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CHAPTER 4

Quality of life is improved for at least 18 months by the addition of exercise to a 16-week very low calorie diet in obese patients with type 2 diabetes mellitus

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ABSTRACT

Objective. To evaluate whether the addition of exercise to a very low calorie diet (VLCD) has beneficial short- and long-term effects on health-related Quality of Life (QoL) in obese patients with type 2 diabetes mellitus (T2DM).

Methods. We included 27 obese, insulin-dependent T2DM patients in a 16-week VLCD study, of whom 13 participated simultaneously in an exercise program (VLCD+E). Before, immediately after and 18 months after the intervention anthropometric measurements, glucoregulation and QoL (SF-36, HADS, NHP and MFI-20) were assessed. Patients were compared to healthy lean and obese (matched for body mass index) controls matched for gender and age.

Results. At baseline, T2DM patients had significantly worse QoL scores in 18 and 14 of the 22 subscales of the QoL questionnaires, compared to lean and obese controls, resp. The 16-week VLCD (n=27) decreased bodyweight (-25.4 ± 1.3 kg, $p < 0.0001$, $p = 0.179$ between groups), and improved glucoregulation (HbA1c $-1.3 \pm 0.3\%$, $p < 0.0001$, $p = 0.488$ between groups) and 9 (VLCD-only) and 11 (VLCD+E) of the 22 subscales of QoL. After 18 months, in the VLCD+E group the QoL subscales did not differ from those in obese controls and only 4 of the 22 subscales were significantly worse compared to lean controls. However, in the VLCD-only group 17 and 13 of the 22 QoL subscales were significantly worse compared to the lean and obese controls, resp.

Conclusion. A 16-week VLCD induces considerable weight loss, metabolic amelioration, and major improvements in QoL in obese T2DM patients. The addition of exercise is of paramount importance for the maintenance of better QoL.

INTRODUCTION

The number of patients with type 2 diabetes (T2DM) is steadily increasing. Almost 90% of T2DM patients are overweight or obese. Medical attention is focused primarily on improving metabolic control to diminish long-term complications. However, patients with chronic diseases such as T2DM also have a poorer health-related quality of life (QoL) compared to healthy control subjects (1). Reduced QoL not only affects individual happiness but may also have impact on participation in the working process, social functioning, compliance to therapy and hence socioeconomic costs.

Improvement of QoL in T2DM patients is associated with an increase in self-management, adherence to therapy and positive changes in lifestyle (2). The magnitude of the effects on QoL is dependent on the type of intervention. Behavioral interventions have the smallest effect, but are nevertheless able to improve QoL, reduce the number of hospitalizations and use of medication (2,3). Bariatric surgery has the largest effect on QoL, mainly through the loss of excess weight and the waning of obesity-associated symptoms (2,4). However, surgery is expensive, invasive, associated with substantial morbidity. Furthermore it is logistically impossible to operate all obese patients with T2DM. Therefore, diet and lifestyle interventions remain the mainstay of therapy for most obese T2DM patients.

Diet-induced weight loss improves QoL in the short-term but not in the long-term, mostly because of regain of bodyweight (3). The effect of exercise on QoL in T2DM patients is less clear (5,6).

Therefore, the aim of this study was to assess whether addition of exercise to a 16-week very low calorie diet (VLCD) in obese, insulin-dependent T2DM patients has greater effects on QoL than a VLCD-only, both immediately after the 16-week intervention and 18 months after the intervention. Secondary aims were to compare QoL in our T2DM patients with lean and obese healthy controls.

PATIENTS AND METHODS

Patients

Twenty-seven obese (body mass index (BMI) 37.2 ± 0.9 kg/m²), insulin-dependent T2DM patients (age 58.0 ± 1.6 years, duration of T2DM 8.9 ± 0.8 years, 58 ± 8 months on insulin therapy) participated in the study. Inclusion criteria were insulin-dependent T2DM patients (who used at least 20 EH of insulin per day) with or without oral glucose-lowering medication; at baseline a BMI above 30 kg/m²; remaining endogenous insulin secretion defined as a fasting plasma C-peptide level greater than 0.8 ng/mL and a 2-fold increase of the basal C-peptide level in response to administration of 1 mg glucagon intravenously. Exclusion criteria were recent weight changes; smoking; any other chronic (endocrine) conditions; signs of depres-

sion or antidepressant medication and silent cardiac ischemia. Patients were recruited via advertisements in local news papers and from the endocrinology and internal medicine out-patient clinics of our hospital.

For each T2DM patient, 2 lean and 2 obese control subjects, matched for age, gender, race and in the obese group for BMI, were included. Control subjects were recruited via advertisements in local news papers.

The Medical Ethics Committee of the Leiden University Medical Center approved the study protocol. Written informed consent was obtained from each subject.

Study design

In all T2DM patients oral blood glucose-lowering medication was discontinued 3 weeks prior to the start of the intervention. One day before the start of the intervention, insulin therapy was stopped as well. The patients did not use any anti-diabetic medication during the whole 16-week intervention period.

At day 0 baseline observations were obtained in all patients (outlined below), followed by a 16-week intervention period. The intervention period consisted of a 16-week VLCD with or without the addition of an exercise program. The VLCD contained a total of ~450 kilocalories per day, divided into 3 sachets of Modifast® (Nutrition & Santé, Antwerpen, Belgium). Modifast® provides all necessary vitamins and micronutrients.

Thirteen of the 27 subjects were randomized to follow an exercise program simultaneously. This exercise program entailed one-hour in-hospital training per week (primarily aerobic exercise, supervised by a physiotherapist) and at least four training sessions at home on a cyclo-ergometer at 70% of their maximum aerobic capacity (VO_{2max}).

At the start, immediately after and 18 months after the 16-weeks intervention period, patients visited the research center after an overnight fast. Height, weight and waist circumference were measured. Fat mass was determined by bioelectrical impedance analysis (Bodystat® 1500 MDD, Bodystat Ltd., Douglas, Isle of Man, UK). Blood samples were obtained for fasting plasma glucose (FPG), insulin and HbA1c levels.

To assess QoL, patients were asked to fill in 4 different questionnaires. Each patient completed the questionnaires before, directly after, and 18 months after the intervention, resulting in a 100% response rate. The healthy (lean and obese) controls were asked to complete the QoL questionnaires only once.

During the 16-week intervention the subjects visited the outpatient clinic weekly, for measurement of weight and to check glucoregulation. Furthermore, compliance with the diet and exercise was established by counting sachets of Modifast that were supplied weekly and reading the heart rate monitor, that was worn during the exercise sessions (Polar S610tm, Polar Electro Oy, Finland). After the 16-week intervention period patients were treated according to current guidelines either in the primary care setting or at the out-patient clinic of our hospital. A follow-up visit for further investigation was scheduled 18 month later. All

patients completed the whole study period of 18 months, there were no dropouts from the study.

Questionnaires

Short Form-36 (SF-36)

The 36 items of the SF-36 record general well-being during the previous thirty days. The items are formulated as questions or statements and are subdivided into nine subscales: (1) physical functioning, (2) social functioning, (3) limitations in usual role activities due to physical problems, (4) limitations in usual role activities due to emotional problems, (5) bodily pain, (6) general health perception and change in health, (7) general mental health and (8) vitality (energy and fatigue) (9) health change. Because the HADS and the MFI-20 (see below) are more specific questionnaires for mental health, vitality and general mental health, these items were left out in this evaluation. Scores vary between 0 and 100. Higher scores are associated with a higher quality of life. (7).

Multidimensional Fatigue Index (MFI-20)

The MFI-20 contains 20 statements to assess fatigue. Five different dimensions of fatigue (four items each) are calculated from these statements: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. Scores fluctuate between 0 and 20; higher scores indicate more fatigue (8).

Hospital Anxiety and Depression Scale (HADS)

The HADS consists of fourteen items pertaining to the three subscales anxiety, depression and total score. Every item is scored on a four-point scale. Scores for the anxiety and depression subscale range from 0 to 21 and the total score from 0 to 42. A higher score indicates more severe anxiety or depression (9).

Nottingham Health Profile (NHP)

The NHP consists of 38 yes/no questions, subdivided in six scales: pain, energy, sleep, emotional reactions, social isolation and disability/ functioning, i.e. physical ability. The scores of the subscales are calculated as a weighted mean of the associated items. The scores are expressed as a value between 0 and 100 and the total score is the mean of the six subscales. A higher score is related to a worse quality of life (10).

Total QoL score

For an integral comparison of the QoL parameters addressed in the 4 questionnaires, our research-group developed a total QoL score which is the sum of all different QoL questionnaires. As described previously (11), all subscales were converted to a 100-point score. The

SF-36 scores were inverted so that a higher score is a worse QoL. Subsequently all subscale scores were added and a mean was calculated, generating a total QoL score (minimum value 0, maximum value 100). A higher score indicates a greater impairment of QoL

Assays

FPG were measured with a fully automated P-800 module (Roche, Almere, the Netherlands). Serum insulin was measured with an immunoradiometric assay (IRMA, Biosource, Nivelles, Belgium). HbA1c was measured with a semi automated HPLC machine Primus Ultra 2 (Kordia, Leiden, the Netherlands)

Homeostatic Model Assessment of Insulin Resistance (HOMA-IR, normal values approach 1) was calculated from FPG and insulin levels according to the updated computed version of the formulae of Wallace et al (12).

Statistical analyses

Data are presented as mean \pm SEM. Data analyses were performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA). Differences between all groups (the two intervention groups and the two healthy controls) were analyzed using a one-way ANOVA. Differences within the group between the three different time points (baseline; directly after the intervention and 18 months after the intervention) were analyzed with a general linear model (GLM) for repeated measures, with time as within-subject factor. LSD post-hoc tests were used in case of a significant F-ratio. Differences in effect of the intervention between both intervention groups were analyzed by calculating a delta between two time points. The delta values were subsequently compared by non-parametric tests for independent samples or, when appropriate, by a two tailed Student's *t*-test for unpaired data. A *p*-value of < 0.05 was considered to be statistically significant.

RESULTS

Baseline characteristics

Clinical characteristics of the patients and healthy controls are shown in Table 1. Baseline characteristics of the two patient groups (VLCD with exercise (VLCD+E) and VLCD-only) were not different. The lean and obese control groups had significantly lower levels of FPG, insulin and HbA1c compared to the patients. The obese controls were well matched with respect to weight, BMI and waist circumference to the T2DM patients.

Short- and long-term effect of a 16-week VLCD on bodyweight and glucoregulation

After the 16-week intervention both groups (VLCD+E and VLCD-only) showed a significant improvement in clinical and metabolic characteristics. There was an impressive loss of weight in

Table 1: Clinical and metabolic characteristics at baseline, directly after and 18 months after a 16-week VLCD only or VLCD with exercise in obese insulin-dependent T2DM patients and comparisons with (obese and lean) healthy controls.

	VLCD + exercise			VLCD only			controls	
	baseline	16 weeks	18 months	baseline	16 weeks	18 months	obese	lean
sex (M/F)	8/5			6/8			28/26	28/26
age (years)	53±3			56±2			56±1	59±2
weight (kg)	114±5 *	86±4 !	98±5 !	113±6 *	89±4 !	103±5 !	112±3 *	73±2
BMI (kg/m ²)	36.4±1.1 *	27.7±1.0!	31.6±1.2 !	37.9±1.4*	30.0±1.1!	34.7±1.3 !	37.6±0.7*	23.8±0.3
waist (cm)	123±3 *	98±3 !	107±4 !	122±3 *	103±3 !	114±3 !	118±2 *	87±1
fat mass (kg)	45.4±3.2*	23.5±2.2!	35.4±2.6 !	49.9±3.6*	33.2±2.8!	44.2±3.0 !	39.2±2.4*	33.4±2.2
HbA1c (%)	7.8±0.4* #	6.3±0.4!	7.5±0.6	7.8±0.3* #	6.7±0.3!	8.2±0.5	5.5±0.1 *	5.2±0.0
fasting glucose (mmol/L)	10.9±0.7* #	6.6±0.8!	9.2±1.0	12.1±0.5* #	7.7±0.6!	12.2±1.1	5.5±0.1 *	4.9±0.1
fasting insulin (mU/L)	25±2 * #	9±1 !	13±2 !	24±4 * #	13±2 !	17±6	14±1 *	5±0
HOMA-IR	12.3±1.3* #	2.5±0.2!	4.7±0.8 !	12.9±2.3* #	4.3±0.8!	9.0±3.1	3.4±0.3*	1.1±0.1

Data are presented as mean ± SEM. ! significant difference vs. baseline values within the group; * significant difference vs. lean controls; # significant difference vs. obese controls

M: male; F: female; BMI: body mass index; HOMA-IR: homeostatic model assessment insulin resistance

all subjects (-27.2±1.9 kg VLCD+E; -23.7±1.6 kg VLCD-only), which consisted mostly of fat mass (-21.8±2.2 kg VLCD+E; -16.6±1.7 kg VLCD-only). There was significantly more loss of fat mass and waist circumference in the VLCD with exercise group. FPG and HbA1C levels improved substantially (respectively p=0.910 and p=0.488 between groups), despite the cessation of all glucose-lowering medication throughout the 16-week intervention period (Table 1).

After 18 months both groups had regained some weight. However, weight was still significantly decreased compared to baseline observations (Table 1). The beneficial effects of the 16-week intervention on HbA1c and FPG levels were also decreased. Nonetheless, the patients still used substantially less glucose-lowering medication than before the intervention (Table 2). Fasting insulin and HOMA-IR levels were only significantly better after 18 months compared to baseline in the VLCD with exercise group.

Table 2: Overview of medication used at baseline, directly after and 18 months after a 16-week VLCD only or VLCD with exercise in obese insulin-dependent T2DM patients.

	VLCD + exercise			VLCD only			controls	
	baseline	16 weeks	18 months	baseline	16 weeks	18 months	obese	lean
insulin (number of pts)	13	0	0	14	0	6	0	0
insulin (EH/day)	77	0	0	86	0	36	0	0
metformin (number of pts)	10	13	12	9	14	12	0	0
SU derivative (number of pts)	3	0	4	1	0	4	0	0
exercise (minutes/week)	34	180	192	24	0	45	82	167

pts: patients; SU: sulfonylureum

Short- and long-term effect of VLCD with or without exercise on QoL

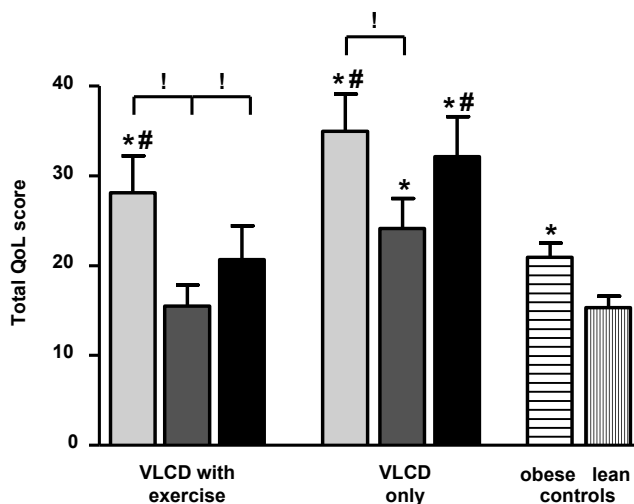
The results of the QoL questionnaires before, immediately after and 18 months after the intervention period are shown in Table 3. At baseline there were no differences in QoL between

Table 3: Quality of life (QoL) at baseline, directly after and 18 months after a 16-week VLCD only or VLCD with exercise in obese insulin-dependent T2DM patients and comparisons with (obese and lean) healthy controls. Short form-36 (SF-36): score 1-100 higher scores are associated with better QoL. Multidimensional fatigue index-20 (MFI-20): score 1-20 higher scores indicate higher experienced fatigue. Hospital Anxiety and depression scale (HADS): scores 0-21, higher score indicated more severe anxiety or depression. Nottingham Health Profile (NHP): score 0-100, higher score is related to a worse QoL.

	VLCD + exercise			VLCD only			controls	
	baseline	16 weeks	18 months	baseline	16 weeks	18 months	obese	lean
SF-36								
Physical functioning	72±6 *#	82±6 ! *	83±5 ! * ?	63±5 *#	78±6 ! *	68±7 *#	81±3 *	94±1
Social functioning	81±6 *#	88±3	87±8	79±5 *#	88±4	80±4 *#	91±2	93±2
Limits due to physical problems	65±11 *#	90±5 !	75±9 *	68±10 *#	71±10 *	59±11 *#	85±4	94±2
Limits due to emotional problems	95±5	100±0	100±0	74±9 *#	86±8	86±8	90±4	94±2
Pain	79±8 *	85±6	82±8	70±6 *	72±6 *	70±6 *	80±3 *	91±2
General health perception	52±6 *#	76±6 !	68±5 ! * ?	51±5 *#	58±5 *#	51±6 *#	74±2 *	80±2
Health change	50±7	92±3 ! *#	67±7 *#	55±7 *#	88±6 ! *#	66±7 #	51±2	55±2
MFI-20								
General fatigue	12±1 *#	7±1 !	9±1 ! ?	14±1 *#	10±1 ! *	12±1 *#	9±1 *	7±1
Physical fatigue	12±1 *#	7±1 ! #	8±1 ! ?	13±1 *#	9±1 ! *	12±1 *#	9±1 *	6±0
Reduction in activity	10±1 *	8±1	7±1 ! ?	12±1 *#	8±1 !	10±1 ! *	8±1	7±1
Reduction in motivation	8±1 *	6±1 !	7±1	10±1 *#	8±1	10±1 *#	7±1	6±0
Mental fatigue	9±1	7±1	8±1	8±1	7±1	8±1	8±1	8±1
HADS								
Anxiety	4±1	3±1 !	4±1	5±1 *#	4±1 !	4±1	3±0	3±0
Depression	3±1	1±0	2±1 ?	5±1 *#	3±1 !	5±1 *#	3±0 *	2±0
Total	7±1	4±1 !	6±1 ?	10±1 *#	7±1 !	9±1 *#	6±1	5±1
NHP								
Energy	18±7 *	2±2 !	11±8 ?	36±11 *#	9±5 !	31±12 *#	7±3	4±2
Pain	13±8 *	9±7	15±9	20±6 *#	21±7 *#	18±6 *	8±2	4±2
Emotional reaction	4±2	5±2	3±2	9±3 *	7±3	9±4 *	4±1	2±1
Sleep	10±6	11±6	15±5 ?	21±7 *#	30±10 *#	30±9 *#	9±2	5±2
Physical ability	14±5 *#	4±2 !	12±5 *	15±5 *#	5±3	15±5 *#	7±2 *	3±1
Social isolation	0±0	0±0	0±0	2±2	0±0	0±0	3±1	1±1
NHP total score	10±3 *	5±2	9±4 ?	17±5 *#	12±3 *#	17±4 *#	6±1 *	3±1

Data are presented as mean ± SEM. ! significant difference vs. baseline values within the group; * significant difference vs. lean controls; # significant difference vs. obese controls; ? significant difference between the VLCD + exercise and VLCD-only.

Figure 1. Total Quality of life (QoL) score before (grey bars), directly after (dark grey bars) and 18 months (black bars) after a 16-week VLCD only or VLCD with exercise in obese insulin-dependent T2DM patients and comparisons with (obese and lean) healthy controls (white bars).



Data are presented as mean \pm SEM. ! significant difference vs. baseline values within the group; * significant difference vs. lean controls; # significant difference vs. obese controls.

the two intervention groups. All patients scored significantly better directly after the 16-week intervention compared to baseline measurements on several subscales but mostly those concerning fatigue and physical ability. The VLCD with exercise group scored significantly better on 11 of the 22 subscales (i.e. the total of subscales of all four questionnaires) after the 16-weeks intervention. These results were partly lasting, since after 18 months still 5 of the 22 subscales remained improved. The VLCD-only group had a similar improvement in 9 of the 22 subscales directly after the 16-week intervention. However, in this group all but one subscale of QoL had returned to baseline levels at 18 months.

The total QoL score (Figure 1) improves equally in both groups directly after the 16-week intervention. However only in the VLCD with exercise group this effect is lasting.

QoL in healthy controls vs. patients

At baseline, T2DM patients scored significantly worse on subscales concerning mostly physical functioning and fatigue compared to both lean and obese healthy controls of the same gender, age and ethnicity (Table 3). Also the total QoL score is significantly worse in both groups compared to lean and obese controls

Immediately after the 16-week intervention program, most QoL scores improved, even to the level of the lean control subjects. In the VLCD with exercise group patients performed worse only at 1 of the 22 subscales compared to lean or obese controls. The VLCD-only group performed worse at 9 and 4 of the 22 subscales compared to healthy lean and obese controls, resp. The total QoL score in the VLCD with exercise group improved to the level of the healthy

lean controls. The patients in the VLCD-only group also improved but not beyond the level of the total QoL score of the obese control group.

The difference between the two intervention groups became more apparent after 18 months. In the VLCD with exercise group the improvements in QoL persisted, none of the subscales differed from obese controls and only 4 of the 22 subscales were significantly worse compared to healthy lean controls after 18 months. The total QoL score also showed a persistent improvement; after 18 months there were still no significant differences in total QoL scores between patients in the VLCD with exercise group and healthy lean and obese controls. However, the QoL scores of the VLCD-only group returned almost back to their original levels; 17 and 13 of the 22 items were significantly worse compared to the lean and obese healthy controls, resp. In addition, the total QoL score of the VLCD-only group after 18 months follow-up was significantly worse than that of healthy lean and obese controls.

In one of the subscales of the SF-36 namely health change both patients groups scored significantly better directly after the intervention compared to both lean and obese control subjects. In the VLCD with exercise group this was a lasting effect up to 18 months after start of the intervention. In the VLCD-only group, patients only scored significantly better compared to the obese control subjects.

DISCUSSION

This study demonstrates that QoL parameters are considerably impaired in obese, insulin-treated T2DM patients. Treatment with a 16-week VLCD with or without an exercise regimen considerably improved QoL, associated with major improvements in anthropometric characteristics and metabolic regulation. However, long-term follow-up shows that exercise is vital in maintaining the achieved anthropometric, biochemical and QoL improvements. Ultimately, in the VLCD with exercise group the total QoL score did not differ and only 4 of the 22 QoL subscales negatively differed from the values obtained in healthy lean controls. In contrast, the achieved improvements in QoL and gluoregulation were completely abolished in patients in the VLCD-only group after 18 months.

Our patients scored slightly better in the HADS items (anxiety and depression) at baseline compared to the T2DM patients described by Pouwer et. al (13). This might be due to the exclusion of patients with psychiatric problems and the use of antidepressant drugs in the present study. In addition, our patients were slightly younger, which is relevant since increasing age is associated with decreased QoL (14). As far as we know, the MFI-20 questionnaire (containing items concerning fatigue) has not been performed previously in T2DM patients. The NHP questionnaire (containing item regarding physical ability, social isolation energy levels) has been used sporadically in T2DM patients (15), whereas the SF-36 is the most used health-related QoL questionnaire (recording general well-being during the previous thirty

days) regardless of the population that is tested. Our patients and T2DM patients from previous other studies had comparable scores for the NHP and SF-36 questionnaire at baseline (4,15,16).

Our finding that diet-induced weight loss can lead to improvements in QoL directly after the intervention is in agreement with other studies (2,16). For example, Kaukua et al. (16) reported improvement in physical functioning and perception of health change related to weight loss after a low caloric diet in combination with Sibutramine or placebo measured by SF-36 in T2DM patients.

Several factors might have contributed to the improvement in QoL in our patients. Firstly, all patients lost a considerable amount of weight. Other studies have already shown that weight loss *per se* (e.g. after bariatric surgery) improves QoL (2). Secondly, insulin therapy was discontinued during the entire 16-week intervention period in our T2DM patients. After the intervention none of the patients in the VLCD with exercise group and almost 2/3 of the patients in the VLCD-only group still did not use insulin at 18 months follow-up. The use of insulin is associated with a lower QoL because of the burden of injections and self-control (1). Thirdly, the oral glucose-lowering medication was stopped as well, which may have decreased potentially present side-effects. However, since these medications were reinstated after the intervention they cannot contribute to the lasting effect on QoL found in the VLCD with exercise group. The same applies to the fourth issue: improved glycemic control. This can ameliorate QoL via a decrease in metabolic oscillations as well as via reduced fear for the occurrence of long-term diabetic complications (1). However, improved metabolic control was only present at 16 weeks, not at 18 months. Fifthly, the undoubtedly better physical condition, due to more minutes of exercise per week at 18 months (Table 2) in the exercise group, might have contributed to the lasting effect on QoL. Lastly, there may also be the confounding effect of participation in a study, because intensive counseling and education has been shown to improve QoL (17). However, this did not apply at 18 months of follow-up. In our study none of the above ascribed factors could independently predict the improvements in QoL (data not shown).

In contrast to what we hypothesized, the addition of an exercise program to a VLCD had no immediate additional positive effect on QoL as compared to a VLCD-only. This has also been reported by some (6,18), but not all previous publications (5,19). One possible explanation for this lack of a direct additional effect of exercise on QoL is that the magnitude of the achieved weight loss masked the effect of exercise. Moreover, it is possible that exercise also had some negative effects. For example, it may have increased muscle or joint pain or interfered with social life (19). However, this study clearly shows that exercise is of paramount importance in maintaining the diet-induced improvements in QoL, weight loss and gluco-regulation.

After the intervention patients were referred to their own health care provider. We were not able to influence treatment strategies, neither with respect to weight loss nor on metabolic regulation. This may be the reason that glycemic control was not as tight as required

by guidelines. Reluctance to reinstitute insulin therapy might have played a role. This makes it difficult to compare the two intervention groups regarding gluoregulation. The improvement in HOMA-IR and insulin levels after the 16-week intervention only lasted in the VLCD with exercise group. Moreover, in none of the patients in this group insulin therapy was restarted. Together these observations are suggestive of a better gluoregulation and less insulin resistance after 18 months in the VLCD with exercise group. We observed a lasting improvement in body weight in both groups. The long-term effect of a VLCD on bodyweight and gluoregulation (20-24) in obese diabetic patients has been addressed before. Some investigators found lasting improvements in gluoregulation but not on body weight (21,24) whereas others found a deterioration of both body weight and gluoregulation (22,23). Our group found improvements in both gluoregulation and body weight (20) 18 months after following a 30-day VLCD.

A limitation of the present study is the relatively small sample size. Nonetheless, our results are in line with the existing literature regarding the effects of bariatric surgery which also causes a significant amount of weight loss, on QoL.

The improvement of QoL in T2DM patients is an important treatment goal. Interventions aimed at improving the perceptions of patients of their physical and mental health can enhance their commitment to self-management and adherence to therapy which will lead to positive lifestyle changes and better diabetes control. Therefore, our finding of an improved QoL after a 16-week VLCD with or without exercise in obese, insulin-dependent T2DM patients is very relevant. The positive effect of weight loss on QoL, in addition to its beneficial effects on glycemic control, insulin resistance and cardiovascular risk factors, should stimulate T2DM patients and health care givers to make a serious effort in achieving and maintaining weight loss. For that matter, we emphasize the paramount importance of exercise in maintaining the positive effects achieved by diet-induced weight loss.

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