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Exercise Training Modalities in Young and Middle-Aged Adults With Prehypertension or Hypertension: A Systematic Review and Network Meta-Analysis

Lu Tian  | Siyu Yang | Yulan Hu | Jinrui Cui | Xiaobei Guo | Zongfeng Liao | Yu Liu

Nursing Department, Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, P.R. China

Correspondence: Yu Liu (504443342@qq.com) | Zongfeng Liao (892123557@qq.com)

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ABSTRACT

Aims: The question of how to choose the right type of exercise to lower blood pressure and cardiovascular risk factors in people worldwide with high blood pressure is not yet fully understood. Thus, the aim of this study was to investigate the effects of various exercise training on blood pressure and cardiovascular risk factors among young and middle-aged adults with prehypertension or hypertension.

Design: Systematic review and network meta-analysis.

Methods: We searched five electronic databases to identify randomized controlled trials that compare exercise training versus a sedentary or sham control group in young and middle-aged adults with prehypertension or hypertension. Review Manager 5.3, Stata15.0, and R4.2.1 software estimated the efficacy of exercise training modalities.

Results: We included 19 eligible articles with 1590 participants to assess five exercise trainings. Our findings indicated that low-middle intensity aerobic exercise (mean difference (MD) = -8.08 , 95% confidence interval (CI) = -13.58 , -2.58) was superior to all exercise strategies (high-intensity aerobic exercise: MD = -6.53 , 95% CI = -12.51 , -0.56 ; high-intensity resistance exercise: MD = -4.95 , 95% CI = -11.07 , 1.17 ; low-middle-intensity resistance exercise: MD = -3.49 , 95% CI = -12.36 , 5.39) compared with control group in lowering systolic blood pressure. Compared with the control strategy, high-intensity resistance exercise (MD = -4.75 , 95% CI = -8.00 , -1.50), high-intensity aerobic exercise (MD = -4.27 , 95% CI = -7.08 , -1.45) could lower diastolic blood pressure. The effects of different exercise patterns on cardiovascular risk factors, the results indicated that only low-middle-intensity aerobic exercise significantly improved body mass index (MD = -0.55 , 95% CI = -7.08 , -1.45), total cholesterol (MD = -19.07 , 95% CI = -36.42 , -1.72), triglycerides (MD = -14.32 , 95% CI = -23.16 , -5.48), high-density lipoprotein (MD = 2.29 , 95% CI = 0.85 , 3.73), and low-density lipoprotein (MD = -13.90 , 95% CI = -22.18 , -5.63). In addition, no intervention affects heart rate.

Conclusion: Compared with other types of exercise, aerobic exercise can significantly improve systolic blood pressure, while high-intensity resistance or aerobic exercise may significantly improve diastolic blood pressure. In addition, AE-LM is effective in the reduction of risk factors that are contributors to the development of cardiovascular disease. Therefore, this study provides strong evidence to support the selection of appropriate exercise modalities for hypertensive patients.

Lu Tian and Siyu Yang made the same contribution.

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1 | Introduction

Worldwide survey data demonstrate that nearly 25%–45% of the population who are above 18 years old are diagnosed with prehypertension or hypertension [1]. Moreover, one in five people with prehypertensive will develop hypertension in 5–10 years if their lifestyles are not well modified [2]. While previous research showed the incidence of hypertension and prehypertension would increase with age ≥ 65 years old [3], growing evidence suggests that hypertension and prehypertension become common concerns among young and middle-aged adults. China Health and Nutrition Survey reveals that the prevalence of prehypertension at 18–39 years is 37.8%, and hypertension at middle age is 17.2% [4]. There is a prevalence of young adults with hypertension of around 7% in India [5] and 33.5% in Bangladesh [6, pp. 2017–2018]. However, the statistics of hypertension and prehypertension among young and middle-aged adults are underestimated because those populations have lower awareness of health and worse living habits, such as irregular sleep patterns [7].

Continuous high blood pressure would result in a series of adverse outcomes among young and middle-aged adults. The new standard of hypertension from the American College of Cardiology (ACC) is defined as a lower blood pressure threshold of 130 mmHg for systolic blood pressure (SBP) or 80 mmHg for diastolic blood pressure (DBP) [8]. With the new classification, nearly half of young and middle-aged adults are potential populations with prehypertension and hypertension [9]. People with prehypertension would increase a 3.01-fold cardiovascular disease risk than people with normal blood pressure in a 15-year follow-up study [10]. Several studies also identify that nearly 50% of stroke and ischemic heart disease are associated with prehypertension and hypertension; hypertension-mediated organ damage and complications in the early lifespan among young adults are reported in some research [7, 10]. In addition, prehypertension and hypertension are considered as significant indicators of coronary artery diseases, aortic dissection, and arrhythmias [11]. Therefore, effective intervention of prehypertension and hypertension among young and middle-aged adults would decrease the incidence of cardiovascular events and associated changes that contribute to several damages in subclinical organs early in its natural history, eventually controlling the risks of later life complications.

2 | Review

Pharmacological therapy is highly recommended for hypertensive patients [1]; however, to our best knowledge, approximately 12%–15% of hypertension patients have resistant hypertension even though they are prescribed to take regular medicine [2]. Thus, some professional organizations support exercise as the first-line therapy to prevent, treat, and control hypertension [12]. A recent study has shown the associations between exercise and hypertension among young and middle adults, which may reduce a high incidence of cardiovascular events for the rest of adulthood [13]. The Chinese Society of Cardiology also claims that exercise is crucial for young and middle-aged with prehypertension to slow the progression of elevated blood pressure [14]. Although regular aerobic and

resistance exercises are proven to achieve blood pressure management [15], the effect of exercise training on blood pressure control and cardiovascular disease prevention may differ with various exercise modalities. Some researchers found that hypertensive and prehypertensive populations should try moderate-intensity and high-intensity aerobic exercise training to control blood pressure [16]. Other studies demonstrated that a significant improvement in blood pressure management for hypertension populations was proven in high-intensity aerobic exercise compared with moderate-intensity exercise [17, 18]. Conflict evidence suggests that aerobic exercise is good, but resistance exercise is better. Emerging evidence concludes that aerobic exercise such as tai chi, swimming, jogging, resistance exercise, or combined training could lower blood pressure [19, 20]. Moreover, most current guidelines are established on the clinical trials of the effect of exercise on the elderly population with hypertension [14].

Therefore, the research aims to conduct a systematic review and network meta-analysis to investigate different high, middle, or low-intensity exercises on the change in blood pressure and cardiovascular biomarkers among young and middle-aged adults with prehypertension and hypertension. Alongside this, the review aims to identify optimal exercise strategies to improve the cardiovascular biomarkers associated with blood pressure.

3 | Materials and Methods

Following the Preferred Reporting Items for Systematic Review incorporating Network Meta-analysis (PRISMA-NMA) [21], this review has been registered on the PROSPERO database (CRD42022354092) and reported according to the International Society for Pharmacoeconomics and Outcomes Research approach on interpreting network meta-analyses for health-care decision-making [22].

3.1 | Data Source and Searches

Two reviewers (L.T. and S.Y.) conducted the systematic literature search independently on PubMed, Embase, CINAL, Cochrane Library, and Web of Science from database inception to September 6, 2023, with limitation to English publication. The following search terms were used in our literature search: “young adults,” “middle-aged adults,” “hypertension,” “prehypertension,” “high blood pressure,” “exercise,” “training,” “physical activity,” “Tachi,” “yoga,” which were developed into tailored search strategies (Supporting Information S1: Appendix 1). We also review the reference lists of included studies, previous systematic reviews or meta-analysis for retrieving additional eligible articles.

3.2 | Study Selection

The network meta-analysis included articles reporting the effect of aerobic or resistance exercise on blood pressure control among prehypertension and hypertension young/

middle-aged population. Studies were included to meet the following criteria according to PICOS (Patient, Intervention, Comparison, Outcome and study type): (i) the subjects were diagnosed with prehypertension (systolic/diastolic blood pressure 120–139/80–89 mmHg) or hypertension (systolic/diastolic blood pressure > 139/89 mmHg) [23]; (ii) the age of participants was described as young (18–35 years old) and middle-aged (36–65 years old) [24]; (iii) eligible intervention were different intensity aerobic exercise or resistance exercise or a combination of both with at least 3-week intervention which researchers observed any changes between pre- and post-intervention outcome measures; (iv) the comparator was a placebo or regular care or received other exercise trainings; (v) the primary outcome indicator were rest systolic blood pressure (SBP) and diastolic blood pressure (DBP), other indicators were reported including mean rest heart rate, body mass index (BMI), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerids (TG); and (vi) the study type were randomized controlled trial or cohort with control groups.

Exclusion criteria were as follows: (i) the enrolled subjects with prehypertension or hypertension are comorbid with heart disease, renal disease, stroke, metabolic disease, or any severe physical problem; (ii) intervention was described as incorporating exercise with other therapeutic methods that affect BP (e.g., diet modification, new medication); (iii) the specific data related to outcome indicators were not provided or no response from authors of included studies after applying for Supporting Information through email.

3.3 | Categorization of Available Evidence

Based on the criteria from previous studies about prehypertension and Frequency, Intensity, Time, and Type (FITT) exercise recommendations for hypertension, exercise strategies in our review were categorized into high-intensity aerobic exercise (AE-H), low-middle intensity aerobic exercise (AE-LM), high-intensity resistance exercise (RE-H), low-middle intensity resistance exercise (RE-LM), combined exercise (COM) which mixed aerobic exercise and resistance exercise and control group (CON) which was classified that regular care or placebo was conducted to control blood pressure and associated risk factors.

The intensity of exercise in this review is classified into high intensity and moderate-low intensity. The high-intensity exercise is defined as meeting one or more following criteria: (1) the heart rate while exercising is $\geq 70\%$ maximum heart rate (HR Max); (2) the oxygen uptake while exercising is $\geq 60\%$ maximal oxygen consumption (VO₂ Max); (3) the power while exercising is $> 80\%$ peak power; (4) 80%–90% of one repetition maximum (1RM) while exercising, 1RM which is an indicator of the resistance exercise intensity is measured by completing an action once against maximal loads, such as correct lifting technique with maximal weight [25]. The moderate-low intensity is defined as meeting one or more following criteria: (1) the heart rate while exercising is 40%–70% maximum heart rate (HR Max); (2) the oxygen uptake while exercising is 40%–60% maximal oxygen consumption (VO₂ Max); (3) the power while

exercising is 40–60 peak power; and (4) 40%–70% of 1RM while exercising [26].

3.4 | Literature Screening and Data Extraction

Two independent reviewers (L.T. and S.Y.) screened the title and abstracts of all search results. Three reviewers (L.T., S.Y., and Y.C.) performed full-text read of all relevant articles based on the inclusion and exclusion criteria. The third reviewer (Y.C.) reached the consensus of eligible articles.

The relevant data of each eligible study was collected by two reviewers (L.T. and S.Y.) following a study characteristics form including the author of the study, year of publication, study country, the age distribution of subjects, intervention type, follow-up time, sample size, details of exercise implementation, and outcome indicators. Any disagreement was resolved by the third reviewer (Y.L.) to judge the difference. The study selection and data extraction were managed through Endnote software.

3.5 | Risk of Bias Assessment and Quality Grading

The risk of bias for each eligible study was evaluated by two reviewers (L.T. and S.Y.) using the Cochrane Collaboration Risk of Bias tool (RevMan 5.3) from six domains: random sequence generation, concealment of distribution, blinding method, data integrity, selective reporting, and other biases. They also evaluated the quality of evidence by rating three grades: A (all items were at low risk), B (some items were at low risk), and C (all items were at high risk). If two reviewers had inconsistent assessments, they were decided by the third reviewer (Y.L.).

3.6 | Data Synthesis

Initially, two independent reviewers (L.T. and S.Y.) preprocess the original data using Microsoft Excel (Version 16.0, Microsoft Corporation, Redmond, WA, USA). When the article was presented, they used the mean change and standard deviation (SDs). We used the methods outlined in the Cochrane Handbook to acquire mean changes and SDs when the article reported pre/post mean difference and SDs. When standard errors (SEs) or 95% confidence interval (CI) was reported, the following formula was used to convert into SDs:

$$SD = SE \times \sqrt{N}, \quad SD = \sqrt{N} \times (\text{upper limit} - \text{lower limit}) \div 3.92.$$

In the eligible studies, we converted the inconsistent units into the same ones for the different measuring units of outcome indicators, such as HDL, LDL, TG, and TC. We used Stata version 15.1 (Stata Crop) to conduct a random-effect network meta-analysis (NMA) and drew a network plot to explore the robustness of the evidence. Each node represents one intervention in the trials, and the node size represents the number of

subjects included in this intervention. The thickness of the line connecting the nodes is proportional to the number of subjects in the trials, directly comparing the two interventions.

All subsequent statistical analyses were performed in the R software package. We conducted the Wald test to identify inconsistency by comparing direct and indirect evidence. We split the network estimates to investigate the significant difference between direct and indirect comparisons. We performed a standard pairwise meta-analysis to compare the effects of different types of exercise interventions using the BUGSnet package in R studio. DerSimonian–Laird method was used to process all direct comparisons. The I^2 statistics ranging from 0% to 100% was calculated to analyze the statistical heterogeneity, and the corresponding p value was also examined. The heterogeneity was considered as not significant ($I^2 < 30\%$), moderate (30%–50%), substantial (50%–75%), and considerable ($> 75\%$).

To examine the probability of each exercise was the most effective intervention, we created rankograms by calculating the surface under the cumulative ranking (SUCRA) of each exercise. The SUCRA value of the most effective intervention would be close to 1, while the SUCRA value of the worst one would be close to 0. A network funnel plot evaluated the

publication bias. The sensitivity analyses were performed by omitting data from high-risk bias.

4 | Results

4.1 | Literature Search and Screening

A total of 3700 articles were identified at an initial search of five electronic databases. After screening the title and abstract, 379 articles were assessed for full-text reading. Finally, 19 articles [1, 2, 4, 17, 18, 27–40] met our inclusion criteria while other articles were excluded with the following reasons: 239 articles did not meet the participant criteria, 15 articles did not report outcomes, 90 articles did not report the exercise training, 10 articles were not RCTs, and 6 did not offer available data although we emailed the corresponding authors. The process of literature selection is illustrated in Figure 1.

4.2 | Study Characteristics

Of total 19 eligible articles [1, 2, 4, 17, 18, 27–40] (Table 1), 6 articles [1, 2, 18, 29, 30, 36] described at least two exercise strategies to

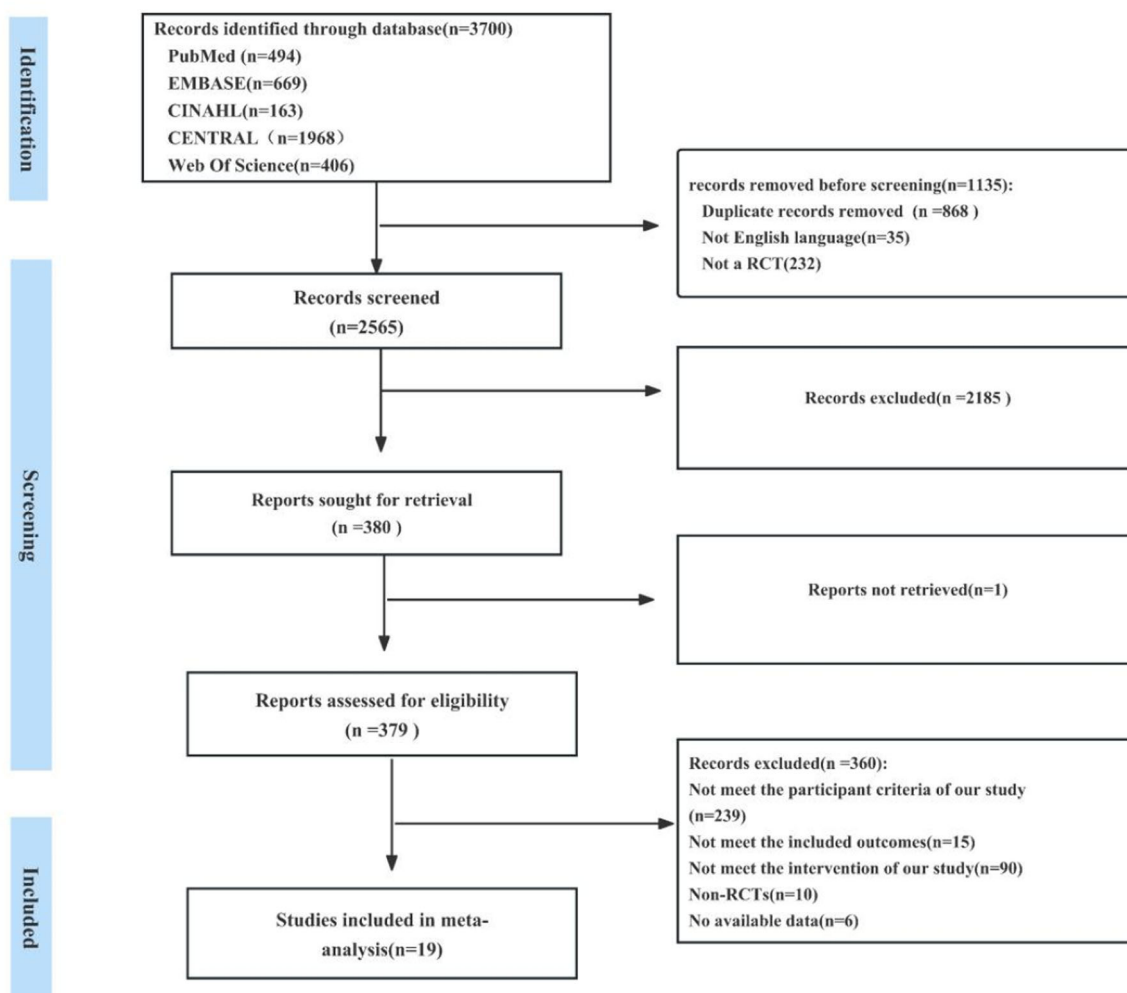


FIGURE 1 | PRISMA flow diagram of included studies.

TABLE 1 | Main characteristics of included studies.

Study (author, year)	Country	The length of intervention	Interventions	Sample (N/F/M)	Age (years \pm SD)	Description of intervention
Blumentha et al. [28]	America	16 weeks	AE-H	39/24/25	44.3 \pm 8.5	Walking/jogging at intensity at least 70% of VO2 Max; 3 times supervised exercise sessions per week
Tanaka et al. [39]	America	10 weeks	RE-LM	31/18/13	46.0 \pm 7.0	Without producing significant cardiovascular training effect; 2–3 times supervised circuit weight training per week
			CON	22/15/7	45.7 \pm 7.8	Maintain previous exercise and diet
			AE-LM	12/7/5	47 \pm 3	60% of VO2 Max; 3 days supervised swimming training program per week on alternate days, 60 min per session
Steffen et al. [38]	America	6 months	CON	6/3/3	49 \pm 5	Remained sedentary
			AE-H	35/16/19	47.5 \pm 8.9	At 70%–85% of reserve HR; 3–4 times supervised exercise program per week
			CON	15/6/9	46.1 \pm 7.6	Maintained usual dietary and exercise/activity habits
Tsai et al. [40]	China	12 weeks	AE-LM	37/19/18	51.6 \pm 16.3	3 times supervised Tai Chi Quan each week
Collier et al. [32]	America	4 weeks	CON	39/19/20	50.5 \pm 9.8	Control group
			AE-LM	15/10/5	49.8 \pm 1.6	65% of VO2 Max, 3 days unsupervised AE training per week; 30 min of treadmill exercise
			RE-LM	15/10/5	47.0 \pm 2.0	Unsupervised RE-ML
Guimarães et al. [33]	Brazil	16 weeks	AE-H	16/7/9	50 \pm 8	At 60% of reserve HR; 40 min exercise training on a treadmill (20 min of submaximal strength training and 10 min of cool-down exercises)
			CON	11/2/9	47 \pm 6	No exercise
Hansen et al. [34]	Norway	12 weeks	AE-LM	28/16/12	53.6 \pm 6.5	Walking/running on treadmill at 60% of VO2 Max; 3 times per week supervised by sports physiologist
Beck et al. [27]	America	8 weeks	CON	29/17/12	51.3 \pm 9.2	No exercise
			RE-H	15/11/4	21.1 \pm 0.6	2 sets of 8–12 repetitions to volitional fatigue on seven variable resistance machines; 3 days per week for 1 h

(Continues)

TABLE 1 | (Continued)

Study (author, year)	Country	The length of intervention	Interventions	Sample (N/F/M)	Age (years \pm SD)	Description of intervention
			AE-LM	13/9/4	20.1 \pm 0.9	Maintain HR between 65% and 85% of their predetermined maximum exercising HR
			CON	15/10/5	21.6 \pm 0.8	No exercise
Carlson et al. [31]	Australia	8 weeks	RE-H	20/7/13	20.0 \pm 7.0	Supervised 30% MVC IRT; 3 days per week
			RE-LM	20/8/12	20.0 \pm 8.0	Supervised 5% MVC IRT; 3 days per week
Park et al. [35]	Korea	12 weeks	AE-LM	25/13/12	54.52 \pm 6.96	Perform supervised qigong: consisted of a warm-up (15 min), main qigong treatment (25 min), and a cool-down (10 min) portion.
			CON	27/22/5	52.93 \pm 8.45	No exercise
Ogbutor et al. [17]	Nigeria	3.3 weeks	RE-H	200/109/91	40.78 \pm 6.04	At 30% MVC; unsupervised IRT 20 min each day
			CON	200/112/88	41.27 \pm 6.31	Control group
Schroeder et al. [37]	America	8 weeks	AE-H	17/7/10	58 \pm 7	Maintain 70% of reserve HR; 3 days supervised AE per week for 60 min per session
			RE-H	17/7/10	57 \pm 9	3 days supervised RE per week for 60 min per session (started with 2 sets of 18–20 maximal repetitions and progressed to 3 sets of 10–14 maximal repetitions with a rest of 1–2 min between sets)
			COM	18/7/11	58 \pm 7	3 days per week for 60 min per session (30 min of AE and 30 min of RE per session)
			CON	17/6/11	58 \pm 6	No exercise
Shou et al. [4]	China	12 weeks	AE-LM	98/48/50	52 \pm 6.46 (male) 51 \pm 7.09 (female)	The target HR during the exercise was set as 50%–60% of the maximal oxygen uptake or 70%–80% of the maximum HR; 24-style simplified tai chi each exercise at 40–90 min
			CON	100/55/45	52 \pm 8.98 (male) 51 \pm 7.54 (female)	No exercise
Boeno et al. [29]	Brazil	12 weeks	AE-H	15/8/7	45.8 \pm 6.8	Performed on a treadmill exercise intensity starting at 60% of HR reserve and increasing by increments of 10% every 4 weeks to 80% of HR reserve; 5 min treadmill walking at a

(Continues)

TABLE 1 | (Continued)

Study (author, year)	Country	The length of intervention	Interventions	Sample (N/F/M)	Age (years \pm SD)	Description of intervention
Cahu et al. [30]	Brazi	12 weeks	RE-H	15/6/7	46.1 \pm 7.2	self-selected intensity, 45–50 min treadmill exercise at the prescribed intensity and 5 min cool down (stretching)
						Consisted of two to three sets of 8–20 submaximal repetitions of bench press, leg press, leg pulldown, leg extension, shoulder press, leg curl, bicep curl and triceps extension.
			CON	12/5/7	44.3 \pm 8.3	Maintain exercise and diet
Pedralli et al. [41]	Brazi	8 weeks	RE-H	17/–/–	61 \pm 2	At 30% of maximal voluntary contraction, a 1-min rest interval; 3 weekly sessions of isometric handgrip training (4 \times 2 min sets, alternating the hands at 30% of maximal voluntary contraction)
			CON	16/–/6	59 \pm 2	Maintain dietary habits and physical activity
			AE-H	14/5/9	50.9 \pm 14.2	At 75% heart rate reserve; 40-min cycling exercise session twice a week
Farhad et al. [1]	Pakistan	8 weeks	RE-H	14/8/6	55.1 \pm 6.9	40-min supervised resistance exercise training session twice a week: 6 resistance exercises, 4 \times 12 repetitions, 60% maximum strength
			COM	14/6/8	53.8 \pm 9.1	2 \times 12 repetitions of RT + 20 min of AT; 40-min exercise session twice a week
			RE-H	43/31/12	30 \pm 4.1	Set to be 60%–80% of 1 repetition maximum; using dumbbells, TheraBand, and free weights 3 days/week
John et al. [2]	Switzerland	5 weeks	AE-H	43/25/18	34 \pm 3.2	Set between 60% to 80% of maximum heart rate; treadmill or static cycling at 5 days/week
			AE-H	12/6/6	21 \pm 0.8	At an 80%–85% heart rate reserve; 20 min of treadmill running with a 1:4 min work to rest ratio

(Continues)

TABLE 1 | (Continued)

Study (author, year)	Country	The length of intervention	Interventions	Sample (N/F/M)	Age (years \pm SD)	Description of intervention
Williamson et al. [18]	Britain	16 weeks	AE-LM	10/6/4	19 \pm 1.3	At an intensity of 40%–60% of their HR-reserve; 20 min of treadmill running with a 1:4 min work to rest ratio
			CON	10/10/-	21 \pm 1.0	No exercise
			AE-H	102/49/53	27.7 \pm 4.2	At 60%–80% peak heart rate; 3 aerobic training sessions per week of 60 min per session
			CON	101/48/53	27.8 \pm 4.1	Control group

Abbreviations: AE-H, high intensity aerobic exercise; AE-LM, low-middle-intensity aerobic exercise; COM, combined exercise; CON, control group; HR, heart rate; IRT isometric resistance training; MVC, maximum voluntary contraction; RE-H, high intensity resistance exercise; RE-LM, low-middle intensity resistance exercise; VO2 Max, maximal oxygen consumption.

control blood pressure. Six articles [27, 28, 32, 37–39] were implemented in America; four articles [29, 30, 33, 36] (21.05%) were implemented in Brazil, and six articles [2, 4, 31, 35, 36, 40] were implemented in Asia. Two articles [18, 34] were implemented in European. One article [17] was implemented in Africa. The duration of exercise training ranged from 3.3 to 16 weeks. The participants in this systematic review were between 18 and 65 years old. Five exercise strategies were compared with controls (placebo, usual care, other exercise strategies): AE-H, A.E.-L.M., RE-H, RE-L.M., and COM.

4.3 | Bias Risk Assessment of Involved Literature

All eligible studies were of middle methodological quality (Figure 2). Seven studies [1, 17, 18, 29, 31, 35, 37] were low risk in allocation concealment while 11 [1, 17, 18, 29, 31–33, 35–37, 40] were at low risk in random sequence generation. Participants and persons blinding was unclear described in eight studies [4, 28, 30, 32–34, 38, 40] and three studies [2, 27, 39] had high risk of bias. Fourteen studies [1, 2, 4, 17, 27, 29–35, 38, 39] showed unclear risk of bias in selective reporting whereas 13 studies [1, 17, 28–31, 33, 34, 4, 18, 35–37] showed unclear risks of other bias (e.g., early trial termination, extreme baseline imbalance).

4.4 | Network Analysis

Figures 3, 5, and 6 show the network structure of exercise training for SBP, DBP, BMI, HR, LDL, HDL, TC, and TG with mixed intervention comparison of different exercise training and control strategies.

4.4.1 | Systolic Blood Pressure

4.4.1.1 | Evidence Network. Fifteen studies [1, 2, 4, 17, 18, 27–33, 35, 39, 40] with 1590 participants involving four exercise training and control strategy reported SBP. The size of the nodes that represent the exercise training indicates the sample size, and the thickness of lines between nodes indicates the number of studies with comparisons of exercise strategies. Four exercise strategies denote direct comparisons, and there is a closed-loop formation. The network evidence of SBP is shown in Figure 3a.

4.4.1.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4a).

4.4.1.3 | Network Meta-Analysis. The network relationship of four exercise strategies and control strategy for SBP is shown in Figure 5a. The SBP score was reported in 15 pieces of literature [1, 2, 4, 17, 18, 27–33, 35, 39, 40] and network comparisons yield a total of 10 pairwise comparisons. There were significant differences between the two exercise strategies and the control group in reducing SBP: AE-LM (MD = −8.08, 95% CI = −13.58, −2.58, $p < 0.05$),

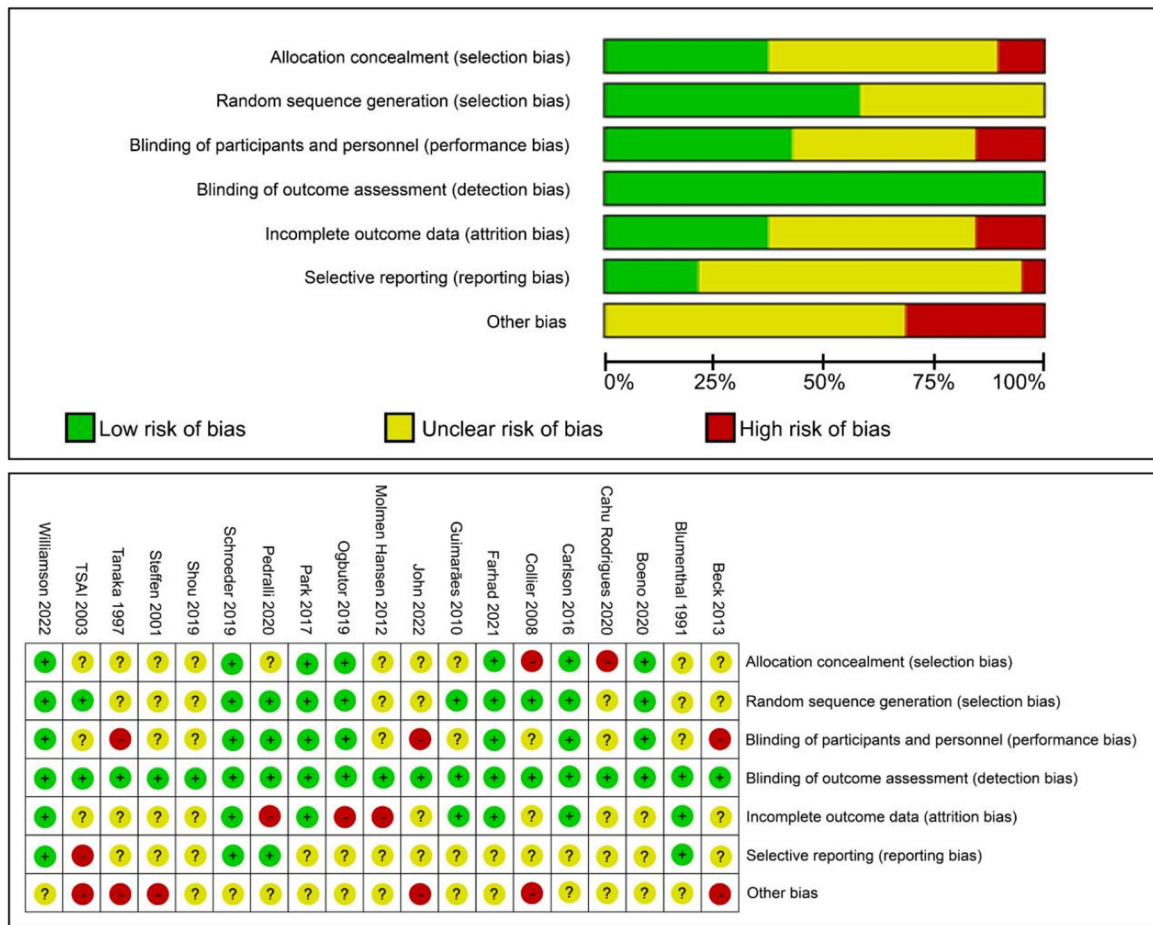


FIGURE 2 | Risk of bias graph.

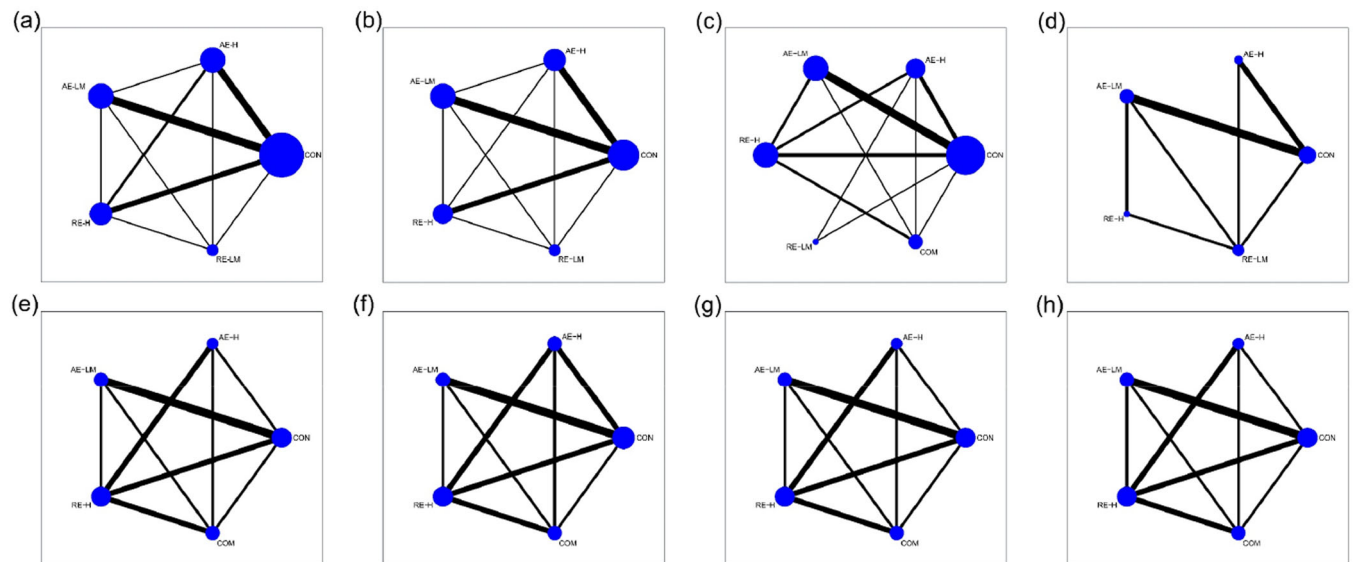


FIGURE 3 | Network plot (a) systolic blood pressure (SBP), (b) diastolic blood pressure (DBP), (c) body mass index (BMI), (d) heart rate (HR), (e) low-density lipoprotein (LDL), (f) high-density lipoprotein (HDL), (g) total cholesterol (TC), and (h) triglyceride (TG).

AE-H (MD = -6.53, 95% CI = -12.51, -0.56), $p < 0.05$). However, there are no significant differences in reducing SBP compared RE-H (MD = -4.95, 95% CI = -11.07, 1.17) and RE-LM (MD = -3.49, 95% CI = -12.36, 5.39) with the control group.

4.4.1.4 | Sucra Probability Ranking. As shown in Figure 6a, the effect of four exercise training and control strategies on a decrease in SBP was ranked probabilistically from high to low as follows: AE-LM (82%) > AE-H (68%) > RE-H (52%) > RE-LM (40%) > CON (7%).

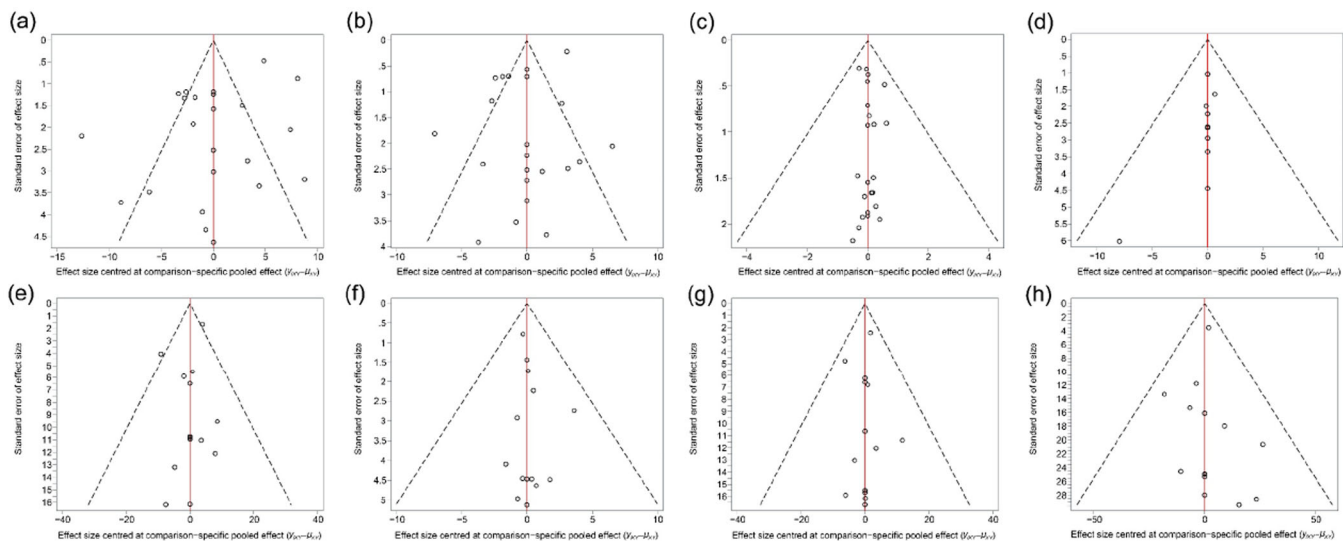


FIGURE 4 | Net funnel: (a) systolic blood pressure (SBP), (b) diastolic blood pressure (DBP), (c) body mass index (BMI), (d) heart rate (HR), (e) low-density lipoprotein (LDL), (f) high-density lipoprotein (HDL), (g) total cholesterol (TC), and (h) triglyceride (TG).

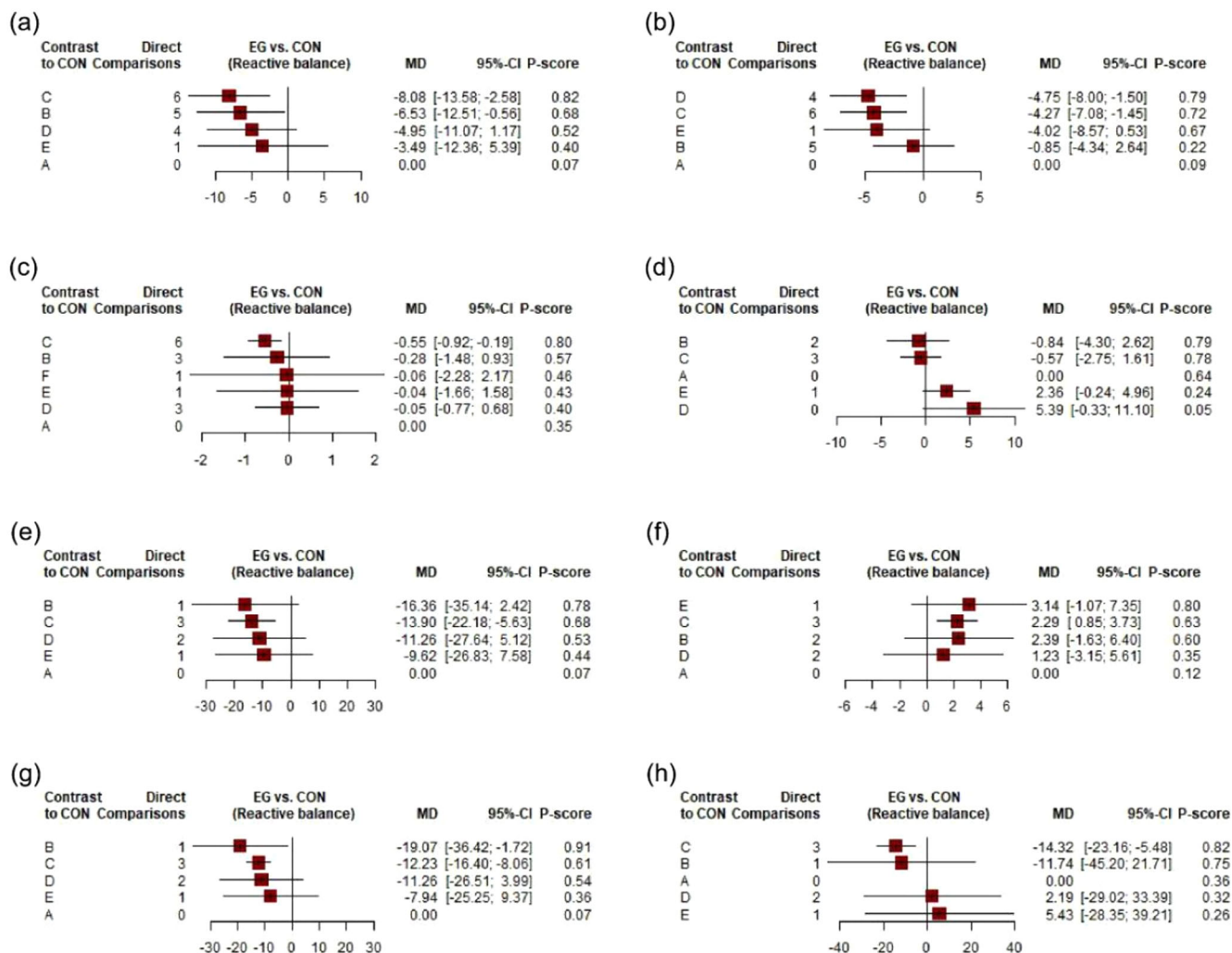


FIGURE 5 | Forest plot: (a) systolic blood pressure (SBP), (b) diastolic blood pressure (DBP), (c) body mass index (BMI), (d) heart rate (HR), (e) low-density lipoprotein (LDL), (f) high-density lipoprotein (HDL), (g) total cholesterol (TC), and (h) triglyceride (TG).

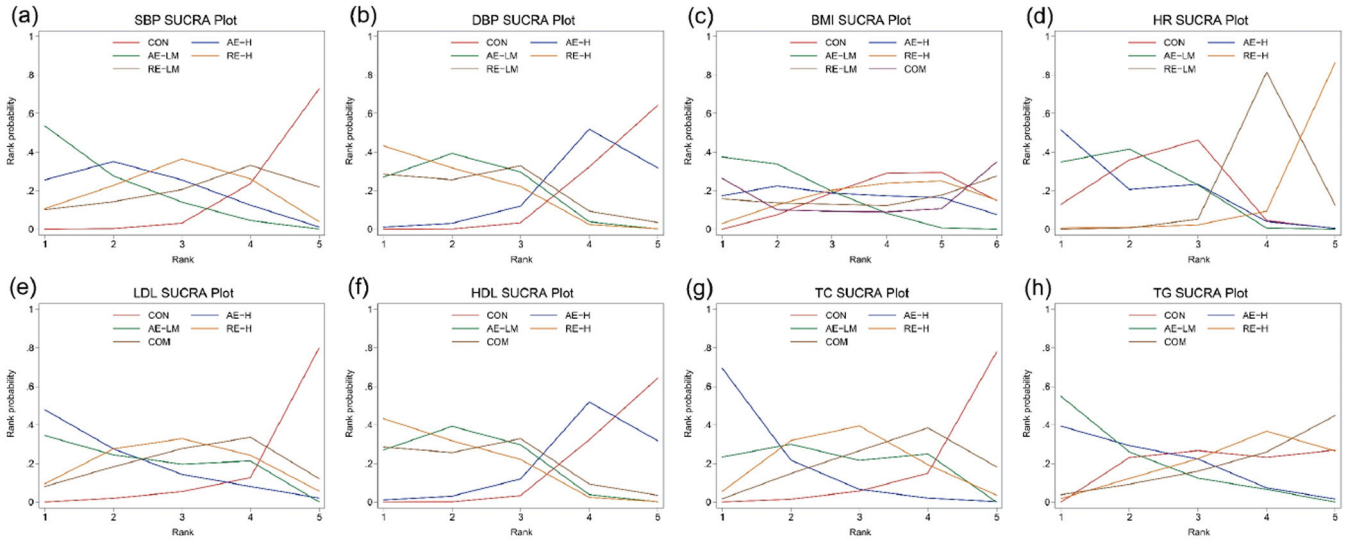


FIGURE 6 | SUCRA plot: (a) systolic blood pressure (SBP), (b) diastolic blood pressure (DBP), (c) body mass index (BMI), (d) heart rate (HR), (e) low-density lipoprotein (LDL), (f) high-density lipoprotein (HDL), (g) total cholesterol (TC), and (h) triglyceride (TG).

4.4.2 | Diastolic Blood Pressure

4.4.2.1 | Evidence Network. Fourteen studies [2, 4, 17, 18, 27–33, 35, 39, 40] involving four exercise training and control strategy reported DBP. The dot size indicates the number of participants in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point intervention. All 10 denote direct comparisons, and there is a closed-loop formation. The network evidence of the DBP is shown in Figure 3b.

4.4.2.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4b).

4.4.2.3 | Network Meta-Analysis. The network relationship of four exercise strategies and control strategy for DBP is shown in Figure 5b. The DBP score was reported in 14 pieces of literature [2, 4, 17, 18, 27–33, 35, 39, 40] and network comparisons yield a total of 10 pairwise comparisons. There were significant differences between the two exercise strategies and the control group in reducing DBP: RE-H (MD = −4.75, 95% CI = −8.00, −1.50), $p < 0.05$), AE-LM (MD = −4.27, 95% CI = −7.08, −1.45, $p < 0.05$). However, there are no significant differences in reducing DBP compared RE-LM (MD = −4.02, 95% CI = −8.57, 0.53) and AE-H (MD = −0.85, 95% CI = −4.34, 2.64) with the control group.

4.4.2.4 | Sucra Probability Ranking. As shown in Figure 6b, the effect of five interventions on reducing DBP was ranked probabilistically from high to low as follows: RE-H (79%) > AE-LM (72%) > RE-LM (67%) > AE-H (22%) > CON (9%).

4.4.3 | Body Mass Index

4.4.3.1 | Evidence Network. Ten studies [4, 27–29, 33–37, 40] involving five exercise training and control strategy reported BMI. The dot size indicates the number of participants

in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point intervention. All 11 denote direct comparisons, and there is no closed loop formation. The network evidence of the BMI is exhibited in Figure 3c.

4.4.3.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4c).

4.4.3.3 | Network Meta-Analysis. The network relationship of five exercise training and control strategy for DBP is shown in Figure 5c. The DBP score was reported in 10 literature [4, 27–29, 33–37, 40] and network comparison yielded a total of 15 pairwise comparisons. There were significant differences between one exercise training (AE-LM) (MD = −0.55, 95% CI = −0.92, −0.19), $p < 0.05$) and control strategy in reducing BMI. However, there are no significant differences in reducing BMI compared AE-H (MD = −0.28, 95% CI = −1.48, 0.93), RE-H (MD = −0.05, 95% CI = −0.77, 0.68), RE-LM (MD = −0.04, 95% CI = −1.66, 1.58), and COM (MD = −0.06, 95% CI = −2.28, 2.17) with the control group.

4.4.3.4 | Sucra Probability Ranking. As shown in Figure 6c, the effect of six interventions on BMI control was ranked problematically from high to low as follows: AE-LM (80%) > AE-H (57%) > COM (46%) > RE-LM (43%) > RE-H (40%) > CON (35%).

4.4.4 | Heart Rate

4.4.4.1 | Evidence Network. Eight studies [27, 28, 31–34, 39, 40] involving four exercise training and control strategy reported heart rate. The dot size indicates the number of participants in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point

intervention. All seven denote direct comparisons, and there is no closed loop formation. The network evidence of the heart rate is exhibited in Figure 3d.

4.4.4.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4d).

4.4.4.3 | Network Meta-Analysis. Eight pieces of literature [27, 28, 31–34, 39, 40] reported heart rate involving four exercise training and control strategy. Network comparison was conducted in five interventions, yielding 10 pairwise comparisons, none of which were statistically significant in affecting heart rate compared AE-H (MD = -0.84, 95% CI = -4.30, 2.62), AE-LM (MD = -0.57, 95% CI = -2.75, 1.61), RE-H (MD = 5.39, 95% CI = -0.33, 11.10), and RE-LM (MD = 2.36, 95% CI = -0.24, 4.96) with the control group.

4.4.4.4 | Sucra Probability Ranking. As shown in Figure 6d, the effect of five interventions on heart rate were ranked problematically from high to low as follows: AE-H (79%) > AE-LM (78%) > CON (64%) > RE-LM (24%) > RE-H (5%).

4.4.5 | Low-Density Lipoprotein

4.4.5.1 | Evidence Network. Five studies [4, 29, 36, 37, 40] involving four exercise training and control strategy reported LDL. The dot size indicates the number of participants in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point intervention. Nine denote direct comparisons, and there is no closed loop formation. The network evidence of the LDL is exhibited in Figure 3e.

4.4.5.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have no publication bias (Figure 4e).

4.4.5.3 | Network Meta-Analysis. The network relationship of four exercise training and control strategy for LDL is shown in Figure 5e. The LDL level was reported in five pieces of literature [4, 29, 36, 37, 40] and network comparison yielded a total of 10 pairwise comparisons. There were significant differences between one exercise training and control strategy in reducing LDL: AE-LM [MD = -13.90, 95% CI (-22.18 to -5.63), $p < 0.05$]. However, there are no significant differences in reducing LDL compared AE-H (MD = -16.36, 95% CI = -35.14, 2.42), RE-H (MD = -11.26, 95% CI = -27.64, 5.12), RE-LM (MD = -9.62, 95% CI = -26.83, 7.58) with the control group.

4.4.5.4 | Sucra Probability Ranking. As shown in Figure 6e, the effect of five interventions on LDL were ranked problematically from high to low as follows: AE-H (78%) > AE-LM (68%) > RE-H (53%) > RE-LM (44%) > CON (7%).

4.4.6 | High-Density Lipoprotein

4.4.6.1 | Evidence Network. Six studies [4, 18, 29, 36, 37, 40] involving four exercise training and control strategy reported HDL. The dot size indicates the number of participants in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point intervention. Nine denote direct comparisons, and there is no closed loop formation. The network evidence of the HDL is exhibited in Figure 3f.

4.4.6.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4f).

4.4.6.3 | Network Meta-Analysis. The network relationship of four exercise training and control strategy for HDL is shown in Figure 5f. The HDL level was reported in six literature [4, 18, 29, 36, 37, 40] and network comparison yield a total of 10 pairwise comparisons. There were significant differences between one exercise training and control strategy in reducing HDL: AE-LM [MD = 2.29, 95% CI (0.85–3.73), $p < 0.05$]. However, there is no significant differences in reducing HDL compared AE-H (MD = -0.28, 95% CI = -1.48, 0.93), RE-H (MD = -0.05, 95% CI = -0.77, 0.68), RE-LM (MD = -0.04, 95% CI = -1.66, 1.58), and COM (MD = -0.06, 95% CI = -2.28, 2.17) with the control group.

4.4.6.4 | Sucra Probability Ranking. As shown in Figure 6f, the effect of five interventions on HDL were ranked problematically from high to low as follows: RE-LM (80%) > AE-LM (63%) > AE-H (60%) > RE-H (35%) > CON (12%).

4.4.7 | Total Cholesterol

4.4.7.1 | Evidence Network. Five studies [4, 29, 36, 37, 40] involving four exercise training and control strategy reported TC. The dot size indicates the number of participants in each intervention, and the line thickness between two nodes represents the number of RCTs using the two-point intervention. All nine denote direct comparisons, and there is no closed loop formation. The network evidence of the TC is exhibited in Figure 3g.

4.4.7.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4g).

4.4.7.3 | Network Meta-Analysis. The network relationship of four exercise training and control strategy for TC is shown in Figure 5g. The TC score was reported in five pieces of literature [4, 29, 36, 37, 40] and network comparisons yield a total of 10 pairwise comparisons. There were significant differences between the two exercise strategies and the control group in reducing TC: AE-H (MD = -19.07, 95% CI = -36.42, -1.72, $p < 0.05$), AE-LM (MD = -12.23, 95% CI = -16.40, -8.06, $p < 0.05$). However, there are no significant differences in reducing TC compared RE-H (MD = -11.26, 95% CI =

−26.51, 3.99) and RE-LM (MD = −7.94, 95% CI = −25.25, 9.37) with the control group.

4.4.7.4 | Sucra Probability Ranking. As shown in Figure 6g, the effect of five interventions on TC were ranked problematically from high to low as follows: AE-H (91%) > AE-LM (61%) > RE-H (54%) > RE-LM (36%) > CON (7%).

4.4.8 | Triglyceride

4.4.8.1 | Evidence Network. Five studies [4, 29, 36, 37, 40] involving four exercise training and control strategy reported TG. The size of the nodes representing the exercise training indicates the sample size, the thickness of lines between nodes indicates the number of studies with comparisons of exercise trainings, four exercise training denote direct comparisons. There is no closed loop formation. The network evidence of TG is shown in Figure 3h.

4.4.8.2 | Publication Bias. The funnel plot of this study showed that most of the scatter points were located on both sides of the vertical line, which demonstrated that they might have a certain degree of publication bias (Figure 4h).

4.4.8.3 | Network Meta-Analysis. The network relationship of four exercise training and control strategy for TG is shown in Figure 5h. The TG score was reported in five pieces of literature [4, 29, 36, 37, 40] and network comparisons yield a total of 10 pairwise comparisons. There were significant differences between one exercise strategy and the control group in reducing TG: AE-LM (MD = −14.01, 95% CI = −20.06, −7.43, $p < 0.05$). However, there is no significant differences in reducing TG compared AE-H (MD = −11.74, 95% CI = −45.20, 21.71), RE-H (MD = 2.19, 95% CI = −29.02, 33.39), and RE-LM (MD = 5.43, 95% CI = −28.35, 39.21) with the control group.

4.4.8.4 | Sucra Probability Ranking. As shown in Figure 6h, the effect of five interventions on TG were ranked problematically from high to low as follows: AE-LM (82%) > AE-H (75%) > CON (36%) > E-H (32%) > RE-LM (26%).

5 | Discussion

5.1 | Main Findings

In this study we found that AE-LM was superior to all exercise strategies and the control group in lowering systolic blood pressure. Compared to the control group, both AE-H and AE-LM were effective in lowering diastolic blood pressure. The results indicated that different exercise patterns significantly influenced cardiovascular risk factors. Specifically, AE-LM notably improved BMI, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides, thereby reducing cardiovascular risk. Importantly, our study found that AE-LM and AE-H were the top two exercise regimens for

managing cholesterol parameters and BMI. Additionally, no intervention had an effect on heart rate.

5.2 | Interpretation

It is acknowledged that aerobic exercise could lower SBP, with many national guidelines recommending it to older people with hypertension and pregnant women who need normalized SBP [42]. Our findings also indicate that different intensities of aerobic exercise contribute to a significant reduction in SBP among young and middle-aged people with prehypertension or hypertension. Especially for AE-LM, our results show the SBP could be lowered by almost 8.08 mmHg, which is similar to the previous meta-analysis that reports AE-LM is superior in reducing SBP in contrast with AE-H [43]. Some studies find AE-LM and AE-H have equal effects on improving SBP in prehypertension people, while others show there are no differences in SBP reduction between AE-LM and AE-H in prehypertension and hypertension population [44, 45]. The effects on SBP may be related to participant selection, such as age, the baseline of blood pressure, and the definition of prehypertension or hypertension.

For improving DBP, RE-H is the best exercise training for young and middle-aged population with prehypertension or hypertension. A meta-analysis of the effect of resistance exercise on hypertension management agrees our findings, which suggests that people with hypertension who choose resistance exercise achieve DBP reduction by 3.2 mmHg [46]. We have similar findings that RE-H significantly reduces DBP by 4.75 mmHg in young and middle-aged populations with prehypertension or hypertension. Pedralli et al. [47] demonstrate a better benefit of DBP control even with RE-LM for the prehypertension and hypertension population. The study by Shaw et al. [48] shows that resistance exercise is an effective way of maintaining DBP among non-hypertensive and hypertensive postmenopausal women. The mechanism for changing DBP with resistance training remains unambiguous, but the effectiveness of resistance exercise on DBP reduction in young and middle-aged populations has been proven in some literature [49, 50]. This could be explained by the fact that the majority of young and middle-aged people were diagnosed with diastolic hypertension, while the SBP of those is at an average level [51].

Aerobic exercise, including AE-H and AE-LM, is the main principle of weight loss in people with hypertension. BMI is the gold standard for identifying average weight, overweight, and obesity by using the equation of weight (kg)/height (m^2) [23]. Obesity is modified as a risk factor for hypertension as massive fat could result in chronic inflammation, which initiates one mechanism for hypertension [52]. Data from Chinese Hypertension Survey show that approximately 277.8 million Chinese adults are abdominal obese, who become potential prehypertensive population [53]. It is worldwide recommended that aerobic exercise could improve blood pressure because aerobic exercise is more related to BMI in hypertension than non-hypertension population [46]. A joint model of BMI and aerobic exercise from G. Hu et al. [54] indicates a decreased risk of hypertension in obese women. Our review suggests that AE-LM significantly affects lower BMI (mean BMI loss ranged from

−0.92 to −0.19) compared with the control strategy. Besides, our network meta-analysis demonstrates that AE-LM ranks as the most effective exercise strategy for BMI reduction from the SUCRA graph.

Our ranking of exercise intervention shows that AE-LM is the most effective intervention for reducing TG, and AE-H is the most effective intervention for improving TC and LDL. Previous published meta-analysis also demonstrates that TC and LDL are significantly decreased after aerobic exercise compared with the control group [55]. A cohort study provides evidence about the longitudinal association between aerobic exercise and reduction in TG from 38% to 57% [56]. Prehypertension and hypertension populations are usually accompanied by metabolic disorders such as hyperlipidemia and obesity. Continuous aerobic exercise could initiate lipoprotein protease activity and activate the skeletal muscle to increase the utilization of fatty acid supply, improving lipid metabolism [57]. Meanwhile, aerobic exercise affects the activity of lecithin-cholesterol acyltransferase, lipoprotein lipase, and hepatic-triglyceride lipase, which participate in the catabolism of lipoprotein [58]. Maintaining cholesterol at an average level may assist hypertension people in preventing damage to the vascular endothelium, reducing the risk of structural changes in the vessels of large arteries that are directly related to cardiovascular disease [59]. Therefore, the best exercise intervention for the prehypertension and hypertension population to control cholesterol may be AE-HL and AE-H.

Our review has several limitations. First, the overall sample size of this study was relatively small, which could have influenced the statistical power of the effect estimates. For example, aerobic exercise was reported in 16 studies, while combined exercise training was only included in 2 studies. Second, the intensity of exercise is considered in the network meta-analysis. However, some studies need to include a description of intensity, which could not be analyzed in our review, leading to heterogeneity among exercise interventions. Third, subgroup analysis could not be conducted due to the variety of lengths and frequency of the blood pressure measurement reference value. Fourth, some studies on ambiguous age criteria of young or middle-aged adults with hypertension or prehypertension participants were excluded, which might be a substantial source of moderate to high risk of bias. In addition, only relevant literature in English was included in our network meta-analysis, which could lead to literature selection bias.

6 | Conclusion

This network meta-analysis synthesizes evidence from previous studies and provides some significant findings about exercise therapy for clinical professionals and researchers. Our study shows that low-to-moderate intensity aerobic exercise and high-intensity resistance exercise are most likely to be the most effective types of exercise for lowering blood pressure. However, considering our meta-analysis's limitations and the insufficient existing literature studies, the results should be interpreted with caution. In the future, more multi-arm randomized controlled trials should be conducted to provide more direct evidence of the relative efficacy of various exercise interventions.

Author Contributions

Lu Tian: conceptualization, methodology, writing – original draft. **Siyu Yang:** methodology, writing – original draft. **Yu Liu:** conceptualization, supervision. **Zongfeng Liao:** data curation, software. **Yulan Hu:** conceptualization. **Jinrui Cui:** methodology, conceptualization. **Xiaobei Guo:** conceptualization, methodology.

Disclosure

Any relevant patents, and so forth are disclosed. Authorship is based on contributions to the research and writing.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

Transparency Statement

The lead authors Yu Liu and Zongfeng Liao affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.