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Outcome of simple decompression of the compressed ulnar nerve at the elbow

influence of smoking, gender and electrophysiological findings

Running title: Simple ulnar nerve decompression and outcome

Original paper

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Outcome of simple decompression of the compressed ulnar nerve

at the elbow

- influence of smoking, gender and electrophysiological

findings

Abstract

Background: Compression of the ulnar nerve at elbow is frequently treated with simple decompression. Knowledge about factors influencing results of surgery of the nerve is limited and contradictory. The primary aim was to evaluate outcome of simple decompression of the nerve using a QuickDASH questionnaire, and to investigate any influence of smoking, gender and preoperative electrophysiological findings. A second aim was to estimate the relation between QuickDASH score and a clinical assessment of outcome by the surgeon. *Methods*: Patients who were operated on with simple decompression of the ulnar nerve,

excluding reoperations, from September 2009 to February 2011 were evaluated before and at one year after surgery using QuickDASH. Data were collected from medical records and from a self-reported health declaration.

Results: There were no differences in QuickDASH scores or change in total score between smokers and non-smokers or between women and men. Nerve pathology, assessed by preoperative electrophysiology, did not affect outcome. The surgeon's assessment of outcome mirrored QuickDASH score. Among all patients, 12/33 (36%) did not have a decrease in QuickDASH score > 8, which is considered as a minimal clinically important difference. *Conclusion*: Smoking, gender and preoperative electrophysiological findings do not affect outcome of surgery. There are a high number of patients who do not benefit from simple decompression of the ulnar nerve at the elbow. Patients who are planned for surgery should be informed that there is a risk for persistent problems. A simple outcome assessment by the surgeon mirrors QuickDASH score at one year.

Key words: ulnar nerve compression; decompression; electrophysiology; smoking; outcome; gender

Introduction

Ulnar nerve compression at the elbow is the second most common nerve compression disorder in the upper extremity. It can be treated by different surgical procedures, most frequently with the cost-effective neurolysis as the primary procedure [1-4], while revision surgery usually involves more extensive procedures, such as subcutaneous or particularly submuscular ulnar nerve transposition. Ulnar nerve compression at the elbow has gained much less interest in the literature than carpal tunnel syndrome (CTS), i.e. median nerve compression at the wrist, and there is a limited agreement of standardized grading systems i.e. how to measure outcome and the indications for surgery [1]. A Cochrane study indicates that the best treatment for ulnar nerve compression is not possible to define due to lack of evidence, including when to treat the patient conservatively or surgically [5].

Several instruments has been used to simply assess outcome in clinical practice, such as the Michigan Hand Outcomes Questionnaire (MHQ), the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire, the Carpal Tunnel Questionnaire (CTQ), and recently a new one was introduced; PRUNE [6, 7]. Interestingly, evaluation of a minimally clinically important difference for these patient-reported outcome questionnaires signifies that small score differences in MHQ and DASH, as well as an even smaller difference in CTQ, after simple ulnar nerve decompression identified satisfied patients; thus, such outcome questionnaires are highly responsive in relation to surgery for ulnar nerve compression [6]. Furthermore, it has been pointed out that smaller sample sizes can be used when such questionnaires are utilized to evaluate outcome up to 12 months post surgery in ulnar nerve compression [6].

There is limited research about factors that influence outcome after ulnar nerve decompression and those that are available show no conclusive result [8], which is in contrast

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to CTS where risk factors for development and for outcome of surgery are described [9, 10]. Smoking is a reported risk factor for ulnar nerve compression [11, 12], but gender seems not to be a risk factor [12]. There is improvement among smokers with CTS, as judged by QuickDASH score, after median nerve decompression, but they may have remaining disability compared to non-smokers [9]. However, outcome of simple decompression in smokers with ulnar nerve compression at the elbow is not described. The relations between the severity of symptoms, nerve conduction staging and outcome of surgery for CTS and ulnar nerve compression are also complex and need more attention [13, 14].

The primary aim of this study was to evaluate outcome of simple decompression of the ulnar nerve at the elbow by using QuickDASH, focusing on the influence of smoking, gender, and preoperative electrophysiological findings. A second aim was to estimate the relation between QuickDASH score and a clinical assessment of outcome by the surgeon.

Material and Methods

Patients, electrophysiology and clinical assessment

A retrospective observational study was performed on patients with ulnar nerve compression at the elbow and operated on at our hospital (identified from the hospital administrative system) with simple decompression from September 2009 to February 2011. All patients were routinely asked to fill in a QuickDASH form both before and at one year after surgery. Data regarding co-existing diseases, smoking, body mass index (BMI), medication and results from electrophysiological examination were obtained from the patients' medical record and from a self-reported declaration of health, which the patients fill in preoperatively. Furthermore, the treating doctor's medical assessment of outcome after the surgery was obtained from the medical records. The electrophysiological findings were graded into four different groups: a) normal findings, b) decreased conduction velocity, c) conduction block and d) axonal degeneration.

The physician's medical assessment after the surgery at the last follow up within one year was extracted from the medical records and was divided into four groups: a) patients who were cured, b) those who were improved, c) patients without improvement and d) those that were considered to be worse.

QuickDASH

The QuickDASH questionnaire is a shortened version of the DASH questionnaire (Disability of Arm, Shoulder and Hand; The Swedish translated version of QuickDASH. [cited 2014 24 May]; Available from:

http://www.dash.iwh.on.ca/system/files/translations/DASH_Swedish.pdf.) QuickDASH is a questionnaire, which the patients fill in before and at one year after surgery. At that time it is considered that the healing process is finished and all temporary side effects has even out [6, 15]. QuickDASH consists of 11 items in which the patients rank their problems on a scale from 1 to 5. After completion of the form a total score is calculated. The total score ranges from 0, meaning no problems at all, to 100, denoting total disability. It is considered that a decrease in total score of more than 8 points, from the preoperative to the postoperative QuickDASH, to reflect a minimal clinically important difference [16]. Furthermore, a postoperative total score of more than 10 is valued as having persistent problems [17].

Excluded patients

Patients were excluded from the study if they had not filled in the postoperative QuickDASH or if the surgery was a revision on the same arm (Figure 1). Also, patients who were operated on as a primary procedure with submuscular or subcutaneous transposition were excluded (Figure 1).

During the study period 121 patients were operated due to symptoms of nerve compression from the ulnar nerve (100 patients with simple decompression; 21 patients with subcutaneous or submuscular nerve transposition or reoperations with simple decompressions). Response with preoperative QuickDASH was received from 61 patients (see below in Results); thus, response rate 50.4%.

Statistical methods

All data are presented as median [interquartile range; IQR] or as number of patients (n, %). For comparison between several groups Kruskal Wallis test was used with the subsequent post hoc method Mann Whitney U-test for continuous data. The chi square-test was used for nominal data. For comparison between the pre- and postoperative QuickDASH results for all patients Wilcoxon signed-rank test was used. Due to the limited number of patients, the subjects were also pooled based on electrophysiological findings (comparison between patients with axonal degeneration and the other three groups) and the surgeons' clinical assessment of outcome (comparison between cured/improved and no improvement/worse). These described groups were compared with Mann Whitney U-test. The Spearman rank correlation test was used to investigate for possible correlations. A p-value of less than 0.05 was considered as statistical significant. Statview for windows (SAS Institute Inc. Cary, NC, USA Version 5.0.1) was used for all analyses.

Ethical considerations

The study protocol was presented to the regional Ethics Committee (#2011/607). They found the study sound, without ethical problems and judged that the study was not applicable to the law in geographical area deleted. Neither advertising nor formal informed consent by each patient was needed. Chief of service at our department approved the quality control. Therefore, no formal permission number has been attached to the study.

Results

All patients

In total, 61 patients were operated on for ulnar nerve compression at the elbow and had filled in a QuickDASH form preoperatively during the study period. Out of these, 42 completed both the pre- and postoperative QuickDASH form, where six procedures were reoperations and three were primary subcutaneous or submuscular transpositions. Therefore, 33 patients, who had primary surgery with simple decompression, were included (Figure 1). There were no differences in age or gender between the patients who only had filled in the preoperative QuickDASH and those who completed both the preoperative and postoperative QuickDASH (results not shown). Out of the patients who had completed both the preoperative and postoperative QuickDASH, the patients who underwent reoperation on the same arm were younger (37 [IQR 18] years) than the patients who had their first surgery done (57 [19] years, p=0.03). There were no differences in gender distribution.

Included patients

The characteristics of the patients are presented in Table I. Out of the 33 patients who answered the QuickDASH questionnaire pre- and postoperatively and underwent simple decompression, 14 were smokers and 19 non-smokers, and 13 were women and 20 men. The age of all the patients was 55 [19.3] years and the patients had a slight overweight, i.e. BMI 25.5 [7.0] (Table I). There was a statistical significant difference between the preoperative (45 [27.5]) and the postoperative QuickDASH scores (30 [43]; p=0.003; Table II). The change in total score between the pre- and postoperative total score was 13 [29]. Twelve (36%) of the patients had a decrease in total score of less than 8 and 22 (66%) had a postoperative total score of more than 10.; i.e. a minimally clinically relevant difference [17]. When plotting the pre- and the postoperative QuickDASH total scores in a scatter diagram there was a weak positive correlation (p=0.02, rho=0.4; Figure 2a).

Smokers

There were no differences between the smokers and the non-smokers regarding age, gender, BMI, hypertension, hypothyroidism or diabetes (Table I). Furthermore, there were no differences in character of symptoms (i.e. constant or intermittent) or the presence of atrophy of the first interosseous muscle (Table I). However, the smokers had a higher frequency of Tinel sign at the elbow [9 (64%) vs. 4 (21%); p=0.01]. There were no differences between the smokers and the non-smokers regarding QuickDASH scores; neither in the pre- or postoperative scores, nor in the change in total score. Furthermore, there was an equal amount of patients who had a decrease in total score of less than 8 and a postoperative total score of more than 10 (Table II).

Patients who did not improve

The patients were divided into two groups depending on the change in total score > or < 8 (Table III). The characteristics of those patients did not differ in any of the variables, although there was a tendency of a higher frequency of more severe electrophysiological stages in those with a change > 8 (p=0.07). The preoperative QuickDASH scores did not differ between the groups (p=0.09), but the patients with a change > 8 had lower total score

postoperatively and naturally a larger change in score (Table III). In addition, the group with a change < 8 had a higher proportion of patients with a postoperative total score > 10.

Gender

There were no differences between the women and men regarding age, BMI, smoking, presence of hypothyroidism, diabetes or statin treatment (Table I). However, a higher frequency of men had hypertension [7 (35%) vs. 0 (0%); p=0.02]. Regarding the character of symptoms and the presence of Tinel sign, no differences were found between women and men, although more men had atrophy of the first interosseous muscle [12 (60%) vs. 3 (23%); p=0.04; Table I]. The QuickDASH scores pre- and postoperatively, the proportion of patients with a change < 8 or a postoperative score > 10 did not differ between women and men (Table II).

Electrophysiological evaluation

Electrophysiological examination was performed in 30 patients, but in six patients the data could not be found. Three patients were graded as having normal electrophysiological values, seven patients as having a decreased conduction velocity, seven patients as having a conduction block and seven patients had signs of axonal degeneration in the ulnar nerve (Table I). A Kruskal Wallis test showed that there were no differences in QuickDASH scores between these four groups (p-values for preoperative QuickDASH score 0.72; postoperative score 0.74 and change in total score 0.15). Furthermore, there were no differences in the number of patients who had a decrease in QuickDASH score of < 8 (p=0.07) or a postoperative QuickDASH score of > 10 (p=0.5). When dividing the patients into two groups, i.e. those with axonal degeneration against the other three groups pooled, no significant differences were found (Table IV). When plotting the preoperative QuickDASH score with

the change in total score, there was a weak positive correlation (rho=0.38, p=0.03; Figure 2b). When separating the patients in the different electrophysiological grading groups (observed with different colours in Figure 2b), the three patients with normal electrophysiology all had a negative change in total score, i.e. judged their results as worse.

Clinical assessment

A clinical assessment, based on the information from the medical records, was available in 31 patients (final discharge from outpatient 42 [60] days) and data were missing in two patients. Five patients were assessed to be cured and 14 patients were improved. In contrast, nine patients were unchanged and three patients were worse than before surgery. There were no differences in the preoperative QuickDASH scores (p=0.72) or in change in total score (p=0.08) among these groups, while the postoperative score differed between the groups (p=0.028). The post hoc analysis showed that the cured (p=0.049; p=0.02, respectively) and improved (p=0.02; p=0.02, respectively) patients (no difference between these two groups) had significantly lower postoperative total scores than the unchanged patients and the patients that were considered as worse (no difference between these two latter groups; Figure 2d; Table IV). As pointed out above, there was a weak positive correlation (rho=0.38, p=0.03; Figure 2c) between preoperative total score and change in total score and data from the pooled groups cured/improved and unchanged/worse are highlighted in Figure 2c. A chi square test showed that more patients in the pooled group no change/worse (8, 66%) had a decrease in total score of < 8 compared to the pooled group cured/improved (4, 21%; p=0.01).

Discussion

The present study on outcome after primary, simple, ulnar nerve decompression at the elbow shows that the overall QuickDASH score improved significantly, but with only 13 points,

which is lower than seen after decompression of the median nerve in carpal tunnel syndrome (i.e. 23 points; [10]), but at a similar level as after partial fasciectomy due to Dupuytren's contracture (i.e. 11 points; [18]). QuickDASH is used at the hospital as a routine to evaluate outcome after different conditions since it is an accepted outcome instrument after simple decompression in the present condition [6]. Malay et al defined a minimal clinical important difference after simple decompression in a population with a similar size as the present study (n=38) and found it as low as 7 points for DASH [6]. It is important to define a minimal clinical important difference in order to establish potential outcome measurements and for the future be able to define relevant sample size estimates in multicentre studies to compare different surgical options. Simple decompression is used as the *primary* surgical procedure to treat ulnar nerve compression at the elbow at the present hospital, when conservative treatment has failed, which is in accordance with other studies [1, 6, 19], although a Cochrane indicates that no differences exist between different procedures [5].

We found that the clinical assessment of the treating surgeon agreed rather well with the QuickDASH scores (see data in Figure 2c-d) with a clear difference between patients considering themselves as cured/improved and unchanged/worse. One has to consider the different time points for follow up; i.e. clinical assessment done at final discharge from outpatient clinic (different in individual patients) and QuickDASH evaluation done at one year, which may explain the discrepancy observed for some individual patients in Fig 2c. Unfortunately, there were 12/33 patients with a change in QuickDASH score < 8 [16], but we could not find any specific causes in data or any concomitant disease(s) that contributed to the explanation of the insufficient outcome. The electrophysiological stages were not more advanced, like axonal degeneration, in these patients with a change in QuickDASH score < 8. Actually, there was a trend towards normal electrophysiology in the ulnar nerve in those

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that did not improve (Table III). One may consider that presence of axonal degeneration in the nerve, observed at the electrophysiological examination, could be detrimental for the outcome, but that was not the case. One reason may be that QuickDASH was assessed one year after surgery, indicating that any regenerative events may have been finished. Furthermore, the patients may have had an additional conduction block, which was treated by the surgical procedure. The study by Malay et al [6] indicates that DASH score rapidly decreases after simple decompression (i.e. 3 months) and remains stable up to one year. A change in QuickDASH score of < 8 was used as a cut off according to Mintken et al [16]. One may argue that the cut off should be < 7 according to Malay et al [6], but none of the present patients had a score of 7 and therefore the conclusions were not affected. However, both the QuickDASH results (from 12/33 patients; 36%) and the clinical assessment (from 12/31 patients; 39%) show that there was a high frequency of patients who did not improve from simple decompression of the ulnar nerve at the elbow; still with a suspicion that the diagnosis may be incorrect. These patients may later be subjected to further clinical examination, laboratory analyses and imaging techniques to exclude other causes of symptoms before considering any future revision surgery. There are no well-defined data in the literature on the frequency of reoperations after simple decompression, but it may be around 7 % [20].

We focused on smoking as a risk factor for unfavourable outcome, since other studies suggests that such a factor may influence the level of QuickDASH pre- and postoperatively in carpal tunnel syndrome [9]. No other studies on ulnar nerve compression at elbow have highlighted this factor for outcome, and smoking is only reported as a risk factor for development of ulnar nerve compression [11]. In the present study, the frequency of smokers was high (i.e. 14/33; 42%) compared to a "normal" population (20-21%; see data from Public Health Agency of Sweden; http://www.folkhalsomyndigheten.se/documents/statistik-

uppfoljning/enkater-undersokningar/nationella-folkhalsoenkaten/resultat-2014/tobaksvanornationella-resultat-och-tidsserier-2014.xls). It was found that the present smokers, without knowing the exact daily consumption, did not have any different QuickDASH scores than those of non-smokers. However, the smokers had a higher frequency of Tinel sign at the elbow, for unknown reasons, indicating a more susceptible and irritable ulnar nerve. Gender, which is not a risk factor for development of ulnar nerve compression at the elbow [11], but may influence QuickDASH score before and after surgery for carpal tunnel syndrome, did not influence the outcome after the present simple decompression of the ulnar nerve at elbow. However, men had a higher frequency of signs of atrophy of the first interosseous muscle indicating more severe and long-term ulnar nerve compression. Thus, no real factor could be pointed out that influenced the outcome.

Study limitations

One limitation is the small number of patients in the present study (n=33), but in the study by Malay et al [6] their number was not very different (i.e. n=38). It should be noted that the excluded patients, who only responded preoperatively, did not differ in character from the included patients [21]. Another limitation is that we did not follow the patients with different clinical tests or with electrophysiological examinations, which has been done in a similar study [15, 19]. The recovery, measured by functional variables, is slower than is seen in the patient-reported questionnaires [15]. Thus, it may be sufficient with information obtained from the questionnaires. A final limitation is that we have only used QuickDASH as evaluation questionnaire, since this is the only one that is available in Swedish language. Although the CTS specific Carpal Tunnel Questionnaire (CTQ) is present in Swedish, it is not specifically designed for ulnar nerve compression at the elbow. Thus, QuickDASH may be sufficient as patient-reported outcome instrument in clinical practice.

Conclusion

Smoking, gender and preoperative electrophysiological findings do not affect the outcome of the surgery as evaluated by QuickDASH or a clinical assessment by the surgeon. However, there are a high number of patients who do not benefit from simple decompression of the ulnar nerve at the elbow. Patients who are planned for surgery should be informed that there is a risk for persistent problems. A simple assessment by the surgeon regarding outcome, mirrors QuickDASH score one year after surgery.

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Table I. Characteristics of patients with ulnar nerve compression at the elbow and treated with simple nerve decompression as a primary surgery.

	All	Smokers	Non-	P-	Women	Men	Р-
	patients		smokers	value			value
	(n=33)	(n=14)	(n=19)		(n=13)	(n=20)	
Women	13 (39%)	6 (43%)	7 (37%)	0.76			N/A
Age	55 [19.3]	54.5 [20]	58 [17]	0.53	47 [17.3]	61 [14]	0.1
BMI	25.5 [7.0]	23.3 [4.1]	27.1 [6.9]	0.06	25.2 [11.4]	25.5 [5.7]	0.5
Smokers	14 (42%)			N/A	6 (46%)	8 (40%)	0.73
Hypertension	7 (21%)	1 (7%)	6 (32%)	0.09	0	7 (35%)	0.02
Hypothyroidism	2 (6%)	1 (7%)	1 (5%)	0.8	1 (8%)	1 (5%)	0.75
Statin treatment	8 (24%)	4 (29%)	4 (21%)	0.6	1 (8%)	7 (35%)	0.07
Diabetes	2 (6%)	0	2 (11%)	0.2	0	2 (10%)	0.24
Constant symptoms	25 (75%)	12 (86%)	13 (68%)	0.25	10 (77%)	15 (75%)	0.9
Tinel present	13 (39%)	9 (64%)	4 (21%)	0.01	3 (23%)	10 (50%)	0.12

Atrophy of first	15 (45%)	6 (43%)	9 (47%)	0.79	3 (23%)	12 (60%)	0.04
interosseous muscle							
Confirmed by	30	12 (64%)	18 (95%)	0.37	12 (92%)	18 (90%)	0.8
electrophysiology							
Electrophysiological	3/7/7/7	0/3/3/3	3/4/4/4	0.56	1/4/4/2	2/3/3/5	0.6
grading [®] :							

Values are median [IQR] and n (%). P-values are calculated with Mann Whitney U-test and chi square-test. ^(a) indicates normal/velocity decrease/conduction block/axonal degeneration; data were missing in six patients.

	All	Smokers	Non-	P-value	Women	Men	P-value
	patients		smokers				
	(n=33)	(n=14)	(n=19)		(n=13)	(n=20)	
QuickDASH	45 [27.5]	56 [31]	43 [24]	0.15	55 [34]	45 [27]	0.6
preoperatively							
QuickDASH	30 [43]	34 [52]	23 [38.5]	0.2	43 [52.5]	24 [33]	0.3
postoperatively							
Change in total score	13 [29]	13.5 [23]	11 [36]	0.82	13 [22]	14 [38]	0.9
Decrease in total score	12 (36%)	5 (36%)	7 (37%)	0.95	4 (31%)	8 (40%)	0.6
less than 8							
Total score	22 (66%)	10 (71%)	12 (63%)	0.62	9 (69%)	13 (65%)	0.8
postoperatively more							
than 10							

Table II. QuickDASH scores in patients with ulnar nerve compression at the elbow and treated with simple nerve decompression as a primary surgery.

Values are median [IQR]. P-values based on Mann-Whitney and chi-square test.

	Decrease in	Decrease in	P-value
	total score <8	total score >8	
	(n=12)	(n=21)	
Women	4 (33%)	9 (43%)	0.59
Age	56.5 [15.5]	54 [21]	0.57
BMI	25.8 [6.9]	24.5 [6.5]	0.56
Smokers	5 (42%)	9 (43%)	0.95
Hypertension	2 (17%)	5 (24%)	0.63
Hypothyroidism	0	2 (10%)	0.27
Statin treatment	2 (17%)	6 (29%)	0.4
Diabetes	1 (8%)	1 (5%)	0.67
Constant symptoms	9 (75%)	16 (76%)	0.93
Tinel present	5 (42%)	8 (38%)	0.8
Atrophy of first interosseous muscle	5 (42%)	10 (38%)	0.74
Confirmed by electrophysiology	12 (100%)	18 (86%)	0.17
Electrophysiological grading:	3/2/1/3	0/5/6/4	0.07
normal/velocity decrease/conduction			
block/axonal degeneration ω			
QuickDASH preoperatively	38 [32]	55 [27]	0.09
QuickDASH postoperatively at one year	45 [35]	23 [30]	0.004
Decrease in total score	-7 [10.5]	22 [31]	<0.0001
Total score postoperatively > 10	11 (92%)	11 (52%)	0.02

Table III. Characteristics and QuickDASH results of patients with a decrease of < or > 8 in QuickDASH scores.

Values are median [IQR] and n (%). P-values are calculated with Mann Whitney U-test and chi square-test.

	Total score	Total score	Change in	Decrease in	Postoperative
	QuickDASH	QuickDASH	totalscore	total score	total score
	preoperatively	postoperatively	QuickDASH	QuickDASH	QuickDASH
				<8	>10
Clinical assessment					
Cured/improved					
(n=19)	43 [33]	23 [28]	18 [22.8]	4 (21%)	11 (58%)
No change/worse					
(n=12)	59 [33]	58 [32]	6.5 [26]	8 (66%)	10 (83%)
p-value	0.12	0.003	0.016	0.01	0.14
Electrophysiology					
staging					
Axonal degeneration	52 [20]	33 [49]	19 [43]	3 (43%)	4 (57%)

Table IV. QuickDASH score in patients with ulnar nerve compression at the elbow evaluated preoperatively and at one year after simple nerve decompression.

(n=	=7)
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All other (n=17)	43 [31]	30 [43]	13 [29]	6 (35%)	12 (70%)
p-value	0.12	0.97	0.82	0.73	0.53

Values are median [IQR]. P-values calculated with Mann Whitney U-test and chi-square test.

Figure legends

Figure 1. Flowchart showing all patients and the included patients at the bottom left.

Figure 2 a) Scattergram showing total score of QuickDASH preoperatively and postoperatively. A weak positive correlation exists; rho=0.42, p=0.02. b) Scattergram showing total score preoperatively and change in total score. A weak positive correlation exists; rho=0.38, p=0.03. The different electrophysiological gradings are highlighted; normal findings; decreased conduction velocity; conduction block; axonal degeneration. c) Same results as panel b) although the clinical assessment groups are highlighted. The patients who were assessed as cured or improved as well as assessed as no change or worse. d) Boxplot showing total score postoperatively for the different clinical assessment groups: cured; improved; no change in symptoms; worse. Kruskal –Wallis test and Mann Whitney U-test shows statistical significant differences between groups cured and no change, cured and worse, improved and no change and finally between improved and worse.



