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Outcome after carpal tunnel release: impact of factors related to metabolic syndrome

Short running title: Carpal tunnel release and metabolic syndrome

Original paper

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**Outcome after carpal tunnel release: impact of factors related to
metabolic syndrome**

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Original paper

Abstract

Objective

The standard surgical treatment of carpal tunnel syndrome (CTS), with an open carpal tunnel release, is reported to relieve symptoms in most patients.

In a retrospective observational study, we evaluated outcome after open carpal tunnel release focusing on factors related to the metabolic syndrome: diabetes, hypertension, obesity (BMI \geq 30) and statin treatment.

Methods

Results from 493 out of 962 patients (531/1044 hands) operated for CTS during 18 months that had filled in QuickDASH questionnaires before and one year after surgery were included in the study.

Results

Patients with diabetes (n=76) had higher QuickDASH scores pre- (56 [36-77]; i.e. median [interquartile range]) and postoperatively (31 [9-61]) compared to patients without diabetes (48 [32-66]; $p < 0.05$ and 16 [5-43]; $p < 0.001$), but the change in total score was equal. A higher proportion of patients with diabetes had a postoperative score of > 10 (74% vs. 61%; $p < 0.05$). The odds of having a change in QuickDASH score < 8 was 2.6 times higher in patients with polyneuropathy than in patients without polyneuropathy.

Patients with hypertension, obesity or statin treatment had a similar improvement after surgery as patients without these factors.

Conclusions

Patients with diabetes without neuropathy, as well as patients with hypertension, obesity or statin treatment, and CTS can expect the same effects of open carpal tunnel release as otherwise healthy patients. Patients with diabetic neuropathy and CTS did not experience the

same improvement as otherwise healthy patients and should be informed about the risk of an unsatisfactory outcome.

Word count abstract: 242

Key words: carpal tunnel syndrome, open carpal tunnel release, diabetic neuropathy, metabolic syndrome, hypertension, obesity, statins

Introduction

Carpal tunnel syndrome (CTS) affects 3-4% of the general population [1]. Idiopathic CTS is more common in females, middle-aged patients and those with an increased body mass index (BMI) [2]. Diseases such as diabetes, rheumatoid arthritis, and hypothyroidism, also carry an increased risk of developing CTS [3]. Open carpal tunnel release (OCTR) as treatment for CTS is considered to give good to excellent results for the majority of patients [4].

The metabolic syndrome, defined by the International Diabetes Federation [5], consists of central obesity or BMI ≥ 30 in combination with two of the following factors: raised triglycerides, reduced HDL-cholesterol, elevated blood pressure and raised fasting plasma glucose. Separately, these elements are known risk factors for development of both diabetic neuropathy and CTS [6]. However, their impact on outcome after surgical treatment of CTS is not known. A recent case-control study [7] suggested that metabolic syndrome is related to more severe forms of CTS, as well as to longer recovery time after OCTR, but not to worse improvement after surgery.

Patients with metabolic syndrome are often treated with statins in order to reduce hypercholesterolemia and thereby decrease the morbidity and mortality of cardiovascular disease [8]. Peripheral neuropathy of the lower extremity, presenting with sensory

disturbances, muscle weakness or atrophy, is a complication to statin treatment [9]. Similar symptoms in the upper extremity could potentially mimic CTS.

Our aim was to evaluate the impact of diabetes, obesity, hypertension and statin treatment on the clinical outcome after OCTR in patients with CTS. We hypothesized that OCTR on patients with diabetes, obesity, hypertension and/or statin treatment would not be as successful as operations on patients with fewer of these factors in their medical history.

We report outcome from 493 patients operated on with open carpal tunnel release and relate results to the components of the metabolic syndrome, i.e. diabetes, hypertension, obesity as well as statin treatment.

Methods

Study design and participants

This retrospective observational study was performed on patients with CTS operated with OCTR at our department from September 2009 to February 2011. Within the hospital administrative register system we identified patients with the operation code ACC51.

Before and one year after surgery, patients were routinely asked to fill in the Swedish version of the QuickDASH (Disability of Arm, Shoulder and Hand) questionnaire. The QuickDASH questionnaire is a shortened version of DASH – Disability of Arm, Shoulder and Hand.

DASH was originally developed as a tool for measuring outcome in terms of impact on function in musculoskeletal disorders and injuries in the upper extremity. QuickDASH consists of 11 items (in contrast to 30 items in DASH) measuring physical performance and symptoms in the upper limb. By scoring the different items [no difficulty/not at all = 1 to extremely/unable = 5] a total score, ranging from 0-100 is calculated where a higher score indicate more disability. Mean DASH score for the general population in the United States is estimated to be 10.1 (standard deviation 14.7) [10], hence a postoperative QuickDASH score

> 10 may be considered as remaining disability [11]. There are no normative data for the Swedish population. A difference of 8 between the preoperative and the postoperative score is considered the minimal clinically important difference [12]. Thus, we present our data as the proportion of patients with a postoperative QuickDASH score > 10 and a total change in QuickDASH score of < 8.

Only patients who had completed the QuickDASH both preoperatively (reply a few days or weeks before surgery) and postoperatively (one year after surgery) were included. We excluded patients who had not completed DASH pre- and postoperatively. Only primary carpal tunnel releases were included. For excluded patients we registered age, gender and, when possible, preoperative scores.

Preoperative information was collected from the medical journal and from the patient's self-reported declaration of health. We recorded diabetes mellitus (DM), diagnosed hypertension, BMI, polyneuropathy (i.e. verified polyneuropathy diagnosis by the referral doctor and/or diagnosed by concomitant electrophysiology) and current statin treatment. In accordance with World Health Organization guidelines obesity was defined as $BMI \geq 30$. If preoperative electrophysiology testing had been performed, median nerve sensory conduction velocity (SCV) across the wrist was recorded. Diagnosis of CTS in this real world study was made by clinical examination, patient history and in uncertain cases verified by electrophysiology testing.

Statistical methods

Data are presented as median [interquartile range, IQR]. Non-parametric Mann-Whitney test was used to compare differences between groups for continuous data. Nominal data are presented as numbers (per cent) and a chi-square test was used to compare differences between groups. A linear regression analysis was used to calculate the effect of individual

variables on change in total score; in model 1 with DM and polyneuropathy as independent variables and in model 2 with BMI \geq 30, DM, hypertension, polyneuropathy and statin treatment as independent variables. A logistic regression analysis was used to calculate Odds Ratio (OR). A p-value $<$ 0.05 was considered statistically significant. StatView for Windows (SAS institute Inc., version 5.0.1, Cary NC, USA) and SPSS Statistics, version 22 (SPSS Inc., Chicago, IL, USA) were used for calculations.

Ethics

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 in the Swedish Ethical Review Act. 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

During the study period, 962 patients (1044 hands) underwent OCTR. Pre- and postoperative QuickDASH were completed in 514 out of 962 patients. Thirty-eight patients were operated bilaterally and included with mean QuickDASH scores for both hands. Twenty-one patients were operated bilaterally during the study period, but had only filled out complete QuickDASH for one of the operations. In these cases, the patient was included with the provided data. Twenty-one patients were not primary releases and were therefore excluded. Thus, the study group consisted of 493 patients (531 hands; data in Tables are presented as patients) (Figure 1).

Demography

Out of the 493 included patients, 343 (70%) were women, 76 (15%) had diabetes, 136 (28%) were obese (i.e. BMI \geq 30), 143 (29%) had diagnosed hypertension, and 86 (17%) were on statin treatment (Table I). In 299 patients (62%), an electrophysiology test had been conducted before surgery. A postoperative score >10 was reported in 308 patients (63%) and in 124 patients (25%) the change in total score was < 8 .

The men were older (median 60 [IQR 48-68] years) than the women (54 [44-64] years; $p<0.05$), had a higher BMI (29 [26-31] vs. 27 [25-31]; $p<0.05$), and a higher frequency of statin treatment (35/145, 24% vs. 51/341, 15%; $p<0.05$). No significant differences were found between men and women regarding diabetes, hypertension, polyneuropathy or in the sensory conduction velocity (SCV) of the median nerve over the carpal tunnel segment. 94 patients (19%) indicated that they were current smokers before the surgery.

The excluded patients, where the patient had filled in only the preoperative QuickDASH ($n=171$), were younger (median 47 [IQR 38-56] years) than the included patients (55 [46-66]; $p<0.0001$) and had a higher preoperative DASH score (median 57 [IQR 41-73]) vs. (50 [32-66]; $p=0.0001$). 277 patients did not fill out any QuickDASH at all.

Diabetes

Patients with CTS and Diabetes Mellitus (DM) were older and had a significantly higher frequency of hypertension, obesity and statin treatment compared to those who did not have diabetes (Table I). Patients with diabetes had lower SCV across the wrist (i.e. carpal tunnel). They scored higher in QuickDASH both pre- and postoperatively (Table II). There was no difference regarding change in QuickDASH score, nor in the number of patients with a change of < 8 in QuickDASH, between those with or without diabetes (Table II).

Significantly more patients with diabetes had a postoperative score > 10 (Table II). Patients

with type 1 (n=18) and type 2 DM (n=58) did not differ in QuickDASH scores (results not shown).

Eighteen patients with DM had been diagnosed with polyneuropathy (22%) compared to seven patients with polyneuropathy in the group without DM (2%; $p<0.0001$). Patients with DM and polyneuropathy (n=18) had, compared to patients that had DM without polyneuropathy (n=58), a higher QuickDASH score preoperatively (78 [IQR 57-85] and 48 [35-71]; $p<0.05$), as well as postoperatively (61 [41-76] and 20 [9-59]; $p=0.001$). All of the patients with DM and polyneuropathy (18/18, 100%) had a postoperative score > 10 compared to 38/58 (66%; $p<0.05$) of the patients with DM without polyneuropathy. There was no significant difference in total score change in QuickDASH score (13 [-6-24] and 24 [5-39]; $p=0.074$). When excluding the patients with polyneuropathy (n=18), the differences in QuickDASH between those with and without DM disappeared (Table III). The odds ratio (OR) of having a change <8 in QuickDASH total score did not differ between patients with DM and patients without DM (Table IV). The OR of having a postoperative score >10 were higher in cases with DM than in cases without DM (Table IV).

Polyneuropathy

Twenty-six patients were diagnosed with polyneuropathy and for these patients the odds of having a change <8 in QuickDASH total score was 2.6 times higher (adjusted OR 2.62 95% CI 1.05-6.54, Table IV) compared to patients without polyneuropathy (controlling for age, female gender, obesity, diabetes mellitus, hypertension and statin treatment). Patients with polyneuropathy had 11.6 times higher odds of having a postoperative score >10 (adjusted OR 11.58 95% CI 1.50-89.70, Table IV).

Obesity

More men had a BMI \geq 30, and patients with obesity demonstrated a higher frequency of DM and hypertension (Table I). However, no differences were found regarding QuickDASH scores (Table II).

Hypertension

Patients with hypertension had significantly higher age and BMI, as well as a higher frequency of diabetes, neuropathy, obesity and statin treatment compared to the patients without hypertension (Table I). They also had lower median nerve SCV over the wrist. There were no significant differences in QuickDASH scores between patients with and without hypertension (Table II).

Statin treatment

Patients that were on statin treatment were older and included more men than the group without statin treatment (Table I). Furthermore, they had a significantly higher frequency of diabetes, hypertension and neuropathy, but there was no difference in median nerve SCV at the wrist (Table I). No significant differences in QuickDASH scores could be found, neither in change in total score nor in scores pre- or postoperatively, between the groups (Table II).

Regression analysis

In model 1 (DM and polyneuropathy as independent variables), DM did not significantly affect change in total score, whereas the presence of polyneuropathy decreased the change in total score with 11.5 points in QuickDASH (Table V). In model 2 (controlling for DM, obesity, hypertension and statin treatment), the presence of polyneuropathy decreased the change in QuickDASH total score with 11.0 points (Table V). None of the other variables turned out statistically significant.

The metabolic syndrome

We did not have enough data to identify the proportion of patients with metabolic syndrome, since we did not have access to e.g. laboratory data of triglycerides etc. In an attempt to assess this proportion, we looked at patients with obesity and their prevalence of hypertension, diabetes and statin treatment in this group. There were no differences in the proportion of patients with a postoperative score > 10 , in the number of patients with a change < 8 , in preoperative score, in postoperative score nor in change in total score between patients with three or more of these factors and the remaining patients.

Discussion

In this study, we focused on a number of factors related to metabolic syndrome and their possible effect on outcome after OCTR. We found that hypertension, obesity and statin treatment were not associated with a negative outcome, while patients with DM *and* neuropathy had more persistent symptoms (i.e. postoperative score > 10) and less symptom relief (i.e. change in QuickDASH < 8) following OCTR.

Diabetes

Diabetes and pre-diabetic stages (i.e. insulin resistance and impaired glucose tolerance) increase the susceptibility to nerve compression [13, 14]. Previous studies [15-17], though not all [18], state that patients with DM benefit from CTR to the same extent as patients without DM. Here, we show that patients with DM *and* neuropathy had higher pre- and postoperative QuickDASH scores and more persistent symptoms after OCTR, whereas patients with DM *without* neuropathy had the same improvement and postoperative scores as patients without DM. It suggests that the neuropathy associated with DM, rather than the diabetes itself,

negatively influences outcome. We defined neuropathy as polyneuropathy diagnosed with electrophysiological testing. By this definition, it is more likely that the widespread peripheral neuropathy comes from the diabetic condition, and that it is not a result of the nerve entrapment in the carpal tunnel or somewhere else. Diabetic neuropathy is a complex condition, depending on both vascular and metabolic factors and is characterized by demyelination and degeneration of nerve fibers [19]. In patients with diabetic neuropathy, it is essential to establish that the sensory symptoms in their hands are due to compression of the median nerve and not to the neuropathy alone. This can, in most cases, be achieved using electroneurography. Interestingly, pathological changes in the posterior interosseous nerve, i.e. a non-compressed nerve in the forearm, are more extensive in patients with diabetes [16]. The presence of pathological changes in the nerves may explain why patients with diabetic neuropathy do not benefit from a nerve decompression procedure to the same degree as patients *without* neuropathy.

Obesity

Obesity is known to be an independent risk factor for developing CTS [20] as well as for development of diabetic neuropathy [8]. It has been speculated that fatty tissue depositing as well as hypercholesterolemia (defined as high LDL, low-density lipoprotein) increase collagen production and deposition in the median nerve and its surrounding tissues may contribute to compression of the nerve [21]. Even though we found that 28% of patients in our study were obese, obesity was not related to an unfavorable outcome after OCTR.

Hypertension

Hypertension, a known risk factor for CTS, is also suggested to be a risk factor for peripheral neuropathy due to changes in the intraneural microcirculation, leading to hypoxia and axonal

degeneration [22]. Our patients with hypertension were generally in poorer health, as indicated by a higher frequency of diabetes, statin treatment and neuropathy. Together with a lower SCV in the median nerve at wrist level it makes interpretation of the mechanisms complex, but hypertension does not seem to be a negative predictor for the outcome of the surgery in CTS.

Statins

Statin treatment is suspected to increase the risk for neuropathy [23]; therefore, with a tentative risk of developing symptoms mimicking CTS. The question of statins as a factor affecting the outcome after OCTR is most complex, since patients treated with statins generally are in poorer health. However, our results do not indicate that the patients with statin treatment had a risk for poor outcome. Dyslipidemia is one of the criteria of the metabolic syndrome, and it is often treated with statins. Aiming to understand the correlation between metabolic syndrome and CTS, one may consider statin treatment a proxy variable for dyslipidemia, but since the indications for statin treatment are wide and statins often are used for secondary prevention, we cannot be certain that the patients treated with statins had altered blood lipid levels.

The metabolic syndrome in CTS and neuropathy

A high prevalence of metabolic syndrome has been found in patients with CTS, but the mechanisms behind this are not fully understood [24, 25]. The current hypothesis is that the metabolic syndrome, and its individual components, is important for the onset and progression of peripheral neuropathy [6], where the underlying mechanisms, including fatty deposition in nerves, extracellular protein glycation, mitochondrial dysfunction, oxidative stress and counter-regulating signaling pathways leading to inflammation, may be different in

type 1 and 2 diabetes [6]. The overall interpretation of mechanisms for development of neuropathy should be done with caution, particularly regarding the pathophysiology in CTS, and it is beyond the scope of the study. More importantly, it is not known if the metabolic syndrome affects the outcome of OCTR in CTS. The present results indicate that factors related to the metabolic syndrome are not detrimental for its outcome, but patients with diabetes and neuropathy have a less favorable outcome.

Study limitations

448 of 962 patients (47%) operated did not complete both the pre-and postoperative QuickDASH questionnaire. Patients who had answered the preoperative QuickDASH only, ranked their symptoms worse than the included patients. We do not know if it indicates the possibility of a worse outcome or a higher capability for improvement. On the other hand, patients who are not satisfied with the surgery may be more prone to answer the postoperative QuickDASH questionnaire than the patients who were pleased with the outcome of surgery. This is a real world study and we did not have the ethical permission to investigate parameters of interest in patients who had not filled in the QuickDASH questionnaires and by that chosen not to participate in any research on the matter. We could not include data on alcohol consumption due to insufficient data.

Conclusions

Patients with diabetes without neuropathy, as well as patients with hypertension, obesity or statin treatment, and CTS can expect the same effects of open carpal tunnel release as otherwise healthy patients. Patients with diabetic neuropathy and CTS did not experience the same improvement as otherwise healthy patients and should be informed about the risk of an unsatisfactory outcome.

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Figure legends

Figure 1. Flow chart to describe the process of including patients.

Table I. Characteristics of included patients with carpal tunnel syndrome and treated with open carpal tunnel release

	All patients n=493	Diabetes n=76	No diabetes n=412^a	Diabetes and polyneuropathy n=18	Diabetes no polyneuropathy n=58	Hyper-tension n=143	No hyper-tension n=342^b	Statin treatment n=86	No statin treatment n=401^c	Obesity (BMI≥30) n=136	No obesity (BMI≤30) n=321^d
Female gender number (%)	343 (70)	46 (60)	295 (72) *	14 (78)	34 (54)	94 (66)	246 (72)	51 (59)	290 (72) *	82 (60)	236 (74) *
Age (years) median [IQR]	55 [45-66]	60 [48-70]	55 [45-66] *	60 [50-72]	60 [48-69]	66 [60-77]	51 [41-59] ***	67 [57-75]	53 [44-63] ***	54 [44-64]	56 [46-68]
BMI median [IQR]	27 [24-31]	29 [25-33]	27 [24-30]*	28 [25-33]	29 [25-33]	29 [26-33]	27 [24-30] ***	29 [25-32]	27 [24-31]*	33 [31-36]	25 [23-27] ***
BMI≥30 number (%)	136 (28)	29 (38)	107 (26) *	6 (33)	23 (40)	56 (39)	80 (23) ***	29 (32)	107 (27)		

Diabetes Mellitus number (%)	76 (15)					37 (26)	37 (11) ***	39 (45)	37 (9) ***	29 (21)	40 (12) *
Hypertension number (%)	143 (29)	37 (49)	106 (26) ***	10 (56)	27 (47)			52 (60)	91 (23) ***	56 (41)	73 (23) ***
Polyneuropathy number (%)	26 (5)	18 (24)	7 (2) ***			14 (9)	11 (3) *	12 (13)	13 (3) ***	9 (6)	16 (5)
Statin treatment number (%)	86 (17)	39 (51)	47 (11) ***	12 (67)	27 (47)	52 (36)	33 (10) ***			29 (21)	52 (16)
SCV median nerve at wrist (m/s) median [IQR]	31 [22-38]	28 (19-36)	32 [24-40] *	29 [23-37]	27 [19-36]	25 [3-33]	34 [26-41] ***	29 [23-37]	32 [22-39]	28 [20-36]	33 [24-40]

*p<0.05 **p<0.001 ***p<0.0001

Comparisons between groups (diabetes vs. no diabetes, diabetes with polyneuropathy vs. diabetes without polyneuropathy, hypertension vs. no hypertension, statin treatment vs. no statin treatment, obesity vs. no obesity). First column for reference. Asterisk indicating statistical significance for comparison with the group found in column to the left of column with asterisk.

Continuous data presented as median [IQR]. Nominal data presented as number of patients (percentage, %).

a= 5 cases were omitted due to missing data; b=8 cases were omitted due to missing data; c=6 cases were omitted due to missing data; d= 37 cases were omitted due to missing data.

IQR= Interquartile range. SCV = Sensory Conduction Velocity. BMI = Body Mass Index.

Table II. QuickDASH results in patients with carpal tunnel syndrome treated with open carpal tunnel release.

	All patients n=493	Diabetes n=76	No diabetes n=412 ^a	Diabetes and poly-neuropathy n=18	Diabetes no poly-neuropathy n=58	Hypertension n=143	No hypertension n=342 ^b	Statin treatment n=86	No statin treatment n=401 ^c	Obesity (BMI≥30) n=136	No obesity (BMI≤30) n=321 ^d
Preoperative score median [IQR]	50 [32-66]	56 [36-77]	48 [32-66] *	78 [57-85]	48 [35-71] *	48 [32-65]	50 [33-67]	48 [34-69]	50 [32-66]	48 [27-64]	50 [34-68]
Postoperative score median [IQR]	18 [5-45]	31 [9-61]	16 [5-43] **	61 [41-76]	20 [9-59] **	20 [5-50]	18 [5-45]	22 [7-54]	18 [5-45]	16 [5-43]	20 [5-45]
Postoperative score >10 number (%)	308 (63)	56 (74)	250 (61) *	18 (100)	38 (66) *	90 (63)	214 (63)	55 (64)	250 (62)	83 (61)	202 (63)
Change in QuickDASH score	21 [8-36]	19 [3-36]	21 [9-36]	13 [-6-24]	24 [5-39]	20 [6-36]	21 [9-36]	20 [7-35]	21 [8-36]	20 [9-36]	21 [7-36]

median [IQR]											
Change in QuickDASH score <8 number (%)	124 (25)	24 (32)	99 (24)	7 (39)	17 (29)	38 (27)	85 (25)	22 (26)	101 (25)	29 (21)	89 (28)

*p<0.05 **p<0.001

Comparisons between groups (diabetes vs. no diabetes, diabetes with polyneuropathy vs. diabetes without polyneuropathy, hypertension vs. no hypertension, statin treatment vs. no statin treatment, obesity vs. no obesity). First column for reference. Asterisk indicating statistical significance for comparison with the group found in column to the left of column with asterisk.

Continuous data presented as median [IQR]. Nominal data presented as number of patients (percentage, %).

a=5 patients were omitted due to missing data; b=8 patients were omitted due to missing data; c= 6 patients were omitted due to missing data; d= 37 patients were omitted due to missing data.

IQR = Interquartile range.

Table III. QuickDASH results in patients with diabetes, *without* neuropathy, and carpal tunnel syndrome treated with open carpal tunnel release compared to patients without diabetes and without neuropathy. All patients with diagnosed polyneuropathy are excluded from this comparison.

	With diabetes (n=58)	Without diabetes (n=399)
Preoperative score median [IQR]	48 [35-71]	48 [30-66]
Postoperative score median [IQR]	20 [9-59]	16 [5-43]
Postoperative score >10 number (%)	38 (66)	240 (60)
Change in QuickDASH score median [IQR]	24 [5-39]	21 [9-36]
Change in QuickDASH score <8 number (%)	17 (29)	93 (23)

None of the calculations reached statistical significance ($p>0.05$).

IQR = Interquartile range

Table IV. Logistic regression. Crude and adjusted odds ratios for change <8 in QuickDASH total score and postoperative score >10

	Dependent variable: change <8 in total score		Dependent variable: postoperative score >10	
	OR	Adjusted OR	OR	Adjusted OR
Age	1.01 (0.99-1.02)	1.00 (0.99-1.02)	1.01 (1.00-1.02)	1.01 (1.00-1.03)
Gender (female)	1.09 (0.71-1.66)	1.17 (0.75-1.85)	0.71* (0.49-1.04)	0.75* (0.49-1.13)
BMI≥30	0.71 (0.44-1.14)	0.66 (0.40-1.10)	0.92 (0.61-1.39)	0.97 (0.62-1.52)
Diabetes Mellitus	1.46 (0.86-2.49)	1.20 (0.61-2.36)	1.81* (1.05-3.14)	1.85 (0.94-3.65)
Hypertension	1.09 (0.70-1.71)	0.99 (0.56-1.75)	1.02 (0.68-1.52)	0.82 (0.49-1.39)
Polyneuropathy	2.70* (1.22-6.02)	2.62* (1.05-6.54)	7.78 *(1.80-33.10)	11.58* (1.50-89.70)
Statin treatment	1.02 (0.60-1.74)	0.91 (0.47-1.73)	1.07 (0.66-1.74)	0.74 (0.40-1.36)

Odds ratio (OR) with 95% confidence interval (CI) in brackets. *p<0.05

Table V. Linear regression analysis. The effect of individual variables on change in total score.

	Model 1. Diabetes Mellitus and polyneuropathy.	Model 2. BMI\geq30, Diabetes Mellitus, hypertension, polyneuropathy, statin treatment.
BMI\geq30		-0.01 (-4.35 – 4.33)
Diabetes Mellitus	-2.62 (-8.21 – 2.96)	-2.95 (-9.28 – 3.39)
Hypertension		-0.93 (-5.62 – 3.76)
Polyneuropathy	-11.5 (-20.7 – -2.36)*	-11.0 (-20.3 – -1.73)*
Statin treatment		-0.64 (-5.21 – 3.76)
Constant	23.5 (21.4 – 25.5)***	23.4 (20.7– 26.0)***
N	481	450
Adjusted R²	0.016	0.011

Dependent variable: Change in total score. Unstandardized b-coefficients, 95% confidence interval (CI) in brackets. BMI = Body Mass Index. *p<0.05, ***p<0.0001