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Effect of combined aerobic exercise and resistance training on postmenopausal women with type 2 diabetes: a systematic review and meta-analysis

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ABSTRACT

Background: There is no strong evidence demonstrating whether or not aerobic exercise in conjunction with resistance exercise improves metabolic diabetes markers in postmenopausal women.

Objective: To evaluate the effect of aerobic exercise and resistance training on metabolic markers in postmenopausal women with type 2 diabetes mellitus (T2DM) by means of a systematic review and meta-analysis.

Methods: The searches were completed using EMBASE, MEDLINE/PubMed, Scopus and Web of Science databases. This study included non-blinded, single or double-blinded randomized control trials and postmenopausal women diagnosed with T2DM. The imposed intervention was aerobic exercise plus any training protocol to strengthen muscle groups for resistance intervention. The outcomes of interest were the blood glucose levels, insulin secretion, homeostasis model assessment-insulin resistance index (HOMA-IR) and glycated hemoglobin (HbA1c). Risk of Bias tools and GRADE were obligatory.

Results: Three studies were included (83 participants). Exercise intervention ranged between two to four days per week. Compared to the control group, in the group submitted to aerobic exercise+resistance training, no significant change was noted for HbA1c (subtotal=mean difference – 0.35 [95% CI: –0.85, 0.15], $p=.17$, and heterogeneity = 0%) (GRADE: very low), nevertheless, HOMA-IR index was significantly improved (subtotal=mean difference –0.52 [95% CI: –0.99, –0.05], $p=.03$, and heterogeneity = 0%) (GRADE: very low).

Conclusion: Despite the very low certainty found in the quality of evidences, our analysis showed that aerobic exercise along with strength exercise seems to improve some metabolic diabetes markers in postmenopausal women with T2DM. There is a need for further studies to support our preliminary findings.

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Introduction

Type 2 diabetes mellitus (T2DM) is a complex metabolic disease that requires continuous self-management to decrease and prevent further complications such as frequent urinary tract infections, skin infections, difficulty of healing wounds, and also causing weight loss, tiredness and weakness. T2DM can also cause serious complications such as diabetic retinopathy and autonomic neuropathy [1]. This epidemic endocrine condition develops as a result of increased blood glucose levels triggered by insulin secretion deficit and/or insulin resistance [2]. In 2021, T2DM and type 1 diabetes have been associated to around 6.7 million deaths globally, which is akin to one death every five seconds. Also, T2DM and type 1 diabetes were responsible for over USD \$966 billion of health-related costs.

The treatment of diabetes helps avoid premature deaths, as well as cardiovascular and metabolic problems [3]. The

pharmacological aim is to prevent severe hyperglycemia, maintain glycemic control and decrease risk factors for chronic complications, for instance dyslipidemia and hypertension [3]. A previous systematic review [4] assessed 179 trials and 25 observational studies in order to better understand the effect of metformin as monotherapy or metformin-based combinations for T2DM. Their key results established moderate to strong evidence that metformin monotherapy was related to lower risk of cardiovascular mortality opposed to sulfonylurea monotherapy. In addition, the 10-year follow-up of the United Kingdom Prospective Diabetes Study [5] stated an enhanced effect of metformin and sulfonylureas in contrast to controlled diets.

In a similar fashion, non-pharmacological complementary and therapeutic interventions typically have the benefits of simple enactment and low financial cost. Consequently, exercise is enforced in the treatment of numerous diseases as an adjunct single therapy [6]. A review of the scientific literature reveals

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that aerobic exercise has been shown to reduce insulin resistance, improve muscle strength, body composition and endothelial function. However, there is currently no convincing evidence to suggest that combining resistance training with aerobic exercise is more effective than either form of exercise alone in reducing glycated hemoglobin (HbA1c) [7–9].

Bearing this in mind, a specific and vulnerable cohort that needs consideration is postmenopausal women. This is because around the time of menopause decreased muscle mass and strength loss [10], elevated cardiovascular risk [11] and metabolic problems [12] are detected. It has been observed that T2DM and postmenopause are two factors involved in higher morbidity and mortality [13]. Non-pharmacological therapeutic interventions to alleviate metabolic problems throughout these conditions are much appreciated.

We sought the following questions: Is aerobic exercise in conjunction with resistance training capable of improving metabolic markers of diabetes in postmenopausal women with T2DM? Is there solid evidence in the research literature supportive of the effect of this combined intervention in this group? With the aim of answering these questions, we performed a systematic review and meta-analysis in order to evaluate the effect of aerobic exercise combined with resistance training exercise on metabolic markers in in postmenopausal women with T2DM.

Methods

Registration

This review was stated consistent with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14] and is registered in the PROSPERO database (CRD42023475538).

Search strategy and study selection

The searches were completed *via* EMBASE, MEDLINE/PubMed (*via* National Library of Medicine), Scopus, and Web of Science databases with the suggestion of the keywords ‘Resistance Training’ OR ‘Weight-Lifting Exercise Program’ OR ‘Strength Training’ OR ‘Strength exercise’ AND ‘Diabetes’ OR ‘Diabetes Insipidus’ AND ‘Postmenopause’ OR ‘Post-Menopause’ OR ‘Postmenopausal Period’ OR ‘Post menopausal Period’.

All acknowledged articles were exported to the Rayyan QCRI program (Qatar Computing Research Institute, Qatar) to remove duplicates. The studies were screened in the Rayyan program by reading the title and abstract. The suitability stage was finalized by two independent reviewers (ASC and ISS) and the authors (ASC, ISS, RDR and VEV) read the whole articles. An additional reviewer (VEV) was invited to decide if there was a disagreement regarding a study.

Eligibility criteria

The studies were those from peer-reviewed journals, published from inception until September 2023. The inclusion and exclusion criteria were compatible with the PICOS (Population, Intervention, Comparison, Outcomes and Study Design) elements, which include:

1. [P] Postmenopausal women diagnosed with T2DM. Included references needed to explicitly include women who are postmenopausal;

2. [I] The intervention was aerobic exercise alongside any training protocol to strengthen muscle groups for resistance intervention;
3. [C] For comparisons, control group was the one that did not receive intervention;
4. [O] The outcomes of interest were metabolic markers of diabetes: blood glucose and insulin levels, homeostatic model assessment for insulin resistance index (HOMA-IR) and HbA1c;
5. [S] Studies that were included were non-blinded, single or double-blind randomized control trials (RCTs). This investigation was restricted to articles published in peer-reviewed journals and written in English. Conference papers, master’s theses, doctoral dissertations, descriptive studies, case studies, editorials or reviews were no included. Studies that did not combine aerobic exercise with resistance training were excluded.

Data extraction

Data regarding the author, year, study location, study design, sample, age of study participants, intervention, controls and outcomes were extracted from primary studies and presented in Table 1. Absent data was requested by contacting the corresponding study authors. This stage was concluded independently by two reviewers (ASC and ISS). When the corresponding author did not respond, the Web Plot Digitizer® was applied to extract the data presented in graphs. The dataset statistics were charted as mean and standard deviations (SD). Values presented ‘standard error’ or ‘confidence intervals’ (CI) in the primary studies were then transformed to SD.

Assessment of the risk of bias

To analyze the risk of bias we used Risk of Bias tool originated in Cochrane organization [15] *via* the Review Manager program (RevMan 5.4.1). Risk of bias is a tool based on the domains [16], and its evaluation is split into seven fields: ‘Random sequence generation’, ‘Allocation concealment’, ‘Blinding of participants and personnel’, ‘Blinding of outcome assessment’, ‘Incomplete outcome data’, ‘Selective reporting’, and ‘Other Bias’. The cataloging was divided into three direct responses: low risk, unclear risk, and high risk. Our assumptions were founded on the table developed by de Carvalho et al. [16], ‘Reviewers’ judgment and criteria for judgment’. Two autonomous authors finalized the risk of bias analysis. An additional was consulted if there were any inconsistencies in their decisions.

GRADE (levels of evidence)

Enforced the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group (GRADE Working Group, 2004) was used to measure the evidences’ certainty. This analysis involves the study design of randomized trials (strong evidence). Study quality (detailed study methods and execution) and limitations in the strength of evidence analysis were also considered [17]. GRADEpro GDT v4® (McMaster University, Ontario, Canada) was used to perform the summary of the findings.

Qualitative analysis (systematic review)

A descriptive synthesis was carried out to define detailed data on how each study was completed. Details of each study were

Table 1. Description of the characteristics of the included studies for analysis by author, year, study location, sample, age (years), intervention, control and outcomes.

Author/Year/ study location	Study Design	Sample	Age (years)	Intervention	Control	Outcomes
Cuff et al. 2003, Canada [19]	Randomized and controlled trial	28 obese postmenopausal women with type 2 diabetes	60.0±2.9 years in control group (n=9), 63.4±2.2 years in Ae+RT group (n=10) and 59.4±1.9 years in the Ae only group (n=9)	A total of 10 women participated in a supervised 16-week structured Ae and RT program, three times per week. Each class consisted of a warm-up, an Ae phase, a RT phase, and a cool-down to total a class time of 75 min. The Ae phase involved individually prescribed exercise at 60–75% of heart rate reserve (based on the initial maximal graded exercise tolerance test), using treadmills, stationary bicycles, recumbent steppers, elliptical trainers, and rowing machines. The RT program consisted of five exercises (leg press, leg curl, hip extension, chest press, and latissimus pull down) for two sets of 12 repetitions using stack weight equipment. RT began with light loads and thereafter progressed as technique permitted	Did not perform any training protocol	Enhanced glucose uptake was seen in postmenopausal women with type 2 diabetes after a combined Ae and RT. This improvement was related to losses of adipose tissue area from abdominal subcutaneous depot and to increases in thigh muscle cross-sectional area and thigh muscle attenuation characteristics
Zois et al. 2009, Greece [20]	Randomized and Controlled trial	20 sedentary postmenopausal women with type 2 diabetes participated in this study	59.4±3.2 years in the control group (n=10) and 55.0±5.2 years in the exercise group (n=10)	The exercise group followed a familiarization-training period of 2 weeks. Ae consisted of walking on the treadmill two times per week. Each session lasted about 75 min including a warm-up period, stretching exercises, the main program with treadmill exercise and a cool-down period. In the initial two months the intensity was 60–70% of HR _{max} thereafter it increased to 70–80% of HR _{max} according to individual adaptation The strength-training program was performed twice a week and consisted of six resistance exercise stations: bench press, seated row, leg extension, pull-down, pec-deck, and leg curl. All subjects performed 3 sets of 12 repetitions for all the exercises at an intensity of 60% of 1-RM	Did not perform any training protocol	The combination of resistance and aerobic training increased muscular strength and endurance and improved glycemic control in postmenopausal women with type 2 diabetes
Jeon et al. 2020, South Korea [21]	Randomized and controlled trial	35 postmenopausal women with type 2 diabetes mellitus were randomly assigned to either exercise or control group.	62.1±7.3 years in exercise group (n=14) and 61.1±7.0 years in control group (n=21)	Ae and RT for 12 weeks. Ae entailed folk dances composed of rhythmic movements to music matching the emotions of older women. Exercise frequency was three times a week for a total of 12 weeks. Exercise duration was 20 minutes each day, including warm-up for 5 minutes and cool-down for 5 minutes RT involved performance of rubber band exercises three times each week. The exercise duration was approximately 30 minutes each day. Rubber band exercises consisted of nine movements to work the large and small muscle groups as described previously: bench press, squat, elbow curl, seated row, knee curl, sit-up, knee extension, overhead press, and seated leg press. Each movement was performed at 70% of the maximal single-repetition resistance. Resistance was increased slowly if the participant could perform 20 repetitions without failure	The participants in the control group performed no additional exercise during the 12-week period	Exercise training did not significantly influence HOMA and HbA1c

*Aerobic plus resistance training (Ae + RT), aerobic only training (Ae only), one repetition maximum (1-RM), glycated hemoglobin (HbA1c), HOMA (homeostatic model assessment), resistance training (RT), maximum heart rate (HR_{max}).

introduced in texts and tables. The individual qualitative analysis per study outcomes were completed by scrutinizing the consequences of the intervention or control protocols.

Quantitative analysis (meta-analysis)

After selecting all relevant references, the possibility of meta-analysis was estimated. In an optimistic situation, outcome values were introduced. The information required to construct the meta-analysis was the post-intervention period. The extraction criterion was implemented with the objective of incorporating all available data in the pre- and post- intervention.

Heterogeneity was calculated *via* the I^2 statistic. Interpreted as low heterogeneity if I^2 was $< 50\%$, moderate if I^2 was between 50% and 75% , and high if I^2 was $> 75\%$. For the '95% CI' and 'Test for overall effect size' values, significant differences were assumed for $p < .05$ (or, $< 5\%$). A random-effect model was imposed as this is a more conservative method that allows the study heterogeneity to deviate beyond chance, providing further generalizable results [18]. All data was obtained using the Review Manager Program (RevMan 5.4.1).

Results

Description of studies

A total of 6,950 references were identified through the searches in the stated databases. After disregarding duplicates ($n=3,769$), 3,181 publications were screened for inclusion. Amongst the cited studies, 2,997 records were omitted after reviewing the title or abstract, and 138 studies were excluded as they were performed among animals. Of the remaining 46 studies, 43 were excluded: 15 because they did not assess postmenopausal women, 26 were non-randomized designs, one did not combine resistance with aerobic exercise and one study because they were not all diabetic patients.

The remaining three papers were designated for full-text reading, risk of bias assessment, GRADE, and qualitative analysis [19–21]. The study features of the included studies are presented in Table 1. Two references [20, 21] were chosen for the quantitative analysis (meta-analysis). The search procedure and selection phases followed the PRISMA protocol flow diagram illustrated in Figure 1.

The studies contained within this review were published between 2003 and 2020 (Table 1). One study originated from Canada [19], one from Greece [20] and one from South Korea [21] for a total of 83 participants.

None of the studies elucidated which criteria was necessary for diabetes diagnosis and postmenopause. There were no contradictions regarding mean age. For the study of Cuff et al. [19] mean age was 60.0 ± 2.9 years in control group, 63.4 ± 2.2 in Aerobic+Resistance Training group and 59.4 ± 1.9 in Aerobic only group; for Zois et al. [20] it was 59.4 ± 3.2 years in the control group and 55.0 ± 5.2 in the exercise group; and for Jeon et al. [21] it was 62.1 ± 7.3 years in exercise group and 61.1 ± 7.0 years in control group.

Regarding exclusion and inclusion criteria, Cuff et al. [19] included postmenopausal women with T2DM controlled by diet or oral agents, were obese and had an inactive lifestyle. Jeon et al. [21] excluded subjects with oral infections prior to the tests, recent history of acute myocardial infarction, stroke, trauma, surgery, neoplastic disorder, occlusive peripheral vascular disease, severe liver dysfunction, use of antidepressants or neurotrophic pharmacotherapies and Alzheimer's disease. Zois et al. [20]

excluded smokers, those with a coronary artery disease history, renal impairment (or, proteinuria), hepatic impairment, gout (or, hyperuricemia), hypertension, diabetic neuropathy or retinopathy.

Pertaining to interventions, the Cuff et al. [19] protocol involved a warm-up, an aerobic phase, a resistance training phase, and a 'cool-down' (75 min each session). During the aerobic exercise program, the agreed exercise was 60% to 75% of heart rate reserve through stationary bicycles, elliptical trainers, recumbent steppers, rowing machines and treadmills. The resistance training intervention involved five exercises (latissimus pull down, leg curl, hip extension, chest press and leg press) for two sets of 12 repetitions, initiated with light loads and further progression. The authors did not define the features of the control group. The exercise intervention persisted for 16 weeks (three times per week).

In the Jeon et al. [21] study, the exercise program continued for 12 weeks and was executed three times per week. The aerobic protocol was based on dancing that involved rhythmic movements. Each session continued for 20 min, including five minutes of warm-up and five minutes of 'cool-down'. Aerobic exercise intensity was monitored by the rated perceived exertion scale 11 to 12 for weeks one to four and 13 to 14 for weeks five to twelve. The resistance training performance of 'rubber band exercises' for 30 min and exercise intensity was monitored also with the rated perceived exertion scale between 11 to 12 for weeks one to four and 13 to 14 for weeks five to twelve. Rubber band exercises involved nine actions at 70% of the maximal single-repetition resistance: knee curl, knee extension, elbow curl, seated row, seated leg press, sit-up, overhead press, squat and bench press. The control group did not perform any exercises during the entire period.

The exercise interventions performed in the study of Zois et al. [20] were split aerobic and resistance training on different days and continued for a total of 16 weeks. The aerobic program was based on jogging or walking on the treadmill twice per week with each session lasting about 75 min. The protocol included a warm-up period (5 to 10 min), stretching exercises (10 min), the main protocol with treadmill exercise (40 to 45 min) and a 'cool-down' period (15 min including stretching). Throughout the first two months, the aerobic exercise intensity was 60% to 70% of maximum heart rate. The strength exercise protocol comprised six exercises (three sets of 12 repetitions with a rest period between sets of 45 to 60 s and two to three-minute intervals between each exercise) with 60% one-repetition maximum (1 RM) twice per week. The exercises were: leg curl, seated row, pectoral-deck, leg extension, pull-down and bench press. Each session started with a 10 to 15-min warm-up and finished with a 10 to 15-min 'cool-down', which included stretching.

Qualitative analysis

Cuff et al. [19] demonstrated that joint aerobic exercise and resistance training interventions significantly improved insulin sensitivity in diabetic postmenopausal women. Glucose uptake was increased after intervention and the variation in insulin resistance was related to changes in visceral adipose, abdominal subcutaneous and muscle cross-sectional area and density.

Jeon et al. [21] established that aerobic and resistance training in diabetic postmenopausal women reduced circulating apolipoprotein J and increased appendicular skeletal muscle mass. Even so, exercise intervention did not significantly affect HOMA-IR values and/or HbA1c.

Zois et al. [20] showed that resistance and aerobic training similarly improved glycemic control in diabetic postmenopausal



Figure 1. PRISMA 2020 flow diagram for new systematic reviews which include searches of databases and registers only.

women. The authors further verified improvements in triglyceride and HDL-cholesterol levels, as well as cardiovascular function, endurance and muscle strength.

Analysis of the risk of bias

The risk of bias in the three detailed studies was not similar. The results of the assessment of risk of bias are summarized in [Figure 2](#).

Random sequence generation (selection bias)

Studies of Cuff et al. [19] and Zois et al. [20] were rated as having a high risk of bias, suggesting potential issues in the randomization process. The study of Jeon et al. [21] presented unclear risk due to insufficient information.

Allocation concealment (selection bias)

The studies of Cuff et al. [19] and Jeon et al. [21] showed unclear risk, indicating ambiguity in whether allocation was adequately concealed. Zois et al. [20] study was rated with a high risk of bias.

Blinding of participants and personnel (performance bias)

None of the studies implemented blinding effectively, resulting in high risk of performance bias across all three studies.

Blinding of outcome assessment (detection bias)

Only Jeon et al. [21] implemented effective blinding for outcome assessment, achieving a low risk of bias. The other two studies did not report blinding, leading to a high risk.

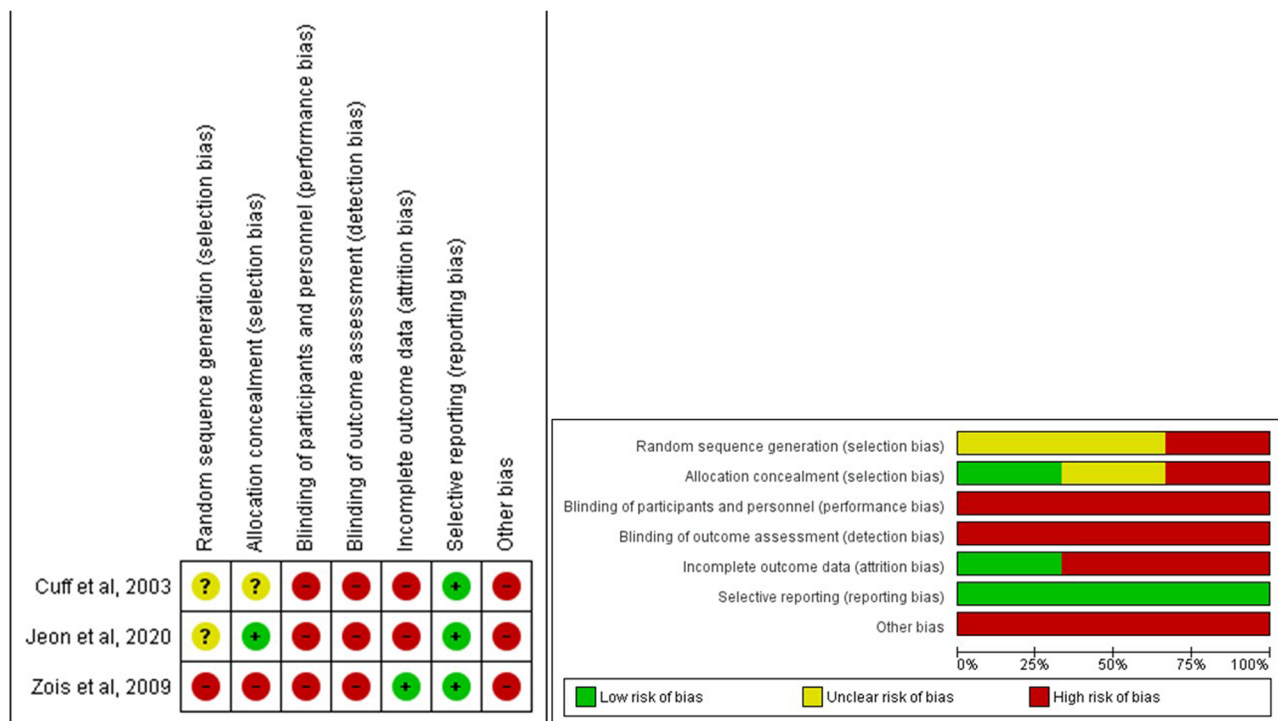


Figure 2. Results of the assessment of risk of bias with the Cochrane risk of bias tool.

Incomplete outcome data (attrition bias)

Jeon et al. (2020) [21] demonstrated robust handling of incomplete outcome data, showing low risk. In contrast, Cuff et al. (2003) [19] and Zois et al. (2009) [20] had a high risk, suggesting significant issues with missing data or attrition.

Selective reporting (reporting bias)

All three studies avoided selective reporting, achieving low risk in this domain.

Other bias

The studies of Cuff et al. [19] and Zois et al. [20] exhibited high risk of other biases, whereas Jeon et al. (2020) [21] did not report additional concerns, reflecting a low risk.

Quantitative analysis

For the HbA1c and HOMA-IR results, a random effect and mean difference (MD) model were carried out to quantify their effect sizes. The black diamond dimension characterizes the 95% confidence interval (CI; Figures 3 and 4). A negative effect size indicates upgraded values in the intervention group compared to the control (no exercise).

HbA1c

No significant adjustment was distinguished for the HbA1c. In the 'Test for overall effect,' we found a subtotal=mean difference -0.35 [95% CI: $-0.85, 0.15$], $p=.17$, and heterogeneity = 0% (Figure 3). The GRADE quality of evidence for this result was extremely low.

Homa-IR

A significant change was documented in the HOMA-IR. In the 'Test for overall effect,' showing a subtotal=mean difference

-0.52 [95% CI: $-0.99, -0.05$], $p=.03$, and heterogeneity = 0% (Figure 4). The GRADE quality of evidence for this result was also extremely low.

Discussion

This systematic review evaluated the effect of aerobic exercise combined with resistance training in postmenopausal women with T2DM. The main findings were that: (1) According to meta-analysis, HOMA-IR was improved because of intervention, yet, no significant effect of exercise was noted on HbA1c; (2) The GRADE quality of evidence for both HOMA-IR and HbA1c presented very low certainty and; (3) Risk of bias assessment emphasized concerns about blinding procedure, further prejudices or bias.

This meta-analysis showed that aerobic exercise combined with resistance training was effective in improving HOMA-IR in postmenopausal diabetic women. This is consistent with a recent study that evaluated postmenopausal non-diabetic women aged 45 or more [22] who partook in a resistance exercise program and revealed a connection between HOMA-IR and muscle strength, meaning that resistance exercise improved this diabetic metabolic indicator. The authors concluded designated that postmenopausal women not submitted to the strength exercise program were associated with a higher probability of developing insulin resistance. Another mechanism that supports this hypothesis is the involvement of adipose tissue. Lesser et al. [23] studied visceral adipose tissue and HOMA-IR in 49 postmenopausal women acquiesced to two 12-week aerobic exercise programs. The key findings exposed significant association between visceral adipose tissue and HOMA-IR, advising that aerobic exercise might improve HOMA-IR *via* adipose tissue mechanisms.

Although a significant effect of the combination of aerobic and strength exercises on HOMA-IR was found, the analysis of the levels of evidence showed a very low inevitability. The main parameters affecting these levels of evidence were risk of bias.

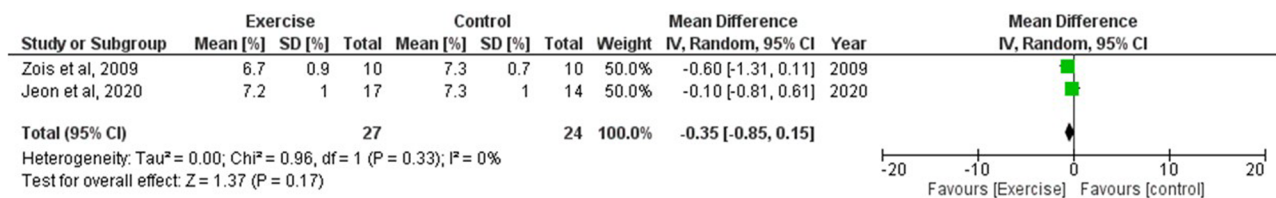


Figure 3. Meta-analysis for overall effects of aerobic exercise combined with resistance training on HbA1c.

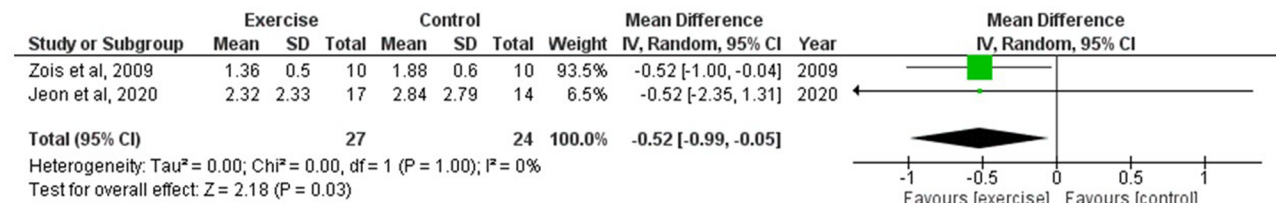


Figure 4. Meta-analysis for overall effects of aerobic exercise combined with resistance training on HOMA-IR values.

Considering that the studies included in the meta-analysis [20, 21] showed low heterogeneity and no wide 95% CI, it was not possible to highlight any significant impact of inconsistency and imprecision. Equally, our quantitative analysis did not reveal a significant effect of aerobic training combined with resistance exercise on HbA1c. Byrkjeland et al. [24] carried out a randomized clinical trial that assessed the effects of aerobic exercise intervention on HbA1c in diabetic patients. The authors observed no significant change of HbA1c levels before and after the exercise program. A further study related the impact of aerobic exercise opposed to resistance training on HbA1c in normal-weight diabetic subjects aged 18 to 80 years [9]. Their main results indicated that resistance exercise alone was preferable to aerobic training alone at reducing HbA1c. Also, it was emphasized that combined aerobic and strength exercise had a transitional impact.

When analyzing the levels of evidence for HbA1c in our review, very low certainty was observed. The main reasons included risk of bias and indirectness, and no significant influence of imprecision (attributable to the low 95% CI) and variability (due to low heterogeneity) was recognized.

Blood glucose and insulin levels were not included in our meta-analysis owing to methodological differences between studies. Cuff et al. [19] and Zois et al. [20] reported improved glycemic control in the studied postmenopausal diabetic women following an aerobic protocol combined with resistance training program. In this regard, a recent meta-analysis of Tan et al. [25] analyzed the influence of exercise programs on metabolic risk factors in postmenopausal and noted that exercise training (continuous, resistance, combined or interval) offered a slight effect in reducing glucose levels (95% CI: -0.60 to -0.16 mmol/L; $p < .001$).

Bearing this in mind, postmenopausal breast cancer patients who endured an aerobic exercise intervention (12-week, 60 min/day, 3–4 days per week) were studied by Viskochil et al. [26]. No significant change was observed in fasting insulin amidst before and after exercise training ($p = .79$).

Regarding our review, some points should be emphasized related to interventional details. Cuff et al. [19] and Jeon et al. [21] interventions were mixed aerobic and anaerobic training through the same day whilst the Zois et al. [20] protocol divided aerobic and resistance training on dissimilar days. In this way, it was problematic to standardize the training protocol for this systematic review. Therefore, exercise intensity was clear in the cited

references. For the aerobic exercise intervention of the study of Cuff et al. [19], they prescribed 60% to 75% of heart rate reserve. In the Jeon et al. [21] study, aerobic exercise intensity was monitored by means of rated perceived exertion scale 11 to 12 for weeks one to four and scale 13 to 14 for weeks five to twelve. Zois et al. [20] submitted the patients to 60% to 70% of maximum heart rate in the first two weeks and then it increased to 70% to 80% of maximum heart rate until intervention concluded. Recently, Kang et al. [27] completed a systematic review with meta-analysis to evaluate the effect of postprandial exercise on glycemic control in obese diabetic patients and overweight individuals. Amongst the stated references exercise intensity ranged between 3 METs and 90% VO₂ max and, their meta-analysis showed improved glycemic response after this intervention. Nevertheless, the authors fixated on postprandial training.

Regarding strength exercise intensity, Jeon et al. [21] submitted the subjects to 70% of the maximal single-repetition resistance (1-RM) by carrying out rubber band exercises. Cuff et al. [19] did not deliver exercise intensity for the resistance protocol. Recent data suggest that resistance exercise with elastic bands, calisthenics, resistance machines and medicine balls between 30% to 70% of 1-RM is capable of improving glycemic response in obese diabetic patients and overweight subjects.

Regarding exercise frequency, the Cuff et al. [19] and Jeon et al. [21] protocols were based on three days per week whereas Zois et al. [20] divided aerobic and resistance training on different days and each modality was achieved two days per week, for a total of four days per week. It has been recently suggested that exercise frequency ranging from two to seven days per week is capable of improving HbA1c, total cholesterol, low-density lipoprotein, high-density lipoprotein and triglyceride values in middle-aged and older adults with T2DM [28]. Together, the aforesaid scientific research literature seems to suggest that the exercise parameters enforced in our analyzed studies [19–21] are able to improve glycemic outcomes.

Our findings underscore the potential benefits of incorporating combined exercise regimens for the management of insulin resistance among postmenopausal diabetic women. This aligns with existing literature suggesting improvements in muscle strength and metabolic markers through resistance training and aerobic activity. Nevertheless, the lack of significant changes in HbA1c and the low quality of evidence limit the generalizability and reliability of these results.

In addition, some key points warrant attention: (1) our meta-analysis included few references and none included blood glucose levels owing to the methodological differences between studies; (2) none of the included studies clarified the definition of postmenopause, such as the measuring of follicle stimulating hormone (FSH) levels (cut-off of ≥ 30 IU/L) and at least one year of amenorrhea; (3) it is impossible to blind exercise, hence, influencing the risk of bias and the analyses of levels of evidence; and (4) although the analysis revealed that the combination of these exercise modalities significantly improved HOMA-IR, it did not yield substantial changes in HbA1c levels.

Despite the mentioned limitations, our meta-analysis showed that aerobic exercise combined with strength exercise exerted in postmenopausal women with T2DM a positive improvement over HOMA-IR, one metabolic diabetes marker but not others. However, the low certainty presented in the quality of evidence evaluation suggests further well-designed randomized studies to support our preliminary findings. It is evident that overall physical exercise plays a pivotal role on menopausal women's health, and in our particular case in postmenopausal diabetic women, providing considerable benefits in terms of glycemic control, that will have a positive impact on cardiovascular health and general well-being. It has been demonstrated that aerobic activities and strength training can assist in enhancing insulin sensitivity and reducing blood glucose levels, which can be exacerbated after the menopause. Furthermore, exercise has been shown to contribute to the maintenance of muscle and bone mass, thereby reducing the risk of osteoporosis and falls. Additionally, it has also been observed that regular physical exercise can lead to improvements in quality of life, which in turn can result in a reduction of menopausal symptoms related to anxiety and depression. Consequently, incorporation of regular physical exercise into the healthcare plan for postmenopausal diabetic women is of paramount importance.

In conclusion, despite the above-mentioned limitations, our study highlights an essential research gap. Robustly designed randomized controlled trials with larger sample sizes, standardized definitions of postmenopause, and rigorous blinding protocols are needed to validate our preliminary findings. Future research should also investigate the optimal frequency, intensity, and duration of combined exercise interventions for the improvement of glycemic control and other metabolic parameters in this postmenopausal population. Addressing these gaps will strengthen the evidence base and enhance therapeutic strategies for the management of postmenopausal women with T2DM.

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Authors' contribution

Vitor Engracia Valenti, André dos Santos Chagas and Rodrigo Daminello Raimundo: conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, writing of original draft.

Vitor Engracia Valenti, André dos Santos Chagas, Peter Chedraui, Ingrid Soares de Souza, Andrey Alves Porto and Rodrigo Daminello Raimundo: data extraction, assessment of the risk of bias, determination of level of evidence and quantitative analysis.

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Data availability statement

The data that support the findings of this study were derived from the following resources available in the public domains: PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>), EMBASE (<https://www.embase.com>), Web of Science (<https://isiknowledge.com>), and Scopus (<https://www.scopus.com>). All required information regarding the study protocol, and collected data, will be made available to researchers upon reasonable request. Proposals should be directed to rodrigo.raimundo@fmabc.br.

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