Original Article

The role of physical exercise in treating people with non-alcoholic fatty liver disease

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ABSTRACT

Objectives: This study aimed to investigate the role of exercise training programs in the prevention and management of non-alcoholic fatty liver disease (NAFLD).Method: the literature review was conducted from January 1, 2020, using the web of science, SCOPUS, and PubMed. Comprehensive exploration was performed with keywords (exercise, NAFLD, liver, and hepatic diseases). Published researches and studies which collected from the exploration were reviewed. Unclear studies were ignored. Results: Many exercise programs were recognized. Most documents confirm a decrease in the fatty liver index, alanine transaminase (ALT), hepatic lipid content, intrahepatic triglyceride (IHTG), improving insulin sensitivity and improving cardiorespiratory fitness. Conclusions: Despite the variations of exercise programs may be adjusted to manage NAFLD, the present review on this issue is restricted in extent. Future studies have to be carried out to strictly clarify which of these changes in daily living may improve obesity-related to NAFLD.

Keywords: NAFLD, physical exercise, resistance exercise, aerobic exercise

Introduction

Like all the organs of the body liver can be affected by many sources.[1-3] NAFLD is a group of liver disorders ranging from isolated hepatic steatosis (fatty liver) to progressive nonalcoholic steatohepatitis (NASH), characterized by the occurrence of swollen hepatocytes, and hepatic fibrosis. NAFLD now affects about15–30% of the community, with a high prevalence ofNAFLD in diabetic and obese individuals, 25% contribute to the creation of NASH, in this manner presenting an expanded hazard for dynamic hepatic fibrosis, the essential determinant of liver-related mortality and morbidity for patients with NASH.[4, 5] Diet-and exercise-prompted weight loss >5% body weight improves NAFLD and reverses hepatic fibrosis and inflammation.[6]

NAFLD practical management guidelines recommended exercise; no specific approach or duration of exercise is otherwise detailed for specialists.[7] The physical activity guidelines for healthy adults recommended the majority of exercise interventions in NAFLD at least 150 min per week of moderate-intensity exercise or 75 min weekly of high-intensity exercise, with resistance training two times per week on non-consecutive days.[8] Therefore, this study aimed to evaluate the evidence of the exercise efficacy in patients with NAFLD and provide guidelines for appropriate physical exercise training to control NAFLD.

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Physical Exercise Training for NAFLD Patients

1) Aerobic Training (see Tables 1 and 2)

Aerobic exercise for NAFLD patients largely depends on the utilization of skeletal muscles for oxygen during aerobic training to produce the energy needed.[9] The primary method for determining the intensity of prescribed exercise is maximum heart rate (Max HR), metabolic equivalent (MET), heart rate reserve (HRR), or maximum oxygen uptake (VO_{2max}). Exercise intensity varies from low to moderate (30–39% of HRR, 57–63% of HRR, 2.0–3.9 METs, and 37–45% of VO_{2max}) moderate (40–59% of HRR, 64–76% of HRR, 4.0–5.9 METs, and 46–63% of VO_{2max}), and vigorous (60–89% of HRR, 77–95% of HRR, 6.0–8.4 METs, and 64–90% of VO_{2max}), exercise modalities include recreational walking, treadmill running, cycle ergometer, cross-training, rowing, and rhythmic exercise.[10]

Aerobic exercises reduce hepatic fat by 3–43% significantly, with various studies showing that weight loss is significantly reduced, however, the frequency, volume, and intensity are still unclear to achieve intrahepatic fat loss. A study by Kistler et al. [11] suggested that high-intensity aerobics, despite its capacity, reduced the level of threat in NAFLD. Whereas, Keating et al. [12] evaluated the effects of exercise intensity and volume on intrahepatic fat, including forty-eight obese participants, different intensities of exercise training did not show significant differences in fatty liver.[13]

Haus et al. evaluated the impact of short-term aerobic exercise, that did not make a significant difference in liver fat levels in NAFLD patients after seven days of high-intensity exercise (treadmill exercise).[14] Thus, a median of 12-week aerobic exercise at high-intensity, 3 sessions per week could be the minimum needed to reduce intrahepatic fat in NAFLD. Additional studies are needed to evaluate the various exercise parameters (mood, frequency, and intensity) present in this plan for liver fat, to identify appropriate NAFLD therapies.

2) Resistance Training (see Tables 1 and 2)

According to the stated guidelines by the American College of Sports Medicine, this paper is about advanced techniques of resisted exercise for good adults. Exercises include shoulder press, latissimus pulling down, chest press, biceps curling, seated rowing, leg curling, leg extending and leg press, three sets, eighteen to twelve repetitions/set, resting between 1-2 min, for 40-minutes. Exercises performed in a public location in the gyms closest to their house or workplace. Given the patient's ability to achieve ten to twelve repetitions, the load gradually increased by two to ten percent in subsequent exercise.[8]

Hashida et al. [15] showed that twelve weeks of resistance training with the medium efficient program, 3 sets per week, 45 min/set with 3.5 METs improved NAFLD with lower energy consumption. Many randomized and non-randomized control studies explored the impacts of resisted exercise on NAFLD, they used device-based resisted exercise; one resisted device with a weight of the body; one utilized solely the participant's body weight; and one weighted-belts, the other one identify 1RM; two individuals did not identify the number of prescribed replications, and oneform of prescribed resistance exercise did not identify the prescribed resistance.[10, 16-22]

Also, in a study by Shamsoddini et al.[16], results in patients with NAFLD showed improvement in cardiac metabolic risk factors; they had used resistance training in circuit training but this dose of circuit training, without concomitant weight loss, it was not enough to improve histology in the NAFLD. The exercise protocol was resisted exercise with fixed intensity with 50% of 1RM, 1-5 circuits for 60 minutes per session, 3 sessions per week.

Moreover, Jakovljevic et al. [23] using resistance exercise, 3 per week, 2 to 3 circuits, 45–60 minutes with intensity: 50% up to 70% 1RM, resistance training can improve hemodynamic regulation and autonomic regulation in NAFLD. A study done by Hallsworth et al. [20] applied resistance exercise: circuit training with the frequency of 3 per week, 2 to 3 circuits, 45–60 minutes, intensity of 50% to 70%, 1RM. Resistance training may improve liver lipid and Lipid oxidationwith no effect on body weight, visceral adipose tissue volume, or whole-body fat mass.

3) Aerobic and Resistance Combination Training (see Tables 1 and 2)

The study by Houghton et al. [24] was conducted in a randomized study in NASH patients, which included twelve weeks of arm cycling for 2 minutes with 1-min rest in between; then tracked by resisted exercise for knee, hip muscles, and chest press, significantly reduced levels of plasma triglyceride and visceral fats in NASH patients, while non-significant changes in inflammatory and circulatory indicators or fibrosis. Exercise training alone without weight control interventions may affect some of the variables, not all factors related to NASH.

Shojaee-Moradie et al. [25] performed a randomized study of twenty-seven NAFLD patients for 16 weeks. This exercise was arm fulfilled whether outdoor or gym-based exercise, tracked by resisted exercise.The intensity was 40–60% of HRR for 20 min; the time was increased to an hour, 4 to 5 times per week for 16 weeks. The results showed an efficient reduction in intrahepatic fat. Combined interventions can provide a new perspective that will create a preceptor training program to target NAFLD patients to gain better outcomes in aerobic or resisted exercises.

4) Novel Training Regimens (see Tables 1 and 2)

Novel training is an exercise that is neither resistance nor aerobic. Accelerated training and hybrid training are an example of novel training. The common form of acceleration training is whole-body vibration: external equipment generates energy and transmits it to the patient's body at various frequencies, enhancing the gravitational speeding up of the skeletal muscle through vibration. Oh et al. [26] conducted a twelve-week accelerated exercise program on eighteen NAFLD patients, with significant improvement in hepatic fat and ALT. The program of accelerating exercise consisted of 3 exercises: first a moving session with 4 stretches, with frequency 30 Hz,

low amplitude, for 30 seconds and two sets for per exercise; the second power session is applied to the larger muscle group with thirty to thirty-five Hz, low amplitude, for 30 seconds and 2 sets training for per group; and third a massage session with the frequency of 40 Hz, high amplitude, for 60 seconds and two training sessions each. Acceleration training was conducted twice a week. The outcomes showed a reduction in hepatic fat, ALT, and improvement of the quadriceps cross-section area.[26] Established that though existence therapy using physical activity and diet have to be emphasized, exercise therapy could have other beneficial effects for NAFLD patients who are unable to modify their lifestyle.

Kawaguchi et al. [27] studied the effect of twelve weeks on thirty-five NAFLD patients. Participants were divided into hybrid training, performed 10 repetitions 3 seconds extension and flexion of the knee joint, twice a week. The findings showed that hybrid training significantly reduced the grade of hepatic steatosis and ALT level. Cross and speeding up exercise may provide new exercise intervention for patients with NAFLD, who cannot contribute to resisted or aerobic exercise, particularly experiencing physical limitations that could otherwise exclude them from such training.[28-32]

Conclusions and Recommendations

From the available literature, it is evident that exercise intervention has a useful influence on NAFLD. Various regimens of resistance training and novel have been shown to reduce hepatic fat content, liver fat and improve liver function, functional capacity, muscle power, and lifestyle, these data justify current guidelines that recommend an exercise regimen that fits with the patient's abilities and preferences, to facilitate long-term compliance with a more active lifestyle.[33-38]

The benefits of exercise in NAFLDare well-recognized. Aerobic, resistance, combination, and narrative exercise programs may enhance systemic indicators of hepatic functions and intrahepatic fats in NAFLD patients either mild or advanced cases. Although the favorable type of exercise training is imprecise, no particular exercise training is likely favorable. Eventually, adherence to exercise training for the long-term has to be highlighted, which could be stated by individual preferences for exercise specifications (mood, frequency, duration, and intensity). When considering exercise training, particular thought must be given to be improving cardiorespiratory fitness and improving musculoskeletal strength through progressive resistance training. Therefore, resisted exercise training in NAFLD patients may be more effective than aerobic exercise, but it has a poor effect on cardiorespiratory capacity in those patients, particularly those who cannot endure or contribute to aerobic training.

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Conflict of Interest

The authors declared no competing interests to disclose.

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Abbreviations

AASLD: American Association for the Study of Liver Diseases
ACSM: According to the American College of Sports Medicine
ALT: Alanine Transaminases
AT: Aerobic Training
CVD: Cardiovascular Diseases
HRR: Heart Rate Reserve
HTG: Hepatic Triglyceride Content
IHCL: Intrahepatocellular Lipid
IHL: Intrahepatic Lipid
IHTG: Intrahepatic Triglyceride
METs: Metabolic Equivalents
MHR: Maximum Heart Rate
NAFLD: Nonalcoholic Fatty Liver Disease
NASH: Nonalcoholic Steatohepatitis
Non-RCT: Non-Randomized Control Trial
RCT: Randomized Control Trial
RM: Repetition Maximum
RPE: Rate of Perceived Exertion
RT: Resisted Training
TG: Triglycerides
VLDL: Very Low-Density Lipoprotein
VO2 peak/max: Maximal oxygen consumption
WBV: Whole-Body Vibration

Table 1. Published Exercise Interventions in Nonalcoholic Fatty Liver Disease RCT randomized control study / NAFLD.

Reference	No of Patients	Exercise Protocol	Main Results
[25]	39	8-week aerobic training (three sessions of 45 minutes per week at 55-75% HRR (heart rate reserve).	Aerobic training was more effective than resistance training in improving blood lipids profile in the elderly with NAFLD and can play a role in the management of this condition.
[21]	24	Combination Ex: Exercise at high distances (cycling) and resistance training. ExerciseFrequency: 3 per week. 45–60 minutes /session. Intensity: Cycling at RPE between 16 to 18, RPE resistance exercise at 14 to 16.	The decrease in HTGC, visceral fat and plasma triglyceride levels. No effect of exercise on liver enzyme levels, metabolic parameters, inflammatory markers of circulation (levels of interleukin 6, tumor necrosis factor-α, or C-reactive protein)

			and fibrosis.
[7]	61	High-intensity Aerobic: Exercise frequency: 3 weekly, 3 sets of 3-minute cycling sessions, 2-minute rest(at a lower VO2 Max)Exercise intensity: 80–85% VO2 Max (50% VO2 Max at rest). Medium-intensity continuous exercise: Exercise frequency: 3 per week, 40 minutes per session. The intensity of exercise: 60–65% VO2 maximum resistance.	Improved hepatic fat accumulation. Weight loss or visceral fat. HIAT also appeared to improve hepatic stiffness.
[26]	69	Aerobic Ex: Treadmill, cross-trainer, bike ergometer, Exercise frequency: 3 to eventually 5 per week, 30 to eventually 45 minutes /session. Exercise intensity: 30% to eventually 60% HRR.	Peripheral insulin sensitivity was significantly increased, decreased liver fat, improved peripheral IR, no significant change in hepatic glucose production, and no changein the control group.
[22]	27	Combination Ex: Gym or outdoor-based aerobic training and resistance training. Exercise frequency: 4–5 per week, 20 to finally 60 minutes practice intensity: 40–60% HRR.	Increased VLDL clearance may contribute to a significant decrease in liver fat after 16 weeks of exercise. longer duration or higher-intensity exercise interventions may be needed to reduce plasma TG and VLDL production rates.
[27]	220	Vigorous-moderate aerobic Ex: Treadmill, exercise frequency: 5 per week, 30 minutes per session. Practice intensity: 65–80% of MHR for 6-months (8–10 METs), 45–55% of MHR for last 6 months (3–6 METs). Moderate intensity: Exercise modality: Treadmill, exercise frequency: 5 per week, 30 minutes per session. Exercise intensity: 45–55% of MHR for 12 months (3–6 METs).	The intense and moderate exercise was equally effective in reducing intrahepatic triglyceride content; this effect appears to be largely mediated by weight loss.
[13]	30	Aerobic Ex: Exercise frequency: 3 per week, 45 minutes per session. Exercise intensity: 60–75% MHR. Resistance Ex: Circuit training. Exercise frequency: 3 per week, 2 to finally 3 circuits per session, 90 s rest between circuits. Exercise intensity: 50% to eventually 70% of 1RM.	RT and AT are equally effective in reducing hepatic fat content and liver enzyme levels in patients with NAFLD. However, aerobic exercise specifically improves NAFLD independent of any change in body weight.
[28]	31	Aerobic Ex: Exercise frequency: 3 to finally 5 per week, 30 to finally 45 minutes per session. Exercise intensity: 30% to eventually 60% HRR.	Exercise training, but not conventional care, significantly improved the VO_2peak. Endothelial dysfunction in the NAFLD cannot be fully explained by excess VAT, but can be reversed by exercise training; this has potential implications for primary prevention of CVD in NAFLD.
[15]	82	Resistance Ex: Exercise frequency: 3 per week, 3 sets per 8–12 reps with 1–2 min rest between sets, for a total duration of about 40 min. Exercise intensity: 1% RM unspecified, load gradually increased 2–10% per week.	Three months of RT improved hepatic fat content accompanied byfavorable changes in body composition and ferritin. RT may serve as a complement to NAFLD treatment.
[14]	40	Aerobic Ex: Exercise Frequency: 3 per week, 60 minutes per session. Exercise intensity: 60–65% HRR. Resistance Ex: 3 per week. 3sets per 10reps per exercise with 1 min recovery between sets. Exercise intensity: 70–80% of 1RM.	Resistance training and aerobic training were equally effective in reducing hepatic fat content in type 2 diabetic patients with NAFLD in both intervention groups.
[18]	21	Resistance Ex: Exercise Frequency: 3 per week, 1 circuit to finally 5 circuits, 12 to finally 60 minutes session. Exercise intensity: Fixed at 50% of 1RM.	Circuit training is safe and effective for improving cardiac metabolic risk factors in patients with NAFLD, however this dose of circuit training, without concomitant weight loss, was not sufficient to improve histology in NAFLD.
[29]	17	Resistance Ex: 3 per week, 2 to finally 3 circuits, 45–60 minutes Exercise intensity: 50% to finally 70% 1RM.	The hemodynamic measures of rest were similar between groups. Resistance exercise therapy seems to improve the autonomic and submaximal exercise hemodynamic regulation in NAFLD.
[30]	13	Aerobic Ex: Exercise frequency: 3 to finally 5 per week, 30 to finally, 45 minutes per session. Exercise intensity: 30% to finally 60% of HRR.	Exercise training improves cutaneous microvascular. NO function compared to conventional care strongly supports the role of exercise in preventing CVD in NAFLD.
[31]	33	Aerobic Ex: Exercise frequency: 5 per week, gradual increase to 30–60 minutes per session. Exercise intensity: 45–55% of VO_2peak.	Decreased IHTG content ($P < 0.05$), no change in total body weight or body fat percentage hepatic VLDL-TG secretion rate.
[17]	19	Resistance Ex: Exercise Frequency: 3 per week, 2 to finally 3 circuits, 45–60 minutes. Exercise intensity: 50% to finally 70% 1RM.	The relative decrease in liver lipid and Lipid oxidationdoes not effect body weight, visceral adipose tissue volume, or whole-body fat mass.
[34]	32	Aerobic Ex: Exercise frequency: 3 per week, 40 minutes per session. Exercise intensity: 80% to 85% of the VO_{2max} with an interval at 50% of the VO_2max.	Significant decrease in BMI, IHTG, visceral adipose fat, plasma lipids, HbA1c, HOMA-IR, and improvement in HRQoL.

Table 2. Distribution of Exercise Interventions in Nonalcoholic Fatty Liver Disease (non-randomized control study) NAFLD.

Reference	No of Patients	Exercise Protocol	Main Results
[19]	53	Exercise frequency: 3 times a week, 3 sets per 10 push-ups and 3 sets per 10 squats at 1 minute intervals per set over 20–30 minutes. Exercise intensity: N/A.	Fat-free mass and muscle mass were significantly increased, whereas hepatic steatosis grade, mean insulin and ferritin levels, and the homeostasis model assessment-estimated insulin resistance index was significantly reduced.
[23]	18	Exercise frequency: 2 times a week, 40 minutes per session. Exercise intensity: Movement session with four stretches, at a 30 Hz frequency, amplitude low, for 30 s and two sets per exercise; Strength and power session that uses larger muscle group contraction, at a 30–35 Hz frequency, low amplitude, for 30 s and two sets for each exercise; Massage session at a 40 Hz frequency, high amplitude, for 60 s and two sets for each exercise.	Total cholesterol and ALT are reduced. TG and AST have not changed. Improved health-related quality of life.
[32]	32	Exercise frequency: 3 per week, 2 sets per 10 reps. Exercise intensity: Starting at 1kg less than 3RM, .5kg was added after each week.	Significant improvement in hepatic fat, truncal subcutaneous fat, and insulin sensitivity.
[11]	17	Exercise frequency: 60 minutes per day for 7 days in a row. Exercise intensity: 80–85% MHR.	HTG reduction.
[10]	90	No specified exercise prescription.	Decreased TG, ALT, and AST.
[33]	13	Exercise frequency: 60 minutes per day for 7 days in a row. Exercise intensity: 80–85% MHR.	Decreased ALT and plasma glucose. AST has not changed. IHL has not changed.
[24]	35	Exercise frequency: 2 per week, 10 sets per 10 reciprocal 3-s knee flexion and extension contractions, 1 min rest between sets, 19 min per day. Exercise intensity: Electrical stimulation intensity was set at a level of 20–25 consecutive knee flexions and extensions.	Decreased liver fat and ALT.

Non-RCT: Non-randomized control trial; TG: Triglycerides; HTG: Hepatic triglyceride content; IHTG: Intrahepatic triglyceride content; IHCL: Intrahepatocellular lipid; IHL: Intrahepatic lipid; IHTG: Intrahepatic triglyceride content; HRR: Heart rate reserve; MHR: Maximum Heart Rate; VO2 peak/max: Maximal oxygen consumption; RM: Repetition maximum; RPE: Rate of perceived exertion.

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