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# Efficacy of aerobic and resistance exercises in improving visceral adipose in patients with non-alcoholic fatty liver: a meta-analysis of randomized controlled trials

## Die Wirksamkeit von aerobem Bewegungs- und Widerstandstraining zur Verbesserung der viszeralen Adipositas bei Patienten mit nichtalkoholischer Fettleber: Eine Meta-Analyse randomisierter, kontrollierter Studien

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**Schlüsselwörter**

Nichtalkoholische Fettlebererkrankung, aerobes Bewegungstraining, Widerstandstraining, randomisierte kontrollierte Studie, Meta-Analyse

**Key words**

non-alcoholic fatty liver disease, aerobic exercise, resistance training, randomized controlled trial, meta-analysis

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## ABSTRACT

**Background** Non-alcoholic fatty liver disease (NAFLD) is a common chronic disease that can cause liver deterioration if insufficiently diagnosed and untreated. The verification of whether exercise interventions improve liver enzymes and lipid and glucose parameters is scant.

**Aim** We conducted this systematic review and meta-analysis to examine the efficacy of aerobic and resistance exercise interventions in patients with NAFLD.

**Methods** We searched the related studies in the PubMed, Embase, Cochrane Library, and Web of Science databases. We screened 1129 articles published before September 1, 2021, based on the inclusion and exclusion standards, after which 17 articles with a total of 1168 participants were finally included. The indices of liver enzymes and lipid and glucose metabolism were gathered and examined by Stata SE.

**Results** The outcomes suggested that aerobic and resistance exercise can markedly improve the parameters of liver enzymes, blood lipids, and glucose, and especially visceral adipose tissue (weighted mean different [WMD] = −8.3 at 95 % CI [−11.59 to −5.00], $p < 0.0001$), in patients with NAFLD.

**Conclusion** This study demonstrated that aerobic and resistance exercises positively affect NAFLD treatment. To further quantify the effects on patients with NAFLD, a more specific and uniform exercise program should be proposed.

## ZUSAMMENFASSUNG

**Hintergrund** Die nicht-alkoholische Fettlebererkrankung (NAFLD) ist eine häufige chronische Erkrankung, die bei unzureichender Diagnose und unzureichender Behandlung zu einer Verschlechterung der Leberwerte führen kann. Es gibt nur wenige Studien, die belegen, dass Sport die Leberenzymwerte sowie die Lipid- und Glukoseparameter verbessert.

**Ziel** In dieser systematischen Übersichtsarbeit und Meta-Analyse wurde die Wirksamkeit von aerobem Bewegungs- und Widerstandstraining bei Patienten mit NAFLD untersucht.

**Methoden** Wir recherchierten in den Datenbanken PubMed, Embase, Cochrane Library und Web of Science die entsprechenden Studien. Anhand der Ein- und Ausschlusskriterien wurden insgesamt 1129 Artikel, die vor dem 1. September 2021 veröffentlicht worden waren, gescreent und schlussend-

lich 17 Artikel mit insgesamt 1168 Teilnehmern eingeschlossen. Die Werte der Leberenzyme sowie des Lipid- und Glukosestoffwechsels wurden erfasst und mit Stata SE untersucht.

**Ergebnisse** Die Ergebnisse legen nahe, dass aerobes Bewegungs- und Widerstandstraining bei Patienten mit NAFLD die Werte der Leberenzyme, der Blutfette und des Blutzuckers und insbesondere des viszeralen Fettgewebes deutlich verbessern können (WMD = –8,3 bei 95 % CI [–11,59 bis –5,00], p < 0,0001).

**Schlussfolgerung** Diese Studie hat gezeigt, dass aerobes Bewegungs- und Widerstandstraining eine positive Rolle bei der Behandlung von NAFLD spielen. Um die Auswirkungen auf Patienten mit NAFLD besser quantitativ beurteilen zu können, sollte ein spezifischeres und einheitlicheres Trainingsprogramm angeboten werden.

**Schlüsselwörter** Nicht-alkoholische Fettlebererkrankung, aerobes Bewegungstraining, Widerstandstraining, randomisierte kontrollierte Studie, Meta-Analyse

## Introduction

Non-alcoholic fatty liver disease (NAFLD) is currently the primary cause of chronic liver disease in the United States and Europe, with a global prevalence of approximately 25 % [1]. It is a metabolic syndrome that can cause obesity, insulin resistance, type 2 diabetes (T2DM), hypertension, and so on. The progression of NAFLD to non-alcoholic steatohepatitis, liver cirrhosis, and liver cancer will increase the incidence of complications and the disease's mortality, thus increasing the burden on the economy and society [2]. Several cohort studies have shown that cardiovascular disease accounts for the significant contribution to death in patients with NAFLD [3]. Therefore, early clinical intervention is particularly vital. However, no effective treatment has been proposed so far. Some studies have pointed out that NAFLD can be treated by increasing satiety, performing weight loss surgery, reducing intestinal energy intake, and using treatments for antioxidation, anti-inflammation, antifibrosis, and so on [4]. However, the above treatment methods are unclear, and some procedures are inconvenient for the patient or may have side effects. Besides, in long-term treatment, drug-induced liver injury and side effects on other organs cannot be ruled out.

Lifestyle interventions, including aerobic exercise and resistance exercise, are beneficial to NAFLD and T2DM [5]. They can reduce intrahepatic fat content, increase the β-oxidation of fatty acids, induce liver protective autophagy, overexpress peroxisome proliferator-activated receptor γ (PPAR-γ), reduce hepatocyte apoptosis, increase insulin sensitivity, and improve non-alcoholic fatty liver [6]. The 2017 AASLD guidelines indicate that early drug intervention only works in patients with non-alcoholic steatohepatitis and fibrosis confirmed by liver biopsies, and exercise can reduce liver steatosis in adult patients with NAFLD [7]. Although several meta-analyses have been published to illustrate the effects of exercise on patients with NAFLD [8, 9, 10, 11, 12], there is no article to summarize as many of the latest articles as possible and evaluate the effect of exercise on visceral adipose tissue. Therefore, this meta-analysis was conducted to analyze the efficacy of aerobic and resistance exercise in patients with NAFLD.

## Materials and Methods

### Literature search

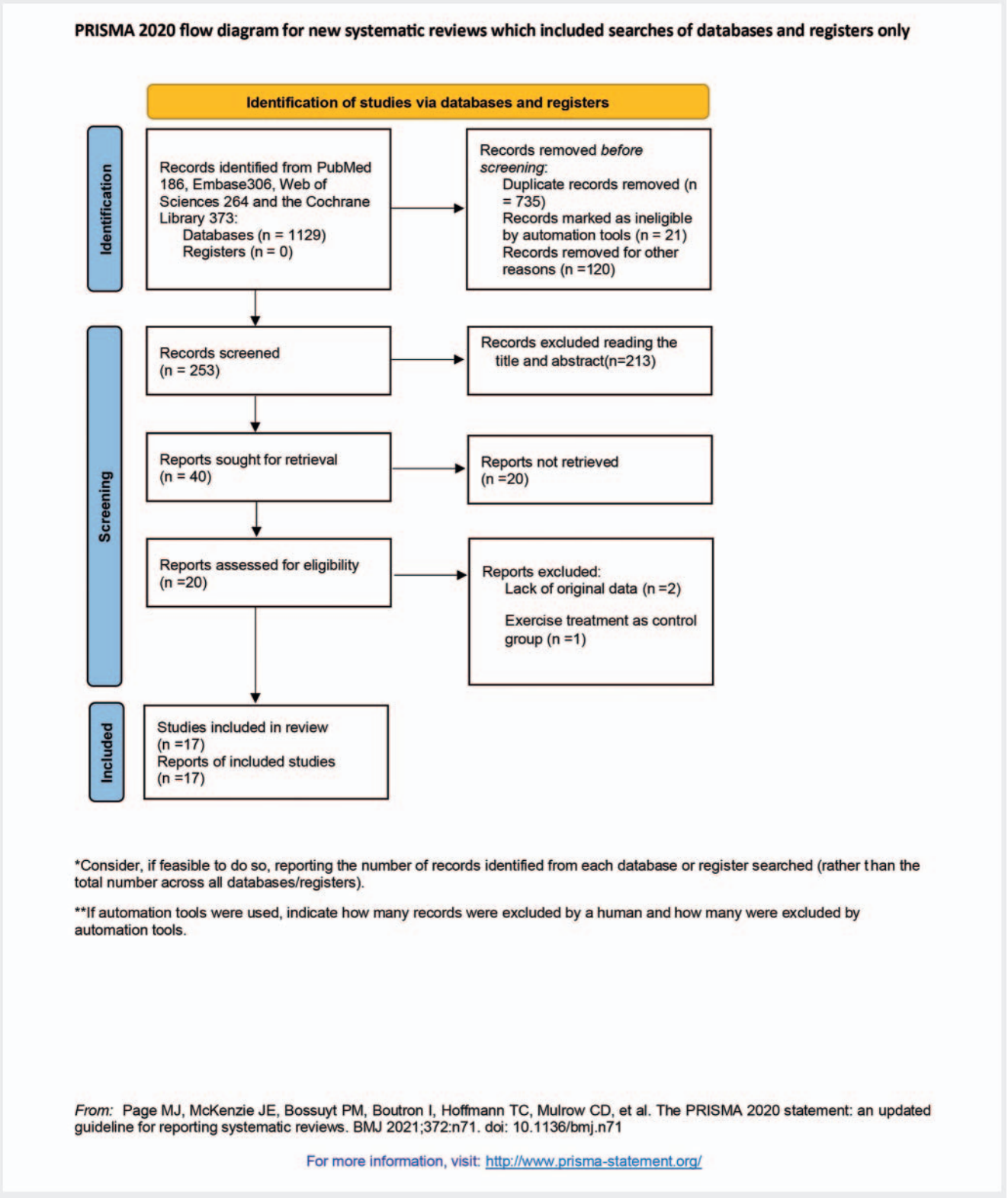
The medical subject heading (MeSH) and related entry terms were applied in Web of Science, PubMed, Embase, and Cochrane Library. We list the key to PubMed here, and the access to the rest of the database can be found in the supplementary materials (S1). We researched it under Title/Abstract in PubMed Advanced Retrieval. The brief expression is as follows: (non-alcoholic fatty liver disease OR NAFLD OR fatty liver, nonalcoholic OR nonalcoholic steatohepatitis OR steatohepatitis, nonalcoholic) AND (exercises OR physical activity OR acute exercise OR isometric exercises OR aerobic exercise OR exercise training) AND (randomized controlled trial [RCT] OR randomized OR placebo). We selected articles published before September 1, 2021, according to the above keyword search.

### Inclusion and exclusion criteria

The 2 authors (Ao and Zheng) independently browsed the retrieved articles through the title and abstract and then screened the articles according to the following inclusion and exclusion criteria. If there was disagreement about inclusion, another researcher (LX Fu) was the arbitrator to decide." The inclusion criteria were as follows: (1) the selected articles were RCTs; (2) patients were adults diagnosed with NAFLD; (3) the experimental group received either aerobic exercise alone or aerobic exercise with resistance exercise; and (4) the data were presented as the mean ± standard deviation (SD). By contrast, the exclusion criteria were (1) pregnant or juvenile; (2) a lack of details even if the authors were emailed; and (3) no control group was used. Because the primary intervention measure in this paper was to evaluate the effect of exercise therapy on patients with NAFLD, if the frequency and mode of exercise were clearly defined, the sample size may be reduced, so the above conditions were not further limited.

### Data extraction

Two authors (LX Fu and WY Zhang) scanned the subjects and abstracts of all potential articles independently. They extracted the number, age, and region of patients, period of intervention, design of the study, and date of publication. Then the authors extracted the outcome indicators such as transaminase, blood glucose (Glu), visceral fat content, and so on. For insufficient or




▶ **Fig. 1** PRISMA flow diagram representing the different phases of this study.

▶ **Table 1** The basic characteristic of included studies.

| Author | Year | N (inter/con) | Age (inter) | Age (cont) | Intervention | Control | Duration | Diagnosis | study design |
|---|---|---|---|---|---|---|---|---|---|
| Houghton D[19] | 2017 | 24(12/12) | 54 ± 12 | 51 ± 16 | aerobic + resistance | standard care | 12 weeks | NASH | randomized controlled trial |
| Abdelbasset WK[24] | 2019 | 32 (16/16) | 54.4 ± 5.8 | 55.2 ± 4.3 | medical + aerobic | medical | 8 weeks | NAFLD with T2DM | randomized controlled trial |
| Abdelbasset WK[23] | 2020 | 47 (31/16) | 54.9 ± 4.7 | 55.2 ± 4.3 | aerobic | medical | 8 weeks | NAFLD with T2DM | randomized controlled trial |
| Jia GY[15] | 2018 | 461 (307/154) | 55.18 ± 7.42 | 54.24 ± 7.51 | aerobic + resistance | standard care | 6 months | NAFLD | randomized controlled trial |
| Shojaee-Moradie F[22] | 2016 | 27 (15/12) | 52.4 ± 2.2 | 52.8 ± 3.0 | aerobic + resistance | advice | 16 weeks | NAFLD | randomized controlled trial |
| Hallsworth K[18] | 2015 | 23 (11/12) | 54 ± 10 | 52 ± 12 | aerobic | standard care | 12 weeks | NAFLD | randomized controlled trial |
| Sullivan S[25] | 2012 | 18 (12/6) | 48.6 ± 2.2 | 47.5 ± 3.1 | aerobic | continue the daily activities | 16 weeks | NAFLD | randomized controlled trial |
| Pugh CJ[20] | 2013 | 11 (6/5) | 50 ± 7.49 | 48 ± 10.83 | aerobic | conventional care | 16 weeks | NAFLD | randomized controlled trial |
| Pugh CJ[21] | 2014 | 21 (13/8) | 48 ± 6.44 | 47 ± 5.77 | aerobic | conventional care | 16 weeks | NAFLD | randomized controlled trial |
| Zelber-Sagi S[30] | 2014 | 64 (33/31) | 46.32 ± 10.32 | 46.64 ± 11.4 | resistance | stretching | 12 weeks | NAFLD | randomized controlled trial |
| Shamsoddini A[28] | 2015 | 30 (20/10) | 45.9 ± 7.3 | 45.8 ± 7.3 | aerobic + resistance | no intervention | 8 weeks | NAFLD | randomized controlled trial |
| Cuthbertson DJ[17] | 2016 | 50 (30/20) | 50 ± 16.76 | 52 ± 14.83 | aerobic | advice | 16 weeks | NAFLD | randomized controlled trial |
| Zhang HJ[16] | 2016 | 208 (135/73) | 54.4 ± 7.4 | 54 ± 6.8 | aerobic | no intervention | 12 months | NAFLD | randomized controlled trial |
| Cheng S[14] | 2017 | 40 (22/18) | 59 ± 4.4 | 60 ± 3.4 | aerobic | no intervention | 6 months | NAFLD | randomized controlled trial |
| Eckard C [26] | 2013 | 20 (9/11) | 52 ± 10 | 51 ± 11 | aerobic | standard care | 6 months | NAFLD | randomized controlled trial |
| Hoseini Z [29] | 2020 | 40 (30/10) | 62.6 ± 1.89 | 62 ± 1.88 | aerobic training | placebo | 2 months | NAFLD with VitD deficiency | randomized controlled trial |
| Franco I[30] | 2021 | 52 (35/17) | 50.45 ± 9.45 | 50.7 ± 8.67 | aerobic | control diet | 12 weeks | NAFLD | randomized controlled trial |

NAFLD, nonalcoholic fatty liver disease; T2DM, type 2 diabetes.

unclear data, the study was excluded if the corresponding authors could not be reached.

### Evaluation of bias

Zhang and Ao evaluated the risk of bias based on the Cochrane Handbook for Systematic Reviews of Interventions. If there was any difference between the 2 scores, it was resolved through discussion [13]. There were 6 points used to evaluate the quality of each study (random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other bias), and the consequences of assessment were illustrated in the form of low risk of bias, unclear risk of bias, or high risk of bias.

### Statistical analysis

We used Stata SE (version 12.0) to test the continuous variables in this meta-analysis. Each study's mean difference and SD were extracted and transformed for the intervention and control groups to calculate the effect sizes for each outcome parameter. The data in the form of the mean ± SE were transferred to mean ± SD by the following formula: $mean_{change}$ = mean (end) − mean (start);

$SD = SE \times \sqrt{\eta}$ (n: number of patients)

and $SD_{change} = \sqrt{(SD\ (start)^2 + SD\ (end)^2 - (2R \times SD\ (start) \times SD\ (end))}$, the r (correlation coefficient) = 0.5 [13]. If the reported results were different from other studies in terms of dimensions and measurement methods, we adopted the standard mean difference (SMD) to summarize the data; otherwise, the outcomes are presented in the form of the weighted mean difference (WMD) with 95 % confidence interval (CI). The random-effects model and 95 % prediction interval (PI) were only used when $I^2 \geq 50\,\%$ and $p < 0.1$; in other cases, the fixed-effects model was used. The results were statistically significant when WMD/SMD had a gap of 0 ($p < 0.05$); however, they were negative when WMD/SMD was close to 0 ($p > 0.05$). In addition, subgroup analyses of the geographical region (Europe, Asia, and North America) and intervention period (≤ 16 weeks and > 16 weeks) were investigated to examine the heterogeneity between studies.

## Results

### Study features

We collected 1129 published articles from 4 databases in the first online search, and we selected a total of 20 studies according to the inclusion and exclusion criteria. Three articles were deleted, including 2 studies that lacked original data and 1 that took exercise intervention as the control group, and so 1168 patients in 17 articles were finally included. The flow diagram is shown in ▶ **Fig. 1**. Among the involved RCTs, 3 trials were performed in China [14, 15, 16], 6 in the UK [17, 18, 19, 20, 21, 22], 2 in Saudi Arabia [23, 24], 1 in the USA [25], 2 in Italy [26, 27], 2 in Iran [28, 29], and 1 in Israel [30], The general exercise frequency of selected studies was 35 times a week, the longest duration was 48 weeks, and the shortest was 8 weeks. The basic characteristics of the involved studies are shown in ▶ **Table 1**.

### Quality assessment

We evaluated each study for the risk of bias based on 6 points of assessment (▶ **Table 2**). Due to the different qualities of each study, the assessment of 6 points was also unequal. The vast majority of enrolled studies were evaluated as low risk of bias, while the remaining portion is marked as unclear in ▶ **Table 2**: only 3 trials were considered unclear for random sequence generation [20, 22, 28], 6 for allocation concealment [17, 21, 25, 26, 28, 29], 7 for blinding [16, 18, 19, 22, 25, 27, 28], and 1 for free of other bias [23].

### The effect of aerobic and resistance exercise on weight and BMI

We analyzed body weight and BMI (▶ **Fig. 2**) in patients with NAFLD. Because the heterogeneity is small, we chose the fixed effect model. Exercise treatment reduced weight by 1.87 kg (95 % CI [−2.43 to −1.32], $p < 0.0001$, $I^2 = 0.0\,\%$) and reduced BMI by 0.38 (95 % CI [−0.57 to −0.18], $p < 0.0001$, $I^2 = 0.0\,\%$).

### The effect of aerobic and resistance exercise on liver enzymes

This meta-analysis shows that aerobic and resistance exercise can reduce alanine aminotransferase (ALT) and aspartate aminotransferase (AST), but the effect on γ-glutamyl transferase (GGT) was not statistically significant. Exercise reduced the ALT level by 3.29 (U/L) (95 % CI [−4.60 to −1.97], $p < 0.0001$, $I^2 = 0.0\,\%$) and AST (WMD = −1.50 at 95 % CI [−2.42 to −0.58], $p = 0.001$, $I^2 = 24.1\,\%$), yet GGT showed less significance (WMD = −2.12 at 95 % CI [−4.49 to 0.25], $p = 0.079$, $I^2 = 0.0\,\%$). The above conclusions will be shown in ▶ **Fig. 3**, ▶ **Fig. 4**, ▶ **Fig. 5**.

### The effect of aerobic and resistance exercise on lipid metabolism

We analyzed cholesterol (TC), triglycerides (TG), intrahepatic triglycerides, and visceral adipose tissue. Considering the different units of TC and TG in the included study, we adopted SMD to summarize the data. It is worth noting that the heterogeneity of TC and TG is significant, so we adopted the random effect model and calculated the 95 % PI. The outcomes implied that the patients in the exercise group had lower TC (SMD = −0.30 at 95 % CI [−0.52 to −0.09], 95 % PI [−0.98 to 0.38], $p = 0.005$, $I^2 = 59.8\,\%$) and TG (SMD = −0.30 at 95 % CI [−0.54 to −0.07], 95 % PI [−1.16 to 0.55], $p = 0.012$, $I^2 = 70.6\,\%$). Furthermore, exercise treatment reduced the visceral adipose tissue level by $-8.30\ cm^2$ (95 % CI [−11.59 to −5.00], $p < 0.0001$, $I^2 = 44.8\,\%$), intrahepatic triglycerides (WMD = −2.36 at 95 % CI [−4.43 to −0.30], $p = 0.025$, $I^2 = 0.0\,\%$) (▶ **Fig. 6**, ▶ **Fig. 7**). Through sensitivity analysis, we concluded that the heterogeneity of TC mainly comes from 3 studies [23, 24, 29]; after deleting these studies, the heterogeneity ($I^2$ index) decreased from 59.8 % to 1.0 %, and the overall effects still exhibited significant differences. Also, 2 studies [23, 24] exhibited significant heterogeneity in TG compared with other

▶ **Table 2** Risk of bias.

| Study | Random sequence generation | Allocation concealment | Blinding | Incomplete outcome data | Selective reporting | Free of other bias |
|---|---|---|---|---|---|---|
| Houghton D, 2017 | L | L | U | L | L | L |
| Abdelbasset WK 2019 | L | L | L | L | L | L |
| Abdelbasset WK 2020 | L | L | L | L | L | U |
| Jia GY 2018 | L | L | L | L | L | L |
| Shojaee-Moradie F, 2016 | U | L | U | L | L | L |
| Hallsworth K, 2015 | L | L | U | L | L | L |
| Sullivan S, 2012 | L | U | U | L | L | L |
| Pugh CJ, 2013 | U | L | L | L | L | L |
| Pugh CJ, 2014 | L | U | L | L | L | L |
| Zelber-Sagi S, 2014 | L | L | L | L | L | L |
| Shamsoddini A, 2015 | U | U | U | L | L | L |
| Cuthbertson DJ, 2016 | L | U | L | L | L | L |
| Zhang HJ, 2016 | L | L | U | L | L | L |
| Cheng S, 2017 | L | L | L | L | L | L |
| Eckard C, 2013 | L | U | L | L | L | L |
| Hoseini Z, 2020 | L | U | L | L | L | L |
| Franco I, 2021 | L | L | U | L | L | L |

L: low risk of bias; U: unclear of bias

studies; the heterogeneity decreased significantly after the deletion of these 2 studies. From another point of view, because of the different intervention times and population regions in the study, we found that they could significantly affect the effect by meta-regression, $p < 0.05$. Based on this conclusion, the subgroup analyses were carried out based on the intervention period (≤ 16 weeks and > 16 weeks) and region of patients (Europe, Asia, and North America). In all subgroups analyses, the heterogeneity of TC decreased only in > 16 weeks of treatment duration times (SMD = −0.16 at 95 % CI [−0.29 to −0.03], $p = 0.020$, $I^2 = 0.0\,\%$). and decreased in Europe group (SMD = 0.03 at 95 % CI [−0.27 to −0.33], $p = 0.849$, $I^2 = 0.0\,\%$); and the heterogeneity of TG decreased only in the Europe group (SMD = −0.14 at 95 % CI [−0.46 to −0.17], $p = 0.375$, $I^2 = 26.0\,\%$), and different intervention cycles have no effect. Even so, these results could not explain all sources of heterogeneity.

### The effect of aerobic and resistance exercise on glucose metabolism

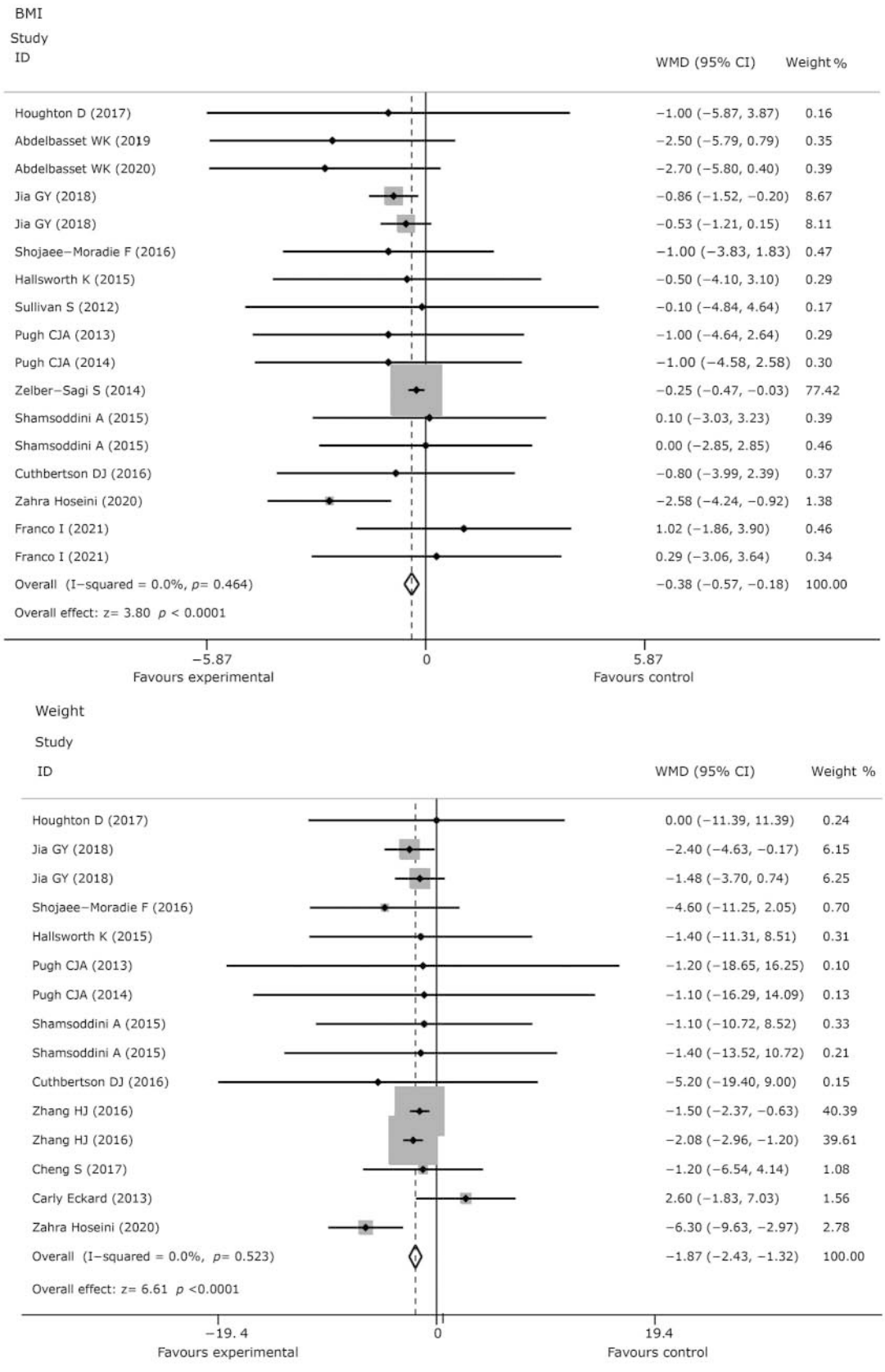
The parameters of this section included Glu, insulin, and HOMA-IR (▶ **Fig. 8**, ▶ **Fig. 9**, ▶ **Fig. 10**). Given the different units of the above indicators, the SMD was used to summarize the Glu, insulin, and HOMA-IR data. Random effect model and heterogeneity in Glu were detected. Aerobic and resistance exercise reduced Glu (SMD = −0.26 at 95 % CI [−0.45 to −0.07], 95 % PI [−0.84 to 0.31] $p = 0.006$, $I^2 = 51.8\,\%$) and HOMA-IR (SMD = −0.36 at 95 % CI [−0.49 to −0.23], $p < 0.0001$, $I^2 = 46.4\,\%$). However, there was no significant statistical difference in insulin ($p = 0.243$). Sensitivity analysis showed that the heterogeneity was mainly due to the source of Hoseini's study [29], and the $I^2$ index decreased from 51.8 % to 21.5 % after deleting this article. Nevertheless, meta-regression did not suggest that regional distribution and intervention cycle were the source of heterogeneity, $p > 0.05$. So no further subgroup analysis was performed.

### Publication bias

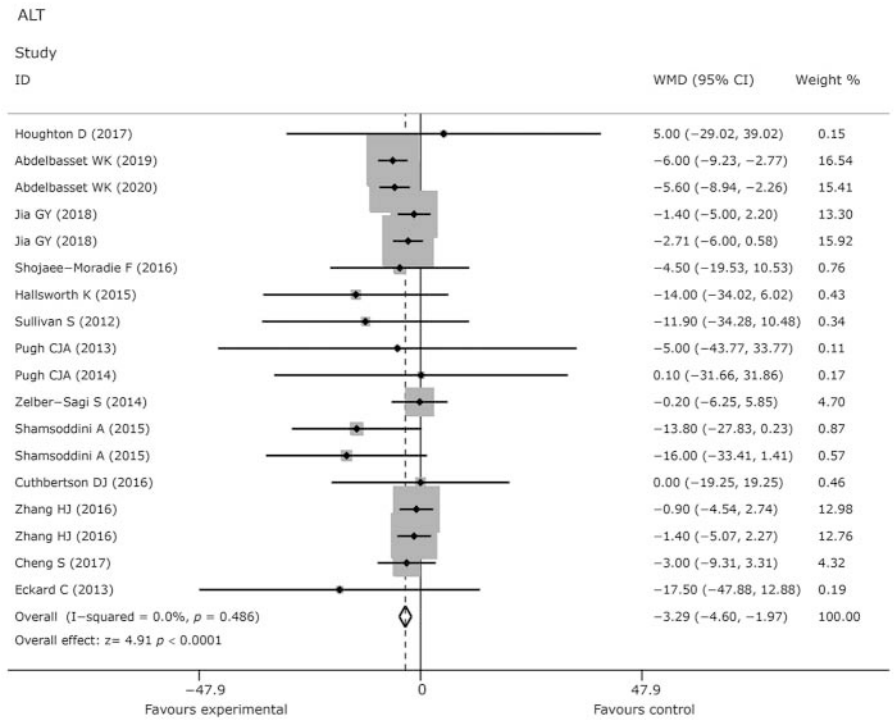
To evaluate publication bias, Egger's test was constructed for BMI ($p = 0.088$), weight ($p = 0.845$), ALT ($p = 0.247$), AST ($p = 0.131$), TC ($p = 0.217$), TG ($p = 0.264$), Glu ($p = 0.609$), and HOMA-IR ($p = 0.361$), which included more than 10 trials. The outcomes were deemed to show no publication bias.

## Discussion

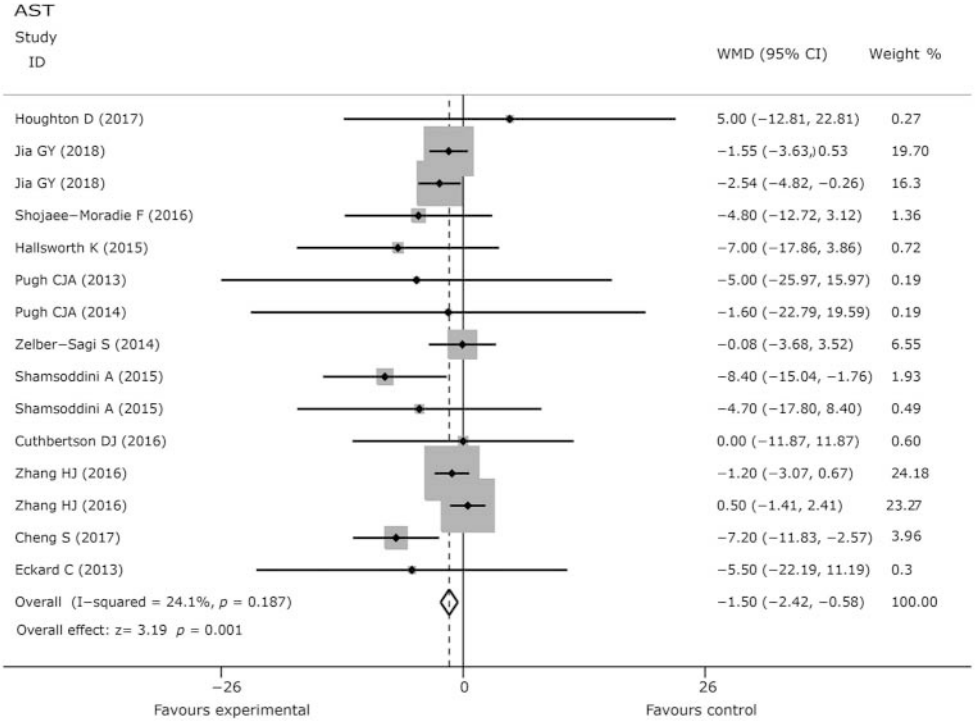
NAFLD is a chronic liver disorder that affects approximately 24 % of the adult population worldwide [31]. Therefore, we aimed to investigate the beneficial impact of aerobic and resistance exercise among patients with NAFLD. Our study outcomes suggested that aerobic and resistance exercise can significantly improve liver enzymes, serum and intrahepatic lipid levels, Glu metabolism levels, and BMI and weight. NAFLD is commonly accompanied by



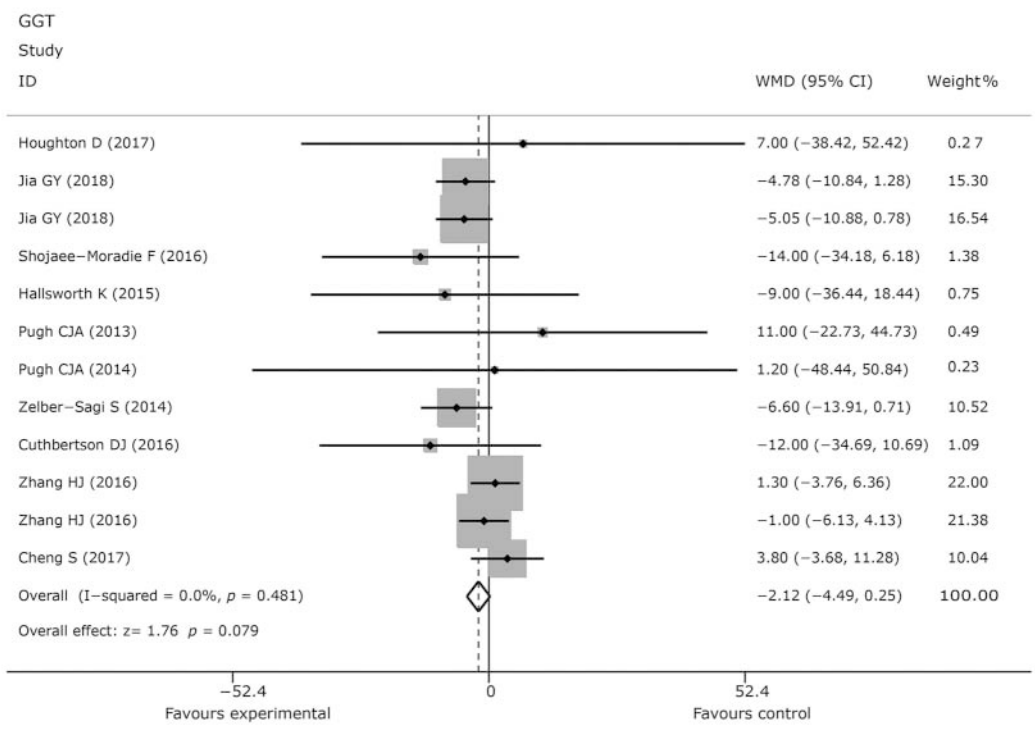

▶ **Fig. 2** Forest plot of the meta-analysis comparing the experimental and control groups in terms of anthropometric parameters.




▶ **Fig. 3** Forest plot of the meta-analysis comparing the experimental and control groups in terms of ALT.




▶ **Fig. 4** Forest plot of the meta-analysis comparing the experimental and control groups in terms of AST.

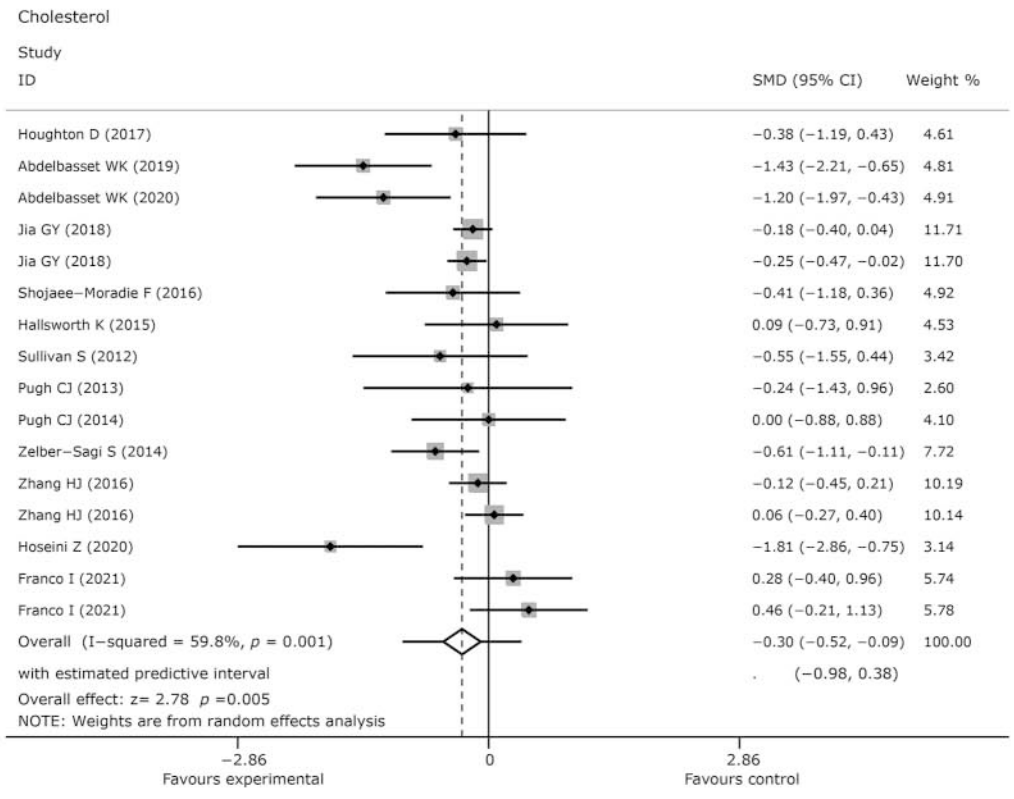


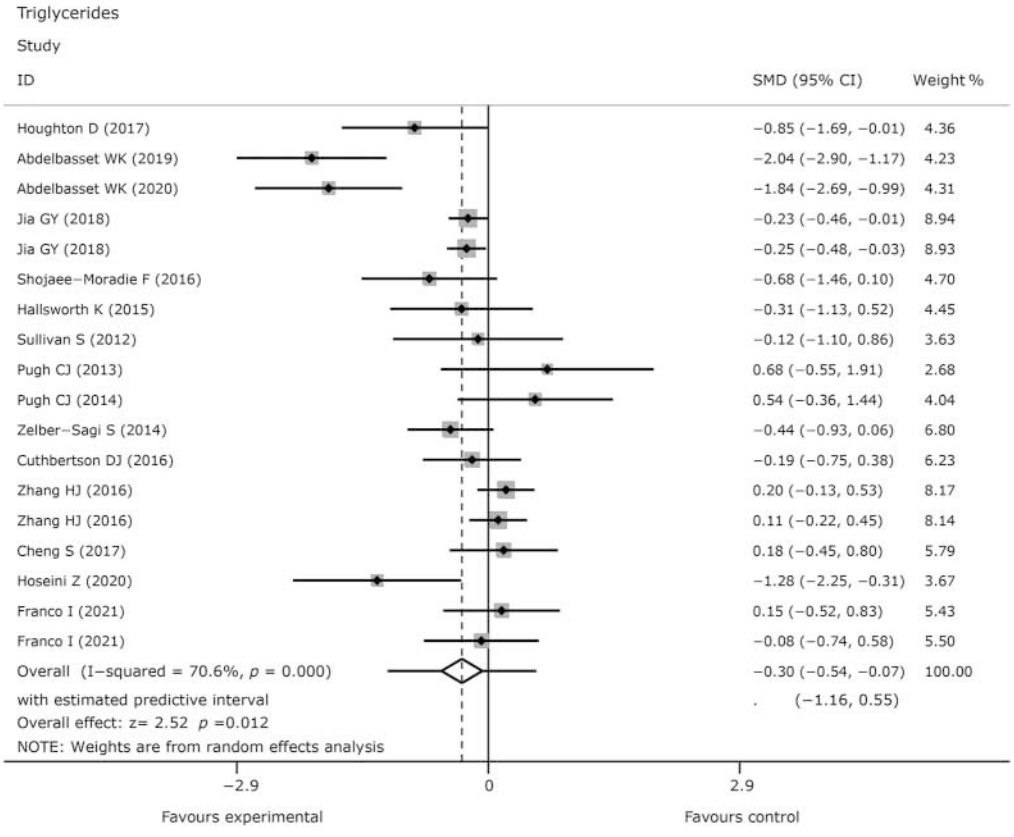

▶ **Fig. 5** Forest plot of the meta-analysis comparing the experimental and control groups in terms of GGT.

T2DM [32], cardiovascular disease, and chronic kidney diseases, so we did not exclude articles that included patients with NAFLD with other complications.

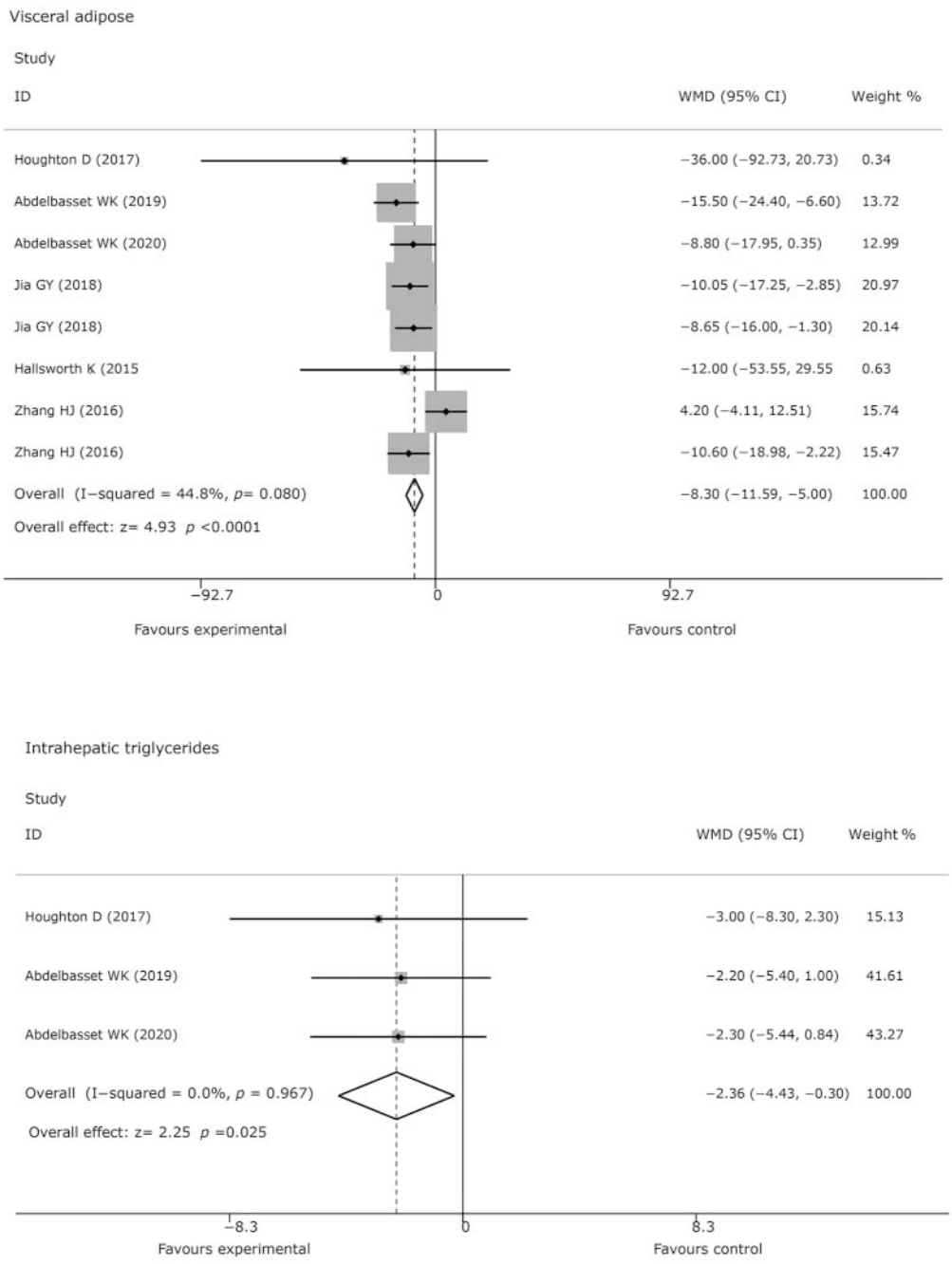
Due to their ability to improve multiple physiological impairments, aerobic and resistance exercises have been applied for chronic diseases at similar frequencies [33, 34, 35]. Studies have suggested that a higher frequency improves chronic inflammation, calories burned, and cardiovascular health [36, 37, 38]. Among the selected studies, the exercise frequencies of patients in the experimental group were 3–5 times/week, and subgroup analysis of exercise frequency was not performed. Although its advantages include its low-cost nonpharmacological nature, low trauma, and ease of implementation, 3 studies reported the side effect of arthralgia during the intervention, which was caused by excessive exercise [15, 16, 30]. Regarding the type of intervention, aerobic exercise (walking, jumping rope, biking, etc.) consumes more energy, is more effective for fat loss, and requires less fitness equipment; however, its requirement of high cardiorespiratory fitness and persistence may make it not beneficial for patients with poor cardiopulmonary function [39]. On the other hand, resistance exercise can enhance muscular strength, muscle mass, and bone density and improve metabolic parameters with less energy consumption [40]. Therefore, resistance exercise is more practicable in patients with NAFLD with poor cardiopulmonary function. In this meta-analysis, subgroups of intervention types were not performed for combined aerobic and resistance exercise in experimental groups. The number of included trials of > 16 weeks was far less than the number of trials ≤ 16 weeks, which may have contributed to the less significant subgroup analysis. Previous studies suggested the beneficial impact of exercise on ALT, AST, Glu, TG, and so on. On these bases, our study also included the latest published articles and analysis of visceral adipose tissue. In this meta-analysis, the changes of liver enzyme index, Glu and lipid metabolism, and visceral adipose tissue can reflect the benefit of an exercise intervention to NAFLD patients. Among them, the reason for the slight decrease in the value of liver enzymes may be that the baseline indicators of the patients included are not high, but overall, it is still meaningful.

There are still some limitations of this study, and the findings should be interpreted cautiously. Firstly, the risk of bias evaluated may be subjective. The primary intervention in this study is exercise therapy; although the trials were performed in a blinded manner, the unclear risk of bias was also hard to avoid. Thus, some “unclear of bias” was changed to “low risk of bias” in the blinding item of risk of bias, which may influence the whole analysis. Furthermore, the exercise assessment may have been greater than the actual amount of exercise performed due to the unblinding measurement in studies. Moreover, 1/3 of the trials were performed in the UK; we cannot rule out that regional factors lead to the research bias. Besides, the bias may be in 4 trials conducted by 2 authors in 2 consecutive years [20, 21, 23, 24]. While this study included more experiments than previously published analyses, some subgroup analyses still lacked correct conclusions due to the relatively small sample quantities. Studies by Shojaee-Moradie et al. and Hallsworth et al. have shown that exercise can not only reduce liver enzymes but also improve diastolic cardiac function [18, 22]. Unfortunately, the included studies also excluded people with poor general conditions, and there were few stud-




▶ **Fig. 6** Forest plot of the meta-analysis comparing the experimental and control groups in terms of cholesterol and triglycerides.




▶ **Fig. 7** Forest plot of the meta-analysis comparing the experimental and control groups in terms of visceral adipose and intrahepatic triglycerides.

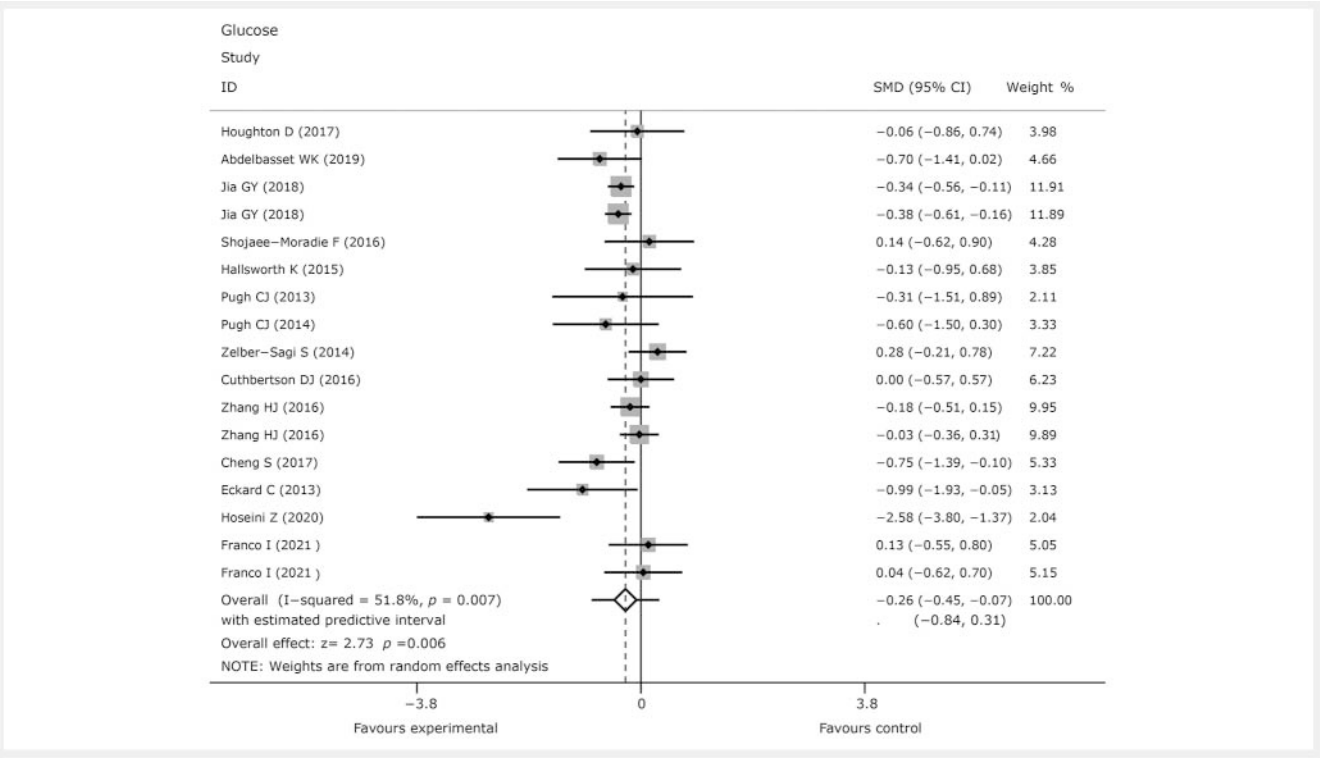
ies on exercise frequency and intensity, so we did not conduct a subgroup analysis, which may not be conducive to individualized therapy. Finally, more articles are needed to analyze and study the above contents in the future to benefit patients with NAFLD.

In summary, our study suggested that aerobic and resistance exercise improved lipids, Glu, liver function, and other indicators in patients with NAFLD, and especially had visceral adipose-lowering effects, which is of great significance to the treatment of NAFLD. This result is not found in other articles. Further studies are needed to determine the effects of long durations of intervention, different geographical regions, and the safety of physical activity.

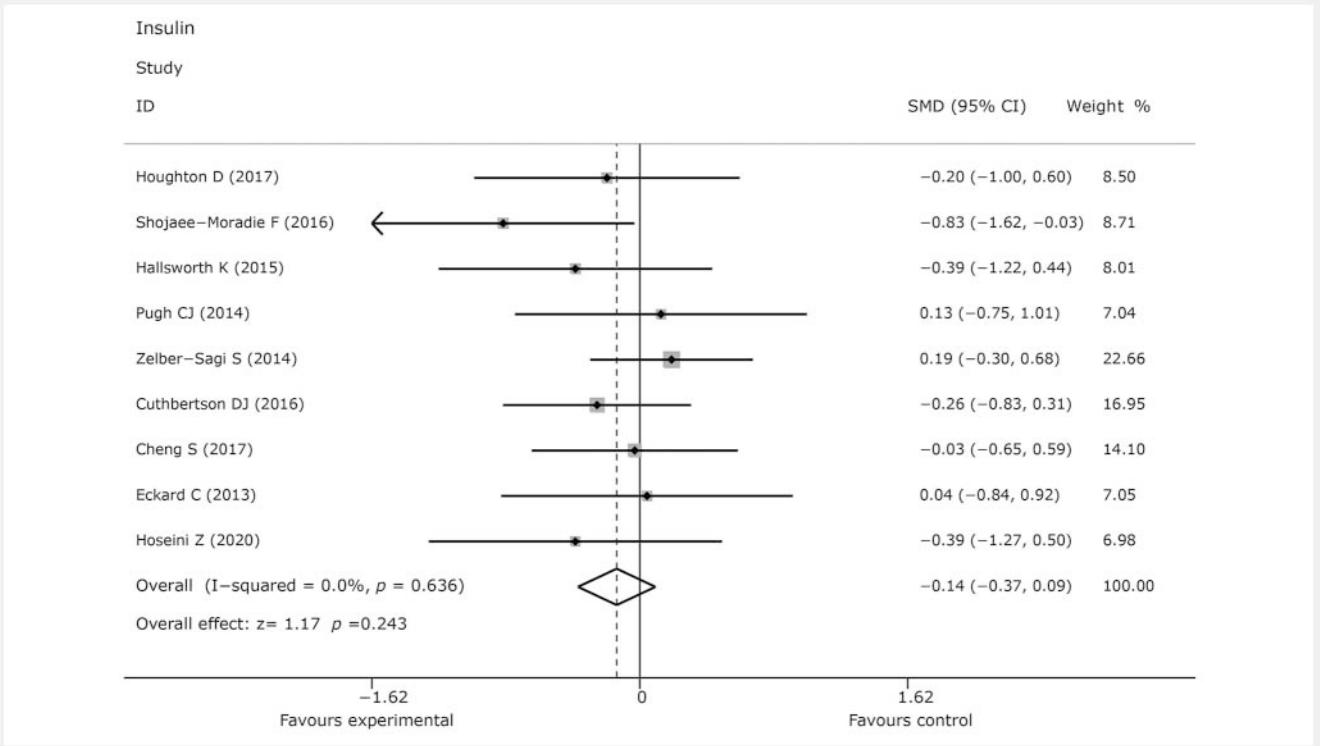
## Declarations

### Registration information

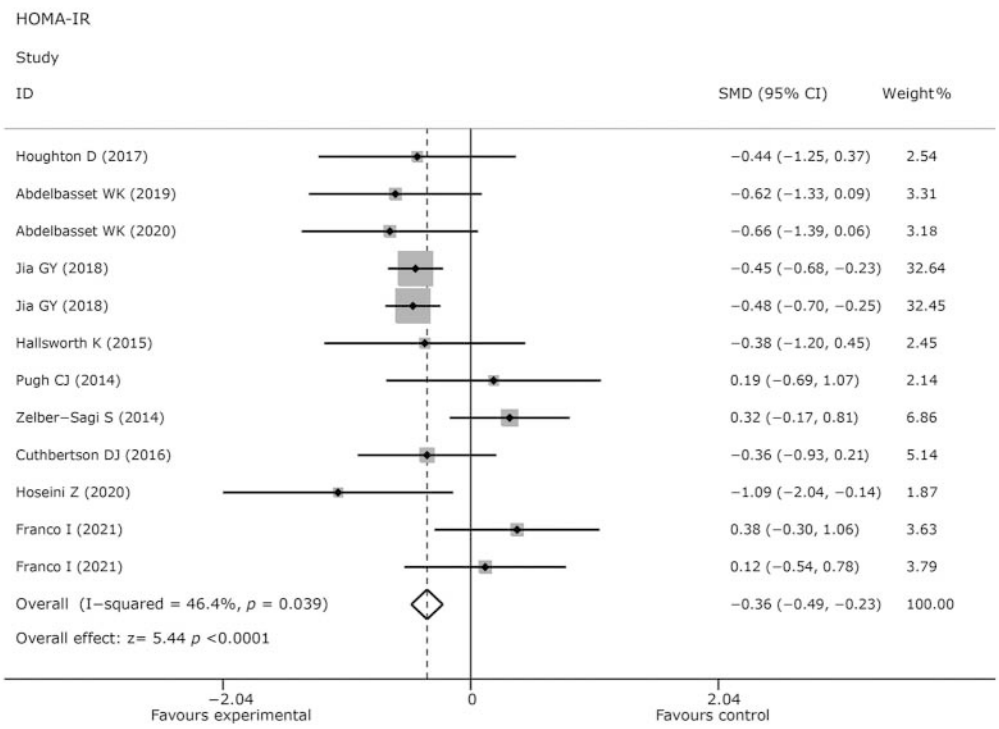
This research has not been registered, and no plan can be provided.




▶ **Fig. 8** Forest plot of the meta-analysis comparing the experimental and control groups in terms of glucose.




▶ **Fig. 9** Forest plot of the meta-analysis comparing the experimental and control groups in terms of insulin.




▶ **Fig. 10** Forest plot of the meta-analysis comparing the experimental and control groups in terms of HOMA-IR.

## Availability of data and material

All data generated or analyzed in the study are included in this article.

## Search strategies

### Web Of Science

#1 TS = (nonalcoholic fatty liver disease OR non alcoholic fatty liver disease OR NAFLD OR nonalcoholic fatty liver disease OR fatty liver, nonalcoholic OR fatty livers, nonalcoholic OR liver, nonalcoholic fatty OR livers, nonalcoholic fatty OR nonalcoholic fatty liver OR nonalcoholic fatty livers OR nonalcoholic steatohepatitis OR nonalcoholic steatohepatitides OR steatohepatitides, nonalcoholic OR steatohepatitis, nonalcoholic )

#2 TS = (exercise OR exercises OR physical activity activities, physical OR activity, physical OR physical activities OR exercise, physical OR exercises, physical OR physical exercise OR physical exercises OR acute exercise OR acute exercises OR exercise, acute OR exercises, acute OR exercise, isometric OR exercises, isometric OR isometric exercises OR isometric exercise OR exercise, aerobic OR aerobic exercise OR aerobic exercises OR exercises, aerobic OR exercise training OR exercise trainings OR training, exercise OR trainings, exercise)

#3 TS = (randomized OR randomized controlled trial)

#4 #1 AND #2 AND #3

### Cochrane Library

#1 MeSH descriptor: [non-alcoholic fatty liver disease] explode all trees

#2 (non alcoholic fatty liver disease):ti,ab,kw OR (NAFLD):ti,ab,kw OR (nonalcoholic fatty liver disease):ti,ab,kw OR (fatty liver, nonalcoholic):ti,ab,kw OR (fatty livers, nonalcoholic):ti,ab,kw OR (liver, nonalcoholic fatty):ti,ab,kw OR (livers, nonalcoholic fatty):ti,ab,kw OR (nonalcoholic fatty liver):ti,ab,kw OR (nonalcoholic fatty livers):ti,ab,kw OR (nonalcoholic steatohepatitis):ti,ab,kw OR (nonalcoholic steatohepatitides):ti,ab,kw OR (steatohepatitides, nonalcoholic):ti,ab,kw OR (steatohepatitis, nonalcoholic):ti,ab,kw

#3 #1 OR #2

#4 MeSH descriptor: [Exercise] explode all trees

#5 (exercises):ti,ab,kw OR (physical activity):ti,ab,kw OR (activities, physical):ti,ab,kw OR (activity, physical):ti,ab,kw OR (physical activities):ti,ab,kw OR (exercise, physical):ti,ab,kw OR (exercises, physical):ti,ab,kw OR (physical exercise):ti,ab,kw OR (physical exercises):ti,ab,kw OR (acute exercise):ti,ab,kw OR (acute exercises):ti,ab,kw OR (exercise, acute):ti,ab,kw OR (exercises, acute):ti,ab,kw OR (exercise, isometric):ti,ab,kw OR (exercises, isometric):ti,ab,kw OR (isometric exercises):ti,ab,kw OR (isometric exercise):ti,ab,kw

#6 #4 OR #5

#7 #3 AND #6

### Embase

#1 ‘nonalcoholic fatty liver’/exp

#2 ‘non alcoholic fatty liver disease’:ab,ti or ‘NAFLD’:ab,ti or ‘nonalcoholic fatty liver disease’:ab,ti or ‘fatty liver, nonalcoholic’:ab,ti or ‘fatty livers, nonalcoholic’:ab,ti or ‘liver, nonalcoholic fatty’:ab,ti or ‘livers, nonalcoholic fatty’:ab,ti or ‘non-alcoholic fatty

liver disease':ab,ti or 'nonalcoholic fatty livers':ab,ti or 'non-alcoholic steatohepatitis':ab,ti or 'nonalcoholic steatohepatitides':ab,ti or 'steatohepatitides, nonalcoholic':ab,ti or 'steatohepatitis, nonalcoholic':ab,ti

#3 #1 OR #2

#4'exercise'/exp

#5'exercises':ab,ti OR 'physical activity':ab,ti OR 'activities, physical':ab,ti OR 'activity, physical':ab,ti OR 'physical activities':ab,ti OR 'exercise, physical':ab,ti OR 'exercises, physical':ab,ti OR 'physical exercise':ab,ti OR 'physical exercises':ab,ti OR 'acute exercise':ab,ti OR 'acute exercises':ab,ti OR 'exercise, acute':ab,ti OR 'exercises, acute':ab,ti OR 'exercise, isometric':ab,ti OR 'exercises, isometric':ab,ti OR 'isometric exercises':ab,ti OR 'isometric exercise':ab,ti OR 'exercise, aerobic':ab,ti OR 'aerobic exercise':ab,ti OR 'aerobic exercises':ab,ti OR 'exercises, aerobic':ab,ti OR 'exercise training':ab,ti OR 'exercise trainings':ab,ti OR 'training, exercise':ab,ti OR 'trainings, exercise':ab,ti

#6 #4 OR #5

#7 'randomized controlled trial':ab,ti OR 'randomized':ab,ti OR 'placebo':ab,ti

#8 #3 AND #6 AND #7

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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