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Prevention and Rehabilitation

Effects of non-linear resistance training and curcumin supplementation on the liver biochemical markers levels and structure in older women with non-alcoholic fatty liver disease

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Background: With increasing age, non-alcoholic fatty liver disease is very common among women with low levels of physical activity. Nonlinear resistance training is one of the new methods to help patients who have low levels of physical activity. Curcumin is an herbal supplement that has anti-inflammatory effects. The present study aimed to examine the effects of nonlinear resistance training and curcumin supplementation on the liver structure and biochemical markers in obese older women with non-alcoholic fatty liver disease.
Methods: Forty-five obese women with non-alcoholic fatty liver disease were randomly assigned into resistance training (RT), curcumin supplement (C), resistance training with curcumin supplement (RTC), and placebo (P) groups. The RT and RTC groups received 12-weeks of nonlinear resistance training while the C and P groups had a normal sedentary lifestyle. Daily, the C and RTC groups received a curcumin capsule while the P and RT groups were given a placebo capsule. Blood sampling and ultrasonography were taken before and after the protocol.
Results: Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels significantly decreased in the RT and RTC groups ($P \leq 0.05$) but not in the C and P groups ($P > 0.05$). Alkaline phosphatase (ALP), total bilirubin (TB) levels, platelet counts (PLT), and liver structure did not significantly change in all groups ($P > 0.05$). Resistance training alone and with curcumin supplementation could significantly improve liver function while taking curcumin alone did not have any significant effect on it.
Conclusion: 12-week non-linear resistance training has beneficial effects on non-alcoholic fatty liver disease in older obese women.

1. Introduction

Many organs lose their ability to function properly due to age-associated changes. One of these organs is the liver that undergoes changes in function and structure with ageing. Increasing age results in reduced liver volume, reduced phase I drug metabolism, impairment of biliary and liver function and decreased protein expression (Schmucker, 2005). Minor age-related changes caused by decreased regenerative capacity of the liver include reduced oxidative-stress response, reduced expression of growth regulator gene, decreased ability to repair DNA leading to liver dysfunction in the elderly (Schmucker, 2005). The prevalence rate of non-alcoholic fatty liver disease is 39% in individuals aged 40 to 50 and 40% in those over the age of 70 (Argo and Caldwell, 2009;

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Okanoue et al., 2011). This disease includes a broad range of hepatic disorders from simple fat accumulation in hepatic cells (simple steatosis) to hepatic tissue inflammation and fibrosis (steatohepatitis) and finally cirrhosis and even hepatocellular carcinoma.

Alanine aminotransferase (ALT) (Kallai et al., 1964; Sheth et al., 1997), aspartate aminotransferase (AST) (Thapa and Walia, 2007), alkaline phosphatase (ALP) (Gowda et al., 2009), platelet counts (PLT) (Liu et al., 2018) and total bilirubin (BT) (Thapa and Walia, 2007; Wong et al., 2004) are factors that are commonly used in clinical medicine tests as indicators of liver diseases (Gowda et al., 2009). In many studies on patients suffering from non-alcoholic fatty liver disease (NAFLD), increased levels of ALT along with diabetes have been considered as independent predictors of moderate to severe fibrosis in patients with fatty liver who are at risk of progression to advanced fibrosis and only these two variables have been shown to have a significant association with steatohepatitis (Hadizadeh et al., 2017).

NAFLD is also common in postmenopausal women (Fan and Farrell, 2009; Hashimoto and Tokushige, 2011). Ageing is inevitable; however, age-related restrictions and diseases in older adults can be controlled. Appropriate physical activities can slow down the loss of physiological capabilities. As homeostasis is altered by resistance training, the mechanical stress placed on the liver can change its chemical levels and structure. Hallsworth et al., (2011) found that eight weeks of resistance training caused a 13% reduction of liver fat cells without weight loss. It has also been reported that antioxidants have a preventative and therapeutic effect against oxidative stress and normalize various factors (Chen et al., 2016; Oliveira et al., 2016). Maintaining physical exercise habits with using antioxidants can be a promising method for the management of NAFLD (Abenavoli et al., 2014; Chen et al., 2016).

Curcumin (diferuloylmethane) has medicinal properties and it originates from the Turmeric plant (a member of the ginger family) (Aggarwal and Sung, 2009). Some studies (Shishodia et al., 2005; Singh, 2007) have revealed that curcumin has health benefits such as antioxidant, anti-inflammatory, antitumoral, anti-fungal, antibacterial, antiviral, antiproliferative and proapoptotic effects. The anti-inflammatory actions of curcumin seem to be closely related to the suppression of pro-inflammatory cytokines and mediators of their release such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 (IL-1). There are reports that curcumin inhibits cytokine-mediated activation of nuclear factor kappa B (NF-kB) by blocking a signal leading to I–B kinase activity in the intestinal epithelial and fibroblast cells of mouse, and also suppresses phorbol ester-induced c-Jun/AP-1 activation (Chun et al., 2003; Jobin et al., 1999). Curcumin inhibits the phosphorylation of Janus kinase 1 (JAK1) and Janus kinase 2 (JAK2) via increased phosphorylation of SHP-2 and its association with JAK1/2, thus attenuating inflammatory response. It acts via a novel anti-inflammatory mechanism and is also a negative regulator of Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway by activation of SHP-2 (Kim et al., 2003). Also, in some studies, pretreatment of endothelial cells for 1 h with curcumin completely blocked their adhesion to monocytes, as well as the cell surface expression of intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion protein (VCAM-1), and endothelial-leukocyte adhesion molecule 1 (ELAM-1) in these cells. Although curcumin inhibited adhesion even when administered 1 h after TNF treatment, maximum inhibition occurred when added either 1 h before or at the same time as TNF. A 30-min treatment with TNF activated NF-kappaB; the activation was inhibited in a concentration-dependent manner by pretreatment with curcumin, indicating that NF-kappaB inhibition may play a role in the suppression of expression of adhesion molecules in endothelial cells. This finding demonstrates that the anti-inflammatory properties of curcumin may be attributable, in part, to the inhibition of leukocyte recruitment (Kumar et al., 1998). Disilvestro et al. found that low doses of curcumin lipidated extraction (80 mg per day) cause changes such as a reduction in ALT levels in middle-aged individuals (DiSilvestro et al., 2012).

2. Objectives

Given the considerable increase in taking herbal supplements due to their few side effects and lack of studies on the effects of nonlinear resistance training concurrent with taking curcumin supplement, this study aims at examining the effects of concurrent nonlinear resistance training and curcumin supplementation on the liver biochemical marker levels and its structure in older women with non-alcoholic fatty liver disease. The findings of the present study can be used to design exercise programs for the elderly, to recognize the impact of curcumin supplementation on the liver function and to provide evidence on the (possible) effects of concurrent training and supplementation in older women.

3. Methods

3.1. Ethical approval

The experimental protocol of the study was approved at the research ethic committee of Islamic Azad University, Kazeroun Branch, Iran with ethical code: IR.IAU.KAU.REC.1398.079. This study was registered at Islamic Azad University, Central Tehran Branch, Iran with registration number: 10121404941010. Also, the researchers received clinical trials code from Iranian Registry of Clinical Trials (IRCT) (IRCT20190103042219N1). This research was conducted in accordance with the principles stated in the Declaration of Helsinki. Before participating in the investigation, the participants were informed about the risks of the study and each participant signed an institutionally approved informed consent document.

All participants were asked to complete the Physical Activity Readiness Questionnaire (PAR-Q: British Columbia ministry of health, 1978) to determine their health background. Seven days before starting the training program, the participants were informed about the objectives and procedures of the study, the number of blood samplings, ultrasound examination times, resistance training program, and the supplement and placebo intake timing.

3.2. Design of the study

This experimental study was designed to examine the effects of nonlinear resistance training and curcumin supplementation on the liver biochemical markers levels and structure of it in older women with non-alcoholic fatty liver disease. This study was designed as a double-blind randomized, placebo-controlled clinical trial. Forty-five obese women with non-alcoholic fatty liver disease (age range: 60–71 years old) were randomly divided into 4 groups, including: resistance training (RT) (age: 65.91 ± 3.31 years, n = 12), curcumin (C) (age: 66.72 ± 3.03 years, n = 11), resistance training with curcumin (RTC) (age: 64.09 ± 3.33 years, n = 11) and placebo (P) (age: 64.36 ± 2.97 years, n = 11) (See Fig. 1). The training program and supplement consumption were carefully supervised. The RT and RTC groups received 12 weeks of non-linear resistance training (Nikseresht et al., 2014). Blood samples were collected before and after the 12-week training program and to survey the participants' liver structure, abdominal ultrasonography before and after the protocol was conducted. Then grades of fatty liver (1-healthy, 2-grade I, 3-grade I-II, and 4-grade II) in the participants were detected. The dietary program for the participants was started

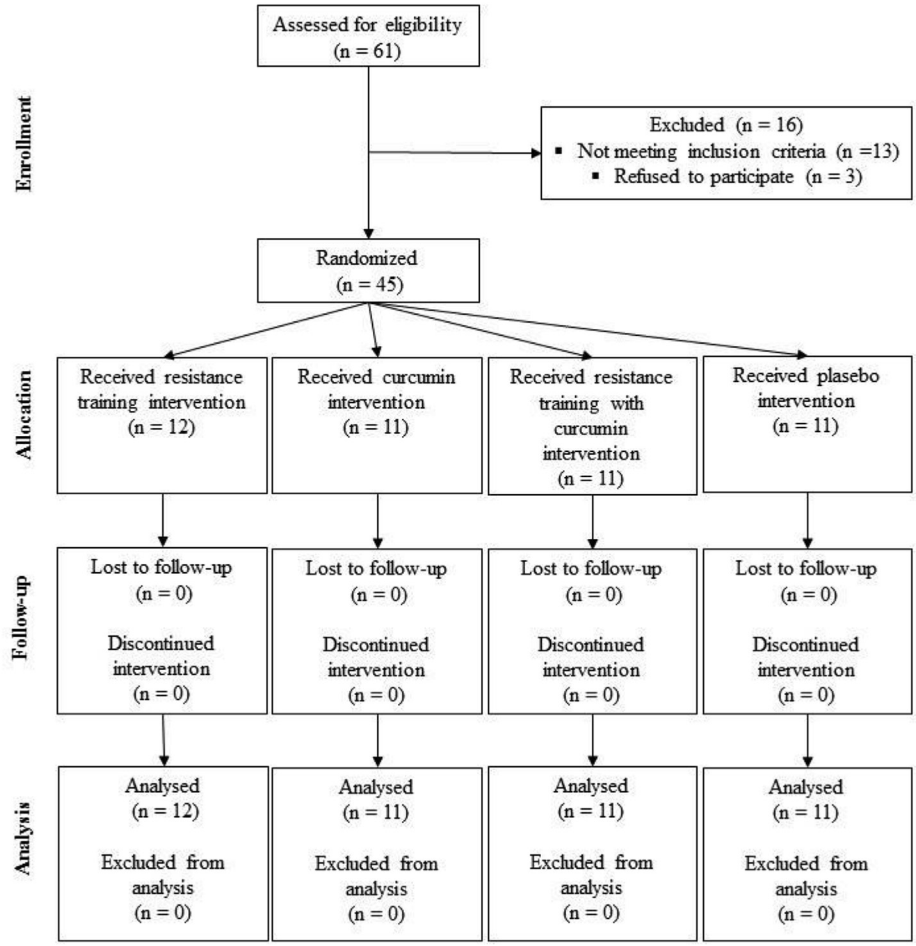

Fig. 1. Process of the study according to consort flow diagram.

one week before the training and continued until the end of the study. The dietary intake was controlled via a food frequency checklist in combination with traditional lecture-based and paper-based instructions according to the classical food pyramid. The calorie expenditure was based on age, BMI, and activity level. Also, the participants were asked to avoid curcumin bioenhancers consumption such as black pepper, long pepper and ginger, especially indiscriminate consumption along the study.

Inclusion criteria consisted of being obese, elderly and female in addition to having fatty liver disease, which was confirmed by ultrasonography. The exclusion criteria were as follows: addiction to smoking, alcohol abuse, doing regular physical exercises in the last 6 months, having lung disease, kidney disease, cardiovascular disease, liver transplantation, estrogen intake, high blood pressure, chronic disorders, taking special medications such as statins, additive effects on insulin sensitivity, hepatotoxic medications intake, having a special dietary program, allergy to curcumin, having a cancer record and taking other supplements.

The present study was a double-blind study. The participants were identified using the codes instead of their actual names. A third party was asked to classify the participants randomly, using the (labelled) codes. Study groups had codes instead of names. The laboratory was uninformed from name of groups and only used the codes. Groups codes were used for statistical analysis. The supplement and placebo participants were unaware of their own group label.

3.3. *Curcumin supplementation*

Participants in the C and RTC groups were asked to take one curcumin capsule (Curcumin 80 mg as Nanomicelle produced by Minoo Pharmaceutical Co.) per day after breakfast, also participants in the P group were asked to take one placebo capsule per day after breakfast for 12 weeks.

3.4. *Exercise training protocol*

To evaluate 1 repetition maximum (1RM), the participants were asked to attend the gym one day before starting the training protocol and after warm-up, the 1RM measurement was performed using the Brzycki's equation (Brzycki, 1993). The equation used is as follows:

$$1\text{RM} = \frac{\textit{weight lifted}}{(1.0278 - (0.0278 \times \textit{number of repetitions}))}$$

The warm-up consisted of working out with a fixed bike for 8 min and 5 min of light stretching exercises.

The nonlinear resistance training program used in this study has been proposed by Nikseresht et al., (2014). Each session took about 60–70 min for main training (plus about 20 min for warm-up and cool-down), three days a week (nonconsecutive) which lasted 12 weeks. Tables 1 and 2 show the details of exercise training program. Also, participants were asked to exhale air during the most

Table 1
Nonlinear resistance training program (Nikseresht et al., 2014). Length of rest period: very light = 1 min; light and moderate = 1–2 min; heavy = 3–4 min; very heavy = 5–7 min †1 set × 20 repetitions, 40% 1RM.

Exercise	Very light	Light	Moderate	Heavy	Very heavy
Knee extension	† 40/20 × 1	60/15 × 2	75/10 × 3	90/4 × 3	95/2 × 4
Bench press	40/20 × 1		75/10 × 3	90/4 × 3	95/2 × 4
Incline bench press		60/15 × 2			
Seated row	40/20 × 1	60/15 × 2	75/10 × 3	90/4 × 3	95/2 × 4
Deadlift	40/20 × 1	60/15 × 2	75/10 × 3	90/4 × 3	95/2 × 4
Pully crunches	1 × 20	2 × 20	3 × 15	3 × 18	3 × 20
Lat pull-downs		60/15 × 2			
Calf raise	40/20 × 1	60/15 × 2	75/10 × 2	90/4 × 2	
Hamstring curl	40/20 × 1	60/15 × 2	75/10 × 2	90/4 × 2	
Press behind neck	40/20 × 1	60/15 × 2	75/10 × 2	90/4 × 2	
Upright row	40/20 × 1	60/15 × 2	75/10 × 2	90/4 × 2	
Arm curl	40/20 × 1	60/15 × 2	75/10 × 2	90/4 × 2	

strenuous phase of the repetition and to inhale it during the less strenuous phase of it. They were also asked to drink enough fluids during and after each training session to prevent dehydration and avoid drinking coffee, energy drinks containing adrenaline, herbal beverages and doing other types of training exercises to prevent any uncontrollable effects on enzymes.

3.5. Blood sampling

Blood samples (approximately 5 cc) were obtained from the antecubital vein between 7:00 a.m. and 9:00 a.m. after 12 h of fast. The samples were drawn in the sedentary condition 48 h before the training protocol and 48 h after that. Then 2 cc of the total whole blood was separated to measure the platelet count. 3 cc of the blood samples was kept at room temperature to separate the clot from serum. The blood tubes were wrapped in the aluminium foil to prevent light exposure and then were centrifuged at 4000 rpm for 5 min. The blood samples were taken before and after the training protocol was performed on the same day in the laboratory. Ultrasonography was conducted between 8:00 a.m. and 11:00 a.m. 24 h before the training protocol and 24 h after that. All participants were monitored regarding the exclusion criteria in order not to show any symptoms of illness in the past 4 days of sampling.

3.6. Variable measurements

Wearing the minimum clothes and no shoes, the participants' weight and height were measured using a balance scale (Seca, 700 Mechanical Column Scales, United Kingdom) calibrated to the nearest 0.1 kg after a 12-h fast. The body mass index was calculated by dividing the human body weight (kg) by squared height (m2).

ALT, AST, ALP, and TB levels were measured by using biochemical analysis kits (Pars Azmoon Chemical co., Iran). The sensitivity of kits was 4 IU/L for ALT, 2 IU/L for AST, 3 IU/L for ALP, and 0.1–30 mg/dl for TB. The photo absorbance change per minute was up to 0.16 for ALT and AST, up to 0.25 for ALP, and it was between 0.1 and 30 mg/dl for TB. To analyze liver enzymes, the auto biochemical analyzer (Mindray BS 800, China), to measure blood platelets (PLT), the auto hematology analyzer (Mindray BC 5800, China), and to ultrasonography from the liver, the color Doppler ultrasonography machine (ESAOTE My lab 40, Italy) were used.

Table 2
The intensity of 12-week nonlinear resistance training (Nikseresht et al., 2014). L = light-intensity workout; M = moderate-intensity workout; VL = very light-intensity workout; H = heavy-intensity workout; VH = very heavy-intensity workout. An active rest day was used after any workout.

	Week											
	1	2	3	4	5	6	7	8	9	10	11	12
Workout Sequence												
Day 1	L	L	M	VL	M	L	VL	H	L	M	L	VL
Day 2	M	VL	H	H	M	M	M	VL	L	M	M	H
Day 3	L	H	L	L	H	H	L	M	VH	VL	VL	L

3.7. Statistical analysis

All data analyses were performed using SPSS (Version 22.0. Armonk, NY: IBM Corp). The data were analyzed regarding normality of distribution (the Shapiro–Wilk test), homogeneity (Levene's test), and were reported as mean ± SD. One-way analysis of covariance (ANCOVA) was used to eliminate the impact of pretest on all variables. Also, Bonferroni's post hoc test was used to find where the differences have occurred if the ANCOVA indicated significant interactions between groups. The partial eta squared statistic was reported for the effect size. The Kruskal-Wallis non-parametric one-way analysis was used to find the differences between groups in the liver structure (to analyze the liver fat). All alpha-levels were set at $p \leq 0.05$ for all statistical comparisons.

4. Results

Physiological characteristics of participants before and after 12 weeks of training are displayed in Table 3. After the protocol, significant differences were not detected in the body mass index and weight ($p < 0.05$) (Table 3).

Liver biochemical markers (ALT, AST, ALP, TB, and PLT) levels and the liver structure of the participants before and after the protocol are presented in Table 4. It was found that ALT levels are significantly different in four groups [$F_{3,40} = 5.652$, $p = 0.013$, Partial eta = 0.298]. The results of Bonferroni's test revealed that ALT levels were significantly decreased in the RT and RTC groups. (Fig. 2). But ALT levels in the C and P groups had no significant difference. Significant difference was found among four groups in AST levels as well [$F_{3,40} = 11.348$, $p = 0.000$, Partial eta = 0.460]. Also, post hoc test showed that AST levels were significantly decreased in the RT and RTC groups. (Fig. 3). ALP [$F_{3,40} = 0.772$, $p > 0.05$, Partial eta = 0.055], TB [$F_{3,40} = 0.336$, $p > 0.05$, Partial eta = 0.025] and PLT [$F_{3,40} = 0.266$, $p > 0.05$, Partial eta = 0.020] levels were not significantly different between groups. Also, the liver structure [Chi-Square = 1.421, df = 3, p = 0.701] was not significantly different. So It was found that nonlinear resistance training could reduce ALT and AST serum levels. However, it did not have any significant effect on other chemical markers (ALP, TB, and PLT). Curcumin supplement intake did not have any significant effect on these markers and nonlinear resistance training concurrent with taking curcumin supplement could reduce ALT and AST levels. The liver structure (liver fat) did not have any significant difference in 4

Table 3
Physiological characteristics of participants among the 12-week protocol. RT: resistance training group, C: curcumin supplement consumption group, RTC: resistance training with curcumin supplement consumption group and P: placebo group.

Variables	RT	C		RTC		P		
	pre	Post	pre	post	Pre	Post	Pre	Post
Height	161.91 ± 3.47	–	160.54 ± 4.76	–	160.72 ± 4.38	–	161.90 ± 4.59	–
Weight (kg)	72.43 ± 4.76	71.95 ± 5.14	71.09 ± 5.63	70.84 ± 6.03	69.80 ± 4.97	69.52 ± 5.20	71.03 ± 4.62	71.23 ± 4.74
BMI (kg.m^{-1})	27.48 ± 1.43	27.46 ± 1.45	27.60 ± 1.26	27.48 ± 1.30	27.03 ± 0.65	26.93 ± 0.84	27.25 ± 1.34	27.21 ± 1.29
1RM Knee extension (kg)	27.22 ± 1.92	35.75 ± 1.96	26.43 ± 2.15	26.09 ± 1.92	25.85 ± 2.06	34.57 ± 1.65	24.72 ± 2.33	24.22 ± 1.80
1RM Bench press (kg)	19.99 ± 1.74	27.14 ± 2.23	20.82 ± 1.63	21.39 ± 1.59	21.16 ± 1.95	28.28 ± 2.04	21.05 ± 1.95	20.66 ± 1.44

Table 4
Non-significant levels serum biochemical markers and liver structural changes during the study. RT: resistance training group, C: curcumin supplement consumption group, RTC: resistance training with curcumin supplement consumption group and P: placebo group.

Variables	RT	C		RTC		P		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
ALP (IU/L)	365.25 ± 84.61	364.66 ± 86.05	376.36 ± 88.45	376.09 ± 86.70	320.09 ± 81.99	317.27 ± 81.75	387.36 ± 79.70	387.81 ± 74.75
TB (mg/dl)	1.20 ± 0.20	1.18 ± 0.20	1.25 ± 0.19	1.21 ± 0.17	1.24 ± 0.19	1.20 ± 0.18	1.23 ± 0.16	1.25 ± 0.16
PLT (× 10^3/μl)	255.25 ± 38.58	256.33 ± 35.62	245.63 ± 38.96	251.81 ± 38.29	273.45 ± 35.00	274.90 ± 35.73	284.18 ± 28.55	286.81 ± 25.70
AST/ALT	1.01 ± 0.15	0.96 ± 0.12	0.98 ± 0.06	0.99 ± .02	0.95 ± 0.06	0.94 ± 0.38	0.97 ± 0.07	0.95 ± 0.12
Liver structure	2.83 ± 0.83	2.66 ± 1.07	3.09 ± 0.83	3.00 ± 1.00	2.72 ± 0.90	2.54 ± 1.12	2.81 ± 0.75	2.90 ± 0.70

groups. One repetition maximum in knee extension [$F_{3,40} = 203.813$, $p < 0.05$, Partial eta = 0.939] and in bench press [$F_{3,40} = 72.222$, $p < 0.05$, Partial eta = 0.844] after 12 weeks of resistance training had significant changes. Post hoc tests revealed that the knee extension and bench press strength were significantly higher in the RT and RTC groups (Table 4).

5. Discussion

The present study is the first research to investigate the effects of concurrent nonlinear resistance training and curcumin supplementation on the liver structure and biochemical markers levels of the liver in older women with the non-alcoholic fatty liver disease. This study differs from other ones in that the load of resistance training is different in each session so various efficiencies of hepatocyte cells to supply necessary energy are required, and consequently, application of different percentages of liver efficiency can be challenging for the physiological capacity.

Undoubtedly, the type of physical activity and physical conditions of older individuals are important features as they are not able to perform heavy training exercises, especially aerobic ones (high-intensity aerobic exercises are recommended for younger individuals). Resistance training requires lower cardiovascular capacity but it could be as useful as aerobic exercises (Hallsworth et al., 2011).

In this regard, some studies concluded that individuals with regular physical activity have lower levels of ALT, AST, and GGT (Limdi and Hyde, 2003). In comparison, according to the research conducted by Slentz et al., (2011), although resistance training does not have significant effects on weight, liver fat, visceral fat, and ALT, aerobic training does. Sigal et al., (2007) did not report a relationship between resistance training and ALT levels and abdominal fat and explained the results based on the type of training and the characteristics of the participants.

Non-alcoholic fatty liver may cause insulin resistance and hyperinsulinemia in obesity (Rantala et al., 2000). A decrease in insulin resistance after training can have various mechanisms such as enhanced post-receptor insulin signaling (Dela et al., 1993),

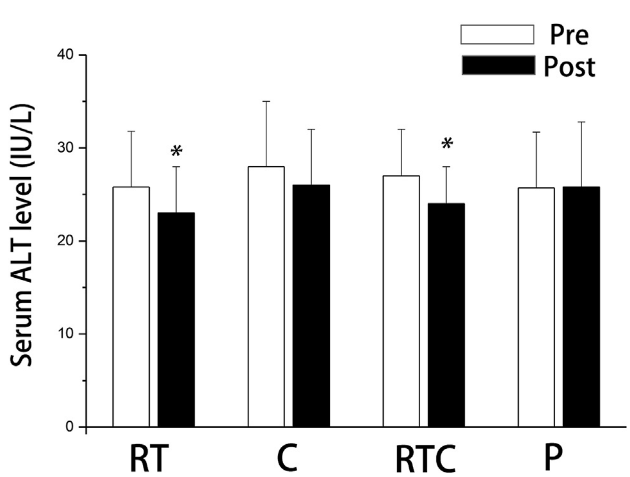

Fig. 2. Serum ALT levels (IU/L) during the study. *: significant changes vs pre-exercise. RT: resistance training group, C: curcumin supplement consumption group, RTC: resistance training with curcumin supplement consumption group and P: placebo group.

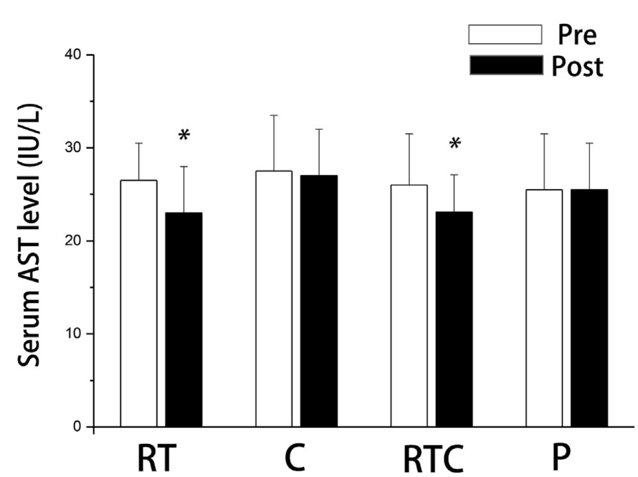

Fig. 3. Serum AST levels (IU/L) during the study. *: significant changes vs pre-exercise. RT: resistance training group, C: curcumin supplement consumption group, RTC: resistance training with curcumin supplement consumption group and P: placebo group.

increased Glucose transporter 4 (GLUT4) protein and mRNA synthesis (Dela et al., 1993), and increased activity of glycogen synthase and hexokinase (Ebeling et al., 1993). However, in this research, mechanism of decrease in insulin resistance cannot be set up. As reported by Duncan et al., (2003) and Poehlman et al., (2000), insulin resistance is not dependent on changes in the body composition. On the other hand, resistance training increases energy consumption. Therefore, improvement in the liver function and a decrease in ALT and AST levels (the ALT and AST enzyme levels are low in the muscles and the highest levels are seen in the liver tissue) (Burger-Mendonca et al., 2008) may result from a decrease in insulin resistance.

Regarding AST to ALT ratio as an index to indicate hepatocyte inflammation and necrosis, the present study showed that there was no significant effect between groups. AST to ALT ratio reduced responses to exercise in the RT group that was nonsignificant. It seems that exercise had a trend to decrease AST to ALT ratio. The present study had a limitation to biopsy. The participant hepatocytes were not surveyed in terms of liver biopsy and histology (because of the age of participants) but the decrease of ALT and AST levels may follow improvement in hepatic steatosis.

ALP levels did not have significant changes in this study. Since ALP can transfer metabolites such as fats across the cell membrane to generate aerobic energy, an increase in ALP after training shows the role of the liver in gluconeogenesis and lipid peroxidation (Burger-Mendonca et al., 2008). With supplying the energy for non-linear resistance training, mostly through an anaerobic system, gluconeogenesis and lipid peroxidation pathways are not required and no increase in ALP level is explainable in this study.

This study found no significant differences in TB and PLT levels after the protocol. Total bilirubin level remains normal as long as hepatocyte cells are not damaged strongly (Garjani et al., 2015). Physical activity has adverse effects on blood platelet counts (Wannamethee et al., 2002). Bobeuf et al. reported that 6-week resistance training in the elderly does not affect platelet counts. An increase in platelet counts reported in some of studies may be due to hemoconcentration (Andrews et al., 1996). Drinking a sufficient amount of fluids during and after training and the absence of severe damages to the liver in this study prevents/inhibits changing in platelet volume.

In the present study, curcumin supplement intake did not have any significant effect on the liver biochemical markers and liver structure. However, some studies (DiSilvestro et al., 2012) have supported the beneficial effects of curcumin on liver function. The antioxidant effects of curcumin play a crucial role in treating non-alcoholic fatty liver disease and liver fibrosis. Moreover, curcumin can harness the attraction of neutrophil granulocytes and myofibroblasts (Nabavi et al., 2014). This supplement improves the liver performance by reducing superoxide production, suppressing pro-inflammatory mediators and activating anti-inflammatory signaling (Naik et al., 2011).

Given the reduction of basal metabolic rate, daily physical activity and total energy with ageing, the weight, visceral fat and liver fat increase. The researchers have found a relationship between increased enzyme levels in postmenopausal women and changes in fat distribution and hormonal and metabolic changes (Suzuki and Abdelmalek, 2009). At ages 20–70, the liver blood flow rate decreases by approximately 33% and the liver size by 25% and the number of mitochondria in the liver cells reduce (Frith et al., 2009). Hence, curcumin supplement intake with antioxidant and anti-inflammatory effects may slow down negative changes in the liver physiological efficiency and can decrease the liver damage. The suppression of pro-inflammatory cytokines and mediators of their release such as TNF-α, IL-1, and NOS are the most possible beneficial consequences of anti-inflammatory actions of curcumin, as there are some reports to show that curcumin inhibits cytokine-mediated activation of nuclear factor kappa B (NF-kB) and phosphorylation of JAK1 and JAK2, which both mechanisms attenuate inflammatory responses (Chun et al., 2003; Jobin et al., 1999; Kim et al., 2003). Also, curcumin inhibits the production of IL-8, MIP-1 alpha, MCP-1, IL-1 beta, and TNF-alpha by PMA- or LPS-stimulated monocytes and alveolar macrophages in a concentration- and a time-dependent manner (Abe et al., 1999). Curcumin effect was not significant in the present study but changes in the dose or duration of curcumin supplement intake may affect the results. Accordingly, concerning the findings of this research, in the RT and RTC groups, levels of ALT and AST decreased but in the C group no difference was seen, so it can be claimed that these beneficial results come from the main effect of non-linear resistance training.

In the present research, the liver structure (liver fat) had no differences in groups, in contrast some studies showed that liver fat can be decreased with resistance training, for example, Kirti et al. reported (Kirti et al., 2014) that 12-week resistance training can reduce the amount of fat in liver (4%) without any changes in ALT, AST and ALP levels in individuals with non-alcoholic fatty liver disease. Concerning the above finding, it is not unlikely that 12 weeks of resistance training with curcumin supplement or per se was not sufficient to improve the liver structure.

In conclusion and with respect to other researches, factors such as the duration and intensity of training protocol, individuals overall physiological condition, blood sampling time and laboratory procedures, balance between practice time and rest time, balance between the endocrine system and the nervous system, weight, body mass index, abdominal obesity, waist-to-hip ratio, research methodology, the type and dose of supplement, lipid profile levels, age and gender of participants can affect the results.

6. Conclusions

12-week non-linear resistance training per se and accompanied with curcumin supplementation could improve ALT and AST levels while no significant change was found in ALP, TB, and PLT levels; however, curcumin supplementation didn't have any significant effect on biochemical markers of the liver. In all groups, the liver structure did not have significant changes. Based on the findings of this research, it can be concluded that non-linear resistance training can be applied as an influential healing factor to improve the liver function and also to treat non-alcoholic fatty liver disease while curcumin supplement did not show any remarkable effects on these variables.

7. Limitations and clinical relevance

In the present study, there were some limitations, including low number of participants and the short duration of study, that could affect the results; also, it could be more reliable to measure liver fat and its enzyme levels via biopsy, however due to the old age of the participants that could delay the recovery of liver cells, the biopsy was not used. On the basis of the results of the present study, non-linear resistance training may be a way to improve the liver function and also to treat non-alcoholic fatty liver disease.

Disclosures & disclaimer

PF and MAA conceived and designed this study. BM and MH collected the materials and performed the experiments. PF and MAA analyzed the data. SRA, PF, and MAA wrote the manuscript. All authors read and approved the final version of the manuscript.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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