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Effects on body weight of strict or liberal adherence to an initial period of VLCD treatment. A randomised, one-year clinical trial of obese subjects

JS:son Torgerson[1,2], L Ågren[2] and L Sjöström*[1,2]

[1]*SOS secretariat, Department of Medicine, Sahlgrenska University Hospital, 413 45 Göteborg, Sweden and* [2]*Clinical Metabolic Laboratory, Department of Medicine, Sahlgrenska University Hospital, 413 45 Göteborg, Sweden*

OBJECTIVES: To examine the impact on early and late weight loss of three different, initial very low calorie diet (VLCD) approaches in a one-year obesity treatment program.
DESIGN: Randomised clinical trial.
SUBJECTS: 121 obese subjects, aged 21–60 y, BMI $\geq 30.0\,kg/m^2$.
INTERVENTIONS: The VLCD-strict group was prescribed a strict outpatient VLCD for 16 weeks, followed by a 36-week hypocaloric diet. The VLCD-mw group received the same treatment, but were hospitalised in a metabolic ward for the initial week. The VLCD-plus group was allowed two small meals weekly, but received otherwise the same recommendations as the VLCD-strict group.
RESULTS: After 16 weeks, there was no difference in weight loss between the treatment groups in the intent-to-treat population, while among completers, the weight loss was about 7 kg larger in the VLCD-strict group compared to the VLCD-plus group ($P < 0.05$). At one year, these groups differed by approximately 4 kg, both according to intention-to-treat and among completers ($P < 0.05$, both differences). These differences were more prominent among females. The weight reduction in the VLCD-mw group was generally not superior to the VLCD-strict group.
CONCLUSIONS: In the short-term, strict VLCD only reduced weight better than a liberal VLCD approach among completers. However, after one year, a strict VLCD regimen seemed beneficial compared to a liberal VLCD for all patients. There was no extra weight loss if the VLCD period was initiated on a metabolic ward.

Keywords: obesity; VLCD; randomised trial; strict *vs* liberal adherence; inpatient *vs* outpatient; females

Introduction

Very low calorie diets (VLCDs) have often been used in the treatment of obesity. Compared with hypocaloric diets, VLCDs are known to produce rapid and profound weight loss in the short-term.[1,2] There are a handful of randomised trials with long-term treatment and follow-up periods, comparing VLCD strategies with hypocaloric diets, within the framework of behavioural support programs.[3–9] Only the trial by Miura *et al*[6] shows a greater weight loss from a VLCD-based treatment compared with a hypocaloric diet. In the other long-term trials, VLCD strategies have not been superior to combinations of hypocaloric diet and behaviour modification.[3–5,7–9] Thus, the initial efficacy of VLCD treatment seems difficult to maintain.

Several authors have pointed at the need for individualised treatment for obesity, in order to improve weight loss and long-term maintenance of weight loss.[5,10] Data on predictors of weight loss and attrition, which would make individualisation possible are, however, scarce or inconsistent.[11] In a two-year study, Torgerson *et al*[9] found that a VLCD, followed by a supportive program (including a hypocaloric diet and behavioural support) was superior to the same supportive regimen alone, in men, but not in women.

The aim of the present one-year trial, was to investigate whether the design of the initial VLCD period could be of importance for early and final weight loss, in total or by gender. Three different 16-week VLCD approaches, followed by 36 weeks of an individualised hypocaloric diet, were compared under randomised conditions. We also wanted to identify baseline differences between drop-outs and patients completing the trial.

Methods

Subjects

Between February 1994 and April 1995, 277 patients were referred to the Clinical Metabolic Laboratory at

*Correspondence: Prof Lars Sjöström, SOS secretariat, Vita Stråket 15, Sahlgrenska University Hospital, 413 45 Göteborg, Sweden.
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Sahlgrenska University Hospital, for treatment of obesity. All patients met a physician for an initial evaluation and discussion of treatment options. Patients were eligible for inclusion in the present trial if they were aged 20–60 y and had a body mass index (BMI) $\geq 30.0\,kg/m^2$. The exclusion criteria were: severe somatic or mental disorder, previous bariatric surgery, abuse, probable non-compliance or participation in another clinical trial of obesity. Of the available patients, 51 did not meet the inclusion criteria and 64 did not comply with the exclusion criteria. Five patients were referred for bariatric surgery and 44 were unwilling to participate, mainly due to lack of time. Finally, the study was not discussed with 12 patients. Thus, 101 subjects wanted to participate and complied with inclusion and exclusion criteria. In addition, 20 patients already known at the Clinical Metabolic Laboratory were randomised after having met the above criteria. In all, 121 subjects were included in the study.

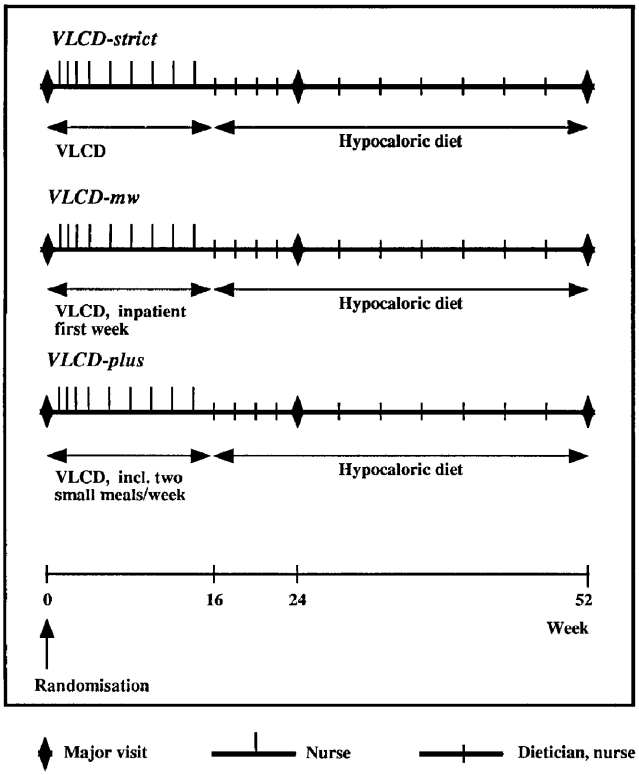

Figure 1 Schedule of all patient visits in the three study groups: very low calorie diet (VLCD)-strict, VLCD-mw and VLCD-plus.

Principal design and randomisation

Patients were randomised to one of three treatment groups: VLCD-strict, VLCD-mw or VLCD-plus. Figure 1 describes the study design and patient visits. The study was approved by the ethics committee at the Faculty of Medicine, University of Göteborg, and all patients gave their written informed consent before randomisation. Patients were stratified into eight groups (male or female, aged ≥ 50 y or less and with a BMI of $\geq 35.0\,kg/m^2$ or less) and randomised consecutively using eight sets of sealed, numbered envelopes. Within each of the eight groups, subjects were randomised in blocks of six (each treatment strategy times two) to optimise patient distribution regarding gender, age and BMI. Baseline data for the study groups are given in Table 1.

The different VLCD approaches

The VLCD period was 16 weeks, irrespective of treatment group. All patients were provided with Modifast® (NOVARTIS Nutrition, Bern, Switzerland) during the VLCD phase and were advised to

Table 1 Baseline characteristics and drop-out rates for 121 obese subjects by treatment group. Means, s.d. and range are shown.

	VLCD-strict			*VLCD-mw*			*VLCD-plus*		
	Mean	*s.d.*	*Range*	*Mean*	*s.d.*	*Range*	*Mean*	*s.d.*	*Range*
n		41			39			41	
Gender (male/female)		10/31			8/31			9/32	
Age (y)	41.4	10.8	23.0–59.0	41.1	11.7	21.0–60.0	45.4	9.6	26.0–59.0
Drop outs		19			15			14	
Weight (kg)	111.4	15.5	84.8–139.5	107.2	16.0	76.9–152.4	109.3	16.0	73.9–145.7
BMI (kg/m^2)	38.5	4.5	30.3–47.7	37.7	4.3	30.4–50.2	37.9	5.0	30.0–52.9
WHR	0.93	0.10	0.75–1.19	0.92	0.10	0.75–1.15	0.91	0.09	0.74–1.09
BF (kg)	49.0	8.0	28.4–64.2	48.0	9.5	28.2–68.4	49.4	9.9	30.9–80.7
FFM (kg)	60.8	13.8	42.6–96.7	59.2	12.8	41.3–89.2	59.9	13.0	43.0–89.3
Systolic BP (mm Hg)	129.1	21.3	100.0–180.0	133.7	24.0	90.0–210.0	128.0	15.2	110.0–160.0
Diastolic BP (mm Hg)	80.0	12.6	60.0–110.0	79.6	12.9	50.0–110.0	80.3	8.4	60.0–100.0
S-Cholesterol (mmol/L)	6.1	1.2	3.3–9.3	5.4	0.9	3.7–7.0	5.7	1.5	2.2–9.6
S-HDL (mmol/L)	1.3	0.3	0.8–2.0	1.2	0.3	0.8–1.8	1.2	0.3	0.7–2.0
S-LDL (mmol/L)	3.7	0.9	1.9–6.0	3.4	0.6	2.2–4.8	3.7	1.3	1.1–7.7
S-TG (mmol/L)	2.6	2.9	0.7–17.0	1.9	0.9	0.6–4.1	3.7	1.3	1.1–7.7
S-Insulin (mU/L)	18.7	8.8	8.0–44.0	18.5	12.0	5.1–65.0	21.4	15.6	6.0–75.0
B-Glucose (mmol/L)	5.0	1.8	3.2–12.2	4.7	2.0	3.3–14.0	5.0	2.6	2.8–15.6

No significant differences were observed between treatment groups.
VLCD = very low calorie diet; BMI = body mass index; WHR = waist-to-hip ratio; BF = body fat; FFM = fat free mass; BP = blood pressure; S = serum; HDL = high density lipoprotein; LDL = low density lipoprotein; TG = triglyceride; B-Glucose = blood glucose

consume three sachets every day, 1909 kJ/d (456 kcal/d). Patients were recommended to drink at least 2.5L of non-caloric fluid a day.

Subjects in the VLCD-strict and VLCD-mw treatment groups were recommended to strictly adhere to the VLCD and avoid other food items. Patients in the VLCD-mw group were hospitalised on a metabolic ward for the first week, then outpatients for 15 weeks and given the same instructions as the VLCD-strict patients. During the week on the metabolic ward, patients lived in a locked, single room to get started under strict VLCD conditions. Twice daily they went for a 30 min walk, accompanied by staff members, who also gave support and guidance.

The VLCD-plus patients were also prescribed a 1909 kJ/d VLCD, but were allowed two small meals weekly, to enable them to take part in a normal social life or to taste something they longed for. They had a free choice of food items, but were strongly encouraged to eat as little as possible, although portion sizes were not standardised.

Except for the first week in the VLCD-mw group, all patients continued their normal daily activities during the entire 16 week period.

Dietary treatment

After the VLCD period, ordinary food was gradually introduced during a three-week refeeding phase. All patients were then advised to consume an individualised hypocaloric diet aiming at an energy deficit of approximately 2100 kJ/d (500 kcal/d), with 15–20% of the energy intake (E%) from protein, 25–30 E% from fat and 50–55 E% from carbohydrates. A high intake of complex carbohydrates and fibre was recommended. Patients were strongly encouraged to adhere to three main meals a day and to avoid unplanned snacks. Food recommendations were based on Swedish nutritional guidelines.[12] Nutrition, food habits and 'every day' strategies to control eating behaviour were discussed with all subjects by experienced dietitians, as described previously.[9] Meal records focusing on the number of meals and when they were eaten were kept by all patients and discussed regularly with the dietitians.

MD and nurse

All the subjects met a physician three times for physical examination and evaluation of treatment and risk factors. The nurses were responsible for medical check-ups during the VLCD phase, and for blood sampling and measurements of body weight, blood pressure and body composition.

Measurements

Weight was measured to the nearest 0.1 kg using electronic scales calibrated monthly. Height was determined to the nearest 0.01 m. BMI (kg/m^2) was calculated from weight and height. Body weight and blood pressure were measured at each visit and waist-to-hip ratio (WHR) on the major visits. Patients were in the fasting state at the major visits.

A standard blood chemistry profile and electrocardiograms (ECGs) were analysed five times during the VLCD phase. Metabolic variables were analysed on all major visits, including fasting blood-Glucose, serum (S)-Insulin, S-Cholesterol (total), S-High density lipoprotein (S-HDL) cholesterol, S-Low density lipoprotein (S-LDL) cholesterol and S-Triglycerides (S-TG). The Department of Clinical Chemistry at Sahlgrenska University Hospital performed all biochemical analyses. The laboratory is accredited according to European norm, EN 45 001.

To describe variations in body composition during weight change, dual energy x-ray absorptiometry (DEXA), (Lunar DPX-L®, Madison, WI) or total body potassium (TBK) examinations were performed on the major visits. For technical reasons, DEXA examinations were performed on patients with body weights of ≤ 115.0 kg and TBK on heavier patients. However, all examinations of a given patient were performed with the same method as on the first major visit.

Using the DEXA technique, body fat (BF), lean tissue mass (LTM) and bone mineral content (BMC) were measured.[13] Gamma radiation from the naturally occurring isotope ^{40}K was measured in the TBK examinations. As ^{40}K constitutes a known fraction of potassium, the total body potassium content (mmol) can be estimated. Potassium is mainly (99%) located intracellularly and the fat free mass (FFM, kg) can thus be determined:[14,15]

$$\text{FFM (women)} = \text{TBK}/62.0$$

$$\text{FFM (men)} = \text{TBK}/64.7$$

$$\text{Body fat is calculated as: BF} = \text{Body weight} - \text{FFM}$$

BF obtained with DEXA and TBK are equivalent. LTM plus BMC obtained with DEXA are equivalent to FFM obtained using TBK. In this paper, FFM will be used as a common term for non-body fat, irrespective of whether DEXA or TBK examinations were performed on a given patient.

Statistics

Analyses of weight change were performed both on the 73 completers and on all 121 subjects on an intention-to-treat basis. For subjects withdrawing during the initial VLCD period, the last weight available was carried forward to the week-16 analyses, and for subjects withdrawing later, to the week 24 and/or week 52 analyses. An α-level of 0.05 and a power of 0.9 was used to calculate sample size. For statistics, the Minitab statistical package was used.[16] For changes in weight and body composition, ANOVA was used as a global test for difference between treatment groups, if the values were normally distributed. If the F-value was significant, Tukey's test was

then used for multiple pairwise comparisons. For changes within each treatment group, a paired *t*-test was used. If changes in weight or body composition were not normally distributed, the Kruskal-Wallis test was used to test for global differences. If significant, the Mann-Whitney-Wilcoxon rank sum test was then used for pairwise comparisons, with the α-level adjusted downwards by a factor of three to compensate for multiple comparisons. The Wilcoxon signed rank test was used for changes within groups if a variable was not normally distributed. A *t*-test or Mann-Whitney-Wilcoxon rank sum test was used for comparisons between completers and drop-outs. The chi-square test was used for analyses of nominal data. In the analyses of weight change between treatment groups, the α-level was not reduced to compensate for repeated comparisons. We argue that reiterated findings of the same type of difference reinforce the results and should not be compensated for. Changes in cardiovascular risk factors were analysed in relation to changes in body weight for all treatment groups pooled. Pitman's non-parametric test was used since the risk factor changes were not normally distributed. Linear regression coefficients were calculated, and used to estimate the magnitude of change in a given risk factor for a 10.0 kg reduction in body weight. To analyse if there were differences in estimated risk factor changes between treatment groups or between time periods, the regression coefficients were compared by use of a special *t*-test.

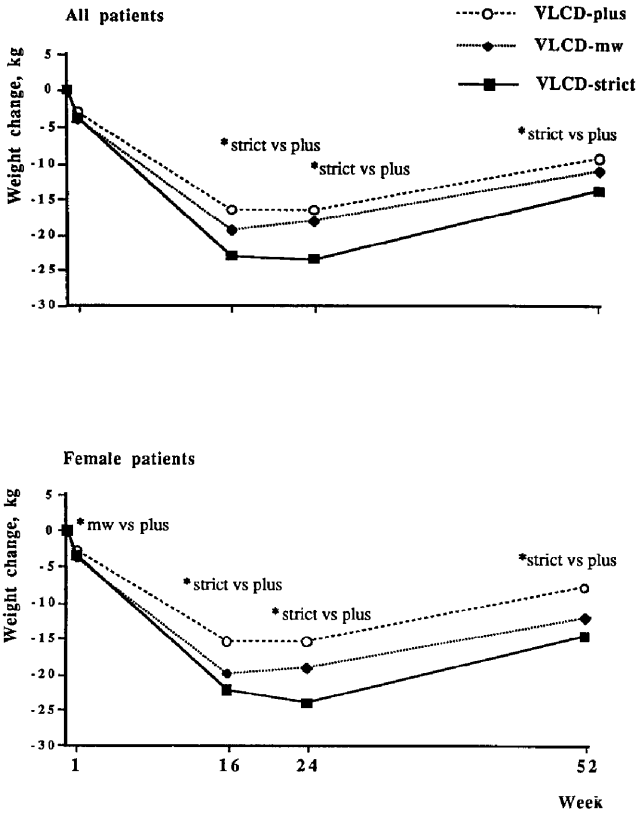

Figure 2 Weight changes by treatment group for patients who completed the trial. Upper panel: all patients, lower panel: female patients. Mean values are shown. Very low calorie diet (VLCD)-plus: open circles; VLCD-mw: filled diamonds; VLCD-strict: filled squares. *$P < 0.05$.

Results

Patient characteristics and safety

There were no significant differences between the treatment groups at baseline (Table 1).

The VLCD treatment was generally well tolerated and no serious or unexpected laboratory or ECG aberrations were seen. One patient with increasing liver test values between baseline and week four, and with elevated baseline values, was lost to follow-up. One female had an acute cholecystectomy due to cholecystitis.

Treatment differences

Figure 2 (upper panel) shows weight changes among completers. After one week there were no significant differences between the groups. After two weeks, subjects in the VLCD-strict group had lost significantly more weight than the VLCD-plus patients, -5.9 ± 2.2 kg *vs* -4.4 ± 1.6 kg ($P < 0.05$), (not shown). The difference between the VLCD-strict and VLCD-plus groups remained significant ($P < 0.05$) at week 16, week 24 and week 52. Weight loss in the VLCD-mw group did not differ significantly from the two other groups at any of the examinations.

In the intent-to-treat population, weight losses after 16 weeks were -16.4 ± 10.8 kg in the VLCD-strict group, -16.0 ± 7.6 kg in the VLCD-mw group and -13.8 ± 8.6 kg in the VLCD-plus group (not statistically significant, NS). At 24 weeks, a significant difference was found between the VLCD-strict group who lost -19.1 ± 10.5 kg and the VLCD-plus patients that lost -13.2 ± 9.8 kg ($P < 0.05$). After one year, the VLCD-strict group had lost -12.3 ± 10.0 kg, the VLCD-mw group -10.2 ± 7.5 kg and the VLCD-plus patients -8.6 ± 11.8 kg ($P = 0.06$ for global difference and $P = 0.03$ for VLCD-strict *vs* VLCD-plus), (not shown).

After 52 weeks, weight losses within each treatment group were highly significant both among completers and in the intent-to-treat population ($P < 0.001$). Among completers, there was no significant difference in the time to maximum weight loss (nadir weight) between treatment groups (not shown). However, the nadir weight differed significantly between the VLCD-strict and VLCD-plus groups, -24.0 ± 9.4 kg and -17.7 ± 11.4 kg, respectively ($P < 0.05$). The nadir weight in the VLCD-mw group was -20.5 ± 7.7 kg, which did not differ significantly from the two other groups.

Gender differences in treatment response

Figure 2 (lower panel) shows the weight changes for female completers. After one week, females in the VLCD-mw group had lost significantly more weight

than women in the VLCD-plus group ($P < 0.05$). At week 16, week 24 and week 52, weight losses in the VLCD-strict group were significantly greater than in the VLCD-plus group ($P < 0.05$, all comparisons).

Analyses on the female intent-to-treat population indicated that after 16 weeks there was no significant difference between the treatment groups. However, after 24 weeks, a significant difference was found between the VLCD-strict group (-18.8 ± 10.4 kg) and the VLCD-plus group (-12.0 ± 9.6 kg), ($P < 0.05$). Also, after 52 weeks, significant differences were found between females in the VLCD-strict group (-12.6 ± 9.9 kg) and in the VLCD-plus group (-7.5 ± 12.1 kg), as well as between the VLCD-mw women, who lost -11.3 ± 7.4 kg and females in the VLCD-plus group ($P < 0.05$, both comparisons), (not shown).

There were no significant differences between the small male treatment groups, neither among completers nor in the intent-to-treat population, (not shown).

Body composition

Table 2 shows the change in body composition, determined by DEXA and TBK examinations, among the majority of the completers after 24 weeks and 52 weeks. There were no significant differences between groups, neither for loss of BF nor for FFM loss. Within treatment groups, BF and FFM were significantly reduced after 24 weeks and 52 weeks. The median loss of FFM, as a percentage of total weight loss, was 25% after 24 weeks and 30% after 52 weeks.

Risk factors

Table 3 shows estimated changes in cardiovascular risk factors, due to a 10.0 kg weight loss, and the relation between weight reduction and changes in risk factors for all treatment groups pooled. After 24 weeks, there were significant associations between weight loss and reductions in WHR, S-Cholesterol and S-TG levels. After one year, significant associations were found between weight reduction and changes in diastolic blood pressure, WHR, S-HDL, S-Insulin and B-Glucose levels. There were no significant difference in the estimates between the two time periods. Neither were there any significant differences in estimated risk factor changes between the treatment groups (not shown).

Drop-outs

Forty-eight subjects (7 men, 41 women), corresponding to 40% of the total study population, did not complete the study. There was no significant difference in attrition rate between treatment groups (Table 1). There were no significant differences in gender distribution, body weight or BMI between drop-outs and completers (not shown). Drop-outs were, however, significantly younger than completers, 38.7 ± 11.2 *vs* 45.2 ± 9.8 y ($P < 0.05$). The mean time until drop-out was 20 ± 13 weeks, with no significant difference between the treatment groups (not shown). Weight loss at drop-out was -7.2 ± 7.4 kg in the VLCD-strict group, -9.0 ± 4.9 kg and -7.3 ± 6.6 kg in the VLCD-mw and VLCD-plus

Table 2 Changes from baseline(Δ) in body fat (BF) and fat free mass (FFM) in obese subjects after 24 weeks and 52 weeks, shown by treatment group. Means and s.d. are shown.

	VLCD-strict		*VLCD-mw*		*VLCD-plus*	
	Week 0–24 Mean ± s.d.	*Week 0–52* Mean ± s.d.	*Week 0–24* Mean ± s.d.	*Week 0–52* Mean ± s.d.	*Week 0–24* Mean ± s.d.	*Week 0–52* Mean ± s.d.
n	15	19	21	23	24	27
Δ BF (kg)	−14.3 ± 7.3	−8.3 ± 7.9	−14.5 ± 7.5	−7.1 ± 8.2	−10.9 ± 6.9	−5.6 ± 10.3
Δ FFM (kg)	−5.9 ± 4.8	−4.3 ± 4.0	−4.4 ± 4.0	−3.6 ± 3.4	−4.7 ± 5.7	−3.5 ± 4.8

VLCD = very low calorie diet
Reductions in BF and FFM were highly significant within each treatment group ($P < 0.001$), except for Δ BF 0–52 weeks in the VLCD-plus group ($P < 0.01$). There were no significant differences between treatment groups.

Table 3 Estimated changes in cardiovascular risk factors due to a 10.0 kg weight loss after 24 weeks and 52 weeks of treatment. Pooled data for all treatment groups are shown.

	Week 0–24		*Week 0–52*	
	Estimated change	*P-value*	*Estimated change*	*P-value*
Systolic BP (mm Hg)	−2.7	$P = 0.18$	−2.8	$P = 0.15$
Diastolic BP (mm Hg)	−1.4	$P = 0.28$	−2.3	$P = 0.04$
WHR	−0.03	$P < 0.001$	−0.03	$P < 0.001$
S-Cholesterol (mmol/L)	−0.3	$P = 0.002$	−0.2	$P = 0.07$
S-HDL (mmol/L)	0.02	$P = 0.56$	0.07	$P = 0.003$
S-LDL (mmol/L)	−0.1	$P = 0.27$	−0.1	$P = 0.16$
S-TG (mmol/L)	−0.6	$P = 0.03$	−0.4	$P = 0.09$
S-Insulin (mU/L)	−1.5	$P = 0.08$	−2.9	$P = 0.01$
B-Glucose (mmol/L)	−0.3	$P = 0.10$	−0.4	$P = 0.02$

BP = blood pressure; WHR = Waist-to-hip ratio; S = serum; HDL = high density lipoprotein; LDL = low density lipoprotein; TG = triglyceride; B-Glucose = blood glucose

groups respectively (NS). Drop-outs occurred both during the VLCD phase ($n = 21$) and during the maintenance phase ($n = 27$).

Discussion

Although VLCDs produce profound initial weight loss, there are in a majority of studies no long-term beneficial effects on weight maintenance compared with treatment programs based on hypocaloric diets and behaviour modification. Nevertheless, the weight reduction achieved with VLCDs is substantial and efforts should be made to further improve the VLCD phase. In the present one-year trial, we focused on the design of the initial VLCD period, comparing strict and liberal VLCD approaches. Our results show that for the intent-to-treat population there was no short-term (16 weeks) difference in weight loss between strict and liberal VLCD regimens. Strict VLCD treatment was, however, clearly more beneficial in the short-term than a liberal VLCD approach, among patients who completed the trial. The strict VLCD treatment also seemed to be beneficial over one year, particularly in women. Initiating the VLCD phase on a metabolic ward, did not increase weight loss compared to the outpatient treatment. Other randomised studies which systematically evaluate strict and liberal approaches to VLCD are not available for comparison.

Many patients find the first VLCD week difficult, with hunger and longing for food. In the present trial, we examined whether efforts to facilitate the start of the VLCD, by reducing unwanted food stimuli and using hospital staff to provide continuous support, could improve weight loss. Patients in the VLCD-mw group were therefore hospitalised for the initial week. Neither early, nor one-year weight loss differed significantly between outpatients in the VLCD-strict group and the VLCD-mw inpatients. This is in accordance with a study by Ohno *et al*[17] in which four inpatient VLCD weeks did not result in greater weight loss than the same outpatient treatment. The cost of hospitalisation for a patient at Sahlgrenska University Hospital was 2600 SEK/d (320 US$) and the average guaranteed daily sickness cash benefit was 344 SEK/individual (43 US$) at the time of the trial.[18] One VLCD week in hospital, instead of outpatient VLCD, thus cost about 21 000 SEK (2600 US $) extra for the health care system. This extra cost does not appear to be justified as no beneficial effect on weight loss was achieved compared with outpatient VLCD treatment.

It has been argued that VLCDs, in spite of their lower energy content, result in less hunger than hypocaloric diets.[19,20] Ketosis could be one reason for this 'therapeutic anorexia', although several reports have found no association between reduced hunger and ketosis.[21,22] The VLCD-preparation itself (sachets of powder), limit the contact with ordinary food and thus may facilitate adherence more than conventional hypocaloric diets.[5] However, some patients long for food during the VLCD phase and it can be difficult to totally avoid ordinary food for three to four months. It has also been discussed that it might be beneficial to add an extra preportioned daily meal to the VLCD treatment to facilitate the refeeding phase.[23] We therefore wanted to examine if allowing two small portions of food twice weekly would change the magnitude of weight loss compared with strict adherence to the VLCD. Patients that completed the treatment program achieved significantly greater weight losses in the VLCD-strict group compared to the VLCD-plus group, both early (16 weeks) and after one year. In the intent-to-treat population, this beneficial effect of strictness was found only in the later phase of the trial and especially among females. Thus, our data may support that intermittent reduction of VLCD-induced anorexia and/or intermittent contact with ordinary food is less effective than strict adherence to the VLCD. The energy content of the allowed meals in the VLCD-plus group was not strictly defined and this might have made overeating more likely than if preportioned meals had been offered.

The drop-out rate was 40%, with no difference between treatment groups. Attrition rates of 10–80% in obesity trials have been reported.[24] The present attrition rate was higher than seen in our previous two-year study.[9] That population was older and heavier according to the study protocol and also recruited from a rural area. They also volunteered to participate after an advertising campaign, while patients in the present trial were referred for obesity treatment. The two populations may therefore not be comparable. Drop-outs in the present study were significantly younger than completers, in accordance with some previous trials.[24,25]

Estimated risk factor changes per 10 kg change in body weight were similar at six and twelve months. Thus, weight related improvements were not ameliorated over time, provided that the weight reduction was maintained. A rebound in risk factors, in spite of weight loss maintenance over two years, has previously been observed.[26]

In a previous two-year study,[9] we found no overall long-term benefit from an initial VLCD phase incorporated in a supportive program, compared with the same support alone. However, there was a gender difference in treatment response; male patients maintained a greater weight loss in the VLCD group than in the support group. Females lost equal amounts of weight, irrespective of treatment. In the present trial, we focused on the structure of the VLCD phase itself, by comparing three initial VLCD approaches incorporated in a one-year treatment program. Among females, weight losses were greater for the more strict VLCD approaches. Thus, female patients in the present trial, lost more weight on a strict rather than on a liberal VLCD approach, but in our previous

study, women had no long-term benefit of a VLCD-period. These seemingly different results could be due to chance or to the different length of the trials, one *vs* two years. It could also be that females in the previous trial tended to be more liberal during the VLCD phase and thereby diluted the VLCD effect. Since the present trial emphasised strictness rather than a more liberal VLCD approach, this might have made female patients in the VLCD-strict and VLCD-mw groups less prone to consume anything but the VLCD. There were only a few men in each group, making the male treatment data difficult to interpret.

Whether the observed differences between treatments would persist beyond one year is not known. The greater one-year weight loss achieved in the VLCD-strict group compared to the more liberal VLCD approach may have been related mainly to the greater weight loss during the initial VLCD phase. In the maintenance phase of the trial, weight regain was similar in all groups, indicating the need for further research efforts directed at optimising the post-VLCD maintenance treatment.

Conclusion

This study showed that strict adherence to an initial VLCD resulted in greater one-year weight loss than a VLCD combined with a few, small weekly meals, especially among females. In the short-term, a strict VLCD approach was beneficial only among completers. Initiating the VLCD period on an inpatient basis did not result in greater weight loss, but was far more expensive.

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