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Original Article

The effects of high- intensity interval training with and without intermittent fasting on body composition and markers of cardiometabolic risk in patients with metabolic-associated fatty liver disease

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Abstract

Background: Increased physical activity participation leads to favorable health benefits for patients with metabolic associated fatty liver disease (MAFLD). However, very few have examined the combined effects of high- intensity interval training (HIIT) and intermittent fasting (IF), especially on cardiometabolic risk factors in patients with MAFLD. Therefore, the purpose of this study was to evaluate the effects of HIIT with and without IF on body composition and markers of cardiometabolic risk in patients with metabolic-associated fatty liver disease.

Materials and Methods: In this quasi-experimental study with a pre-test-post-test design, 48 patients with MAFLD were randomly assigned into HIIT (HIIT, n = 15), HIIT plus intermittent fasting (HIIT+IF, n = 16), or intermittent Fasting (IF, n = 17) groups. HIIT training program were performed, 3 times/week with 80–95% HR peak intensity in 14 min/sessions for 12 weeks. The 5:2 IF groups restricted energy intake for two non-consecutive days per week for 12 weeks. Serum levels of fasting glucose, insulin, insulin resistance, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein and body composition measurements (weight, body mass index) were measured before and after 12 weeks of study.

Results: Significant reduction in weight, body mass index, serum levels of TC, TG, LDL-C in the HIIT+IF and IF groups compared to the HIIT alone group and significant increase in the HDL-C in the HIIT+IF and HIIT alone compared to the IF group ($p>0.05$). Although there was a significant decrease in the levels of fasting glucose, insulin and insulin resistance in all three groups after 12 weeks of study compared to the baseline ($p>0.05$), however, no significant difference was observed between the groups ($p\geq0.05$).

Conclusion: The results suggest that HIIT combined with intermittent calorie restriction (ICR) can reduce body composition and lipid profile more effectively than either HIIT or ICR alone in in obese women. The results of the present study showed that HIIT combined with IF can help to improve body composition and cardiometabolic risk markers in patients with MAFLD.

Keywords: Fasting glucose, Insulin, TC, TG, LDL-C, HDL-C, HIIT, IF, MAFLD

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Introduction

Metabolic-associated fatty liver disease (MAFLD), previously termed non-alcoholic fatty liver disease (NAFLD), is characterized by excessive accumulation of fat in liver cells (>5% of liver weight) not caused by viral infection, alcohol consumption, or drugs [1]. It is the most common chronic liver disease in the world [2,3]. MAFLD is becoming a major public health problem as a significant increase in prevalence has been observed in recent years, with an estimated annual cost of €35 billion in Europe and €89 billion in the United States. These potential costs were determined based on the construction of a Markov model that was simulated by considering the progression from a healthy population to age-related incidence and progression data, although limitations of the method may lead to an underestimate of the true burden [4].

In 2013, it was reported that up to 50% of obese men may suffer from MAFLD [5]. It is also estimated that 23–44% of patients with MAFLD develop non-alcoholic steatohepatitis (NASH) and subsequently lead to fibrosis and, in the worst case, cirrhosis, which leads to hepatocellular carcinoma (HCC) in 40–60% of patients within 5–7 years and in 40–60% of patients within 3–7 years [6]. The European Society for the Study of the Liver recommends dietary changes and a gradual increase in aerobic or resistance exercise in patients with MAFLD [7]. Factors such as early detection, prevention, treatment of risk factors and lifestyle changes [4] are also important, especially because of the association of MAFLD with insulin resistance, dyslipidemia, diabetes, hypertension or metabolic syndrome [8–12] and an increased risk of mortality related to liver and cardiovascular diseases [13,14].

Lifestyle modification, including diet and exercise, is considered the primary treatment of choice with the aim of reducing weight and improving the risk of developing insulin resistance and metabolic syndrome [14, 15]. Although, limited studies have been conducted to date to determine the effect of diet on the development of MAFLD, the use of various nutritional modifications during the course of this disease suggests that diet is a key factor in both the development and treatment of the disease [16–19]. Intermittent fasting (IF) is a new weight loss regimen that has been steadily increasing in popularity over the past decade [20, 21]. According to research reports, intermittent fasting has been used in many diseases, for example, obesity, type 2 diabetes or cardiovascular disease, with measurable effects [15, 22, 23]. It should be noted that these are diseases that often coexist with MAFLD [24] and cause it, it is logical to investigate the use of intermittent fasting in patients with MAFLD.

Physical activity influences metabolic health by influencing skeletal muscle composition and mitochondrial function. Regular physical activity is an effective strategy for improving cardiometabolic health. It prevents obesity and visceral fat accumulation and reduces the risk of metabolic and cardiovascular diseases [25]. High-intensity interval training (HIIT) is a training mode that alternates periods of high-intensity exercise with periods of rest, which has been shown to promote weight loss and improve cardiometabolic health [26,25]. Although there is growing evidence for a link between body weight regulation and genetic changes, there is little information on changes in cardiometabolic risk markers in relation to weight loss in MAFLD followed by a HIIT training program. Furthermore, well-controlled exercise studies such as MAFLD in HIIT are scarce, and in particular, analyses of specific biochemical responses such as cardiometabolic factors are lacking to date [27].

Therefore, due to the lack of research in this area and the gaps in the efficacy of exercise interventions combined with weight-loss diets, the aim of this study was to evaluate the effect of HIIT combined with IF on body composition and cardiometabolic risk factors in patients with MAFLD. In addition, the relationship between clinically relevant metabolic and anthropometric variables and cardiovascular risk factors before and after HIIT and IF in patients with MAFLD will be assessed.

Materials and Methods:

This is a quasi-experimental and applied study that was conducted cross-sectionally. The design used in this study was a pre-test-post-test with a control group. The statistical population includes men with metabolic fatty liver disease aged 38-50 years in Izeh city who used two exercise and diet interventions during a 12-week intervention. Based on the inclusion and exclusion criteria, 48 patients with MAFLD were selected from among the eligible patients based on the inclusion and exclusion criteria in a convenient way as a statistical sample and then randomly assigned to 3 groups: high-intensity interval training or HIIT (n=15), intermittent fasting or IF (n=17), and HIIT + IF (n=16).

Data collection method

The weight of the subjects was recorded in kilograms using a SEGA scale. Standing height was recorded in centimeters. A SEGA height gauge made in Germany was used to measure height with an accuracy of half a centimeter. In this study, body mass index was calculated using the formula. In this study, all participants consciously accepted all responsibilities and consequences of participating in the study.

High-intensity interval training protocol

The modified HIIT protocol of Reljik et al., (2018) is given in Table 1. In this protocol, all training sessions were performed on a foot ergometer. This protocol consisted of three parts: a 2-minute warm-up phase, the main exercise consisting of 5 repetitions of 1 minute at an intensity of 80 to 95% of the participants' peak heart rate, and considering 1-minute intervals of low-intensity recovery period in the exercise intervention groups, and a 3-minute cool-down phase. The total training time was about 14 minutes per session. The minimum training intensity (HR) increased in the subjects according to the following pattern:

Table 1: High-intensity, low-volume interval training

Week	Rest (minute)	Repetition (minute)	Intensity (%)
1-4	1	5×1	80-85
5-8	1	5×1	85-90
9-12	1	5×1	90-95

Diet Fasting Do you have Intermittent

In this study, intermittent fasting was used in a 5:2 ratio, twice a week, on non-consecutive days, for 12 weeks. Therefore, subjects consumed 25% of their total daily energy requirements (totaling about 600 kcal/two meals) on IF days, while on the other days of the week, food consumption was allowed ad libitum. In the IF diet, subjects underwent a 6-hour period when participants were only allowed to consume two meals, followed by a complete fast for the next 18 hours. It should be noted that during this 18-hour complete fast, participants were only allowed to drink water and unsweetened tea and coffee. In this study, they received a list of meal options containing 300 kcal on IF days. Of course, the distribution of macronutrients was prioritized. 40% of protein sources were also provided in the IF diet menu. It should be noted that weekly meetings with the groups were supervised by a nutritionist to monitor the follow-up of the dietary intervention.

Measurement Variables Bloody Dependent

To assess the concentrations of metabolic factors and lipid profiles, blood samples of 7 ml were taken from the subjects of the study groups during two stages (48 hours before the start of the study and 48 hours after the end of the study) after 10-12 hours of fasting. In this study, serum levels of fasting blood glucose, insulin, total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein were measured by ELISA using special kits. It should be noted that all subjects were asked to refrain from strenuous exercise or taking supplements for two days before blood sampling.

Method Execution Research

During a call at health centers in Isfahan, eligible subjects were selected based on the inclusion and exclusion criteria. Before the study began, subjects were asked to complete a medical history questionnaire, physical activity, and an informed consent form. In the next stage, they participated in an explanatory session to familiarize themselves with the objectives of the study, how to perform the tests, the research steps, and the method of work. Then, according to the research design, they were randomly assigned to three groups: high-intensity interval training or HIIT (n=15), intermittent fasting or IF (n=17), and HIIT + IF (n=16).

Then, the training groups underwent HIIT for 12 weeks, and the IF group performed under the supervision of a nutritionist for 12 weeks in a ratio of 5:2. Before and after the last intervention session, dependent variables such as fasting blood glucose, insulin, insulin resistance, total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, weight, and body mass index were measured and recorded on a specific day and time as a pretest and posttest.

Analysis and Analysis Statistical Data

The collected data were analyzed in two parts: descriptive and inferential statistics. In the descriptive statistics section, central tendency indicators including mean and standard deviation were used, and in the inferential statistics section, the Kolmogorov-Smirnov test was used to evaluate the normal distribution of the data. In establishing the desired hypothesis, the dependent t-test was used for intragroup comparison and the analysis of covariance test was used for comparison between groups. If significant, the difference between groups was used with the Bonferroni test. All data analysis operations were performed using SPSS 23 statistical software at a significance level of $p<0.05$.

Results

In Table 2, the mean and standard deviation of some physical characteristics of the participants are presented by group separation, such as age, height, weight, and body mass index.

Table 2: Mean and standard deviation of physical characteristics of research participants by group before the study

Variable (Group)	IF	HIIT+IF	HIIT
Age (Year)	42.94±3.51	44.00±3.56	43.93±3.43
Height (centimeter meters)	171.65±4.22	174.56±4.77	175.11±4.75
Weight (kg)	85.18±3.57	84.88±6.09	87.42±4.68
Index Mass Body(kg/m2)	28.96±1.77	27.82±1.00	28.54±1.76

HIIT= Practice Periodic Severe (n=15); HIIT+IF= Practice Periodic Intense + fasting Do you have Intermittent (n=16); IF =Fasting Do you have Intermittent (n=17).

The results in Table 3 showed a significant decrease in the mean weight of all three intervention groups compared to baseline ($p\geq0.05$).

Table 3: Results of the paired t-test for comparing weight before and after the study period by group

Statistical Indexs	Average±Deviation Standard		df	t	Sig
Variables	Pre Test	Post Test			
HIIT	87.42±4.68	86.22±4.87	14	-5.583	0.000
HIIT+IF	84.88±6.09	78.23±4.87	15	-16.177	0.000
IF	85.18±3.57	80.62±13.3	16	-11.187	0.000

According to the significant effect of group from the analysis of covariance test, it is observed that there is a significant difference between the weight values in the studied groups after a 12-week period ($p\geq0.05$). Therefore, there is a significant difference between the effects of twelve weeks of high-intensity interval training with and without intermittent fasting on weight in patients with metabolic fatty liver disease. According to the significant difference between the groups ($p<0.001$, $F=634.77$), and the results of the Bonferroni post hoc test, a significant decrease in weight values was observed in the HIIT+IF group compared to the HIIT and IF alone groups and in the IF group compared to the HIIT group (p≥0.05).

The results of Table 4 showed a significant decrease in the mean body mass index of all three intervention groups compared to baseline (p≥0.05).

Table 4: Results of the paired t-test to compare body mass index before and after the study period by group.

Statistical Indexs	Average±Deviation Standard		df	t	Sig
Variables	Pre Test	Post Test			
HIIT	28.54±1.76	28.15±1.77	14	-5.571	0.000
HIIT+IF	27.82±1.00	25.66±0.08	15	-19.025	0.000
IF	28.96±1.77	27.42±1.72	16	-11.283	0.000

According to the significant group effect of the analysis of covariance test, it is observed that there is a significant difference between the mean body mass index in the study groups after a 12-week period (p≤0.05). Therefore, there is a significant difference between the effects of twelve weeks of high-intensity interval training with and without intermittent fasting on body mass index in patients with metabolic-related fatty liver disease. According to the significant difference between the groups (p<0.001, F=65.951), and the results of the follow-up test, a significant decrease in the mean body mass index of the HIIT+IF group was observed compared to the HIIT and IF alone groups and the IF group compared to the HIIT group (p≤0.05).

According to Table 5, the results of the dependent t-test showed a significant decrease in fasting blood glucose values in each intervention group after 12 weeks compared to baseline (p≤0.05).

Table 5: Results of paired t-test for comparing blood glucose before and after the study period by group.

Statistical Indexs	Average±Deviation Standard		df	t	Sig
Variables	Pre Test	Post Test			
HIIT	141.20±8.59	122.40±22.52	14	-2.630	0.015
HIIT+IF	140.75±17.65	117.84±18.26	15	-2.738	0.015
IF	141.41±57.12	122.40±22.52	16	-2.926	0.010

According to the results of the analysis of covariance, it is observed that there is no significant difference between the mean fasting blood glucose in the study groups after a 12-week period (p≤0.05). Therefore, there is no significant difference between the effects of twelve weeks of HIIT with and without IF on fasting blood glucose in patients with metabolic fatty liver disease.

According to Table 6, the results of the dependent t-test showed a significant decrease in insulin values in the intervention groups after the intervention compared to the baseline ($p \geq 0.05$).

Table 6: Results of paired t-test for comparing insulin before and after the study period by group

Statistical Indexs	Average±Deviation Standard		df	t	Sig
Variables	Pre Test	Post Test			
HIIT	14.60±8.06	18.07±9.67	14	-3.483	0.002
HIIT+IF	14.27±8.14	16.70±3.18	15	-2.803	0.014
IF	15.13±3.46	13.53±8.63	16	-2.333	0.035

According to the results of the analysis of covariance, it is observed that there is no significant difference between the mean insulin in the study groups after a 12-week period ($p \leq 0.05$). Therefore, there is no significant difference between the effects of twelve weeks of HIIT with and without IF on insulin in patients with metabolic fatty liver disease.

According to Table 7, the results of the dependent t-test showed a significant decrease in HOMA-IR values in the intervention groups after the intervention compared to the baseline ($p \geq 0.05$).

Table 7: Results of paired t-test for comparing HOMA-IR before and after the study period by group

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	2.60±8.60	1.07±19.67	14	-3.483	0.002
HIIT+IF	27.3±18.14	2.70±30.18	15	-2.803	0.014
IF	13.2±13.46	1.53±18.63	16	-2.333	0.035

According to the results of the analysis of covariance, it is observed that there is no significant difference between the mean HOMA-IR in the study groups after a 12-week period ($p \leq 0.05$). Therefore, there is no significant difference between the effects of twelve weeks of HIIT with and without IF on HOMA-IR in patients with metabolic fatty liver disease.

According to Table 8, the results of the dependent t-test showed a significant decrease in HbA1C values in each intervention group after 12 weeks of intervention compared to baseline ($p \geq 0.05$).

Table 8: Results of paired t-test for comparing HbA1C before and after in each group

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	8.71±2.06	7.70±1.78	14	-347.3	0.005
HIIT+IF	15.9±0.85	6.88±0.92	15	-6.006	0.000
IF	8.95±0.85	7.44±0.88	16	-5.475	0.000

According to the results of the analysis of covariance, it is observed that there is a significant difference between the HbA1C values in the study groups after a 12-week period ($p \geq 0.05$). Therefore, there is a difference between the effects of 12 weeks of HIIT with and without IF on HbA1C in patients with metabolic fatty liver disease. According to the significant difference between the groups ($p<0.05$, $F=3.606$), and the results of the Bonferroni post hoc test, a significant decrease in HbA1C values was observed in the HIIT+IF group compared to the HIIT alone group ($p \geq 0.05$).

According to Table 9, the results of the dependent t-test showed a significant decrease in TC values in all three intervention groups after 12 weeks of the study period compared to baseline ($p \geq 0.05$).

Table 9: Results of the paired t-test for comparing TC before and after the study period by group.

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	275.13±38.35	258.27±29.96	14	-3.675	0.002
HIIT+IF	285.50±47.55	223.75±40.58	15	-4.883	0.000
IF	296.47±53.10	248.29±48.56	16	-4.351	0.000

According to the results of the analysis of covariance, it is observed that there is a significant difference between the TC values in the studied groups after a 12-week period ($p \geq 0.05$). Therefore, there is a difference between the effects of 12 weeks of HIIT with and without IF on TC in patients with metabolic fatty liver disease. According to the significant difference between the groups ($p<0.01$, $F=5.246$), and the results of the Bonferroni post hoc test, a significant decrease in TC values was observed in the HIIT+IF group compared to the HIIT alone group ($p \geq 0.05$).

The results of the dependent t-test in Table 10 showed a significant decrease in TG values in the HIIT+IF and IF groups after 12 weeks of intervention compared to baseline ($p \geq 0.05$), while this difference was not significant in the HIIT group.

Table 10: Results of paired t-test for comparing TG before and after in each group

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	219.00±50.48	193.13±63.85	14	-1.673	0.116
HIIT+IF	195.50±47.05	131.56±31.88	15	-5.037	0.000
IF	196.18±26.57	146.29±35.73	16	-5.694	0.000

According to the results of the analysis of covariance in Table 10, it is observed that there is a significant difference between the TG values in the study groups after a 12-week period ($p \geq 0.05$). Therefore, there is a difference between the effects of 12 weeks of HIIT with and without IF on TG in patients with metabolic fatty liver disease. According to the significant difference between the groups ($p < 0.01$, $F = 8.849$), and the results of the Bonferroni post hoc test, a significant decrease in TG values was observed in the HIIT+IF group compared to the HIIT alone group ($p \geq 0.05$).

According to Table 11, the results of the paired t-test showed a significant decrease in LDL values in each of the three groups after the study period compared to the baseline ($p \geq 0.05$).

Table 11: Results of paired t-test for comparing LDL before and after the study period by group

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	135.27±20.18	125.00±18.21	14	3.447	0.004
HIIT+IF	148.50±21.61	110.38±15.55	15	8.266	0.000
IF	154.53±30.30	120.59±23.75	16	6.434	0.000

According to the results of the analysis of covariance in Table 11, it is observed that there is a significant difference between the LDL values in the study groups after a 12-week period ($p \geq 0.05$). There is a difference between the effects of 12 weeks of HIIT with and without IF on LDL in patients with metabolic fatty liver disease. According to the significant difference between the groups ($p < 0.01$, $F = 8.849$), and the results of the Bonferroni post hoc test, a significant decrease in LDL values was observed in the HIIT+IF and IF groups compared to the HIIT alone group ($p \geq 0.05$).

According to Table 12, the results of the dependent t-test showed a significant increase in HDL values in the HIIT intervention and HIIT+IF combination groups after the intervention compared to the baseline (p≥0.05). While this difference was not significant in the IF group (p≤0.05).

Table 12: Results of paired t-test for comparing HDL before and after the study period by group.

Statistical Indexs	Average±Deviation Standard		df	t	sig
Variables	Pre Test	Post Test			
HIIT	34.07±18.2	38.07±1.71	14	14.491	0.001
HIIT+IF	35.31±2.09	39.69±3.16	15	8.234	0.001
IF	34.94±2.58	35.47±2.72	16	1.774	0.100

According to the results of the analysis of covariance in Table 12, it is observed that there is a significant difference between the HDL values in the study groups after a 12-week period (p≥0.05). Therefore, there is a difference between the effects of 12 weeks of HIIT with and without IF on HDL in patients with metabolic fatty liver disease. According to the significant difference between the groups (p<0.001, F=30.506), and the results of the Bonferroni post hoc test, a significant increase in HDL values was observed in the HIIT+IF groups and also in the HIIT alone group compared to the IF group (p≥0.05).

The results generally showed that although a significant decrease in the weight values of each group was observed compared to the baseline, this difference was only significant between the exercise+intermittent calorie restriction and intermittent calorie restriction groups compared to the exercise group after 12 weeks of intervention. A significant decrease in body mass index values was observed in each group compared to baseline, but this difference was only significant between the exercise + intermittent calorie restriction groups and also intermittent calorie restriction compared to the exercise group after 12 weeks of intervention.

Also, a significant increase in peak oxygen consumption of obese patients was observed after the interventions of exercise alone and high-intensity interval training in combination with intermittent calorie restriction compared to the intermittent calorie restriction intervention alone. However, a significant decrease in serum concentrations of total cholesterol, triglyceride, and low-density lipoprotein was observed after the interventions of intermittent calorie restriction, high-intensity interval training in combination with intermittent calorie restriction compared to the intervention of exercise alone. Finally, a significant increase in serum concentrations of high-density lipoprotein was observed after the interventions of exercise alone and high-intensity interval training in combination with intermittent calorie restriction compared to the intervention of intermittent calorie restriction alone.

Discussion and Conclusions

Weight gain in the form of adipose tissue plays a key role in the pathogenesis of cardiometabolic diseases. Lifestyle changes that are accompanied by continuous calorie restriction and exercise are more effective in reducing weight and, consequently, in reducing adipose tissue and cardiovascular risk factors. The present study investigated the effects of 12 weeks of intermittent calorie restriction in combination with high-intensity interval training on body composition and cardiovascular risk factors in obese women. This study was designed to investigate the effects of 12 weeks of exercise and HIIT with and without IF on body composition and cardiometabolic risk markers in patients with MAFLD. The main findings of this study indicated a significant effect of the combination of IF and HIIT on improving weight and body mass index values and improving cardiometabolic risk markers in patients with MAFLD after 12 weeks of intervention.

Although many studies have shown that IF is beneficial for human health and is suitable for a wide range of metabolic diseases, this dietary model is rarely promoted in practice. The main reason for this lack of implementation is that people are accustomed to eating three meals a day. When switching to an IF program, some people experience hunger, irritability, and loss of concentration. In addition, IF has side effects in humans. Previous studies have shown that the level of exercise performance of athletes during fasting is significantly reduced due to hypoglycemia (28). There are also disturbances in sleep architecture. A recent study by Lu et al. (29) showed that IF, in the absence of controlled food intake, will lead to a decrease in muscle mass. Improper fasting time can lead to gastrointestinal diseases. In unhealthy individuals, the use of therapeutic fasting can lead to a decrease in physical fitness. Ultimately, IF involves various fasting methods, time intervals, and energy restrictions that require consultation with a dietitian or physician to adopt an appropriate fasting plan to ensure the patient's nutritional needs are met, while gradually reducing the daily eating interval to prevent side effects, while providing ongoing counseling and education.

The findings of a meta-analysis provide strong evidence for the role of aerobic exercise in the management of patients with MAFLD [30]. Recent evidence suggests that exercise can provide important health benefits [30]. The World Health Organization (WHO) recommends that adults should engage in at least 150–300 min of moderate-intensity exercise or 75–150 min of vigorous-intensity exercise per week for optimal health [32]. The American College of Sports Medicine (ACSM) and the Centers for Disease Control and Prevention, National Institutes of Health have concluded that moderate-intensity aerobic exercise is effective in reducing the overall risk of chronic disease [33]. In addition, the ACSM and the American Diabetes Association recommend at least 150 min per week of moderate-intensity or 75 min per week of vigorous-intensity physical activity for all adults to reduce the risk of cardiovascular disease and type 2 diabetes, as well as to improve cardiorespiratory fitness [34]. However, it remains unknown whether the levels of physical activity recommended at least according to the guidelines are sufficient to reduce the risk of MAFLD. Is there a dose-response relationship?

A meta-analysis showed that all types of aerobic exercise: continuous, intermittent, and combined, had a significant effect on intramuscular triglyceride levels and body mass index compared with usual care or another type of intervention (35). The results of our study are consistent with previous meta-analyses. Smart et al. (36) showed that exercise programs, regardless of dietary intervention, may be beneficial in terms of changes in intrahepatic fat, body mass, BMI < FFA, insulin, liver enzymes, blood lipids, and peak oxygen consumption. Interestingly, the authors concluded that exercise programs with a total caloric intake of more than 10,000 kcal may be more effective in reducing intrahepatic fat than programs with a lower caloric intake. In contrast to Smart et al., Catsagoni et al. noted significant effects of a physical exercise program on reducing cardiometabolic risk factors (37).

Effects on body composition

Overall, there was a significant positive correlation between BMI and weight loss during IF in terms of body composition (i.e., the higher the starting BMI, the greater the weight loss during the fasting period). This suggests that IF may be more effective for individuals with a higher BMI. The results regarding the effect of IF on body composition were similar to those obtained in a previous meta-analysis (38) that included 11 trials that showed that TRF was effective in reducing weight and FBG compared with no mealtime restriction. It comes close. In addition, IF was more effective in reducing weight than a conventional control diet. It was also more effective than CER in reducing FM levels (39). In a meta-analysis on religious fasting (40), overweight participants were found to have greater weight loss and fat percentage than normal individuals. A recent meta-analysis of RCTs showed that ADF effectively reduced body composition (BMI, weight, and FM) in overweight adults over a 6-month period compared with a control group (41). However, in another meta-analysis of 12 RCTs, investigators confirmed that lean mass was relatively preserved in the IF group and no significant weight loss was detected (42). Furthermore, a recent study by Lu et al. (38) on 16:8 time-restricted eating (TRE), an IF program that encourages the consumption of all dietary foods within an 8-hour eating window, showed that IF did not play a significant role in weight loss in the absence of controlled food intake. This, in turn, may lead to a decrease in muscle mass. There were no significant differences in FM, FINS, glucose levels, HbA1C, or blood lipids between the TRE group and the control group. The results of Lu's study are in contrast to those of most fasting studies. This may be due to the time window of fasting. In the meantime, our meta-analysis is also included in this study, but a comprehensive assessment of IF on body composition is useful.

Effects on Blood Lipids and Blood Sugar Control

In the lipid module analysis, the findings of a recent meta-analysis of the effects of IF and energy-restricted diets on blood lipids were similar to those in our review. Results showed that, compared with the HIIT intervention group alone, IF significantly reduced TC and TG concentrations, but had no significant effect on HDL-C concentrations (43). However, the two meta-analyses are inconsistent in terms of LDL-C levels. The lack of standardization of the timing of blood lipid measurements across individual studies may have led to variations in LDL-C concentrations in some studies. In healthy adults, the longer the week of fasting, the higher TC, LDL-C, and other markers (44). This meta-analysis included energy restriction during uninterrupted time, which may be the main reason for this difference. Although we did not observe a significant effect of IF on HDL-C concentrations, some previous studies have shown an effect of dietary intervention on this lipid marker. Morrow et al. reported a modest increase in HDL-C concentrations in subjects who exercised for 8 weeks as part of a normal calorie diet (45). Previous studies have shown that IF is not only beneficial in reducing free radical production or weight loss. It also has several health benefits (46). IF can induce an evolutionarily conservative adaptive cellular response, improve blood glucose regulation, enhance anti-stress capacity, and inhibit inflammation between and within organs. During fasting, cells activate pathways that enhance the body's defenses against oxidative and metabolic stress, as well as remove or repair damaged molecules. IF improves healthy physiological markers related to metabolism, which provides the basis for improved metabolic properties of the animal (47). Fat is the main source of energy for cells and is stored in adipose tissue as TG after a meal. During fasting, TGs are broken down into fatty acids and glycerol, which are used to provide the energy consumed by the organism (48).

Conclusion

Overall, this randomized controlled trial showed that IF may improve body composition parameters (weight and BMI) and lipid profile (TC, TG) and metabolic factors (fasting blood glucose, insulin and insulin resistance), but may not have an effect on LDL-C, HDL-C, which are risk factors for developing diabetes and CVDs. However, this study provides strong evidence that 12 weeks of HIIT training combined with IF at a ratio of 5:2 is effective in improving body composition, serum levels of fasting blood glucose, insulin, insulin resistance and blood lipids in patients with MAFLD. Therefore, high-quality and long-term RCTs are needed to provide data on the sustainability of the effect and strengthen the certainty of the evidence.

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Conflicts of interest

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