Reviews in Cardiovascular Medicine

Systematic Review

Effects of aerobic, resistance, and combined exercise on metabolic syndrome parameters and cardiovascular risk factors: a systematic review and network meta-analysis

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This study examines the effects of aerobic, resistance, and combined exercise on metabolic syndrome parameters and cardiovascular risk factors, to identify the most effective way of improving metabolic syndrome and preventing cardiovascular disease. We searched EMBASE, the Cochrane Library, PubMed, MEDLINE, Ovid, the Chinese Biological Medicine Database (CBM), the Wanfang Database, the China National Knowledge Infrastructure (CNKI) database, and the Chinese Scientific Journal Database (VIP), for randomized controlled trials (RCTs), identifying 15 comparing the effects of aerobic, resistance, and combined exercise on metabolic syndrome parameters and cardiovascular risk factors (e.g., glucose, triglyceride, blood pressure, body mass index, etc.). We assessed the quality of the articles and performed a network meta-analysis with a Bayesian random effects model to synthesize direct and indirect evidence. Combined exercise was most effective at controlling glucose and total triglyceride (TG) levels. Aerobic, resistance, and combined exercise groups achieved significant effects regarding body fat. Aerobic exercise was superior to resistance exercise regarding body mass index (BMI). There was no statistically significant difference in weight, waist circumference (WC), levels of high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), insulin, systolic blood pressure (SBP), and diastolic blood pressure (DBP) among the exercise groups. Combined exercise was the best exercise scheme for improving weight, WC, DBP, TG, TC, glucose, and insulin levels. Resistance exercise was most effective at ameliorating body fat, LDL-C levels, and SBP. Aerobic exercise was the optimal way of improving BMI and HDL-C levels. This network meta-analysis suggests combined exercise is the most effective choice in improving the metabolic syndrome and cardiovascular risk parameters, whereas aerobic exercise reveals the minimum effect. Further studies should certify the role resistance exercises play in metabolic syndrome and cardiac rehabilitation.

Keywords

Cardiovascular disease; Metabolic syndrome parameters; Aerobic exercise; Resistance exercise; Combined exercise; Network meta-analysis

1. Background

Cardiovascular disease (CVD) is a disorder of the heart and blood vessels; it includes coronary heart disease, cerebrovascular disease, rheumatic heart disease, and other conditions. CVD, the predominant clinical manifestation of systemic atherosclerosis, accounted for 31% of all deaths worldwide in 2017 [1]. Approximately 17.9 million individuals died of CVD in 2015, representing a 12.5% global increase between 2005 and 2015 [2, 3]. Evidently, our understanding and knowledge of potential risk factors are imperative to preventing the risk of CVD and related morbidity and mortality rates.

Metabolic syndrome (MS) affects approximately one-fourth of all adults [4] and is closely related to cardiovascular disease (CVD) and premature death [5, 6]. MS is defined as a cluster of metabolic abnormalities that include obesity, insulin resistance, hypertriglyceridemia, hypertension, hypercholesterolemia, and reduced high-density lipoprotein cholesterol (HDL-C) level [7]. It could dramatically increase the prevalence of type 2 diabetes and cardiovascular disease [7]. Type 2 diabetes characterized by insulin resistance is a kind of metabolic disease [8] that has adverse effects on metabolic abnormalities. Diabetes develops together with obesity, hypertension, and hypercholesterolemia, which results in poor glucose control, hypertension, hypercholesterolemia, and endothelial dysfunction [8]. It leads to an increased risk of CVD development [9], a twofold to fourfold higher risk of stroke, and a threefold to fourfold higher risk of myocardial infarction [10]. Accumulating evidence has identified the following as risk factors for CVD: obesity, Type 2 diabetes, and metabolic syndrome, including hypertension and hypercholesterolemia [11, 12].

The World Health Organization and other international and national agencies have documented that the risk factors of CVD and metabolic syndrome are worthy of attention in order to prevent and alleviate the burden of CVD [12]. The "Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020" emphasizes the reduction of widespread insufficient physical activity and the prevention of noncommunicable diseases, including diabetes, obesity, MS, and CVD [13, 14].

There is extensive evidence that aerobic training triggers greater improvement in aerobic capacity and associated cardiopulmonary and metabolic variables and more effectively ameliorates CVD risk factors, while resistance training enhances endurance, muscular strength, and muscle mass to a greater degree [15]. Resistance training is always perceived as a complement to, rather than a replacement for, aerobic exercise [15]. However, there is also substantial evidence that qualitative changes in resistance-trained muscle could lead to improved glucose uptake that has effects comparable to aerobic training on body composition, glycemic control, and insulin sensitivity and signaling [8]. More evidence is needed to prove whether resistance training presents a viable complement to aerobic exercise or whether it is an effective intervention independently. Resistance training may provide "cross-protection" against the oxidative stress produced by aerobic exercise; resistance training combined with aerobic exercise possibly enhances the effects on metabolic variables and CVD risk factors [15]. But there is limited literature comparing the three modes of exercise, and evidence of which is the best exercise mode for improving metabolic problems and cardiovascular risk factors is lacking [8]. In some studies meta-analyses were conducted to compare any two means of aerobic, resistance, and combined exercise; however, patients with high-risk factors for CVD were neglected in these meta-analyses. Clinicians have no standards to follow in deciding which exercise program is best for patients to improve metabolic syndrome and prevent the development of CVD. Network analysis, comparing two modes or all of them, can pool three modes of exercise together to collect substantial evidence. Therefore, conducting a network meta-analysis (NMA) is essential.

2. Study aims

The aim of this NMA is to evaluate the effects of aerobic, resistance, and combined exercise on metabolic syndrome parameters and cardiovascular risk factors, as well as to provide additional insights into the selection of the most effective exercise pattern, so as to improve metabolic syndrome and prevent the development of CVD.

3. Methods

3.1 Selection criteria

The selection criteria were formulated in line with the PICOs checklist [16]. Studies were included if the following criteria were met: (1) Trials must have utilized randomization to assign groups, regardless of the application of blinding methods; (2) Participants must include those at high risk of metabolic syndrome, metabolic syndrome problems, or obesity/being overweight, assessed by metabolic syndrome parameters, or those with cardiovascular risk factors, such as hypertension, diabetes, being elderly, or having a sedentary lifestyle, with no limitations in regard to race, age, sex, or duration of intervention; (3) Randomized controlled trials (RCTs) must have been conducted regarding the following interventions: non-exercised controls, aerobic exercise, resistance exercise, and resistance and aerobic exercise (combined exercise); and (4) Outcomes must include BMI, weight, waist circumference (WC), body fat, HDL-C, LDL-C, TG, TC, glucose, insulin, SBP, and DBP (participants whose effect outcomes were unchanged were regarded as invalid). Studies were excluded if any of the following criteria were met: (1) The course of the intervention was ambiguous; (2) The study did not report a statistical method; (3) There were no baseline results; or (4) There was a lack of precise or complete data.

3.2 Identification of trials

All relevant RCTs in EMBASE, the Cochrane Library, PubMed, MEDLINE, Ovid, the Chinese Biological Medicine Database (CBM), the Wanfang Database, the China National Knowledge Infrastructure (CNKI) database, and the Chinese Scientific Journal Database (VIP) were screened from the databases' respective times of inception to April 2020. The references of each study were searched to screen relevant systematic reviews, and other possible relevant articles were identified through a manual search of related journals and by perusing meeting abstracts. No restrictions were placed on the language, blinding methods, or publication year of the studies. Research objects and research designs formulated the search terms used in the strategy. The research object included participants with metabolic syndrome, dyslipidemia, and obesity, and those carrying out aerobic exercise, resistance exercise (muscle strengthening), and resistance and aerobic exercise (combined exercise). The research type was RCTs. Related words and their synonyms were collected and combined with the logical operators "OR" and "AND" to develop a complete search strategy.

3.3 Data extraction and quality assessment

Preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines were adopted for this systematic review and meta-analysis. The PICOS (patients, intervention, comparison, outcome, and study design) framework was applied to select relevant studies. Two investigators independently screened the titles, abstracts, and full texts of the studies according to the inclusion eligibility. Conflicts were resolved by reaching a consensus or arbitration by a third party. The following data were extracted: (1) The characteristics of the included studies, such as the name of the first author and publication year; (2) Features of the participants, including country, sex, age, number of participants, and proportion of male/female patients; (3) Details of the intervention, including training frequencies and durations, and follow-up time; (4) The main effect outcomes; and (5) Quality scores for the study [17]. The Cochrane Risk of Bias Tools (Cochrane Handbook, version 5.1.0) [18] and the modified

Jadad scale [19] were used by two investigators to independently perform a quality assessment. The Cochrane Risk of Bias included the following items: (1) Selection bias (allocation concealment random sequence generation); (2) Detection bias (blinding of the outcome assessment); (3) Performance bias (blinding of the participants and personnel involved); (4) Reporting bias (selective reporting); (5) Attrition bias (incomplete outcome data); and (6) Other biases. Each item was evaluated as low, high, or unclear. The Modified Jadad scale concerned aspects including randomization, concealment of allocation, blinding, inclusion and exclusion criteria, withdrawals and dropouts, adverse effects, and statistical methods. Each item was scored −1, 0, or 1, with 1–3 points indicating a low-quality study and 4–7 points indicating a study of sufficient quality. Discordant results were arbitrated by a third investigator.

3.4 Statistical analysis

OpenBUGS 3.2.3 (Free Software Foundation 51 Franklin Street, Fifth Floor Boston, MA) and STATA 15.0 software (StataCorp LLC, 4905 Lakeway Drive College Station, Texas, USA) (OpenBUGS 3.2.3: GNU GENERAL PUBLIC LICENSE Version 3, 29 June 2007, Copyright (C) 2007 Free Software Foundation, Inc. http://fsf.org/. STATA 15.0 software: copyright 1985-2017 StataCorp LLC.) were employed to implement the NMA and to draw graphics. A Bayesian random effects model was utilized to directly compare the outcomes in the NMA. The Bayesian approach offered probabilistic distributions of the estimates of each effect by simulating the posterior distribution of the parameters, using the Markov Chain Monte Carlo (MCMC) method [19]. A total of 200,000 simulation and 20,000 adaptation iterations were set for the analysis. Continuous outcomes are presented with mean differences (MDs) and their 95% confidence intervals (95% CIs). When the 95% CIs of the MDs did not reach zero, the outcome effects among the groups were considered to be significantly different. The model fit was evaluated with a deviance information criterion. The consistency of NMA was examined by comparing the difference values of differences in conditions (DIC) between the direct and indirect evidence. A difference value of DIC >5 indicated an inconsistent model. In such cases, inconsistency was assessed by node splitting, comparing indirect evidence with direct evidence from the entire network on each node. If inconsistent, a further meta-regression analysis was carried out to determine the potential sources of the inconsistency. Sensitivity analysis was also performed by eliminating studies with a high risk of bias or poor quality.

In addition, STATA 15.0 software was adopted to present graphs of the NMA. The network graph was used to show the comparative relationships among the groups. The thickness of the lines in the network graph corresponded to the number of comparison trials, and the node sizes were proportional to the sum of the sample sizes [20]. The surfaces under the cumulative ranking curve (SUCRA) probability values were used to rank the intervention outcomes. SUCRA values of 0% and 100% were assigned to the worst and best interventions, respectively [21].

4. Results

4.1 Results of the literature search

Initially, 1441 potentially eligible articles were identified through the electronic databases. After removing duplicates and irrelevant articles, 463 articles remained. Subsequently, after reading the full text, 448 articles were further excluded for the following reasons: the intervention did not meet the inclusion criteria (n = 115); the intervention was vague (n = 47); the study did not include related outcomes (n = 185); the study did not report a statistical method (n = 38); there were no baseline results (n = 52); and the study incorrectly generated a random sequence (n = 11). Eventually, a total of 15 RCTs were included in this systematic review [22–36]. The process of study identification, screening, and inclusion is shown in Fig. 1.

A total of 15 articles involving 536 participants were eligible. Participants in RCTs with a high risk of metabolic syndrome/metabolic syndrome problems, obesity/being overweight, and diabetes mellitus accounted for 40%, 46.7%, and 13.3% of the participants, respectively. Four nodes were included in the NMA. Each node denoted different interventions: non-exercise control, aerobic exercise, resistance exercise, and resistance and aerobic exercise (combined exercise) (Fig. 2). Aerobic exercise was performed on a treadmill, by walking or running, or through other forms of exercise, such as jogging and cycling. Resistance exercise focused on the main muscle groups. It was performed through stretching exercises, jogging, or using elastic resistance bands, weight resistance machines, or Technogyms. Combined exercise refers to the combination of aerobic and resistance exercise. The total training time was 177.5 to 181 minutes a week. The median follow-up was 14.5 weeks (range: six to 48 weeks). The basic features of the study are depicted in Appendix Table 3. Thirteen studies (86.7%) reported age and sex. None of the articles reported significant differences in baseline characteristics, such as age, sex, and metabolism indexes.

4.3 Quality assessment

All studies were evaluated according to the Cochrane Risk of Bias Assessment Tool (Fig. 3). The modified Jadad scale was applied to perform a quality evaluation of the included studies. Jadad scores of 4 to 7 were necessary to ensure the studies were of sufficient quality. According to the evaluation, all studies presented data on follow-up, withdrawal, statistical methods, research ethics, and inclusion and exclusion criteria. Only three studies reported details about the randomized method used. None of them utilized a blinded method or allocation concealment. The results of the quality evaluation indicated that 12 and three RCTs obtained Jadad scores of 5 (80%) and 6 (20%), respectively. The results of the detailed evaluations are presented in Appendix Table 3. As a whole, the overall quality of the included studies was moderate.

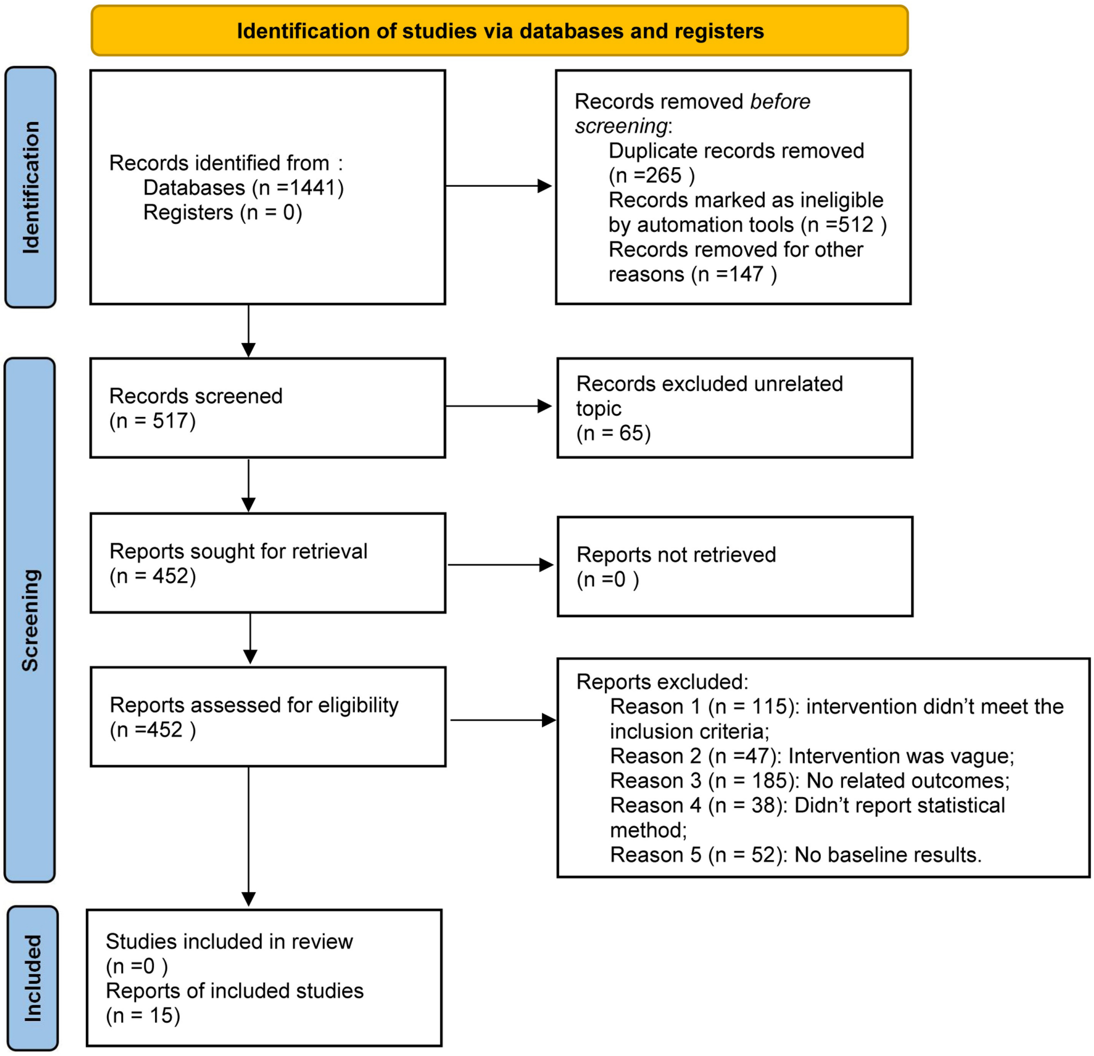

Fig. 1. PRISMA flow chart.

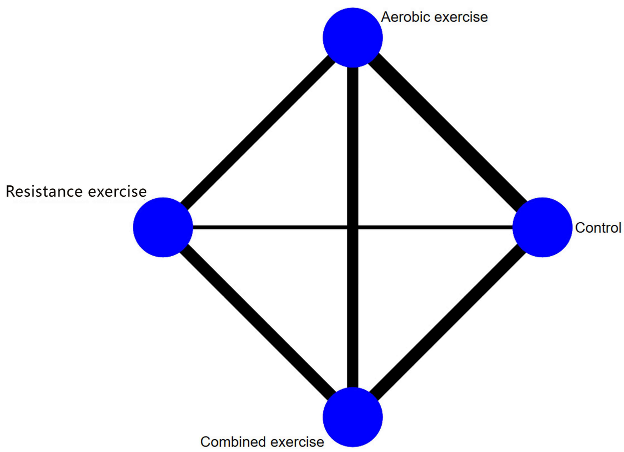

Fig. 2. Network geometry.

4.4 Outcomes (results of overall outcomes and ranking results based on SUCRA)

A consistency model was applied to analyze the data. The model fit was good for all of the results. No relevant inconsistency was indicated. The alternative models for NMA showed similar results. The SUCRA results of the 12 outcomes are illustrated in Table 1. A regression analysis of the duration of the interventions was applied to determine the model's sensitivity, which is shown in Table 2.

4.5 Changes in glucose and insulin

A total of eight RCTs observed glucose and insulin [23, 25–27, 31, 32, 34, 36]. Regarding the glucose parameter, statistically significant differences were found between the control and combined exercise groups (MD = –9.456, 95% CI: –13.78 to –5.141), the aerobic exercise and combined exercise groups (MD = –8.427, 95% CI: –13.06 to –3.814), and the resistance exercise and combined exercise groups (MD = –8.899, 95% CI: –14.28 to –3.519), which revealed that combined exercise had a significant advantage in regard to im-

Table 1. SUCRA values of different interventions for outcomes.

	BMI	Weight	Body fat	HDL-C	LDL-C	TG	TC	Insulin	Glucose	SBP	DBP	WC
CT	65.9%	62.3%	0.4%	20.1%	63.4%	3.1%	18.4%	60.8%	25.8%	9.2%	21.4%	41.9%
AE	87.2%	44.7%	67.8%	71.5%	10.7%	57.3%	46.2%	24.6%	40.4%	48.8%	30.3%	35.4%
RE	7.6%	25.7%	80.9%	63.2%	73.7%	39.9%	54.4%	40.9%	33.8%	89.1%	60.3%	29.6%
CE	39.3%	67.3%	50.9%	45.3%	52.3%	99.8%	81.0%	73.7%	100%	53.0%	88.0%	93.1%

Abbreviations: AE, aerobic exercise; BMI, body mass index; CE, combined exercise; CT, control; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol (LDL-C); RE, resistance exercise; SBP, systolic blood pressure; SUCRA, surfaces under the cumulative ranking curve; TC, total cholesterol; TG, total triglyceride; WC, waist circumference.

Table 2. Results of the subgroup analysis of duration.

Covariate effect	Mean (95% CI)
BMI	0.14 (−0.93 to 1.28)
Weight	−1.52 (−7.46 to 4.68)
Waist circumference	−2.06 (−4.58 to 0.63)
Body fat	0.60 (−2.30 to 3.56)
HDL-C	0.59 (−6.38 to 7.74)
LDL-C	10.85 (−0.44 to 22.15)
Triglycerides	4.83 (−10.46 to 20.28)
Total cholesterol	15.30 (3.31 to 27.42)
Glucose	−5.86 (−13.87 to 2.52)
Insulin	−0.139 (−4.27 to 4.31)
SBP	2.99 (−5.11 to 11.12)
DBP	2.76 (−2.55 to 8.25)

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

proving glucose control. Moreover, combined exercise had the highest probability of being the best option for improving glucose control, based on the SUCRA values (SUCRA = 100%). However, the insulin levels were not statistically significantly different among these groups. According to the SUCRA values, combined exercise had the best performance in regard to improving insulin resistance (SUCRA = 73.7%).

4.6 Changes in blood lipid composition

A total of nine RCTs observed blood lipid compositions, such as HDL-C, LDL-C, TG, and TC [23–25, 27–29, 31, 33, 36]. The combined exercise group showed a more significant reduction in TG than the other groups (control, aerobic, and resistance groups), showing MDs of 20.39 (95% CI: 12.03 to 28.74), 10.5 (95% CI: 2.37 to 18.17), and 13.28 (95% CI: 4.94, 21.76), respectively. Moreover, combined exercise was regarded as the most efficacious protocol for improving TG, according to the SUCRA values (99.8%). In addition, the control group showed inferior results compared to the aerobic exercise group (MD: −9.885, 95% CI: −19.24 to −0.77). No significant difference was observed in regard to HDL-C, LDL-C, and TC among these groups, as shown in Fig. 4. In terms of TC, the ranking probability based on the SUCRA values indicated that combined exercise had the highest probability of being the best option (SUCRA = 81.0%). Furthermore, the results of the regression analysis for the duration of the interventions showed that TC was the only significant index (Table 2). Moreover, TC increased along with increasing time, with an MD (95% CIs) of 15.3 (3.31, 27.42). With respect to reducing LDL-C, resistance exercise had a 73.7% probability of being the best training program, whereas aerobic exercise was the best option for improving HDL-C (SUCRA = 71.5%).

4.7 Changes in body composition

A total of 14 RCTs [22–26, 28–36] observed the following body compositions: body fat, BMI, weight, and WC. Aerobic, resistance, and combined exercise yielded significant effects on body fat compared with the non-exercise controls. The MD and 95% CIs of body fat in the aerobic, resistance, and combined exercise groups were −1.991 (95% CI: −3.245 to −0.6525), −2.181 (95% CI: −3.339 to −0.7661), and −1.709 (95% CI: −2.935 to −0.4744), respectively. Resistance exercise was regarded as the best exercise regimen to reduce body fat, based on the SUCRA values (80.9%). The aerobic exercise group showed better outcomes in BMI than the resistance exercise group did (MD = 0.70, 95% CI: 0.08 to 1.32), and displayed a trend of being the best intervention measure for reducing BMI (SUCRA = 87.2%). Regarding weight and WC, no statistically significant difference was observed among the three groups, as shown in Fig. 3. Combined exercise was the most favorable intervention for reducing weight and WC, based on the SUCRA values (SUCRA = 67.3% and 93.1%, respectively).

4.8 Changes in blood pressure

A total of nine RCTs [22–27, 29, 33, 36] observed blood pressure. SBP and DBP were not significantly different among the groups. The SUCRA value revealed that combined exercise ranked the highest in terms of reducing DBP (SUCRA = 88.0%), whereas resistance exercise ranked as most effective in terms of reducing SBP (SUCRA = 89.1%).

5. Discussion

The benefits of aerobic exercise training on the modulation of cardiovascular risk factors were widely recognized whereas resistance training was regarded as a complement to, instead of a replacement for, aerobic exercise [15]. Interestingly, in studies where resistance training has been evaluated, it has been proved that this has exerted analogous effects to aerobic training on glycemic control and insulin sensitivity-signaling and body composition. Resistance training appears

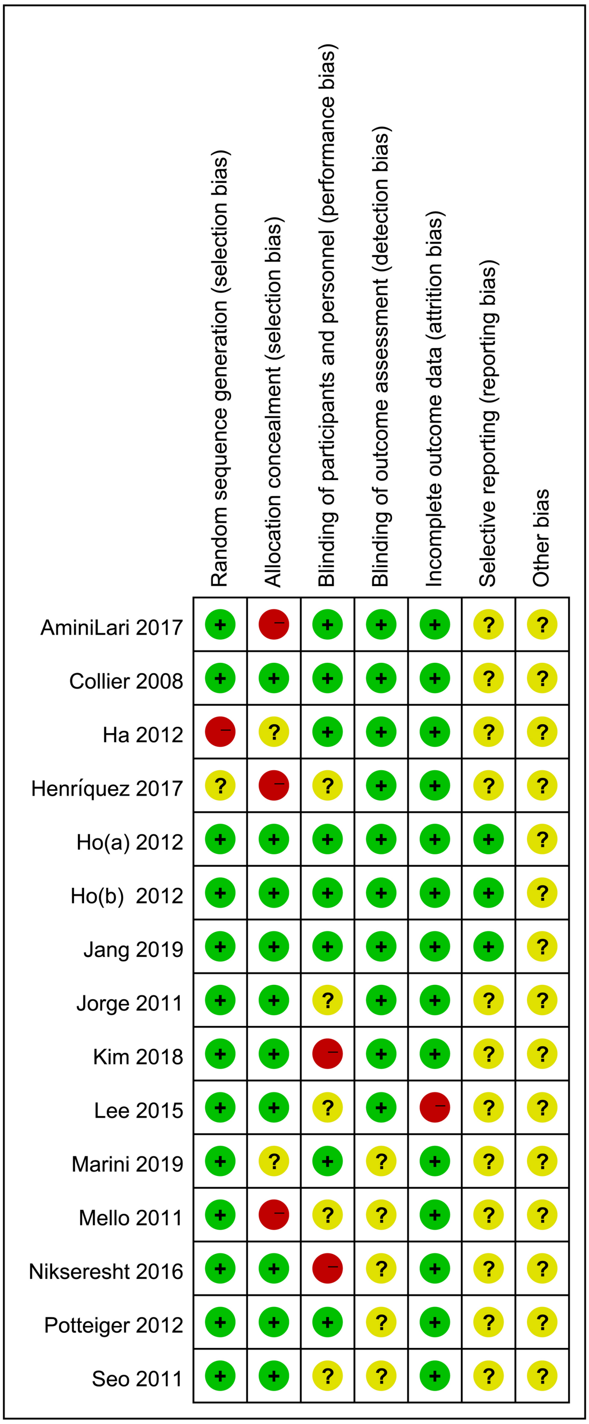

Fig. 3. Cochrane risk of bias results.

to be a feasible alternative to aerobic training or to play an independent role in cardiovascular risk factors [37]. This recommendation supports the result of our study that resistance exercise leads to more effective outcomes in improving the metabolic syndrome and cardiovascular risk parameters compared to aerobic exercise. The result of our study revealed that resistance exercise was the most significant effective training method in ameliorating body fat while aerobic exercise was best in improving BMI significantly. And body

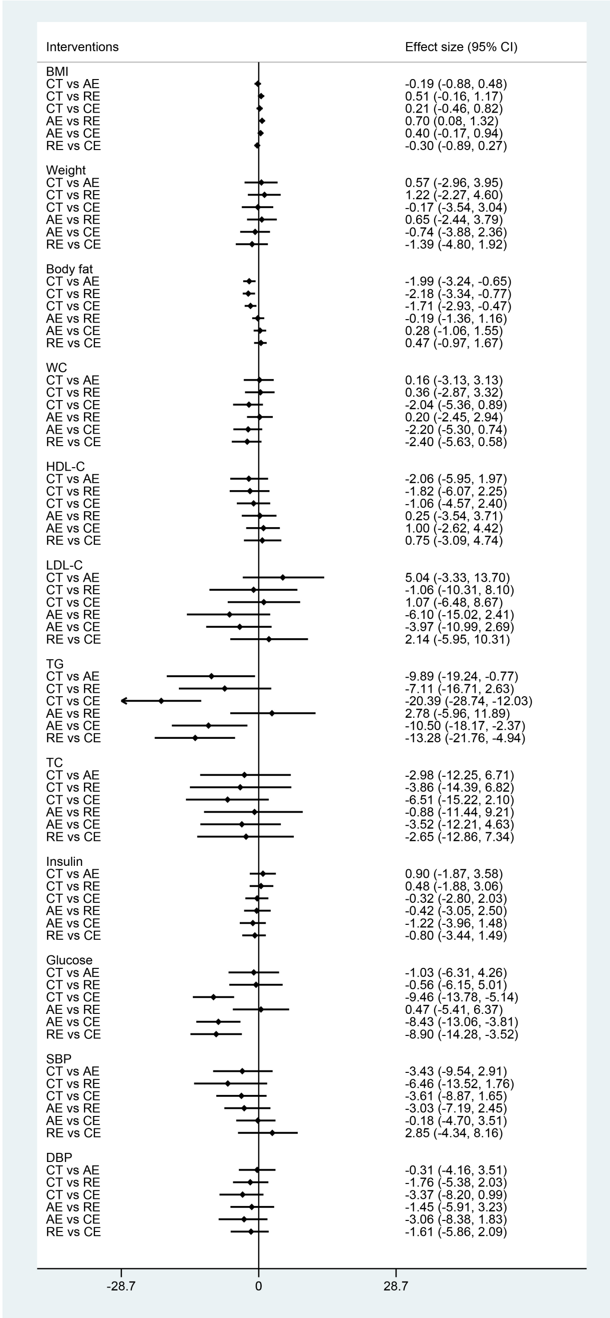

Fig. 4. Effect size of pairwise intervention comparison.

fat was proved to have a stronger correlation than BMI with CVD and all causes of death [37]. From this evidence, it can be seen that resistance exercise is better than aerobic exercise in preventing cardiovascular risk factors. Compared to aerobic exercise, resistance exercise increases muscular strength, endurance, and muscle mass to a greater extent [15]. Muscle mass engaged during exercise stimulates more IL-6 release that involved in lipid metabolism [38]. Excessive fat tissue stimulates uncontrolled inflammatory responses, resulting in systemic low-grade inflammation and metabolic disorders [39]. These processes are key pathophysiological components of cardiovascular disease [40]. Thus, resistance exercise is effective in lowering body fat and has an indispensable role in the prevention of cardiovascular disease.

In addition, based on the SUCRA values, resistance exercise showed the best results in regard to lowering LDL-C, but it had no statistical significance. Besides, aerobic exercise was superior to resistance exercise in regard to improving HDL-C. The systemic IL-6 response to exercise, the key intermediary agent to lipid degradation, relied on the duration and intensity of exercise [38]. An experimental study confirmed that a bout of exercise induces significant anti-inflammatory actions [38]. However, the intensity in our study was mostly moderate, which may account for the absence of superiority of resistance exercise in improving HDL-C. In addition, some studies inferred that low-volume resistance exercise provides maximal benefits in regard to lowering the risk of CVD [41, 42]. Recent studies also revealed no extra benefits of higher levels of resistance exercise [43]. The maximum benefits of resistance exercise were achieved with patients performing under one hour a week of training, especially at 58 minutes a week of training [41]. Total training time in our analyzed studies was 177.5–181 minutes of training a week, with a median follow-up of 14.5 weeks. Moreover, a regression analysis of the duration of the intervention showed that none of the outcomes changed along with the increasing training time. This suggests that a high volume of resistance exercise doesn't necessarily lead to better results in improving LDL-C and HDL-C. It also suggested that high intensity and an appropriate amount of resistance may be more effective in decreasing fat, but the safe levels of intensity and amount of exercise for CVD patients needs further research.

Furthermore, resistance exercise represents improving endothelial function. This network meta-analysis study revealed resistance exercise was most effective at ameliorating SBP. Regular resistance exercise training may mediate a reduction in blood pressure as a result of reducing systemic vascular resistance by enhancing endothelial sensitivity to nitric oxide, thereby reducing the sympathetic tone and salt load [44]. This was supported by a study aiming to prescribe exercise as therapy in 26 different chronic diseases. It revealed resistance training lowers SBP, while there was no statistical significance when aerobic exercise was added to it. Nevertheless, aerobic exercise is extensively recommended by international guidelines in the treatment of hypertension [45]. However, existing evidence from the general population indicates that aerobic exercise interventions showed less remarkable effects on SBP and DBP in normotensive participants (minimal reduction in DBP and no effect on SBP), whereas more beneficial effects were observed in hypertensive participants [46]. Only one report included in our study involved participants with pre- or stage one essential hypertension, which may have led to our result showing that aerobic exercise demonstrated minimal effects on blood pressure. Thus, it can be seen that, for normotensive participants, resistance exercise exerts more of an effect on blood pressure control than aerobic exercise.

While the role of aerobic exercise in preventing CVD is demonstrated with anti-oxidant and anti-inflammatory function, aerobic exercise stimulated mitochondrial biogenesis. As main "actor" during exercise, mitochondrial biogenesis presents excess glucose needs in the muscular tissue; this process results in glucose reduction. This is similar to the result of our study that aerobic exercise is better at reducing glucose than resistance exercise. A study conducted by Lee *et al.* [47] concluded that aerobic exercise had more advantages than resistance exercise in regard to improving insulin sensitivity and reduced glucose level. Besides, our study revealed combined exercise was the most significant in monitoring glucose; it also indicated that resistance has some additional effect on glucose monitoring. Improvement of body fat and skeletal muscle, resulting from the benefit of resistance training, are conducive to glucose storage and disposal. This process may contribute to glucose reduction and a long-lasting effect in metabolic parameters.

As discussed above, resistance excise is superior in lipid degradation while aerobic exercise is better at glucose control. Combined exercise has the advantages of both these types of exercise. It may reveal an additive effect in certain parameters. For example, combined exercise results in better outcomes than a single mode of exercise; however, this doesn't mean it maximizes all outcomes. In our study, aerobic exercise is the most effective method in improving patients' BMI. The reason for this is presumably that the exercise group reduced fat mass but increased muscle mass. Moreover, resistance exercise is the best way to reduce body fat. Lee *et al.* [47] concluded that aerobic and combined exercise showed similar benefits in ameliorating insulin sensitivity. This indicates balance is needed in combining aerobic and resistance exercise to achieve maximal effect.

5.1 Strengths and limitations

This was the first NMA focusing on metabolic syndrome parameters and cardiovascular risk factors. The main results of our study suggested an appropriate exercise program to improve metabolic syndrome and prevent CVD, which might attract the attention of more researchers focusing on this field. Millions of individuals would benefit, and social and medical burdens would be alleviated if our results could be applied in clinical practice. Second, we included a large sample size involving 536 participants. Studies published in English and Chinese were within the range of our research, there were no publication restrictions, and all eligible data were included, thereby increasing the power of the study. This meta-analysis also has several limitations. First, although all studies included were RCTs, merely one-fifth of them adequately described the randomization process. None of them identified blinding allocation concealment or the blinding of outcome assessments. Finally, the lack of controlling for age and sex was another limitation of the meta-analysis.

Table 3. Basic Characteristics of included studies.

Study ID	N	Sex (M/F)	Age	Interventions	Training type	Training intensity	Training frequencies and duration	Study participants	Outcomes	JADAD
Lee 2015 [30]	27	0/27	68.01 ± 2.88	AE vs CE	AE: treadmill, CE: treadmill + EMMG	Moderate to high (40–70% HRR, Borg's scale 10–13)	50 min/time, 5 times/week, 8 weeks	Healthy older women	① ④	5
de Mello 2011 [23]	30	No detail	16.71 ± 1.47	AE vs CE	AE: treadmill, CE: treadmill + EMMG	Moderate (50–70% VO2peak, B/A × 3/6–20)	60 min/time, 3 times/week, 48 w	Obese adolescents	①③⑤⑥⑦⑧⑨⑩⑪⑫	5
Marini 2019 [36]	30	No detail	49.3 ± 10.3	CT vs CE	CT: SA, CE: Treadmill+ EMMG	Moderate (50–70% HRR, 50%/A × N/1)	90 min/session, 2 sessions/week, 12 week	Outpatients with Metabolic Syndrome	① ②③⑤⑥⑦⑧⑩⑪⑫	5
Seo Dl 2011 [25]	20	0/20	No detail	CT vs CE	CT:SA, CE: treadmill + EMMG	Moderate (60–70% HRR, B/A × 3/10)	60 min/day, 3 days/week, 12 w	Obese middle-aged women	②④ ⑤⑦⑨⑪⑫	5
Ha 2012 [26]	15	0/15	20.96 ± 1.78	CT vs CE	CT: SA, CE: Treadmill + EMMG	Moderate to high (60–80% HRR, B/A × 3/10–15)	80 min/day, 3 day/week, 12 w	Obese female college students	①②③④ ⑤⑥⑦⑧⑨⑪⑫	5
Henríquez 2017 [33]	42	0/42	56.5 (53–60)	AE vs RE	AE: no detail, RE: EMMG	Light to Moderate (60–65% VO2peak, 20–30%/A × N/10)	40 min/day, 3 day/week, 24 w	Postmenopausal women	① ②③⑤⑦⑧⑪⑫	5
Potteiger 2012 [29]	22	22/0	36.35 ± 4.8	AE vs RE	AE: treadmill and jogging, RE: EMMG	Moderate to high (65–80% MCF, 80–100%/(5–10) × N/5–10)	45 min/day, 3–4 day/week, 24 w	Overweight, physically inactive males	①③④ ⑤⑦⑪⑫	5
Collier 2008 [22]	30	20/10	48.2 ± 1.3	AE vs RE	AE: treadmill, RE: EMMG	Moderate to high (65% VO2peak, 80–100%/(5–10) × N/5–10)	AE: 30 min/day, 3 day/week, 4 w, RE: 45–50 min/day, 3 day, 4 w	Pre-or stage-1 essential hypertensives	① ④ ⑪⑫	5
Jang 2019 [35]	24	0/24	55.46 ± 3.77	CT vs AE vs RE	CT: SA, AE: treadmill, RE: EMMG	Moderate (60–75% HRR, 60–70%/A × N/1)	50 min/time, 4 time/week, 8 w	Middle-calss, middle-aged women	① ②③④	6

Table 3. Continued.

Study ID	N	Sex (M/F)	Age	Interventions	Training type	Training intensity	Training frequencies and duration	Study participants	Outcomes	JADAD
Nikseresht 2016 [31]	33	33/0	39.63 ± 2.77	CT vs AE vs RE	CT: SA, AE: treadmill, RE: EMMG	Light to high (65–90% MHR, 40–90%/(4–20) × (1–4)/C)	55 min/sessions, 3 sessions/week, 12 w	Obese men	②③④ ⑤⑥⑦⑧⑨	5
Kim 2018 [34]	35	0/35	73.2 ± 4.9	CT vs RE vs CE	CT:SA, RE: Stretching, CE: EMMG	Moderate to high (Borg scale 6–8)	RE: 70 min/time, 3 time/week, 6w, CE: 90 min/time, 3 time/week, 6 w	Healthy elderly participants	① ②③④ ⑨⑩	5
Ho 2012 [28]	64	10/54	53 ± 1.35	CT vs AE vs RE vs CE	CT: SA, AE: treadmill, RE: EMMG, CE: AE + RE	Moderate (60% HRR ± 10 beats/min, B/(8–12) × 4/10)	30 min/day, 5 day/week, 12 w	Overweight and obese adults	①②③④ ⑤⑥⑦⑧⑨⑩	6
AminiLari 2017 [32]	52	0/52	No detail	CT vs AE vs RE vs CE	CT: SA, AE: Running, RE: EMMG, CE: AE + RE	Moderate (50–55% MHR, 50–55%/1 × N/1)	60 min/day, 3 day/week, 12 w	Type2 diabetic middle-aged women	① ②④ ⑨⑩	5
Jorge 2011 [24]	48	18/30	53.9 ± 9.9	CT vs AE vs RE vs CE	CT: light stretching exercise, AE: cycling, RE: EMMG, CE: AE + CE	The lactate threshold, B/A × N/1	60 min/day, 3 day/week, 12 w	Patients with type 2 diabetes mellitus	①③⑤⑥⑦⑧⑪⑫	5
Ho 2012 [27]	64	10/54	53 ± 1.35	CT vs AE vs RE vs CE	AE: treadmill, RE: EMMG, CE: AE + RE	Moderate (60% HRR ± 10 beats/min, B/(8–12) × 4/10)	30 min, 5 day/week, 12 w	Overweight and obese adults	⑪⑫	6

① BMI ② weight ③ WC ④ body fat ⑤ HDL ⑥ LDL ⑦ TG ⑧ TC ⑨ Glucos ⑩ Insulin ⑪ SBP ⑫ DBP.

HRR, heart rate reserve; CT, control; AE, aerobic exercise; RE, resistance exercise; CE, combined exercise; HRR, heart rate reserve; RM, repetitions maximum; MHR, maximal heart rate; MCF, maximal cardiorespiratory fitness; SA, sedentary activities; EMMG, exercise for the main muscle groups, such as leg extension, prone leg curl, abdominal crunch, biceps, triceps, and seated calf leg press, bench press, lat pull down, seated rowing, shoulder press, abdominal curlsa and kness curls. B/A × N/C represents N set of A repetitions at B% of the C-repetition maximum.

6. Conclusions

Endothelial dysfunction, oxidative stress, and inflammatory processes may act as mediators, as these are key pathophysiological components of metabolic dysfunction and CVD. The mechanism of effective exercise to prevent CVD is based on these pathophysiological components. Resistance exercise has an important effect on inhibiting the inflammation process and improving endothelial function; it also has stronger function in lipid degradation. Aerobic exercise has improved anti-oxidant and anti-inflammatory function; it has advantages with regards to glucose metabolism. Combined exercise cumulates the benefits of both types of exercise. However, a balanced combination of exercises that is safe and effective to prevent CVD still needs to be defined.

Abbreviations

BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; DIC, differences in conditions; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol (LDL-C); NMA, network Meta-analysis; MCMC, Markov Chain Monte Carlo (MCMC); MD, mean differences; RCT, randomized controlled trials; SBP, systolic blood pressure; SUCRA, surfaces under the cumulative ranking curve; TC, total cholesterol; TG, total triglyceride; WC, waist circumference.

Author contributions

MYL, YZ, ASKC—designed the study; MYL, YP, TZ—conducted literature search and appraisal of study quality; YZ, ASKC—revised the manuscript.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

Appendix

See Table 3.

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