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Effects of Mediterranean diet, exercise, and their combination on body composition and liver outcomes in metabolic dysfunction-associated steatotic liver disease: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of liver-related morbidity and mortality. Lifestyle interventions like the Mediterranean diet (MD) and exercise are recommended for management, but the most effective lifestyle approach remains unclear.

Methods A comprehensive literature search was conducted in Embase, MEDLINE via Ovid, Cochrane Central, and Web of Science Core Collection from inception to April 1, 2025, without language restrictions. We included randomized controlled trials (RCTs) in adults with MASLD or metabolic dysfunction-associated steatohepatitis (MASH) assessing the MD and/or exercise interventions on anthropometric measures, liver enzymes, and indices or grades of liver steatosis and fibrosis. The mean difference and corresponding 95% confidence interval (CI) were pooled using a random-effects model. Risk of bias was assessed with ROB-2, and evidence certainty was evaluated using GRADE.

Results From a total of 4806 search results, 37 unique RCTs met the inclusion criteria, from which 11 assessed the MD and 27 exercise, either aerobic, resistance, or in combination, and two RCTs assessed the effect of the MD and exercise combination. Meta-analyses showed that the MD in comparison with the control significantly reduced body weight [weighted mean difference (WMD = −2.38 kg, 95% CI −4.11 to −0.66), body mass index (WMD = −0.70 kg/m^2, 95% CI = −1.03 to −0.36), waist circumference (WC) (WMD = −1.56 cm, 95% CI −3.02 to −0.09), and alanine aminotransferase (ALT) (WMD = −3.96 IU/L, 95% CI −6.54 to −1.38). Aerobic and combined aerobic-resistance

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exercises in comparison with the control group reduced body weight (WMD = − 1.56 kg, 95%CI − 2.31 to − 0.82; WMD = − 1.90 kg, 95%CI − 3.59 to − 0.22, respectively). In addition, aerobic exercise significantly decreased WC (WMD = − 2.14 IU/L, 95%CI − 2.87 to − 1.41) and resistance exercise reduced ALT (WMD = − 15.40 IU/L, 95%CI − 28.60 to − 2.20) in patients with MASLD/MASH compared to the control group.

Conclusions The MD and aerobic exercise, whether alone or combined with resistance training, support weight loss and improve liver health in patients with MASLD/MASH. Standardized methods for measuring and reporting outcomes are essential to build robust evidence on the impact of lifestyle changes on clinical outcomes.

Trial registration PROSPERO registration code.

CRD42024577846.

Keywords Lifestyle, Metabolic dysfunction-associated steatotic liver disease, Non-alcoholic fatty liver disease, Metabolic dysfunction-associated steatohepatitis, Mediterranean diet, Exercise, Systematic review, Meta-analysis

Background

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the leading cause of liver-related morbidity and mortality worldwide. Its prevalence in the adult population ranges from 32% [1] to 37% [2], with even higher rates in individuals with obesity (up to 75%) [3] and type 2 diabetes (T2D) (56%) [4]. As metabolic diseases continue to become more widespread, the prevalence of MASLD is expected to rise at an alarming rate [1]. Previously known as non-alcoholic fatty liver disease (NAFLD) [5], MASLD is a complex and heterogeneous condition characterized by abnormal hepatic fat accumulation unrelated to alcohol consumption or specific liver toxins [6, 7]. The clinical spectrum of MASLD is broad, encompassing simple steatosis and progressing to metabolic dysfunction-associated steatohepatitis (MASH), which may lead to fibrosis and, ultimately, hepatocellular carcinoma [7].

Various pharmacological and nutraceutical interventions have been explored; however, their application in clinical settings remains constrained due to concerns about their efficacy, the limited number of high-quality research, and potential side effects [8]. In view of this and given that MASLD is highly prevalent in overweight/obesity patients, and it is associated with cardiometabolic risk, there is growing interest in lifestyle interventions to address steatotic liver disorders [9]. Moreover, interventions in diet and physical activity are considered to be the cornerstone of management in the whole MASLD spectrum [7, 10]. Current guidelines recommend weight loss through dietary modifications, increased physical activity, or both combined in MASLD patients [7, 11, 12]. Evidence suggests that achieving a 7–10% reduction in body weight through a low-fat, hypocaloric diet combined with regular exercise can effectively resolve steatosis, reduce inflammation, and regress fibrosis in MASLD [11–13]. However, there is no consensus on the most effective lifestyle strategy [10, 11].

Over the years, several dietary strategies have been extensively studied, such as energy-restricted diets, moderate-to-high protein intake patterns, and the Mediterranean diet (MD). Although there is no consensus on the optimal diet for treating MASLD, the EASL-EASD-EASO guidelines recently recommended the MD as the preferred option [7, 10]. Previous systematic reviews and meta-analyses have evaluated the effects of interventions on the MD [14, 15] or exercise [16] on metabolic and liver-related outcomes. A meta-analysis by Del Bo et al. [15] showed that adherence to the MD appeared to reduce liver stiffness, and no significant effects were observed for liver enzymes or waist circumference (WC) in MASLD patients. In contrast, Haigh et al. [14] reported that the MD interventions were associated with favourable reductions in alanine aminotransferase (ALT) levels based on their meta-analysis. Similarly, the evidence surrounding exercise interventions for MASLD remains heterogeneous. Xiong et al. [17] demonstrated that aerobic exercise is associated with significant improvements in ALT, aspartate aminotransferase (AST), and body mass index (BMI), while resistance training appears to only reduce AST levels. However, a meta-analysis by Chai et al. [18] has reported reductions in intrahepatic lipid content and liver enzymes in response to physical activity, though their findings were drawn from populations with diverse metabolic disorders. In addition, the level of evidence presented by the published meta-analyses has not been addressed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Such variability underscores the need for an updated and methodologically rigorous meta-analysis focusing exclusively on adults with MASLD to provide more comprehensive evidence on the efficacy of the MD and exercise in this specific population. Therefore, we aimed to summarize and critically assess the evidence on the effect of the MD, exercise, and their combination on

anthropometric and liver outcomes in patients with MASLD/MASH.

Methods

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [19] (Additional file 1: PRISMA Checklist). The protocol for this study has been registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration code: CRD42024577846).

Literature search

The systematic search was conducted in Embase, MEDLINE via Ovid, Cochrane Central, Web of Science Core Collection until April 1, 2025, to find related articles without language or any other restriction. A combination set of keywords was used to find potentially relevant studies. The complete search strategy is provided in Additional file 2: Table S1. The literature search was also supplemented by performing search in Google Scholar and screening the reference lists of all included studies. No language, publication date, or other restrictions were applied.

Selection of studies

Studies were included if they met the following criteria: (1) conducted on the adult population (≥18 years old) diagnosed with MASLD/NAFLD, metabolic dysfunction-associated steatohepatitis, MASH/NASH by either ultrasonography, Transient Elastography, or biopsy; (2) randomized controlled trials (RCTs) with at least one arm in which the participants received MD, exercise (resistance or aerobic, or their combination), or a combination of the MD and exercise (including high-intensity interval training (HIIT)); (3) presence of control or usual/standard care group (or another diet in case of the MD as intervention); (4) assessed at least one of the following outcomes: body weight, BMI, WC, liver enzymes including alanine transaminase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT), and measurements of liver steatosis (including only liver fat percentage or grades) and liver fibrosis as indices/scores or grades.

We excluded studies in cell cultures, animals, children and adolescents (<18 years), and pregnant women. Case reports/series, letters to the editor, conference proceedings, posters, protocols, narrative reviews, systematic reviews and/or meta-analyses, and book chapters were also excluded. In addition, studies without a control group or a clear definition for control group, with no summary effect sizes, were excluded from the present study.

After deduplication of the retrieved studies, two groups of independent reviewers (V.A.A., J.H.V., N.M., H.RD., C.D., R.D., J.P.U., and M.T.) screened the titles and abstracts according to the eligibility criteria. The full texts were further evaluated independently by two groups (V.A.A., N.M., H.RD., C.D., J.H.V., R.D., J.P.U., and M.T.). Discrepancies between reviewer screening decisions were resolved by consensus or, if not possible, evaluated by an independent (S.B.). Finally, references of the selected articles were checked to detect additional related articles.

Data extraction

Relevant data were extracted and double-checked from eligible studies by two independent groups of reviewers (V.A.A., N.M., H.RD., C.D., J.U.P., R.D., S.D., and M.T.) and disagreements were resolved by discussing with an independent reviewer (S.B.). Collected information included the first author's name, publication year, study location, study design (parallel/cross-over, etc.), number of male and female participants, number of participants in the intervention and control groups, participants' health condition, the assessment method of the disease, number of study arms, intervention duration, washout period duration (if applicable), intervention protocol, control group approach, the unit and assessment method of the outcomes, as well as the effect size measures for the effect of interest. In case a study involved more than one intervention group that met the inclusion criteria, data for the intervention groups were combined using a method recommended by the Cochrane Handbook [20]. HIIT interventions in this meta-analysis were categorized under the aerobic-resistance combination group due to their composite training features. Given the heterogeneous nature of HIIT protocols and the absence of clear classification in some studies, grouping such interventions with combined training was deemed appropriate and has been applied in previous literature [21, 22]. Therefore, given the physiological overlap and mixed characteristics, these HIIT protocols were considered representative of aerobic-resistance combination interventions. In case a study involved more than one intervention group that met the inclusion criteria, data for the intervention groups were combined using a method recommended by the Cochrane Handbook [20].

When multiple RCTs were identified from the same population and reporting on the same outcomes, we included the version with the longest follow-up to avoid duplicate inclusion of participants and double counting.

Risk of bias assessment and certainty of evidence

We assessed the risk of bias using the RoB-2 tool from Cochrane specifically for RCTs [23]. The RoB-2 tool

estimates quality based on five domains, including (1) random sequence generation (selection bias), (2) allocation concealment (selection bias), (3) blinding of participants and personnel (performance bias), (4) blinding of outcome assessment (detection bias), (5) incomplete outcome data (attrition bias), (6) selective outcome reporting (reporting bias), and (7) compliance to the diet as another possible source of bias. Each domain was judged as "low risk of bias", "high risk of bias", or "unclear risk of bias". Since blindness is not possible for studies that examine the effects of diet and exercise, the blinding of participants, personnel, and reviewers was not considered a major factor in assessing the risk of bias. Finally, the overall quality of each eligible trial was categorized as "low risk" ("low risk" for all key domains), "unclear risk" ("unclear risk of bias" in 1 or more domains), and "high risk" ("high risk" for 1 or more domains). The factors contributing to study quality were seven domains (confounding factors, selection of participants, interventions classification, deviations from intended interventions, missing data, outcomes measurement, and selective reporting), and the overall risk of bias was reported as "low risk", "high risk", or "some concerns". Quality assessment of RCTs was conducted by two authors independently (L.B. and R.D.) and any disagreements were resolved by contacting the senior researcher (S.B.).

The certainty of evidence was assessed with the GRADE tool by investigators independently (H.RD. and S.B.). According to GRADE, high or moderate certainty of evidence can be interpreted as, it is very likely or probable that the true effect lies close to the estimated finding, and a recommendation can be made, while low or very low certainty of evidence indicates that our confidence in the result is limited or very weak, respectively [24].

Statistical analysis

Difference in mean changes ± standard error (SE) of considered outcomes (change in intervention group/period minus the change in the control group/period) was estimated in each included study to be used as an effect size. Moreover, a random-effects model was used to synthesize pooled estimates. Between-study heterogeneity was assessed using the I^2 statistic, ranging from 0 to 100%, reflects the proportion of total variation across studies attributable to heterogeneity [25, 26]. I^2 values were categorized as follows: < 25% for low heterogeneity, 25–50% for moderate heterogeneity, and > 50% for high heterogeneity. However, as I^2 depends on the sample size, we additionally calculated τ^2, which is independent of study size and quantifies the between-study variation in effect estimates. Sensitivity analyses were also conducted to assess the robustness of the overall estimates through exploring the effect of removing each individual study from meta-analyses ("leave-one-out" analysis). Publication bias was assessed by visual inspection of funnel plots and the application of Begg's and Egger's asymmetry tests [26]. Overall, two RCTs on the MD [27, 28] and one on aerobic exercise intervention [29] reported geometric means derived from log-transformed weight data due to skewed distributions, while the remaining studies reported arithmetic means. As geometric means are not directly comparable to arithmetic means [20], these two studies were not included in the pooled meta-analysis. Similarly, studies that reported effect sizes only in figures or used heterogeneous outcome metrics (e.g. different scoring systems or percentages) were not pooled in the meta-analysis and were instead summarized narratively. All analyses were conducted using STATA, version 18 (Stata Corp, College Station, TX) and two-sided P-values < 0.05 were considered significant.

Results

The PRISMA flowchart summarizes the selection process of the studies for the systematic review and meta-analysis (Fig. 1). A total of 4806 studies were identified through search in databases. Duplicate references were identified and removed ($N = 2231$). After screening the titles and abstracts, 63 studies were further screened by full text. In total, 37 unique RCTs including, 11 studies assessing the MD, 27 studies assessing exercise, and two studies assessing combined the MD and exercise were included in the systematic review and furthered in the meta-analysis if information was sufficient and standardized. Additional file 2: Table S2 [30–54] provides a list of excluded studies along with the reasons for exclusion.

Study characteristics

Characteristics of the included RCTs on the MD are shown in Table 1. Eligible studies were published between 2013 and 2023. Three studies were conducted in Australia [55–57] and three studies in Italy [28, 58, 59]. We also included one study conducted in Spain [60], one in Greece [61], one in Serbia [62], one in Iraq [63], and one in China [64]. Eleven studies had a parallel design, and one study was cross-over RCT [57] (Table 1). All studies were performed on both sexes, except two studies which one of them was done in females only [64] and the other one was conducted in males only [62]. As mentioned in the "Methods" section, for studies with overlapping populations, only the trial with the longer follow-up duration was included to avoid double-counting participants. Accordingly, the RCT by Montemayor et al. [60], which reported 12-month follow-up outcomes, was included, and the shorter-term RCT by Abbate et al. [65], which reported only 6-month outcomes on the same population, was excluded.

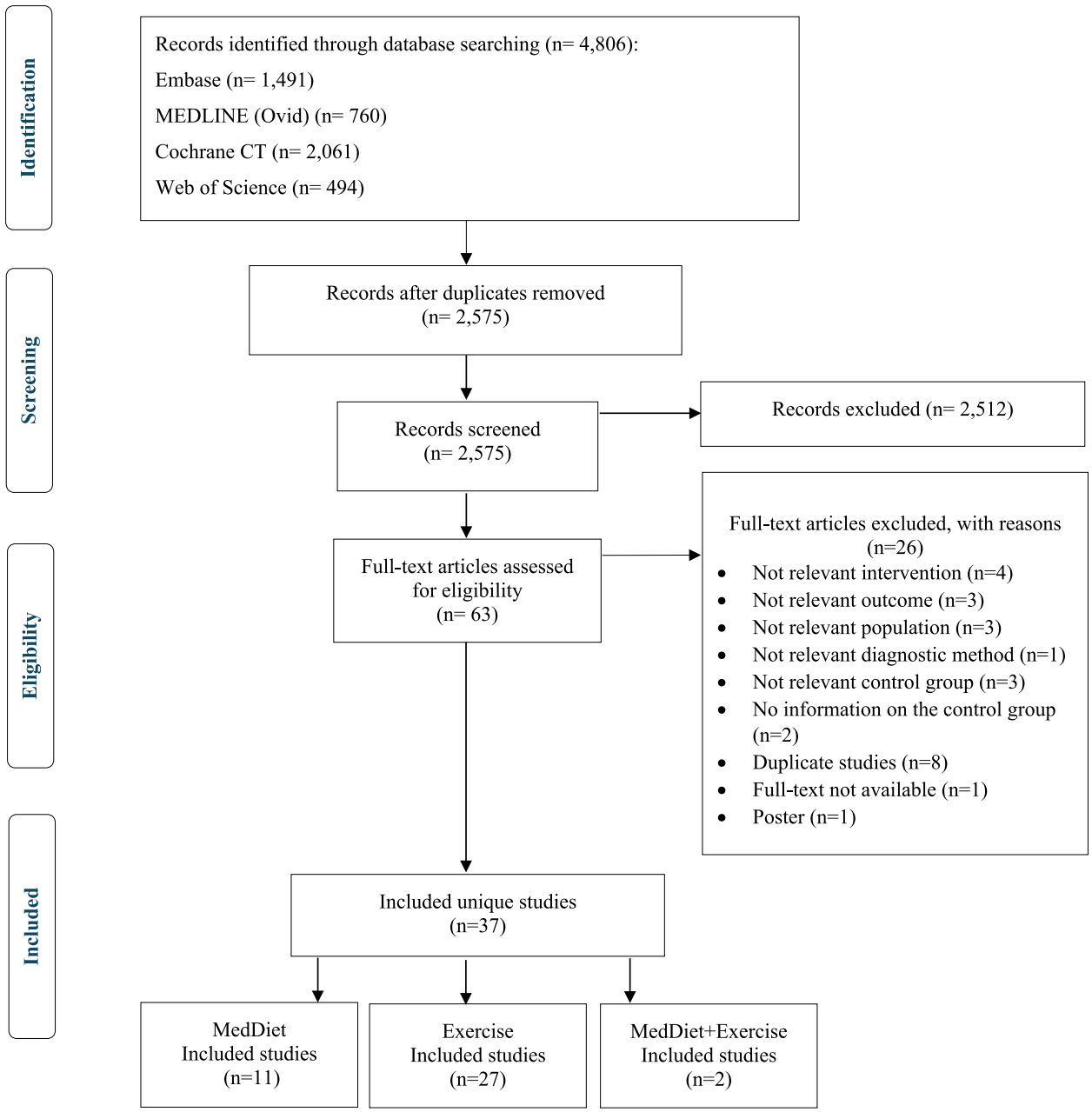

Fig. 1 PRISMA flowchart of the study selection process

Twenty-seven eligible RCTs on exercise interventions are presented in Table 2. Included RCTs were published between 2011 and 2024 and with the duration between 1.5 and 20 months. Fifteen studies assessed only aerobic interventions [29, 66–79], four studies performed only resistance interventions [80–83], seven studies conducted combined aerobic-resistance [84–87] or HIIT [88, 89] interventions, and two studies assessed both aerobic and resistance as separate arms [90, 91]. In overall, ten studies were performed in Iran [66, 72, 73, 81–84, 86, 87, 90], seven in the UK [29, 68, 69, 78, 80, 85, 88], four in the USA [70, 71, 75, 76], three in China [67, 79, 91], one in Germany [89], one in Turkey [77], and one in Brazil [74]. All these RCTs were performed on both sexes, except for two studies on only men [81, 90] and six studies on women [66, 73, 74, 82, 84, 86]. All exercise interventions performed in included RCTs were supervised, except for one [77].

Table 1 Characteristics of included articles with Mediterranean diet and combined Mediterranean diet + exercise intervention

Study (first author's name, year)	Country	Design[1]	Participants demographics	No. of participants (Age, SD/IQR/range)	Diagnosis method	Diet intervention(s) description	Control description	Duration (months)	Reported outcome(s)
Abenavoli et al. [59]	Italy	1	NAFLD patients Male & Female BMI over 25 kg/m^2	MD: $n=20$ (MAge: 52, IQR: 40–60) CG: $n=10$ (MAge: 33, IQR: 28–43)	Ultrasonography	MD (1400–1600 kcal/day intake)	Standard care	6	Weight, BMI, WC, ALT, AST, GGT, fatty liver index, and fibrosis
Chooi et al. [64]	China	1	NAFLD patients Female only BMI 23 to 35 kg/m^2	MD: $n=28$ (MAge: 35.7, SD: 1.3) CG: $n=29$ (MAge: 34.6, SD: 1.5)	Ultrasound	MD (500–1000 kcal/day deficit)	Habitual diet	3	Weight, BMI, WC, and liver fat percentage
Curci et al. [58]	Italy	1	NALFD patients Male & Female BMI over 25 kg/m^2	Low Glycemic MD: $n=23$ (MAge: 50.74, SD: 1.75) PA1 + Low Glycemic MD: $n=27$ (MAge:50.32, SD: 9.61) PA2 + Low Glycemic MD: $n=24$ (MAge:36.75, SD: 10.50) C: $n=22$ (MAge: 50.70, SD: 8.67)	Fibro scan	Low Glycemic MD Low Glycemic MD with 2 physical activity variations	CD	3	BMI, WC, and fibrosis
Fateh et al. [63]	Iraq	1	NAFLD patients Male & Female	MD: $n=45$ (MAge: 47.3, SD: 15.75) CG: $n=45$ (MAge: 44.04, SD: 13.2)	Ultrasound	MD	CD	3	ALT, AST, and fatty liver index
George et al. [55]	Australia	1	NAFLD patients Adult male & Female BMI of 32 ± 6 kg/m^2	MD: $n=18$ (MAge: 52.6, SD: 11.7) LFD: $n=21$ (MAge: 62.1, SD: 13.6)	Ultrasound or Biopsy	MD	LFD	3	Weight, BMI, WC, ALT, AST, GGT, liver fat percentage, and fibrosis
Katsagoni et al. [61]	Greece	1	NAFLD patients Male & Female BMI 25–40 kg/m^2	MD: $n=21$ (MedAge: 44, IQR: 41–60) CG: $n=21$ (MedAge: 47, IQR: 42–60)	Ultrasound, compatible liver histology	MD (1500 energy/day (women); 1800 kcal/day (men) deficit)	Dietary guidelines for healthy lifestyle (1500 kcal/day (women); 1800 kcal/d (men) deficit)	6	Weight, BMI, WC, ALT, GGT, and fibrosis
Misciagna et al. [28]	Italy	1	NAFLD patients Adult male & Female	Low Glycemic MD: $n=50$ CG: $n=48$	Ultrasonography	Low Glycemic MD	Standard care (healthy diet lifestyle)	6	BMI, GGT, and fatty liver index
Montemayor et al. [60]	Spain	1	NAFLD patients with MetS Male & Female BMI 27–40 kg/m^2	MD –high meal frequency: $n=43$ (MAge: 52.3, SD: 7.1) MD–physical activity: $n=42$ (MAge: SD: 52.2, 5.8) CD: $n=43$ (MAge: 54.1, SD: 8.9)	MRS	MD- high meal frequency (25–30% kcal/day deficit) MD with physical activity	CD	12	Weight, BMI, WC, ALT, AST, GGT, and fatty liver percentage

Table 1 (continued)

Study (first author's name, year)	Country	Design[1]	Participants demographics	No. of participants (Age, SD/IQR/range)	Diagnosis method	Diet intervention(s) description	Control description	Duration (months)	Reported outcome(s)
Properzi et al. [56]	Australia	1	NAFLD patients with overweight Male & Female	MD: *n* = 24 (MAge: 51, SD: 13.36) LDF: *n* = 24 (MAge: 53, SD: 9.07)	MRS	MD	LFD	3	Weight, BMI, WC, ALT, GGT, and liver fat percentage
Ristic-Medic et al. [62]	Serbia	1	NAFLD patients and overweight Male only BMI 25 to35kg/m^2	MD: *n* = 12 (MAge: 34.2, SD: 4.66) LFD: *n* = 12 (MAge: 39.92, SD: 3.78)	Ultrasonography	MD (30% or 600–800 kcal/day deficit)	LFD (30% or 600–800 kcal/day deficit)	3	Weight, BMI, WC, ALT, AST, GGT, and fatty liver index
Ryan et al. [57]	Australia	2	NALFD patients with MetS Male & Female	MD: *n* = 12 CG: *n* = 12 (MAge, SD: 55, SD: 14)	MRS	MD	Low fat-high carbo-hydrate diet	1.5	Weight, BMI, WC, ALT, GGT, and liver fat percentage

ALT alanine aminotransferase, *AST* aspartate transaminase, *BMI* body mass index, *CD* conventional diet, *CG* control group, *GGT* γ-glutamyl transferase, *IQR* interquartile range, *LFD* low-fat diet, *MAge* mean age, *MD* Mediterranean diet, *MedAge* median age, *MetS* metabolic syndrome, *MRS* magnetic resonance spectroscopy, *SD* standard deviation, *WC* waist circumference

[1] Design: 1 Parallel/2 Cross-over

Table 2 Characteristics of included articles with exercise (aerobic, resistance, and combination) intervention

Study (first author's name, year)	Country	Design[1]	Participants demographics	No. of participants analysed (Age, SD/IQR/range)	Diagnosis method	Intervention(s) description	Control description	Duration (months)	Reported outcome(s)
Aliniya et al. [84]	Iran	1	NALFD patients with obesity Female Only	AT + RT: *n* = 10 (MAge: 51.2, SD: 6.82) CG: *n* = 10 (MAge: 53.5, SD: 6.39)	Ultrasonography and blood tests	AT + RT	No intervention	3	Weight and BMI, and liver fat percentage
Astinchap et al. [66]	Iran	1	NALFD patients with T2D Female Only BMI 25 to 36 kg/m	AT: *n* = 15 RT: *n* = 15 CG: *n* = 15 (MAge: 51, SD: 8)	Ultrasonography	AT RT	No intervention	2	Weight, BMI, ALT, AST, and fatty liver grade
Cheng et al. [67]	China	1	NALFD patients who are pre-diabetic Male & Female	AT: *n* = 22 (MAge: 59, SD: 4.4) CG: *n* = 18 (MAge: 60, SD: 3.4)	Ultrasound	AT	No intervention	6	Weight, ALT, AST, GGT, and liver fat percentage
Cuthbertson et al. [69]	UK	1	NALFD patients Male & Female	AT: *n* = 29 (MAge: 50, CI 46, 58) CG: *n* = 31 (MAge: 52, CI 46, 59)	Clinically by a hepatologist	AT	No intervention	4	Weight, BMI, WC, ALT, AST, and GGT, and liver fat percentage
Cuthbertson et al. [68]	UK	1	MASLD/MASH Patients Male & Female	AT: *n* = 54 (MAge: 51.8, SD: 11.1) CG: *n* = 34 (MAge: 50.9, SD: 11.6)	MRI or liver biopsy	AT	No intervention	12–20	Fibrosis
Ezpeleta et al. [70]	USA	1	NAFLD patients with obesity Male & Female	AT: *n* = 15 (MAge: 44, SD: 13) CG: *n* = 20 (MAge: 44, SD: 12)	Ultrasonography	AT	No intervention	3	Weight, BMI, WC, ALT, AST, liver fat percentage, and fibrosis
Hallsworth et al. [80]	UK	1	NAFLD patients Male & Female	RT: *n* = 11 (MAge: 52, SD: 13.3) CG: *n* = 8 (MAge: 62, SD: 7.4)	MRI-PDFF/MRS	RT	No intervention	2	Weight, BMI, WC, and ALT, and liver fat percentage
Hallsworth et al. [88]	UK	1	NAFLD patients Male & Female	HIIT: *n* = 12 (MAge: 54, SD: 11) CG: *n* = 11 (MAge: 52, SD: 12)	MRI-PDFF/MRS	HIIT	No intervention	3	Weight, BMI, ALT, AST, and GGT, and liver fat percentage
Harris et al. [71]	USA	1	MASLD patients Male & Female	AT: *n* = 15 (MAge: 55.2, SD: 10.6) CG: *n* = 8 (MAge: 46.1, SD: 11)	Biopsy	AT	No intervention	5	Weight, WC, liver fat percentage, and fibrosis
Hassabi et al. [72]	Iran	1	NAFLD patients Male & Female	Moderate-intensity AT: *n* = 13 (MAge: 53.2, SD: 9.60) High-intensity AT: *n* = 13 (MAge: 47.5, SD: 9.65) CG: *n* = 14 (MAge: 49.8, SD: 11.2)	Transient Elastography	Moderate-intensity AT High-intensity AT	No intervention	6	Weight, BMI, WC, ALT, AST, and liver fibrosis

Table 2 (continued)

Study (first author's name, year)	Country	Design[1]	Participants demographics	No. of participants analysed (Age, SD/IQR/range)	Diagnosis method	Intervention(s) description	Control description	Duration (months)	Reported outcome(s)
Hoseini et al. [73]	Iran	1	NALFD patients with vitamin D deficiency Female only	AT: *n* = 10 (MAge: 62.6, SD: 1.8) CG: *n* = 10 (MAge: 62, SD: 1.8)	Clinically by a hepatologist	AT	No intervention	2	Weight and BMI
Houghton et al. [85]	UK	1	NAFLD patients Male & Female	AT + RT: *n* = 12: (MAge: 54, SD:12) CG: *n* = 12 (MAge: 51, SD: 16)	Biopsy	AT + RT	No intervention	3	Weight, BMI, ALT, AST, GGT, liver fat percentage, and fibrosis
Jafarikhah et al. [81]	Iran	1	NALFD patients Male only	RT: *n* = 8 (MAge: 48.6, SD: 2.5) CG: *n* = 8 (MAge: 46.2, SD: 5.4)	Clinically by a hepatologist	RT	No intervention	2	BMI, AST, and ALT
Moradi Kelardeh et al. [82]	Iran	1	NAFLD patients with obesity Female only	RT: *n* = 12 (MAge: 65.9, SD: 3.3) CG: *n* = 11 (MAge: 64.3, SD: 2.9)	Ultrasonography	RT	No intervention	3	Weight, BMI, ALT, and AST
Pugh et al. [29]	UK	1	NAFLD patients with obesity Male & Female	AT: *n* = 13 (MAge: 48, CI: 44, 51) CG: *n* = 8 (MAge: 47, CI 43, 51)	MRS	AT	No intervention	4	ALT, AST, GGT, and liver fat percentage
Rajabi et al. [86]	Iran	1	NAFLD patients Female only	AT + RT: *n* = 11 (MAge: 44.4, SD: 6.4) RT + HIIT: *n* = 11 (MAge: 42.1, SD: 9.0) CG: *n* = 11 (MAge: 43.8, SD: 7.5)	Ultrasonography	AT + RT	No intervention	3	Weight and BMI
Reljic et al. [89]	Germany	1	NAFLD patients Male & Female	HIIT: *n* = 29 (MAge: 52.1, SD: 9.6) CG: *n* = 17 (MAge: 56.7, SD: 9.8)	Metabolic equivalent of task	HIIT	No intervention	3	Weight, BMI, WC, ALT, AST, GGT, and fibrosis
Rezende et al. [74]	Brazil	1	NAFLD patients Female only	AT: *n* = 19 (MAge: 56.2, SD: 7.8) CG: *n* = 21 (MAge: 54.5, SD: 8.9)	Biopsy	AT	No intervention	6	BMI, WC, ALT, AST, and GGT, liver fat grade, and fibrosis
Shamsoddini et al. [90]	Iran	1	NAFLD patients Male only	AT: *n* = 10 (Mage: 39.7, SD: 6.3) RT: *n* = 10 (Mage: 45.9, SD: 7.3) CG: *n* = 10 (MAge: 45.8, SD: 7.3)	Ultrasonography	AT RT	No intervention	2	Weight, BMI, WC, AST, ALT, and liver fat grade
Shojaee-Moradie et al. [87]	UK	1	NAFLD patients Male & Female	AT + RT: *n* = 15 (MAge: 52.4, SD: 2.2) CG: *n* = 12 (MAge: 52.8, SD: 3.0)	Ultrasound/biopsy	AT + RT	No intervention	4	Weight, BMI, WC, ALT, AST, GGT, and liver fat percentage

Table 2 (continued)

Study (first author's name, year)	Country	Design[1]	Participants demographics	No. of participants analysed (Age, SD/IQR/range)	Diagnosis method	Intervention(s) description	Control description	Duration (months)	Reported outcome(s)
Stine et al. [75]	USA	1	NAFLD patients Male & Female	AT: *n* = 18 (MAge: 45.0, SD: 10.2) CG: *n* = 10 (MAge: 52.9, SD: 11.5)	Biopsy	AT	No intervention	5	Weight, BMI, WC, ALT, AST, liver fat percentage, and fibrosis
Sullivan et al. [76]	USA	1	NAFLD patients with obesity Male & Female	AT: *n* = 12 (MAge: 48.6, SD: 2.2) CG: *n* = 6 (MAge: 47.5, SD 3.1)	MRI-PDFF/MRS	AT	No intervention	4	Weight, BMI, ALT, and liver fat percentage
Us Altay et al. [77]	Turkey	1	NAFLD patients Male & Female	AT: *n* = 16 (age range 40–75) CG: *n* = 16 (age range 30–75)	Ultrasonography	AT	No intervention	3	Weight, BMI, ALT, AST, and GGT
Varmazyar et al. [83]	Iran	1	NAFLD patients Overweight or obesity Male & Female	RT: *n* = 10 (MAge: 31.6, SD: 9.3) CG: *n* = 9 (MAge: 32.8, SD: 8.2)	Ultrasonagraphy	RT	No intervention	3	Weight, BMI, AST, and ALT
Willis et al. [78]	UK	1	NALFD with overweight/obesity Male & Female	AT: *n* = 11 (MAge: 61, SD: 17) CG: *n* = 13 (MAge: 63, SD: 18)	MRS	AT	No intervention	1.5	Weight, BMI, WC, ALT, AST, GGT, and liver fat percentage
Yao et al. [91]	China	1	NALFD patients Male & Female	AT: *n* = 29 (MAge: 61.28, SD: 7.5) RT: *n* = 34 (MAge: 55.80, SD: 12.2) CG: *n* = 31 (MAge: 58.06, SD: 9.7)	Clinically by a hepatologist	AT RT	No intervention	5	Weight, BMI, and ALT
Zhang et al. [79]	China	1	NALFD patients Male & Female	Moderate AT: *n* = 73 (MAge: 54.4, SD: 7.4) Vigorous-Moderate AT: *n* = 73 (MAge: 53.2, SD: 7.1) CG: *n* = 74 (MAge: 54.0, SD: 6.8)	Ultrasonography	Moderate AT Vigorous-Moderate AT	No intervention	12	Weight, BMI, and WC, ALT, AST, GGT, and liver fat percentage

AT aerobic training, *ALT* alanine aminotransferase, *AST* aspartate transaminase, *AT* aerobic training, *BMI* body mass index, *CG* control group, *CI* 95% confidence interval, *GGT* γ-glutamyl transferase, *HIIT* high-intensity interval training, *MAge* mean age, *MetS* metabolic syndrome, *MD* Mediterranean diet, *MRI* magnetic resonance imaging, *MRS* magnetic resonance spectroscopy, *RT* resistance training, *SD* standard deviation, *T2D* type 2 diabetes, *WC* waist circumference

[1] Design: 1 Parallel/2 Cross-over

Two RCTs published between 2022 and 2023 also assessed the combination of the MD and exercise in patients with MASLD/MASH [58, 60], one in Italy [58] and one in Spain [60]. Both studies included men and women.

Findings from systematic review and meta-analyses

The effect of Mediterranean diet on body weight and composition and liver outcomes

Six studies were included in the meta-analysis of the effect of the MD on weight [56, 57, 59, 60, 62, 64] (Table 3, Additional file 2: Figure S1). The overall results showed that the MD significantly reduced weight [weighted mean difference (WMD = −2.38 kg, 95% CI −4.11 to −0.66, $P=0.01$) in comparison to standard care or control diet. In total, seven studies reported data revealed that the MD significantly reduced BMI [56–60, 62, 64](WMD = −0.70 kg/m^2, 95% CI = −1.03 to −0.36, $P<0.001$) and WC [56–60, 62, 64] (WMD = −1.56 cm, 95% CI = −3.02 to −0.09, $P=0.04$) in comparison to standard care or control diet (Table 3, Additional file 2: Figure S1).

In addition, the overall results of six RCTs [56, 57, 59, 60, 62, 63] showed a significant effect of the MD on ALT levels (WMD = −3.96 IU/L, 95% CI = −6.54 to −1.38, $P<0.001$). However, the effect sizes obtained from four RCTs [59, 60, 62, 63] did not show any significant effect of the MD on AST levels (WMD = −2.14 IU/L, 95% CI = −5.63 to 1.34, $P=0.23$). Findings from five RCTs [56, 57, 59, 60, 62] showed no changes in GGT levels (WMD = −3.55 IU/L, 95% CI = −11.57 to 4.47, $P=0.39$) (Table 3, Additional file 2: Figure S1).

Misciagna et al. [28], which assessed fatty liver by fatty liver index, reported a significant reduction in this index after 6 months low-glycaemic MD intervention in patients with NAFLD in comparison to INRAN guidelines. Abenavoli et al. [59] also showed a significant lower fatty liver index in the MD intervention group than the control group. Fateh et al. [63] found a significant lower fatty liver index in the MD intervention group compared to the control group at the end of the follow-up. One study reported decrease in liver steatosis by changes in magnetic resonance by comparing the MD to the American Association for the Study of Liver Disease diet [60], while two others reported significantly lower liver fat percentages in the MD group compared to either a low-fat–high-carbohydrate diet [57] or a standard control group [64]. However, another RCT showed no changes in liver steatosis between the two groups [56]. Similarly, Goerge et al. [55] showed no significant difference in liver fat percentage between the MD and low-fat diet groups after 3 months intervention. Regarding liver fibrosis, four RCTs showed improvements in fibrosis outcomes with the MD compared to standard care [59, 61], Research Center for Food and Nutrition diet [58], and low-fat diet [55].

All heterogeneity values for the meta-analyses assessing the effect of the MD are presented in Table 3 and Additional file 2: Figure S1.

The effect of exercise on body weight and composition and liver outcomes

Thirteen studies on aerobic exercise [66, 67, 69–79, 90], five on resistance exercise [66, 80, 83, 90, 91], and six studies on the combined aerobic-resistance interventions [84–89] reported weight measurements and were included in the meta-analysis (Tables 4, 5, and 6, Additional file 2: Figure S2-S4). Interventions on aerobic

Table 3 The overall effect of Mediterranean diet on the outcomes using random-effects model

Study group	Number of studies	Number of participants	Meta-analysis			Heterogeneity			
			WMD	95% CI	*P*-effect	Q statistic	*P*-value	τ^2	I^2%
Weight, kg									
Overall	6	272	−2.38	-4.11 to -0.66	0.01	6.42	0.27	1.04	22.12
BMI, kg/m^2									
Overall	7	317	-0.70	-1.03 to -0.36	<0.001	2.29	0.89	0.0	0.0
WC, cm									
Overall	7	317	-1.56	-3.02 to -0.09	0.04	1.73	0.94	0.0	0.0
ALT, IU/L									
Overall	6	305	-3.96	-6.54 to -1.38	<0.001	1.83	0.8	0.0	0.0
AST, IU/L									
Overall	4	330	-2.14	-5.63 to 1.34	0.23	3.84	0.28	3.10	21.97
GGT, IU/L									
Overall	5	215	-3.55	-11.57 to 4.47	0.39	1.28	0.86	0.0	0.0

ALT alanine aminotransferase, *AST* aspartate transaminase, *BMI* body mass index, *cm* centimetre, *CI* confidence interval, *GGT* gamma-glutamyl transferase, *IU/L* international units per litre, *kg* kilogramme, *kg/m2* kilogramme per square metre *WC* waist circumference, *WMD* weighted mean difference

Table 4 The overall effect of aerobic exercise on the outcomes using random-effects model

Study group	Number of studies	Number of participants	Meta-analysis			Heterogeneity			
			WMD	95% CI	*P*-effect	Q statistic	*P*-value	τ^2	I^2%
Weight, kg									
Overall	13	599	− 1.56	− 2.31 to − 0.82	< 0.001	21.25	0.05	0.57	43.52
BMI, kg/m^2									
Overall	12	409	− 0.26	− 0.54 to 0.02	0.07	9.77	0.55	0.0	0.0
WC, cm									
Overall	9	499	− 2.14	− 2.87 to − 1.41	< 0.001	4.68	0.79	0.0	0.0
ALT, IU/L									
Overall	12	626	− 1.43	− 3.96 to 1.10	0.27	27.56	< 0.001	7.90	60.08
AST, IU/L									
Overall	9	479	− 1.01	− 3.64 to 1.61	0.45	7.76	0.01	7.76	58.91
GGT, IU/L									
Overall	5	356	0.55	− 2.46 to 3.56	0.72	0.89	0.93	0.0	0.0

ALT alanine aminotransferase, *AST* aspartate transaminase, *BMI* body mass index, *cm* centimetre, *CI* confidence interval, *GGT* gamma-glutamyl transferase, *IU/L* international units per litre, *kg* kilogramme, *kg/m*^{2} kilogramme per square metre, *WC* waist circumference, *WMD* weighted mean difference

Table 5 The overall effect of resistance exercise on the outcomes using random-effects model

Study group	Number of studies	Number of participants	Meta-analysis			Heterogeneity			
			WMD	95% CI	*P*-effect	Q statistic	*P*-value	τ^2	I^2%
Weight, kg									
Overall	5	159	− 0.74	− 3.72 to 2.23	0.63	0.19	0.99	0.0	0.0
BMI, kg/m^2									
Overall	6	111	− 0.17	− 1.01 to 0.66	0.69	0.79	0.98	0.0	0.0
ALT, IU/L									
Overall	5	136	− 15.40	− 28.60 to − 2.20	0.02	25.61	< 0.001	170.59	84.38

ALT alanine aminotransferase, *BMI* body mass index, *CI* confidence interval, *IU/L* international units per litre, *kg* kilogramme, *kg/m*^{2} kilogramme per square metre, *WMD* weighted mean difference

Table 6 The overall effect of combined aerobic-resistance exercise (including HIIT) on the outcomes using random-effects model

Study group	Number of studies	Number of participants	Meta-analysis			Heterogeneity			
			WMD	95% CI	*P*-effect	Q statistic	*P*-value	τ^2	I^2%
Weight, kg									
Overall	6	173	− 1.90	− 3.59 to − 0.22	0.03	0.31	0.99	0.0	0.0
BMI, kg/m^2									
Overall	5	146	− 1.08	− 2.81 to 0.64	0.22	6.29	0.18	1.44	36.37
ALT, IU/L									
Overall	4	120	− 2.46	− 9.27 to 4.35	0.48	1.80	0.61	0.0	0.0
AST, IU/L									
Overall	4	120	− 1.70	− 5.59 to 2.19	0.39	2.43	0.49	0.0	0.0
GGT, IU/L									
Overall	4	120	1.53	− 5.29 to 8.35	0.66	3.05	0.38	2.03	1.78

ALT alanine aminotransferase, *AST* aspartate transaminase, *BMI* body mass index, *CI* confidence interval, *GGT* gamma-glutamyl transferase, *IU/L* international units per litre, *kg* kilogramme; *kg/m*^{2} kg/m kilogramme per square metre, *WMD* weighted mean difference

and aerobic-resistance combination showed weight reduction in comparison to control (WMD = −1.56 kg, 95%CI −2.31 to −0.82, $P < 0.001$ and WMD = −1.90 kg, 95%CI −3.59 to −0.22, $P = 0.03$, respectively). Twelve aerobic [67, 69, 70, 72–78, 90, 91], six resistance [80–83, 90, 91], and five combined aerobic-resistance interventions [84–86, 88, 89] reported BMI and were included in the meta-analysis (Tables 4, 5, and 6, Additional file 2: Figure S2-S4). No significant changes were observed in BMI in any of these interventions. Nine aerobic interventions reported WC [69–72, 74, 75, 78, 79, 90], but no differences were found in comparison to control (Tables 4, 5, and 6, Additional file 2: Figure S2-S4).

Twelve aerobic [67, 69, 70, 72, 74–79, 90, 91], five resistance [80, 81, 83, 90, 91], and four combined aerobic-resistance [85, 87–89] interventions reported ALT levels were included in the meta-analysis (Tables 4, 5, and 6, Additional file 2: Figure S2-S4). Resistance exercise showed significant reduction in ALT levels compared with control groups (WMD = −15.40 IU/L, 95%CI −28.60 to −2.20, $P < 0.001$); however, no significant changes were observed in ALT levels in interventions on aerobic and combined aerobic-resistance exercises. Nine aerobic [67, 70, 72, 74, 75, 77–79, 90] and four combined aerobic-resistance [85, 87–89] interventions reported levels of AST (Tables 4, 5, and 6, Additional file 2: Figure S2-S4). Neither aerobic nor combined aerobic-resistance interventions showed changes in AST levels in comparison to control. Five studies on aerobic [67, 74, 77–79] and four on combined aerobic-resistance intervention included in the meta-analysis showed no changes in GGT in comparison to control (Table 4, Table 6, Additional file 2: Figure S2, and Additional file 2: Figure S4). Two RCTs showed a significant reduction in ALT and AST in the resistance exercise group compared with the control group [66, 82].

Twelve RCTs assessed aerobic [29, 66, 67, 69–71, 74–76, 78, 79, 90], three resistance [66, 80, 90], and four combined aerobic-resistance [84, 85, 87, 88] interventions on liver fat content, though units of measurement varied. Six RCTs on aerobic exercise showed a significant reduction in liver fat compared to controls [67, 69, 71, 75, 76, 79], while three reported no significant changes [29, 74, 78]. Two RCTs found both aerobic and resistance training significantly reduced liver steatosis [66, 90]. Hallsworth et al. [80] assessed the effects of only resistance exercise on liver steatosis in participants with NAFLD, showing no differences between the intervention group and control. Among combined interventions, four RCTs showed reductions in liver fat or steatosis grade compared to controls [84, 85, 87, 88].

Five RCTs on aerobic exercise [68, 70, 72, 74, 75] and two on combined aerobic-resistance (including HIIT) [85, 89] exercise assessed the liver fibrosis. With regard aerobic exercise, all RCTs showed no difference between liver fibrosis indices/stages between the aerobic exercise group and the control group [68, 70, 72, 74, 75]. Houghton et al. [85] found no difference in fibrosis between combined aerobic-resistance intervention group and the control group. However, Reljic et al. [89] showed that the reduction in NFS was significantly greater in the HIIT group than in the control group.

Effect of combined Mediterranean diet and exercise interventions

Two studies assessing the MD and structured exercise intervention assessed the outcomes of interest in patients with NAFLD [58, 60]. In a RCT involving patients with metabolic syndrome and NAFLD, a 6- and 12-month intervention with the MD and structured exercise significantly reduced intrahepatic fat content measured by MRI, with no significant differences between the groups [60]. In another study by Cruci et al. [58] evaluating the effects of a low-glycemic index MD (LGIMD), LGIMD with aerobic exercise, and LGIMD with combined aerobic-resistance exercise, no significant differences in BMI, WC, and AST were observed between the groups after 3 months. Although the controlled attenuation parameter (CAP) score decreased in all groups compared to baseline, the changes were not significantly different between the groups.

Risk of bias and certainty of evidence

In total 37 trials were assessed (Table 7). Regarding the RCTs on the MD, three were defined as "Low Risk" [56, 60]; seven studies were defined as "Some concerns" [28, 55, 57, 59, 61, 62, 64]; and two studies were defined as "High-Risk" [58, 63]. Regarding RCTs on exercises, five studies were defined as "Low Risk" [74, 79, 82, 83, 89]; Ten RCTs were defined as "Some concerns" [67, 70, 73, 75, 77, 78, 80, 87, 88, 91]; and 12 RCTs were defined as "High-Risk" [29, 66, 68, 69, 71, 72, 76, 81, 84–86, 90].

The GRADE assessments of the included studies are presented in Additional file 2: Tables S3-S6. Our findings revealed that the certainty of evidence for the MD impact on AST was rated as very low, while the evidence for its effects on weight, BMI, WC, ALT, and GGT was classified as low (Additional file 2: Table S3). For aerobic exercise, the evidence quality was very low for its effects on ALT, AST, and liver steatosis, whereas the evidence was considered low for weight, BMI, and WC, and moderate for GGT (Additional file 2: Table S4). Regarding resistance exercise, the certainty of evidence for its impact on ALT was very low, and the evidence for its effects on weight and BMI was also low (Additional file 2: Table S5). Finally, the combined aerobic-resistance exercise

Table 7 Risk of bias assessment of articles included in meta-analysis

Study	Randomization process	Deviations from intended interventions based on adherence	Missing outcome data	Measurement of the outcome	Selection of the reported result		Overall Assessment
					Anthropomorphic Measures	Liver Measures	
Mediterranean diet							
Abenavoli et al. [59]	Some concerns	Some concerns	Low risk	Low risk	Some concerns	Some concerns	Some concerns
Chooi et al. [64]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
Curci et al. [58]	Some concerns	Some concerns	Low risk	Low risk	N/A	High risk	High risk
Fateh et al. [63]	High risk	Low risk	Low risk	Low risk	N/A	Low risk	High risk
George et al. [55]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
Katsagoni et al. [61]	Some concerns	Low risk	Low risk	Low risk	N/A	Low risk	Some concerns
Misciagna et al. [28]	Some concerns	Low risk	Low risk	Low risk	N/A	Some concerns	Some concerns
Montemayor et al. [60]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Properzi et al. [56]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ristic-Medic et al. [62]	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns
Ryan et al. [57]	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns
Exercise							
Aliniya et al. [84]	Some concerns	High risk	Low risk	Low risk	N/A	Some concerns	High risk
Astinchap et al. [66]	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	High risk
Cheng et al. [67]	Low risk	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Cuthbertson et al. [69]	Low risk	Some concerns	High risk	Low risk	Low risk	Low risk	High risk
Cuthbertson et al. [68]	Low risk	Some concerns	High risk	Low risk	Low risk	Low risk	High risk
Ezpeleta et al. [70]	Some concerns	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Hallsworth et al. [80]	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns
Hallsworth et al. [88]	Some concerns	Low risk	Some concerns	Low risk	Some concerns	Some concerns	Some concerns
Harris et al. [71]	Some concerns	Low risk	Low risk	Low risk	N/A	High Risk	High risk
Hassabi et al. [72]	Some concerns	High risk	Some concerns	Low risk	N/A	Some concerns	High risk
Hoseini et al. [73]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
Houghton et al. [85]	High risk	Low risk	Low risk	Low risk	Some concerns	Low risk	High risk
Jafarikhah et al. [81]	Some concerns	High risk	Low-Risk	Low risk	Some concerns	Some concerns	High risk
Moradi Kelardeh et al. [82]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Pugh et al. [29]	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk
Rajabi et al. [86]	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns	High risk
Relijc et al. [89]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rezende et al. [74]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Shamsoddini et al. [90]	Some concerns	High risk	High risk	Low risk	Some concerns	Some concerns	High risk

Table 7 (continued)

Study	Randomization process	Deviations from intended interventions based on adherence	Missing outcome data	Measurement of the outcome	Selection of the reported result		Overall Assessment
					Anthropomorphic Measures	Liver Measures	
Shojaee-Moradie et al. [87]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
Stine et al. [75]	Some concerns	Low risk	Low risk	Low risk	Low risk	Low risk	Some concerns
Sullivan et al. [76]	Low risk	High risk	High risk	Low risk	N/A	Low risk	High risk
Us Altay et al. [77]	Low risk	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Varmazyar et al. [83]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Willis et al. [78]	Low risk	Low risk	Some concerns	Low risk	Some concerns	Some concerns	Some concerns
Yao et al. [91]	Low risk	Low risk	Low risk	Low risk	Some concerns	Some concerns	Some concerns
Zhang et al. [79]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

(including high-intensity interval training, HIIT) demonstrated very low-quality evidence for its effects on weight, BMI, ALT, AST, and GGT (Additional file 2: Table S6).

Additional analysis

Findings of additional analyses including publication bias and leave-one-out are reported in Additional file 2: Figure S5-S8 and Additional file 2: Figure S9-S12.

Discussion

In the current systematic review and meta-analysis, the effects of lifestyle interventions including the MD, exercise, and their combination and related clinical parameters (anthropometric measures, liver enzymes and parameters) were summarized. Additionally, the effects of exercise were differentiated among aerobic, resistance, and its combination (aerobic and resistance or high-intensity interval training) interventions. Our meta-analysis showed that the MD reduces body weight, BMI, WC, and the levels of ALT in MASLD/MASH patients. In addition, aerobic exercise intervention showed a significant reduction in body weight and WC, and aerobic exercise in combination with resistance exercise significantly reduced body weight in patients with MASLD/MASH. Resistance exercise intervention also significantly reduced the levels of ALT in MASLD/MASH patients.

In line with our findings, a previous meta-analysis revealed that the MD intervention reduced ALT and liver stiffness in patients with MASLD [14]. While Del Bo et al. [15] found no significant effect of the MD on WC and the level of liver enzymes including ALT, and GGT in MASLD patients. The controversies between our findings and previous meta-analysis might be due to differences in search strategies, inclusion and exclusion criteria, methodological approaches, and statistical power. In general, the MD favourable effects in patients with MASLD/MASH can be attributed to several components of this diet pattern, such as olive oil, fish, vegetables, and fruit, which have been associated with a reduction in liver steatosis content and liver enzymes [92, 93]. Weight reduction has been consistently shown to exert beneficial effects on MASLD. The MD, rich in dietary fibre from legumes and whole grains, contributes to weight management primarily through enhanced satiety, thereby reducing overall energy intake [93]. Additionally, the quality of dietary fat plays a key role. Diets high in saturated and trans fats have been associated with increased adiposity and central fat accumulation, whereas the MD pattern emphasizes the consumption of unsaturated fats, particularly omega-3 polyunsaturated fatty acids (n-3 PUFAs) derived from fish and olive oil. These fats help reduce inflammation and activate PPAR-alpha, a nuclear receptor that regulates fat metabolism in the liver [93]. Activation of PPAR-α promotes β-oxidation of fatty acids, lowers circulating triglyceride levels, increases HDL cholesterol, and improves liver function [94, 95]. They also influence several key processes in the liver, such as decreasing fat production, increasing fat oxidation, and improving lipid transport and storage, helping to protect against liver fat accumulation and dysfunction [95].

Our meta-analysis demonstrated that both aerobic and combined aerobic-resistance exercise interventions significantly reduced body weight compared to controls, consistent with previous studies showing the benefits of exercise for weight management in patients with MASLD [96, 97]. The observed weight reduction with aerobic exercise may be attributed to increased energy expenditure and improved metabolic efficiency, while combined

aerobic-resistance training likely benefits from enhanced muscle mass, which promotes a higher resting metabolic rate [98, 99]. The significant reduction in liver fat percentage observed with aerobic exercise may be attributed to enhanced fat oxidation and improved hepatic insulin sensitivity [100, 101]. Regular aerobic activity increases mitochondrial capacity and promotes fatty acid oxidation, leading to greater utilization of fat as an energy source [102]. Moreover, enhanced hepatic insulin sensitivity reduces de novo lipogenesis and improves glucose regulation, effectively lowering lipid accumulation within the liver [100]. Together, these mechanisms highlight the complex, multifaceted effects of aerobic exercise on liver health and MASLD pathophysiology, emphasizing its role in improving key metabolic pathways and reducing disease progression. However, our findings also highlighted inconsistencies. Despite significant weight reduction and lower liver fat with aerobic and combined exercise, BMI, ALT, AST, and GGT remained largely unaffected. These results are in line with several studies showing that exercise may not always lead to significant changes in BMI or WC due to the concurrent gain in muscle mass [103]. Findings from a meta-analysis by Smart et al. [104] showed no significant changes in the levels of ALT and AST following the aerobic and resistance exercise interventions.

In the present study, resistance exercise alone did not significantly reduce body weight, a finding supported by previous research indicating that resistance training primarily increases muscle mass rather than reducing fat mass [105]. However, our results showed that resistance exercise was associated with a significant reduction in ALT levels. This effect on ALT aligns with previous findings, suggesting that resistance training may improve hepatic enzyme levels through enhanced insulin sensitivity and reduced hepatic fat accumulation [101]. In addition, a meta-analysis by Wang et al. [106] in non-diabetic patients with MASLD showed that resistance training led to significant reductions in ALT and AST. Mechanistically, resistance exercise may increase muscle glucose uptake, reduce circulating glucose levels and subsequently decrease hepatic fat synthesis [8]. Nevertheless, in light of recent evidence, further research is warranted to reassess the comparative effects of aerobic and resistance exercise on metabolic risk factors in patients with MASLD/MASH. Current guidelines recommend focusing on dietary modifications, physical activity, or, optimally, a combination of both, with the goal of achieving weight reduction [10, 107] and our findings demonstrate that the MD and aerobic exercise could improve both anthropometric measures and liver outcomes in MASLD/MASH patients.

Our findings provide insights into the potential benefits of lifestyle interventions, specifically the MD and aerobic exercise, for the management of MASLD. The observed improvements in body weight, BMI, waist circumference, and ALT levels suggest that these interventions may offer clinically meaningful benefits in reducing hepatic fat content and inflammation. Given the rising global prevalence of MASLD, these lifestyles strategies represent accessible and effective non-pharmacological options for disease management. However, further research is needed to optimize intervention protocols, including the type, intensity, and duration of dietary and exercise regimens. Long-term studies are crucial to assess the sustainability of these interventions and their impact on liver histology and other clinical outcomes. As the evidence base expands, lifestyle interventions are expected to play an increasingly central role in the management of MASLD, offering a promising avenue for improving liver health and reducing the risk of progression to more severe liver conditions.

This study presents a comprehensive systematic review and meta-analysis evaluating the effects of the MD, exercise, and their combination on anthropometric and liver outcomes in patients with MASLD/MASH. We included only RCTs and used a random-effects model to account for between-study variability. In addition, most of the eligible exercise interventions were supervised, which improves intervention fidelity and participant adherence. However, several limitations should be acknowledged. Lifestyle interventions involving diet and physical activity are inherently heterogeneous in both design and implementation, which presents a significant challenge for evidence synthesis. In particular, variability in exercise intensity, frequency, and adherence across studies complicated the interpretation of pooled effects. Moreover, due to the behavioural nature of these interventions, blinding of participants and investigators was not feasible in any of the included RCTs, introducing a potential source of performance bias. Although all included studies employed a Mediterranean-style dietary intervention, there was notable variation in how the diet was defined and operationalized. Some trials implemented energy-restricted or low-glycemic index versions, while others adhered more closely to traditional Mediterranean dietary patterns. Similarly, the composition of control groups varied widely, ranging from usual diets to other specific dietary prescriptions, limiting comparability across trials and potentially affecting the observed effect sizes. Many of the included studies were also limited by small sample sizes and relatively short intervention durations, which may constrain the generalizability and long-term applicability of the findings. While we systematically evaluated the quality of evidence using the

GRADE framework, several outcomes were supported by evidence of low or very low certainty. These limitations underscore the need for future high-quality, large-scale RCTs employing standardized definitions of the MD, harmonized intervention protocols, and extended follow-up periods to better elucidate the effects of lifestyle interventions on body composition and liver outcomes in MASLD.

Conclusions

In conclusion, the MD and aerobic exercise favour weight reduction and hepatic profile in patients with MASLD/MASH. Lifestyle interventions remain a pillar treatment in patients with MASLD/MASH. Standardized procedures to measure and report outcomes in patients with MASLD/MASH are needed to provide accumulated robust evidence on the effects of lifestyle on clinical profiles.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
CAP	Controlled attenuation parameter
EASD	European Association for the Study of Diabetes
EASL	European Association for the Study of the Liver
EASO	European Association for the Study of Obesity
GGT	Gamma-glutamyl transferase
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HITT	High-intensity interval training
LGIMD	Low-glycemic index Mediterranean diet
MASLD	Metabolic dysfunction-associated steatotic liver disease
MD	Mediterranean diet
NAFLD	Non-alcoholic fatty liver disease
PRISMA	Systematic reviews and meta-analyses
PROSPERO	Prospective register of systematic reviews
PUFA	Polyunsaturated fatty acid
RCT	Randomized controlled trials
SE	Standard error
T2D	Type 2 diabetes
WC	Waist circumference
WMD	Weighted mean difference

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04320-7.

Additional file 1: PRISMA Checklist.

Additional file 2: Tables S1-S6 and Figures S1-S12.

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Authors' contributions

V.AA. and S.B. conceptualized the study. S.T, J.H.V., and S.B. conducted the literature search. V.AA., J.H.V., H.RD., N.M., C.D., R.D., J.U., M.Tushuizen., and S.B. contributed to literature screening. V.AA., H.RD., N.M., C.D., R.D., J.U., S.D., M.Tushuizen., and S.B. extracted the data. L.B., H.RD., R.D., and S.B. performed the quality assessment. S.B. analysed the data. V.AA., J.H.V., S.T., L.B., and S.B. contributed to writing the first draft. M.CC., M.Tushuizen., M.Tawfik., K.B., J.M., A.G.H., D.G, O.F., and S.B. provided critical revision of the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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