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The Effect of Lifestyle Modification on the Recovery of Non-Alcoholic Fatty Liver Disease in Health Insurance Staff in Tabriz, Iran: A Randomized Clinical Trial

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Abstract

Objectives: Non-alcoholic fatty liver disease (NAFLD) is among the most common liver diseases. In recent years, the prevalence of fatty liver disease has been mostly attributed to obesity, an unhealthy lifestyle, and poor eating habits, which, in addition to Western countries, have also been reported in Iran. This study aimed to evaluate the effect of lifestyle modification (physical activity and diet) on the recovery of NAFLD in health insurance staff in Tabriz, Iran.

Materials and Methods: This randomized controlled clinical trial was conducted on 42 male and female NAFLD patients aged 20 to 55. The participants were randomly divided into intervention (diet along with aerobic exercise) (n=21) and control (without diet and exercise) (n=21) groups. The level of disease recovery was evaluated by measuring the level of liver enzymes (AST and ALT), liver ultrasound (to determine the degree of fatty liver), and body mass index (BMI) before and after three months of intervention. Paired and independent t-test, Mann-Whitney U test, and Wilcoxon test were performed using SPSS version 22 software. The clinical significance of the study was estimated using an epidemiological tool known as the number needed to treat (NNT).

Results: No significant difference was observed between the two groups in anthropometric and biochemical parameters, as well as fatty liver grade. However, the decrease in BMI index in the intervention group was insignificant compared to the control group. The degree of liver recovery in the intervention and control groups was calculated to be 69.9% and 33.3%, respectively. Also, the decrease in fatty liver grade in the intervention group was significant compared to the control group ($P = 0.028$). There was a statistically significant reduction in the severity of fatty liver disease in the intervention group at the end of the research (NNT = 3.5), meaning that for every 3.5 patients with NAFLD treated with diet and exercise for 3 months, one patient showed improvement.

Conclusions: This study showed that lifestyle modifications, such as physical activity and dietary habits, significantly affected fatty liver in NAFLD patients.

Keywords: Lifestyle, Modification, Recovery, NAFLD

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide, mainly caused by a sedentary and unhealthy lifestyle (1). This disease is characterized by fat accumulation, especially triglycerides, in the cytoplasm of liver cells at a rate of 5%-10% of liver weight in the absence of alcohol consumption (1). NAFLD is closely related to an unhealthy lifestyle, including increased calorie intake and reduced physical activity and exercise.

The last three decades have witnessed a significant increase in the average body mass index (BMI) and obesity, which are the pathophysiological drivers of NAFLD (2). Currently, there are different therapeutic strategies for the management of NAFLD. However, proven treatments for this disease have yet to be found (3).

The first step in treating the disease is to modify the patient's lifestyle and control the risk factors for the disease (4). Randomized controlled trials have shown that lifestyle interventions reduce body weight in NAFLD patients, improve hepatic triglyceride content determined by magnetic resonance techniques, and mitigate the complications of NAFLD (combination of steatosis, inflammation, and hepatocyte ballooning), as determined by liver biopsy (5–11).

A recent systematic review and meta-analysis showed that the overall prevalence of NAFLD worldwide was 32.4%, and its frequency was significantly higher in men (12). A clinical trial on 261 patients with NASH (proven by biopsy) who underwent frequent liver biopsy after 12 months of low-calorie and low-fat diet intervention (750 kcal less than the daily requirement) and walking (200 min/wk) reported the effect of weight loss induced by a healthy lifestyle on liver histology (13). In another 18-month study involving 278 subjects with dyslipidemia or central obesity (half of whom had NAFLD), exercise and diet interventions did not affect liver fat content or cardiovascular risk parameters (5).

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Key Messages

- Considering the high prevalence of NAFLD in most countries and its economic effects on the individual and the society, making changes in lifestyle, including the level of awareness about the type of diet and increasing physical activity, can reduce the incidence of complications caused by the progression of the disease. Therefore, in order to manage fatty liver, in addition to treatment, there is a need for self-management of patients to improve the quality of life and reduce costs caused by the progression of the disease.

Similarly, an 8-week study involving 45 patients with type 2 diabetes (with and without NAFLD) found that exercise combined with high monounsaturated fats or a high-carbohydrate/low-glycemic index diet had no significant effect on reducing liver triglycerides content (14).

In contrast, in a study of 130 severely obese subjects (BMI >35 kg/m^2), exercise with diet resulted in greater weight loss and liver fat reduction than a 6-month dietary intervention (15). A 6-month trial on obese subjects older than 65 years showed similar reductions in hepatic triglyceride content and body weight in the diet group compared to the diet-exercise group. However, the diet-exercise group observed a significant decrease in serum lipids and blood pressure (16).

Clinical trials on the effect of lifestyle modifications on the improvement of NAFLD are limited, and no study in this field has been conducted on sedentary employees. This study aimed to evaluate the effects of lifestyle modification, including physical activity and diet, on the recovery of NAFLD in health insurance employees in Tabriz, Iran.

Materials and Methods

Study Design

The study was a double-blind, randomized, controlled clinical trial. Men and women aged 20 to 55 were divided into intervention and control groups using the random blocking method and blocks 4 and 6 through random assignment software (RAS) with a 1:1 assignment ratio by a person not involved in the research. The feature was hidden by placing the group's name in a sealed, numbered, opaque envelope. The allocation was conducted by a researcher who had no direct clinical participation in the study, and the statistical data analyzer remained blinded throughout the investigation.

Subjects

All participants gave their informed consent after receiving a detailed explanation of the study's purpose and methods. The inclusion criteria were: men and women aged 20–55 with NAFLD. Ultrasound of the liver and bile ducts using a Medison SonoAce X6 confirmed the presence of NAFLD. Also, an experienced radiologist at the ultrasonic center of Tabriz University of Medical Sciences performed the liver ultrasound. The exclusion criteria were as follows: pregnant and lactating women; individuals with cardiovascular, thyroid, kidney, inflammatory, or autoimmune disease; individuals with diabetes, hepatitis A, B, or C; individuals with hemochromatosis, Wilson's disease or inflammation; use of vitamin supplements, including vitamins A, E and C; use of prebiotic/probiotic supplements and alcohol consumption.

Sample Size

Sampling for this study was performed using the convenience method. The participants were divided into two study groups: intervention (diet and aerobic exercise) and control (physical activity without diet) by random allocation. The required sample size was at least 20 patients per group based on the mean change in Aspartate aminotransferase (AST) according to the Keymasi et al study (17). The number of participants in each group was increased to 25 to account for a 10% dropout rate.

The participants were matched for age and sex and randomly divided into an intervention (n=21) and a control group (n=21) using a computer-generated randomization scheme. Over three months, the first group participated in a diet and aerobic exercise program, while the second group served as a control and exercised without changing their food. We followed up on the two groups by phone and social groups every two weeks.

All measurements, including anthropometric assessments, dietary intake records, and blood tests, were taken before and after the intervention. The primary outcome of the study was the difference in AST serum levels. The remaining variables (i.e., ALT, BMI, and weight) were considered secondary outcomes. The BMI was calculated through anthropometric assessments of each patient's height and weight using standard anthropometric techniques (18).

Physical Activity

In addition to the diet, the intervention group participated in aerobic exercise for 12 weeks and three sessions per week for 45 minutes. Based on Karvonen's formula, physical activity, including walking at an intensity of 60% heart rate, was considered (19).

*Heart rate reserve = [(220-age)-rest heart rate * %60 HR] + rest heart rate*

To determine the walking pace, the Karvonen method and the following formula were used to calculate the heart rate of each patient at the time of measurement and according to 60% of their reserve heart rate. The device adjusts the heart rate during walking to match the calculated rate.

Blood Tests
At the study's beginning and end, 5 mL of venous blood samples were obtained after an overnight fasting (12 hours). The AST and ALT were measured via the enzymatic method by PARS AZMUN (Tehran, Iran) kits using an auto-analyzer machine (Alcyon 300, Abbott, USA), which was calibrated before beginning the tests.

Dietary Intakes
The participants' dietary intake was assessed using a three-day food record (two weekdays and one weekend). Nutritionist IV (First Databank, Inc., Hearst Corporation) was used to compile a database of the content and nutritional value of Iranian food products, which was then used to assess the dietary data.

Diet
A weight loss diet (500 calories less than calculated energy) containing 60% carbohydrates, 25% fat, and 15% protein was prescribed to the intervention group by a nutritionist, along with general training on healthy eating based on increasing the consumption of vegetables and legumes and reducing the consumption of sweets and saturated fats.

Ultrasonography
To measure patients' lifestyles at the onset of the study, physical activity was measured by patients' self-reports, and the quantity of daily food intake was determined using a three-day food record questionnaire and the Nutritionist IV software.

Then, for each food item, the individual's intake in grams was manually calculated. Using the Nutritionist IV, the individual's daily energy intake was calculated, and a diet containing 500 fewer calories than the calculated energy was suggested. The control group did not receive the interventions of education, diet, and physical activity.

An experienced radiologist at the Ultrasonic Center of Tabriz University of Medical Sciences performed the liver ultrasound.

The liver was evaluated for size, echogenicity, structure, and ultrasound beam penetration using the Medison SonoAce X6. Based on echogenicity, beam penetration, and portal vessel wall distinction, non-alcoholic fatty livers were classified into three subscale grades (grade I, II, and III) (20).

Statistical Analysis
Statistical analyses were performed using SPSS V 22.0 (IBM, Armonk, NY). The normal distribution of all variables was checked with the Kolmogorov-Smirnov test. The paired t-test was used for intra-group changes and the independent t-test was utilized for inter-group changes for variables with normal distribution. In addition, Mann-Whitney U and Wilcoxon tests were employed for variables with non-normal distributions. Demographic indicators were analyzed, and the primary indicators and distribution of the main variables were extracted, using descriptive statistics. Clinical significance was estimated using the epidemiology method number needed to treat (NNT), which is computed using the following formula:

$1/ARR = NNT$

Which ARR stands for absolute risk reduction.

Statistical significance was set to a P value < 0.05.

Results
The present study randomly divided 50 patients with NAFLD (male=24, female=26) into two groups. Of these, eight subjects were excluded from the study before the intervention because of COVID-19 disease, and 42 patients (male=19, female=23) continued the study (Figure 1). According to Table 1, 43% of the intervention group and 67% of the control group, and 55% of the study subjects were women. The mean age of the intervention and control groups was (43.9±5.21-45.4±5.52) years, respectively. As shown in Table 2, the mean BMI in the intervention group was 29.7±3.5 kg/m^2 and 27.9±4.7 kg/m^2 in the control group. At the end of the trial, a significant decrease in BMI was observed in the treatment group compared to the beginning of the study, but no significant decrease was observed between the groups (P = 0.751). Also, serum levels of AST and ALT in both groups were not significantly reduced compared to the beginning of the trial (P = 0.62) and (P = 0.42), respectively (Table 2).

Results showed that 33.3% of those with grade 1 fatty liver in the control group observed improvement. Also, 85.7% of the intervention group had a reduction in the fatty liver grade, of which 61.9% recovered completely (Table 3).

According to Table 4, the relative risk (RR) in the intervention group was 57.1% compared to the control group. The RR reduction in the intervention group was 42.9%. The ARR, the absolute benefit of the intervention, was 28.6%.

Based on the NNT test results, the NNT number in the intervention group was 3.5, indicating that in 3.5 patients with NAFLD under diet and physical activity for 3 months, one patient exhibited a significant decrease in fatty liver degree compared to the beginning of the study (P = 0.028).

Discussion
It has been proposed that lifestyle modifications, including physical activity and diet, significantly affected fatty liver grade in NAFLD patients.

Findings Related to AST and ALT Indices in the Studied Groups
The liver transaminase enzymes, AST and ALT, are important but non-specific indicators of liver damage. The serum concentration of these enzymes in patients with NAFLD sometimes increases up to 10 times the

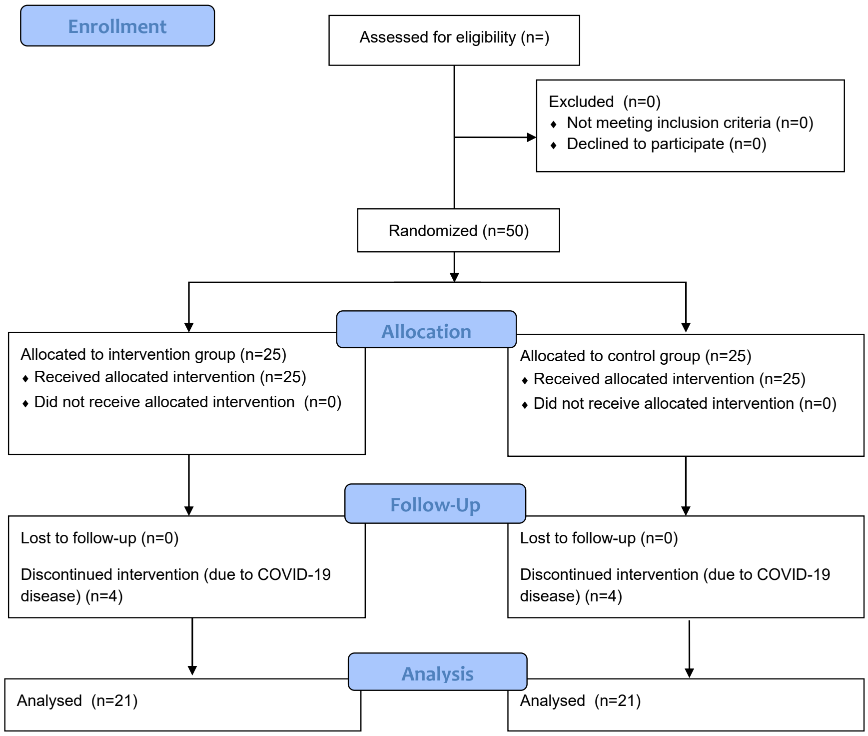

Figure 1. Flowchart of the Study.

normal range (21). Over 78% of those with fatty liver have normal liver enzyme levels, and an enzyme elevation is not a sensitive indicator of the condition (20). Our results showed that after three months of diet and exercise, the ALT and AST indices of NAFLD patients did not differ significantly from those of the control group.

Several studies have demonstrated the effect of exercise and diet on liver enzymes and liver fat content. Keymasi et al investigated the effect of exercise training on liver fat content and liver enzymes in middle-aged men with fatty liver and found a decrease in AST and ALT enzymes, which conflicted with our results (17).

Also, a decrease in AST and ALT enzymes was observed in studies where patients with NAFLD were subjected to weight loss intervention for 6 months (22,23), which contradicted the results of our study in terms of liver enzymes.

Yoshimura et al conducted two types of diet intervention and diet with exercise on NAFLD patients and found no significant relationship between liver enzymes and

Table 1. Demographic Characteristics of the Study Subjects

Variable	Intervention Group (n = 21)	Control Group (n=21)	Total
Age, Mean ± SD	43.9±5.21	45.4±5.52	44.67±5.35
Gender, No. (%)			
Male	12 (57.1)	7 (33.3)	19(45.2)
Female	9 (42.9)	14 (66.7)	23 (54.8)
Education level, No. (%)			
Diploma	0 (0.0)	2 (9.5)	2 (4.8)
Associate degree	0 (0.0)	1 (4.8)	1 (2.4)
Master	10 (47.6)	13 (61.9)	23 (54.8)
High master	11 (52.4)	4 (19.0)	15 (35.7)
Doctoral degree	0 (0.0)	1 (4.8)	1 (2.4)
Marital status, No. (%)			
Single	2 (9.5)	1 (4.8)	3 (7.1)
Married	19 (90.5)	20 (95.2)	39 (92.9)
Smoking, No. (%)	2 (9.5)	2 (9.5)	4 (9.5)

Table 2. Comparison of the Transaminase Enzyme and Anthropometric Index at Baseline and at the End of trial Between the Two Groups

Variables		Intervention Group (n=21) Mean ± SD	Control Group (n=21) Mean ± SD	*P* Value[a]
AST, U/L	Before	28.3±6.8	27.3±7.5	0.62
	After	26.9±5.5	27.8±6.2	
	P value[b]	0.79	0.43	
ALT, U/L	Before	24.4±11.3	19.9±14	0.42
	After	23.0±9	24.8±21.9	
	P value[b]	0.917	0.08	
BMI, kg/m^2	Before	29.7±3.5	27.9±4.7	0.751
	After	28.1±3.1	27.7±4.2	
	P value[b]	0.005	0.201	

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; BMI, body mass index.
[a] Independent samples *t* test; [b] paired *t* test.
$P < 0.05$ is significant.

Table 3. Frequency of Subjects Studied Based on Fatty Liver Grade at the Beginning and End of the Study

Group	Status	Normal (Grade 0)	Grade I	Grade I-II	Grade II	Grade III
Intervention (n = 21), No. (%)	Before	0 (0)	11 (52.4)	2(9.5)	8 (38.1)	2(9.5)
	After	13 (61.9)	6 (28.6)	2 (9.5)	0 (0)	2 (9.5)
Control (n = 21), No. (%)	Before	0 (0)	14 (66.7)	3 (14.3)	4 (19)	3 (14.3)
	After	7 (33.3)	7 (33.33)	3 (14.3)	4 (19)	3 (14.3)

Table 4. Effect of Lifestyle Modification (Physical Activity and Diet) on Grade Fatty Liver in NAFLD Patient

Groups	Recovery, %	NNT (95% CI)	ARR (95% CI)	RRR (95% CI)	RR (95% CI)	*P* value[a]	*P* value[b]
Intervention	61.9%	3.5%	28.6%	42.9%	57.1%	0.000	0.028
Control	33.33%					0.08	

Abbreviations: NAFLD, nonalcoholic fatty liver disease; ARR, absolute risk reduction; RRR, Relative risk reduction; RR, risk reduction; NNT, number needed to treat.
[a] *P* value resulted from Wilcoxon test.
[b] *P* value resulted from Mann-Whitney U test.
$P < 0.05$ is significant.

fat accumulated in the liver with aerobic exercise. In other words, reducing calorie intake with and without exercise can have a beneficial effect on fatty liver and its complications such as heart diseases (24). Contradictory results were reported in Orci and colleagues' study that physical activity independent of diet reduces ALT and AST liver enzymes in patients with NAFLD (25). However, in our study, aerobic exercise and diet did not affect liver enzymes, which may be related to the normal range of liver enzymes in most study subjects. Also, a long-term intervention with a limited-calorie diet is needed to observe significant changes in the level of liver enzymes.

Findings Related to Fatty Liver Grade Index in the Studied Groups

Although liver biopsy is the gold standard for diagnosing fatty liver, NAFLD is often diagnosed using the routine and non-invasive method of liver ultrasound. Moreover, the sensitivity and specificity of this diagnostic method is 80-100% (26). In a normal state, fat accumulation in the liver of healthy people is less than 5% (27).

Our study showed that 3-month physical activity and diet reduce the grade index of fatty liver in patients with NAFLD compared to the control group. Our study is similar to several studies showing that liver fat content decreases in people with NAFLD following moderate weight loss through caloric restriction (28,29).

In Scaglioni and colleagues' study, short-term changes in lifestyle, including diet and physical activity, were associated with improved liver fat, which was evaluated by ultrasonography (30). Hickman et al. also reported the reduction of hepatic steatosis following diet therapy and exercise and weight loss for three months in people with chronic hepatitis C and hepatic steatosis. In this study, the rate of reduction of steatosis had a significant correlation with the rate of weight loss (29). At the end of Huang and colleagues' study, patients with a 7% weight loss compared to patients with a 2% weight loss showed a significant improvement in hepatic steatosis (31).

Findings Related to Anthropometric Indices in the Studied Groups

Obesity is one of the risk factors involved in the pathogenesis of NAFLD, and it has been reported that 7%-10% weight loss can be considered a way to manage NAFLD (3). On the other hand, obesity is related to insulin resistance and the severity of inflammation in NAFLD patients, and total abdominal fat distribution, waist circumference index, and BMI have been introduced as predictors of metabolic risk factors (32).

Although our study showed no difference in BMI reduction between the intervention and control groups after three months of exercise and diet, the results were statistically significant when comparing the intervention group to its baseline state. Several studies have found that obesity is significantly associated with NAFLD, so weight loss through changes in diet can lead to significant improvement in fatty liver (33). For example, studies have shown that the probability of developing NAFLD is 30 times higher in people with a BMI of more than 25 than those with a BMI of less than 25 (34). A study showed that reducing calorie intake reduces NAFLD by 42%-81%, and weight loss is directly proportional to the rate of NAFLD (35). A cohort study was conducted on 995 Australian teenagers in two healthy and unhealthy diet groups. The results showed a significant difference in developing NAFLD between the healthy diet group who consumed yellow and red vegetables, such as tomatoes and fruits, compared to unhealthy teenagers who consumed ready meals, red meat, meat products, potatoes, chips, soft drinks, fried foods, sauce, and roasted nuts (36). Most previous studies reported weight loss of 2%-11% with calorie-restricted diets (37- 39).

In the study of Thomas et al, prescribing a diet with a limit of 500 kcal per day in patients with NAFLD caused a 3.4% weight loss with a significant decrease in other anthropometric indices (22). In Ghaemi et al.'s study, weight loss, even by 2% in three months, resulted in a significant decrease in BMI, waist circumference, and WHR in patients with NAFLD (39).

Limitations of the Study

- Not using liver biopsy as a gold standard method due to its invasiveness and using non-invasive ultrasound method to diagnose fatty liver.
- The impossibility of examining the consequences of hepatic steatosis due to the limited duration of the study.

Conclusion

The results of this study showed that lifestyle modifications, including physical activity and diet, had significant effects on fatty liver grade in patients with NAFLD.

Authors' Contribution

Conceptualization: Leila Javadi.
Data curation: Soraya Moradi.
Formal analysis: Soraya Moradi.
Funding acquisition: Vahid Majidi.
Investigation: Leila Javadi.
Methodology: Leila Javadi.
Project administration: Leila Javadi.
Resources: Vahid Majidi.
Software: Soraya Moradi.
Supervision: Leila Nikniaz.
Validation: Mohamadhossein Amirpour.
Visualization: Vahid Majidi.
Writing–original draft: Leila Javadi.
Writing–review & editing: Leila Javadi.

Conflict of Interests

Authors have no conflict of interest.

Ethical Issues

The Ethics Committee of Tabriz University of Medical Sciences approved the current study with the university ethical code TBZMED. REC. 1400.303. The study was also registered in the Iranian Registry of Clinical Trials on 2022-02-28(identifier: IRCT20210808052106N1, http://www.irct.ir).

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References

1. Johnson NA, Keating SE, George J. Exercise and the liver: implications for therapy in fatty liver disorders. Semin Liver Dis. 2012;32(1):65-79. doi:10.1055/s-0032-1306427
2. NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016;387(10026):1377-1396. doi:10.1016/s0140-6736(16)30054-x
3. Malhotra N, Beaton MD. Management of non-alcoholic fatty liver disease in 2015. World J Hepatol. 2015;7(30):2962-2967. doi:10.4254/wjh.v7.i30.2962
4. Patel NS, Doycheva I, Peterson MR, et al. Effect of weight loss on magnetic resonance imaging estimation of liver fat and volume in patients with nonalcoholic steatohepatitis. Clin Gastroenterol Hepatol. 2015;13(3):561-568.e1. doi:10.1016/j.cgh.2014.08.039
5. Gepner Y, Shelef I, Komy O, et al. The beneficial effects of Mediterranean diet over low-fat diet may be mediated by decreasing hepatic fat content. J Hepatol. 2019;71(2):379-388. doi:10.1016/j.jhep.2019.04.013
6. St George A, Bauman A, Johnston A, Farrell G, Chey T, George J. Effect of a lifestyle intervention in patients with abnormal liver enzymes and metabolic risk factors. J Gastroenterol Hepatol. 2009;24(3):399-407. doi:10.1111/j.1440-1746.2008.05694.x
7. Sun WH, Song MQ, Jiang CQ, et al. Lifestyle intervention in non-alcoholic fatty liver disease in Chengyang district, Qingdao, China. World J Hepatol. 2012;4(7):224-230. doi:10.4254/wjh.v4.i7.224
8. Wong VW, Chan RS, Wong GL, et al. Community-based lifestyle modification programme for non-alcoholic fatty liver disease: a randomized controlled trial. J Hepatol. 2013;59(3):536-542. doi:10.1016/j.jhep.2013.04.013
9. Promrat K, Kleiner DE, Niemeier HM, et al. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. Hepatology. 2010;51(1):121-129. doi:10.1002/hep.23276
10. Eckard C, Cole R, Lockwood J, et al. Prospective histopathologic evaluation of lifestyle modification in nonalcoholic fatty liver disease: a randomized trial. Therap Adv Gastroenterol. 2013;6(4):249-259. doi:10.1177/1756283x13484078

11. Ueno T, Sugawara H, Sujaku K, et al. Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. J Hepatol. 1997;27(1):103-107. doi:10.1016/s0168-8278(97)80287-5
12. Riazi K, Azhari H, Charette JH, et al. The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2022;7(9):851-861. doi:10.1016/s2468-1253(22)00165-0
13. Vilar-Gomez E, Martinez-Perez Y, Calzadilla-Bertot L, et al. Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. Gastroenterology. 2015;149(2):367-378.e5. doi:10.1053/j.gastro.2015.04.005
14. Bozzetto L, Prinster A, Annuzzi G, et al. Liver fat is reduced by an isoenergetic MUFA diet in a controlled randomized study in type 2 diabetic patients. Diabetes Care. 2012;35(7):1429-1435. doi:10.2337/dc12-0033
15. Goodpaster BH, Delany JP, Otto AD, et al. Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial. JAMA. 2010;304(16):1795-1802. doi:10.1001/jama.2010.1505
16. Shah K, Stufflebam A, Hilton TN, Sinacore DR, Klein S, Villareal DT. Diet and exercise interventions reduce intrahepatic fat content and improve insulin sensitivity in obese older adults. Obesity (Silver Spring). 2009;17(12):2162-2168. doi:10.1038/oby.2009.126
17. Keymasi Z, Sadeghi A, Pourrazi H. Effect of pilates training on hepatic fat content and liver enzymes in men with nonalcoholic fatty liver disease. J Appl Health Stud Sport Physiol. 2017;4(2):49-56. doi:10.22049/jassp.2019.26576.1241
18. Marfell-Jones MJ, Stewart AD, de Ridder JH. International Standards for Anthropometric Assessment. Wellington, New Zealand: International Society for the Advancement of Kinanthropometry; 2012.
19. She J, Nakamura H, Makino K, Ohyama Y, Hashimoto H. Selection of suitable maximum-heart-rate formulas for use with Karvonen formula to calculate exercise intensity. Int J Autom Comput. 2015;12(1):62-69. doi:10.1007/s11633-014-0824-3
20. Khov N, Sharma A, Riley TR. Bedside ultrasound in the diagnosis of nonalcoholic fatty liver disease. World J Gastroenterol. 2014;20(22):6821-6825. doi:10.3748/wjg.v20.i22.6821
21. Brun P, Castagliuolo I, Di Leo V, et al. Increased intestinal permeability in obese mice: new evidence in the pathogenesis of nonalcoholic steatohepatitis. Am J Physiol Gastrointest Liver Physiol. 2007;292(2):G518-525. doi:10.1152/ajpgi.00024.2006
22. Thomas EL, Brynes AE, Hamilton G, et al. Effect of nutritional counselling on hepatic, muscle and adipose tissue fat content and distribution in non-alcoholic fatty liver disease. World J Gastroenterol. 2006;12(36):5813-5819. doi:10.3748/wjg.v12.i36.5813
23. Cankurtaran M, Tayfur O, Yavuz BB, Geyik S, Akhan O, Arslan S. Insulin resistance and metabolic syndrome in patients with NAFLD but without diabetes: effect of a 6 month regime intervention. Acta Gastroenterol Belg. 2007;70(3):253-259.
24. Yoshimura E, Kumahara H, Tobina T, et al. Lifestyle intervention involving calorie restriction with or without aerobic exercise training improves liver fat in adults with visceral adiposity. J Obes. 2014;2014:197216. doi:10.1155/2014/197216
25. Orci LA, Gariani K, Oldani G, Delaune V, Morel P, Toso C. Exercise-based interventions for nonalcoholic fatty liver disease: a meta-analysis and meta-regression. Clin Gastroenterol Hepatol. 2016;14(10):1398-1411. doi:10.1016/j.cgh.2016.04.036
26. Baršić N, Lerotić I, Smirčić-Duvnjak L, Tomašić V, Duvnjak M. Overview and developments in noninvasive diagnosis of nonalcoholic fatty liver disease. World J Gastroenterol. 2012;18(30):3945-3954. doi:10.3748/wjg.v18.i30.3945
27. Morgan B. Fatty liver disease: the liver labyrinth. Nature. 2014;516(7529):S8-9. doi:10.1038/516S8a
28. Tiikkainen M, Bergholm R, Vehkavaara S, et al. Effects of identical weight loss on body composition and features of insulin resistance in obese women with high and low liver fat content. Diabetes. 2003;52(3):701-707. doi:10.2337/diabetes.52.3.701
29. Hickman IJ, Clouston AD, Macdonald GA, et al. Effect of weight reduction on liver histology and biochemistry in patients with chronic hepatitis C. Gut. 2002;51(1):89-94. doi:10.1136/gut.51.1.89
30. Scaglioni F, Marino M, Ciccia S, et al. Short-term multidisciplinary non-pharmacological intervention is effective in reducing liver fat content assessed non-invasively in patients with nonalcoholic fatty liver disease (NAFLD). Clin Res Hepatol Gastroenterol. 2013;37(4):353-358. doi:10.1016/j.clinre.2012.10.009
31. Huang MA, Greenson JK, Chao C, et al. One-year intense nutritional counseling results in histological improvement in patients with non-alcoholic steatohepatitis: a pilot study. Am J Gastroenterol. 2005;100(5):1072-1081. doi:10.1111/j.1572-0241.2005.41334.x
32. Cheung O, Kapoor A, Puri P, et al. The impact of fat distribution on the severity of nonalcoholic fatty liver disease and metabolic syndrome. Hepatology. 2007;46(4):1091-1100. doi:10.1002/hep.21803
33. Dehghan P, Miwechi M, Izadi E, Sohrabi MR. Comparison of nutritional behaviors and body mass index in patients with and without non-alcoholic fatty liver diseases. Community Health. 2015;2(2):80-87. [Persian].
34. Jun DW. The role of diet in non-alcoholic fatty liver disease. Korean J Gastroenterol. 2013;61(5):243-251. doi:10.4166/kjg.2013.61.5.243
35. Viljanen AP, Iozzo P, Borra R, et al. Effect of weight loss on liver free fatty acid uptake and hepatic insulin resistance. J Clin Endocrinol Metab. 2009;94(1):50-55. doi:10.1210/jc.2008-1689
36. Oddy WH, Herbison CE, Jacoby P, et al. The Western dietary pattern is prospectively associated with nonalcoholic fatty liver disease in adolescence. Am J Gastroenterol. 2013;108(5):778-785. doi:10.1038/ajg.2013.95
37. Arefhosseini SR, Ebrahimi-Mameghani M, Farsad Naeimi A, Khoshbaten M, Rashid J. Lifestyle modification through dietary intervention: health promotion of patients with non-alcoholic fatty liver disease. Health Promot Perspect. 2011;1(2):147-154. doi:10.5681/hpp.2011.016
38. Yamamoto M, Iwasa M, Iwata K, et al. Restriction of dietary calories, fat and iron improves non-alcoholic fatty liver disease. J Gastroenterol Hepatol. 2007;22(4):498-503. doi:10.1111/j.1440-1746.2006.04548.x
39. Ghaemi A, Taleban FA, Hekmatdoost A, et al. How much weight loss is effective on nonalcoholic fatty liver disease? Hepat Mon. 2013;13(12):e15227. doi:10.5812/hepatmon.15227