


Effect of Exercise Training on Arterial Stiffness in Overweight or Obese Populations



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ABSTRACT

The purpose was to analyze the effects of exercise training (ET) on arterial stiffness in all-age overweight or obese individuals. Sixty-one trials were included with ET improving flow-mediated dilation (FMD), pulse wave velocity (PWV), and intima-media thickness (IMT). In the subgroup analysis: (i) ET improved FMD in overweight or obese children and adolescents with a large effect size (SMD = 0.83, 95% CI 0.42–1.25). PWV was decreased after ET regardless of age. IMT was decreased by ET in participants younger than 60, (ii) ET improved FMD, PWV, and IMT in participants whose BMI were smaller than 30 kg/m², but ET only improved PWV of participants whose BMI were larger than 30 kg/m². (iii) AE improved FMD, PWV, and IMT. High-intensity interval training (HIIT) decreased IMT. (iv) The increase of FMD only happened when training duration was longer than eight weeks. However, ET decreased PWV when the training duration was no longer than 12 weeks. IMT was decreased when the training duration was longer than eight weeks. ET instigated an improvement in endothelial function and arterial stiffness in overweight or obese populations, but depending on the different characteristics of exercise intervention and participants' demographics.

Introduction

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. In 2016, more than 1.9 billion adults were overweight worldwide, of which over 650 million were obese. Moreover, the prevalence of overweight or obese children and adolescents increased more than four-fold, from 4 to 18% globally. Overweight and obesity are major risk factors for cardiovascular diseases and diabetes [1].

It is well established that obesity significantly increases the progression of atherosclerosis [2]. Endothelial dysfunction has been identified as an early event that causes the development of atherosclerosis, followed by gradual remodeling of the arterial wall [3]. Therefore, the endothelial function, stiffness, and elasticity of arteries can be used as important indicators to evaluate the progress of atherosclerosis. Endothelial function can be quantified by flow-mediated dilation (FMD). Vascular intima-media thickness (IMT)

can be measured as a sign of vascular remodeling. It is considered as an intermediate phenotype of atherosclerosis that is suitable in large-scale population studies [4]. The assessment of pulse wave velocity (PWV) is recommended as the “gold standard” measurement of aortic stiffness. It is a simple, non-invasive and reproducible method. Sufficient clinical evidence supports the predictive value of aortic stiffness for cardiovascular diseases [5].

Exercise training (ET) can help with weight loss. Its effect on decreasing arterial stiffness also attracts much attention. However, the ET's influences on the vascular structure and function for overweight or obese patients are still not determined. The meta-analysis of Son et al. [6] reveals that exercise intervention programs significantly improve FMD in overweight and obese adults, and their effect may rely on the different characteristics of exercise interventions and participants' demographics. It was reported that arterial stiffness did not lessen in middle-aged or older obese populations in response to aerobic training [7]. Previous meta-analysis studies have investigated the impact of exercises on FMD and IMT in obese pediatric populations [8, 9], but not on all-age stage populations. It is not clear what kind of training protocol is more effective to improve arterial stiffness. Moreover, training modality would be a key factor that induced different results. It seemed that resistance training would not be an effective way to improve arterial stiffness [10]. It is also unclear that whether a training duration threshold exists at which an overweight or obese patient's vascular function can be improved.

Therefore, this systematic review and meta-analysis aimed to summarize the effect of ET on arterial stiffness, assessed by FMD, PWV, and IMT, in all-age overweight or obese individuals.

Materials and Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) as the protocol for designing this review [11].

Search strategy and selection criteria

A systematic search of the literature was conducted using the bibliographic databases PubMed/Medline, Embase, and Web of Science from their inception to August 5, 2021. The search terms used were “exercise”, “training”, “physical activity”, “obesity”, “overweight”, “excess weight”, “BMI”, “body mass index”, “vascular compliance”, “vascular stiffness”, “arteriosclerosis”, “flow mediated dilation”, “FMD”, “homa”, “pulse wave velocity”, “PWV”, “intima media thickness” and “IMT”. We looked for research with human participants and restricted the language to English. Reference lists of the included studies were also searched as an additional check for further studies that could be included in the review.

Inclusion criteria

Studies were selected for review if they met the following criteria: (1) they were randomized controlled trials (RCTs) or non-RCTs; (2) participants were overweight or obese but had no other complications; (3) participants were intervened for a period of longer than two weeks' ET with a clear protocol; (4) FMD or PWV or IMT were measured to assess vascular function; and (5) results were demon-

strated with a mean and standard deviation (SD) or standard error of the mean (SEM), both before and after ET.

Study selection and data extraction

Two reviewers extracted the data independently using a standardized Excel template. Disagreements were resolved through discussion between the two reviewers, with a third reviewer stepping in if the first two reviewers could not agree. Extracted data included the author's last name, year of publication, participants' characteristics (age, sex, weight, and BMI), criteria of overweight or obesity, exercise prescriptions (intensity, frequency, type, session time, and duration), and outcomes (body composition, blood pressure, glycemia, blood lipids, exercise capacity, and vascular function outcomes). If any included study did not provide relevant information, the corresponding author was contacted and asked to provide the data by email.

Study quality and reporting

Two reviewers independently assessed the identified articles using the ‘Tool for assessment of study quality and reporting in exercise’ (TESTET) scale, which consists of 5 available points for study quality and 10 for study reporting [12]. Higher scores represent better study quality and reporting. Disagreements in scores between the two reviewers were resolved by discussion with a third party.

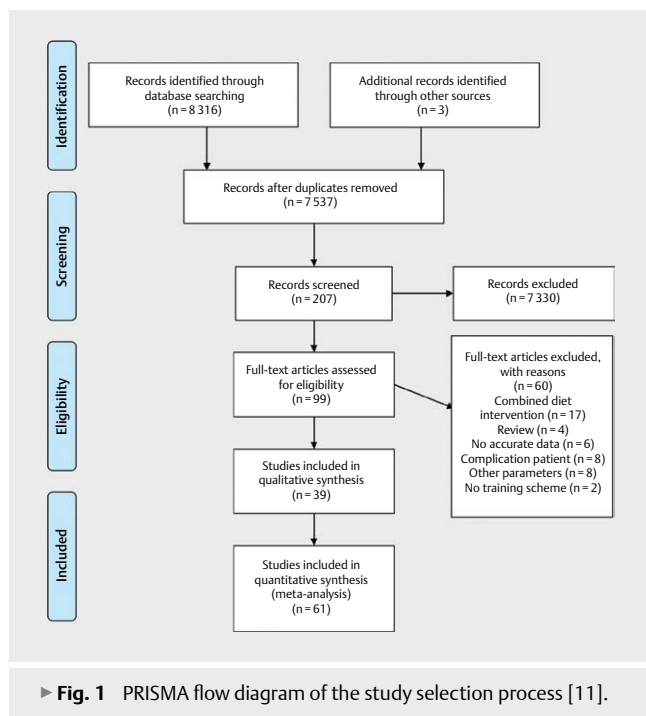
Data analysis

Analyses were carried out using STATA 16.0 to measure the between-trial standardized mean difference (SMD) and 95% confidence intervals (95% CI). The effect size (ES) of SMD was classified as large (>0.8), moderate (0.5–0.8), small (0.2–0.5), or trivial (<0.2). Studies were eliminated if they indicated potential bias. Heterogeneity for the between-study association was evaluated using the I^2 statistic. Regarding statistical significance for I^2 , values of 25 to \leq 50% were considered low heterogeneity, 50 to \leq 75% moderate heterogeneity, and >75% high heterogeneity. Testing for an overall effect (Z score) was significant when $p < 0.05$. The randomized effect model was used when heterogeneity was moderate or high, and the fixed-effect model was used when heterogeneity was low. Publication bias was assessed by examining the asymmetry of the funnel plots using the Egger's test. A sensitivity analysis was conducted to test the robustness of the overall SMD by extracting results for the first time point available after the intervention ended. To examine possible variables that may have affected training effectiveness, subgroup analyses were also performed based on participants' age, health status, training intensity, and duration. We also analyzed the effect of ET on BMI if it was reported in the studies included.

Results

Study selection

The literature search strategy is outlined in ► **Fig. 1**. Our initial database search identified 8,316 potentially eligible articles, with a further three identified through manual search. Following the screening of titles and abstracts, 7,537 articles were excluded, based on the inclusion criteria. The remaining 99 papers under-



went full-text screening, after which 60 further studies were excluded. The final analysis included a total number of 61 trials in 39 studies.

Characteristics of included studies

The included studies evaluated a total of 1,245 participants of both genders. Participants' mean age ranged from 8.9 years to 73.5 years. Twenty-three trials focused on children and adolescents, and 38 trials included adult participants. Overweight or obesity was defined by BMI or percentile or waist circumference or the percentage of body fat. Aerobic exercise (AE), resistance training (RT), high-intensity interval training (HIIT), and combined training protocols were conducted. The training duration ranged from 6 to 48 weeks. Details can be seen in ► **Table 1**.

Study quality and reporting

► **Table 3** includes an overview of the scores assessed with TESTET. Median values regarding criteria matching were three (1–3) for study quality and eight (6–9) for study reporting. The overall median score is 11 out of 15 possible points. The lowest scoring study scored 7, with the highest scoring 12. Studies scored highly for eligibility criteria specified, intention-to-treat analysis, between-group statistical comparisons of the primary outcome, measures and variability, intensity control, and report of ET parameters. In contrast, studies scored poorly for the specification of the randomization procedure as well as blinding of participants and assessors.

The effect of exercise on FMD

Comparisons in 12 trials included data for conducting a meta-analysis of FMD. The pooled SMD estimate showed high heterogeneity ($I^2 = 70.85\%$, $p = 0.00$). Accordingly, randomized-effect models were applied for further meta-analysis. Results represented that the FMD

was increased by ET with a moderate ES (SMD = 0.67, 95% CI = 0.32–1.02, ► **Fig 2a**). The funnel plot was symmetrical (► **Fig. 2b**), indicating little publication bias risk detected for the effect of ET on FMD.

The effect of exercise on PWV

Comparisons in 23 trials included data for conducting a meta-analysis of PWV. The pooled SMD estimate showed low heterogeneity ($I^2 = 5.41\%$, $p = 0.37$). Accordingly, fixed-effect models were applied for further meta-analysis. Results represented that the PWV was significantly decreased by ET with a small ES (SMD = -0.19 , 95% CI = -0.29 to -0.1 , ► **Fig. 3a**). The funnel plot was symmetrical (► **Fig. 3b**). This means there was little publication bias risk detected for the effect of ET on PWV.

The effect of exercise on IMT

Comparisons in 12 trials included data for conducting a meta-analysis of IMT. The pooled SMD estimate showed low heterogeneity ($I^2 = 45.79\%$, $p = 0.02$). Accordingly, fixed-effect models were applied for further meta-analysis. Results represented that the IMT was significantly decreased by ET with a small ES (SMD = -0.26 , 95% CI = -0.43 to -0.13 , ► **Fig. 4a**). The funnel plot was symmetrical (► **Fig. 4b**). This means there was little publication bias risk detected for the effect of ET on IMT.

Subgroup analysis

Age

We conducted a subgroup analysis according to participants' age (adolescent, adult, and aged) to determine whether endothelial function and arterial stiffness response to ET differed according to this factor (See ► **Table 2**). ET improved FMD in children and adolescents who were overweight or obese with a large ES (SMD = 0.83, 95% CI 0.42 to 1.25, ► **Table 2**). In contrast, the FMD in adult participants ranged from 18 to 60 did not change after ET (SMD = 0.38, 95% CI -0.23 to 0.99; ► **Table 2**). PWV was decreased after ET in each subgroup regardless of age. IMT decreased after ET in participants younger than 60, but the ES in the aged subgroup was not significant (SMD = -0.18 , 95% CI -0.59 to 0.22; ► **Table 2**).

BMI

The level of obesity would be a potential factor that induced the training effect. We compared the effect according to participants' BMI ($< 30 \text{ kg/m}^2$ and $> 30 \text{ kg/m}^2$). BMI in both subgroups was decreased by ET (BMI $< 30 \text{ kg/m}^2$ MD = -0.55 kg/m^2 95% CI -0.87 to -0.24 ; BMI $> 30 \text{ kg/m}^2$ MD = -1.04 kg/m^2 95% CI -1.59 to -0.49), and the mean difference is larger in participants whose BMI was less than 30 kg/m^2 (see Supplementary figure ► **Fig. 5**). ET increased FMD and decreased PWV and IMT in participants whose BMI was less than 30 kg/m^2 (see ► **Table 2**). The PWV of participants whose BMI was larger than 30 kg/m^2 was decreased after ET, but the FMD and IMT did no change after ET (see ► **Table 2**).

Training modality

According to the scheme of ET, we divided the training modality into AE, RT, HIIT, and combined training subgroups. AE training can improve FMD, PWV, and IMT (see ► **Table 2**). IMT was decreased

► **Table 1** Characteristics of the included research studies.

Study	Country	Age	Sex (male/ female)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/ week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Watts 2004a [33]	Australia	8.9±0.6	8/6	29.9±1.3	BMI>30 kg/m ²	AE	Dodge and tag, jogging, soccer, and other active recreational	60min	HR: 140–180	3	8	BW ↔, BMI ↔, WC ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, HbA1c ↓, SBP ↔, DBP ↔	NM	Brachial FMD ↑
Kelly 2004 [34]	US	11.0±0.63	5/5	30.4±1.3	BMI>85th percentile	AE	Cycling	30–50min	50–80% VO _{2max}	4	8	BW ↔, BMI ↔, WC ↔, BF% ↔	TG ↔, TC ↔, HDL ↑, LDL ↔, FG ↔, SBP ↔, DBP ↔	VO _{2max} ↑	Brachial FMD ↔
Watts 2004b [35]	Australia	14.3±1.5	9/10	34.4±0.8	BMI>30 kg/m ²	Combine	Cycle ergometer+RT	60min	AE:65–85% HR; RT:55–75% 1RM	3	8	BW ↔, BMI ↔, WC ↔, BF% ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, HbA1c ↔, MBP ↔	Muscle strength ↑, exercise capacity ↑	Brachial FMD ↑
Olson 2006 [36]	US	38±1	0/15	27.5±0.9	BMI>25 kg/m ²	RT	Quadriceps, hamstrings, gluteals, pectorals, latissimus dorsi, rhomboids, deltoids, biceps, and triceps	NM	8RM–6RM	At least 2	48	BW ↔, BMI ↔, WC ↔, BF% ↔, LBM ↑	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↔, DBP ↔, MBP ↔, HbA1c ↔, HOMA-IR ↔	1RM ↑	Brachial FMD ↑, Carotid IMT ↓
Meyer 2006 [37]	Germany	13.7±2.1	17/16	29.8±5.93	BMI>97th percentile for the German pediatric population	AE	Swimming, sports games, walking	60–90min	NM	3	24	BMI ↓, BF% ↔, Waist/hip ratio ↓	TG ↓, TC ↔, HDL ↔, LDL ↓, SBP ↓, HbA1c ↓, HOMA-IR ↓	Wmax ↑	Radial FMD ↑, Radial IMT ↓
Farpour-Lambert 2009 [38]	Switzerland	9.1±1.4	9/13	25.4±4.6	BMI>97th percentile	Combine	Fast walking, running, ball games, or swimming+RT	60min	55–65% VO _{2max}	3	12	BW ↑, BMI ↔, BF% ↔, LBM ↔	TG ↔, TC ↓, HDL ↔, LDL ↓, SBP ↓, DBP ↔, FG ↑, Insulin ↔, HOMA-IR ↔	VO _{2max} ↑	Carotid FMD ↔, Carotid IMT ↔
Murphy 2009 [39]	US	7–12	NM	27.9±4.8	BMI>85th percentile	AE	Dance Dance Revolution	10–30min	NM	5	12	BW ↑, BMI ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↔, DBP ↔, HOMA-IR ↔	VO _{2max} ↑	Brachial FMD ↑

► Table 1 Continued.

Study	Country	Age	Sex (male/ female)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Lee 2010 [40]	South Korea	12–14	NM	26.12 ± 2.44	BMI > 95th percentile	Combine	AE + RT	60 min	70–80% RM	3	10	BMI ↔, WC ↓	TG ↔, TC ↔, HDL ↑, LDL ↓, MBP ↔	1-mile running ↑, physical strength ↑	Brachial Left baPWV ↔, Right baPWV ↔
		12–14	NM	26.34 ± 2.25	BMI > 95th percentile	AE	Soccer, basketball, football, baseball, hockey, badminton, heartthrobs, rope skipping, and mountain	60 min	60–80% VO _{2max}	3	10	BMI ↔, WC ↓	TG ↔, TC ↔, HDL ↑, LDL ↓, MBP ↔	1-mile running ↑, physical strength ↑	Brachial Left baPWV ↔, Right baPWV ↔
Kim 2011 [41]	South Korea	17.63 ± 0.49	18/0	28.60 ± 3.41	BMI ≥ 25 kg/m ²	AE	running, stretching, jumping rope, badminton, basketball, and aerobic dance	50 min	1500–2500 kcal/wk	5	12	BW ↓, BMI ↓, WC ↓, BF ↓, BF% ↓	TG ↔, TC ↓, HDL ↑, LDL ↓, SBP ↓, DBP ↔, FG ↔, Insulin ↓, HOMA-IR ↓	VO _{2max} ↑	Carotid IMT ↔
Vinet 2011 [42]	France	51.3 ± 3.2	10/0	33.2 ± 1.0	30 kg/m ² < BMI < 40 kg/m ²	AE	Walking or cycling	45 min	Maximum lipid-oxidation point HR ± 5 b.p.m	3	8	BW ↔, BMI ↔, LBM ↔, BF% ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↔, DBP ↔, Insulin ↔, HOMA-IR ↔	VO _{2max} ↑	Brachial FMD ↑, Carotid IMT ↓
Yang 2011 [43]	South Korea	45.3 ± 9.5	0/40	27.6 ± 2.4	BMI ≥ 25 kg/m ²	Combine	Treadmill walking/ running and cycling	45 min aerobic + 20 min RT	60–75% HRmax	5	12	BW ↔, BMI ↓, WC ↓	TG ↓, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↓, DBP ↓, HOMA-IR ↔	NM	baPWV ↓
Figueroa 2012 [44]	US	22.4 ± 1.8	0/10	29.9 ± 0.8	BMI ≥ 25 kg/m ²	AE	Whole-body vibration training	NM	5 and 10% of body weight	3	6	BW ↔, BF ↔	SBP ↓, DBP ↔	leg strength ↑	baPWV ↓
Park 2012 [45]	South Korea	12.1 ± 0.1	7/8	24.4 ± 0.4	BMI ≥ 85th percentile	Combine	Walking, running + RT	80 min	AE: 60–70% HRR; RT: 60% 1RM	3	12	BW ↔, BMI ↔, WC ↓	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↔, DBP ↔	VO _{2max} ↑	Carotid IMT ↓

► Table 1 Continued.

Study	Country	Age	Sex (male/fe-male)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Figueroa 2013 [46]	US	54 ± 1	0/14	32.6 ± 1.0	BMI ≥ 25 kg/m ²	RT	Leg press, leg extension, leg flexion, and calf raise	NM	20 RM	3	12	BW ↔, BF ↔	SBP ↓, DBP ↔, MBP ↓, Insulin ↔		Aortic PWV ↔, baPWV ↔
Wong 2014 [47]	US	57 ± 1	0/14	34.2 ± 1.2	BMI ≥ 30 kg/m ²	AE	Stretching training	50 min, 38 stretches	RPE > 18	3	8	BW ↔, BMI ↔	SBP ↓, DBP ↓	Sit and reach ↑	Aortic PWV ↔, faPWV ↔, baPWV ↔
Kurose 2014 [48]	Japan	46.4 ± 14.8	11/32	35.5 ± 5.0	BMI ≥ 30 kg/m ²	Combine	Cycle ergometer or treadmill + RT	30 min	Anaerobic threshold	3	24	BW ↓, BF % ↓	SBP ↔, DBP ↔, HOMA-IR ↔	VO _{2max} ↑	baPWV ↔
Kearney 2014 [49]	North-ern Ireland	45 ± 6.2	11/41	29.19 ± 4.32	BMI ≥ 25 kg/m ²	AE	Brisk walking	30 min	Slightly out of breath	5	24	BMI ↔, Waist/hip ratio ↔, BF % ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, SBP ↔, DBP ↔	VO _{2max} ↑	Carotid radial PWV ↓
Franklin 2015 [50]	US	30.3 ± 5.4	0/10	34.2 ± 3.0	30 kg/m ² < BMI < 40 kg/m ²	RT	Circuit-based resistance training	NM	80–90% 10 RM	2	8	BW ↔, BMI ↔, WC ↔, BF % ↔	TC ↔, HDL ↔, LDL ↔, SBP ↔, DBP ↔, FG ↔	Aerobic capacity ↔	Brachial FMD ↓
Horner 2015 [51]	Canada	14.7 ± 1.8	15/15	34.4 ± 5.2	BMI ≥ 95th percentile	AE	treadmill, elliptical or stationary bike	60 min	60–75% VO _{2max}	3	12	NM	NM	NM	cPWV ↔, Carotid IMT ↔
		14.6 ± 1.9	14/13	35.7 ± 3.3	BMI ≥ 95th percentile	RT	10 Whole-body exercises	60 min	NM	3	12	NM	NM	NM	cPWV ↔, Carotid IMT ↔
Sawyer 2016 [52]	US	35.1 ± 8.1	9 (NM)	36.0 ± 5.0	BMI ≥ 30 kg/m ²	HIIT	Cycle ergometers	20 min	90–95% HRmax	3	8	BW ↔, BMI ↔, WC ↓, BF % ↓, BF ↔, LBM ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FC ↔, Insulin ↔, HOMA-IR ↔	VO _{2max} ↑	Brachial FMD ↓
		35.1 ± 8.1	9 (NM)	36.0 ± 5.0	BMI ≥ 30 kg/m ²	AE	Cycle ergometers	30 min	70–75% HRmax	3	8	BW ↔, BMI ↔, WC ↓, BF % ↓, BF ↔, LBM ↔	TG ↔, TC ↔, HDL ↔, LDL ↔, FC ↓, Insulin ↔, HOMA-IR ↔	VO _{2max} ↑	Brachial FMD ↑

▶ Table 1 Continued.

Study	Country	Age	Sex (male/ female)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Jefferson 2016 [53]	US	68 ± 3	8/8	31.1 ± 2.7	27 kg/m ² < BMI < 35 kg/m ²	RT	Seated leg curl, leg press, leg extension, seated calf raises, triceps press, biceps curl, incline press, and compound row	10 rep × 3sets	70% 1RM	3	20	BW ↔, BMI ↔, WC ↔, Waist-to-hip ratio ↔, BF ↔, BF ↔, LBM ↔	SBP ↔, DBP ↔	knee strength ↑	baPWV ↔
Robinson 2016 [54]	US	34 ± 8	3/7	32 ± 5	BMI: 25–40 kg/m ²	AE	Treadmill	30–45 min	75% HRmax	3	8	BW ↓, BMI ↓, WC ↓, BF ↓	TG ↔, TC ↔, HDL ↔, LDL ↔, FG ↔, SBP ↔, DBP ↓	VO _{2max} ↑	Brachial FMD ↑
Hunter 2016 [55]	US	43 ± 12	4/18	32.6 ± 4.3	BMI ≥ 25 kg/m ²	AE	Bikram yoga	90 min	NM	3	8	BF % ↓, WC ↔	TG ↔, TC ↓, HDL ↔, LDL ↔, SBP ↓, DBP ↓	grip strength ↑	baPWV ↓
Park 2017a [56]	South Korea	73.5 ± 7.1	0/25	27 ± 1.4	BMI ≥ 25 kg/m ²	Combine	Elastic exercise + walking	50–80 min	RPE 13–17	5	24	BF % ↓, WC ↔	TG ↔, TC ↓, HDL ↔, LDL ↔, SBP ↓, DBP ↓	grip strength ↑	Carotid IMT ↓
Park 2017b [57]	South Korea	70.4 ± 4.5	0/21	25.8 ± 1.6	Body fat mass > 32%	Combine	Walking + chest press, seated row, shoulder press, biceps curl, triceps extension, trunk extension, abdominal crunch, squats, leg press, calf raise	40–80 min	Moderate intensity (5–6 scale) on a scale of 0–10	5	24	BMI ↔, BF % ↓, WC ↓, LBM ↑	SBP ↓, DBP ↔	grip strength ↑, VO _{2max} ↑	Carotid IMT ↓
Alvarez-Alvarado 2017 [58]	US	20 ± 1	0/25	30.7 ± 0.7	BMI: 27–40 kg/m ²	AE	Whole-body vibration training	11–30 min	Frequency: 30 to 35 Hz; amplitude: low–high	3	6	BW ↔, BMI ↔, WC ↔, BF % ↔	SBP ↓, DBP ↓	NM	baPWV ↓, cPWV ↓, faPWV ↓

► Table 1 Continued.

Study	Country	Age	Sex (male/fe-male)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Chuensiri 2018 [59]	Thailand	11.0±0.3	11/0	26.5±0.9	BMI> 2 standard deviation above the growth reference data for boys	HIIT	Cycling	24 min	90% Peak power	3	12	BW ↔, BMI ↔, WC ↔, Waist/hip ratio ↔, BF% ↔, LBM ↔	TG ↓, TC ↓, HDL ↔, LDL ↓, SBP ↔, DBP ↔, MBP ↔	Muscle strength ↑, VO _{2max} ↑	Brachial FMD ↑, baPWV ↓, Carotid IMT ↓
Bharath 2018 [60]	US	14.6±1	0/20	30±2.2	BMI> 2 standard deviation above the growth reference data for boys	Combine	AE + RT	60 min	40–70% HRR	5	12	BW ↓, BMI ↓, WC ↓, BF% ↓, LBM ↑	SBP ↔, DBP ↔, FG ↓, Insulin ↓, HOMA-IR ↓	VO _{2max} ↑	Brachial FMD ↑, baPWV ↓, Carotid IMT ↓
Fernandez-del-Valle 2018 [61]	US	22.69±3.35	0/6	34.19±3.03	30 kg/m ² ≤ BMI ≤ 39.99 kg/m ²	RT	Circuit of seven exercises in the following order: LP, row, back squat, weighted crunches, deadlift, BP, and squat jumps with weights.	50 min	70–75% 1RM, 70–85% HR max	3	3	BW ↔, BMI ↔, Waist/hip ratio ↔, BF% ↔, LBM ↓	SBP ↔, DBP ↔	Strength ↑, cardiorespiratory fitness ↑	Aortic PWV ↔
Wong 2018 [62]	US	15.2±1.2	0/15	30.1±2.2	BMI> 95th percentile for age and sex	Combine	resistant band exercises + treadmill walking	60 min	40–70% HRR	3	12	BW ↓, BMI ↓, WC ↓, BF% ↓, LBM ↑	SBP ↔, DBP ↔, FG ↓, Insulin ↓, HOMA-IR ↓	NM	baPWV ↓
Park 2020a [63]	South Korea	69.1±0.9	10/0	26.2±0.5	BMI> 25 kg/m ²	Combine	Elastic-band resistance training + treadmill walking	90–120 min	60–70% of 1 RM(RT), 60–70% HRmax (AE)	3	12	BW ↓, BMI ↓, BF ↔, BF% ↓	TG ↔, TC ↔, HDL ↔, LDL ↓, FG ↔, SBP ↓, DBP ↔, MBP ↓	Grip strength ↑, VO _{2max} ↑	baPWV ↓
Park 2020b [64]	South Korea	45±3	10/0	27.9±0.9	BMI> 25 kg/m ²	AE	Walking and/ or light jogging	40–60 min	60–85% HRmax	3	12	BW ↓, BMI ↓, BF% ↓	SBP ↔, DBP ↔	VO _{2max} ↑	baPWV ↓

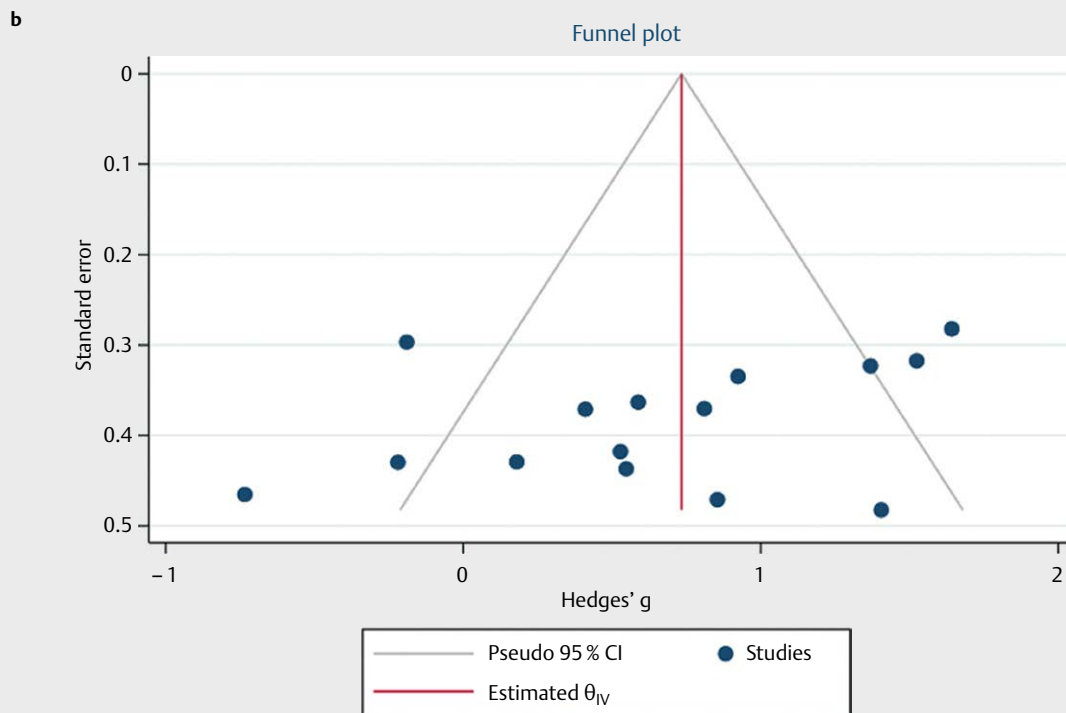
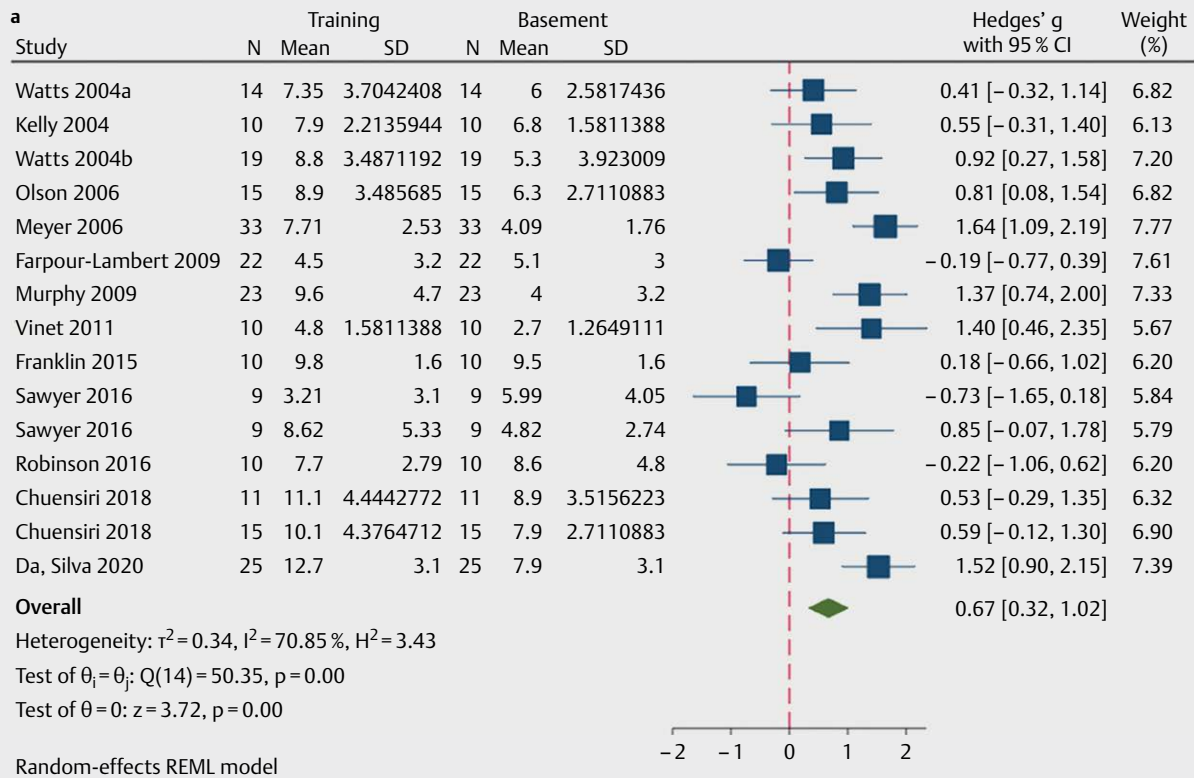
▶ Table 1 Continued.

Study	Country	Age	Sex (male/ female)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/ week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
		52 ± 3	11/0	27.5 ± 0.6	BMI > 25 kg/m ²	AE	Walking and/ or light jogging	40–60 min	60–85%HR-max	3	12	BW ↓, BMI ↓, BF% ↔	SBP ↔, DBP ↔	VO _{2max} ↑	baPWV ↔
Da, Silva 2020 [65]	Brazil	15.1 ± 1.0	25 (NM)	28.2 ± 3.4	NM	HIIT	Running sprints	45 min	NM	3	12	BW ↔, BF% ↔, WC ↓	TG ↑, TC ↔, HDL ↔, LDL ↔, FG ↔, HbA1c ↔	Endurance capacity ↑	Brachial FMD ↑
Inoue 2020 [66]	Japan	66.5 ± 2.1	5/10	25.9	BF% ≥ 25.0% for men and ≥ 35.0% for women	AE	Cycle ergometer	45 min	60–70% VO _{2max}	3	8	BW ↔, BF% ↓	TG ↔, TC ↔, HDL ↔, SBP ↔, DBP ↔	VO _{2max} ↑	cfPWV ↓
Lee 2020 [67]	South Korea	14.4 ± 1.6	13/25	> 30	BMI > 85th percentile	AE	Brisk walking or light jogging	60 min	~50–65% VO _{2max}	3	24	BW ↔, BF ↓, SM ↔	TG ↔, TC ↓, HDL ↔, LDL ↔, SBP ↔, DBP ↔	NM	cfPWV ↔, Carotid IMT ↔
		14.4 ± 1.6	15/25	> 30	BMI > 85th percentile	RT	Eight whole-body resistance exercises	12–15 reps × 2 sets	~60% 1RM	3	24	BW ↓, BF ↓, SM ↑	TG ↓, TC ↔, HDL ↔, LDL ↔, SBP ↔, DBP ↔	NM	cfPWV ↔, Carotid IMT ↔
		14.5 ± 1.7	14/26	> 30	BMI > 85th percentile	Combine	AE + RT	30 min treadmill or elliptical + 1 set eight whole-body resistance exercises	AE:50–65% VO _{2max} RT:60% 1RM	3	24	BW ↔, BF ↓, SM ↑	TG ↔, TC ↔, HDL ↔, LDL ↔, SBP ↔, DBP ↔	NM	cfPWV ↔, Carotid IMT ↔
de Oliveira 2020 [68]	Brazil	29.4 ± 4.6	0/11	34.1 ± 3.6	30 kg/m ² ≤ BMI ≤ 39.99 kg/m ²	HIIT	Running track	16 min	85–95% HRmax	NM	8	NM	SBP ↓, DBP ↔, MBP ↓	NM	cfPWV ↓
		27.0 ± 5.0	0/14	35.7 ± 2.4	30 kg/m ² ≤ BMI ≤ 39.99 kg/m ²	AE	Running track	41 min	65–75% HRmax	NM	8	NM	SBP ↔, DBP ↓, MBP ↓	NM	cfPWV ↓
Wong 2020 [69]	US	22 ± 1	0/14	34.3 ± 0.8	30 kg/m ² ≤ BMI ≤ 39.99 kg/m ²	AE	Mat Pilates training	60 min	NM	3	12	BW ↔, BMI ↔, BF% ↓, BF ↓, LBM ↔	SBP ↓, DBP ↓	NM	baPWV ↓
Clark 2020 [70]	Australia	30 ± 6	16/0	29.0 ± 3.1	25 kg/m ² ≤ BMI ≤ 35 kg/m ²	HIIT	Cycle ergometers	24 min	~90% HRmax; RPE ~ 15	3	6	NM	SBP ↔, DBP ↓, MBP ↓	NM	cfPWV ↔
		26 ± 8	12/0	28.2 ± 2.5	25 kg/m ² ≤ BMI ≤ 35 kg/m ²	AE	Cycle ergometers	30 min	65–75% HRmax, RPE 11	3	6	NM	SBP ↔, DBP ↓, MBP ↓	NM	cfPWV ↔

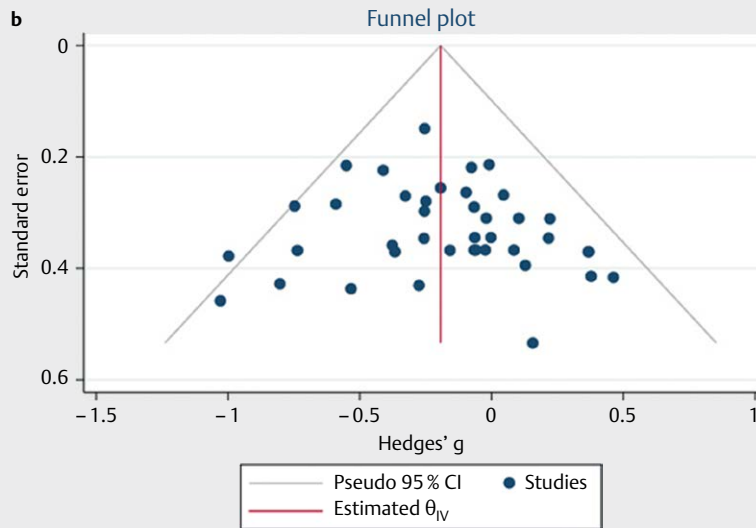
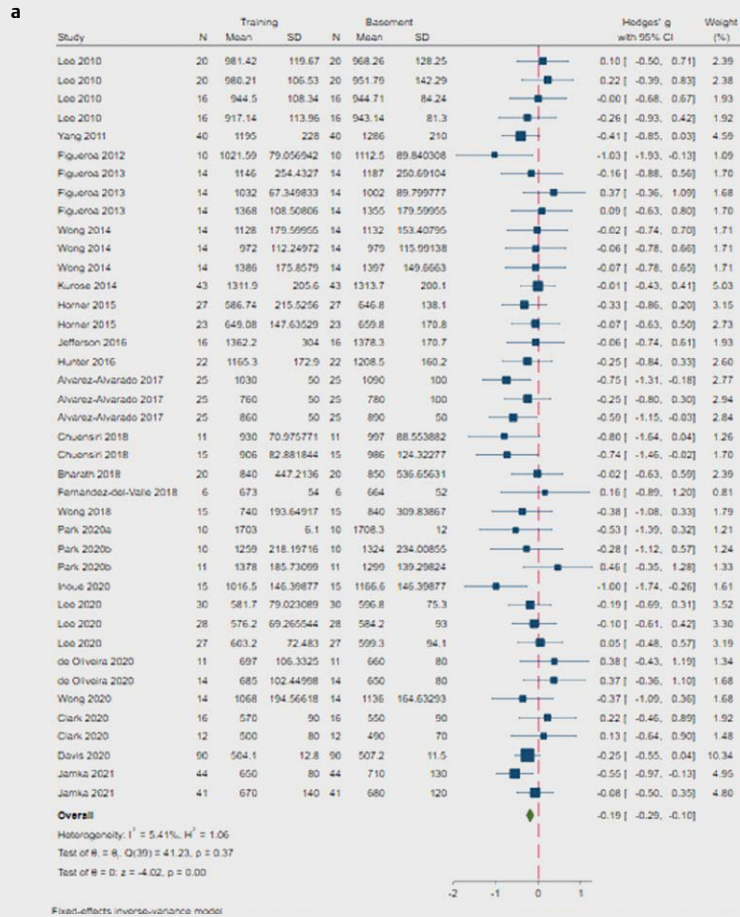
► **Table 1** Continued.

Study	Country	Age	Sex (male/fe-male)	BMI (kg/m ²)	Obesity criteria	Training modality	Training scheme	Session time	Intensity	Frequency (times/week)	Duration (weeks)	Body composition	Blood	Exercise capacity	Vascular function
Davis 2020 [71]	US	9.6 ± 0.7	30/60	25.9 ± 4.6	BMI ≥ 85th percentile	AE	Tag, jump rope	40 min	HR > 140	NM	32	BMI ↑, WC ↑, BF % ↓	TG ↔, TC ↔, HDL ↑, LDL ↓, FG ↔, SBP ↔, DBP ↔, Insulin ↔, HOMA-IR ↔	VO _{2max} ↑	cfPWV ↔
Farahati 2020 [72]	Iran	42.80 ± 2.69	0/10	29.20 ± 2.28	BMI > 27 kg/m ²	HIIT	treadmill walking or running	16 min	85–95% HRmax	3	12	NM	TG ↓, TC ↓, LDL ↓	NM	Carotid IMT ↔
Jamka 2021 [73]	Poland	43.90 ± 3.80	0/11	30.79 ± 2.79	BMI > 27 kg/m ²	AE	Treadmill walking or running	47 min	60–70% HRmax	3	12	NM	TG ↓, TC ↓, LDL ↔	NM	Carotid IMT ↔
		55 ± 7	0/44	35.87 ± 4.43	BMI > 30 kg/m ²	AE	Cycle ergometer	55 min	50–70% HRmax	3	12	BW ↓, BMI ↓, WC ↓	SBP ↓	NM	cfPWV ↓
		55 ± 7	0/41	35.98 ± 5.10	BMI > 30 kg/m ²	Combine	RT + cycling	20 min RT + 25 min AE	RT: 50–60% HRmax 1RM, AE: 50–70% HRmax	3	12	BW ↓, BMI ↓, WC ↓	SBP ↔	NM	cfPWV ↔

AE, aerobic exercise; RT, resistance training; HIIT, high-intensity interval training; Combine, AE + RT; BMI, body mass index; min, minute; HR, heart rate; HRR, heart rate reserve; NW, not mentioned; BW, body weight; WC, waist circle; BF, body fat; BF %, body fat percentage; SM, skeletal muscle mass; LBW, lean body weight; TC, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; FG, fast glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HbA1c, glycated hemoglobin | glycosylated hemoglobin; FMD, flow-mediated vasodilatation; cfPWV, carotid-femoral pulse wave velocity; baPWV, brachial-ankle pulse wave velocity; IMT, intima-media thickness; ↑, increased; ↓, decreased; ↔, no change



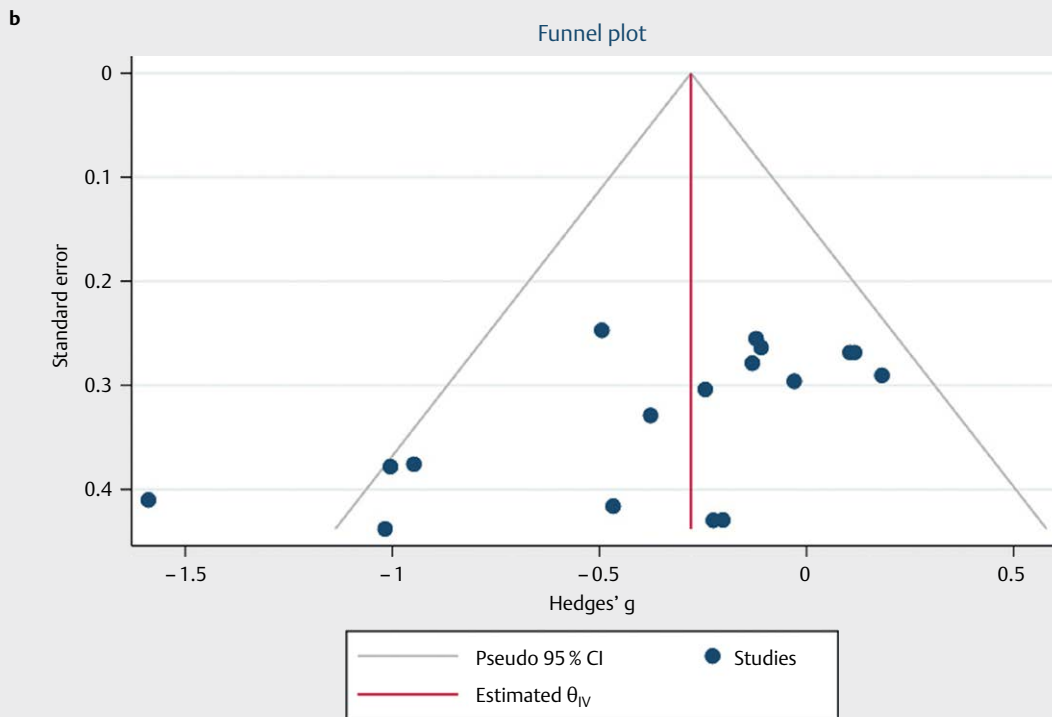
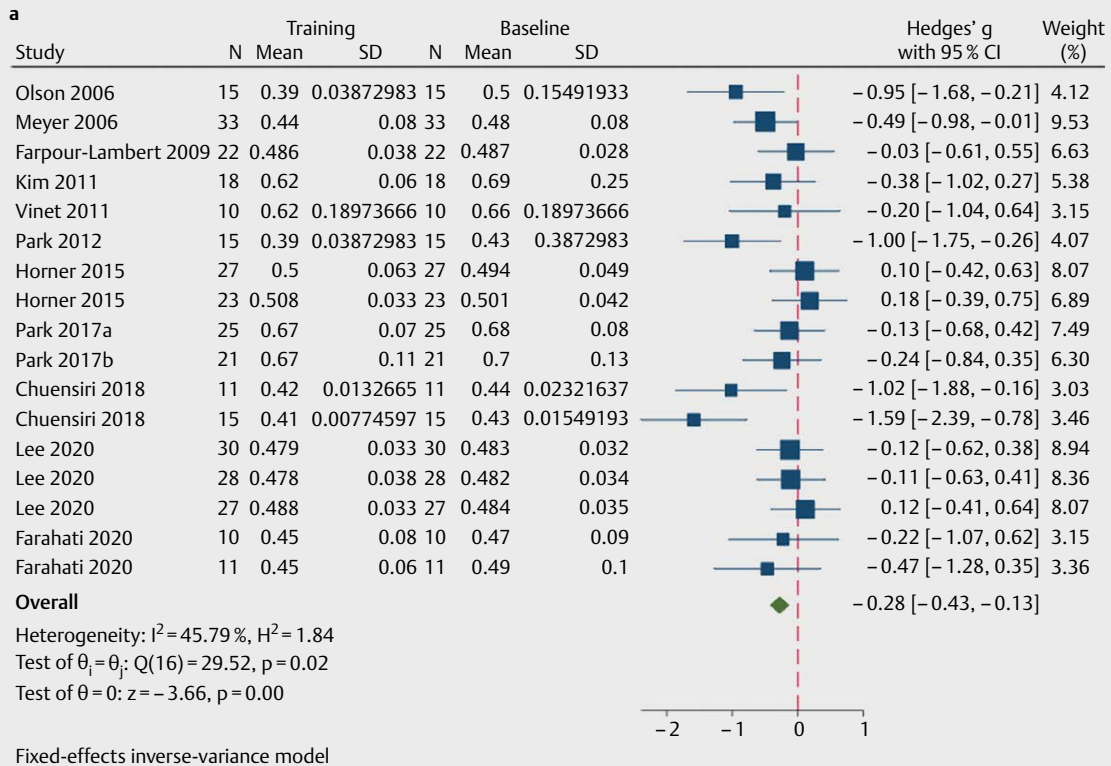
► **Fig. 2** **a.** Forest plot of meta-analysis of ET on FMD. The dotted line represents the mean treatment effect and the diamond represents the overall treatment effect and 95% confidence interval (CI). **b.** Funnel plot for FMD including 95% CI lines. The vertical line represents zero size. SMD represents the standard mean difference.



► **Fig. 3** **a.** Forest plot of meta-analysis of ET on PWV. The dotted line represents the mean treatment effect while the diamond represents the overall treatment effect and 95% confidence interval (CI). **b.** Funnel plot for PWV including 95% CI lines. The vertical line represents zero size. SMD represents the standard mean difference.

after HIIT training. However, there was no change of FMD, PWV, and IMT after RT and combined training (see ► **Table 2**).

Training duration
The change of vascular function and structure would be the cumulative effect of exercise training. Thus, we analyzed the results ac-



► **Fig. 4** **a.** Forest plot of meta-analysis of ET on IMT. The dotted line represents the mean treatment effect and the diamond represents the overall treatment effect and 95% confidence interval (CI). **b.** Funnel plot for IMT including 95% CI lines. The vertical line represents zero size. SMD represents the standard mean difference.

► **Table 2** Results of subgroup meta-analysis.

Subgroup analysis	FMD				PWV				IMT			
	Number of Studies	SMD	95% CI	I ² (%)	Number of Studies	SMD	95% CI	I ² (%)	Number of Studies	SMD	95% CI	I ² (%)
Age	7-18 years	0.83	0.42-1.25	71.13	14	-0.18	-0.32 - -0.03	0	11	-0.26	-0.43 - -0.08	61.15
	18-60 years	0.38	-0.23-0.99	67.09	23	-0.18	-0.31 - -0.05	17.11	4	-0.49	-0.90 - -0.09	0
	>60 years	-	-	-	3	-0.50	-0.93 - -0.07	40.15	2	-0.18	-0.59-0.22	0
BMI (kg/m ²)	<30	0.85	0.39-1.31	74.13	15	-0.25	-0.40 - -0.09	33.23	10	-0.50	-0.71 - -0.30	47.61
	>30	0.43	-0.1-0.95	63.15	25	-0.16	-0.28 - -0.04	0	7	-0.02	-0.24-0.19	0
Training modality	AE	0.89	0.38-1.39	67.35	21	-0.30	-0.43 - -0.18	6.31	6	-0.24	-0.48-0.00	0
	RT	0.53	-0.08-1.15	19.17	7	0.00	-0.25-0.25	0	3	-0.18	-0.52-0.16	65.53
	Combine	0.36	-0.73-1.45	83.85	8	-0.04	-0.23-0.16	0	3	-0.18	-0.44-0.08	36.57
	HIIT	0.52	-0.38-1.41	82.27	4	-0.22	-0.59-0.16	60.08	3	-0.96	-1.44 - -0.48	52.21
	6 ≤ Duration ≤ 8	0.43	-0.02-0.87	56.80	14	-0.24	-0.42 - -0.06	38.66	1	-0.20	-1.04-0.64	-
Duration (week)	8 < Duration ≤ 12	0.77	0.13-1.40	78.06	20	-0.20	-0.34 - -0.06	0	9	-0.34	-0.57 - -0.12	63.65
	Duration > 12	1.26	0.45-2.07	68.64	6	-0.13	-0.31-0.05	0	7	-0.23	-0.44 - -0.03	13.93
	Overall	0.67	0.32-1.02	70.85	40	-0.19	-0.29 - -0.10	5.41	17	-0.28	-0.43-0.13	45.79

ording to training duration. The increase of FMD happened only when the training duration was longer than eight weeks (see ► **Table 2**). However, ET decreased PWV when the training duration was no longer than 12 weeks (see ► **Table 2**). IMT was decreased when the training duration was longer than eight weeks, but only one study measured IMT was included in the subgroup whose training duration was shorter than eight weeks (see ► **Table 2**).

Discussion

The main finding of this meta-analysis, which included 1,245 overweight and obese patients, was that ET could improve endothelial function and arterial stiffness in overweight or obese populations as measured by FMD, PWV, and IMT. However, the ET effect may depend on the different characteristics of exercise intervention and participants' demographics. Subgroup analyses revealed that endothelial function and arterial stiffness in overweight or obese children and adolescents could be improved by ET, but the effect of FMD in adults and IMT in aged adults was insignificant. ET improved endothelial function and arterial stiffness for those with a BMI less than 30, whereas FMD and IMT did not change after ET in participants whose BMI was larger than 30. AE was an effective modality in improving and remodeling vascular function. In contrast, RT did not improve endothelial function and arterial stiffness. PWV may react early to ET when training duration ranged from 6 to 12 weeks, while the improvement diminished when duration was longer than 12 weeks. The improvement of FMD and IMT induced by ET might have a threshold if the training duration was no less than eight weeks.

Our results demonstrated that exercise benefited overweight and obese populations by improving endothelial function and arterial stiffness in exercise intervention studies. Obesity is a risk factor for endothelial dysfunction, and the mechanism may increase inflammation and decrease NO bioavailability in adipose tissue [13]. It was reported that a 1% increase in FMD was associated with a 13% decrease in cardiovascular events for adults [14]. Dias et al. [8] found the improvement effect of ET on FMD in child obesity, which was consistent with this meta-analysis. Son et al. [6] revealed that ET increased FMD in obese adults, contrasting with our results that showed that ET did not change FMD in overweight or obese adults. The reason for this inconsistency probably was the difference in the inclusion criteria. We excluded studies that included obese patients who had other chronic complications.

The overall results indicated that ET decreased arterial stiffness as measured by PWV and IMT. Montero et al. [7] revealed that arterial stiffness was generally not reduced in middle-aged and older obese populations when responding to aerobic training. However, the parameters included measuring arterial stiffness were different. Our result indicated that ET had a significant beneficial effect on PWV with low heterogeneity. The decreasing effect was also discovered in healthy participants after ET [15, 16]. Thus, PWV would be a sensitive indicator for the reaction to ET, whereas it seems that the effect of ET on IMT depended on participants' age. A meta-analysis revealed that the effects of aerobic endurance exercise on IMT did not show any statistical significance in healthy adults [15]. The decrease of IMT was proved in obese children and adolescents [9, 17]. In this meta-analysis, ET improved IMT in overweight or

obese participants who were younger than 60 years, but the effect was insignificant in aged participants.

We speculate that the response of the vascular structure to ET was blunt in aged overweight or obese populations. Compared with obese or overweight children whose baseline age was 13.0 years old, the age of the obese or overweight was 42.8 years. In young individuals, arteries tend to be more elastic [18]. The aging process, oxidative stress, production of free radicals, neuroendocrine changes and genetic predisposition contribute to the increase of wall diameter, vascular calcification, and elasticity loss, leading to collagen deposition and elastin fragmentation in the media layer, and subsequently lead to myocyte proliferation and vascular stiffness [19]. Thus, obesity and aging were factors inducing vascular dysfunction and stiffness together. Importantly, compensation of vascular structure may occur in overweight and obese youth [20], however vascular plasticity was attenuated in older people in response to exercise training [21], especially for central cardiovascular plasticity [22]. The potential mechanisms were blunted NO signaling and age-related pro-/antioxidant imbalance [23, 24].

The benefit for vascular function and structure induced by ET depended on the level of obesity [25, 26]. Though ET decreased BMI no matter whether participants' BMI was larger than 30 kg/m², ET did not change FMD and IMT in participants whose BMI was larger than 30 kg/m². The progress of atherosclerosis was highly associated with BMI, and an adverse long-term adiposity status change was more prominently related to advanced subclinical atherosclerosis [25]. Endothelial dysfunction was also linked with obesity [26]. The development of atherosclerosis would attend the accumulation of obesity. A higher BMI would be a long-term accumulation of weight gain and subsequently induce the development of vascular dysfunction and arterial structure remodeling. Vascular function improved by ET immediately, but endothelial function and arterial structural remodeling was difficult to reverse by a short-term ET. Therefore, the difficulty of reversing vascular remodeling induced by ET was related to obesity development.

Training modality is a key factor that induces different training effects. AE improved FMD, PWV, and IMT. HIIT only decreased IMT to reverse vascular remodeling. However, RT and combined training did not affect all three indicators. The effectiveness of RT on vascular function was consistent with previous studies. Ashor et al. found that RT and combined exercise had no effect on PWV in healthy participants [16]. Ceciliato et al. [10] reported that RT did not elicit changes in arterial stiffness in healthy subjects. An insignificant effect of FMD intervened by RT was also reported in overweight and obese adults [6]. Conclusively, AE was a good modality to improve atherosclerosis, while RT and combined training did not improve vascular function and structure in overweight or obese patients.

The reaction of endothelial function and stiffness to ET varied by training duration. Kobayashi et al. [27] indicated that regular aerobic exercise reduced arterial stiffness in healthy participants regardless of the intensity or duration of aerobic exercise. However, a meta-analysis revealed that arterial stiffness improved by aerobic exercise training required a prolonged duration in pre- and hypertensive subjects [28]. The health status would be the reason for the declined reaction of FMD and IMT to ET in the early training stage. In this meta-analysis study, PWV reacted early to ET when

training duration ranged from 6 to 12 weeks, while the improvement diminished when duration was longer than 12 weeks. The improvement of FMD and IMT induced by ET may have a threshold on which training duration was no less than eight weeks. The vascular function and structure did not react in a synchronized manner to pathological intervention or exercise. Endothelial cells could sense shear stress, and release nitric oxide, which lowers the active tone of VSMCs, leading to (flow-mediated) vessel dilation to counteract the initial increase in wall shear stress [29]. When the vessel wall is continuously exposed to pathological signals, the biomechanical and biochemical stressors elicit functional and adaptive responses. Long-term changes in wall shear stress provoke diameter adaptation [30]. Wall thickness changes are seen in response to increased wall stress (or wall tension), due to high blood pressure [31]. Thus, the structure remodeling was later than vascular function. Meanwhile, vascular function changed immediately after exercise. Repeated episodic bouts of exercise induce chronic functional adaptation and ultimately structural arterial remodeling [32]. Therefore, PWV was improved after shorter training duration, but the improvement of FMD and IMT needed a longer training duration. Training intensity may also be a factor in interpreting the training result, but the intensity had high heterogeneity among studies included in this meta-analysis. The effect of different categories of training intensity on vascular function and arterial stiffness of training intensity needs to be investigated.

Limitations

This study has some limitations. Training intensity was a potential factor to affect the training effect. Since studies included in this review had high heterogeneity, we did not perform subgroup analysis according to training intensity categories. Methodological differences and confounding factors of selected studies were unavoidable, so SMD was chosen instead of the mean difference. Thus, we are unable to compare and evaluate the subgroup results quantitatively. We excluded the studies that intervened by combined diet intervention and recruited participants who had more complications. Network meta-analysis is needed to interpret the training effect comprehensively.

Conclusion

ET can improve overweight or obese populations' endothelial function and arterial stiffness based on FMD, PWV, and IMT measurement. However, ET effect may depend on the different characteristics of exercise intervention and participants' demographics. The improvement of endothelial function and arterial stiffness induced by ET was effective in overweight or obese children and adolescents and participants whose BMI was less than 30. AE was an effective modality to improve vascular function and remodeling. The improvement of FMD and IMT induced by ET may have a threshold that requires a training duration of fewer than eight weeks.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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