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REVIEW ARTICLE

Effects of resistance training on cardiovascular risk factors in patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Aims Type 2 diabetes mellitus (T2DM) is prevalent worldwide, often manageable through lifestyle changes like physical activity. This meta-analysis aimed to determine the effect of resistance training (RT) on cardiovascular risk factors in adults with T2DM.

Methods Four databases were searched up to March 2024. The mean difference (MD) was calculated by a random effect model with 95% confidence interval (CI).

Results Forty-eight articles were included in the review. There was a significant pooled effect size for the meta-analysis comparing RT vs. control on hemoglobin A1C (MD = -0.49, 95% CI: -0.66, -0.33; $P < 0.00001$), fasting blood sugar (MD = -11.58, 95% CI: -18.61, -4.55; $P = 0.001$), insulin (ES = -1.65, 95% CI: -2.87, -0.42; $P = 0.008$), HOMA-IR (MD = -1.20, 95% CI: -1.85, -0.55; $P = 0.0003$), triglyceride (MD = -18.14, 95% CI: -30.32, -5.96; $P = 0.004$), and high-density lipoprotein (MD = 2.71, 95% CI: 0.78, 4.64; $P = 0.006$). Moreover, RT was effective for reducing body weight (MD = -0.81, 95% CI: -1.50, -0.13; $P = 0.02$), fat percentage (MD = -0.92, 95% CI: -1.62, -0.22; $P = 0.010$), and waist circumference (MD = -2.14, 95% CI: -3.00, -1.28; $P < 0.00001$).

Conclusion RT effectively improves cardiovascular risk factors in T2DM adults, suggesting potential as treatment or prevention. Future studies can consider investigating the optimal RT regimen to achieve effective T2DM management in adults.

Keywords Diabetes · Exercise training · Strength training · Glycemic control · Meta-analysis

Introduction

According to the International Diabetes Federation (IDF), the estimated number of individuals worldwide affected by diabetes mellitus was 537 million in 2021, with projections demonstrating an increase to 783 million by the year 2045 [1]. The urbanization and development of the global economy have significantly contributed to the rise in diabetes cases, driven by factors such as reduced physical activity, unhealthy dietary habits, and aging [2, 3].

Insulin resistance impairs the ability of muscle cells to take up and store glucose and triglycerides, leading to high levels of glucose and triglycerides in the bloodstream. Additionally, insulin resistance is linked to a higher likelihood of developing cardiovascular diseases (CVDs) and mortality [4, 5]. Previous studies have shown that various factors, including inflammatory factors, indices of insulin

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resistance, and lipid profile contribute to the development of CVDs [3].

According to the American College of Sports Medicine (ACSM), physical exercise is a therapeutic approach for individuals with T2D. The current recommendation suggests that a minimum cumulative energy expenditure of 1000 kcal per week should be achieved through engaging in aerobic activities [6]. The recommendations from the American Diabetes Association (ADA) align with the aforementioned guidelines, suggesting at least 150 min per week of moderately intense aerobic exercise, or alternatively, 90 min per week of vigorous aerobic exercise [7]. Consequently, aerobic exercise has been the primary area of focus in studies examining exercise training, as it consistently demonstrates improvements in glucose control [8]. Nevertheless, long-term adherence to these recommendations remains low, highlighting the need for research into effective strategies that can enhance compliance rates.

Over the past decade, there has been an increasing interest in investigating the impacts of resistance training (RT) on glycemic control and insulin sensitivity. This interest stems from the acknowledgement that RT operates through both overlapping mechanistic pathways with aerobic training, as well as distinct pathways that deliver additional benefits for insulin signaling [9]. The emphasis on RT is driven, in part, by the understanding that people with T2D, who often have obesity or other co-morbidities, may face challenges in achieving the required volume and intensity of aerobic training to elicit significant improvements [9]. Consequently, there is a possibility of higher adherence to RT regimens.

Moreover, it has been found that RT enhances muscular strength and endurance, improves flexibility, positively impacts body composition, and declines the likelihood of developing CVDs [4]. In contrast to aerobic exercise, the recommendation for resistance exercise by the ADA was only initiated in 2006. If there are no contraindications, it is advisable to encourage diabetic patients to engage in RT three times a week, focusing on all major muscle groups and progressing to three sets of 8–10 repetitions using a weight that cannot be lifted more than 8–10 times [2]. The popularity of RT has grown due to its positive impact on body composition and muscular strength. Additionally, it has been recognized for its role in promoting health and combating disease [2]. Such advantages comprise ameliorated glycemic control, blood lipids, and bone mineral density in healthy populations [2].

The most recent systematic review and meta-analysis, conducted by Jansson et al. [8] explored the impact of RT on hemoglobin A1c in adults with T2DM across 20 studies up until January 2021. However, additional randomized controlled trials (RCTs) have been published since then [1, 2, 4, 10–13], indicating the need for an updated meta-analysis. Moreover, despite its growing recognition, the full scope of RT's impact on cardiovascular risk factors in T2D remains to be fully elucidated. Therefore, this meta-analysis aimed to fill this gap by synthesizing only recent level 1 (RCT) evidence to offer fresh perspectives on the effects of RT on cardiovascular risk factors in patients with T2DM.

Materials and methods

Design

The present systematic review was prospectively registered in the PROSPERO international register of systematic reviews (CRD42024509820). It was executed and documented adhering to the PRISMA guidelines [14].

Information sources and search strategy

The scoping search for similar systematic reviews utilized the systematic review databases, PROSPERO and Cochrane Library [15]. Then, comprehensive searches were conducted across four online databases, including CINAHL (EBSDCO), PubMed, MEDLINE (Ovid), and EMBASE (Ovid). The search strategies were developed according to the PICO [16] method with detailed strategies provided in Supplementary Table S1. Additionally, reference lists and grey literature databases, such as Google Scholar, were screened to ensure the inclusion of relevant studies. The search was restricted to studies published in English from the inception of each database to March 1, 2024. To identify relevant RCTs, the inclusion and exclusion criteria to the titles and abstracts of all papers were independently applied by two investigators (LX, ZhS). The full text of any RCTs that were not expressly excluded by the abstract or title was examined by both investigators. Disagreements between investigators were settled by consultation until an agreement was reached. In cases where the potentially eligible studies reported data that could not be distinguished, the corresponding authors were contacted for further clarification.

Inclusion and exclusion criteria

RCTs published in English were appropriate for inclusion if they assessed the effect of a resistance exercise training intervention in comparison to usual care (i.e., no intervention, standard care, sham exercise control group, or brief advice/recommendation only) on cardio-metabolic markers (hemoglobin A1C, fasting blood sugar, insulin, HOMA-IR,

triglyceride, cholesterol, high-density lipoprotein, and low density lipoprotein) and body composition (body weight, body mass index, fat%, and waist circumference) in men and women (aged ≥ 18) with T2D. We defined a resistance workout as an exercise mode that requires exertion of force against a resistance and is completed in a dynamic fashion [17]. Studies were excluded if the intervention group was not RT only (e.g., RT was combined with aerobic and/or dietary intervention). Trials without control or studies dealing with animals were also excluded. Finally, if the participants were pregnant women with gestational diabetes, trials were also excluded.

Outcome measures

The outcomes measures included various cardio-metabolic markers: hemoglobin A1C, fasting blood sugar, insulin, HOMA-IR, triglyceride, cholesterol, high-density lipoprotein, and low-density lipoprotein. Additionally, body composition variables such as body weight, body mass index, fat percentage, and waist circumference were assessed.

Data extraction

One author (LX) completed data extraction and the second author (ZhS) checked for accuracy. We applied a data extraction form according to the Cochrane Data Collection. The following information from each included study was extracted: first author's last name, publication year, country, intervention features (duration, frequency and duration of each exercise session), exercise intensity and progression, number of participants in each group, gender, mean age in each group, and mean body mass index. Means and standard deviation (SD) were extracted from the data; where standard errors were reported, we converted them to SD.

Quality assessment and risk of bias

The validated Tool for the Assessment of Study Quality and Reporting in Exercise (TESTEX) [18], a 15-point scale specific to exercise training interventions was applied to determine the study quality. A score of 10 or higher is regarded as good reporting and study quality [19].

The risk of bias of the included studies was assessed using the revised Cochrane risk of bias, version 2 (RoB 2) tool [20]. The assessment of risk of bias in each study was conducted based on the appropriateness of sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of follow-up, and selecting reporting. Each criterion was assessed as adequate, inadequate, or unclear, in accordance with Cochrane risk of bias criteria [21]. The risk of bias in each RCT was classified as either low (all criteria graded adequate), moderate (one criterion graded inadequate, or 2 graded unclear) or high (2 or more criteria graded inadequate, or more than 2 graded unclear). The two authors divided the included RCTs at random, cross-checked the studies' quality and accuracy of the data extraction, and then evaluated the results.

Data analysis

Meta-analyses and forest plots were created using RevMan 5 [22], and meta-regression analyses were conducted using Comprehensive Meta-Analysis software (V.3 for Windows, Biostat, Englewood, New Jersey, USA). The p-value was set at 5% for the effect size. We performed meta-analyses to demonstrate the impact of RT versus control on outcome measures. Random-effects model and inverse variance methods were applied in the meta-analyses to estimate the mean difference (MD) and 95% confidence interval (CI). Data on outcomes were extracted using mean and SD values. The difference between the mean at baseline and post-intervention was calculated, and the SD change was determined by considering the sample size in the study, along with the group p-values or the 95% CI, in cases where the mean and SD were not reported. In addition, we converted standard error of the mean (SEM) to SD in instances where SEM was provided instead of SD [23]. GetData Graph Digitizer software was utilized to extract data from figures if data were not presented in the text or tables, as well as authors were not available.

The I^2 statistic was utilized to assess statistical heterogeneity, with I^2 values exceeding 50% indicating considerable heterogeneity [24]. In cases where high levels of heterogeneity were observed in a meta-analysis, we examined study features and data-related factors to identify the source of heterogeneity. Sub-group analyses were conducted, considering intervention duration (≤ 12 weeks and > 12 weeks), gender (men, women, or mix), baseline hemoglobin A1C (< 7.5% and ≥ 7.5%), and baseline BMI (< 30 kg.m^2 and ≥ 30 kg.m^2) as potential causes of heterogeneity. Additionally, meta-regression was performed to further explore potential sources of heterogeneity, including year of publication, number of sessions per week, mean sample age, sample size, and study quality scores (using TESTEX). Furthermore, sensitivity analyses were conducted to assess the reliability and stability of the outcomes. The risk of publication bias was evaluated using funnel plots [25].

Results

Study selection

Our initial combined search yielded a total of 1436 articles, subsequently yielding 677 articles for evaluation after removal of duplicates, based on their titles and abstracts. The full screening process resulted in 60 articles, out of which 12 were eliminated due to the following reasons: (1) the absence of a control group; (2) the utilization of combined exercise training interventions; (3) the replication of a previously conducted study; (4) the inclusion of an active control group; and (5) the utilization of an acute intervention. Finally, 48 article met the inclusion criteria and were consequently incorporated into the meta-analysis. The article selection process adhered to the guidelines outlines by the PRISMA, as illustrated in Fig. 1.

Participant, and intervention characteristics

Supplementary Table S2 shows the details of participant, and intervention characteristics. A total of 2191 participants (intervention: 1148; control: 1043) were included. Among these, 1056 participants were female, 1006 were male; and the remaining 129 participants were not classified. The minimum mean age was 21.29 ± 1.90 years [11], while the maximum mean age was 73.2 ± 2.6 years [26]. Prior to the study, all participants led a sedentary lifestyle, and the control groups were instructed to maintain their routine lifestyle throughout the study. The studies were conducted across

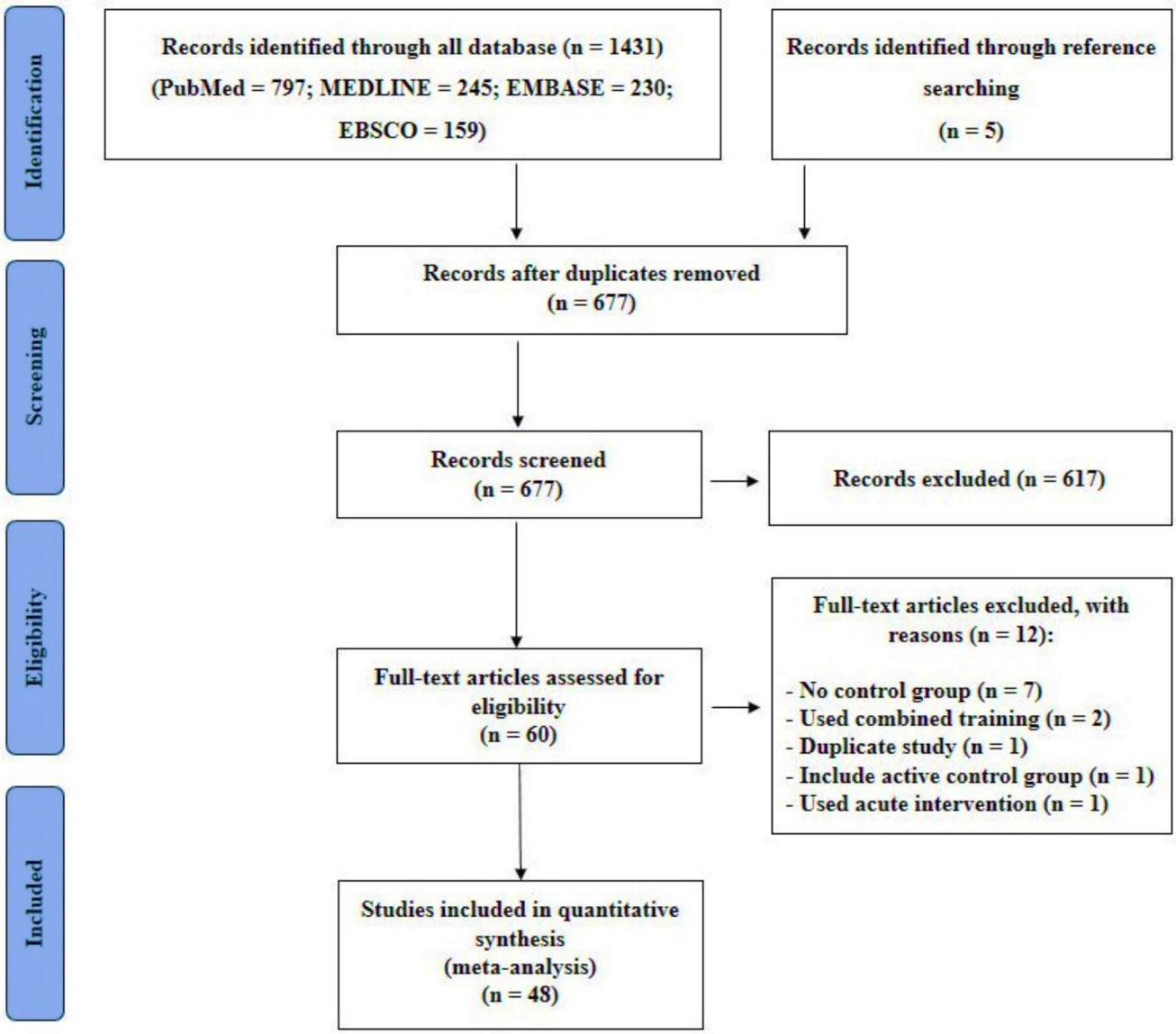

Fig. 1 Flow chart for selection of studies for systematic review

various countries: 11 in Iran, five in the USA, four in India, four in Brazil, three in Australia, three in Korea, two in Germany, two in China, two in Japan, and one each in New Zealand, Finland, Ireland, Portugal, Taiwan, Greece, Sri Lanka, Malaysia, Canada, Belgium, Ethiopia, and Columbia. The duration of the interventions ranged from 4 to 6 weeks [27] to 12 months [28, 29]. Among the included RCTs, only 14 [30–43] reported the anti-diabetic medications used by participants during the intervention, including biguanides, sulfonylureas, and metformin.

RT exercise prescription

Supplementary Table S2 displays a summary of RT exercise prescriptions in each included study. The number of exercises included in each workout ranged from 3 [44] to 12 [31, 45, 46]. Most studies utilized weight machines or free weights, except for three studies [26, 40, 42] which employed elastic bands. Studies used a workout frequency of either seven [26, 46], five [27, 40, 47], four [11], three [1, 2, 4, 10, 13, 28–31, 34, 36, 37, 41, 42, 45, 48–64], two to three [65], two [12, 32, 33, 39, 43, 44, 66, 67], or one [38] sessions per week.

Effects of RT interventions on cardio-metabolic markers

Hemoglobin A1C. A meta-analysis of 43 trials involving 1953 participants demonstrated a statistically significant reduction in hemoglobin A1C with RT, as illustrated in Fig. 2 (MD: − 0.49, 95% CI: − 0.66, − 0.33; $P < 0.0001$), with high heterogeneity ($I^2 = 85\%$). Subgroup analyses demonstrated that the decrease in hemoglobin A1C levels after RT was statistically significant in: (1) both those with an exercise training duration of more than 12 weeks (MD: − 0.50, 95% CI: − 0.79 to − 0.21; $I^2 = 93\%$) and those with a duration of ≤ 12 weeks (MD: − 0.42, 95% CI: − 0.65 to – 0.30; $I^2 = 65\%$) (see Supplementary Table S3), (2) in women (MD: − 0.68, 95% CI: − 1.08 to – 0.28; $I^2 = 54\%$), men (MD: − 0.89, 95% CI: − 1.39 to – 0.40; $I^2 = 44\%$) and both sexes combined (MD: − 0.42, 95% CI: − 0.60 to – 0.24; $I^2 = 88\%$) (see Supplementary Table S3), (3) in studies with a baseline hemoglobin A1C of < 7.5% (MD: − 0.15, 95% CI: − 0.31 to 0.00); $p = 0.05$; $I^2 = 62\%$) and those with ≥ 7.5% (MD: − 0.81, 95% CI: − 1.06 to − 0.55; $p < 0.00001$; $I^2 = 88\%$), and (4) in studies with a baseline BMI of < 30 kg/m^2 (MD: − 0.53, 95% CI: − 0.72 to – 0.33); $p < 0.00001$; $I^2 = 79\%$) and those with ≥ 30 kg/m^2 (MD: − 0.44, 95% CI: − 0.72 to – 0.15; $p = 0.003$; $I^2 = 90\%$) (see Supplementary Table S3). Sensitivity analysis displayed that the exclusion of individual studies did not result in any statistically significant differences, indicating a notable level of robustness in these effects.

Fasting blood sugar. A meta-analysis of 34 trials involving 1444 participants demonstrated a statistically significant reduction in fasting blood sugar with RT, as depicted in Fig. 3 (MD: – 11.58 mg/dl, 95% CI: − 18.61, − 4.55; $P = 0.001$), with high heterogeneity ($I^2 = 93\%$). Subgroup analyses demonstrated that the decrease in fasting blood sugar after RT was statistically significant in: (1) both exercise training duration exceeding 12 weeks (MD: − 9.52 mg/dl, 95% CI: − 17.73 to – 1.32; $I^2 = 70\%$) and those ≤ 12 weeks (MD: − 11.60 mg/dl, 95% CI: − 20.72 to – 2.47; $I^2 = 94\%$) (see Supplementary Table S3), (2) in women (MD: − 17.89 mg/dl, 95% CI: − 33.97 to – 1.81; $I^2 = 95\%$) and men (MD: − 10.98 mg/dl, 95% CI: − 15.88 to – 6.08; $I^2 = 0\%$), but not in both sexes (MD: − 7.72 mg/dl, 95% CI: − 17.32 to 1.89; $I^2 = 91\%$) (see Supplementary Table S3), (3) in studies with a baseline hemoglobin A1C of < 7.5% (MD: − 8.58, 95% CI: − 14.28 to – 2.87); $p = 0.003$; $I^2 = 64\%$) and those with ≥ 7.5% (MD: − 14.98, 95% CI: − 27.91 to – 2.05; $p = 0.02$; $I^2 = 96\%$), and (4) in studies with a baseline BMI of < 30 kg/m^2 (MD: − 12.10, 95% CI: − 24.01 to – 0.19); $p = 0.05$; $I^2 = 94\%$) and those with ≥ 30 kg/m^2 (MD: − 11.58, 95% CI: − 18.61 to – 4.55; $p = 0.005$; $I^2 = 89\%$) (see Supplementary Table S3). Sensitivity analysis exhibited that the exclusion of individual studies did not result in any statistically significant differences, demonstrating a notable level of robustness in these effects.

Insulin. A meta-analysis of 15 trials involving 528 participants demonstrated a statistically significant reduction in insulin with RT, as depicted in Fig. 4 (MD: – 1.65, 95% CI: − 2.87, − 0.42; $P = 0.008$), with high heterogeneity ($I^2 = 90\%$). Subgroup analyses based on intervention duration demonstrated that insulin did not significantly change after RT in either exercise training duration exceeding 12 weeks (MD: − 4.19, 95% CI: − 10.91 to 2.53; $I^2 = 90\%$) or those ≤ 12 weeks (MD: − 1.22, 95% CI: − 2.57 to 0.14; $I^2 = 89\%$) (see Supplementary Table S3). However, subgroup analyses based on gender demonstrated that insulin levels significantly decreased only in men (MD: − 3.20, 95% CI: − 6.07 to – 0.32; $I^2 = 91\%$), but not in women (MD: 0.18, 95% CI: − 1.01 to 1.38; $I^2 = 21\%$) or in both sexes combined (MD: − 2.05, 95% CI: − 4.29 to 0.19; $I^2 = 92\%$) (see Supplementary Table S3). Additionally, subgroup analyses based on baseline A1C levels revealed that insulin levels did not significantly change in studies with baseline A1C < 7.5% (MD: -0.57, 95% CI: -1.78 to 0.64; $p = 0.35$; $I^2 = 29\%$) but significantly decreased in those with A1C ≥ 7.5% (MD: -2.42, 95% CI: -4.18 to -0.65; $p = 0.007$; $I^2 = 94\%$). Finally, analyses based on baseline BMI levels showed no significant change in insulin levels for studies with BMI < 30 kg/m² (MD: -0.61, 95% CI: -2.33 to 1.12;

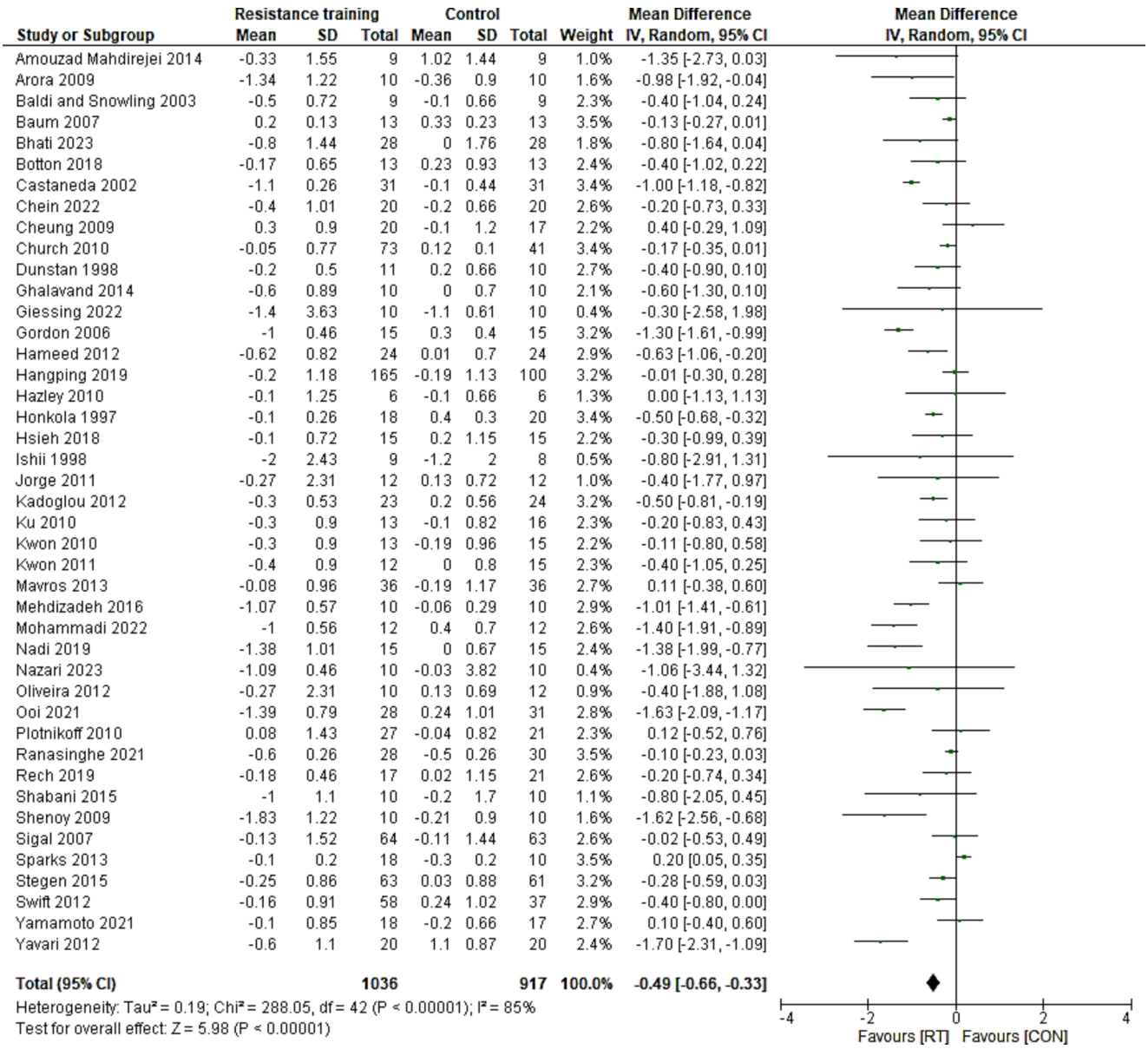

Fig. 2 Forest plot of effect on hemoglobin A1C level post-exercise intervention program

$p = 0.49$; $I^2 = 84\%$), whereas a significant decrease was observed in those with BMI ≥ 30 kg/m² (MD: -2.8, 95% CI: -4.61 to -1.00; $p = 0.002$; $I^2 = 91\%$) (see Supplementary Table S3). Sensitivity analysis displayed that when Gordon et al. [55] was removed, the overall effect of RT became insignificant (MD: − 1.10, 95% CI: − 2.25, 0.05; $I^2 = 88\%$).

HOMA-IR. A meta-analysis of nine trials involving 276 participants demonstrated a statistically significant reduction in HOMA-IR with RT, as represented in Fig. 5 (MD: – 1.20, 95% CI: − 1.85, − 0.55; $P = 0.003$), with high heterogeneity ($I^2 = 91\%$).

Triglyceride. A meta-analysis of 23 trials involving 880 participants revealed a statistically significant reduction in triglyceride levels with RT, as illustrated in Figure S1 (MD: – 18.14 mg/dl, 95% CI: − 30.32, − 5.96; $P = 0.004$), with moderate heterogeneity ($I^2 = 59\%$). Subgroup analyses based on intervention duration confirmed that triglyceride significantly decreased after RT in exercise training duration ≤ 12 weeks (MD: − 23.90, 95% CI: − 37.43 to – 10.37; $I^2 = 53\%$), but not in studies lasted > 12 weeks (MD: − 5.87, 95% CI: -34.81 to 23.07; $I^2 = 67\%$) (see Supplementary Table S3). However, subgroup analyses based on gender demonstrated that triglyceride levels significantly decreased only in studies conducted on both sexes (MD: − 14.51, 95% CI: − 20.20 to − 8.82; $I^2 = 0\%$), but not in studies with isolated men (MD: 4.5, 95% CI: − 100.74 to 109.74; $I^2 = 88\%$) or women (MD: − 4.02, 95% CI: − 67.66 to 59.62; $I^2 = 89\%$) (see Supplementary Table S3). Additionally, sensitivity

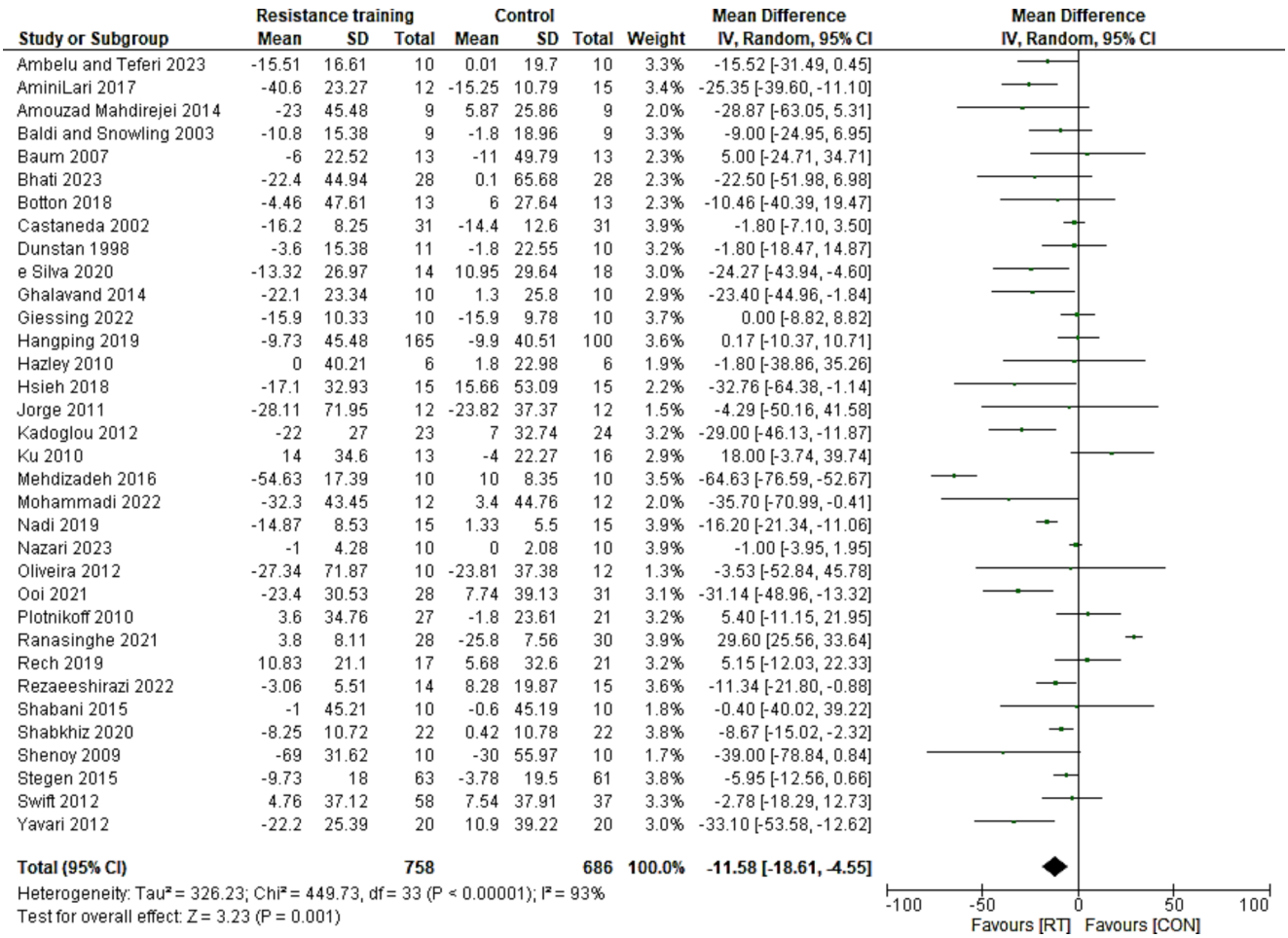

Fig. 3 Forest plot of effect on fasting blood sugar level post-exercise intervention program

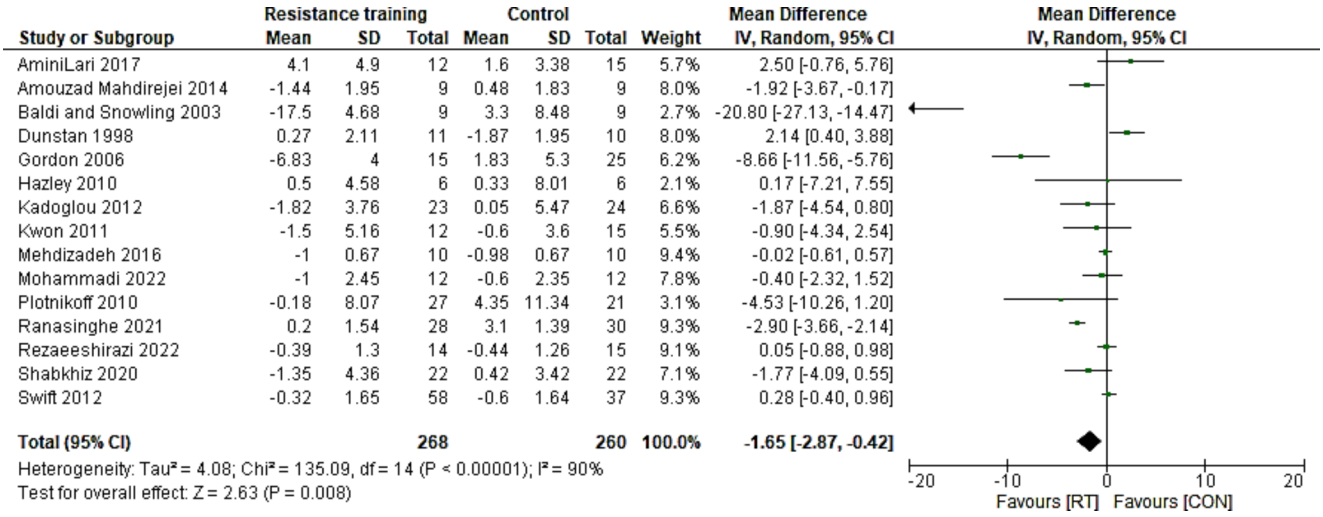

Fig. 4 Forest plot of effect on insulin level post-exercise intervention program

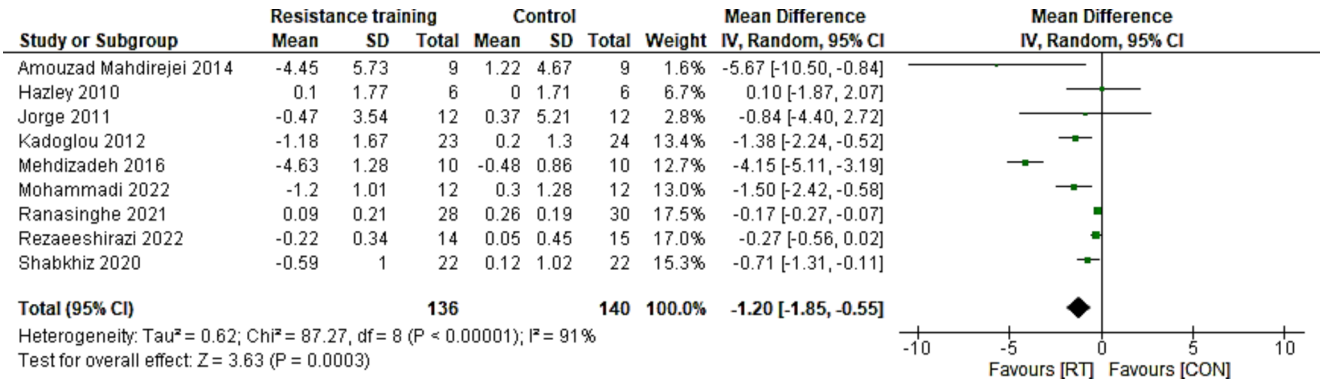

Fig. 5 Forest plot of effect on HOMA-IR post-exercise intervention program

analysis exhibited that the exclusion of individual studies did not result in any statistically significant differences, demonstrating a notable level of robustness in these effects.

Cholesterol. A meta-analysis of 21 trials comprising 713 participants revealed non-significant improvements in cholesterol levels with RT (MD: – 8.81, 95% CI: − 19.17, 1.54; $P = 0.10$), with high heterogeneity ($I^2 = 94\%$) (Figure S2).

High-density lipoprotein. A meta-analysis of 22 trials involving 853 participants revealed a statistically significant increase in high-density lipoprotein levels with RT, as indicated in Figure S3 (MD: 2.71 mg/dl, 95% CI: 0.78, 4.64; $P = 0.006$), with moderate heterogeneity ($I^2 = 77\%$). Subgroup analyses based on intervention duration demonstrated that high-density lipoprotein significantly increased after RT in studies lasted 12 weeks or less (MD: 3.02, 95% CI: 0.18 to 5.86; I2 = 72%), but no in those lasted > 12 weeks (MD: 1.94, 95% CI: − 0.96 to 4.85; $I^2 = 79\%$) (see Supplementary Table S3). Moreover, subgroup analyses based on gender demonstrated that high-density lipoprotein levels significantly increased in men (MD: 5.07, 95% CI: − 0.08 to – 10.22; $I^2 = 0\%$) and in both sexes combined (MD: 2.17, 95% CI: − 0.04 to 4.37; $I^2 = 80\%$), but not in women (MD: 5.44, 95% CI: − 2.14 to 13.03; $I^2 = 77\%$) (see Supplementary Table S3). Sensitivity analysis exhibited that the exclusion of individual studies did not result in any statistically significant differences, demonstrating a notable level of robustness in these effects.

Low-density lipoprotein. Meta-analysis of the effect of RT on low-density lipoprotein found no evidence of a change as demonstrated in Figure S4 (MD: – 7.07 mg/dl, 95% CI: − 17.83, 3.70; $P = 0.20$). However, we observed high heterogeneity among studies ($I^2 = 91\%$; $p < 0.00001$).

Effects of RT interventions on body composition

Body weight. A meta-analysis of 19 studies involving 880 participants demonstrated a statistically significant decline in body weight with RT, as revealed in Figure S5 (MD: – 0.81 kg, 95% CI: − 1.50, − 0.13; $P = 0.02$), with no heterogeneity ($I^2 = 0\%$). Subgroup analyses based on intervention duration demonstrated that body weight did not significantly change after RT in either exercise training duration exceeding 12 weeks (MD: − 0.86, 95% CI: − 1.81 to 0.09; $I^2 = 0\%$) or those ≤ 12 weeks (MD: − 0.76, 95% CI: − 1.75 to 0.23; $I^2 = 0\%$) (see Supplementary Table S3). Subgroup analyses based on gender demonstrated that body weight significantly decreased only in both sexes combined (MD: − 0.79, 95% CI: − 1.51 to – 0.07; $I^2 = 0\%$), but not in men (MD: -1.85, 95% CI: − 6.09 to 2.38; $I^2 = 0\%$) or women (MD: − 0.72, 95% CI: − 3.17 to 1.73; $I^2 = 0\%$) (see Supplementary Table S3). Sensitivity analysis displayed that when Honkola et al. [39] was removed, the overall effect of RT became insignificant (MD: − 0.68, 95% CI: − 1.40, 0.03; $I^2 = 0\%$).

Body mass index. Meta-analysis of the effect of RT on body mass index found no evidence of a change as demonstrated in Figure S6 (MD: – 0.21 $kg.m^2$, 95% CI: − 0.44, 0.01; $P = 0.06$). Moreover, we observed low levels of heterogeneity among studies ($I^2 = 10\%$).

Fat percentage. A meta-analysis of 18 studies involving 739 participants demonstrated a statistically significant decline in fat percentage with RT, as revealed in Figure S7 (MD: – 0.92, 95% CI: − 1.62, − 0.22; $P = 0.010$), with low levels of heterogeneity ($I^2 = 45\%$; $p = 0.02$). Subgroup analyses based on intervention duration confirmed that fat percentage significantly decreased after RT in exercise training duration exceeding 12 weeks (MD: − 1.36, 95% CI: − 2.01 to -0.71; $I^2 = 0\%$), but not in those ≤ 12 weeks (MD: − 0.73, 95% CI: − 1.71 to 0.25; $I^2 = 0\%$) (see Supplementary Table S3). Moreover, subgroup analyses based on gender demonstrated that fat percentage significantly decreased in women (MD: − 1.20, 95% CI: − 2.30 to – 0.11; $I^2 = 0\%$) and in both sexes combined (MD: − 1.21, 95% CI: − 2.18 to − 0.25; $I^2 = 36\%$), but not in men (MD: − 0.23, 95% CI: − 1.87 to 1.41; $I^2 = 64\%$) (see Supplementary Table S3). Sensitivity analysis exhibited that the exclusion of individual studies

did not result in any statistically significant differences, demonstrating a notable level of robustness in these effects.

Waist circumference. A meta-analysis of 16 studies involving 732 participants demonstrated a statistically significant decrease in waist circumference with RT, as revealed in Figure S8 (MD: – 2.14 cm, 95% CI: − 3.00, − 1.28; $P < 0.00001$), with low levels of heterogeneity ($I^2 = 22\%$). Subgroup analyses based on intervention duration demonstrated that waist circumference significantly reduced after RT in both exercise training duration exceeding 12 weeks (MD: − 2.88, 95% CI: − 3.94 to -1.81; $I^2 = 16\%$) and those ≤ 12 weeks (MD: − 1.24, 95% CI: − 2.10 to − 0.37; $I^2 = 0\%$) (see Supplementary Table S3). Moreover, subgroup analyses based on gender demonstrated that waist circumference significantly reduced only in both sexes combined (MD: − 2.35, 95% CI: − 3.41 to – 1.29; $I^2 = 36\%$), but not in women (MD: − 1.79, 95% CI: − 5.55 to 1.97; $I^2 = 0\%$). Additionally, only one trial [68] was conducted in men, with no evidence of change (MD: − 0.49, 95% CI: − 2.82 to 1.84) (see Supplementary Table S3). Sensitivity analyses found the overall effect of RT is robust when removing studies one by one.

Meta-regression analyses

Meta-regression analyses revealed that none of the considered variables significantly contributed to the observed heterogeneity in hemoglobin A1C, fasting blood sugar, insulin, triglyceride, high-density lipoprotein, or body weight changes (all $p > 0.05$). Yet, in the analysis of fat percentage, mean sample age emerged as a significant predictor of heterogeneity ($Q = 4.13$, $p = 0.0420$). Similarly, in the analysis of waist circumference, both mean sample age ($Q = 8.52$, $p = 0.0035$) and year of publication ($Q = 13.16$, $p = 0.0003$) were found to significantly affect the RT effect (see Supplementary Tables S4-S43).

Risk of bias, publication bias, and quality of evidence

In total, only five studies [2, 13, 51, 53, 54] were deemed to have an unclear risk of bias, and all other studies were identified as having a high risk of bias. The risk-of-bias assessment for each individual study can be found in Supplementary Figure S9.

According to the TESTEX tool, the quality of the studies presented in this meta-analysis is good, median score was 10 (from a maximum score of 15; range 8–13) (see Supplementary Table S44).

To further explore the possibility of publication bias, we conducted funnel plots and Egger's test for variables with significant changes. The funnel plots for these variables did not indicate asymmetry, suggesting a low likelihood of publication bias (Supplementary Figures S10-17). Furthermore, the results of Egger's test showed no significant evidence of publication bias for the analyzed variables, including hemoglobin A1C ($p = 0.06613$), fasting blood sugar ($p = 0.10525$), insulin ($p = 0.20041$), triglyceride ($p = 0.85490$), HDL ($p = 0.86846$), body weight ($p = 0.35908$), fat% ($p = 0.39111$), and waist circumference ($p = 0.86321$). These findings suggest that the observed effects are unlikely to be influenced by publication bias.

Discussion

This systematic review and meta-analysis included 48 studies and 2,191 participants, and making it the most extensive study to explore the effects of RT on cardiovascular risk factors in people with T2DM. We observed significant improvements in glycemic control, HDL levels, as well as some anthropometric variables.

Consistent with previous meta-analyses [8, 27, 69, 70], we found that RT interventions reduce hemoglobin A1C levels, indicative of improved long-term glycemic control among T2DM participants engaged in RT. Similarly, fasting blood sugar levels exhibited a significant decrease post-intervention, suggesting enhanced glucose regulation. Notably, the observed reductions in insulin levels and HOMA-IR further underscore the beneficial effects of RT on insulin sensitivity, a crucial aspect in the management of insulin resistance and T2DM. Previous research has highlighted that even a modest decrease of 0.3% in hemoglobin A1C holds clinical significance [71, 72]. Thus, the results of our meta-analysis hold clinical relevance, as we observed a 0.49% reduction in hemoglobin A1C. Notably, our study revealed a larger effect size for hemoglobin A1C compared to the effect sizes reported by Liu et al. (-0.45%), Ishiguro et al. (-0.34%) and Jansson et al. (-0.39%) for the same variable [8, 69, 73], possibly due to the inclusion of additional studies.

There are some possible pathways through which RT may enhance glycemic control. One possible mechanism involves skeletal muscle facilitating substantial glucose uptake via glucose transporters [74], particularly glucose transporter type 4 (GLUT4), which mediates insulin-induced glucose uptake [75]. RT has the capacity to augment the protein content of GLUT4, and increased muscle mass can boost glucose uptake [76]. Consequently, features of RT regimens that promote muscular hypertrophy may contribute to improved glycemic control. Nonetheless, single session of RT has demonstrated reductions in glucose levels among individuals with T2DM [77], indicating that

certain features of RT may enhance glycemic control irrespective of muscular hypertrophy.

Our meta-analysis demonstrated that RT interventions significantly reduce body weight, fat percentage, and waist circumference-key anthropometric markers associated with metabolic health and cardiovascular risk [78, 79]. These findings align with studies highlighting RT's role in improving body composition through enhanced muscle mass and decreased fat mass, which contribute to better metabolic outcomes in T2DM [78]. The reductions in fat percentage and waist circumference directly influence insulin sensitivity and glucose metabolism [79–81], further supporting the role of RT in improving metabolic health.

Subgroup analyses based on intervention duration also demonstrated notable decreases in hemoglobin A1C and fasting blood sugar levels in both medium- and long-term interventions (≤ 12 weeks and > 12 weeks). These findings are consistent with studies conducted by Ishiguro and colleagues [73] and Jansson and colleagues [8], which similarly found that intervention duration did not significantly influence the impact of RT on hemoglobin A1C. Furthermore, another meta-analysis, which categorized included studies into two subgroups (8–20 weeks and 21–48 weeks), reported no differences in hemoglobin A1C between the subgroups of RT [82]. This suggests that the duration of intervention may not play a substantial role in reducing hemoglobin A1C levels, as both shorter and longer regimens may yield comparable effects. However, it is important to note that this finding may not extend to other crucial indicators of glycemic control and insulin resistance, such as insulin and the HOMA-IR, as our analysis revealed no significant changes in insulin levels following RT, regardless of whether the exercise training duration exceeded 12 weeks or was ≤ 12 weeks.

Our analysis revealed significant reductions in triglyceride levels, a key lipid variable associated with cardiovascular risk, particularly in studies with intervention durations of 12 weeks or less. This suggests that the initial phases of RT are especially effective in improving lipid profiles, likely due to early metabolic adaptations. During these early weeks, individuals may experience enhanced lipoprotein lipase (LPL) activity, which are subsequently taken up and oxidized by muscles [83]. However, this reduction in triglycerides was not observed in studies lasting longer than 12 weeks, which may be due to the body's adaptation to the exercise regimen, leading to a plateau in lipid metabolism improvements [84]. As training progresses, the relative intensity or progression of the exercise regimen might decrease, reducing the stimulus for further triglyceride reduction. Additionally, the body may shift its focus from reducing circulating triglycerides to mobilizing and utilizing other lipid stores, such as intramuscular fat, which could explain the lack of further reductions in longer interventions. Interestingly, subgroup analyses based on gender revealed that the decrease in triglyceride levels was significant only in studies involving both sexes, while studies with isolated male or female participants did not show significant changes. The notable improvements in high-density lipoprotein levels further support the favorable impact of RT on lipid profiles, which are paramount in mitigating cardiovascular risk factors [85]. While non-significant changes were observed in cholesterol and low-density lipoprotein levels, the significant increase in high-density lipoprotein and concurrent decrease in triglycerides suggest a favorable shift in lipid metabolism with RT interventions. These findings collectively underscore the multifaceted benefits of RT in ameliorating metabolic health variables and reducing cardiovascular risk in individuals with metabolic disorders.

The impact of RT on anthropometric measures is likely mediated by increased muscle mass and enhanced metabolic activity, facilitating greater glucose uptake and utilization. The reduction in fat percentage also indicates a shift towards a more favorable body composition, which has been linked to decreased insulin resistance and lower cardiovascular risk in individuals with T2DM [78–80]. The consistent effects of RT on body composition across different intervention durations suggest that both short- and long-term RT programs can be effective in improving body composition in T2DM patients, although factors such as training intensity and baseline fitness levels may influence the degree of improvement.

Overall, our findings suggest that the effects of RT on lipid profiles are influenced by various factors, including intervention duration and gender composition. Moreover, on the basis of the available evidence, the varied responses of lipids may be linked to other factors such as the volume and intensity of training [44]. These insights can inform the development of tailored RT interventions aimed at optimizing lipid profiles in individuals with metabolic disorders. Further research is warranted to explore the mechanisms underlying these subgroup differences and to guide personalized approaches to RT-based interventions for lipid management.

In the pathophysiological development of T2DM, weight issues are often associated with insulin resistance, a key risk factor. Effective management of T2DM involves not only controlling blood glucose levels but also addressing insulin resistance and achieving weight loss [86]. In this systematic review and meta-analysis, RT programs were found to significantly reduce fasting blood sugar levels, body weight, and fat percentage. These results align with previous reports demonstrating the effectiveness of exercise in individuals with T2DM, showing improvements in blood glucose control and insulin resistance by facilitating glucose uptake and

utilization in skeletal muscle [87–89]. Moreover, an elevation in plasma-free fatty acids can result in the inactivation of cellular insulin receptors, leading to reduced stimulation of the insulin signaling pathway and consequently, insulin resistance [44, 90]. Given that exercise promotes increased metabolism, utilizing fats both during and after physical activity, it is likely that changes in body fat (i.e., fat percentage) have also contributed to enhancing cellular glucose uptake.

Meta-regression analyses revealed that none of the considered variables significantly contributed to the observed heterogeneity in several outcomes, including hemoglobin A1C, fasting blood sugar, insulin, triglyceride, high-density lipoprotein, or body weight changes. However, in fat percentage analysis, mean sample age emerged as a significant predictor of heterogeneity, suggesting that differences in the age composition of study populations may influence the observed effects of interventions on fat percentage. Similarly, in waist circumference analysis, both mean sample age and year of publication were found to significantly affect the observed effects. These findings highlight the importance of considering demographic factors such as age and temporal trends in study outcomes when interpreting results and designing interventions targeting metabolic health. Nonetheless, future research should aim to further investigate the factors contributing to heterogeneity in metabolic outcomes to advance our understanding and improve interventions aimed at promoting metabolic health.

There are several key strengths to our study. First, to the best of our knowledge, this is the first meta-analysis to explore the efficacy of RT regimens on cardio-metabolic variables and body composition in adults diagnosed with T2DM. Second, it adheres to the PRISMA reporting guidelines, ensuring transparency and adherence to best practices in systematic review methodology. Furthermore, only studies employing a RCT design were included, enhancing the rigor and reliability of the findings. Third, the review utilized TESTEX [18], a quality assessment tool not previously employed in similar systematic reviews, to evaluate the methodological quality of the included studies. Finally, a rigorous inclusion/exclusion protocol was followed to minimize confounding factors among study populations, guided by established methodologies proposed by Berman and Parker (2002) [91]. This study also has some limitations. First, the majority of the RCTs included in our analysis demonstrated methodological quality ranging from low to moderate, potentially introducing bias into the analyses and limiting the strength of evidence to levels ranging from low to medium. However, despite this limitation, we accounted for study quality in our meta-regression analysis and found that it did not significantly impact the findings. Additionally, both meta-analyses revealed statistical heterogeneity, promoting us to conduct further analyses such as meta-regression and sub-group analyses to explore potential sources of variation. Second, it is important to acknowledge the possibility of publication bias, where studies that fail to demonstrate statistical and/or clinical significance may be less likely to be published. This can occur either due to authors' decisions to refrain from publication or due to rejection of such articles by scientific journals. As a result, the findings of our meta-analysis should be interpreted with caution. Fourth, although our review focused on assessing the effects of resistance exercise training on cardio-metabolic variables in individuals with T2DM, it is essential to recognize that the use of other type 2 diabetes medications, such as metformin, was not explicitly accounted for or reported in the included studies. This limitation could potentially impact the generalizability of our findings and the interpretation of the results. Future research should aim to investigate the effects of RT regimens among individuals with T2DM who are on various medications, thereby offering a more comprehensive understanding of its efficacy across diverse patient populations. Lastly, the inclusion of RCTs published exclusively in English may introduce publication bias, potentially limiting the generalizability of the findings. Consequently, it is crucial to approach the interpretation of the review results with caution.

In conclusion, this meta-analysis with meta-regression provides further evidence supporting the effectiveness of RT regimens in reducing cardiovascular risk factors, including hemoglobin A1C, fasting blood sugar, insulin, HOLA-IR, triglyceride, and high-density lipoprotein, as well as body weight, fat percentage, and waist circumference in patients with T2DM. Therefore, RT programs can be considered as a viable option for T2DM patients, either as a prescribed treatment or as a preventive measure. Future studies can consider investigating the optimal RT regimen to achieve effective T2DM management in adults.

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Author contributions LXJ and ZhSG designed the study and wrote the initial draft of the paper. ZhSJ performed the original data analysis. YS re-analyzed the data and revised the statistical methods and results sections. MS contributed to the interpretation of the meta-analysis results and assisted in rewriting the discussion, particularly framing the findings within the context of current literature. XZ played a crucial role in reformatting the manuscript, addressing reviewer comments, and ensuring the manuscript's alignment with journal guidelines. All authors reviewed the results and approved the final version of the manuscript.

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Declarations

Conflict of interest The authors declare that they have no competing interest.

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