

Review Article

Aerobic training reduces blood pressure and waist circumference and increases HDL-c in metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials



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Abstract

The objective of this study is to estimate the effect of aerobic training (AT) on metabolic syndrome (MetS) outcomes. The Medline, EMBASE, SPORTDiscus, The Cochrane Library, and PEDro databases were searched from inception to May 2017. Two independent reviewers selected the studies and assessed their quality and data. The pooled mean differences between intervention groups and the control group were calculated using a random-effect model. Only randomized controlled trials that compared the effect of AT on MetS with a control group were included. Seventeen published studies were included in the meta-analysis. Systolic and diastolic blood pressure were significantly reduced (-5.11 mmHg [95% confidence interval [CI] $-7.36, -2.85$] and -2.97 mmHg [$-4.99, -0.94$], respectively), following AT. There was also a significant reduction in waist circumference (-2.18 cm [95% CI $-3.75, -0.62$]) and a significant increase in high-density lipoprotein cholesterol (95% CI -3.15 mg/dL [$-5.30, -1.01$]). The pooled effect showed a reduction of -7.64 mg/dL [95% CI $-17.65, 2.37$] in triglycerides and -1.36 mg/dL [95% CI $-4.11, 1.40$] in fasting glucose. This systematic review and meta-analysis provides an overview of the evidence supporting AT as an effective approach to reduce blood pressure levels and waist circumference and increase high-density lipoprotein cholesterol levels. These changes may help to reduce the risk of stroke mortality and mortality from heart disease in people with MetS. *J Am Soc Hypertens* 2018;12(8):580–588. © 2018 American Heart Association. All rights reserved.

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Introduction

Metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors, such as elevated blood pressure, waist circumference, triglycerides and fasting glucose, and decreased high-density lipoprotein cholesterol (HDL-c).¹ The presence of MetS increases the risk of developing cardiovascular diseases and type 2 diabetes mellitus and, therefore, have an increased risk of death.^{1,2}

Aerobic training (AT) has been shown to be an effective strategy to treat and prevent cardiovascular disease,^{3,4} type 2 diabetes mellitus,⁵ stroke,⁶ and other chronic diseases.^{7,8} In

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fact, AT has been studied in people with MetS^{9,10}; however, the results are not always consistent. Some studies have demonstrated positive effects on systolic and diastolic blood pressure^{11,12} and waist circumference,^{11,13} whereas other studies have not found significant results.^{14,15} The same inconsistency can be observed regarding metabolic parameters. Some studies have shown positive effects on triglycerides¹⁶ and fasting glucose,¹⁴ whereas other studies did not demonstrate significant results on HDL-c, triglycerides, or fasting glucose.^{17,18}

A previous systematic review and meta-analyses have investigated the effect of resistance training (RT) on MetS. The authors found that RT reduces systolic blood pressure and may help to prevent stroke mortality and mortality from cardiovascular diseases in people with MetS.¹⁹ Regarding AT, to the best of our knowledge, there is one meta-analysis published recently investigating the effect of exercise training on clinical outcomes in patients with MetS.²⁰ Although the authors have performed an excellent work, some limitations may have underestimated or overestimated the results. The authors indicated that studies with interventions including diet or medications would be included only if this intervention (diet or medication) was equal across the exercise and control groups. However, in the study from Oh et al.,²¹ the experimental group received a multicomponent intervention (health monitoring, counseling, health education, exercise, and diet), whereas the control group received only an educational booklet. Furthermore, although the authors have stated that included studies were randomized controlled trials, one of the studies was not randomized.²² Finally, the authors did not evaluate the overall quality of evidence and the strength of the recommendation of the meta-analysis results.

Thus, considering the potential benefit of AT on several health outcomes, and the absence of a meta-analysis of randomized controlled trials to evaluate the effects of AT on MetS, the aim of this study was to summarize the available evidence of AT on MetS in comparison with a control group in randomized controlled trials.

Methods

The protocol for this systematic review was previously registered in an international database of systematic reviews in health and social care (registration number CRD42016033862). Protocol registration provides explicit hypotheses, methods and analysis of the systematic review.²³ In addition, it reduces authors' biases by publicly documenting the planned methods.²⁴ The preferred reporting items for systematic review and meta-analyses guidelines were followed to improve the reporting of this systematic review and meta-analysis.²⁵

Search Strategy

The MEDLINE, EMBASE, SPORTDiscus, The Cochrane Library, and PEDro databases were searched from their

inception until May 2017, to identify randomized controlled trials addressing AT as an exercise treatment for MetS. The search strategy used a combination of terms related to AT, MetS, and randomized controlled trial ([Supplementary Data 1](#)). The reference lists of the included studies were checked to find potential studies that could also be used in this review. We included only studies published in English.

Study Selection

Only randomized controlled trials that compared AT with a control group were included in this review. Studies that used diet intervention were included if this intervention was equal for all groups in the study. Trials were eligible if they included participants with MetS and assessed its components: fasting plasma glucose, triglycerides, HDL-c, blood pressure, and waist circumference. All types of supervised AT, irrespective of intensity, frequency, or duration, were eligible for inclusion. Two independent researchers (I.R.L. and B.C.T.-L.) applied the study selection criteria. Disagreements were resolved by consensus. If necessary, a third researcher (H.L.M.) was consulted.

Data Extraction

Extracted data included baseline and final values of means, standard deviation, and sample sizes of blood pressure, waist circumference, triglycerides, HDL-c, and fasting glucose. If final values were not available, change scores were used. When necessary, authors were contacted to provide detailed information. As standard deviation values are not always reported by researchers, where necessary, these data were imputed or calculated using methods recommended in the Cochrane Handbook for Systematic Reviews of Interventions.²⁴ Blood pressure values were expressed in millimeter of mercury; waist circumference in centimeters; and triglycerides, HDL-c, and fasting glucose in milligrams per deciliter. If necessary, data were converted to these units of measurement.

Risk of Bias Assessment and Overall Quality

The PEDro scale was used to evaluate the risk of bias of individual studies.^{26,27} Two reviewers (I.R.L. and S.N.L.) independently assessed the risk of bias of individual studies using the PEDro scale. If trials were already listed on the PEDro database (<http://www.pedro.org.au/>), these scores would be adopted. As participant blinding and therapist blinding are not possible in training interventions, a PEDro score of 6 or greater was considered of “high quality”, studies with a score of 4 or 5 were considered of “moderate quality,” and those with a score of 3 or less were deemed of “poor quality.”^{19,28–30} Any disagreements in the scoring of trials were resolved consensually. The PEDro scale is a valid measure of the methodological quality of clinical trials and is

based on the Delphi list developed by Verhagen et al.³¹ Methodological quality was not an inclusion criterion.

The GRADE approach was used by two independent reviewers (I.R.L. and S.N.L.) to evaluate the overall quality of evidence and the strength of the recommendation,^{32,33} as advocated by the Cochrane Handbook.²⁴ It is a systematic and explicit approach that allows judgments to be made about strength of evidence and is an effective method for linking evidence quality and clinical recommendations. The overall quality of evidence was initially regarded as “high” but was downgraded by one level for each of the four factors encountered: limitations in the design (>25% of participants from studies with low-quality methods—PEDro score < 6 points); inconsistency of results ($I^2 > 50\%$); imprecision (<400 participants in total for each outcome); and publication bias (assessed with a funnel plot and quantified using the Egger test). If the Egger test result were statistically significant (2-tailed $P > .100$) for at least one result, we would downgrade the quality of evidence of all meta-analyses conducted in this review by one level.³⁴ Indirectness was not considered for this review because of the presence of a specific population, relevant outcome measures, and direct comparisons.

The following factors were used to define the quality of evidence: high quality—further research is unlikely to change our confidence in the estimate of effect; moderate quality—further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate; low quality—further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality—we are uncertain about the estimate.

Statistical Analysis

The inverse variance weighting random-effect model was used to compute a pooled estimate of mean difference (MD) and respective 95% confidence interval (95% CI). The heterogeneity of results across studies was evaluated using the I^2 statistic. In addition, although not planned a priori in our protocol, we performed a stratified subgroup analysis using the same procedures as the main analysis, comparing high (PEDro ≥ 6) versus low/moderate (PEDro ≤ 5) methodological quality, short-term (<6 months) versus long-term (≥ 6 months) interventions, and continuous versus interval training interventions. Meta-analysis was conducted on appropriate data using RevMan (The Cochrane Collaboration; V.5.3).

Results

Systematic Review

The search strategy performed resulted in a total of 6167 publications. After the removal of duplicates, the

search strategy identified 4343 titles. Screening of titles and abstracts identified 100 potentially eligible studies, and 14 publications were included.^{9,11–14,16–18,35–40} Three more studies were included after checking the reference lists of included trials and after a hand search.^{10,15,41} The reasons for exclusion were conference abstract, other languages than English, no AT or control group, no evaluation of MetS risk factors, no population with MetS, and not a randomized controlled trial (Figure 1). After data extraction, all the 17 included studies provided sufficient information for meta-analysis. A total of 299 men and 196 women were included in the meta-analysis. Three studies^{9,11,35} included only men, two studies^{14,36} included only women, and 12 studies included a mixed sample of men and women, with 42.5% ($n = 17$),¹² 70.6% ($n = 24$),¹⁸ 70.0% ($n = 28$),¹⁶ 16.7% ($n = 6$),¹⁰ 64.5% ($n = 20$),³⁷ 8.3% ($n = 2$),¹⁵ 36.4% ($n = 8$),¹⁷ 40.0% ($n = 16$),³⁸ 53.6% ($n = 15$),¹³ 55.0% ($n = 11$),³⁹ and 71.4% ($n = 24$)⁴¹ of women, respectively. Watkins et al.⁴⁰ did not report the percentage of women, so we adopted a 50% distribution (13 men and 12 women). The training period ranged from 6 weeks to 12 months. [Supplementary Data 2](#) shows the characteristics of the included studies.

Aerobic Training on MetS Components

The results of the meta-analysis comparing the effects of AT with a control group show that AT is significantly superior in terms of reducing systolic blood pressure (15 studies, $n = 482$, $I^2 = 35\%$, MD -5.11 mmHg [95% CI -7.36 to -2.85]), diastolic blood pressure (14 studies, $n = 449$, $I^2 = 55\%$, MD -2.97 mmHg [95% CI -4.99 to -0.94]) (Figure 2), and waist circumference (16 studies, $n = 515$, $I^2 = 31\%$, MD -2.09 cm [95% CI -3.91 to -0.26]) (Figure 3), and increasing HDL-c (16 studies, $n = 496$, $I^2 = 57\%$, MD -3.15 mg/dL [95% CI -5.30 to -1.01]) (Figure 4). However, the results of pooling data show that AT is not superior to control groups in reducing triglycerides (16 studies, $n = 507$, $I^2 = 0\%$, MD -7.64 mg/dL [95% CI -17.65 to 2.37]) (Figure 4) and fasting glucose (15 studies, $n = 469$, $I^2 = 27\%$, MD -1.36 mg/dL [95% CI -4.11 to 1.40]) (Figure 5).

Subgroup Analysis

Subgroup-stratified analysis was performed comparing high (PEDro ≥ 6) versus low/moderate (PEDro ≤ 5) methodological quality, short-term (<6 months) versus long-term (≥ 6 months) interventions, and continuous versus interval training (Supplementary Data 3).

High-quality studies presented greater reduction than low-/moderate-quality studies for systolic blood pressure (3 studies, $n = 92$, $I^2 = 17\%$, MD -8.68 mmHg [95% CI -12.85 to -4.52]; P -value $\leq .01$) and diastolic blood

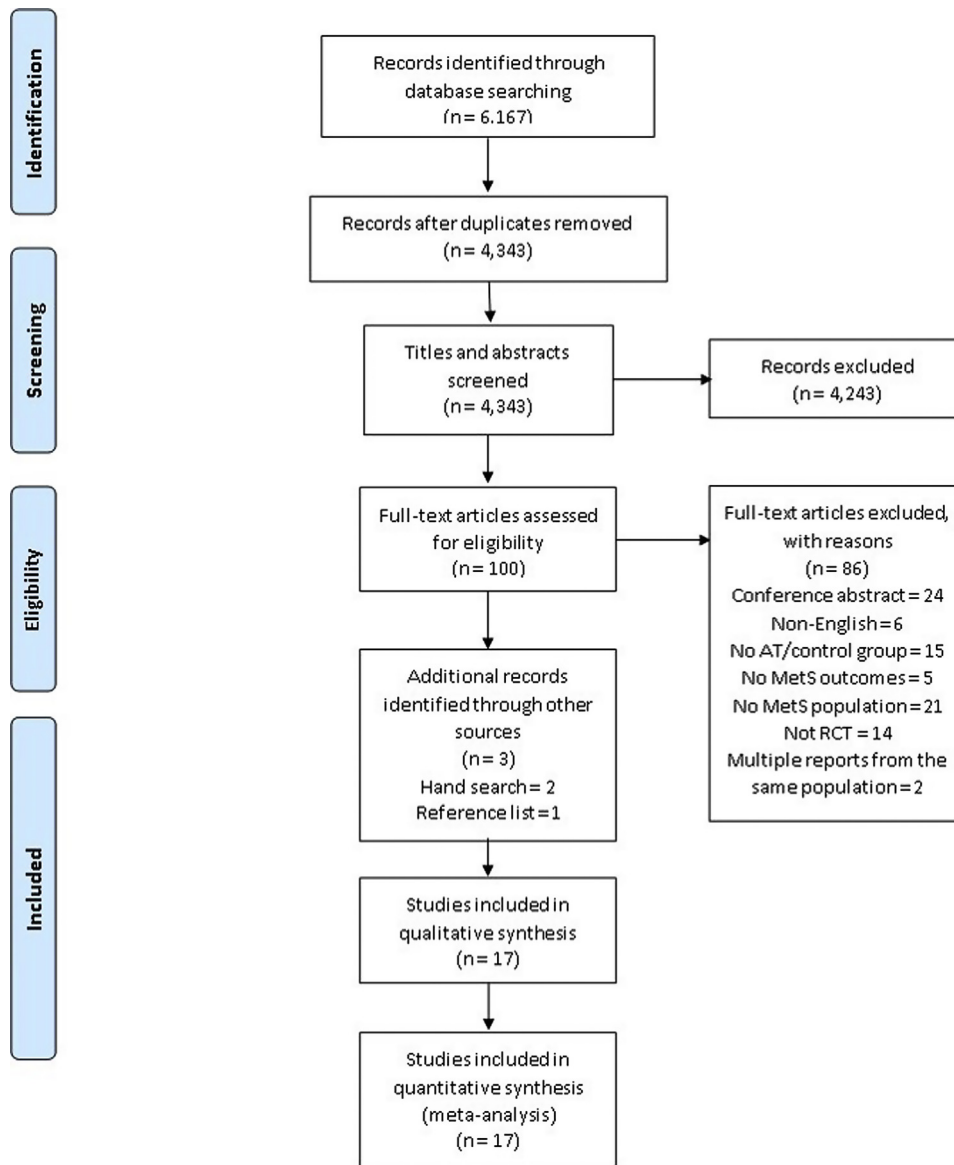


Figure 1. Flow chart of included studies.

pressure (3 studies, $n = 92$, $I^2 = 0\%$, MD -5.54 mmHg [95% CI -6.58 to -4.49]; P -value $\leq .01$). Potential influences of the duration and type of AT training, that is, short-term vs. long-term trials and continuous vs. interval training, were not detected as comparisons of subgroups revealed no differences in pooled estimates.

Methodological Quality

All included trials had random allocation and provided points and estimates of variability. The concealed allocation was performed only in one study.¹⁷ Owing to the nature of the interventions, blinding of participants and

therapists was not possible. Assessor blinding was implemented in two of included studies.^{15,37} In addition, seven studies^{10,12,16,17,37–39} had adequate follow-up, and two studies^{12,35} included an intention-to-treat analysis. Three studies^{12,17,37} were considered “high quality,” thirteen studies^{9–11,13–16,18,35,38–41} were considered “moderate quality,” and one study³⁶ was considered “poor quality.” Complete details are reported in [Supplementary Data 2](#).

Overall Quality of Evidence

On the basis of the GRADE system ([Supplementary Data 2](#)), pooled data of all meta-analyses were

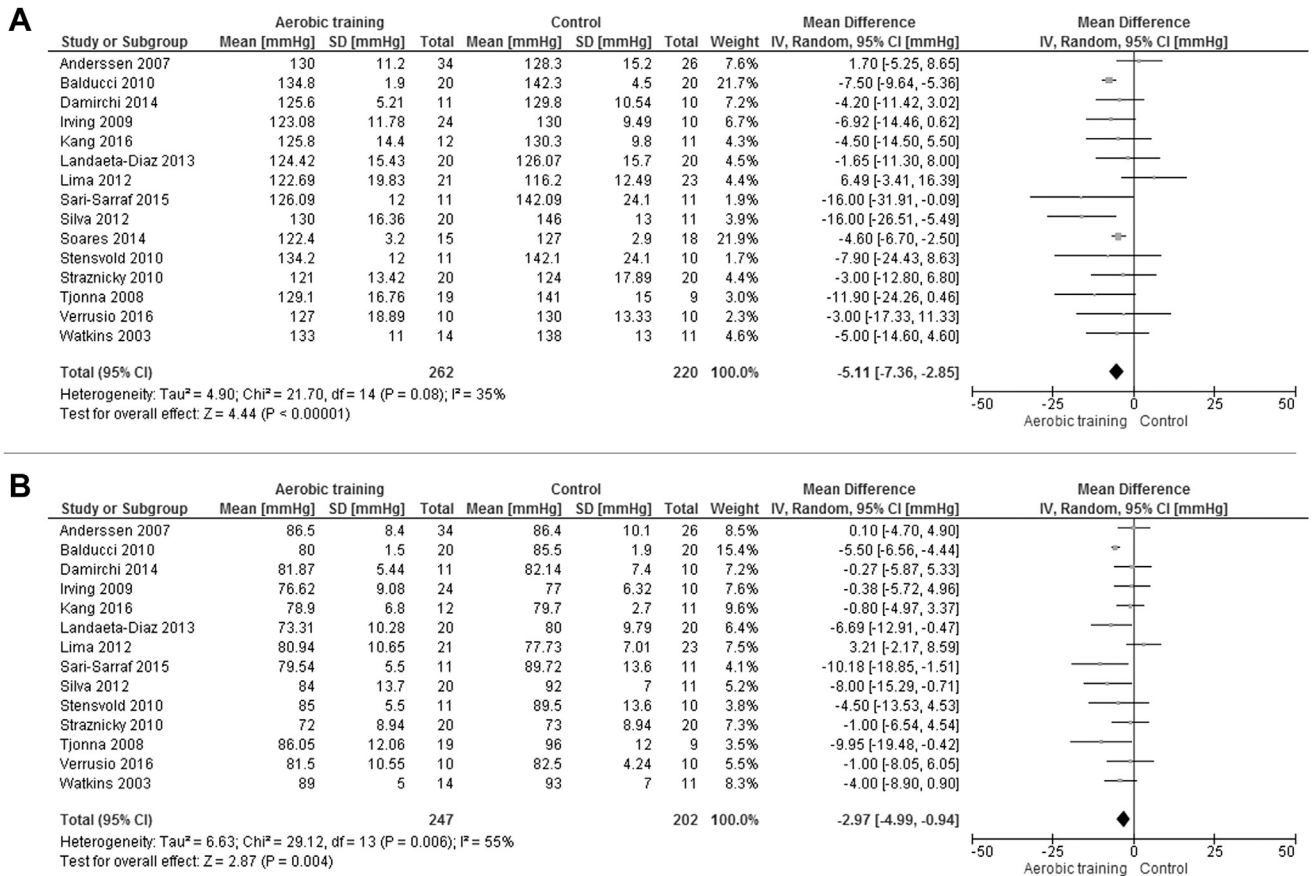


Figure 2. Effects of aerobic training on systolic blood pressure (A) and diastolic blood pressure (B) in adults with MetS.

classified as low-quality evidence. All variables were downgraded one level owing to the presence of risk of bias (more than 25% of participants from studies of low/moderate methodological quality) and one level owing to the presence of publication bias (assessed with a funnel plot and two-tailed Egger test) (Supplementary Data 3).

Discussion

This systematic review provides evidence that AT is effective in reducing systolic and diastolic blood pressure and waist circumference, and increasing HDL-c in adults with MetS. AT did not affect triglycerides and fasting glucose. The quality of evidence is low for all variables.

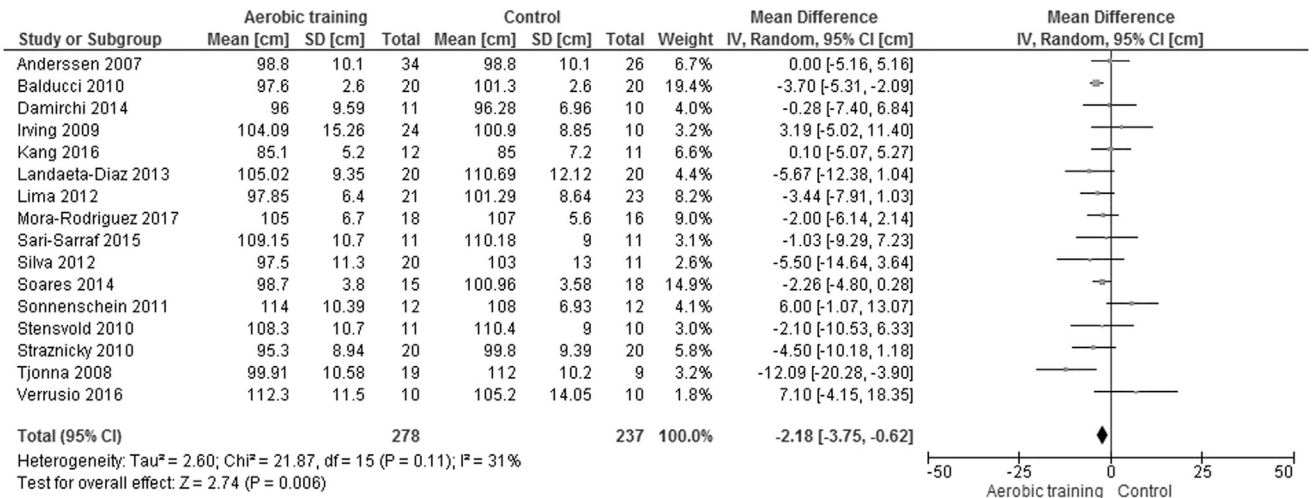


Figure 3. Effects of aerobic training on waist circumference in adults with MetS.

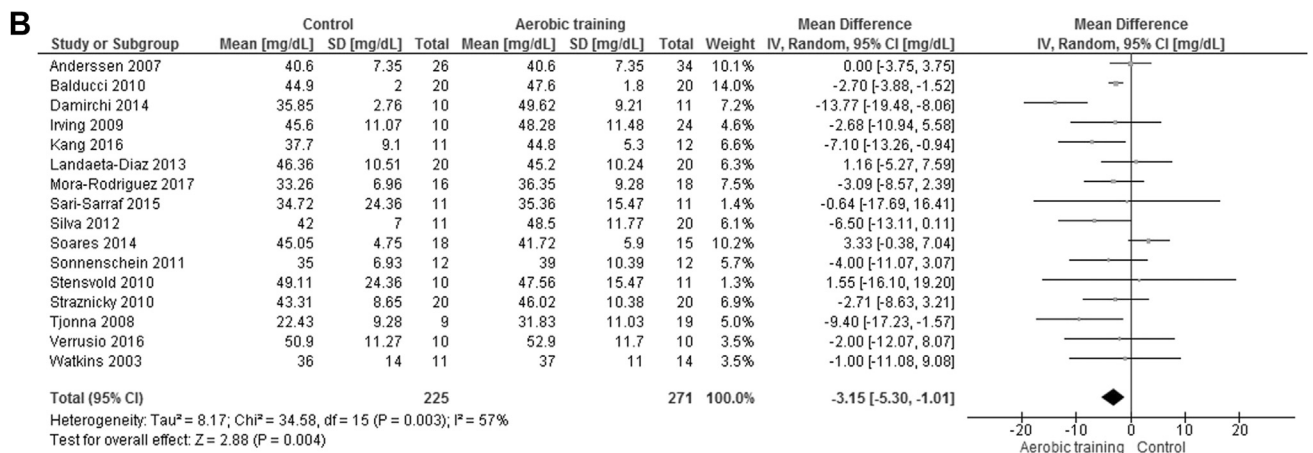
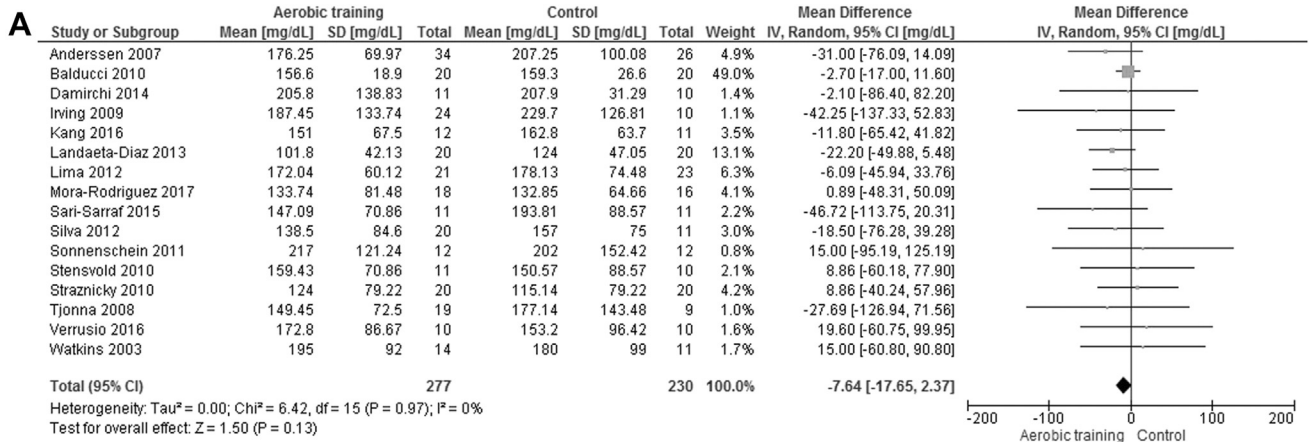


Figure 4. Effects of aerobic training on triglycerides (A) and HDL-c (B) in adults with MetS.

MetS Components Improved by Aerobic Training

Systolic blood pressure was reduced by 5 mmHg and diastolic blood pressure by 3 mmHg. These results are in accordance with previous finding regarding AT and blood

pressure.^{7,42–44} The blood pressure reduction found in the present study was higher than that observed in a previous meta-analysis of RT.¹⁹ Reducing blood pressure can be associated with 40% lower risk of mortality by stroke and 30% lower risk of mortality from heart disease.⁴⁵

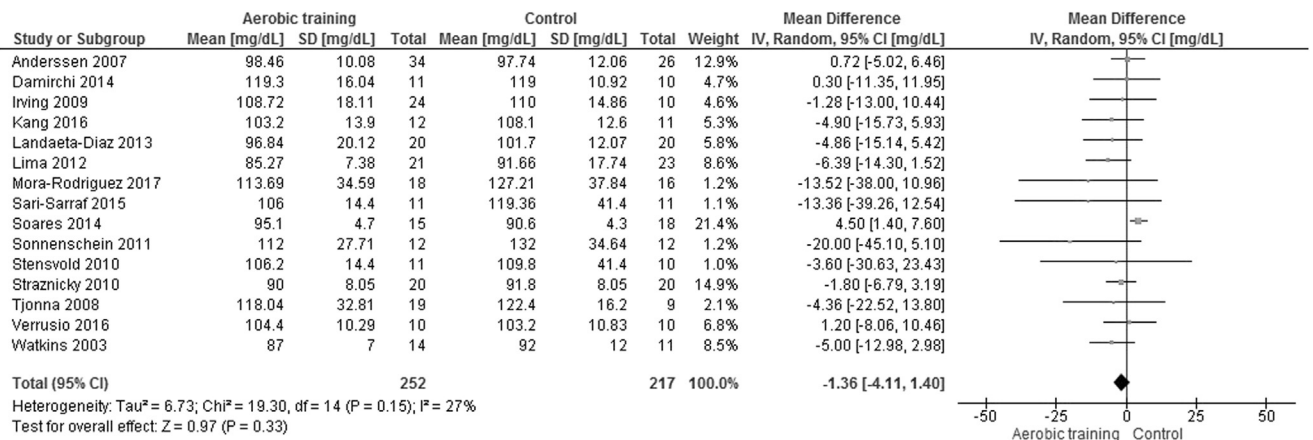


Figure 5. Effects of aerobic training on fasting glucose in adults with MetS.

Therefore, promoting aerobic exercise in adults with MetS might be more helpful in reducing blood pressure than RT alone. We believe that a combination of aerobic and RT may be even more effective; however, a comprehensive study investigating the effect of combined training, AT only, RT only, and a control group still need to be done.

Regarding waist circumference, we found a reduction of 2 cm in favor of AT. A previous meta-analysis has shown that aerobic exercise was effective in reducing visceral adiposity when compared to a control group.⁴⁶ Also, RT alone was not capable of reducing waist circumference in adults with MetS.¹⁹ When compared with RT, AT seems to be more effective, however, without statistical significance.⁴⁶ Although the reduction found in the present study seems small, or not clinically relevant, a small change in visceral adiposity can significantly reduce the risk of chronic diseases.⁴⁷ We believe that a combined intervention, with aerobic and resistance components, would be even more beneficial than any intervention alone.

We observed an increase of 3 mg/dL in HDL-c after AT intervention. The literature regarding this outcome is controversial. Although some studies found positive results regarding HDL-c after aerobic exercise,^{48,49} others did not find significant results after the intervention.^{17,50} Although more days of aerobic exercise was associated with higher HDL-c in men and women,⁵¹ there is evidence that exercise provides modest effects on HDL-c.⁵²

It is worthy to mention the consistency found in the meta-analyses of the present study. Such consistency may be due to the similarity of the effect sizes. A specific population of similar age affected by the same disease and submitted to similar interventions probably contributed to this lack of significant heterogeneity. However, it is important to note that the absence of heterogeneity, as measured by I^2 , does not imply homogeneity. Considering our results, AT can be applied as part of the treatment and prevention of MetS, reducing blood pressure and waist circumference, and might help to improve the HDL-c profile.

Strengths and Limitations

The strengths of this systematic review are its search protocol, comprehensive search strategy, and have randomized designs as an inclusion criterion. Inconsistency (I^2) was assessed to evaluate the consistency of the results. It is important to show that the variation in findings is compatible with chance alone. Also, the overall quality of the evidence was assessed using the GRADE approach, which evaluates the quality of evidence and is an effective method for linking evidence quality and clinical recommendations. Another strength is that we were able to identify nine different publications that were not included in the previous meta-analysis. A limitation of this review is that we included only studies published in English. Another limitation is that we did not perform analysis stratified by sex. Twelve of the included

studies used a mixed sample of men and women, three studies used only male, and two studies used only female. Metabolic changes caused by menopause may influence the results of the MetS components.⁵³ Finally, another limitation, not of this study particularly, is the low number of participants composing this meta-analysis. Despite the advancement of exercise science in the past few years, there is a lack of randomized controlled trials, with appropriate sample size, evaluating these conditions (AT and MetS).

In summary, AT is an effective intervention for reducing blood pressure levels by approximately 5 mmHg, waist circumference by 2 cm, and increasing HDL-c by 3 mg/dL in adults with MetS. These results are clinically meaningful because they would translate to a reduction in mortality by stroke, heart disease, and other chronic diseases if achieved at a population level. The quality of evidence is low for all variables.

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Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jash.2018.06.007>.

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