Research Article

Journal of Nutritional Biology

Fasting Therapy versus Standard Weight Reduction Diet Combined with Naturopathic Complex Treatment in Patients with Overweight and Obesity

Wiebelitz KR^{1*}, Wessely DK², Ismar LE², Pötschke T³, Weidner B³ and Beer AM³

¹Clinic for Children and Adolescents, Prignitz Hospital, Medizinische Hochschule Brandenburg Theodor Fontane, Germany

²Department of Neurology, St. Johannes-Hospital, Germany

³Department of Naturopathy, Blankenstein Hospital, Ruhr-Universität Bochum, Germany

***Correspondence:** Wiebelitz KR, Clinic for Children and Adolescents, Prignitz Hospital, Dobberzinerstrasse 112, D-19348 Perleberg, Germany, Tel: +49 3876303816; Fax: +49 3876303183; E-mail: ruediger.wiebelitz@gmx.de, r.wiebelitz@krankenhaus-prignitz.de

Received: Feb 02, 2018; Accepted: Apr 12, 2018; Published: Apr 16, 2018

Abstract

Background: Overweight and obesity are major risk factors for many chronic diseases in modern societies. A retrospective follow-up study showed an advantage of weight reduction diet (WRD) to fasting therapy concerning long-term weight loss.

Objective: Prospective comparison of WRD to fasting therapy concerning long-term weight loss.

Methods: From 08/2007 to 02/2009 90 patients with overweight or obesity were observed with a follow-up period of 6 months, who received either a fasting therapy or a WRD in the context of naturopathic complex in-patient treatment including physical activity.

Results: During the in-patient treatment the fasting patients loosed significantly more weight than the WRD patients, but regained weight during the follow-up, while the weight loss of the WRD patients persisted. 32% of the fasting and 81% of the WRD patients achieved a 5% weight loss after 6 months. Total and LDL-cholesterol were significantly more reduced, controlled eating habits, physical leisure activity and tendentially physical quality of life increased more after 6 months in the WRD group, while the systolic blood pressure declined more in the fasting patients.

Conclusion: Weight loss and improvement of obesity-associated parameters were long-term significantly inferior in fasting patients compared to patients treated with a WRD. The reduced success of the fasting patients is probably caused by the minor lifestyle modification.

Keywords: Naturopathic fasting; Weight loss; Overweight; Weight-reducing diet; Lifestyle modifications; Fasting triglyceride levels; Interventions to increase physical activity; Hypertension

Abbreviations: WRD: Weight Reduction Diet; LDL: Low Density Lipoprotein; m: mean; sd: standard deviation; min-max: minimum - maximum; sm=small; me=medium; st=strong; pat.=patients; hypertens.=hypertensive

Introduction

Overweight and obesity are major risk factors for the development of other chronic diseases. These comorbidities include, among others, cardiovascular disease, diabetes mellitus, dyslipidemia and malignancy [1-4]. The dietetic standard therapy is the moderately energy-restricted mixed diet with a daily energy deficit of 2100-3350 kJ (500-800 kcal) [5]. To raise the energy consumption an increase in physical activity in everyday life and recreation time is desired.

A retrospective follow-up study [6] examined the question whether a therapeutic weight reduction achieved by an in-patient naturopathic fasting therapy [7] can be maintained over a longer period in patients with overweight or obesity and compared the effects of fasting with a weight reduction diet (WRD). The retrospective results with a mean follow-up of 6.8 years showed an advantage of WRD concerning sustained weight loss, changes in eating habits, increased leisure time activity and improvement in quality of life in relation to body weight.

Regarding arterial hypertension and other diet-related disorders like lipid metabolism many authors point out the need for research on the long-term therapeutic effect of fasting [8-10]. Data describing the development of blood pressure and serum lipids exist only for the period of treatment, but no follow-up data are published. Concerning total, LDL- and HDL-cholesterol and triglycerides case reports and studies suggest a reduction and in some cases normalization of these values during fasting therapy [11,12], but the progress after cessation of fasting is unknown.

Methods

Present investigation

A prospective comparison of fasting effects and the impact of a WRD is published for the first time in this manuscript.

Design

The presented single-center study is an open two-armed quasi-experimental study with follow-up. In-patients with overweight or obesity receiving either a modified Buchinger fasting therapy (Table 1) [13] or a WRD as part of a naturopathic complex treatment in the department of naturopathy during the period from August, 2007 to August, 2008 were studied.

Nutrition interventions

The sequence of therapeutic fasting is shown in table 1. WRD means a diet with reduced caloric feed charge. Patients receive a well-balanced low-fat and modified fat wholefood basic diet with a daily energetic deficit of 2100-3350 KJ (500-800 kcal). The food contains ~50% carbohydrates, ~30% fat and ~20% proteins. Restriction of animal fat leads to less than 7% of saturated fatty acids. Dietary fibers and complex carbohydrates ensure a prolonged feeling of satiety.

Additionally, patients got as part of the naturopathic complex in-patient treatment concomitant non medicinal treatments [14]. Details of the inpatient naturopathic complex therapy are defined by the OPS 8-975.2x in the German DRG-System [15]. Details of this OPS are given in table 2.

Naturopathic complex therapy consists of body-mind-therapy {"Ordnungstherapie"}, nutritional therapy, exercise therapy, phytotherapy and hydro-/thermo- and balneotherapy as well diverting and detoxifying measures. Exercise therapy consisted of 60 minutes guided walking in the nature (up and downhill) five times per week. Assuming a mean body weight of 91 kg the caloric consumption of this guided walking for 60 minutes amounts to approximately 675 large calories [kcal] or approximately 3380 kcal per week. Hydrotherapy included exercise therapy in a swimming bath under physiotherapeutic guidance for 30 minutes three times per week. Assuming a mean body weight of 91 kg the caloric consumption of exercise therapy in a swimming bath for 30 minutes amounts to approximately 429 large calories [kcal] or approximately 1290 kcal per week (Note: the factual use and distribution of the other naturopathic treatments in both treatment groups is delineated in table 9).

After dismissing from hospital no further intervention related to the study happened with the exception of the telephone interviews after 3 and 6 months. Patients were advised on dismissing to continue with physical activity and altered nutrition as taught during the hospital stay.

Primary and secondary objectives

The primary objective of the present study is the weight loss after 6 months of patients who received in-patient fasting treatment in comparison to those receiving a WRD. A mean difference of 3 kg between the treatment groups was considered clinically significant:

A permanent reduction of 5% of the starting weight is considered a success [1,16] and a general goal of therapy in both German [5] and U.S. American guidelines [17]. On the other hand, health benefits arise already from an absolute weight reduction of more than 2.25 kg [16,18].

Secondary objectives are a weight loss of $\geq 5\%$ of the initial weight after completion of in-patient treatment and after 6 months, the development of systolic and diastolic blood pressure, serum concentrations of total, LDL- and HDL-cholesterol, triglycerides and glucose, the change in the eating habits with the dimensions of cognitive control, distractibility of eating behavior and hunger feelings as well as changes in physical activity and quality of life.

Statistical analysis

Data entry, statistical analysis and generation of graphs were performed using the software SPSS version 17.0 and OpenOffice.org 3.0.1.

The necessary sample size for an α -error of 0.05 and a β -error of 0.2 (meaning a power of the study of 80%) was calculated using the software G* Power Version 3.0.10 [19]. The standard deviation was estimated according to the results of a meta-analysis for the dietary treatment of obesity at 4.3 kg [20]. Under these conditions the minimal total number of required patients for the two-tailed t-test for independent samples is 68 subjects (34 per group). An expected drop-out rate of 25% led to the planned inclusion of 90 patients in this study.

Statistical testing of the primary objective was performed using the Student's t-test for dependent samples after verifying the prerequisites Gaussian distribution and homogeneity of variance by the Kolmogorov-Smirnov test and the Levene test.

Secondary objectives were characterized by mean, median, minimum, maximum and standard deviation. Frequencies were calculated for nominal and ordinal data as absolute number and relative ratio. If applicable (Gaussian distribution and homogeneity of variance) statistical testing of metric data was performed using the Student's t-test for dependent and independent samples, otherwise the Mann-Whitney U test and the Wilcoxon signed-rank test. Statistical testing of ordinal and nominal scaled data was performed using the chi-square test (Pearson or Fisher's Exact test). The significance level was generally set to 5%. As an empirical measure for the effect of statistically significant results the effect size was calculated ex-post [21].

Ethical approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki in its revised version of 1975 and its amendments of 1983, 1989, and 1996. All procedures involving human patients were approved by the Ethics Committee of the Ruhr University Bochum (registration number 2977, 9th August, 2007). Written informed consent was obtained from all patients.

Trial registration

The study is registered at the DRKS (Deutsches Register Klinischer Studien, number DRKS00006343). Universal Trial Number (UTN): U1111-1159-2725. URL for the registry: https://www.drks.de/drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00006343.

Questionnaires and measurements

The following questionnaires were used: Questionnaire on eating behavior (Poodle and Westenhöfer; FEV - expanded German translation of the TFEQ) [7,22], Freiburg questionnaire on physical activity by Frey and Berg (FFKA) [23], general health questionnaire (SF-12; shortened form of SF-36) [24]. At the beginning of the study the general medical history and the specific history of obesity was recorded.

The parameters were measured at six points of time: The day before the start of the nutritional therapy (t_0), the fourth treatment day (t_1), the seventh day of therapy (t_2), the day of hospital discharge (t_3), follow-up three months (t_4) and six months (t_5) after the discharge.

At all times (t_0 - t_5), weight, blood pressure and laboratory parameters serum glucose, triglycerides, total cholesterol, LDL and HDL cholesterol were measured. Blood samples were taken in the morning after 12 h of fasting and before taking any medication. The body weight was determined with the calibrated electronic scale Omron BF500, using a standardized scheme: fasting state in the morning and light clothing. The arterial blood pressure was determined indirectly by the Riva-Rocci method in the morning in the fasting state and after five minutes of rest in a sitting position using a mechanical aneroid-manometer and a stethoscope. Before the nutritional therapy (t_0) and at the follow-up appointments (t_4 , t_5) eating behavior, health related quality of life and the physical activity of the patients were examined by the questionnaires described above.

Subjects

Patients aged from 18 to 75 years with overweight or obesity ($\text{BMI} \geq 25 / \geq 30 \text{ kg/m}^2$) and who were prescribed fasting therapy or a WRD as a form of nutritional therapy in the context of in-patient naturopathic complex treatment were included. Exclusion criteria were pregnancy, lactation, participation in another study simultaneously or in an organized weight-reduction program, actual medication against obesity, condition after extensive bowel resection or bariatric treatment, inflammatory bowel disease, malignant disease, postoperative nutritional deficit, hepatic or renal failure, insulin-dependent diabetes mellitus, not compensated hypothyroidism or hyperthyroidism, coronary heart disease or acute or chronic cardiac arrhythmia, eating disorders like anorexia nervosa, bulimia or binge-eating disorder, severe psychiatric disorders, addictive disorders and dementia. The acquisition of patients from August 2007 to August 2008 is outlined in figure 1. After checking the inclusion and exclusion criteria the patients were allocated to the test group (fasting therapy) and the control group (WRD) by medical prescription (Figure 1).

The mean length of hospital stay in both groups was 16.2 ± 2.2 days. Patients with WRD were given the appropriate nutrition therapy diet throughout the entire inpatient stay, 15.1 ± 2 days. The fasting therapy lasted on average 8.2 ± 1.6 days with a subsequent fare buildup of 3.4 ± 0.5 days. All fasting patients were given a WRD for the remaining in-patient stay of 3.3 ± 2.5 days. Biometric and demographic characteristics of the study population are given in table 3.

Table 4 shows the main diagnoses of both study groups, table 5 the secondary metabolic and vascular diagnoses and table 6 the other diagnoses of the study participants at the baseline interview.

In table 7 medication with potential weight-increasing effect at baseline is listed, table 8 shows the total medication at baseline.

A summary of the therapies applied in in-patient complex naturopathic treatment is given in table 9.

Results

2 patients per study group withdrew their informed consent during their in-patient treatment, participation ended prematurely. 2 patients discontinued the prescribed fasting therapy, 2 patients felt the requirements of the

study to be too strenuous in the context of their diseases. Of the 86 (95.6%) at discharge still participating patients 75 (83.3%) appeared at the first follow-up after 3 months. 1 patient of the fasting group was hospitalized due to diverticulitis, another patient developed malignant disease. Another 2 patients after fasting therapy and 4 patients after WRD withdrew their informed consent before the first follow-up. One previously fasting patient and 2 patients of the WRD group could neither be reached by phone nor by mail and were lost to follow-up. In between the two follow-up observations another 5 persons terminated their participation in the study: 1 patient of the fasting group experienced a strong progression of her chronic polyarthritis requiring hospitalization, 1 patient of the WRD group suffered a herniated disc, which immobilized her. 2 other patients, 1 each per treatment group, lost their motivation for the second follow-up and one person after WRD gave no reasons for the withdrawal of his informed consent. 38 patients (80.9%) after fasting therapy and 32 patients (74.4%) after WRD appeared for the second follow-up after 6 months (overall follow-up rate of 77.8%).

At the beginning of the treatment, there were no significant group differences regarding all evaluated parameters (Table 10).

Only significant differences at 6 months are described in detail:

In the fasting group mean weight reduction after 6 months was 3.2% (mean effect size), in the WRD group 8.4% (strong effect size; significant difference). Regarding the 5% success criterion significantly more WRD (81%) than fasting (32%) patients were successful.

After 6 months total cholesterol and LDL-cholesterol was significantly reduced only in the WRD group (7.1%, strong effect size respectively 11.3%, medium to strong statistical effect), with a significant difference between the groups in favor of WRD. HDL cholesterol increased in the fasting group by 5% and in the WRD group by 5.7% (both significant, small to medium effect, no significant difference between groups).

The systolic and the diastolic blood pressure decreased significantly in the fasting group (4.8%, mean effect size, respectively 2.6%, small to medium effect size), in the WRD group only by trend (3.2% respectively 2.6%, but no significant differences between groups).

Table 1: Sequence of therapeutic fasting modified according to Buchinger at the naturopathic department

	Relieving day	1st–7th fasting day	1st day after fasting	2nd day after fasting	3rd day after fasting
fasting provisions	Balanced diet Evening meal: 1 piece of fruit or stewed fruit	Thrice daily 250ml vegetable stock and 150 ml juice (sauerkraut, beetroot, carrot, tomato) 3 cups (150 ml) fasting tea (nettle, hawthorn, dandelion, field horsetail licorice) 3 x 1 table spoon freshly squeezed plant juice (dandelion, nettle, birch) in daily rotation Daily. 2 pouches potassium citrate Herbal teas, mineral water Liquid intake at least 3-4 l/day	in the morning: fasting stock with bran + flax seed + 1 glass vegetable juice at noon: breaking of fasting with 2 grated apples or whole apples or apple sauce at night: potato soup	in the morning: fasting stock with bran + flax seed, plums + curd at noon: potatoes, curd or vegetables, yoghurt at night: Mixtum (wheat bran, flax seed, figs, raisins boiled) or bread with eupeptic spread	in the morning: fasting stock with bran + flax seed, figs, curd, fruit, yoghurt, bran at noon: fresh food or potatoes, curd or vegetables yoghurt at night: cereals pulp or bread with eupeptic spread
		~628 kJ	~2093 kJ	~3140 kJ	~4186 kJ
		(~150 kcal)	(~ 500 kcal)	(~750 kcal)	(~ 1000 kcal)
other measurements		bowel cleanse: 1st fasting day: purging with 20-40 g Glauber's salt or FX-passage salt high enema every 2-3 days, alternatively Glauber's salt or FX-passage salt daily at noon liver packing fasting laboratory: days 4 and 7	1 capsule <i>Saccharomyces boulardii</i> daily Stopping of fasting tea, freshly squeezed plant juices, potassium citrate and liver packings		

In hypertensive patients the systolic and the diastolic blood pressure decreased in the fasting group (n=15) significantly (6%, strong effect size, respectively 4.9%, medium effect size). The mean decrease in the WRD group (n=13) was not significant (4.7% respectively 3.8%, but no significant differences between groups).

Concerning eating behavior the increase of the cognitive control score and the rigid control score increased and the experienced feeling of hunger decreased in the fasting group only by trend (11.7% respectively 15.6% respectively -9.8%), while the changes were significant in

the WRD group (28.2%, moderate to strong effect size, respectively 19.6%, small effect size, respectively -20%, but only significant difference between groups for the second parameter, medium effect size).

The flexible control score increased and the distractibility scores decreased significantly in both groups (33.2%, medium effect size, and -11.5%, small effect size, respectively 58.5%, strong effect size, and 25.4%, medium effect size, with significant respectively borderline group differences, medium effect size).

Figure 1: Recruitment of patients and course of the study.

Leisure time activities such as walking, cycling, dancing and bowling increased significantly in both groups (37% respectively 114%, significant difference between groups).

Physical quality of life improved significantly in both groups (12%, small to medium effect size, respectively 20%, mean effect size, no significant difference between groups).

Discussion

This prospective study confirms the main findings of our previous retrospective study [6] concerning weight development. The retrospective study also showed

already a clear and statistically highly significant difference between the groups regarding the long standing post discharge dietary changes, the persistent increase of leisure activity and the sustained improvement in quality of life in relation to body weight.

Both treatment groups of this prospective study achieved a clinically significant mean weight loss of more than 2.25 kg. Several studies demonstrated the health benefit arising from a weight loss of this magnitude [16,25]. So far available therapies reach an average loss of weight after 6 months between 2.4 and 8.4 kg dependent on the type of intervention. Thus the fasting group (2.9 kg) is in the lower part and the WRD group (7.5 kg) in the upper range [20]. Sustained weight reduction by more

Table 2: Details of the OPS 8-975.24 defining the minimal standards of the inpatient naturopathic complex therapy in the German DRG-System

Criterion	Details
Therapy	> 120 minutes of therapy/day Clinical naturopathic team Leadership: Consultant with naturopathic specialisation and > 3 years experience in classical naturopathy
Team	Physicians Naturopathic experienced nurses Minimal 3 three of the following: <ul style="list-style-type: none"> • Physiotherapist/masseur/medical pool attendant/trainer (sport) • Occupational therapist • Psychologist • Nutrition scientist/dietician • Art therapist/music therapist
Therapeutic concept	Compilation of an individual specific naturopathic diagnostic and therapeutic concept at the beginning of the treatment
Team briefing	At least twice a week (at Blankenstein hospital 5 times per week) Topics to be included <ul style="list-style-type: none"> • somatic aspects • mind-body ("Zordnungstherapeutische" aspects) • social aspects Patient-centered documentation of <ul style="list-style-type: none"> • hitherto achieved results of treatment • additional goals of treatment
Nursing	Naturopathic extended care by nurses specialised in naturopathy
Therapeutical methods	Minimal 5 of the following 8 sectors: <ul style="list-style-type: none"> • Nutritional therapy • Hydro-/thermotherapy • Other physical methods • Phytotherapy • Body-mind-therapy ("Ordnungstherapie") • Exercise therapy • Detoxifying measures One additional method: <ul style="list-style-type: none"> • Manual therapy • Acupuncture/traditional chinese medicine • Homeopathy • Neural Therapy • Art therapy/music therapy
Duration	≥ 21 treatment days or ≥ 14 treatment days and minimal 2520 therapeutical treatment minutes

Bold: realised at Blankenstein Hospital

than 5% is associated with significant health benefits and therefore frequently used to quantify the effect of a obesity treatment [1,16]. It is the first general treatment goal in the German and U.S. guidelines for obesity treatment [5,17]. Concerning this criterion the WRD group is more successful (81% versus 32%). Besides the absolute weight loss the prevention of subsequent weight increase after the end of a therapy is a significant problem in the treatment of obesity [26]. The fasting patients regained almost half of the initially achieved weight loss (2.7 of 5.6

kg) after 6 months in the present study. In contrast the WRD patients were able to continue their weight loss at discharge (3.1 kg) leading to more than double weight loss (7.5 kg) after 6 months. The effects of fasting on glucose homeostasis are one possible explanation for the observed weight regain after fasting therapy. Chaput et al. showed in a recent study on energy-restricted diet that post-therapeutic low serum glucose concentrations in the oral glucose tolerance test correlate with a long-term weight gain by increased energy intake [27]. In this

Table 3: General biometric and demographic characteristics of the patients before treatment

	Fasting Therapie n = 47		WRD n = 43		All n = 90	
	mD	SD	m	SD	m	
	(min-max)		(min-max)		(min-max)	
Age [years]	54.6	8.5	56.8	10.8	55.7	9.7
	(40-72)		(27-74)		(27-74)	
Weight [kg]	92.7	17.6	89.2	16	91	16.9
	(67.9-135)		(63.8-134.1)		(63.8-135)	
BMI [kg/m²]	33.3	5.9	32.5	5.5	32.9	5.7
	(25.2-48)		(25.9-46.8)		(25.2-48)	
	n (percentage)		n (percentage)		n (percentage)	
Gender						
male	8 (17%)		2(5%)		10 (11%)	
female	39(83%)		41 (95%)		80 (89%)	
Situation of life						
alone living	9 (19%)		8 (19%)		17 (9%)	
living with child	3 (6%)		1 (2%)		4 (4%)	
living with partner	22 (47%)		22 (61%)		48 (53%)	
living with partner and child	12 (26%)		8 (19%)		20 (22%)	
living with parents	1 (2%)		0 (0%)		1 (1%)	
Graduation						
no school leaving certificate	3 (6%)		1 (2%)		4 (4%)	
secondary modern school	23 (49%)		27 (63%)		50 (56%)	
junior high school	9 (19%)		5 (12%)		14 (16%)	
university-entrance diploma /university degree	12 (26%)		10 (23%)		22 (24%)	
Employment situation						
employed	32(68%)		28 (65%)		60 (67%)	
employment seeking	1(2%)		2 (5%)		3 (3%)	
retired	14 (30%)		13 (30%)		27 (30%)	

m: mean, sd: standard deviation, min-max: minimum - maximum. No significant group differences

Table 4: Main diagnoses (ICD-10 groups) in the study population (baseline). No significant group differences

	Fasting therapie n = 47	WRD n = 43	All n = 90
	n (%)	n (%)	n (%)
Diseases of the musculoskeletal system and connective tissue	44 (94%)	42 (98%)	86 (96%)
Diseases of the skin and subcutis	1 (2%)		1 (1%)
Diseases of the nervous system	1 (2%)		1 (1%)
Endocrine, nutritional and metabolic disorders	1 (2%)		1 (1%)
Diseases of the digestive organs		1 (2%)	1 (1%)
Total	47 (100%)	43 (100%)	90 (100%)

Table 5: Metabolic and vascular secondary diagnoses in the study population (baseline). No significant group differences

	Fasting Therapie	WRD	All
	n = 47	n = 43	n = 90
	n (%)	n (%)	n (%)
Arterial hypertension	22 (47%)	17 (40%)	39 (43%)
Diabetes mellitus type 2	12 (26%)	10 (23%)	22 (24%)
Impaired glucose tolerance	1 (2%)	0 (0%)	1
Hypercholesterolaemia	40 (85%)	38 (88%)	78 (87%)
Hypertriglyceridamia	10 (21%)	11 (26%)	21 (23%)
Total [n]	85	76	161

study fasting patients reduced their serum glucose level before food-intake in the morning within the first 7 days much more (27%) than WRD patients (7%).

Studies on obesity treatment showed a significant correlation between the decrease in serum leptin and the increase of perceived hunger [28,29]. This mechanism is also a possible trigger of a positive energy balance through increased food intake after fasting therapy. The observed weight curves after fasting therapy resemble the results of VLED (very low energy diet) and VLCD (very low calorie diet; daily energy intake <3350 KJ [<800 kcal]). A systematic review of randomized controlled trials that administered a VLED for obesity therapy showed a higher initial weight loss than other diets. Cessation of therapy resulted - similar to the fasting group in this study - in a regain of about 40% of the achieved reduction after 6 months [20]. The failure was attributed to the lack of change in diet after treatment, since no healthy diet was “learned” by “passive” taking prepared meals, in spite of regularly nutritional counseling - as in the present study. Lack of the practical experience that “healthy food” with moderate reduced energy content and reduced fat content can be tasty and satiable probably cause the absent weight stabilization after fasting therapy.

The guidelines of the “Medical Society for Therapeutic Fasting and Nutrition” include hyperlipidemia and type 2 diabetes mellitus as well-established indications for fasting therapy [30]. But long-term effects of fasting on serum lipids and serum glucose were not previously published. The WRD group experienced significantly greater reductions in total cholesterol and LDL-cholesterol than the fasting group after 6 months. The changes of HDL-cholesterol, triglycerides and glucose were not significantly different after 6 months. Regarding the continued weight loss in the WRD group the reduction in LDL cholesterol is probably caused by a systematic

change of diet. The trend of serum glucose in diabetic patients suggests an inferiority of fasting therapy to WRD. The reason might be again the better implementation of lifestyle modification and eating behavior in the WRD group.

Summing up no clinically important changes in serum lipids and serum glucose were detected in patients after fasting therapy in the long-term course.

The observed reduction of blood pressure in the fasting group corresponds to the results of other studies on therapeutic fasting [11,31]. In literature and in the present study a greater reduction was observed in patients with arterial hypertension [11]. The four times higher weight adjusted blood pressure reduction of fasting patients cannot be explained by weight loss alone. The present study suggests a continuous long-term effect of fasting therapy on blood pressure beyond the sole effect of weight loss, confirming the hypothesis of McCarty [10] of specific blood pressure lowering mechanisms induced by fasting therapy. Hyperinsulinemia caused by adipositas is blamed to raise blood pressure by sodium retention, activation of the sympathetic nervous system and reduction of endothelial nitric oxide [10]. Kolanowski et al. showed a significant decrease of insulin levels and triggering of natriuresis by fasting [32]. Both serum insulin levels and insulin response to glucose strain are reduced by fasting and may contribute to the reduction of blood pressure [12]. Another effect of fasting on the regulation of the natriuretic peptides ANP and BNP may also lower blood pressure [33]. However, the initial advantage of fasting therapy compared to WRD did not last for the 6 month follow-up period. But regarding the hypertensive subpopulation the blood pressure parameters (systolic and diastolic) remained significantly lowered after 6 months in the fasting group-in contrast to the WRD group, though statistical comparison between the groups was

Table 6: Other diagnoses (baseline) of the study participants.

Diagnoses	Fasting Therapie	WRD	All
	n = 47	n = 43	n = 90
	n %	n %	n %
Chronic back pain, spondylosis	43 (91%)	40 (93%)	83 (92%)
Slight depressive episode	19 (40%)	23 (53%)	42 (47%)
Fibromyalgia	17 (36%)	16 (37%)	33 (37%)
Hypothyreosis	15 (32%)	13 (30%)	28 (31%)
Gonarthrosis	15 (32%)	12 (28%)	27 (30%)
Polyarthrosis	5 (11%)	10 (23%)	15 (17%)
Tinnitus	7 (15%)	3 (7%)	10 (11%)
Gastroesophageal reflux disease	4 (9%)	6 (14%)	10 (11%)
Cervicocephal syndrome	5 (11%)	5 (12%)	10 (11%)
Cervicobrachial syndrome	4 (9%)	6 (14%)	10 (11%)
Varicosis	6 (13%)	3 (7%)	9 (10%)
Bronchial asthma	3 (6%)	6 (14%)	9 (10%)
Intervertebral disc displacement	5 (11%)	4 (9%)	9 (10%)
Osteoporosis	3 (6%)	5 (12%)	8 (9%)
Migraine	4 (9%)	3 (7%)	7 (8%)
Sleep disorders	4 (9%)	2 (5%)	6 (7%)
Diverticulosis	2 (4%)	4 (9%)	6 (7%)
Finger polyarthrosis	3 (6%)	3 (7%)	6 (7%)
Periarthropathia humeroscapularis	2 (4%)	4 (9%)	6 (7%)
Coxarthrosis	6 (13%)	0 (0%)	6 (7%)
Chronic polyarthritits	5 (11%)	0 (0%)	5 (6%)
Tension headache	1 (2%)	3 (7%)	4 (4%)
CVI	0 (0%)	4 (9%)	4 (4%)
Chronic constipation	3 (6%)	1 (2%)	4 (4%)
Chronic gastritis	1 (2%)	3 (7%)	4 (4%)
OSAS	1 (2%)	3 (7%)	4 (4%)
Chronic sinusitis	4 (9%)	0 (0%)	4 (4%)
Arthrosis of the ankle joint	1 (2%)	3 (7%)	4 (4%)
Carpal tunnel syndrome	3 (6%)	1 (2%)	4 (4%)
Hyperhidrosis	2 (4%)	1 (2%)	3 (3%)
Hiatal hernia	2 (4%)	1 (2%)	3 (3%)
Trochanteric bursitis	2 (4%)	1 (2%)	3 (3%)
Rhizarthrosis	0 (0%)	3 (7%)	3 (3%)
Heberden's nodes	1 (2%)	2 (5%)	3 (3%)
Iron deficiency anemia	1 (2%)	1 (2%)	2 (2%)
Hallux valgus	2 (4%)	0 (0%)	2 (2%)
Hepatic steatosis	1 (2%)	1 (2%)	2 (2%)
Diabetic polyneuropathy	0 (0%)	2 (5%)	2 (2%)
Psoriasis	2 (4%)	0 (0%)	2 (2%)
Enthesiopathy	2 (4%)	0 (0%)	2 (2%)
Chondromalacia patellae	1 (2%)	1 (2%)	2 (2%)
Meniscus lesion	2 (4%)	0 (0%)	2 (2%)
Spinal canal stenosis	1 (2%)	1 (2%)	2 (2%)
COPD	2 (4%)	0 (0%)	2 (2%)
Meniere's disease	1 (2%)	0 (0%)	1 (1%)
Photodermatosis	1 (2%)	0 (0%)	1 (1%)
Multiple sclerosis	1 (2%)	0 (0%)	1 (1%)
Horner's syndrome	1 (2%)	0 (0%)	1 (1%)
Restless legs syndrome	1 (2%)	0 (0%)	1 (1%)
Bell's palsy	1 (2%)	0 (0%)	1 (1%)
Irritable bowel syndrome	1 (2%)	0 (0%)	1 (1%)
Myositis	1 (2%)	0 (0%)	1 (1%)
Atopic eczema	1 (2%)	0 (0%)	1 (1%)
Allergic rhinitis	0 (0%)	1 (2%)	1 (1%)
Psoriatic arthritis	1 (2%)	0 (0%)	1 (1%)
Omarthrosis	1 (2%)	0 (0%)	1 (1%)
Radial epicondylitis	0 (0%)	1 (2%)	1 (1%)
Wrist arthrosis	0 (0%)	1 (2%)	1 (1%)
Baker cyst	1 (2%)	0 (0%)	1 (1%)
Post-nucleotomy syndrome	0 (0%)	1 (2%)	1 (1%)
Total (inclusive metabolic and vascular diagnoses)	309	280	589
Diagnoses/patient	6,57	6,51	6,54

Table 7: Medication with potential weight-increasing effect.

	Fasting therapie n = 47	WRD n = 43	All n = 90
Prescriptions	n	n	n
Antidepressants (tricyclics, SSRI, MAO inhibitors, mirtazapine)	5	9	14
Antihistamines	4	2	6
β-blocker (per os)	7	8	15
Hormone replacement therapy (estrogens, progestins)	0	4	4
Corticosteroids	2	0	2
Oral antidiabetics (glitazones, sulfonylureas, glinides)	2	2	4
Anticonvulsants, pizotifen, antipsychotics, insulin	0	0	0
Total	20	21	41
	n (%)	n (%)	n (%)
Number of patients with ≥ 1 of these medicaments	16 (34%)	17 (40%)	33 (37%)

Only one significant difference between the groups in the hormone replacement therapy (p=0.048).

not significant. Because of these ambiguous results the evaluation of therapeutic fasting in arterial hypertension remains an interesting topic.

Cognitive control of eating behavior increased in both groups, distractibility of eating behavior and feelings of hunger were reduced after 6 months. In particular the increase of the flexible control is related to an advantageous weight development [34]. While the increase of the rigid control is similar in both groups, the increase of the flexible control is nearly twofold in the WRD group (59%) compared to the fasting group (33%). This suggests that fasting patients were not able to apply the content of nutrition teaching as well as the WRD patients. The probable cause is the practical exercise during the in-patient treatment in the WRD group: These patients trained their skills by choosing the foods from the buffet and experienced their weight loss in association with altered behavior. Fasting patients learned this first as a theoretical concept and experienced the greatest weight reduction without a change in diet convertible into daily life.

Current reviews as well as evidence-based guidelines of the American College of Sports Medicine and the American Heart Association recommend a daily exercise target of 60-90 minutes of mild to moderate activity for long-term stabilization of a reduced body weight [35-37]. This claim was met by the WRD patients (77 minutes / day), while the fasting patients remained below the target range (57 minutes / day). The increase in physical activity was generated by enhancement of leisure time activity, not base or sports activity. Recreational activity increased

by 0.76 h/week (37%) in the fasting and 2.44 h/week (114%) in the WRD group (significant difference). The increase of recreational activity correlated significantly in both groups with the loss of weight.

A clear negative association exists between increasing body weight and decreasing self-rated physical health and vitality as well as social functioning [38]. Weight reduction is associated with a significant improvement of these limitations [18]. In the present study the HRQL (SF-12) increased in both groups, with a tendency of the physical quality of life (KSK) towards greater improvement after 6 months in the WRD group (20% vs. 12%, p=0.354), which can be explained by the greater weight loss of the WRD patients.

Limitations of this study arise from the recruitment of the participants: Only female multimorbid patients, who were so ill that an inpatient treatment for two to three weeks was justified, though multimorbidity may be a characteristic of overweight elderly members of our society. The intense individual and group nutritional therapy, the individual and group "Ordnungstherapie" (body-mind-medicine) and the individual and group physiotherapy and exercise therapy could probably hardly be achieved in an ambulant setting.

A pilot phase revealed that a randomized attribution of the patients to the treatment arms was impossible - for individual reasons of the patients, for example existing or missing motivation for fasting, but also for medical reasons and individual decisions of the treating physician when considering the whole disease complex of a patient

Table 8: Total medication (baseline) by therapy group. Number of ordinances.

	Fasting therapie n = 47	WRD n = 43	All n = 90
Prescriptions	n	n	n
Analgesics	33	31	64
Antiallergics	4	2	6
Antianemics	0	1	1
Antidiabetics	10	6	16
Antiemetics/Antivertiginosa	2	0	2
Antitussives	0	1	1
Antihypertensives	32	23	55
Bronchodilators/Antiasthmatics	5	7	12
Corticoids (internal)	2	0	2
Diuretics	8	10	18
Gout medications	2	2	4
Gynaecological drugs	5	3	8
Hypnotics/sedatives	7	3	10
Cardiac agents	3	2	5
Laxatives	0	1	1
Lipid-lowering agents	4	8	12
Gastro-intestinal agents	29	31	60
Migraine medication	2	0	2
Mineral supplements	15	11	26
Muscle relaxants	2	1	3
Neuropathy drugs	0	1	1
Ophthalmics	1	2	3
Parkinson's disease remedies	2	0	2
Psychotropic drugs	13	21	34
Thyroid therapeutics	15	13	28
Sex hormones	0	6	6
Thrombocyte aggregation inhibitors	4	7	11
Retuning remedies	17	15	32
Urological drugs	3	2	5
Vitamins	12	8	20
Cytostatic drugs	5	0	5
Unregistered homeopathic remedies	3	1	4
Total	240	219	459
Drugs / Patient	5,11	5,09	5,10

including psychiatric concomitant disease. Therefore there may be uncontrolled confounders between the treatment groups. For example motivation to change was certainly higher in the fasting group. But usually it would be expected that higher motivation for change would lead to a better long term outcome. In fact the opposite was the case.

Reverse causation concerning the main target criterion should not occur because of the prospective character of this study. Possible reverse causation between treatment results, for example decreasing weight causing more ability and motivation for exercise therapy, and on the other hand more exercise therapy causing burning of fat and by this weight reduction, would not be a problem but a desired side effect, if occurring.

Table 9: Therapies of the complex naturopathic in-patient therapy

	Fasting therapy	WRD (Weight)	All
	n (percentage)	n (percentage)	n (percentage)
Nutrition therapy	47 (100%)	43 (100%)	90 (100%)
Exercise therapy*	47 (100%)	43 (100%)	90 (100%)
Phytotherapy	47 (100%)	43 (100%)	90 (100%)
Phytobalneotherapy	43 (92%)	(92%)	39 (91%)
“Ordnungstherapie”	41 (87%)	(87%)	39 (91%)
Hydro-/ thermotherapy	40 (85%)	(85%)	35 (81%)
Detoxifying therapies	36 (77%)	(77%)	30 (70%)
Akupuncture	29 (62%)	(62%)	28 (65%)
Neuraltherapy	13 (28%)	(28%)	15 (35%)
CO2 - therapy	7 (15%)		7 (16%)
Heliotherapy	3 (6%)	(6%)	6 (14%)
Elektrotherapy	3 (6%)	(6%)	4 (9%)
Total patients	47	43	90

No significant differences between the groups

* Physical activity: Swimming, walking, treadmill, training bike, physiotherapy

“Placebo treatment” was not possible, nor a third group with WRD diet alone, because participants of the study were recruited in an in-patient setting. In Germany an inpatient treatment of more than 2 weeks for WRD alone would not be paid by the health insurances. An ambulant control group with written instructions would probably perform the WRD in a different way and with less compliance. It is generally accepted that the combination of nutritional therapy and physical activity is essential for the treatment of obesity - as happened in our in-patient setting and was [partially] continued during the ambulant follow-up-phase. Placebo effects therefore cannot be judged with certainty. The topic of this study concerning weight development over time after a special intervention depends on the scientifically known factors of nutritional intake, physical exercise, metabolic and endocrinologic particularities of the individual patient. The latter may be susceptible to placebo effects, but there are no recognizable reasons for essential differences between the treatment groups. Even the numerous additional diagnoses of the participants are distributed equally in both treatment groups at start (Tables 4 and 6), although randomization was impossible.

Conclusions

This study shows long-term inferiority of in-patient therapeutic fasting - modified according to Buchinger - compared to a WRD as a standard therapy for obesity, with respect to the main objective of this study - the loss

of weight after 6 months - as well as most secondary objectives of this study. The lesser extent of lifestyle modification in the fasting group appears to be causative. Whether these findings can be conferred upon other types of fasting therapies or upon fasting for healthy persons, remains subject for future research.

Conflicts of Interest

All authors declared no conflict of interest.

References

1. Anderson JW, Konz EC (2001) Obesity and disease management: effects of weight loss on comorbid conditions. *Obes Res* 4: 326S-334S.
2. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 348: 1625-1638.
3. Diabetes Prevention Program Research Group (2002) Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. *N Engl J Med* 346: 393-403.
4. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, et al. (2016) ESC Pocket Guidelines: Prävention von Herz-Kreislauf-Erkrankungen. *Eur Heart J* 37: 2315-2381.
5. Wirth A, Berg A, Bischoff SC, Colombo-Benkmann M, Ellrott T, et al. (2014) Evidenzbasierte Leitlinie: Prävention und Therapie der Adipositas.

Table 10: Overview of the findings in the two treatment groups receiving a modified Buchinger fasting therapy respectively a weight reduction diet.

Parameter		Fasting patients (according to Buchinger, modified)										Weight reduction diet patients (WRD)										Comparison of groups																
		Before Treatment					Result					Before treatment					Result					Signif-icance p	Effect size δ															
		n	m	sd	Day 4	Day 7	Discharge	3 months	6 months	Diff. Δ	Signif-icance p	Effect size δ	n	m	sd	Day 4	Day 7	Dis-charge	3 months	6 months	Diff. Δ			Signif-icance p	Effect size δ													
Weight	[kg]	38	91.7	17.3	88.5	16.5	87.2	16	86.1	16.0	86.7	15.1	88.8	16.5	-	<0.001	0.69 me	32	88.8	16.9	87.3	16.7	86.6	16.4	85.7	16.0	82.4	14.7	81.3	14.4	-7.5	<0.001	1.44 st	<0.001	0.98 st			
Number of pat	with 5%-weight reduction	38							78.9	52.6	31.6							9.4	75.0							9.4	75.0		81.3				<0.001	0.501 st				
Cholesterol-line	Total [mg/dl]	38	240.1	36			217	36	192.9	33	237.6	40	236.8	32	-3.3	0.469						226.8	41	219.4	42	227.2	43	225.6	43	-17.2	0.001	1.33 st	0.039	0.51 me				
	HDL [mg/dl]	38	152.9	29			146.9	34	120.8	31	149.5	33	148.3	28	-4.6	0.236						146.0	39	142.9	41	139.8	43	134.6	36	-17.1	<0.001	0.7 me/st	0.036	0.51 me				
	LDL [mg/dl]	38	58.5	16			47.2	14	45.1	11	59.3	14	61.4	15	+2.9	0.019	0.4 sm/me					54.3	13	51.7	12	60.6	14	63.2	14	+3.4	0.012	0.5 sm/me	0.744					
Tri-glycerides	[mg/dl]	38	141.6	64			112.8	47	135.2	61	142.2	73	135.9	71	-5.7	0.292						129.4	62	129.7	66	133.3	65	138.1	70	-18.2	0.065		0.450					
	[mg/dl]	38	102.5	21			74.6	17	95.6	16	97.3	19	100.2	18	-2.3	0.392						94.7	16	95.4	19	95.7	18	96.5	18	-5.1	0.144		0.520					
Glucose	in diabetic patients [mg/dl]	9	129.1	24			94.7	18	112.8	20	123.8	14	125.4	15	-3.7	0.696						110.8	22	113.1	28	113.0	25	116.8	13	-9.7	0.460							
Pressure all pat.	systolic [mm/Hg]	38	126	14			118	11	114	9	117	10	120	12	-6	<0.00	0.66 me	32	125	11		122	11	120	13	122	9	121	10	-4	0.086		0.325					
	diastolic [mm/Hg]	38	78	8			74	7	73	7	74	7	76	8	-2	0.010	0.4 sm/me	32	76	8		75	8	75	7	76	7	74	8	-2	0.120		>0.05					
Pressure hypertens. pat.	systolic [mm/Hg]	15	134	13			125	11	119	8	123	9	126	11	-8	0.002	0.88 st	13	129	13		127	13	125	13	125	9	123	12	-6	0.085		>0.05					
	diastolic [mm/Hg]	15	82	6			77	6	75	5	76	7	78	7	-4	0.027	0.67 me	13	79	9		78	9	78	8	77	6	76	8	-3	0.377		>0.05					
Nutritional behaviour	cognitive control [score]	38	10.18	3.43							12.11	3.3	11.37	3.17	+1.2	0.070		32	10.44	4.16												<0.001	0.90 me/st	0.048	0.49 me			
	flexible control [score]	38	2.53	1.52							3.39	1.67	3.37	1.58	+0.8	0.003	0.52 me	32	2.84	1.61												<0.001	1.16 st	0.049	0.49 me			
	rigid control [score]	38	3.00	1.56							3.71	1.52	3.47	1.45	+0.47	0.101		32	3.16	1.55												0.031	0.4 sm	0.705				
	Distractibility [score]	38	6.84	2.63							5.72	2.41	6.05	2.48	-0.79	0.015	0.41 sm	32	7.00	2.68												<0.001	0.76 me	0.050				
number of patients	Feeling of hunger [score]	38	4.47	2.21							3.76	2.53	4.03	2.22	-0.44	0.11		32	4.38	2.45												0.017		0.393				
	with basis activity [%]	38	84								92		90		+6	0.287		32	75												+16	0.156						
	with leisure activity [%]	38	76								87		84		+8	0.656		32	75												+9	0.588						
	with sport activity [%]	38	53								61		53		0			32	53												0							
Physical activity	Basal activity [h/week]	38	1.87	2.48							2.58	2.42	1.96	2.4	+0.09	0.344		32	1.95	2.16											2.83	2.57	2.52	2.54	+0.57	0.298	0.754	
	Leisure activity [h/week]	38	2.08	2.12							2.81	2.55	2.84	3.00	+0.76	0.049		32	2.14	2.31											3.95	4.46	4.58	4.51	+2.44	0.002	0.039	
	Sportive activity [h/week]	38	1.82	3.71							2.36	4.25	1.9	3.63	+0.08	0.527		32	2.07	3.55											2.16	3.75	1.87	3.56	-0.20	0.121	0.359	
Quality of life	physical sum scale [score]	38	32.2	9.60							36.5	10.9	36.2	10.3	+4	0.007	0.5 sm/me	32	30.0	9.8											35.0	11.2	36.1	11.2	+6.1	<0.001	0.67 me	0.354
	psychological sum scale	38	43	10.5							46.2	11.4	45.3	11.7	+2.3	0.153		32	42.7	12.1											45.5	10.6	44.8	10.0	+2.2	0.058	0.983	

Short cuts: m=mean; sd=standard deviation; sm=small; me=medium; st=strong; pat.=patients; hypertens.=hypertensive

6. Beer AM, Ismar LE, Wessely DK, Pötschke T, Weidner B, et al. (2014) Retrospective Long-Term Comparison of Naturopathic Fasting Therapy and Weight Reduction Diet in Overweight Patients. *Evid Based Complement Alternat Med*.
7. Pudiel V, Westenhöfer J (1989) Fragebogen zum Eßverhalten (FEV). Handanweisung. Hogrefe Verlag für Psychologie, Göttingen, Toronto, Zürich.
8. Goldhamer AC, Lisle DJ, Sultana P, Anderson SV, Parpia B, et al. (2002) Medically supervised water-only fasting in the treatment of borderline hypertension. *J Altern Complement Med* 8: 643-650.
9. von Herz U, Müller MJ (1996) Heilfasten. *Aktuelle Ernährungsmedizin* 21: 25-28.
10. McCarty MF (2003) A preliminary fast may potentiate response to a subsequent low-salt, low-fat vegan diet in the management of hypertension - fasting as a strategy for breaking metabolic vicious cycles. *Med Hypotheses* 60: 624-633.
11. Göhler L, Hahnemann T, Michael N, Oehme P, Steglich HD, et al. (2000) Reduction of Plasma Catecholamines in Humans during Clinically Controlled Severe Underfeeding. *Prev Med* 30: 95-102.
12. Huber R, Nauck M, Ludtke R, Scharnagl H (2003) Effects of one week juice fasting on lipid metabolism: a cohort study in healthy subjects. *Forsch Komplementarmed Klass Naturheilkd* 10: 7-10.
13. Pötschke T, Weidner B (2012) Ernährungstherapie Beer AM, Adler M: Leitfaden Naturheilverfahren für die ärztliche Praxis. Urban & Fischer Elsevier Verlag, München 1: 115-154.
14. Beer AM, Ostermann T, Matthiessen PF (2001) Evaluation stationärer Naturheilkunde – Das Blankensteiner Modell. Teil I: Patientenklimentel und therapeutische Konzepte. *Forsch Komplementarmed Klass Naturheilkd* 8: 6-13.
15. The International Statistical Classification of Diseases and Related Health Problems, 10th revision, German Modification (ICD-10-GM) (2018) Systematisches Verzeichnis, Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme, 10. Revision, German Modification edited by Deutsches Institut für Medizinische Dokumentation und Information (DIMDI).
16. Vidal J (2002) Updated review on the benefits of weight loss. *Int J Obes Relat Metab Disord* 26: S25-S28.
17. Pi-Sunyer FX. NHLBI Obesity Education Initiative (2000) The Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults.
18. Fine JT, Colditz GA, Coakley EH, Moseley G, Manson JE, et al. (1999) A prospective study of weight change and health-related quality of life in women. *JAMA* 282: 2136-2142.
19. Faul F, Erdfelder E, Lang AG, Buchner A (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 39: 175-191.
20. Franz MJ, VanWormer JJ, Crain AL, Boucher JL, Histon T, et al. (2007) Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *J Am Diet Assoc* 107: 1755-1767.
21. Bortz J, Döring N (2006) Forschungsmethoden und Evaluation. Für Human- und Sozialwissenschaftler. Springer Medizin Verlag, Berlin, Heidelberg.
22. Stunkard AJ, Messick S (1985) The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *J Psychosom Res* 29: 71-83.
23. Frey I, Berg A, Grathwohl D, Keul J (1999) Freiburger Fragebogen zur körperlichen Aktivität-Entwicklung, Prüfung und Anwendung. *Sozial- und Präventivmedizin/Social and Preventive Medicine* 44: 55-64.
24. Bullinger M, Kirchberger I (1998) Der SF-36 Fragebogen zum Gesundheitszustand - Handanweisung. Hogrefe Verlag für Psychologie, Göttingen.
25. Williams LT, Young AF, Brown WJ (2006) Weight gained in two years by a population of mid-aged women: how much is too much. *Int J Obes (Lond)* 30: 1229-1233.
26. Ulen CG, Huizinga MM, Beech B, Elasy TA (2008) Weight Regain Prevention. *Clin Diabetes* 26: 100-113.
27. Chaput JP, Tremblay A (2009) The glucostatic theory of appetite control and the risk of obesity and diabetes. *Int J Obes (Lond)* 33: 46-53.
28. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, et al. (1996) Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 334: 292-295.
29. Mars M, de Graaf C, de Groot CP, van Rossum CT, Kok FJ (2006) Fasting leptin and appetite responses induced by a 4-day 65%-energyrestricted diet. *Int J Obes (Lond)* 30: 122-128.
30. Wilhelmi de Toledo F, Buchinger A, Burggrabe H, Gaisbauer M, Hölz G, et al. (2002) Leitlinien zur Fastentherapie. *Forsch Komplementarmed Klass Naturheilkd* 9: 189-198.
31. Michalsen A, Schlegel F, Rodenbeck A, Ludtke R, Huether G, et al. (2003) Effects of short-term modified fasting on sleep patterns and daytime vigilance in

non-obese subjects: results of a pilot study. *Ann Nutr Metab* 47: 194-200.

32. Kolanowski J (1981) Influence of insulin and glucagon on sodium balance in obese subjects during fasting and refeeding. *Int J Obes* 1: 105-114.
33. Potter LR, Abbey-Hosch S, Dickey DM (2006) Natriuretic peptides, their receptors, and cyclic guanosine monophosphate-dependent signaling functions. *Endocr Rev* 27: 47-72.
34. Ellrott T, Pudel V (1998) *Adipositastherapie. Aktuelle Perspektiven*. Georg Thieme Verlag, Stuttgart.
35. Catenacci VA, Wyatt HR (2007) The role of physical activity in producing and maintaining weight loss. *Nat Clin Pract Endocrinol Metab* 3: 518-529.
36. Haskell WL, Lee I, Pate RR, Powell KE, Blair SN, et al. (2007) Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 116: 1081-1093.
37. Saris WH, Blair SN, van Baak MA, Eaton SB, Davies PS, et al. (2003) How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obes Rev* 4: 101-114.
38. Larsson U, Karlsson J, Sullivan M (2002) Impact of overweight and obesity on health-related quality of life - a Swedish population study. *Int J Obes Metab Disord* 26: 417-424.

Copyright: © **Wiebelitz et al.** This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.