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# The Effect of Combined Aerobic and Resistance Training on Hepatic Enzymes in Males With Nonalcoholic Fatty Liver

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## Abstract

**Background:** Nonalcoholic fatty liver disease (NAFLD) is a common liver disease associated with inactivity and obesity. Physical activity and exercise could affect the risk of NAFLD progression by improving the hepatic lipid profiles.
**Objectives:** The current study aimed to evaluate the efficacy of combination of aerobic and resistance training on hepatic enzymes in males with NAFLD.
**Patients and Methods:** The study was a randomized controlled trial. Thirty-two untrained males with NAFLD (aged = 32.93 $\pm$ 2.15 years, weight = 86.01.51 $\pm$ 8.40 kg) were recruited and randomly divided into equal experimental and control groups. The trained group took part in a combination aerobic and resistance training program for eight weeks (three times per week). The control group continued their routine life. The weight, body mass index (BMI) and serum levels of total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), very low density lipoprotein (VLDL), HDL/LDL, TC/HDL, aspartate aminotransferase (AST) and alanine transaminase (ALT) were measured before and after the protocol.
**Results:** Statistical analysis demonstrated that the training group had significant changes in weight, BMI, TC, TG, LDL, VLDL, HDL/LDL, TC/ HDL, AST and ALT, whereas there was no significant change in HDL in NAFLD patients ($P < 0.05$).
**Conclusions:** The results suggest that physical activity improves metabolic parameters, which interfere in the development of fatty liver and has a protective role against the development of NAFLD.

*Keywords:* Fatty Liver, Exercise, Lipid Profiles, Hepatic Enzymes

## 1. Background

Nonalcoholic fatty liver disease (NAFLD) is one of the common liver diseases (1) strongly linked to lifestyle habits (2). The prevalence of NAFLD in the general population of Western countries is 20% - 30%, whereas, it is 6.3% - 33% worldwide (3). In Asian countries it is 12% - 24% (4) and the prevalence of NAFLD in South and North of Iran is 21.5% (5) and 43.8% (6), respectively. The most common cause of liver disease in Iran is likely NAFLD (7). The most predictive factors of NAFLD are metabolic syndrome and obesity, which are increasing in Iran (8); therefore, the prevalence of NAFLD is predicted to increase in the future. The prevalence of NAFLD increases with increasing waist-to-hip circumference ratio (WHR) (9). Racial background influences the relationship between body mass index (BMI) and NAFLD (10). Also high risk of developing dyslipidemia [(high plasma triglycerides (TG) and/or low plasma high-density lipoprotein cholesterol (HDL)], diabetes type 2 and hypertension could be associated with NAFLD. Besides overweight, alanine aminotransferase (ALT) and aspartate aminotransferase are markers of liver dysfunction (11). Studies suggested that the fatty liver metabolic parameters could improve by lifestyle modification by increasing physical activity and changing bad eating habits (12, 13); therefore the relationship between physical activity (PA) and liver enzyme levels aspartate aminotransferase (AST) and AST/ALT are shown (11, 14). Haus et al. noted that short-term exercise reduces the risk of NAFLD progression by improving the hepatic lipid profiles (15). The differences of HDL concentrations between athletes and sedentary show the beneficial effects of exercise on NAFLD (16).

## 2. Objectives

There are several studies on the effect of different methods of exercise and different subject on NAFLD. The current study aimed to evaluate the efficacy of combination of aerobic and resistance training on males with NAFLD.

## 3. Patients and Methods

### 3.1. Subjects

The current study was conducted from April to June 2015 under the auspices of the Islamic Azad university Najafabad branch. The study was approved by the research ethics committee of Isfahan University of Medical Science and health services (IUMS) (No. 494128). All subjects were volunteers and signed a written informed consent.

### 3.2. Study Design

The study was randomized controlled trial. Thirty-two untrained males with NAFLD (mean age = 32.93 $\pm$ 2.15 years, weight = 86.01.51 $\pm$ 8.40 kg and BMI= 28.21 $\pm$ 0.19 kg/m$^2$) were randomly selected out of 48 eligible male volunteers with NAFLD. They were randomly divided into two equal groups, experimental (E) and control (C). The inclusion criteria were male with NAFLD diagnosis and not to have taken part in regular exercises for at least six months prior to enrollment. The exclusion criteria were any orthopedic problem that would interfere with the protocol of training.

The training group took part in a combination of aerobic and resistance training programs for eight weeks (three times per week). The duration of each session was 60 minutes divided into four sections consisting of 10 minutes warm-up, 10 minutes aerobic training, 30 minutes resistance training, and 10 minutes cool-down. The warm-up section consisted of stretching movements and rhythmic movements with low intensity. The aerobic training section consisted of rhythmic movements and the resistance training section consisted of three sets of 8 - 12 repetitions at 60% - 80 % of maximum voluntary contraction (MVC) (17) in biceps, triceps, pectoralis, quadriceps, and hamstring muscles in the position of dumbbell biceps (seated concentration curl), dumbbell triceps (triceps kickback), bench press, knee extension and knee flexion, respectively. The subjects had three minutes rest after completing the three sets.

The intensity of aerobic training was 65% - 85% heart rate reserve (HRR) by the Polar FT4 HR Monitor and the intensity of resistance training was 60% - 80 % MVC. The cool-down section consisted of rhythmic movements with low intensity and stretching movements with deep breathing. The control group continued their normal lifestyle. There was no dropped outs due to the study.

### 3.3. Anthropometric Measurements

The digital scale (Seca Bella 840, Seca GmbH and Co, Hamburg, Germany) was used to measure body weight (BW) To measure height, the stadiometer was used (0.1 cm precision) (Seca, Modell 214, Hamburg, Germany). Quetelet index (kg/m$^2$) was used to calculate BMI (18).

### 3.4. Blood Sample Measurement

Venous blood samples were obtained from the antecubital vein of the subjects in a seated position before and after the intervention. The blood samples were collected at the same time of the day to reduce any diurnal variation of the hormonal response. Following the overnight fasting of 9 - 12 hours, the subjects came to the laboratory from 7:00 to 8:00 am, and took a rest for 30 minutes prior to the first blood collection. The serum levels of TG, total cholesterol (TC) (6), low density lipoprotein (LDL), HDL, AST and ALT were measured by ROSHE full automated auto-analyzer using Pars Azmoon kits. Very low density lipoprotein (VLDL) by the formula VLDL = TG/5, and also the ratio TC/ HDL and HDL/ LDL were calculated.

### 3.5. Statistical Analysis

Relevant statistical analyses were performed using SPSS version 15 on a personal computer; $P < 0.05$ was considered as the level of significance. Descriptive analyses were adopted for demographic and clinical characteristics and reported as means $\pm$ SD. Before the statistical analysis Kolmogorov-Smirnov test was used to determine the normality of the distributions ($P > 0.05$), and the Levene test was used to show homogeneity of variances between the two groups before the start of the protocol ($P > 0.05$). Differences among groups were assessed by analysis of covariate (ANCOVA) ($P < 0.05$).

## 4. Results

Thirty-two subjects completed the training program and the follow-up test in the experimental group. Kolmogorov-Smirnov test showed the normal distribution of the variables ($P > 0.05$), and the Levene test showed homogeneity of variances between the two groups before the start of the protocol reported in Table 1 ($P > 0.05$).

The thirty-two patients with NAFLD recruited for the investigation, completed the study. Demographic and clinical characteristics are shown in Table 2. There were no significant differences in the baseline of age, weight and BMI between the two groups ($P \leq 0.05$). The means of lipid profiles components and liver enzymes before and after eight weeks in both groups are presented in Table 1 ($P \leq 0.05$).

The ANOVA test demonstrated that after the eight weeks of combined aerobic and resistance training, the E group had 2.25% significant decrease in weight, 2.01% in BMI, 8.48% in LDL, 3.07% in TC, 7.44% in TG, 7.44% in VLDL, 11.09% in TC/ HDL, 12.32% in AST, 12.85% in ALT, and 6.09% significant increase in HDL/LDL, but there was no significant change in the HDL ($P \leq 0.05$) (Table 1).

**Table 1.** Blood Test Results of the Study Subjects Before and After Eight Weeks of Combination Aerobic and Resistance Training Program[a]

| Variables | Pre-test | Post-test | *LevenTest* | F | P | $\eta^2$[b] | Observed Power |
|---|---|---|---|---|---|---|---|
| **Weight, kg** | | | 0.06 | 61.24 | 0.01* | 0.66 | 1.00 |
| E | 86.05 ± 8.77 | 84.11 ± 8.78 | | | | | |
| C | 85.97 ± 8.02 | 86.73 ± 8.11 | | | | | |
| **BMI, Kg.m$^{-1}$** | | | 0.07 | 9.82 | 0.01* | 0.24 | 0.86 |
| E | 28.35 ± 2.73 | 27.78 ± 2.57 | | | | | |
| C | 27.65 ± 1.85 | 28.07 ± 1.79 | | | | | |
| **TC, mg.dL$^{-1}$** | | | 0.05 | 12.98 | 0.00* | 0.30 | 0.93 |
| E | 234.56 ± 32.78 | 252.25 ± 26.79 | | | | | |
| C | 233.43 ± 21.14 | 227.50 ± 19.74 | | | | | |
| **TG, mg.dL$^{-1}$** | | | 0.05 | 4.53 | 0.04* | 0.13 | 0.53 |
| E | 237.87 ± 53.79 | 238.68 ± 51.77 | | | | | |
| C | 260.62 ± 38.23 | 291.87 ± 62.56 | | | | | |
| **LDL, mg.dL$^{-1}$** | | | 0.20 | 33.13 | 0.00* | 0.53 | 1.00 |
| E | 153.43 ± 16.47 | 147.06 ± 14.82 | | | | | |
| C | 148.00 ± 17.38 | 178.50 ± 28.11 | | | | | |
| **HDL, mg.dL$^{-1}$** | | | 0.12 | 2.54 | 0.12 | 0.08 | 0.33 |
| E | 34.30 ± 6.63 | 35.38 ± 7.58 | | | | | |
| C | 41.07 ± 13.50 | 32.98 ± 17.71 | | | | | |
| **VLDL, mg.dL$^{-1}$** | | | 0.05 | 4.53 | 0.04* | 0.13 | 0.53 |
| E | 47.77 ± 10.75 | 47.53 ± 10.35 | | | | | |
| C | 52.12 ± 7.64 | 58.37 ± 12.51 | | | | | |
| **HDL/ LDL** | | | 0.84 | 15.01 | 0.00* | 0.34 | 0.96 |
| E | 0.22 ± 0.05 | 0.24 ± 0..06 | | | | | |
| C | 0.28 ± 0.22 | 0.18 ± 0..09 | | | | | |
| **TC/ HDL** | | | 0.12 | 8.03 | 0.00* | 0.21 | 0.78 |
| E | 7.11 ± 1.93 | 6.68 ± 1.51 | | | | | |
| C | 8.29 ± 4.96 | 9.58 ± 4.91 | | | | | |
| **AST, U.L$^{-1}$** | | | 0.96 | 86.22 | 0.01* | 0.74 | 1.00 |
| E | 97.88 ± 48.89 | 85.82 ± 39.80 | | | | | |
| C | 70.11 ± 44.77 | 75.70 ± 48.47 | | | | | |
| **ALT, U.L$^{-1}$** | | | 0.98 | 91.01 | 0.01* | 0.77 | 1.00 |
| E | 54.94 ± 13.17 | 47.88 ± 11.62 | | | | | |
| C | 52.23 ± 17.57 | 57.84 ± 21.57 | | | | | |

Abbreviations: AST, aspartate aminotransferase; ALT, alanine transaminase; BMI, body mass index; C, control group; E, exercise group; HDL, high density lipoprotein; TC, total cholesterol; TG, triglycerides; LDL, low density lipoprotein; VLDL, very low density lipoprotein.
[a] Number of control group and exercise group = 16, df = 1,30.
[b] $\eta$, Partial eta-squared (demonstrated the changes of variable); observed power (to indicate an adequate number of subjects); values are mean ± SD.

## 5. Discussion

Obesity is the background of the diseases, and NAFLD is concomitant with it, moreover decreased physical activity and the lack of controlled calorie intake impact on the progressive disease process (19). The NAFLD's prevalence has increased, especially in the middle aged subjects (20), and often occurs more in males than females (21).

**Table 2.** Demographic Data of Subjects in the Experimental and Control Groups[a]

| Variables | Experimental Group | Control Group |
|---|---|---|
| **Age, y** | 34.46 ± 7.29 | 31.41 ± 8.89 |
| **Weight, kg** | 86.05 ± 8.77 | 85.97 ± 8.02 |
| **BMI , kg.m$^{-1}$** | 28.35 ± 2.73 | 28.07 ± 1.79 |

[a] No. = 16

In results of the current study showed a significant decrease in BW, BMI, LDL and TC, TG, LDL, VLDL, TC/HDL and significant increase in HDL/LDL after eight weeks of physical training in males with fatty liver, whereas there was no significant change in the HDL. Although there were significant changes in many variables, the changes did not lead to a desirable point. Pinto et al. noted significant decrease in BM, HDL and TG levels in active males with fatty liver (12). Also Khaoshbaten showed significant decrease of lipid profiles after three months of aerobic exercise (22). Zelber-Sagi et al. noted the adjustment of body mass index and significant decrease in lipid profiles and body composition after resistance training in patients with NAFLD (23).

The current study results indicated significant decrease of AST and ALT, which was in line with those of Hazar et al. (24) and Khaoshbaten et al. (22); they reported significant decrease of AST and ALT in patients with NAFLD following exercise training. Hallsworth et al. demonstrated that eight weeks of resistance exercise specifically improves NAFLD by 13% and relative reduction in liver lipid, without any changes in BW and FM (25).

Habitual physical activity enhances hepatic fatty acid oxidation and reduces fatty acid synthesis (26). Histological features of NAFLD have an inverse relationship with fat oxidation (27). Incomplete lipid oxidation in the high-fat-diet leads to metabolic deregulation by including $\beta$-oxidation elevation, which is not matched with enhanced Krebs cycle activity. The accumulation of acetyl Co-A, in the cell cytosol or leak into plasma may impact on mitochondrial oxidative stress factors or insulin sensitivity which have important roles in hepatic function (28). Koves et al. also found that exercise training increased the flux of both $\beta$-oxidation and Krebs cycle in both liver and skeletal muscles (29). Ordonez suggested that weight loss associated with exercise and proper diet is the main factor to prevent and treat NAFLD (30). Fat oxidation as a dominate energy resource in physical activity with mild to moderate intensity improves hepatic lipid composition. The first step in the NAFLD management is lifestyle modification (30). Therefore, lifestyle is a main factor with progressive effects on NAFLD, whereas health-related fitness (HRF), physical activity (PA) are beneficial factors are necessary to improve lifestyle and reduce the associated risk factors of NAFLD (14).

In conclusion, the prevalence of NAFLD has recently increased due to the rise of obesity and diabetes type 2, affected by lifestyle changes and industrialization. Therefore, lifestyle modifications are the best strategy to prevent and control NAFLD. Exercise as a valid and low-cost therapy could be added to NAFLD therapies to adjust fatty liver disorders.

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