

Sustainability of diet-based moderate calorie restriction among obese patients with metabolic-associated fatty liver disease

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Abstract

Background and Aim: The long-term sustainability of weight loss continues to be a subject of investigation. This study was designed to examine the effects of weight loss and the long-term sustainability of lifestyle modifications among obese patients with metabolic-associated fatty liver disease (MAFLD).

Materials and Methods: A total of 40 patients who were prescribed a hypo-caloric diet (~500 calories reduction for each patient), and who were followed up for 12 weeks in 4 face-to-face interviews were enrolled in the study. The patients were contacted at the 36th month, and their current weight was recorded.

Results: The mean weight at baseline of 87±13 kg decreased to 79±11 kg after 12 weeks of intervention ($p<0.001$). The mean weight at the 36th month did not significantly differ from that measured at the baseline ($p=0.563$). The mean controlled attenuation parameter decreased from 320±13 dB/m to 273±37 dB/m ($p<0.001$), while the median liver stiffness measurement decreased from 8.7 kPa (3.6–45.7 kPa) to 5.7 kPa (2.2–29.9 kPa) ($p<0.001$).

Conclusion: Strict follow-up through nutritional consultation can help achieve weight loss in obese patients with MAFLD. However, for long-term results, the collaboration of nutritionists and gastroenterologists is essential to prevent weight regain.

Keywords: Diet sustainability; fibrosis; metabolic-associated fatty liver disease.

Introduction

An increased prevalence of type 2 diabetes mellitus (T2DM), obesity, and nonalcoholic fatty liver disease (NAFLD) reflects the close relationship between these disease etiologies.^[1] Based on the available insights of the disease pathophysiology, it has been proposed that NAFLD may be an hepatic manifestation of systemic metabolic dysfunction;

therefore, international collaborative efforts have renamed this disease for the sake of competently reflecting the disease's pathophysiology.^[2–4] Metabolic (dysfunction)-associated fatty liver disease (MAFLD), formerly called NAFLD, is a recently proposed nomenclature that is defined as evidence of hepatic steatosis in addition to being overweight, with T2DM or metabolic dysfunction criteria.^[5]

MAFLD has been estimated to affect approximately one-quarter of the world population.^[6] As the problem of widespread obesity grows, MAFLD constitutes a major public health burden.^[7,8] The growing prevalence notwithstanding, there is currently no approved pharmacotherapy to address this health concern. The most established treatment remains a recommendation for lifestyle modifications that are targeted at weight reduction.^[9,10] A weight loss of >10% of body weight has been demonstrated to show improvement in hepatic steatosis, steatohepatitis, and fibrosis by at least one stage. Even a modest weight loss of >5% produces beneficial improvement in the disease.^[11] The benefit of weight reduction has been proven;^[12–14] however, it has been shown that only a minority of patients achieve the targeted sustained weight loss using standard lifestyle interventions.^[15] Scragg et al.^[16] demonstrated that an extremely low-calorie diet may help to achieve a targeted weight loss of >10% and maintain the loss with continued use in 9 months of follow-up. However, weight regain has been reported in long-term follow-up even when the targeted weight loss was achieved.^[17] Nonetheless, Haufe et al.^[18] observed that the effects of weight loss persisted in terms of insulin resistance and hepatic fat content, despite weight regain.

A few studies notwithstanding,^[15–18] there is a paucity of studies that have investigated the sustainability of an effective diet in the long-term follow-up. Here, we have referred to this issue with respect to our obese MAFLD population using a calorie-restriction diet.

Materials and Methods

Patients

Forty consecutive obese patients who were followed up at Marmara University Institute of Gastroenterology between December 2017 and March 2018 with a MAFLD diagnosis were recruited for this study. Obesity was defined as a body mass index (BMI) of ≥ 30 kg/m² according to the diagnostic criteria of the World Health Organization.^[19] The diagnosis of MAFLD was made based on the presence of the following metabolic risks: overweight/obesity, diabetes mellitus, and evidence of metabolic dysregulation. Metabolic dysregulation has been defined as the presence of 2 or more of the following conditions: 1) waist circumference ≥ 102 cm in men and 88 cm in women; 2) blood

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Table 1. Comparison of anthropometric measurements, laboratory parameters, and transient elastography outcomes of patients before and after dieting for 12 weeks

	Before	After	p
Body weight, kg	87±13	79±11	<0.001
Body mass index, kg/m ²	32.7 (30.0–45.3)	29.7 (26.4–41.1)	<0.001
Waist circumference, cm	107 (82–132)	99 (78–122)	<0.001
Fasting blood glucose, mg/dL	114 (84–207)	98 (84–159)	<0.001
Insulin, mg/dL	18.4±8.4	14.0±5.8	<0.001
Hemoglobin A1c, %	5.9 (4.5–11.8)	5.4 (4.0–7.3)	<0.001
Total cholesterol, mg/dL	210±45	172±43	<0.001
Triglycerides, mg/dL	183±66	133±53	<0.001
Low-density lipoprotein, mg/dL	130±37	105±30	0.003
High-density lipoprotein, mg/dL	43 (30–75)	45 (26–80)	0.168
Aspartate transaminase, U/L	32 (16–135)	20 (12–43)	<0.001
Alanine transaminase, U/L	47 (14–190)	29 (12–58)	<0.001
Gamma glutamyl transferase, U/L	41 (10–316)	26 (9–184)	<0.001
Controlled attenuation parameter, dB/m	320±46	273±37	<0.001
Liver stiffness measurement, kPa	8.7 (3.6–45.7)	5.7 (2.2–29.9)	<0.001

The normally distributed data are presented as mean±SD and were compared using a paired t-test. The non-normally distributed data are presented as median [minimum–maximum] and were compared with the Wilcoxon signed-rank test. The significant p values are marked in bold type.

pressure ≥130/85 mmHg or undertaking a specific drug treatment; 3) TG ≥1.70 mmol/L or undertaking a specific drug treatment; 4) HDL cholesterol (HDL-C) <1.0 mmol/L in men and <1.3 mmol/L in women; 5) prediabetes (i.e., fasting glucose levels of 5.6–6.9 mmol/L, or 2-hour post-load glucose levels of 7.8–11.0 mmol/L, or HbA1c 5.7%–6.4%); 6) homeostasis model assessment-insulin resistance (HOMA-IR) score ≥2.5; and 7) a C-reactive protein level of >2 mg/L.^[5]

Diet prescription and follow-ups. A 12-week with a hypocaloric diet was prescribed by a dietician (B.E.T) after assessing the patients' individual requirements. The total caloric consumption was reduced by ~500 kcal for each patient. The macro-nutritional ingredients were 45%–60% carbohydrates, 10%–20% proteins, and 25%–35% fat. Complex carbohydrates and nutrition with a low glycemic index were recommended. During the visits, the patients were also educated about healthy cooking methods and nutrition. The study involved 4 face-to-face interviews, conducted at initiation, 4, 8, and 12 weeks. The patients were interviewed again by phone after 36 months to assess adherence to lifestyle modifications and their current weight.

At baseline, the nutritional status of the patients was assessed based on a 3-day food consumption record using Nutritional Information System software (BeBIS; Ebispro for Windows, Stuttgart, Germany; Turkish version 8.1). The laboratory data included the values of total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein, aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase, serum insulin, hemoglobin A1c, and fasting blood glucose. Elevated AST and ALT levels were defined as >37 U/L and >40 U/L, respectively.^[20] Bioimpedance analysis was performed using a Tanita MC 780 P device (Tanita Corp., Tokyo, Japan) to estimate body composition data. A baseline FibroScan (Echosens SA, Paris, France) examination was also performed. Face-to-face interviews were conducted in the fourth and eighth weeks to evaluate patient compliance with the therapy. Anthropometric measurements, laboratory tests, and FibroScan results were reassessed in the twelfth week.

Transient Elastography

Transient elastography using the FibroScan device was performed by a single operator according to the manufacturer's instructions detailed elsewhere.^[21] At least 10 valid measurements were performed during each examination and an interquartile range-to-median ratio of ≤0.3 was achieved.^[22] Hepatic steatosis was defined as a controlled attenuation parameter cut-off of ≥238 dB/m.^[23] A liver stiffness measurement of ≥8.95 kPa and ≥11 kPa indicated significant (F≥2) and advanced fibrosis (F≥3), respectively.^[24]

Statistical Analysis

All of the study analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The normality of distribution was analyzed using the Kolmogorov-Smirnov test. Normally and not-normally distributed data were expressed as mean±SD and median [minimum–maximum], respectively. Dependent continuous variables were compared using a paired t-test and the Wilcoxon signed-rank test. Dependent categorical dependent data were compared using McNemar's test. The level of statistical significance was set at p<0.05.

Ethics

This study was conducted according to the Declaration of Helsinki and approved by the ethics committee of Bahcesehir University (date: 18.10.2017, number: 2017-16/01). Written informed consent was obtained from all of the patients.

Results

The study population comprised 40 patients with MAFLD (mean age: 56±10 years; 25 women [66%], 13 men [34%]). Initially, 25 patients (63%) were categorized as class I obesity, 8 (20%) as class II, and 5 (13%) as class III. The baseline anthropometric, laboratory, and FibroScan parameters are provided in Table 1, as well as the compar-

ison to the values determined at the 12th week of follow-up. All of the patients complied with their diet. A weight loss of 5% to 10% of the body weight was recorded for 27 patients (68%). The remaining patients achieved a weight loss of >10%. At the end of the 12th week, regression in both hepatic steatosis and fibrosis was observed. The initial prevalence of significant and advanced fibrosis decreased from 47.4% (n=18) and 31.6% (n=12) to 15.8% (n=6) and 10.5% (n=4), respectively (p<0.001 and p=0.008, respectively). Elevated transaminase levels were recorded in 58% (n=23) of the patients at baseline and in only 25% (n=10) after the weight reduction. The change in hepatic fibrosis is depicted in Figure 1.

According to the patients' statements, the daily mean caloric consumption was 1480±373 kcal (range: 725–2701 kcal). At the 36th month, 23 patients (61%) had abandoned their diet plan completely, while 15 patients (39%) still partially followed the diet. The change in the weight and BMI of these patients is illustrated in Figure 2. The weight at baseline did not significantly differ from the final weight at the 36th month (p=0.563); however, the BMI decreased significantly (p=0.046).

Discussion

Our results demonstrated successful improvement in the status of hepatic fibrosis and steatosis in obese patients with MAFLD following weight reduction and nutritional consultation; however, the long-term observation after termination of follow-up revealed weight regain and noncompliance with the recommended diet.

Successful and sustained weight loss has been previously defined as a loss of 10% of the body weight maintained for >12 months.^[25] Franz et al.^[26] reported in a systematic review of weight loss interventions that weight loss (5%–9%) plateaued at the 6th month and stabilized at the 12th month (4.8%–8%) in some patients. Most patients regained 30% of the lost weight in the first 12 months following the discontinuation of the intervention. As observed in our research, most patients with MAFLD report having regained the weight lost by dieting.^[27–29] Therefore, it appears that the period after reaching the plateau at the 6th month should be targeted with a change in the diet strategy and a focus on lifestyle and weight loss maintenance.^[30] For MAFLD patients in particular, sustained lifestyle modifications that include improved eating and the inclusion of physical activity constitute the cornerstone of disease management. Amelioration of laboratory and histological parameters has consistently been reported following use of a hypocaloric diet.^[31]

Surgical interventions, such as sleeve gastrectomy, Roux-en-Y gastric bypass (RYGB), and adjustable gastric banding, have offered an alternative means to achieve long-term weight loss in patients with MAFLD. All of these options have been associated with the improvement of MAFLD.^[32–34] Unlike lifestyle modification, bariatric surgery is associated with sustained weight loss in 40% to 70% of patients. In the systematic review of Hafeez et al.,^[35] for instance, complete regression of NAFLD was reported to be 60% to 83%, and fibrosis resolution occurred in 35% to 50% of the patients who underwent bariatric surgery. However, there were also some incidences of worsening fibrosis after RYGB, which may be associated with the surgical intervention or inadequate replacement of macro/micronutrients;^[36–38] therefore, recent MAFLD guidelines suggest that bariatric surgery is most appropriate for patients with at least obesity class II and without liver cirrhosis.^[10]

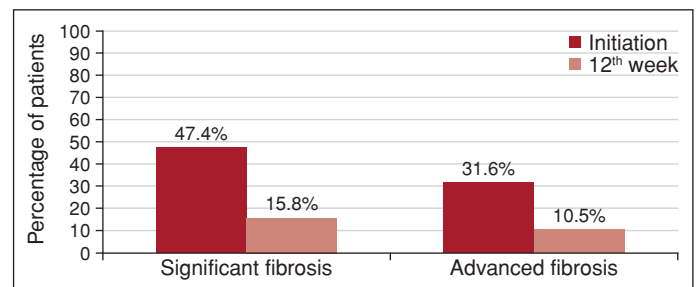


Figure 1. Change in hepatic fibrosis status over the course of follow-up.

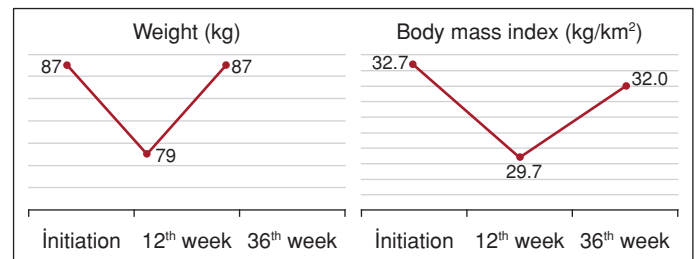


Figure 2. Changes in weight and body mass index over the course of follow-up.

The main strength of this study lies in the long-term observation of 36 months. In addition, we used FibroScan, a diagnostic tool that has been recognized as an accurate means to evaluate hepatic steatosis and fibrosis status.^[39–41] Limitations of this study include the fact that, due to the ongoing coronavirus 2019 pandemic, we could not conduct face-to-face interviews in the 36th month. The information about current weight was provided in a phone interview; we could not conduct FibroScan or laboratory examinations. Second, only 3 days of food consumption were recorded, which may have influenced the low caloric consumption data.

In conclusion, obese patients with MAFLD can benefit from weight reduction and strict follow-up with a nutritional consultation. For long-term success, it appears that a more flexible follow-up with a nutritional specialist may prevent weight regain. The collaboration of gastroenterologists and nutritional specialists plays a significant role in disease management.

Ethics Committee Approval: The Bahcesehir University Clinical Research Ethics Committee granted approval for this study (date: 18.10.2017, number: 2017-16/01).

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Author Contributions: Study concept and design: HG, BET, TO, EBK, EK; Acquisition of data: BET, TO, EBK, EK; Statistical analysis and interpretation of data: EBK, TO, BET, EK; Drafting of the manuscript: TO, EBK, EK, BET; Critical revision of the manuscript: HG; Study supervision: HG, BET, TO, EBK, EK. All authors approved its final version and agree to be accountable for all aspects of the study.

Conflict of Interest: The authors have no conflict of interest to declare.

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