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## Enhancing Sleep Quality in Non-Alcoholic Fatty Liver with Combined Accelerated Aerobic Training: a Randomized Control Study

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## ABSTRACT

**INTRODUCTION.** Exercise constitutes a crucial and well-established component of changing lifestyle to control non-alcoholic fatty liver disease (NAFLD). Accelerating training (AT) involves activating skeletal muscles through heightened gravity acceleration using vibration, rendering it a recommended therapeutic intervention.

AIM. To determine the impact of incorporating AT with aerobic exercise on sleep quality and liver function in NAFLD.

**MATERIALS AND METHODS.** This randomized control trial recruited 60 female NAFLD patients aged 35–45 years from Al-Shrouk General Hospital in Cairo. The participants were equally allocated at random into two groups: A (control group) received aerobic exercise, and B (intervention group) received AT plus aerobic exercise and followed a three-month intervention program. Before and after the interventions, sleep quality was assessed through the Pittsburgh Sleep Quality Index (PSQI), and liver function was evaluated by measuring alanine transaminase (ALT) and aspartate transferase (AST) hepatic enzymes in the blood.

**RESULTS.** Both PSQI scores (p < 0.05) and ALT enzyme levels were significantly (p was 0.005 and 0.006, respectively) improved in groups A and B after the three-month intervention program. However, the AST levels exhibited a non-significant change in both groups (p was 0.569 and 0.027, respectively).

**CONCLUSION.** Combining aerobic exercise and AT may provide the best clinical benefits to NAFLD patients.

**KEYWORDS:** non-alcoholic fatty liver disease, accelerating training, aerobic exercise, whole-body vibration, sleep quality.

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## Улучшение качества сна при неалкогольной жировой дистрофии печени с помощью комбинированных аэробных тренировок с ускорением силы тяжести: рандомизированное контрольное исследование

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### РЕЗЮМЕ

**ВВЕДЕНИЕ.** Физические упражнения являются важнейшим и хорошо зарекомендовавшим себя компонентом изменения образа жизни для борьбы с неалкогольной жировой болезнью печени (НЖБП). Ускоряющая тренировка (УТ) предполагает активацию скелетных мышц за счет повышенного гравитационного ускорения с помощью вибрации, что делает ее рекомендованным терапевтическим вмешательством.

**ЦЕЛЬ.** Определить влияние сочетания тренировок с ускорением силы тяжести и аэробных упражнений на качество сна и функцию печени при НЖБП.

**МАТЕРИАЛЫ И МЕТОДЫ.** В рандомизированном контрольном исследовании приняли участие 60 пациенток с НЖБП в возрасте 35–45 лет из больницы общего профиля Аль-Шрук в Каире. Участники были распределены методом случайного отбора поровну на две группы: пациенты группы А (контрольная группа) получали аэробные упражнения, пациенты группы В (экспериментальная группа) — тренировки с ускорением силы тяжести и аэробные упражнения и выполняли трехмесячную программу. До и после вмешательств качество сна оценивалось с помощью Питтсбургского индекса качества сна (ПИКС), функция печени — путем измерения уровня печеночных ферментов аланинтрансаминазы (АЛТ) и аспартаттрансферазы (АСТ) в крови.

**РЕЗУЛЬТАТЫ.** Как показатели ПИКС (*p* < 0,05), так и уровень фермента АЛТ были значительно улучшены (*p* составил 0,005 и 0,006 соответственно) в группах А и В после трехмесячной программы вмешательства. Однако уровни АСТ в обеих группах изменились незначительно (*p* составил 0,569 и 0,027 соответственно).

**ЗАКЛЮЧЕНИЕ.** Сочетание аэробных упражнений и с тренировками с ускорением силы тяжести может принести наибольшую клиническую пользу пациентам с НЖБП.

**КЛЮЧЕВЫЕ СЛОВА:** неалкогольная жировая болезнь печени, тренировки с ускорением силы тяжести, аэробные упражнения, вибрация тела, качество сна.

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#### INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) represents a major contributor to liver disease globally, accounting for 25–30 % of cases [1]. The numbers of Americans with NAFLD and those with non-alcoholic steatohepatitis (NASH) are anticipated to rise by 21 % to 101 million by 2030 and by 63 % to 27 million, respectively. Inactivity is associated with NAFLD onset and its development into NASH, with an increased NAFLD risk by 4 % for every hour spent sedentary [1]. Considering the absence of a pharmaceutical remedy for NAFLD and NASH, lifestyle adjustments, including exercising and dietary changes, have become the primary focus of treatment [1]. The NAFLD encompasses a range of clinic-pathologic diseases, from isolated fatty liver to advanced NASH, which is identified by necroinflammation, hepatic fibrosis, and inflated hepatocytes [2]. Patients with NAFLD were more prone to experiencing obstructive sleep apnea, especially those exhibiting severe daytime sleepiness [3]. Prior investigations could not determine the causal relation relationship between sleep quantity and duration and NAFLD. However, sleep disruptions could impact their quality of life and probably impair their prognosis [4].

Although exercise can alleviate NAFLD regardless of weight loss, the ideal exercise intensity and the pathophysiologic processes remain unclear [5]. The best way to cure NAFLD is to adapt to a more active lifestyle because the present pharmacologic treatments are ineffective. This enhances vascular endothelial function, lowers liver inflammation and hepatic steatosis, alters body composition favorably, boosts cardiorespiratory fitness, and may cause a histologic reaction [1]. The American Association for the Study of Liver Diseases has suggested exercise practice guidelines for managing NAFLD. Nonetheless, they do not provide practitioners with specific guidelines about the type or duration of exercise [6]. Exercise reduces fatty acid synthesis, boosts fatty acid oxidation in the liver, and lowers releasing molecules linked to hepatocellular and mitochondrial damage. Despite physical activity being proven efficacy for improving fatty liver disease [7], the most efficient exercise protocol for NAFLD remains unclear. However, most patients are unable to consistently participate in exercise programs due to experiencing early fatigue [8]. Aerobic exercise mostly depends on the ability of the skeletal muscle to use oxygen during aerobic respiration to create the energy source adenosine triphosphate [9]. Aerobic training techniques included optional gym workouts, treadmills, bicycles, Nordic quick walks, and walking. Aerobic exercise has been found to be a cost-effective and practical way to improve NAFLD and address obesity effectively [10]. Therefore, managing NAFLD requires at least 20 min of aerobic exercise daily [11].

Because the most efficient way to induce positive effects on the human body has been thought to be through vertical acceleration [12], AT, an innovative and simple whole-body vibration (WBV) based rehabilitation exercise, has been suggested as an intervention for managing NAFLD. The AT is a training program conducted on a three-dimensional vibrating platform that produces the vibration device in the sagittal (y), frontal (x), and vertical (z) directions and incorporates different physical movements or static postures customized for particular purposes. Moreover, AT is beneficial for resistance exercise without requiring heavy lifting or dynamic movements, especially for obese patients struggling with joint pain during exercise [13]. Additionally, AT can reduce visceral and abdominal fat, lower insulin resistance, improve cardiovascular fitness, improve body composition, improve activity of daily living (ADL), and improve mood [14]. Furthermore, AT enhances physical function and body adiposity in obese NAFLD patients by lowering hepatic and intramyocellular fat contents, besides improving abnormal liver function test results, constituting a useful clinical approach in treating NAFLD [15].

Accordingly, we hypothesized that incorporating AT exercises into aerobic training would enhance liver function and sleep quality.

#### AIM

To determine the impact of incorporating AT with aerobic exercise on sleep quality and liver function in NAFLD.

#### MATERIALS AND METHODS Study Design and Participants

This single-blinded randomized controlled trial recruited 60 female patients with NAFLD aged 35–45 years from Al-Shrouk General Hospital in Cairo. The study was conducted between January 2022 and December 2023 and approved by the Physical Therapy Faculty's Ethical Committee at Cairo University on 27.02.2022 (No: P.T.REC/012/003658).



Fig. 1. The study flowchart

16

The study objectives and potential risks were clearly explained to the participants, who signed an informed consent before participation.

The participants had a body mass index (BMI) of 35-39.9 kg/m<sup>2</sup>, indicating class II obesity. The NAFLD diagnosis was determined by excessive food consumption or lack of physical exercise, high serum alanine transaminase (ALT) levels, and confirmed with ultrasound testing. This study excluded patients using anti-diabetic or weight loss medications, pregnant and breastfeeding patients, and patients with liver disease, heart block or complex ventricular arrhythmia, recent myocardial infarction, cardiopulmonary dysfunction, cerebrovascular disorders, vision or hearing impairments, psychiatric disorders, neurological diseases affecting balance or cognitive function (e.g., epilepsy), marked lower limb fixed deformity or tightness, congenital or acquired lower limb deformities. Each patient received lifestyle advice for NAFLD nutrition and physical activity from a gualified dietitian and a medical nutritional doctor. Figure 1 depicts the study flowchart.

#### Procedures

All participants underwent a physical evaluation conducted by an experienced physiotherapist at the trial's commencement to assess their participation eligibility. A survey was used to collect demographic information. Each participant's height and weight were measured with an analog weight and height scale to calculate their BMI: weight (kg) divided by the square of height (m<sup>2</sup>).

A coin flip was used to randomly assign participants to groups A or B, with an equal chance of being allocated to either group. A researcher who was unaware of the group assignments observed the coin and then allocated the patients accordingly.

#### Interventions

#### The AT Program

Group B received AT training plus aerobic exercise through walking. Instructions for completing the AT activities were given to each participant during the initial visit prior to the program's start. The training was performed at a faster pace, according to Oh S. et al. [15]. The AT training was scheduled for 12 weeks, twice a week. Thirty participants completed upper, lower, and wholebody exercises on a vertical vibration machine (Super fit massage VG 200B-SFM, China) using a protocol of three phases: warming up, strength and power, and cooling down. The sessions lasted 30 min in the first one and a half

Table 1. Comparison of subject characteristics

months and 40 min in the second one and a half months, with a 30-S rest period in between each movement [15].

The phases of the training were conducted as the following [15]: (1) Warming up phase: A stretching exercise for 5 min including upper and lower limb and whole-body stretching exercise (low mode, low amplitude, frequency: 16.5 Hz); (2) A strength and power phase: The first one-and-a-half-month sessions included 20 min upper and lower limb strength exercises and whole-body exercises (moderate mode, low amplitude, frequency 20 Hz) and the second one-and-a-half-month sessions included 30-min upper and lower limb strength exercises and whole-body exercises (high mode, low amplitude, frequency 22 Hz); (3) Cooling down phase: A stretching exercise of 5 min including upper and lower limb and whole-body stretching exercises (low mode, low amplitude, frequency: 16.5 Hz).

#### **Aerobic Exercise**

All participants in both groups were required to complete aerobic training consisting of an electronic treadmill (AC5000M, China) walking that lasted for three days weekly for three months. Moderate aerobic training involves a 10-min warm-up walking on the treadmill at 30–40 % HR max subsequent by 45 min of aerobic exercise on an electronic treadmill with a heart rate maintained at 60–75 % of the maximum heart rate (MHR); the heart rate was monitored by a link connected to the treadmill [16].

The workout program ends with a 10-minute cooldown period walking on the treadmill at 30-40 % HR max [16]. The Karvonen formula was employed to calculate MHR for each participant as follows: MHR = 220 - age [17]. The speed was adjusted according to target intensity.

#### Outcome Measures Sleep Quality

The Arabic version of the Pittsburgh Sleep Quality Index (PSQI), a five-minute self-administered questionnaire, Arabic version as deployed to measure sleep quality preand post-study. The PSQI consists of 19 separate items that collectively create 7 components, resulting in a total global score. A lower score indicates better sleep quality [18].

#### **Blood Analysis**

Blood samples,5mls were collected from the right median cubital vein utilizing a small needle pre- and post-study while the patient was fasting to measure aspartate transferase (AST) and Alanine transaminase (ALT) using standard methods (Autoanalyzer, Mindary BS 800, China) [15].

literree	Group A (Walking)	Group B (Accelerating and walking)	T-value	<i>p</i> -value
items	M ± SD ( <i>n</i> = 30)	M ± SD ( <i>n</i> = 30)		
Age, years	$40.8\pm3.4$	41.07 ± 3.3	0.306	0.760
Height, cm	$159.2 \pm 5.9$	$157.8 \pm 5.2$	0.977	0.333
Weight, kg	91.9 ± 8.4	91.1 ± 6.6	0.459	0.648
BMI, kg/m²	36.2 ± 1.3	36.6 ± 1.5	1.105	0.274

**Note:** *M* — mean; SD — standard deviation; *p*-value — probability value; \* — statistical significance of differences between groups.

#### **Statistical Analysis**

The software SPSS (Version 22; SPSS Inc., Chicago, II, USA) was employed to perform all statistical analyses. The demographic features of all participants in both groups were analyzed utilizing the Independent Sample T-test. Furthermore, MANOVA was deployed to determine the differences between the groups pre- and post-intervention, and pairwise comparisons were conducted to detect the significant variations within groups. p < 0.05 indicated a significant difference.

#### RESULTS

Table 1 indicates that the participant characteristics, including age, height, weight, and BMI, exhibited a nonsignificant difference between both groups.

## *Treatment Effects on ALT, AST, and Sleep Quality* Within-Group Comparison

Both AST and ALT levels and PSQ scores did not significantly differ between both groups pre- or post-intervention (p < 0.05). Furthermore, ALT had a significant improvement of 8.1 % in group A and 6.9 % in group B. Nonetheless, AST levels showed a nonsignificant change in groups A and B, with 2.2 % and 5.7 % percentages of change, respectively (Table 2). In addition, significant alterations of PSQ scores (p < 0.05) were detected in groups A and B with 50.5 % and 63.5 % percentage change, respectively (Table 2).

#### **Between-Group Comparison**

The results indicated a nonsignificant difference (p > 0.05) between groups pre-intervention. However,

the post-treatment comparison of groups revealed that sleep quality (p-value 0.037) and ALT levels significantly improved in group B more than in group A. However, AST levels exhibited a nonsignificant variation (p-value 0.076) between both groups post-treatment (Table 2).

#### DISCUSSION

The primary finding of our research was that the sleep quality was significantly improved in group A, which received AT combined with aerobic training. During the 12-week training session, liver enzymes decreased significantly. However, group B, which performed aerobic exercise without the AT, showed greater improvement in ALT levels. Our results demonstrated nonsignificant differences in all parameters between both groups pre-treatment (p > 0.05). These results confirmed our hypothesis that incorporating AT exercises into aerobic training would enhance liver function and sleep quality.

Several clinical trials have validated the efficacy of exercise intervention in treating NAFLD [18]. Although aerobic exercise was not related to weight loss in terms of its impact on ALT and AST, engaging in aerobic activities for 8–12 weeks can enhance AST and ALT levels in patients suffering from NASH or NAFLD. However, ALT levels have been observed to be normal in various NAFLD cases. Therefore, caution is advised when using AST and ALT as alternative markers for distinguishing changes in NAFLD resulting from exercise training [19].

Moderate-intensity treadmill training has been revealed to significantly improve mean ALT and AST levels in ten ultrasound-confirmed NAFLD patients from

Variables		Group A (Walking) $M \pm SD$	Group B (Accelerating and walking) M ± SD	Comparison between Groups	
AST (U/L)	Pre-treatment	23 ± 6.6	26.2 ± 7.2	3.152	0.081
	Post-treatment	22.5 ± 7.1	24.7 ± 6.9	1.394	0.243
	Change %	2.2 %	5.7 %		
	Within-group Comparison	0.569	0.027		
ALT (U/L)	Pre-treatment	27.3 ± 6.4	30.3 ± 6.8	3.142	0.082
	Post-treatment	25.1 ± 5.9	28.2 ± 7.3	3.258	0.076
	Change %	8.1 %	6.9 %		
	Within-group Comparison	0.005*	0.006*		
PSQI	Pre-treatment	9.1 ± 2.9	9.6 ± 2.7	0.617	0.435
	Post-treatment	4.5 ± 1.8	3.4 ± 1.5	4.551	0.037*
	Change %	50.5 %	63.5 %		
	Within-group Comparison	p < 0.05*	p < 0.05*		

**Table 2.** AST, ALT, and PSQI comparison within and between groups

**Note:** AST — aspartate transferase; ALT — alanine transaminase; PSQI — Pittsburgh Sleep Quality Index; WC — waist; M — mean; SD — standard deviation; MD — mean difference; p-value — probability value; \* — significance; change % — percentage of change.

#### BULLETIN OF REHABILITATION MEDICINE | 2024 | 23(3)

 $36.9 \pm 16.4$  and  $29.7 \pm 9.0$  U/L to  $24.4 \pm 7.2$  and  $20.9 \pm 4.4$  U/L, respectively [20]. The current findings support and broaden the recent discovery by Hoseini Z. et al. [21] that aerobic exercise significantly impacts liver lipid content and can effectively reduce liver fat, promote weight loss, and decrease liver enzymes (AST and ALT) and cholesterol.

Our findings align with earlier studies investigating the effects of aerobic exercise on sleep quality and duration in obese people, demonstrating improvements in sleep quality, even without significant weight reduction [22, 23]. Physical exercise can be a natural sleep approach by boosting relaxation and lowering insomnia-related hyperarousal. Engaging in physical activities enhances sleep quality, cognitive performance, physical health, and psychological well-being [24].

Our results align with the assumptions that various exercise methods effectively impact liver function. Physical activity was elucidated to be strongly linked to decreased inflammation and improved steatohepatitis and fibrosis in experimental models. Similarly, aerobic and resistance exercises have been revealed to lower liver fat, improve insulin resistance, and enhance blood lipids, independent of weight reduction in human trials [25].

Previous clinical trials on NAFLD pathogenesis have provided evidence supporting the beneficial effects of AT by revealing that a 24-week WBV has improved liver function tests, specifically AST and ALT. This suggests that WBV is a beneficial exercise alternative for NAFLD patients who struggle to participate in regular exercise [15].

Furthermore, Oh S. et al. [12] have shown that hepatic fat content and intramyocellular lipid levels significantly decreased through a 12-week program involving 20min aerobic training sessions twice weekly. Additionally, AST (p = 0.29) and ALT (p < 0.05) levels were significantly improved, possibly because of restoring insulin sensitivity and reducing abnormal fat accumulation in the liver. This can be accomplished by resolving adipokine imbalance, which alleviates oxidative stress and inflammation in the liver. Improvements in liver conditions were established using abdominal tomography in obese patients with NAFLD, showing changes in liver steatosis and stiffness levels [12].

Consistently, Torres-Nunes L. et al. [26] have manifested that WBV exercise can generate biological changes that lead to significant physiological responses in blood pressure, an expected result of physical activity. Their results also indicated that central, mean, maximum, and lowest temperatures increased 15 min postinterventions. Additionally, WBV exercise induced slight changes in muscle tone and several body composition measures, accompanied by a positive change in the sleep cycle. Limited scientific data supports the benefits of AT for NAFLD patients, and the most effective exercise therapy intensity and method remain uncertain.

#### **Sagnificance & Limitations**

Our study had several limitations. First, the absence of post-training follow-up because the participants were unavailable; last the limited research conducted on AT and aerobic training in NAFLD, particularly on different age levels. Therefore we recommended further investigation into the effect of AT and aerobic training in NAFLD utilizing a wide range of inclusion criteria, using other evaluating methods (such as lipid profile) and a larger sample size.

#### CONCLUSION

The study indicates that integrating aerobic exercise with AT significantly enhances sleep quality scores and enhances liver function test abnormalities in NAFLD patients. Moreover, AT is a promising new strategy expected to be used in therapeutic exercise programs.

#### **ADDITIONAL INFORMATION**

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**Data Access Statement.** The data that support the findings of this study are available on reasonable request from the corresponding author.

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