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Effects of Long-term Regular Exercise Intervention on NAFLD-related Parameters: A Meta-analysis

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Abstract:

Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent forms of chronic liver disease across the globe, affecting a significant portion of the population. Long-term regular exercise therapy can improve the relevant clinical indicators of NAFLD patients, and is one of the effective means to treat the disease. This study conducted a meta-analysis of relevant literature published in PubMed up to September 2024 to assess the effects of exercise on various clinical markers in NAFLD patients. A total of nine articles were included, involving 254 patients, with intervention duration ranging from 8 to 26 weeks. Analysis results showed that long-term adherence to exercise significantly reduced ALT(MD=-5.98 , 95% CI [-7.99,-3.97]),AST(MD=-2.92, 95% CI [-5.30,-0.53]),LDL-C(MD=-5.38 , 95% CI [-7.70,-3.06]) levels and increased HDL-C(MD=3.78 , 95% CI [0.4,7.15]) levels in NAFLD patients. However, there was little effect on HbA1c(MD=-0.13 , 95% CI [-0.28,0.02]) levels in NAFLD patients. To sum up, consistent physical activity is a potent means of enhancing the well-being of individuals suffering from NAFLD.

Keywords: Meta-analysis; exercise; non- alcoholic fatty liver disease.

1. Introduction

Non-alcoholic fatty Liver disease (NAFLD) refers to a type of disease caused by excessive accumulation of fat in the liver in the absence of excessive alcohol intake. With the global economic growth and the improvement of people's quality of life, NAFLD has evolved into a key global public health challenge, and about one quarter of the world's population is affected by the disease [1]. Although there is no specific treatment for NAFLD, it can be effectively managed with a proper diet and regular exercise [2]. The study by Slentz et al. confirmed that exercise is an economical and convenient intervention that can effectively improve NAFLD [3]. Therefore, this study systematically reviewed the relevant literature and conducted a meta-analysis to explore the specific effects of exercise intervention on related physiological and biochemical indicators of NAFLD patients, clarify the role of exercise in the treatment of NAFLD, and provide a basis for exercise therapy of NAFLD. Ultimately, we hope that these findings can help NAFLD patients achieve better health outcomes, reduce the risk of disease progression, and improve quality of life through exercise therapy.

2. Materials and Methods

2.1 Data Sources and Search Strategy

A search of the literature from inception to September 2024 was conducted using the PubMed database in accordance with PRISMA guidelines. While performing the literature search, using both subject and free word methods, the constructed search expression is as follows:
(((((Non-alcoholic Fatty Liver Disease[Title/Abstract]) OR (Fatty Liver, Nonalcoholic[Title/Abstract])) OR (NAFLD[Title/Abstract])) OR (Nonalcoholic Fatty Liver Disease[Title/Abstract])) OR (Nonalcoholic Steatohepatitis[Title/Abstract])) AND ((Sports[Title/Abstract]) OR (Exercise[Title/Abstract])).

2.2 Criteria for Exclusion and Inclusion

The inclusion criteria for articles in this study are as follows: (1) The article is written in English; (2) The subjects were adults; (3) NAFLD was diagnosed by pathology or imaging examination. (4) conduct a study of any type of exercise for at least eight weeks; (5) The control group did not receive any intervention including exercise intervention. (6) Prior to the implementation of the intervention, comparisons between the experimental and control groups did not show statistically significant differences. In addition, race, sex, and nationality were not restricted.
Exclusion criteria: (1) cross-sectional studies, uncontrolled studies or prospective studies; (2) no exercise intervention alone; (3) The required data could not be obtained; (4) Conference abstracts, review articles, animal studies, case reports, and republished papers.

2.3 Data Extraction

According to established inclusion and exclusion criteria, ineligible studies were excluded by reviewing abstracts or full content of articles, and the following information was extracted from selected studies: name of the lead author, year of publication, size of study sample, frequency of exercise, and number of weeks of intervention duration.

2.4 Statistical Analysis

The levels of liver parameters (ALT, AST), glucose metabolism parameters (HbA1c), and lipid parameters (LDL-C, HDL-C) in NAFLD patients were statistically analyzed by Review Manager (RevMan 5.3.) software, and the mean difference (MD) and 95% confidence interval (CI) were calculated. To determine the extent to which the intervention affected the outcome. Heterogeneity was determined by the I2 statistic, with I2≥50% as high heterogeneity and I2 < 50% as low heterogeneity. According to the degree of heterogeneity between the study data, the decision was made to use a fixed effect model (when I2≥50%) or a random effect model (when I2 < 50%) to analyze the data.

3. Results

3.1 Results of the Search

Figure 1 illustrates the detailed process of the initial screening and full-text review of the literature.

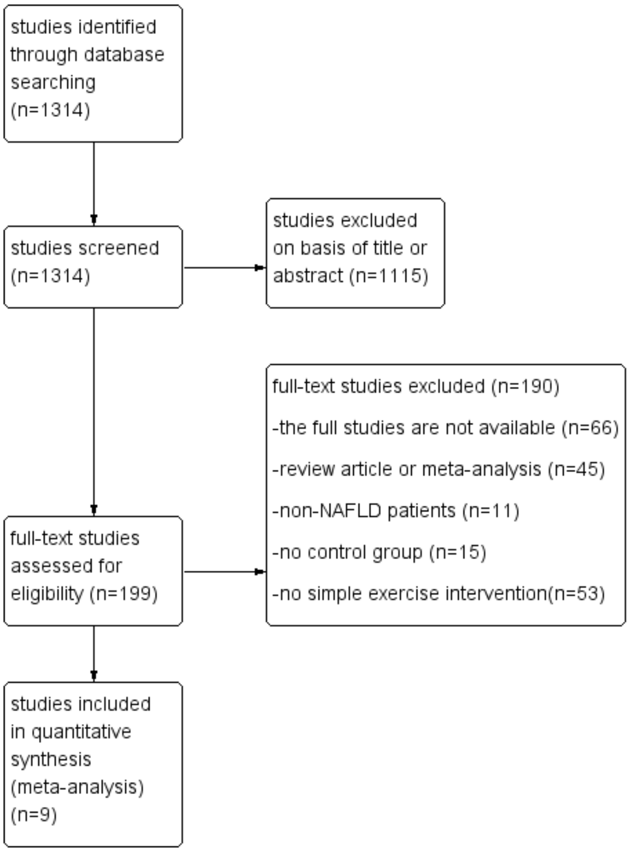

Fig.1 Selection of studies for review and meta-analysis. (picture credit: original)

After screening, 9 articles were included in the analysis as shown in Table 1 [4-12].

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Table 1. Characteristics of included studies.

Author, Year	Sample Size	Disease	Training Sessions/Week	Intervention Duration(Weeks)
Shi-Ming Chen 2008	38	NAFLD	Not mentioned	10
Kate Hallsworth 2011	21	NAFLD	3	8
Carly Eckard 2013	20	NAFLD	4to7	26
Alireza Shamsoddini 2015	20	NAFLD	3	8
Mohammad Ebrahim Ghamarchehreh 2019	18	NAFLD	3	8
Walid Kamal Abdelbasset 2020	32	NAFLD	3	8
Hector-Center for Nutrition 2021	46	NAFLD	Not mentioned	8
Ambrin Farizah Babu 2022	42	NAFLD	Not mentioned	12
Mohammad Hassabi 2023	17	NAFLD	5	26

3.2 Effects on ALT

As shown in Figure 2, ALT levels (MD=-5.98, 95% CI[-7.99,-3.97]) in the exercise group was significantly lower than that in the control group after the intervention.

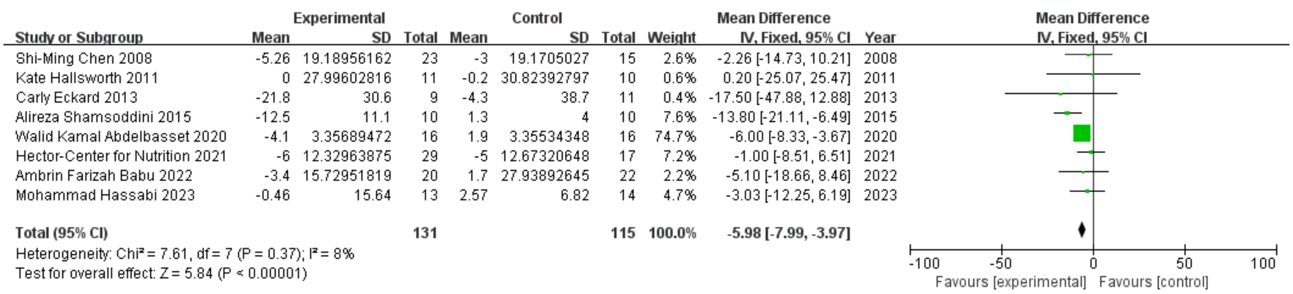


Fig 2. Forest plot of the effect of exercise on ALT. (picture credit: original)

3.3 Effect on AST

It can be observed in Figure 3 that after exercise intervention, AST levels (MD=-2.92, 95% CI [-5.30,-0.53]) in the exercise group decreased significantly compared with those in the control group.

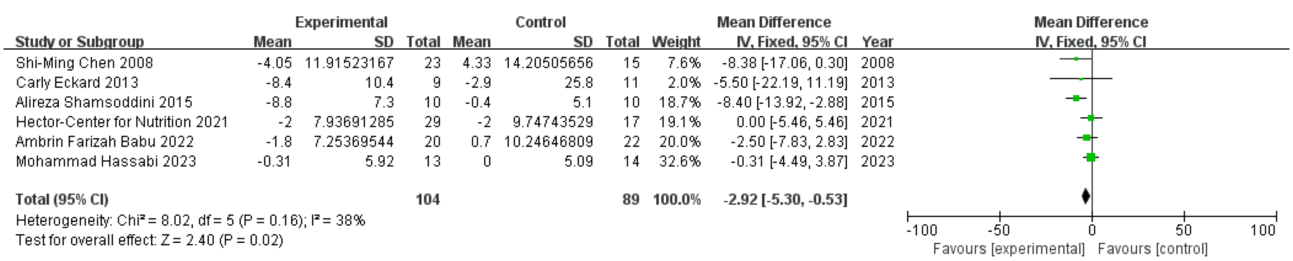
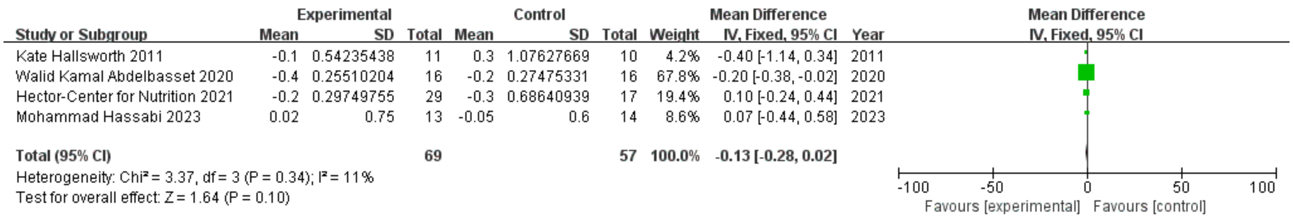


Fig 3. Forest plot of the effect of exercise on AST. (picture credit: original)

3.4 Effect on HbA1c

The results in Figure 4 show that after the exercise intervention, there was no statistically significant difference in HbA1c levels (MD=-0.13, 95% CI[-0.28,0.02]) between the exercise group and the control group.

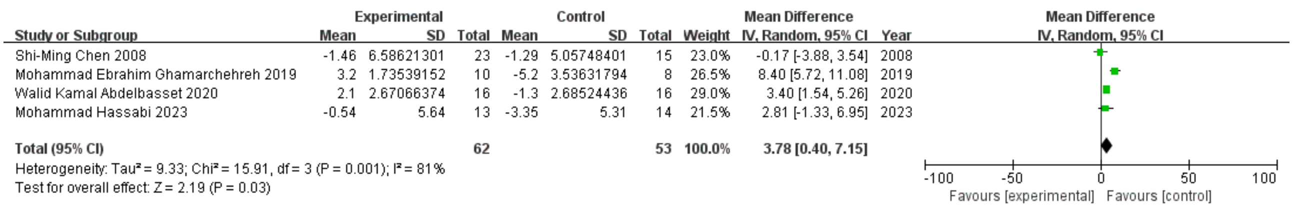


Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Kate Hallsworth 2011	-0.1	0.54235438	11	0.3	1.07627669	10	4.2%	-0.40 [-1.14, 0.34]	2011
Walid Kamal Abdelbasset 2020	-0.4	0.25510204	16	-0.2	0.27475331	16	67.8%	-0.20 [-0.38, -0.02]	2020
Hector-Center for Nutrition 2021	-0.2	0.29749755	29	-0.3	0.68640939	17	19.4%	0.10 [-0.24, 0.44]	2021
Mohammad Hassabi 2023	0.02	0.75	13	-0.05	0.6	14	8.6%	0.07 [-0.44, 0.58]	2023
Total (95% CI)			**69**			**57**	**100.0%**	**-0.13 [-0.28, 0.02]**	

Fig 4. Forest plot of the effect of exercise on glycated hemoglobin (HbA1c). (picture credit: original)

3.5 Effect on HDL-C

The results in Figure 5 reveal that HDL-C levels (MD=3.78, 95%CI [0.4,7.15]) in the exercise group significantly exceeded those in the control group after receiving exercise therapy.

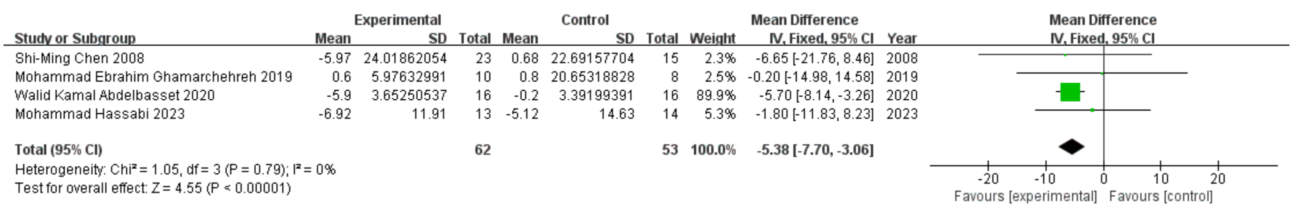


Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Shi-Ming Chen 2008	-1.46	6.58621301	23	-1.29	5.05748401	15	23.0%	-0.17 [-3.88, 3.54]	2008
Mohammad Ebrahim Ghamarchehreh 2019	3.2	1.73539152	10	-5.2	3.53631794	8	26.5%	8.40 [5.72, 11.08]	2019
Walid Kamal Abdelbasset 2020	2.1	2.67066374	16	-1.3	2.68524436	16	29.0%	3.40 [1.54, 5.26]	2020
Mohammad Hassabi 2023	-0.54	5.64	13	-3.35	5.31	14	21.5%	2.81 [-1.33, 6.95]	2023
Total (95% CI)			**62**			**53**	**100.0%**	**3.78 [0.40, 7.15]**	

Fig 5. Forest plot of the effect of exercise on HDL-C. (picture credit: original)

3.6 Effect on LDL-C

Figure 6 shows that compared with the control group, the LDL-C level (MD=-5.38, 95% CI[-7.70,-3.06]) was significantly reduced in the exercise group.



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Shi-Ming Chen 2008	-5.97	24.01862054	23	0.68	22.69157704	15	2.3%	-6.65 [-21.76, 8.46]	2008
Mohammad Ebrahim Ghamarchehreh 2019	0.6	5.97632991	10	0.8	20.65318828	8	2.5%	-0.20 [-14.98, 14.58]	2019
Walid Kamal Abdelbasset 2020	-5.9	3.65250537	16	-0.2	3.39199391	16	89.9%	-5.70 [-8.14, -3.26]	2020
Mohammad Hassabi 2023	-6.92	11.91	13	-5.12	14.63	14	5.3%	-1.80 [-11.83, 8.23]	2023
Total (95% CI)			**62**			**53**	**100.0%**	**-5.38 [-7.70, -3.06]**	

Fig 6. Forest plot of the effect of exercise on LDL-C. (picture credit: original)

3.7 Bias Analysis

Bias risk assessment was carried out for each of the eventually included studies, and the assessment results were shown in Figure7,8.

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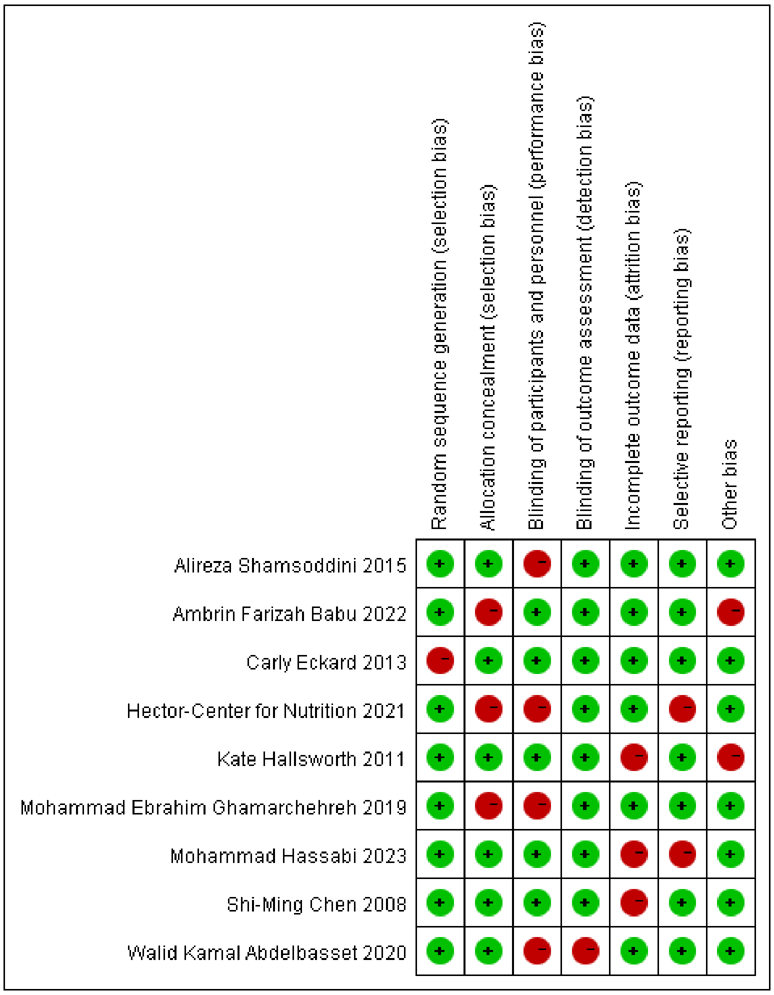

Fig7. Risk of bias summary. (picture credit: original)

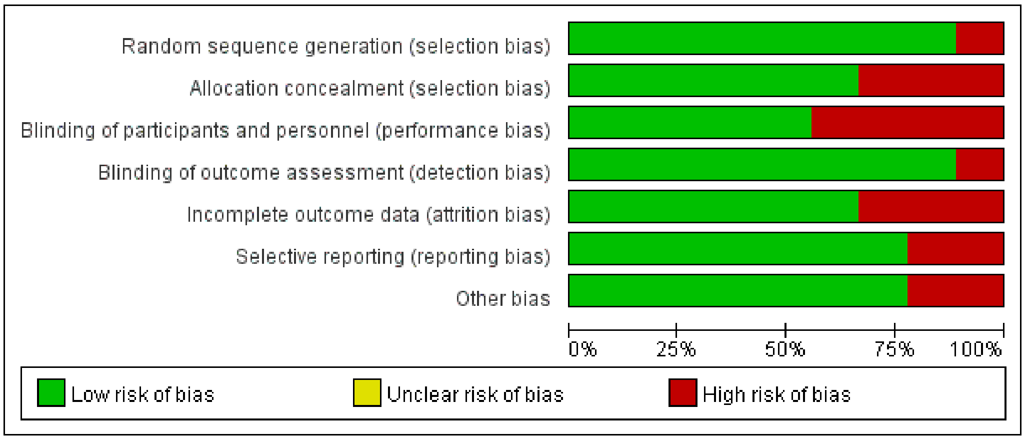

Fig 8. Risk of bias graph. (picture credit: original)

4. Discussion

This meta-analysis comprehensively evaluated the effects of long-term and regular exercise intervention on transaminase indicators (ALT and AST), blood glucose indicators (HbA1c), and lipid levels (LDL-C and HDL-C) in patients with NAFLD.

The concentration of glutamic oxalic aminotransferase (AST) and alanine aminotransferase (ALT) in blood are important markers to evaluate the degree of liver injury

[13].The combined results suggest that consistent and regular physical exercise can reduce AST and ALT levels in NAFLD patients. A similar conclusion was reached by Babu et al [14]. In addition, Bianchi et al. have revealed that exercise intervention can decrease liver inflammation by increasing the activity of SIRT, which in turn more effectively deacetylates metabolic transcription factors and key inflammation, such as PGC-1α and NF-κB [15], thus having a therapeutic effect on NAFLD.

Glycosylated hemoglobin (HbA1c) is a stable compound that reflects the non-enzymatic reaction of hemoglobin in the presence of serum sugars and is present in red blood cells. As one of the parameters of glucose metabolism, HbA1c is an important marker to assess the level of NAFLD patients. This analysis revealed that exercise had no noticeable effect on glycosylated hemoglobin (HbA1c) levels in NAFLD patients. This finding may be related to the inclusion of only four studies. In addition, the findings of this study are consistent with the conclusions of previous studies by Babu et al [14].

High density lipoprotein cholesterol (HDL-C), which helps prevent arteriosclerosis, is produced in the liver and carries cholesterol from other parts of the body back to the liver for processing and elimination in the bile. The higher the level of HDL-C in the blood, the lower the risk of CVD. Low-density lipoprotein cholesterol (LDL-C), the major lipoprotein component in the blood, is responsible for transporting cholesterol throughout the body and is generally regarded as a key risk factor for the development of atherosclerosis. A significant feature of NAFLD is the dysregulation of lipid metabolism. Elevated HDL-C and decreased LDL-C are one of the manifestations of this symptom. Severe lipid metabolism abnormalities may lead to the occurrence and development of pathological states such as type 2 diabetes mellitus and atherosclerosis [16]. Therefore, reducing the level of LDL-C and increasing the level of HDL-C are important measures to improve lipid metabolism and delay the disease in patients with NAFLD. This study clearly indicates that long-term adherence to regular exercise can positively affect LDL-C and HLD-C levels in NAFLD patients. This regulation of lipid levels is essential for remission and overall recovery in NAFLD patients.

5. Conclusion

The results of this meta-analysis reveal an important finding: long-term and regular exercise therapy can significantly optimize multiple physiological indicators in NAFLD patients, including the levels of alanine aminotransferase ALT, AST, HDL-C and LDL-C. However, the exercise intervention did not show statistically significant improvement in HbA1c, a key measure of glycemic control.

Although these findings provide valuable information for our understanding of the role of exercise in the treatment of NAFLD, it must be noted that the results of this meta-analysis are based on a limited number of studies that included relatively small sample sizes. This limitation may affect the generality and reliability of the results, and therefore caution should be exercised when interpreting these results.

In view of this, more in-depth and extensive studies are necessary to more accurately determine the optimal strategy of exercise intervention in improving the condition of NAFLD patients. These studies should include larger sample sizes and more diverse exercise regimens and durations to better understand how exercise affects the pathophysiological processes in NAFLD patients. In addition, future research should also take into account individual differences and the type and intensity of exercise to provide more personalized and effective exercise therapy recommendations for NAFLD patients.

6. References

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