Submitted: 11 January, 2021 Accepted: 08 February, 2021 Online Published: 31 March, 2021 DOI:10.31083/jomh.2021.025

JOMH Journal of Men's Health

Original Research

Effect of a combination of aerobic exercise and dietary modification on liver function in overweight and obese men

Xiao-Guang Zhao[1,2,*], Hui-Ming Huang[1,2], Chen-Ya Du[2]

[1]Research Academy of Grand Health, Ningbo University, Ningbo City, Zhejiang, P. R. China
[2]Faculty of Sport Science, Ningbo University, Ningbo City, Zhejiang, P. R. China

***Correspondence:** xiaoguangzhao1985@gmail.com (Xiao-Guang Zhao)

Abstract

Background: Obesity is not only associated with cardiovascular diseases but also a primary cause of liver dysfunction and other related diseases. This study's aim was to determine the impact of a combination of dietary modification and aerobic exercise on liver function in overweight and obese adult males.

Methods: 45 overweight or obese men were randomly divided between the control group (n = 22) and intervention group (n = 23). Subjects in the intervention group were provided with dietary modification and aerobic exercise programmes. Dietary modification is a diet which restricts calorie intake and balances nutrients. Before and after 12 weeks of intervention, participants' anthropometric characteristics and biochemical parameters relating to liver function including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) were measured.

Results: 12 weeks of aerobic exercise and dietary modification resulted in average weight loss of 10.6%, and body mass index, waist circumference and fat percentage decreased by 10.2%, 9.4% and 14.5% ($P < 0.05$). AST, ALT, GGT and ALP in the intervention group reduced by 20.6%, 18.1%, 37.7% and 6.1% ($P < 0.05$). Compared to the control group, AST, ALT, GGT and ALP in the intervention group were markedly lower ($P < 0.05$). Furthermore, there was a markedly positive relationship between the reduction rates of body weight and GGT ($P < 0.05$).

Conclusion: 12 weeks of aerobic exercise and dietary modification caused significant weight, waist circumference and body fat percentage reduction in overweight and obese men and their liver function was improved. The findings can provide a scientific reference for the improvement of liver function and prevention of liver diseases among overweight and obese people.

Keywords

Aerobic exercise; Dietary modification; Liver function; Overweight and obesity; Weight reduction

1. Introduction

Due to high energy intake and low levels of physical activity, the prevalence of obesity has increased rapidly [1]. Obesity, as a chronic disease, has become one of the most serious public health threats of the 21st century [2]. Many studies have noted that obesity and being overweight are generally accompanied by one or more risk factors of cardiovascular disease [3–5]. Obesity not only has an association with cardiovascular diseases but also a major cause of liver dysfunction and other related diseases. Recent studies have proven that being overweight or obese can result in liver dysfunction including impaired hepatic mitochondrial function, liver cirrhosis and fibrosis, and can even lead to the occurrence of non-alcoholic fatty liver disease [6–8]. Therefore, for overweight and obese people, improving their liver function and preventing fatty liver diseases is of great significance.

The liver plays a crucial role in lipid metabolism. Lipids can accumulate in the liver due to an imbalance that exists between the delivery of fat derived from adipose tissue stores or food intake to the liver and the consumption of fat as an ingredient of lipoproteins [9]. This partly explains why such a close relationship exists between liver diseases and obesity. At the same time, several epidemiological research projects have demonstrated that almost all patients who suffer from non-alcoholic steatohepatitis are between 10% and 40% over their ideal weight. Although adults with normal body weight can suffer from non-alcoholic steatohepatitis, it is more frequently detected in those who are overweight or obese [10].

It is essential for overweight and obese individuals to choose an appropriate method for reducing their body weight. Generally, aerobic exercise and dietary modification are considered to be effective and non-medical treatments for the monitoring and management of body weight. Previous studies have proven that aerobic exercise intervention is better for improving cardiopulmonary function and decreasing the risk of cardiovascular disease in comparison to dietary modification intervention [11, 12]. At the same time, dietary modification intervention may be more effective than aerobic exercise intervention for facilitating a reduction in body weight and body fat [13, 14]. Therefore, a combined aerobic exercise and dietary modification intervention is more frequently used to facilitate weight reduction among overweight and obese people. However, there is still debate surrounding whether this combined intervention can improve liver function in different individuals [15–17] and the impact the combined intervention has on the liver function of overweight and obese adults remains unclear.

Liver function is measured by several biochemical parameters including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) [18, 19]. This study's aim was to examine the effect of a combined aerobic exercise and dietary modification intervention on weight reduction and liver function in adult overweight and obese males. The study's hypothesis was that 12 weeks of dietary modification and aerobic exercise intervention could reduce body weight and improve the liver function of overweight and obese adult males.

2. Methods

2.1 Study design

The study was a randomised controlled trial which used a control group. By utilising a random number generator, participants were randomly assigned to either the control group (n = 22) or the intervention group (n = 23) and participants were provided with aerobic exercise and dietary modification for 12 weeks. Participants' anthropometric characteristics and blood biochemical indicators relating to liver function were measured both before and after the 12-week intervention period. The purposes and procedures of the research were all explained to participants and it was requested that they read and sign an informed consent form before participation. The research protocol was in full compliance with the latest modification of the Ethics Guidelines of the Declaration of Helsinki which was reviewed and approved by the Human Ethics Board of Ningbo University.

2.2 Participants

In this study, overweight was defined as a body mass index (BMI) of 24.0 to 27.9 kg/m^2 and obesity was regarded as a BMI $\geq$ 28.0 kg/m^2, based on the guidelines for preventing and controlling obesity in Chinese adults [20]. Subjects were recruited using local newspaper advertisements and posters for this study. Subjects who fulfilled the following inclusion criteria were included in our study: 1) adult men aged 20 years or older; 2) a BMI now more than 24 kg/m^2; 3) body weight change of no more than 5 kg in the previous 6 months; 4) no exercise habits, meaning a total exercise time of less than 150 minutes per week; 5) no current or past disorders relating to the respiratory or cardiovascular systems; 6) no injuries or musculoskeletal disorders which affect participation in physical activity. A total of 45 men fulfilled these criteria. The subjects' baseline characteristics are shown in Table 1.

TABLE 1. The baseline characteristics of the subjects

	Control group (n = 22)	Intervention group (n = 23)	*P*-value
Age (yrs)	49.5 ± 11.4	50.8 ± 10.9	0.92
Height (cm)	167.2 ± 5.6	167.9 ± 6.8	0.36
Weight (kg)	80.0 ± 9.8	81.1 ± 10.6	0.52
BMI (kg/m^2)	28.3 ± 2.1	28.7 ± 2.6	0.14

2.3 Measurements

2.3.1 Anthropometric characteristics

Subjects were required to wear light clothing with no shoes when their body height and weight were measured. BMI was then calculated as body weight in kilograms divided by the square of body height in metres (kg/m^2). Each subject's waist circumference was measured with a measuring tape. Bioelectrical impedance analysis was used for assessing body fat percentage using the bipolar foot-to-foot technique (BF-689; Tanita). Before measurements were taken, participants were required to fast for 10 to 12 hours and they had to have an empty bladder. Accuracy was 0.1 kilogram (kg) for the measuring of fat mass and 0.1% for the assessing of body fat percentage with a 50 kHz intensity of frequency of induction. It was reported that the repeatability coefficient of the measurements was 0.985 and the technical error was 0.639 [21].

TABLE 2. Changes in anthropometric characteristics following 12 weeks of the intervention programme

	Control group		Intervention group	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
Weight (kg)	80.0 ± 9.8	80.2 ± 9.5	81.1 ± 10.6	72.4 ± 9.2$^{*,\$}$
BMI (kg/m^2)	28.3 ± 2.1	28.3 ± 2.4	28.7 ± 2.6	25.7 ± 2.3$^{*,\$}$
Waist circumference (cm)	98.5 ± 9.0	98.8 ± 9.7	99.0 ± 8.4	89.6 ± 7.8$^{*,\$}$
Body fat percentage (%)	25.4 ± 4.6	25.6 ± 5.1	25.0 ± 4.3	21.5 ± 5.0$^{*,\$}$

Note: * means $P < 0.05$ vs. pre-intervention; $ means $P < 0.05$ vs. control group.

2.3.2 Liver function

Following 10 to 12 hours of fasting, each participant's venous blood sample was obtained from the antecubital vein and delivered directly to the central laboratory for the analysis of liver function parameters, including AST, ALT, GGT and ALP. Liver enzymes were tested enzymatically using an automatic analyser (Ci8200; Abbott Architect) which used standard protocols based on the manufacturer's instructions. All laboratory assays were tested without knowing any of the subjects' information.

2.4 Interventions

2.4.1 Aerobic exercise

The intervention was a moderate-intensity aerobic exercise programme consisting of a 90-minute session for 12 weeks (three times per week). Each 90-minute session included 15 minutes of warm-up and stretching exercises, 60 minutes of jogging or brisk walking and 15 minutes of cool-down and stretching exercises. Exercise intensity was expressed by the percentage value of maximal oxygen consumption (VO_2max) and each subject's VO_2max and corresponding heart rate were obtained before the intervention. The linear relationship between the VO_2, ratings of perceived exertion and heart rate has been proven [22]. Subjects exercised at 50% to 60% of their VO_2max for the first four weeks of the intervention and this was gradually increased. For the final four weeks, the exercise intensity was set 60% to 70% of the subject's VO_2max. Indoor exercises were conducted on rainy days (seven times) using stair-stepping or ergometric cycling and the intensity of the indoor exercise matched that of the outdoors exercise as closely as possible. Several principal researchers and experienced fitness trainers were involved in the aerobic exercise intervention.

2.4.2 Dietary modification

The dietary modification programme consisted of one 90-minute session each week for 12 weeks and included theoretical and practical knowledge of diet management. During the session, participants were taught how to restrict their calorie intake to 1,680 kcal per day (a mean of 840 kcal of carbohydrates, 420 kcal of fat and 420 kcal of protein). The dietary modification programme's main objective was to help subjects restrict their calorie intake and obtain a well-balanced intake of carbohydrates, protein, fat, vitamins, minerals and amino acids. Our research team had more than 10 years of experience in instructing subjects with this dietary modification. Their experience has proven that the dietary modification intervention is incredibly effective and safe for decreasing body weight and helping subjects form healthy eating habits. Additional detailed information relating to the dietary modification programme has been previously published [23].

2.5 Statistical analyses

In this study, the test data were presented as mean ± SD. Within-group differences between baseline and follow-up changes were tested using a paired *t*-test. Univariate analyses of variance (ANOVA) were conducted to assess between-group statistical differences. Pearson's correlations were used for determining the relationship of reduction rate between anthropometric characteristics and liver function. Data analysis was conducted using the IBM Statistical Package for Social Sciences (SPSS, version 22.0). For statistical analysis, $P < 0.05$ was considered to be statistically significant.

3. Results

3.1 Changes in anthropometric characteristics following the intervention programme

The results of differences in anthropometric characteristics following 12 weeks of the intervention programme are shown in Table 2. No significant changes in body weight, waist circumference, BMI and body fat percentage were observed after 12 weeks in the control group ($P > 0.05$). However, in the intervention group, body weight decreased from 81.1 ± 10.6 kg to 72.4 ± 9.2 kg (a decrease of 10.6%, $P < 0.05$), BMI decreased from 28.7 ± 2.6 kg/m^2 to 25.7 ± 2.3 kg/m^2 (a reduction of 10.2%, $P < 0.05$), waist circumference decreased from 99.0 ± 8.4 cm to 89.6 ± 7.8 cm (a decrease of 9.4%, $P < 0.05$) and body fat percentage decreased from 25.0 ± 4.3% to 21.5 ± 5.0% (a reduction of 14.5%, $P < 0.05$) after 12 weeks of intervention. The intervention group's body weight, waist circumference, BMI and body fat percentage showed significant decreases in comparison to the control group ($P < 0.05$).

3.2 Changes in liver function parameters after the intervention programme

The results of changes in liver function parameters following 12 weeks of the intervention programme are shown in Table 3. In the control group, no significant changes were observed in AST, ALT, GGT and ALP after 12 weeks ($P >$

TABLE 3. Changes in liver function parameters following 12 weeks of the intervention programme

	Control group		Intervention group	
	Pre-intervention	Post-intervention	Pre-intervention	Post-intervention
AST (U/L)	27.1 ± 10.4	27.3 ± 9.8	26.4 ± 9.7	19.7 ± 5.6*,$
ALT (U/L)	32.8 ± 20.7	34.4 ± 19.3	32.4 ± 22.7	23.0 ± 10.4*,$
GGT (U/L)	39.5 ± 18.4	41.4 ± 19.2	40.5 ± 19.0	23.2 ± 9.9*,$
ALP (U/L)	200.7 ± 50.6	207.2 ± 45.7	203.0 ± 46.0	188.7 ± 42.4*,$

Note: AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase.

* means $P < 0.05$ vs. pre-intervention; $ means $P < 0.05$ vs. control group.

0.05). However, in the intervention group, AST decreased from 26.4 ± 9.7 U/L to 19.7 ± 5.6 U/L (a decrease of 20.6%, $P < 0.05$), ALT decreased from 32.4 ± 22.7 U/L to 23.0 ± 10.4 U/L (a reduction of 18.1%, $P < 0.05$), GGT decreased from 40.5 ± 19.0 U/L to 23.2 ± 9.9 U/L (a decrease of 37.7%, $P < 0.05$) and ALP decreased from 203.0 ± 46.0 U/L to 188.7 ± 42.4 U/L (a reduction of 6.1%, $P < 0.05$) following the intervention programme. The intervention group's AST, ALT, GGT and ALP showed significant decreases in comparison to the control group ($P < 0.05$).

3.3 Correlations of reduction rate between anthropometric characteristics and liver function parameters

The results of correlations of reduction rate between anthropometric characteristics and liver function parameters are shown in Table 4. It can be seen from the table that only the GGT reduction rate displays a marked correlation with the decline rate of body weight, waist circumference, BMI and body fat percentage (r = 0.56 to 0.79, $P < 0.05$). No significant correlation was found between the decline rate of obesity and the reduction rates of AST, ALT and ALP ($P > 0.05$).

TABLE 4. Correlations of reduction rate between anthropometric characteristics and liver function parameters

	AST Δ	ALT Δ	GGT Δ	ALP Δ
Weight reduction	-0.12	-0.09	0.76*	-0.10
BMI reduction	-0.11	-0.06	0.72*	-0.16
Waist circumference reduction	0.03	0.04	0.79*	0.04
Body fat percentage reduction	-0.26	-0.28	0.56*	0.28

Note: AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase.

Δ means reduction rate; * means the significance level $P < 0.05$.

4. Discussion

Being overweight or obese makes individuals more vulnerable to liver dysfunction. Previous studies have shown that liver cirrhosis and fibrosis, impaired hepatic mitochondrial function and non-alcoholic fatty liver disease are all related to obesity [6–8]. Weight reduction can be helpful in facilitating the improvement of liver function. A combined aerobic exercise and dietary modification intervention is frequently used to aid weight reduction in overweight and obese individuals, but its effect on liver function remained unclear. Therefore, the aim of this study was to conduct an exploration of the impact of a combination of aerobic exercise and dietary modification on liver function in overweight and obese adult males. The results showed that 12 weeks of aerobic exercise and dietary modification led to significant weight, waist circumference and body fat percentage reduction in overweight and obese men and improved their liver function.

Obesity has become an increasing global public health problem in recent years. According to World Health Organization statistics [24], the prevalence of being overweight and obese among individuals aged 18 years and older is 39%, among which the prevalence of obesity is 13%. The fundamental cause of being overweight and obese is believed to be an increased intake of energy-dense foods and low levels of physical activity. Being overweight or obese can lead to a variety of metabolic disorders, including hypertension, hyperlipidaemia, type 2 diabetes and non-alcoholic fatty liver disease [25–27]. Many studies have shown that weight reduction significantly prevents the occurrence and development of the aforementioned metabolic disorders [28, 29]. Therefore, it is both beneficial and healthy for overweight and obese adults to control their body weight or lower their BMI.

The liver is an important organ which is involved in maintaining the balance of lipid metabolism. When the body is in a state of illness, there are abnormalities in the lipid metabolism and a large number of lipid components enter the liver cells in order to make the liver synthesise the fat which has increased and accumulated, causing swelling, degeneration and even apoptosis in the liver cells and thereby resulting in impaired liver function [30, 31]. Being overweight or obese can cause abnormal lipid metabolism, which can result in liver dysfunction. Verrijken *et al.* [32] reported that obesity is positively and significantly related to liver function parameters, including AST, ALT, GGT and ALP, and participants with high levels of visceral adipose tissue ($\geq$ 113 cm^2) have a poorer liver function than those with low levels of visceral adipose tissue (< 113 cm^2). This study further demonstrated that weight reduction among overweight and obese men can dramatically enhance the values of AST, ALT, GGT and ALP. The study's findings were consistent with those of Skrypnik *et al.* [15], who reported that exercise intervention causes a significant improvement to liver function among individuals with abdominal obesity. Based on the above results, it can be concluded that 12 weeks of a combination of aerobic exercise and dietary modification significantly improves the liver function of overweight and obese adult males.

Obesity and fatty liver have a close relationship. Previous research has highlighted that being overweight or obese is an independent factor that affects liver fibrosis in those with non-alcoholic fatty liver disease [33, 34]. There is a greater likelihood that obesity will cause non-alcoholic steatohepatitis by disturbing Kupffer cell function and sensitising oxidant stress and hepatocytes to endotoxin [35]. Hannah and Harrison [36] demonstrated that a 3% to 5% weight reduction is related to decreased steatosis, while weight reduction of 7% to 10% is associated with fibrosis regression and non-alcoholic steatohepatitis remission. In this study, it was discovered that body weight decreased by 10.6% and the AST, ALT, GGT and ALP decreased by 20.6%, 18.1%, 37.7% and 6.1% following the combination of aerobic exercise and dietary modification intervention. The results show that liver function improvement may be concerned with weight reduction in overweight and obese adult males.

Aerobic exercise has been reported to decrease liver fat and insulin among obese individuals [37, 38]. Keating *et al.* [39] documented that 45 to 60 minutes of aerobic exercise with 50% VO_2max (four days per week) can significantly decrease 28% of intrahepatic lipid and that 30 to 45 minutes of aerobic exercise with 70% VO_2max (three days per week) can reduce 29% of intrahepatic lipid. Huang *et al.* [40] further noted that a combination of dietary modification and aerobic exercise at 70% of the target heart rate can be effective for improving the liver histology of adults with non-alcoholic steatohepatitis (BMI > 25 kg/m^2). In addition, Baba *et al.* [17] discovered that 60% to 70% of maximal heart rate exercise combined with dietary modification can help decrease ALT concentrations among those with non-alcoholic steatohepatitis. The study also discovered that the normalisation of ALT is independent of weight loss. Similarly, this study showed that a combination of 50-70% of maximal heart rate exercise and dietary modification caused significantly improved liver function. In particular, the intervention can be used for the improvement of liver dysfunction and diseases that are triggered by being overweight or obese.

GGT is produced by the hepatocyte mitochondria and confined to the cytoplasm and intrahepatic bile duct epithelium [41]. Previous studies have demonstrated that GGT is significantly and negatively associated with an increase in physical activity [42, 43]. GGT concentrations greater than 109 U/L and exercise times of less than 60 minutes per week are considered to be risk factors for diabetes [44]. Therefore, increased physical activity or an exercise intervention can help reduce GGT concentrations. Chen *et al.* [45] noted that a 10-week exercise programme in combination with diet improvement can significantly reduce GGT among those with fatty liver disease. Ohno *et al.* [46] observed that GGT values decreased by 50% following a 10-week exercise programme for sedentary individuals. In this study, it was also discovered that GGT values demonstrate a significant downward trend following 12 weeks of intervention. Further analysis showed that a reduction in GGT is significantly associated with a decrease in weight, waist circumference, BMI and percentage fat ($r = 0.56$ to 0.79, $P < 0.05$). To summarise, exercise alone or exercise combined with dietary improvement can improve GGT and the improvement of GGT is associated with a reduction in body weight.

5. Conclusions

It is incredibly important for overweight and obese individuals to reduce their weight and improve their liver function. The results of this study suggest that 12 weeks of a combination of aerobic exercise and dietary modification significantly reduce weight, waist circumference and body fat percentage among overweight and obese men, while significantly improving their liver function. The findings can provide a scientific reference for the improvement of liver function and prevention of liver diseases in overweight and obese people.

Author contributions

Xiao-Guang Zhao is contributed in study design, manuscript writing, and submission; Hui-Ming Huang is contributed in study design and data analysis; Chen-Ya Du is contributed in manuscript writing and data collecting.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Human Ethics Board of Ningbo University (No: RAGH20190715).

Acknowledgment

The authors thank numerous subjects participated in this study. The authors express their gratitude to all the editors and peer reviewers for their comments and suggestions.

Funding

This research was supported by the Fundamental Research Funds for the Provincial Universities of Zhejiang (SJWY2020005), the Zhejiang Philosophical and Social Science Programme (21NDJC004Z), and the National Social Science Foundation in China (18BTY100).

Conflict of interest

The authors declare no competing interests.

References

[1] Hruby A, Manson JE, Qi L, Malik VS, Rimm EB, Sun Q, *et al.* Determinants and consequences of obesity. American Journal of Public Health. 2016; 106: 1656-1662.
[2] Sorrie MB, Yesuf ME, GebreMichael TG. Overweight/Obesity and as-

sociated factors among preschool children in Gondar City, Northwest Ethiopia: a cross-sectional study. PLoS ONE. 2017; 12: e0182511.
[3] Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. Nature. 2006; 444: 875-880.
[4] Nayyar M, Lastra G, Acevedo CM. Mineralocorticoids and Cardiovascular Disease in Females with Insulin Resistance and Obesity. Current Hypertension Reports. 2018; 20: 88.
[5] Nikolopoulou A, Kadoglou NPE. Obesity and metabolic syndrome as related to cardiovascular disease. Expert Review of Cardiovascular Therapy. 2012; 10: 933-939.
[6] Vimaleswaran KS, Cavadino A, Verweij N, Nolte IM, Leach IM; LifeLines Cohort Study, *et al*. Interactions between uncoupling protein 2 gene polymorphisms, obesity and alcohol intake on liver function: a large meta-analysed population-based study. European Journal of Endocrinology. 2015; 173: 863-872.
[7] Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: from pathophysiology to therapeutics. Metabolism: Clinical and Experimental. 2019; 92: 82-97.
[8] Ruiz JR, Lasa A, Simon E, Larrarte E, Labayen I. Lower plasma NAMPT/visfatin levels are associated with impaired hepatic mitochondrial function in non-diabetic obese women: a potential link between obesity and non-alcoholic fatty liver disease. Nutrition, Metabolism, and Cardiovascular Diseases. 2012; 22: e1-e2.
[9] Goodman ZD. The impact of obesity on liver histology. Clinics in Liver Disease. 2014; 18: 33-40.
[10] Chitturi S, Farrell GC. Etiopathogenesis of nonalcoholic steatohepatitis. Seminars in Liver Disease. 2001; 21: 27-41.
[11] Dobrosielski DA, Papandreou C, Patil SP, Salas-Salvadó J. Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk. European Respiratory Review. 2017; 26: 160110.
[12] Fock KM, Khoo J. Diet and exercise in management of obesity and overweight. Journal of Gastroenterology and Hepatology. 2013; 28: 59-63.
[13] Ho SS, Dhaliwal SS, Hills AP, Pal S. The effect of 12 weeks of aerobic, resistance or combination exercise training on cardiovascular risk factors in the overweight and obese in a randomized trial. BMC Public Health. 2012; 12: 704.
[14] Weiss EP, Albert SG, Reeds DN, Kress KS, McDaniel JL, Klein S, *et al*. Effects of matched weight loss from calorie restriction, exercise, or both on cardiovascular disease risk factors: a randomized intervention trial. The American Journal of Clinical Nutrition. 2016; 104: 576-586.
[15] Skrypnik D, Ratajczak M, Karolkiewicz J, Mądry E, Pupek-Musialik D, Hansdorfer-Korzon R, *et al*. Effects of endurance and endurance-strength exercise on biochemical parameters of liver function in women with abdominal obesity. Biomedicine & Pharmacotherapy. 2016; 80: 1-7.
[16] Katsagoni CN, Georgoulis M, Papatheodoridis GV, Panagiotakos DB, Kontogianni MD. Effects of lifestyle interventions on clinical characteristics of patients with non-alcoholic fatty liver disease: a meta-analysis. Metabolism: Clinical and Experimental. 2017; 68: 119-132.
[17] Sreenivasa Baba C, Alexander G, Kalyani B, Pandey R, Rastogi S, Pandey A, *et al*. Effect of exercise and dietary modification on serum aminotransferase levels in patients with nonalcoholic steatohepatitis. Journal of Gastroenterology and Hepatology. 2006; 21: 191-198.
[18] Hann H, Wan S, Myers RE, Hann RS, Xing J, Chen B, *et al*. Comprehensive analysis of common serum liver enzymes as prospective predictors of hepatocellular carcinoma in HBV patients. PLoS ONE. 2012; 7: e47687.
[19] Liu C, Zhou W, Lu Z, Wang X, Qiu Z. The associations between liver enzymes and the risk of metabolic syndrome in the elderly. Experimental Gerontology. 2018; 106: 132-136.
[20] Zhou B. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults–study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomedical and Environmental Sciences. 2002; 15: 83-96.
[21] Ramírez-Vélez R, Rodrigues-Bezerra D, Correa-Bautista JE, Izquierdo M, Lobelo F. Reliability of health-related physical fitness tests among colombian children and adolescents: the FUPRECOL study. PLoS ONE. 2015; 10: e0140875.
[22] Jacobs PL, Klose KJ, Guest R, Needham-Shropshire B, Broton JG, Green BA. Relationships of oxygen uptake, heart rate, and ratings of perceived exertion in persons with paraplegia during functional neuromuscular stimulation assisted ambulation. Spinal Cord. 1997; 35: 292-298.
[23] Zhao X, Tsujimoto T, Kim B, Katayama Y, Ogiso K, Takenaka M, *et al*. Does weight reduction affect foot structure and the strength of the muscles that move the ankle in obese Japanese adults? The Journal of Foot and Ankle Surgery. 2018; 57: 281-284.
[24] World Health Organization. Obesity and overweight. 2020. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (Accessed: 27 September 2020).
[25] van Dijk SJ, Tellam RL, Morrison JL, Muhlhausler BS, Molloy PL. Recent developments on the role of epigenetics in obesity and metabolic disease. Clinical Epigenetics. 2015; 7: 66.
[26] Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot N. Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. Diabetes Research and Clinical Practice. 2014; 105: 141-150.
[27] Zeyda M, Stulnig TM. Obesity, inflammation, and insulin resistance-a mini-review. Gerontology. 2009; 55: 379-386.
[28] Westerterp-Plantenga MS, Nieuwenhuizen A, Tomé D, Soenen S, Westerterp KR. Dietary protein, weight loss, and weight maintenance. Annual Review of Nutrition. 2009; 29: 21-41.
[29] Palmer BF, Clegg DJ. Strategies to Counter Weight Loss-Induced Reductions in Metabolic Rate. Current Sports Medicine Reports. 2019; 18: 258-265.
[30] Alves-Bezerra M, Cohen DE. Triglyceride metabolism in the liver. Comprehensive Physiology. 2017; 8: 1-8.
[31] Ponziani FR, Pecere S, Gasbarrini A, Ojetti V. Physiology and pathophysiology of liver lipid metabolism. Expert Review of Gastroenterology & Hepatology. 2015; 9: 1055-1067.
[32] Verrijken A, Francque S, Mertens I, Talloen M, Peiffer F, Van Gaal L. Visceral adipose tissue and inflammation correlate with elevated liver tests in a cohort of overweight and obese patients. International Journal of Obesity. 2010; 34: 899-907.
[33] Angulo P, Keach JC, Batts KP, Lindor KD. Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. Hepatology. 1999; 30: 1356-1362.
[34] Hossain N, Afendy A, Stepanova M, Nader F, Srishord M, Rafiq N, *et al*. Independent predictors of fibrosis in patients with nonalcoholic fatty liver disease. Clinical Gastroenterology and Hepatology. 2009; 7: 1224-1229.
[35] Yang SQ, Lin HZ, Lane MD, Clemens M, Diehl AM. Obesity increases sensitivity to endotoxin liver injury: implications for the pathogenesis of steatohepatitis. Proceedings of the National Academy of Sciences of the United States of America. 1997; 94: 2557-2562.
[36] Hannah WN, Harrison SA. Effect of Weight Loss, Diet, Exercise, and Bariatric Surgery on Nonalcoholic Fatty Liver Disease. Clinics in Liver Disease. 2016; 20: 339-350.
[37] van der Heijden G, Wang ZJ, Chu ZD, Sauer PJJ, Haymond MW, Rodriguez LM, *et al*. A 12-week aerobic exercise program reduces hepatic fat accumulation and insulin resistance in obese, Hispanic adolescents. Obesity. 2010; 18: 384-390.
[38] Lee S, Deldin AR, White D, Kim Y, Libman I, Rivera-Vega M, *et al*. Aerobic exercise but not resistance exercise reduces intrahepatic lipid content and visceral fat and improves insulin sensitivity in obese adolescent girls: a randomized controlled trial. The American Journal of Physiology-Endocrinology and Metabolism. 2014; 305: E1222-E1229.
[39] Keating SE, George J, Johnson NA. The benefits of exercise for patients with non-alcoholic fatty liver disease. Expert Review of Gastroenterology & Hepatology. 2015; 9: 1247-1250.
[40] Huang MA, Greenson JK, Chao C, Anderson L, Peterman D, Jacobson J, *et al*. One-year intense nutritional counseling results in histological

improvement in patients with non-alcoholic steatohepatitis: a pilot study. the American Journal of Gastroenterology. 2005; 100: 1072-1081.

[41] Mei Y, Chen L, Zeng P, Peng C, Wang J, Li W, *et al*. Combination of serum gamma-glutamyltransferase and alkaline phosphatase in predicting the diagnosis of asymptomatic choledocholithiasis secondary to cholecystolithiasis. World Journal of Clinical Cases. 2019; 7: 137-144.

[42] Shephard RJ, Johnson N. Effects of physical activity upon the liver. European Journal of Applied Physiology. 2015; 115: 1-46.

[43] Smart NA, King N, McFarlane JR, Graham PL, Dieberg G. Effect of exercise training on liver function in adults who are overweight or exhibit fatty liver disease: a systematic review and meta-analysis. British Journal of Sports Medicine. 2018; 52: 834-843.

[44] Arase Y, Suzuki F, Ikeda K, Kumada H, Tsuji H, Kobayashi T. Multivariate analysis of risk factors for the development of type 2 diabetes in nonalcoholic fatty liver disease. Journal of Gastroenterology. 2009; 44: 1064-1070.

[45] Chen S, Liu C, Li S, Huang H, Tsai C, Jou H. Effects of therapeutic lifestyle program on ultrasound-diagnosed nonalcoholic fatty liver disease. Journal of the Chinese Medical Association. 2008; 71: 551-558.

[46] Ohno H, Yahata T, Yamashita K, Yamamura K, Sato Y, Yamamoto C, *et al*. Effect of physical training on immunoreactive gamma-glutamyltransferase in human plasma. Enzyme. 1988; 39: 110-114.