

High-intensity circuit weight training versus aerobic training in patients with nonalcoholic fatty liver disease

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Background

Nonalcoholic fatty liver disease (NAFLD) has become one of the most common causes of liver disease worldwide and has been recognized as a major health burden. To date, no evidence-based therapy has proven to be effective for NAFLD, except for exercise and dietary interventions. The unsuitability of weight-oriented aerobic training for obese people with NAFLD because of the difficulty in maintaining weight loss necessitates the development of alternative strategies such as resistance training.

Objective

The aim of the study was to evaluate the effect of high-intensity circuit weight training (CWT) compared with aerobic training in NAFLD patients.

Materials and methods

A randomized controlled trial enrolling 32 NAFLD patients of both sexes (15 men and 17 women) with ages ranging from 30 to 55 years without secondary liver disease (e.g. without hepatitis B virus, hepatitis C virus, or alcohol consumption) was conducted. Patients were randomly allocated either to CWT or to aerobic exercise training, three times weekly, for 3 months. Anthropometrics, lipid profile, liver enzymes, and liver steatosis were assessed. Steatosis was quantified with the hepatorenal-ultrasound index (HRI) representing the ratio between the brightness level of the liver and the right kidney.

Results

All baseline characteristics were similar for the two treatment groups with respect to demographics, anthropometrics, lipid profile, liver enzymes, and liver steatosis on imaging. HRI score was significantly reduced in the CWT group as compared with the aerobic exercise training group (-0.38 ± 0.37 vs. -0.17 ± 0.28 , $P = 0.017$), representing an 18 versus 8.54% relative reduction from baseline in the two groups, respectively. CWT also improved body composition, most importantly waist circumference, which was positively correlated with the change in HRI ($r = 0.645$ and $P = 0.009$).

Conclusion

This randomized controlled trial demonstrated a significant reduction in steatosis, as assessed by HRI, after 3 months of CWT accompanied by favorable anthropometric, lipid profile, and liver enzyme changes. CWT may serve as a complement to the treatment of NAFLD.

Keywords:

aerobic exercise, circuit weight training, liver steatosis, obesity

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide [1]. The presentation of the disease ranges from what can be considered ‘silent liver disease’, or fatty steatosis, to nonalcoholic steatohepatitis [2].

Nonalcoholic steatohepatitis is considered a major cause of cryptogenic cirrhosis and is associated with an increased risk for developing cardiovascular disease, insulin resistance (IR), type 2 diabetes, and chronic kidney disease [3,4]. The prevalence of NAFLD is influenced by several factors such as age, sex, ethnicity, and the presence of sleep apnea and endocrine dysfunctions (hypothyroidism, hypopituitarism, hypogonadism, and polycystic ovary syndrome) [5,6].

Obesity is a chronic disease defined by a BMI greater than 30 kg/m^2 , and morbid obesity, one of the most rapidly growing subgroups, is defined as a BMI greater than 40 kg/m^2 [7]. Considered as a state of chronic low-grade inflammation, obesity has been associated with complications such as type 2 diabetes, cardiovascular disease, hypertension, stroke, gallbladder disease, osteoarthritis, and psychosocial problems [8,9]. Obesity has also been associated with a spectrum of cancer types (colon, breast, endometrium, kidney, esophagus, stomach, pancreas, and gallbladder), and, together with IR,

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represents a risk factor for developing hepatocellular carcinoma [10].

NAFLD is strongly linked to obesity, with a reported prevalence as high as 80% in obese patients and only 16% in individuals with a normal BMI and without metabolic risk factors [11,12]. Fatty liver severity in the morbidly obese also correlates with the degree of impaired glycemic status [13].

Hepatic steatosis is correlated with BMI, but is more closely associated with visceral adiposity (measured as waist circumference), as visceral adipose tissue is more lipolitically active on a per-unit-weight basis than subcutaneous fat [14,15]. However, it was identified as a form of metabolically benign obesity in which insulin-sensitive, obese individuals have a lower percentage of accumulated liver fat compared with IR obese subjects. This implies that the prevention and reduction of hepatic fat accumulation may lower IR even in patients with increased adiposity [16,17].

To date, no evidence-based therapy has proven to be effective for NAFLD, except exercise and dietary interventions [18]. The role of physical activity (PA) as a potential treatment for NAFLD has been tested in several observational studies and in a few clinical trials, mostly testing the effect of aerobic training [19,20].

However, obese people have an extra burden on the knee and hip joints that tend to discourage continued adherence to aerobic exercise programs. Furthermore, fatigue is a common symptom in NAFLD patients, and they report low scores for vitality [21]. Although NAFLD patients understand the benefits of exercise, they lack the confidence to perform it and express a fear of falling [22].

For those patients who may have physical limitation or low motivation that prevents them from performing aerobic PA, resistive training (RT) can serve as an alternative option. Therefore, there is an unmet need for the development of a safe and effective exercise therapy that can be sustainably adopted by NAFLD patients to achieve long-term weight loss. Thus, the main aim of this randomized controlled trial was to evaluate the effect of high-intensity circuit weight training (CWT) on NAFLD patients.

Materials and methods

Patients

Thirty-two patients of both sexes (15 men and 17 women) with ultrasound-diagnosed fatty liver attending the liver clinic at the National Nutrition Institute were screened and selected randomly to be enrolled into

this 12-week blinded randomized controlled trial after they had fulfilled the inclusion criteria of the study and had provided informed consent for participation in the study and for publication of the results. This study was approved by the Ethics Committee for scientific research of the Faculty of Physical Therapy, Cairo University.

Inclusion criteria were as follows: age between 30 and 55 years, BMI of 30 or more, and a diagnosis of fatty liver on ultrasound in the past 6 months and on the baseline ultrasound examination. The diagnosis of NAFLD was based on overeating or physical inactivity, elevated serum alanine aminotransferase (ALT) levels, and the presence of at least two of three abnormal findings using abdominal ultrasonography: diffusely increased liver echogenicity (bright) greater than for kidney, vascular blurring, and deep attenuation of the ultrasound signal according to the diagnostic guidelines for NAFLD [23].

Exclusion criteria were any known secondary liver diseases, including the presence of hepatitis B surface antigen or anti-hepatitis C virus antibodies, alcohol consumption, administration of medical treatment that may elevate ALT or lead to hepatic steatosis, known diabetes, and major chronic diseases including renal, cardiovascular, and lung diseases, uncontrolled hypertension, inflammatory bowel disease, active cancer, autoimmune disorders, and orthopedic contraindications for resistance training (RT). Adults with diabetes were excluded to avoid a confounding effect, as it is unclear whether they would have the same response to physical training and as changes in antidiabetic medications might occur during the trial. Patients who had been regularly performing RT in the 3 or 6 months before study enrolment and patients with recent weight reduction (more than 3 kg in the last 3 months) were also excluded.

To avoid a type II error, a preliminary power analysis [power (1- β error probability) = 0.85, α = 0.01, effect size = 0.5] determined a sample size of 32 for this study. This effect size was chosen because it yielded a realistic sample size [24].

To avoid bias after patients had been assessed for eligibility and recruited, patients were randomly assigned to either group A or group B. Group A patients participated in a CWT program (2–3 circuits), with 10 repetitions (with a 2 min rest between each circuit), 3 days/week for 12 weeks; group B patients participated in an aerobic training program (30–40 min) 3 days/week for 12 weeks. Patient allocation was by means of random numbers using opaque envelopes prepared by an independent person.

Low-calorie diet

A low-calorie diet (LCD) must be lower than the person's energy requirement and energy expenditure. It usually produces an energy deficit of 500–1000 calories per day. Diets consisting of between 800 and 1200 kcal/day are classified as LCDs. The constituents of LCDs should be as follows: fat 30% of total caloric intake (TCI), complex carbohydrates such as grains and fruits 55% of TCI, protein 15% of TCI (low-fat meat, fish, chicken, and high-protein bean), and 20–30 g fiber/day [25].

Outcome measures

Initially, data on the patients' characteristics were collected in the first session – namely, height (measured to the nearest 0.1 cm with the participant standing in an erect position against a vertical scale of a portable stadiometer), and weight (kg) (measured to the nearest 0.1 kg using a standard weight scale).

Resting heart rate (beats/min), resting respiratory rate (cycle/min), and blood pressure were measured during the sessions to exclude any signs or symptoms that may interfere with the continuity of the study. BMI (kg/m^2) was calculated as weight in kilograms divided by squared height in meters. Waist circumference was measured using an anthropometric tape at the level of the umbilicus.

Laboratory determinations

Each participant underwent biochemical testing for liver enzymes and serum lipid profile. Blood samples were drawn from the median cubital vein at baseline and at week 12 after fasting for 12 h.

Ultrasonographic examination for determination of nonalcoholic fatty liver disease

Fatty liver was assessed by abdominal ultrasonography using standardized criteria [26]. Ultrasonography was performed with the same equipment (EUB-8500 scanner; Hitachi Medical Corporation, Tokyo, Japan) and by the same experienced radiologist. The radiologist was blinded to patient allocation and to laboratory values and medical history of the participants. During the ultrasonography, a histogram of brightness levels – that is, a graphical representation of echo intensity within a region of interest (ROI) – was obtained. In the liver, the ROI was measured in the seventh or eighth intercostal space in the mid or anterior axillary line in the superficial aspect of the liver. In the right kidney, the ROI was determined as the cortical area between the pyramids.

The brightness level for each organ was recorded and the ratio between the median brightness level of the

liver and the right kidney cortex was calculated to determine the hepatorenal-ultrasound index (HRI). The HRI has been previously demonstrated to be highly reproducible ($r = 0.77$, $P < 0.001$, $k = 0.86$) and was validated against liver biopsy [27]. HRI of 1.5 or more indicates fatty liver.

Exercise training protocols

Sufficient warm-up and cooling down (about 10–15 min) in the form of stretching of major muscle groups, flexibility movements, active movements of limbs, breathing exercises, and walking at low intensity (50% of maximum heart rate) was performed before and after both CWT and aerobic training sessions. Sufficient time was taken to familiarize the participants in the CWT group with the RT machines by making the participants do one set of each exercise on different weight machines, which were repeated 10 times. Sufficient time was also taken to familiarize the participants in the aerobic training group with the treadmill and safety measures.

For both groups closely supervised exercise training was regularly held at a frequency of three sessions per week. Participants were encouraged to have sweetened eatables or beverages during training to compensate for probably occurring hypoglycemic episodes. Also they were advised not to eat heavy meals at least 2 h before training.

Resistance circuit weight training program

The American College of Sports Medicine (2011) specified the following parameters: load: 70–80% 1RM; number of repetitions: 10; number of circuits: 2–3; rest between circuits: 2 min; frequency: 3 days/week.

The following exercises (stations) were performed: bench press, seated row, shoulder press, chest press, lateral pull down, abdominal crunches, leg press, leg extension, triceps pushdown, and seated bicep curls. Sixteen patients participated in a CWT exercise program performed for 30 min, three times per week, for 12 weeks. Closely supervised training techniques were adopted for participants of this group after proper warm-up to minimize the risk of musculoskeletal injuries. The program progressed gradually in frequency and intensity. The protocol initially consisted of twice weekly sessions for the first month, which was increased to 3 nonconsecutive days' sessions per week for the following 2 months [28].

The intensity progress for the CWT group followed a stepwise manner in which there was a gradual increase by 2.5% of one-repetition maximum

(1RM) every 2 weeks. Moderate resistance was used in which 60–65% of 1RM was used during the first month, and then the intensity was increased to 70–80% of 1RM in the subsequent months. The training program started with one to two sets of 10 repetitions of 10 different exercises for upper and lower body during the first month, which was increased to three sets of 10 repetitions of 10 different exercises (stations) for upper and lower body for the subsequent 2 months. CWT exercises were performed with a 90–120 s rest between each exercise group (station). Between each station the patient performed treadmill exercise, maintaining their rate of perceived exertion between 13 and 14 on the Borg's score scale [29].

Aerobic exercise program

After warming up, the participants of this group performed treadmill walking three times per week (on nonconsecutive days). The duration of exercise was increased from 20 min per session (at 60% of maximum heart rate) to 30 min (at 75% of maximum heart rate) per session [30].

Aerobic exercise intensity was determined by the Karvonen formula in which target heart rate = [(max HR–resting HR) × intensity] + resting HR, where maximum heart rate = 220–age [31]. All 32 participants willingly adhered to and completed the training programs. No serious adverse effect was reported in either training group.

Results

This study was conducted to investigate the effect of high-intensity CWT versus aerobic training in patients with NAFLD by exploring the effect of 3 months of high-intensity CWT versus aerobic training on anthropometric parameters, lipid profile, liver enzymes, and liver steatosis assessed by abdominal ultrasound using the HRI as a quantitative objective measurement of steatosis.

Baseline (pretraining) demographic and anthropometric characteristics of patients in both groups

The baseline (pretraining) evaluation revealed nonsignificant statistical differences between the two groups (CWT group (A) and aerobic training group (B)) regarding the demographic and anthropometrics characteristics, including gender, age, height, weight, body mass index, and waist circumference ($P > 0.05$), as shown in Table 1.

Baseline (pretraining) clinical parameters in both groups

The results of this study revealed that there were nonsignificant statistical differences between the two groups before treatment in the measured clinical parameters with respect to blood tests, including lipid profile [total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL)], liver enzymes [ALT and aspartate aminotransferase (AST)], and liver steatosis on imaging as assessed by the HRI ($P > 0.05$), as shown in Table 2. Results are illustrated in Figs. 1–3.

Table 1 Baseline (pretraining) demographic and anthropometric characteristics of patients in the two groups (mean ± SD)

Variables	Circuit weight training group (N = 16)	Aerobic training group (N = 16)	t-Value	P-value
Age (years)	43.32 ± 10.32	44.64 ± 11.4	1.94	0.17
Height (m)	1.62 ± 0.04	1.64 ± 0.05	2.87	0.09
Weight (kg)	89.03 ± 5.84	89.11 ± 6.33	0.002	0.96
BMI (kg/m ²)	33.99 ± 2.57	33.13 ± 2.11	1.35	0.25
Waist circumference (cm)	105.05 ± 10.77	106.71 ± 10.16	0.46	0.527
Sex (female)	55.5%	58.1%	0.53 ^a	0.44

^aThe value is calculated using the χ^2 -test; Level of significance at $P \leq 0.05$.

Table 2 Baseline (pretraining) clinical parameters in the two groups

Variables	Mean ± SD		t-Value	P-value
	Circuit weight training group (N = 16)	Aerobic training group (N = 16)		
Cholesterol (mg/dl)	194.18 ± 45.81	183.35 ± 32.92	0.76	0.288
Triglycerides (mg/dl)	145.88 ± 75.69	143.65 ± 55.15	0.007	0.894
HDL (mg/dl)	47.32 ± 12.29	45.65 ± 9.96	0.41	0.553
LDL (mg/dl)	114.94 ± 40.37	106.23 ± 24.22	0.74	0.296
ALT (U/l)	52.00 ± 35.61	49.13 ± 37.20	0.640	0.733
AST (U/l)	33.30 ± 17.49	32.50 ± 14.76	0.39	0.572
HRI (score)	2.11 ± 0.44	1.99 ± 0.46	1.55	0.203

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; HRI, hepatorenal-ultrasound index; LDL, low-density lipoprotein; N, sample size; Level of significance at $P \leq 0.05$.

Anthropometric and clinical parameters in the two groups after 3 months of training

Anthropometric and clinical parameters in the circuit weight training group

Anthropometric parameters: Regarding anthropometric parameters (weight, BMI, and waist circumference) results revealed that there

were statistically significant differences between pretraining and post-training values. Concerning group A, the percentage changes were -12.36, -9.85, and -9.49% and *P*-values were 0.001, 0.001, and 0.002, respectively. Results are presented in Table 3 and illustrated in Fig. 4.

Clinical parameters

Lipid profile

Regarding lipid profile (total cholesterol, triglyceride, HDL, and LDL), results revealed that there were statistically significant differences between pretraining and post-training values. Concerning group A, the percentage changes were -4.43, -9.22, -4.64, and -5.29% and *P*-values were 0.007, 0.001, 0.004, and 0.015, respectively. Results are presented in Table 3 and illustrated in Fig. 5.

Liver enzymes

Regarding liver enzymes (ALT and AST), results revealed that there were statistically significant differences between pretraining and post-training values. Concerning group A, the percentage changes were -10.19 and -8.28% and *P*-values were 0.018 and 0.008, respectively. Results are presented in Table 3 and illustrated in Fig. 6.

Liver steatosis

Regarding liver steatosis on imaging as assessed by the HRI, results revealed that there was a statistically significant difference between pretraining and post-training values. Concerning group A, the percentage change was -18.00% and *P*-value was 0.002. Results are presented in Table 3 and illustrated in Fig. 7.

Anthropometric and clinical parameters in the aerobic training group

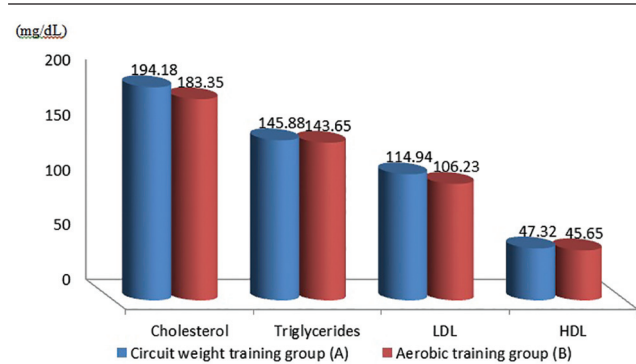
Anthropometric parameters: Regarding anthropometric parameters (weight, BMI, and waist circumference), results revealed statistically significant differences between pretraining and post-training values. Concerning group B, the percentage changes were -5.31, -5.22, and -3.91% and *P*-values were 0.001, 0.001, and 0.001, respectively. Results are presented in Table 4 and illustrated in Fig. 8.

Clinical parameters

Lipid profile

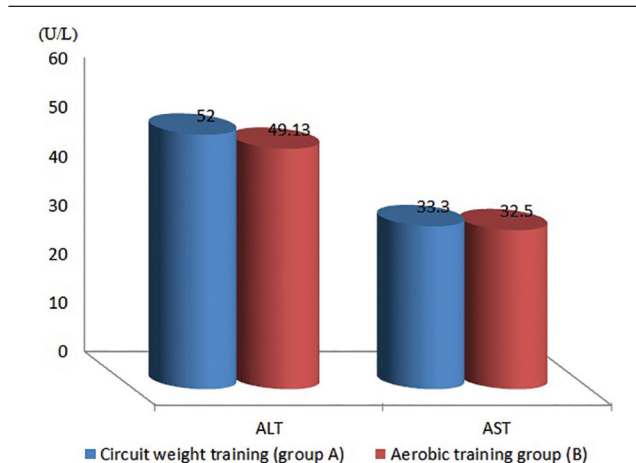
Regarding the lipid profile (total cholesterol, triglycerides, HDL, and LDL), results revealed statistically significant differences between pretraining and post-training values. Concerning group B, the

Figure 1



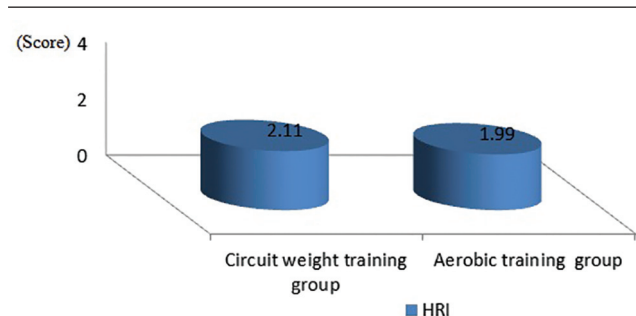
Baseline (pretraining) clinical parameters in the two groups.

Figure 2



Baseline (pretraining) clinical parameters in the two groups.

Figure 3



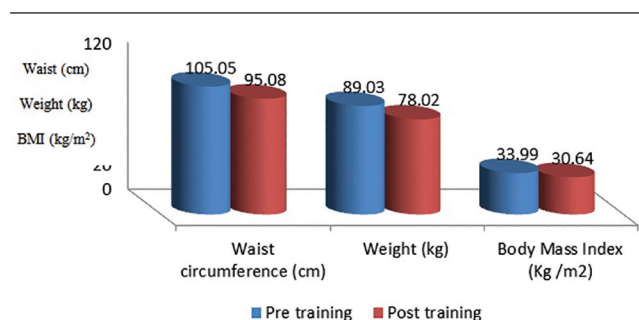
Baseline (pretraining) hepatorenal-ultrasound index (HRI) in the two groups.

percentage changes were -2.14, -2.17, -0.28, and -2.63% and *P*-values were 0.038, 0.019, 0.023, and 0.040, respectively. Results are presented in Table 4 and illustrated in Fig. 9.

Liver enzymes

Regarding liver enzymes (ALT and AST), results revealed statistically significant differences between

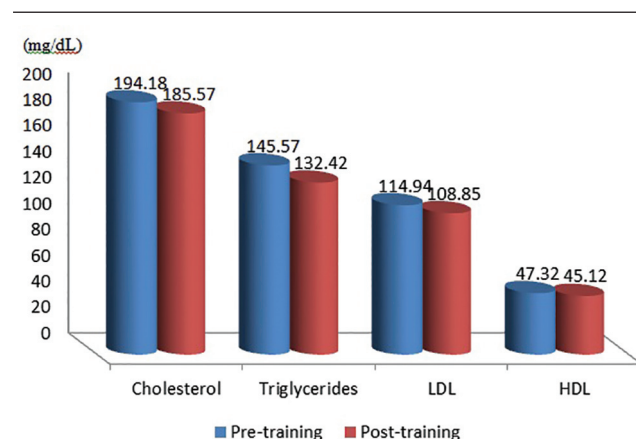
Figure 4



Anthropometric parameters in the circuit weight training group.

pretraining and post-training values. Concerning group B, the percentage changes were -7.55 and -5.47% and *P*-values were 0.007 and 0.009, respectively. Results are presented in Table 4 and illustrated in Fig. 10.

Figure 5



Clinical parameters (lipid profile) in the circuit weight training group after 3 months of training.

Table 3 Anthropometric and clinical parameters in the circuit weight training group

Variables	Circuit weight training group (group A) (N = 16)				
	Mean ± SD		Percentage of change	t-Value	P-value
	Pretraining	Post-training			
Weight (kg)	89.03 ± 5.84	78.02 ± 3.84	-12.36%	11.366	0.001*
BMI (Kg/m ²)	33.99 ± 2.57	30.64 ± 2.89	-9.85%	10.629	0.001*
Waist circumference (cm)	105.05 ± 10.77	95.08 ± 8.80	-9.49%	6.553	0.002*
Cholesterol (mg/dl)	194.18 ± 45.81	185.57 ± 29.2	-4.43%	5.490	0.007*
Triglycerides (mg/dl)	145.88 ± 75.69	132.42 ± 62.30	-9.22%	4.822	0.001*
HDL (mg/dl)	47.32 ± 12.29	45.12 ± 6.43	-4.64%	1.910	0.004*
LDL (mg/dl)	114.94 ± 40.37	108.85 ± 26.38	-5.29%	1.263	0.015*
ALT (U/l)	52.00 ± 35.61	46.70 ± 9.65	-10.19%	1.297	0.018*
AST (U/l)	33.30 ± 17.49	30.54 ± 7.75	-8.28%	5.21	0.008*
HRI (score)	2.11 ± 0.44	1.73 ± 0.37	-18.00%	6.77	0.002*

ALT, alanine transaminase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; HRI, hepatorenal-ultrasound index; LDL, low-density lipoprotein; N, sample size; *Significant; *level of significance at *P* < 0.05.

Table 4 Anthropometric and clinical parameters in the aerobic training group

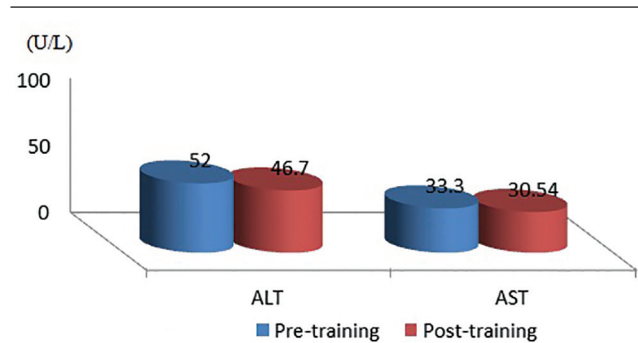
Variables	Aerobic training group (group B) (N = 16)				
	Mean ± SD		Percentage of change	t-Value	P-value
	Pretraining	Post-training			
Weight (kg)	89.11 ± 6.33	84.37 ± 12.08	-5.31%	6.886	0.001*
BMI (Kg/m ²)	33.13 ± 2.11	31.40 ± 2.89	-5.22%	7.976	0.001*
Waist circumference (cm)	106.71 ± 10.16	102.53 ± 7.55	-3.91%	7.313	0.001*
Cholesterol (mg/dl)	183.35 ± 32.92	179.42 ± 17.25	-2.14%	1.095	0.038*
Triglycerides (mg/dl)	143.65 ± 55.15	140.53 ± 29.68	-2.17%	2.040	0.019*
HDL (mg/dl)	45.65 ± 9.96	45.52 ± 5.64	-0.28%	1.320	0.023*
LDL (mg/dl)	106.23 ± 24.22	103.43 ± 14.57	-2.63%	1.274	0.040*
ALT (U/l)	49.13 ± 37.20	45.42 ± 14.43	-7.55%	5.983	0.007*
AST (U/l)	32.50 ± 14.76	30.72 ± 6.95	-5.47%	4.875	0.009*
HRI (score)	1.99 ± 0.46	1.82 ± 0.28	-8.54%	7.471	0.001*

ALT, alanine transaminase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; HRI, hepatorenal-ultrasound index; LDL, low-density lipoprotein; N, sample size; *level of significance at *P* < 0.05; *Significant.

Liver steatosis

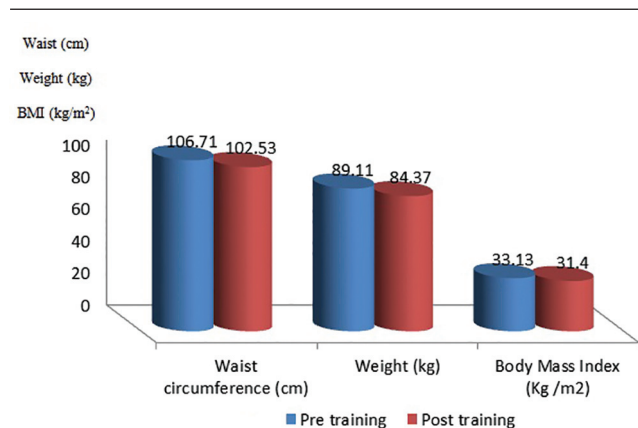
Regarding liver steatosis on imaging as assessed by the HRI, results revealed a statistically significant difference between pretraining and post-training values. Concerning group B, the percentage change was -8.54% and P -value was 0.001. Results are presented in Table 4 and illustrated in Fig. 11.

Figure 6



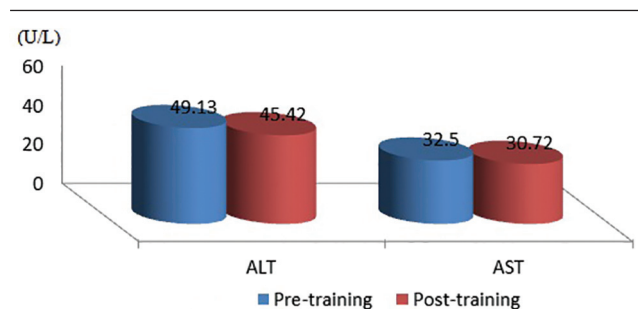
Clinical parameters (liver enzymes) in the circuit weight training group after 3 months of training.

Figure 8



Anthropometric parameters in the aerobic training group after 3 months of training.

Figure 10



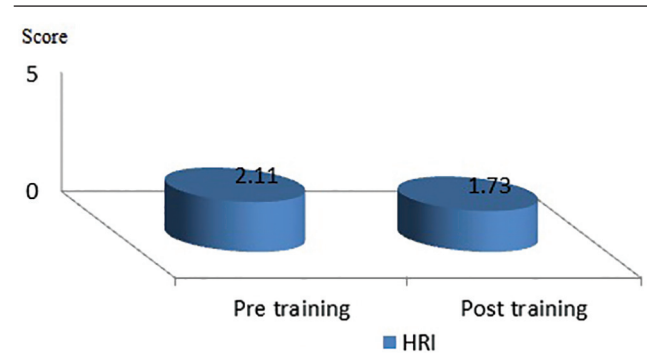
Clinical parameters (liver enzymes) in the aerobic training group after 3 months of training.

Comparison between the two groups regarding anthropometric and clinical parameters after 3 months of training

Anthropometric parameters

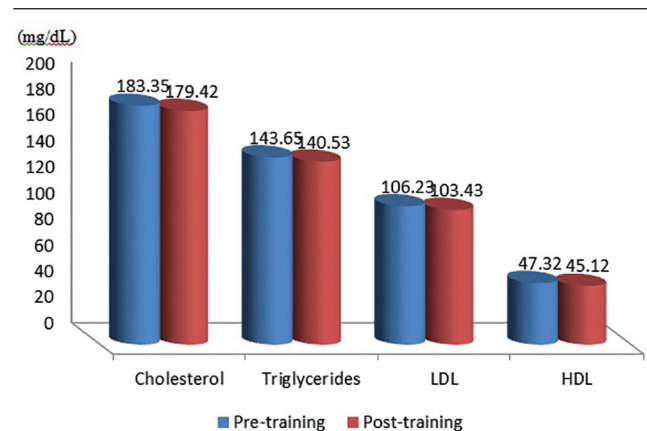
Regarding anthropometric parameters (weight, BMI, and waist circumference), the results of this study

Figure 7



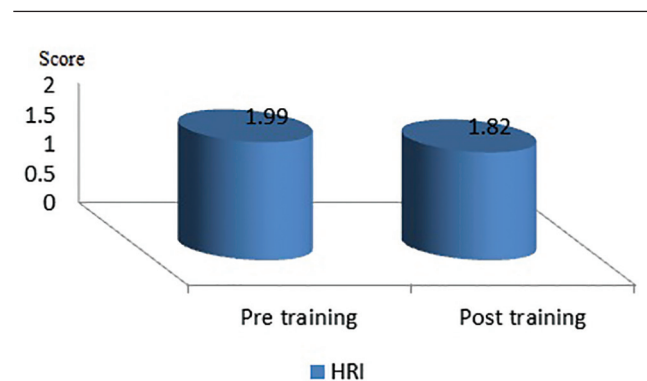
Hepatorenal-ultrasound index (HRI) in the circuit weight training group after 3 months of training.

Figure 9



Clinical parameters (lipid profile) in the aerobic training group after 3 months of training.

Figure 11



Hepatorenal-ultrasound index (HRI) in the aerobic training group after 3 months of training.

revealed statistically significant differences between the two groups after 3 months of training, except for BMI, with P -values of 0.036, 0.293, and 0.012, respectively, favoring the CWT group (group A). Results are presented in Table 5 and illustrated in Fig. 12.

Clinical parameters

Lipid profile

Regarding lipid profile parameters (triglycerides, HDL, and LDL), the results of this study revealed no statistically significant differences between the two groups after 3 months of training ($P = 0.086$, 0.984, and 0.076, respectively). However, there was a statistically significant difference between the two groups with regard to total cholesterol ($P = 0.018$), favoring group B. Results are presented in Table 5 and illustrated in Fig. 13.

Liver enzymes

Regarding liver enzyme levels (ALT and AST), results revealed no statistically significant difference between

the two groups after 3 months of training ($P = 0.946$ and 0.965, respectively). Results are presented in Table 5 and illustrated in Fig. 14.

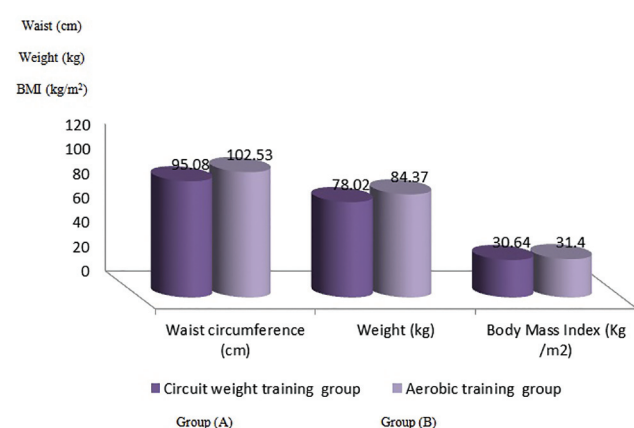
Liver steatosis

Regarding liver steatosis on imaging as assessed by the HRI, results revealed a statistically significant difference between the two groups after 3 months of training ($P = 0.017$), favoring group A. Results are presented in Table 5 and illustrated in Fig. 15.

Correlation between the changes in waist circumference and hepatorenal-ultrasound index in the two groups after 3 months of training

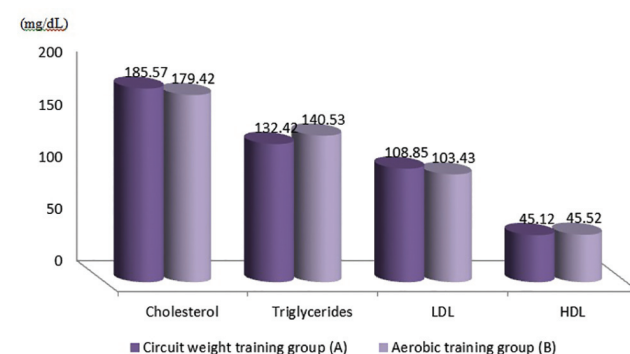
Pearson's correlation was used to correlate between the changes in waist circumferences and the reduction in HRI in the two groups after 3 months of training. In both groups, there was a strong positive correlation between waist circumference and HRI ($r = 0.645$ and 0.561, respectively). Results are presented in Table 6 and illustrated in Fig. 16.

Figure 12



Comparison between the two groups regarding anthropometric parameters after 3 months of training.

Figure 13



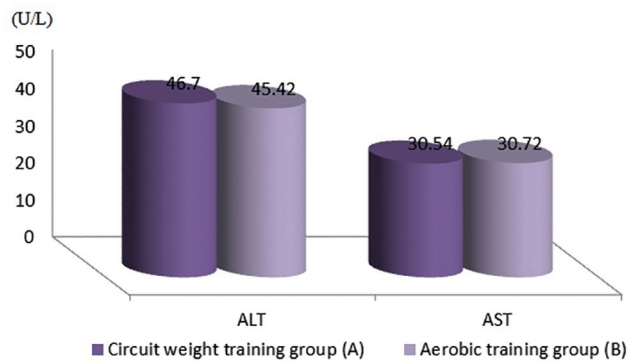
Comparison between the two groups regarding clinical parameters (lipid profile) after 3 months of training.

Table 5 Comparison between the two groups regarding anthropometric and clinical parameters after 3 months of training

Variables	Post-training			
	Mean \pm SD		t-Value	P-value
	Circuit weight training group (N = 16)	Aerobic training group (N = 16)		
Weight (kg)	78.02 \pm 3.84	84.37 \pm 12.08	1.120	0.036*
BMI (kg/m ²)	30.64 \pm 2.89	31.40 \pm 2.89	0.74	0.293
Waist circumference (cm)	95.08 \pm 8.80	102.53 \pm 7.55	2.140	0.012*
Cholesterol (mg/dl)	185.57 \pm 29.2	179.42 \pm 17.25	2.120	0.018*
Triglycerides (mg/dl)	132.42 \pm 62.30	140.53 \pm 29.68	1.032	0.086
HDL (mg/dl)	45.12 \pm 6.43	45.52 \pm 5.64	0.008	0.984
LDL (mg/dl)	108.85 \pm 26.38	103.43 \pm 14.57	1.087	0.076
ALT (U/l)	46.70 \pm 9.65	45.42 \pm 14.43	0.089	0.946
AST (U/l)	30.54 \pm 7.75	30.72 \pm 6.95	0.037	0.965
HRI (score)	1.73 \pm 0.37	1.82 \pm 0.28	2.164	0.017*

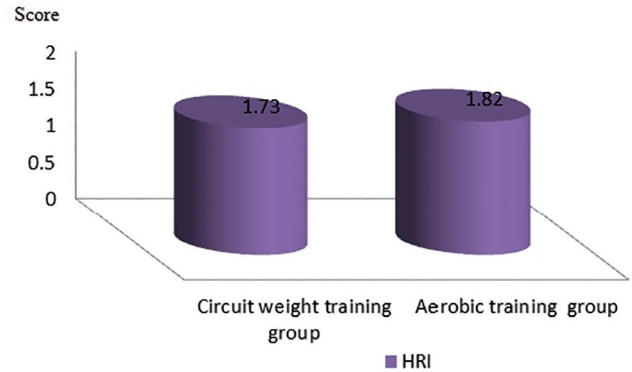
ALT, alanine transaminase; AST, aspartate aminotransferase; HDL, high-density lipoprotein; HRI, hepatorenal-ultrasound index; LDL, low-density lipoprotein; N, sample size; *level of significance at $P < 0.05$; *Significant.

Figure 14



Comparison between the two groups regarding clinical parameters after 3 months of training.

Figure 15



Comparison between the two groups regarding hepatorenal-ultrasound index (HRI) after 3 months of training.

Table 6 Correlation between the changes in waist circumference and hepatorenal-ultrasound index in the two groups after 3 months of training

Waist circumference	Hepatorenal-ultrasound index			
	Group A (N = 16)		Group B (N = 16)	
	r	P-value	r	P-value
	0.645	0.009**	0.561	0.030*

N, sample size; r, correlation coefficient; *Correlation is significant at the 0.05 level (two-tailed); **Correlation is significant at the wvel (two-tailed).

Discussion

In this randomized controlled trial, NAFLD patients underwent either CWT or aerobic exercise training for 3 months. The results suggest that CWT exerts beneficial effects on several anthropometric and clinical parameters, including liver steatosis and body composition.

The HRI score was significantly reduced in the CWT group as compared with the aerobic exercise training group (-0.38 ± 0.37 vs. -0.17 ± 0.28 , $P = 0.017$), representing an 18 versus 8.54% relative reduction from baseline in the two groups, respectively. CWT also improved body composition, most importantly waist circumference, which was positively correlated with the change in HRI.

PA is a documented modality for weight reduction in NAFLD therapy. In an observational analysis of 348 patients with NAFLD, after 1 year Suzuki *et al.* [32] demonstrated an improvement in transaminase levels with weight loss, and they concluded that reducing weight by at least 5% with subsequent weight control and exercising regularly may be beneficial in treating NAFLD.

The beneficial effect of aerobic exercise in NAFLD is supported by clinical trials demonstrating a relative reduction of hepatic triglyceride concentration by

21–35% following supervised training such as cycling. However, in a trial of a more modest activity that included brisk walking, there was a relative reduction of 10.3% in liver fat, similar to the one observed in the present study [33,34].

Cross-sectional studies have shown that higher levels of PA are associated with lower levels of intrahepatic triglyceride IHTG [35,36]. Previous studies have reported a beneficial effect of aerobic exercise on liver function, independent of weight reduction [33,37].

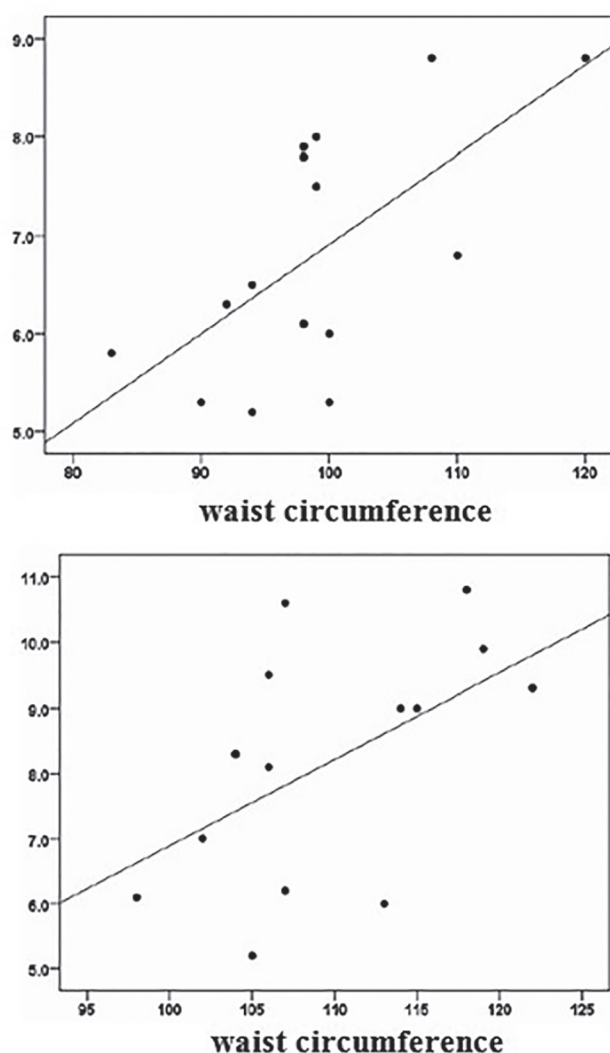
In recent years, there has been increased attention on RT as a useful adjunctive tool of exercise. Johnson *et al.* showed that RT without a concomitant weight-loss diet significantly improved insulin sensitivity and fasting glycemia and decreased abdominal fat [33].

The 2007 update of the American Heart Association dealing with resistance exercise (RE) concludes that RT should be viewed as a complement to aerobic exercise [38]. However, the beneficial effect of RT for patients with steatosis was so far not supported by strong evidence.

The benefit of PA alone in the absence of any changes in body weight was examined in NAFLD patients. Hallsworth *et al.* assigned 19 sedentary adults with NAFLD to 8 weeks of RE. Eleven were assigned to RE and eight to normal treatment; they showed a benefit of RE as a lipid-lowering treatment for NAFLD independent of weight loss [39].

In previous published trials on the effect of RT in adult NAFLD patients, there was a significant improvement in glycemic control and no improvement in liver enzymes [40,41]. Our study did not demonstrate improved glucose metabolism. This discrepancy may stem from the exclusion of diabetic patients from

Figure 16



Correlation between the changes in waist circumference and hepatorenal-ultrasound index (HRI) in the two groups after 3 months of training.

our study. It was previously shown that RT improves hyperglycemia only in patients with disturbed glucose metabolism or diabetes [42,43]. Our study showed significant improvement in liver enzyme levels (ALT and AST) within groups but with no difference between groups.

Another beneficial effect of RT in our study was a significant reduction in serum cholesterol. Although data regarding the effect of RT on lipid metabolism are equivocal, reduction in serum total cholesterol and LDL by RT has been previously demonstrated in a meta-analysis of randomized controlled trials [44]. It is well established that liver steatosis is associated with IR and lipid abnormalities, including alteration in cholesterol metabolism [45,46]. Recent data show that increased IR contributes to the shift in cholesterol metabolism to increased synthesis and decreased

absorption, independent of body weight [47,48]. Several studies have demonstrated that RT improves IR, including hepatic IR [46,49], and therefore may contribute to decreased synthesis of hepatic cholesterol.

Induction of adipose tissue loss by RT through an increase in metabolic rate has been reported previously [40]. One possibility is that myogenesis induced by CWT leads to recruitment of a large number of muscle fibers, resulting in an increase in the metabolic potential to burn fat. Another possibility is that of activation of the sympathetic nervous system by CWT, which induces lipolysis in white adipose tissue, resulting in reduction of body fat [50].

Recently, skeletal muscle has been identified not only as a component of the locomotor system but also as a metabolic organ engaged in glucose and fatty acid metabolism similar to the liver and adipose tissue [51]. RT is hypothesized to reduce the amount of hepatic fat through a mechanism involving insulin sensitivity and fatty acid metabolism [52].

In NAFLD, the level of intrahepatic lipid increases through induction of de-novo lipogenesis resulting from induced expression and activation of transcription factors, such as sterol regulatory element-binding protein-1c and carbohydrate response element-binding protein, in response to increased insulin levels. In addition, increased levels of triglyceride intermediates inhibit insulin-stimulated glucose uptake, suggesting a vicious cycle whereby inhibition of insulin action by high intrahepatic lipid levels in the liver triggers a further increase in intrahepatic lipid levels [53].

It has been reported that RT restores insulin sensitivity and increases systemic glucose metabolism through induction and activation of skeletal muscle glucose transporter type 4, followed by an increase in glucose uptake by skeletal muscle and induction of glycogen synthesis [54,55]. RT has also been shown to reduce hepatic fatty acid uptake and increased utilization of fatty acids by skeletal muscle through enhanced myogenesis, leading to a reduction in hepatic fat content [55].

The effect of WBV training on the endocrine system in normal male individuals was investigated by Di Loreto and colleagues under the hypothesis that application of vibrations would be effective in the treatment of obesity. They showed that WBV training improved glucose utilization by increasing the consumption of circulating plasma glucose for muscle contraction, indicating that WBV training improves insulin sensitivity. Thus, long-term WBV training is believed to attenuate IR in obese and diabetic patients by repeated vibratory

stimulation of skeletal muscles, subsequently leading to muscle contractions. A similar mechanism is assumed to be relevant in AT [56].

Conclusion

In NAFLD patients, compliance may be even lower because fatigue has been demonstrated to be markedly higher in NAFLD patients compared with controls, and is associated with inactivity and excessive daytime sleepiness. Therefore, an alternative or a complement form of exercise that may be easier to perform or to adhere to, such as RT, may be helpful in the treatment of NAFLD patients. This randomized controlled trial demonstrated a significant reduction in steatosis, as assessed by HRI, after 3 months of CWT, accompanied by favorable anthropometric and lipid profile, and liver enzyme changes. CWT may serve as a complement to the treatment of NAFLD.

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Conflicts of interest

There are no conflicts of interest.

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