed rank test for paired data. The Bonferroni adjustment was applied to correct for multiple testing.

The Mann-Whitney U-test was used to compare the scores on the individual items of the BCTQ between the two age groups preoperatively and one year postoperatively. In addition the differences between the post- and preoperative scores were compared between the age groups, using the Mann-Whitney U-test. Again, the Bonferroni adjustment was applied to

correct for multiple testing. We did this by multiplying the p-values by 11, since this is the number of items of the BCTQ. The significance level was set at p<0.05.

RESULTS

During the inclusion period 1023 patients underwent CTR. A total of 345 patients filled in questionnaires before surgery. Of these, 227 patients filled in questionnaires before and after surgery ('participants'). The remaining 118 patients were either lost to follow-up or declined long term participation ('non-participants') The sex distribution did not differ between participants (74% women) and non-participants (67%; p=0.16). Median preoperative BCTQ score did also not differ between participants and non-participants; median score 2.7 (2.3-3.2) vs 2.7 (2.4-3.2), p = 0.62. Participants were older than non-participants: median age 58 (49-73) vs 53 years (43-61), p < 0.001.

The age of participants ranged from 23 to 90 years; 75 patients were 70 years of age or older. Table 1 shows a comparison of the baseline data between the older and younger patients. The proportion of men in the older group was twice as high as in younger patients. The absence of a measurable SNAP of the median nerve occurred almost twice as often in the older than in the younger patients, indicating far more severe NCS abnormalities in the elderly. The incidence of diabetes mellitus and joint disorders was significantly higher in the elderly. The total preoperative BCTQ score did not differ between the two age groups.

Table 1. Baseline data.

Baseline data	Younger (<70 years) n = 152	Older (≥70 years) n = 75	p-value	Missing data
Age (years)	51.8 ± 10.2	77.6 ± 5.5	n.a.	0
Male	30 (19.7%)	30 (40.0%)	**0.002**	0
Preoperative BCTQ score	2.7 ± 0.7	2.8 ± 0.7	0.353	6
Alcohol intake (glasses/week)	2 (0-6)	2 (0-10)	0.218	13
Diabetes mellitus; present	6 (4.0%)	10 (13.3%)	**0.019**	5
Joint disorder; present	16 (10.5%)	18 (24.0%)	**0.010**	2
NCS abnormality*			**<0.001**	9
CV difference <10m/s	9 (6.0%)	4 (5.3%)		
CV difference ≥10 and <20 m/s	63 (41.4%)	8 (10.7%)		
CV difference ≥20 m/s	37 (24.3%)	11 (14.7%)		
median SNAP present, ulnar SNAP absent	42 (27.6%)	41 (54.7%)		
median SNAP absent, ulnar SNAP absent	0	3 (4.0%)		

BCTQ = Boston Carpal Tunnel Questionnaire. * These percentages do not add up to 100% because of missing data (n=9). SNAP = sensory nerve action potential

One year after CTR, the total BCTQ differed significantly between the age groups, but the difference of 0.2 points was small. The occurrence of palmar pain and the degree of patient satisfaction did not differ between the groups. (table 2)

Table 2. Outcome of patients <70 and ≥ 70 years old one year after carpal tunnel release.

Outcome one year after surgery	Younger (<70 years) n = 152	Older (≥70 years) n = 75	p-value	Missing data
BCTQ	1.3 ± 0.5	1.5 ± 0.5	**0.030**	11
	1.1 (1.0-1.5)	1.3 (1.0-1.9)		
Palmar pain score	1.3 ± 1.9	1.1 ± 1.7	0.511	18
	0.0 (0.0-2.0)	0.0 (0.0-2.0)		
Palmar pain score = 0	73 (5.9%)	41 (57.7%)	0.109	18
Patient satisfaction			0.122	12
Resolved completely	97 (68.3%)	39 (53.4%)		
Severely worsened	2 (1.4%)	1 (1.4%)		

BCTQ = Boston Carpal Tunnel Questionnaire. The BCTQ scores were postoperatively not normally distributed, but data are also presented as mean ± standard deviation (SD) to enable the comparison with the preoperative data.

The preoperative scores of individual items of the BCTQ did not differ between groups either. However, one year after surgery, persisting numbness and tingling sensations; items 6 and 8 of the BCTQ, occurred more often in older than in younger patients. There was a trend towards older patients reporting a higher score on question 11. (table 3). The total BCTQ and the scores for all items of the BCTQ were significantly lower one year after than before surgery in both age groups ($p < 0.001$). Furthermore, the difference between the postoperative and the preoperative score for the individual BCTQ items did not differ significantly between the age groups, with the exception of item 8: Older patients showed less improvement on item 8, tingling sensations, than younger patients (1.4 points improvement versus 2.0 points, $p < 0.001$) (table 3).

Table 3. Comparison of the 11 individual items of the Boston Carpal Tunnel Questionnaire (BCTQ) pre- and postoperatively between patients <70 and 70 years and older.

BCTQ items	Preoperative			Postoperative			Delta (postop minus preop)		
	Younger n = 152	Older n = 75	p-value	Younger n = 152	Older n = 75	p-value	Younger n = 152	Older n = 75	p-value
1. Severity nocturnal pain	2.7 ± 1.0	3.0 ± 1.0	0.074	1.2 ± 0.5	1.4 ± 0.6	0.037	1.5 ± 1.1	1.6 ± 1.2	0.214
2. Awakening due to nocturnal pain	2.7 ± 1.1	2.9 ± 0.9	0.106	1.2 ± 0.5	1.3 ± 0.7	0.118	1.5 ± 1.2	1.6 ± 1.1	0.488
3. Do you have diurnal pain	2.3 ± 0.8	2.4 ± 0.9	0.899	1.4 ± 0.7	1.4 ± 0.6	0.136	0.9 ± 0.8	1.0 ± 1.0	0.510
4. Frequency diurnal pain	3.5 ± 1.4	3.4 ± 1.3	0.521	1.6± 1.3	1.8 ± 1.3	0.224	1.9 ± 1.7	1.6 ± 1.7	0.372
5. Duration diurnal pain	2.9 ± 1.4	3.2 ± 1.5	0.087	1.6 ± 1.2	1.7 ± 1.2	0.310	1.3 ± 1.7	1.5 ± 1.6	0.253
6. Do you have numbness	2.6 ± 1.0	2.6 ± 1.0	0.807	1.3 ± 0.6	1.6 ± 0.8	**0.001***	1.3 ± 1.2	1.0 ± 1.2	0.108
7. Do you have weakness	2.1 ± 0.9	2.4 ± 1.2	0.082	1.6 ± 0.8	1.8 ± 0.9	0.333	0.5 ± 1.0	0.6 ± 1.3	0.591
8. Do you have tingling sensations	3.2 ± 0.9	3.0 ± 0.9	0.048	1.2 ± 0.6	1.6 ± 0.9	**0.001***	2.0 ± 1.0	1.4 ±1.2	**<0.001***
9. Severity nocturnal tingling sensations	3.0 ± 0.9	3.0 ± 1.0	0.764	1.2 ± 0.6	1.4 ± 0.6	0.017	1.8 ± 1.0	1.6 ± 1.2	0.220
10. Awakening due to nocturnal tingling	3.0 ± 1.0	3.0 ± 0.9	0.792	1.2 ± 0.5	1.4 ± 0.8	0.069	1.8 ± 1.1	1.6 ± 1.2	0.218
11. Dexterity	2.0 ± 0.9	2.2 ± 1.2	0.107	1.4 ± 0.7	1.6 ± 0.8	0.011	0.6 ± 0.9	0.6 ± 1.3	0.929

As median scores on almost every item were 1 or 2 points in each group, there was no use in expressing these data in median and interquartile range as should actually be done in not-normally distributed data. Therefore, means and standard deviations were presented in this table. P-values are the original values before Bonferroni correction for multiple testing, p-values multiplied by 11, was applied. * p <0.05 after Bonferroni correction.

DISCUSSION

In this study we showed that older patients with CTS differed from younger patients on several aspects. Older patients had more severe NCS abnormalities. Before CTR, the symptom profile did not differ significantly between the age groups, but one year after CTR the older group exhibited more residual numbness and paraesthesiae. Yet, patient satisfaction and the occurrence of postoperative palmar pain did not differ between the age groups. The older group contained more men and showed higher rates of diabetes mellitus and joint disorders.

NCS, age and preoperative symptoms of CTS

In accordance with previous studies, we found a higher proportion of severely abnormal NCS in the patients aged ≥70.[2,14,15,29] The higher severity of NCS in the older group may be expected to be accompanied by more complaints preoperatively, but this was not the case. There may be various reasons for this relatively low subjective severity. Either elderly patients were less likely to complain than younger patients, or their symptoms were no worse than those of younger patients. For example, with advancing age, the quality of sleep decreases, older people have more arousals during the night[30] and they probably get out of bed more frequent e.g. because of nocturia. When they are already used to frequent awakenings, elderly are probably less bothered by nocturnal tingling caused by their CTS. In addition, these paraesthesiae might actually occur less frequent because of the shorter sleep duration in aged persons. [30] Older patients are likely to have decreased sensory function, which might reduce the perception of CTS symptoms. Furthermore, regardless of age, the lack of concordance between nerve conduction findings and some clinical features of CTS has been found by others and was previously described as the "clinical and neurophysiological dissociation". [5,31-33] The absence of a correlation between the first part of the BCTQ and NCS and between pain and NCS has been reported previously.[33] Similar results were found in another study that described 83 hands of patients over 70 years of age.[11] A partial explanation for this dissociation may be that pain/painful paraesthesiae are transmitted through small unmyelinated C fibres and that the function of these fibres is not reflected by any NCS parameter.[34] Another reason could be that pain and tingling are experienced more intensely during the first phase of nerve entrapment, when NCS are still normal or only moderately abnormal.[33]

Our results concerning no significant difference in symptomatology of older and younger patients at presentation, is in line with two other prospective studies with large numbers of patients of various ages.[9,14] A study from 1991 in 296 patients found diurnal paraesthesiae to be particularly frequent in patients > 70 years compared to patients aged 50-60 years.[15] Unfortunately, since the BCTQ does not contain a question on diurnal paraesthesiae in specific, we were not able to evaluate this item in our patients.

Postoperative symptoms and outcome of CTS

All items of the BCTQ improved one year after CTR in both age groups, but older patients showed significantly less improvement on the occurrence of paraesthesiae (item 8) than

younger patients, resulting in a difference in the postoperative score of 0.4 points. The postoperative score for numbness of the hand (item 6), was 0.3 points higher for older patients than for younger patients, but the improvement on this item was not statistically different between the age groups. The degree of improvement may have failed to reach statistical significance due to the relatively stringent correction for multiple testing.

Numbness and paraesthesiae are likely caused by median nerve damage due to prolonged compression. The regenerative capacity of nerves decreases with advancing age,[17,19-21] which might explain why older patients have more remaining numbness and paraesthesiae postoperatively than younger patients. However, then it is remarkable that the results concerning pain and motor function were not different from those of younger patients. This might be explained by the fact that pain is probably not caused by actual nerve damage, but by increased excitation of fibers due to compression. The absence of a significant difference in motor function could be due to the nature of the BCTQ that may not be sensitive to motor dysfunction, as only two items consider motor function, and not exclusively so. The first, dexterity (item 11) depends on an interplay between sensory and motor functions and the second, weakness of the hand, (item 7) may be aggravated by pain or stiffness.

We found only one other study that compared the individual items of the BCTQ between older and younger patients pre- and postoperatively. [6] Unfortunately there were only 14 patients aged ≥ 70 in this study and outcome was assessed six months after surgery, while it is known that improvement after surgery continues after six months.[22,35] This makes a comparison to our results of limited value.

Overall, the total BCTQ was only 0.2 points higher in our group of older patients, and the occurrence of palmar pain and patient satisfaction were similar in both age groups. Apparently, having more residual numbness and paraesthesiae is no reason for older patients to be less satisfied than younger patients.

Age, gender and comorbidity

In the group aged ≥70 years the proportion of male patients was 40%, which was twice as high as in the patients <70 years. This is in line with a large study on the demographics of CTS from New Zealand that showed that the annual incidence of CTS for middle-aged patients was much higher in women than in men and was equal in men and women aged 70-75.[2] Several other studies showed a similar sex distribution in elderly patients CTS to ours.[9,12,14] The most likely explanation for the effect of age on sex proportions is the decrease of the influence of hormonal factors as risk factor for CTS in older women.[2,36,37]

We found higher rates of diabetes mellitus and joint disorders in our older patients. This was not unexpected as these conditions are more prevalent with increasing age; similar results were found previously.[7,9,14] This higher burden of degenerative changes of bones and joints in elderly patients was however not reflected in a higher score on the preoperative questions of the BCTQ regarding weakness (item 7) or dexterity (item 11).

Strengths and limitations

The strengths of this study are its prospective design, the large number of patients with NCS-confirmed CTS, the systematic application of a validated, widely used questionnaire on symptoms of CTS and the long follow-up period. The follow-up period is important as it takes approximately ten months before maximum symptom relief is achieved after CTR.[35]

A limitation is the relatively high percentage of patients who did not participate in follow-up. These patients were younger than the participants, perhaps because older patients were more willing to fill in time-consuming questionnaires. Non-participants did not differ from participants on preoperative BCTQ and we do not expect that this difference in age affects the validity of our conclusions.

The use of the Bonferroni correction for multiple testing is open to debate. There obviously is some degree of correlation between the clinical aspects of the individual items of the BCTQ and one could argue that the Bonferroni correction is too stringent here. Nevertheless, we felt this correction was justified, since a relatively high number of statistical tests was performed.

CONCLUSION

The symptom profile of patients with CTS at presentation did not differ between older and younger patients, but older patients presented with more severe NCS abnormalities. One year after CTR, older patients reported more residual numbness and paraesthesiae than younger patients, which might be partly due to the decrease of the regenerative capacity of nerves with advancing age. However, we feel that older patients with CTS should be encouraged to undergo CTR just as much as younger patients, since neither reported patient satisfaction nor the occurrence of palmar pain differed between age groups.

APPENDIX

The Boston Carpal Tunnel Questionnaire, symptom severity scale[25]

The following questions refer to your symptoms for a typical twenty-four-hour period during the past two weeks (circle one answer to each question).

1.How severe is the hand or wrist pain that you have at night?

I do not have hand or wrist pain at night
Mild pain
Moderate pain
Severe pain
Very severe pain

2.How often did hand or wrist pain wake you up during a typical night in the past two weeks?

Never
Once
Two or three times
Four or five times
More than five times

3.Do you typically have pain in your hand or wrist during the daytime?

I never have pain during the day
I have mild pain during the day
I have moderate pain during the day
I have severe pain during the day
I have very severe pain during the day

4.How often do you have hand or wrist pain during the daytime?

Never
Once or twice a day
Three to five times a day
More than five times a day
The pain is constant

5.How long, on average, does an episode of pain last during the daytime?

I never get pain during the day
Less than 10 minutes
10-60 minutes
Greater than 60 minutes
The pain is constant throughout the day

6.Do you have numbness (loss of sensation) in your hand?

No
I have mild numbness
I have moderate numbness
I have severe numbness
I have very severe numbness

7.Do you have weakness in your hand or wrist?

No weakness
Mild weakness
Moderate weakness
Severe weakness
Very severe weakness

8.Do you have tingling sensations in your hand?

No tingling
Mild tingling
Moderate tingling
Severe tingling
Very severe tingling

9.How severe is numbness (loss of sensation) or tingling at night?

I have no numbness or tingling at night
Mild
Moderate
Severe
Very severe

10.How often did hand numbness or tingling wake you up during a typical night during the past two weeks?

Never
Once
Two or three times
Four or five times
More than five times

11.Do you have difficulty with the grasping and use of small objects such as keys or pens?

No difficulty
Mild difficulty
Moderate difficulty
Severe difficulty
Very severe difficulty

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