***Journal of Physical Activity and Health*, 2022, 19, 855-867**
https://doi.org/10.1123/jpah.2022-0372

Human Kinetics
REVIEW

Effect of Exercise on Carotid Artery Intima–Media Thickness in Adults: A Systematic Review and Meta-Analysis

Yiyan Wang,[1] Hengjing Wu,[2] Jie Sun,[1] Minqian Wei,[3] Jiaqi Wang,[1] Husheng Li,[1] Xubo Wu,[3] and Jing Wu[1]

[1]Department of Fundamental Nursing, School of Nursing, Shanghai University of Traditional Chinese Medicine, Shanghai, People's Republic of China; [2]Clinical Center for Intelligent Rehabilitation Research, Shanghai YangZhi Rehabilitation Hospital (Shanghai Sunshine Rehabilitation Center), School of Medicine, Tongji University, Shanghai, People's Republic of China; [3]Department of Rehabilitation Therapy, Shanghai Seventh People's Hospital, Shanghai, Peoples Republic of China

Background: Carotid intima–media thickness (cIMT) is a validated surrogate marker of atherosclerosis that is independently associated with the risk for cardiovascular disease. Recent studies on the effect of exercise on cIMT have yielded conflicting results. ***Methods:*** Studies that were available up until October 30, 2021 from the PubMed, Cochrane Library, Embase, and Web of Science databases were included in the analysis. Subgroup analyses were performed to determine the effects of the type, intensity, and duration of exercise on cIMT. ***Results:*** This review included 26 studies with 1370 participants. Compared with control participants, those who engaged in exercise showed a decline in cIMT (weighted mean difference [WMD] –0.02; 95% confidence interval [CI], –0.03 to –0.01; $I^2 = 90.1\%$). Participants who engaged in aerobic (WMD –0.02; 95% CI, –0.04 to –0.01; $I^2 = 52.7\%$) or resistance (WMD –0.01; 95% CI, –0.02 to –0.00; $I^2 = 38.5\%$) exercise showed lower cIMT compared with control participants. An exercise duration of >6 months was associated with a 0.02 mm reduction in cIMT. In participants with low cIMT at baseline (<0.7 mm), exercise alone was not associated with a change in cIMT (WMD –0.01; 95% CI, –0.03 to 0.00; $I^2 = 93.9\%$). ***Conclusions:*** Exercise was associated with reduced cIMT in adults. Aerobic exercise is associated with a greater decline in cIMT than other forms of exercise. Large, multicenter, randomized controlled trials are required to establish optimal exercise protocols for improving the pathological process of atherosclerosis.

Keywords: atherosclerosis, sports, vascular health

Carotid atherosclerosis is the leading cause of ischemic stroke.[1] At the population level, early detection of carotid plaque formation is possible through the routine use of Doppler ultrasound.[2,3] Carotid intima–media thickness (cIMT) is a marker of vascular structure and a well-established surrogate of atherosclerosis.[4–6] Epidemiological studies have indicated that an increase in cIMT is present in the general population, especially in middle-aged and older adults. Li et al[7] reported that among 14,322 participants, the mean cIMT was 0.74 (0.11) mm, with almost 40% of the participants having cIMT >1 mm and early atherosclerotic lesions.

Evidence shows that the use of pharmacological agents and lifestyle interventions reduces the rate of increase in cIMT.[8–10] It is well-known that a cIMT ≥0.7 mm is associated with an increased risk for cardiovascular disease.[11,12] cIMT can be used to evaluate cardiovascular disease risk in asymptomatic adults.[13,14] In nonpharmacological treatments, the regression of atherogenesis, as demonstrated by cIMT, has been observed in trials of lifestyle interventions.[15–17] Lifestyle modification may be key to treating subclinical atherosclerosis as it affects vascular and endothelial function.[18,19] Meanwhile, the separate effect of exercise on cIMT, an important component of lifestyle intervention, remains unclear. Conflicting results have been obtained among the studies. Glodzik et al[20] reported that controlled aerobic exercise reduced cIMT in healthy adults, whereas Bjarnegard et al[21] found that the effect of exercise on cIMT was negligible. Although several previous systematic reviews and meta-analyses have explored exercise interventions, they only focused on a particular form of exercise (such as tai chi, yoga, or walking) and extensively evaluated a particular outcome, such as quality of life and cardiovascular events.[22–25]

In this systematic review and meta-analysis, we aimed to summarize the current evidence regarding the effects of exercise on cIMT in adults and determine the impact of the 3 characteristics of exercise (duration, intensity, and type) on cIMT. We hope to provide a basis for the development of appropriate exercise prescriptions for adults.

Methods

This meta-analysis was conducted based on the recommendations of the Preferred Reporting Items for Systematic Reviews statement.[26]

Eligibility Criteria

Populations. Adult participants (aged ≥ 18 y) who were not restricted by health status were eligible.

Interventions. Studies that treated PA as a single intervention as opposed to a component of a broader intervention were eligible. Furthermore, studies that included the intervention and control groups, where the only difference between the 2 groups was the addition of exercise in the intervention group, were included. We excluded studies that combined exercise with cognitive training, diet control, or drug therapy to assess the independent effect of exercise on cIMT. We classified the exercise included in the studies into 5 types: aerobic exercise, resistance exercise, combined

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J. Wu (jingwuclose@126.com) is corresponding author, https://orcid.org/0000-0002-2492-5118

aerobic and resistance exercise (CARE), high-intensity interval exercises (HIIE), moderate-intensity continuous exercise (MICE), and endurance exercise.

Comparisons. Studies in which the control group received usual care (allowed participation in unplanned, unstructured, daily exercises) were eligible. Sedentary behavior is reportedly associated with increased cIMT.[27–29] Therefore, we excluded studies in which individuals who had a sedentary lifestyle were used as controls.

Outcomes. Studies in which the outcome was cIMT of the participants and those in which there were no restrictions on the band of the measuring instrument and measuring sites (the common carotid artery, internal carotid artery, common carotid artery bifurcation, and carotid bulb) were all eligible.

Information Sources and Search Strategy

We searched the PubMed, Cochrane Library, Embase, and Web of Science databases until October 11, 2021. The reference lists in relevant reviews and meta-analyses were another source of information. Two researchers (H. Wu and J. Wu) independently searched the electronic databases using the same search strategy. The complete search strategy for PubMed is presented in Table S1 (see Supplementary Material [available online]), the other databases were searched using the same index terms.

Selection Process

We imported records from the database searches into EndNote and deleted duplicate records. For initial screening of the eligible studies, 2 researchers (Y. Wang and Wei) independently reviewed the titles and abstracts of all records and discussed inconsistencies until they reached a consensus. To determine the studies to be included, 2 researchers (Wei and Sun) independently screened the full texts according to the inclusion criteria and discussed disagreements with other researchers until they reached an agreement. Only studies published in English were included.

Data Collection Process

We designed an extraction form into which 2 researchers (Y. Wang and JW) independently inputted data extracted from the included studies. Other researchers examined and resolved the conflicting data. The information extracted from each included study were as follows: (a) characteristics of the articles (first author, year of publication, and the country where the study was carried out), (b) characteristics of the participants (health status, male/female, sample size, and mean age), (c) characteristics of exercise (type, form, duration of session, frequency, intensity, and duration of exercise), and (d) effects of treatment.

Data Items

We extracted the mean and SD of the cIMT in the intervention and control groups after the intervention. With the participant in the supine position, the thickness of the intima and media of the carotid artery wall was measured using B-mode sonography. The measurement sites included the common, internal, and external carotid arteries, bifurcation of the common carotid artery, and carotid bulb. The final recorded result was the measurement of 1 vascular site or the average of measurements at multiple sites.

Study Risk of Bias Assessment

Two review authors (Y. Wang and Sun) independently assessed the quality of the included studies using the Cochrane risk-of-bias tool[30] and resolved any differences through discussions with other authors. The tool evaluates each study based on the areas of randomized controlled trials related to deviations: selection, performance, detection, attrition, reporting, and other biases. Based on the description in a study, it was evaluated as having “low,” “unclear,” or “high” risk of bias in these areas.

Synthesis Methods

Statistical analyses were performed using Stata (version 15.0, Stata Corporation).

In different studies, consistent methods were used to measure cIMT, and the units were all in millimeters. Therefore, we expressed the effect measures as weighted mean differences (WMDs) and 95% confidence intervals (CIs). An individual study group was used as the unit of analysis. Studies that reported multiple intervention groups and a single control group were treated as multiple studies. To avoid double counting, we referred to the method described by Coventry et al[31] and divided the sample size of the control group equally.

The I^2 statistic was calculated to assess the heterogeneity among studies and select the effect model. A random-effects model was selected if I^2 was >50%, indicating statistical heterogeneity among the studies. Otherwise, a fixed-effects model was used. Meta-regression analysis was used to examine the causes of heterogeneity. Forest plots were used to graphically demonstrate the meta-analysis results. Egger regression analysis was performed to assess potential publication bias and visually inspect the funnel plots.

Results

Study Selection

We searched 4 electronic databases and reference lists (6 citations) and identified 1681 citations. After removal of duplications, titles and abstracts were screened, and 204 records were identified for full-text review. Finally, 26 studies[20,21,32–55] (32 study groups) that met the eligibility criteria were included in the meta-analysis. The detailed selection process and reasons of exclusion of some studies are presented in the Preferred Reporting Items for Systematic Reviews flow diagram (Figure 1).

Study Characteristics

Twenty-six studies identified 32 study groups with 1370 participants, and all study groups were included in the meta-analysis. Most of the studies were conducted in Asia (n = 14), the United States (n = 6), and Europe (n = 5). Twenty-four study groups evaluated participants with diseases. The duration of the intervention ranged from 2 to 12 months for the intervention arms, but lasted ≤6 months[20,33–35,38–40,42–44,46,49–55] for most studies. The effect of aerobic exercise was reported in 9 of the 32 study groups. Fifteen study groups reported that exercise reduced cIMT in adults. However, 17 study groups maintained that exercise did not affect the cIMT. The relevant characteristics of these studies are summarized in Table 1.

Risk of Bias in Studies

Details of the quality assessment using the Cochrane Collaboration tool are presented in Table S2 (see Supplementary Material

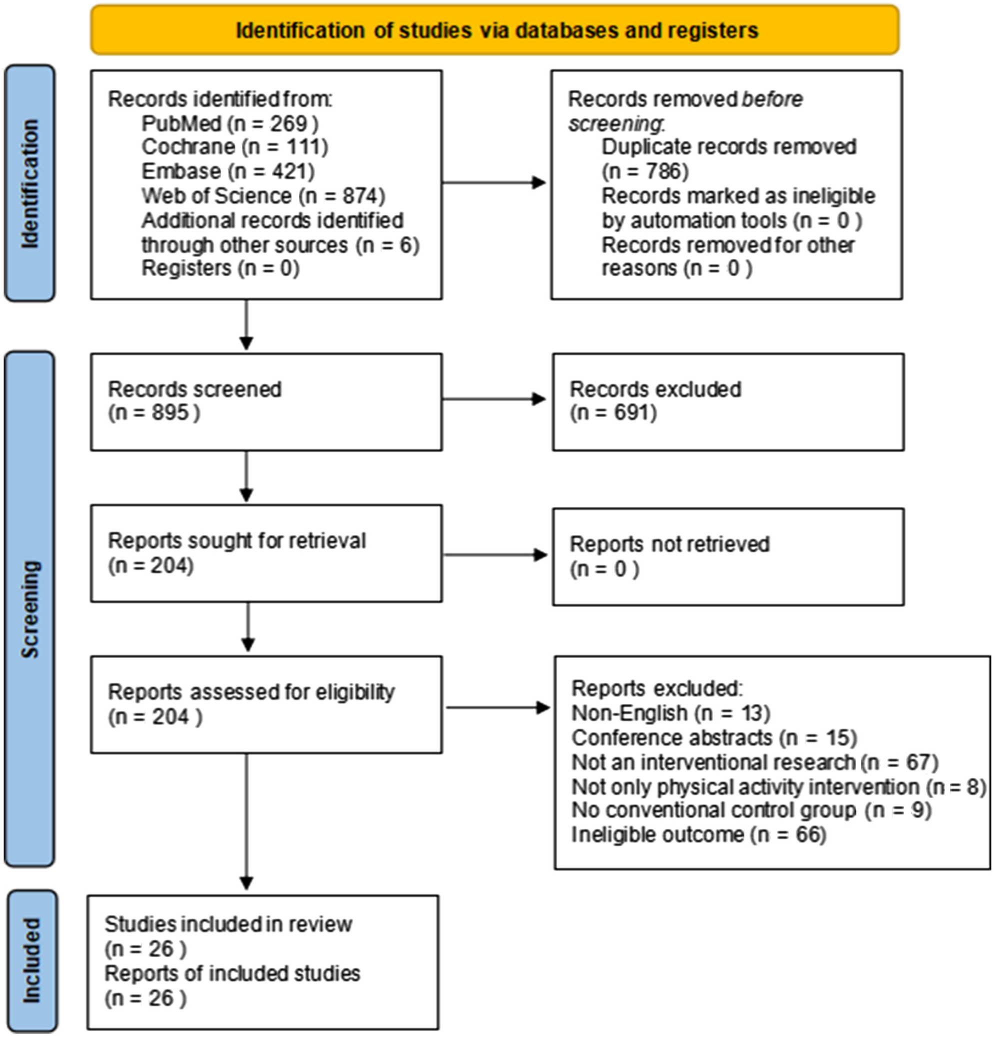

Figure 1 — Flowchart of study selection for the meta-analysis.

[available online]). No included study provided a clear explanation for the concealment of allocation, and most of them did not mention blinding of the evaluator. Although blinding of participants and personnel was not feasible in this setting, we assessed all studies as having a high risk of performance to avoid potential bias.

Results of Syntheses

In the pooled analyses, exercise (WMD –0.02; 95% CI, –0.03 to –0.01; $I^2 = 90.1\%$), compared with usual care controls had a more significant effect on cIMT in adults, which presented substantial heterogeneity (Figure 2). We conducted a random-effects meta-regression to explore the heterogeneity among the studies (Table S3, see Supplementary Material [available online]). A subgroup analysis was performed based on the variables included in the meta-regression model. We used a random-effects model to calculate total and subgroup effects.

Subgroup Analysis

Duration of Exercise. Subgroup analyses by duration showed a variation in the effects of different durations of exercise on cIMT. Figure 3 shows that studies with a higher exercise duration (>6 mo; WMD –0.02; 95% CI,–0.02 to –0.02; $I^2 = 0.0\%$) reported a more significant effect on cIMT. Studies with a lower exercise duration (≤6 mo; WMD –0.02; 95% CI, –0.04 to –0.00; $I^2 = 91.1\%$) reported a tendency toward reduction in cIMT at the end of the intervention.

Exercise Types. In the subgroup analysis by type, aerobic exercise showed a more significant effect on cIMT compared with the other types of exercise. The results of the meta-analysis of the different types of exercise were as follows: aerobic exercise (WMD –0.02; 95% CI, –0.04 to –0.00; $I^2 = 52.7\%$), resistance exercise (WMD –0.01; 95% CI, –0.02 to –0.00; $I^2 = 38.5\%$), CARE (WMD –0.01; 95% CI, –0.02 to –0.00; $I^2 = 0.0\%$), HIIE (WMD –0.03; 95% CI, –0.09 to 0.02; $I^2 = 95.6\%$), MICE (WMD –0.02; 95% CI, –0.09 to 0.05; $I^2 = 59.4\%$), and endurance exercise (WMD –0.04; 95% CI, –0.13 to 0.05; $I^2 = 73.4\%$; Figure 4).

Intensity of Exercise. The effects of medium- to low-intensity exercise (WMD –0.02; 95% CI, –0.04 to –0.00; $I^2 = 59.4\%$) on cIMT were little or no different from those of medium to high-intensity exercise (WMD –0.02; 95% CI, –0.04 to 0.00; $I^2 = 59.8\%$; Figure 5).

Table 1 Characteristic of Included Studies

Studies	Country	Health status	Male/ female	Exercise		Control		Types	Forms	Session duration	Frequency (times/wk)	Intensity	Duration	Effect
				n	Age	n	Age							
Adams et al[49]	Canada	TCS	63/0	35	44.0 (11.6)	28	43.3 (9.9)	HIIE	Treadmill walk/ running	35 min	3	75%–95% VO_2peak	12 wk	Decrease
Bjarnegard et al[21]	Sweden	Nonsmoking	0/42	21	34 (7)	21	35 (6)	Aerobic	Cycling	45–60 min	3	High effort	12 mo	NS
Byrkjeland et al[48]	Norway	T2DM	115/22	61	63.5 (8.0)	62	63.2 (7.2)	Aerobic and resistance	—	60 min	2	RPE ≥ 15	12 mo	NS
Croymans et al[51]	United States	Obese young men	—	28	21.5 (2.22)	8	21.72 (1.57)	Resistance	DB	60 min	3	6–8 RM	12 wk	Decrease
Donley et al[33]	United States	Metabolic syndrome	8/14	11	46 (4)	11	44 (3)	Aerobic	Treadmills	60 min	3	85% HR_{max}	8 wk	NS
		Healthy adults	6/15	11	41 (4)	10	40 (4)	Aerobic	Treadmills	60 min	3	85% HR_{max}	8 wk	NS
Farahati et al[52]	Iran	Overweight	0/20	11	43.90 (3.80)	9	44.22 (3.63)	MICE	Treadmill walk/ running	30 min	3	85%–95% HR_{max}	12 wk	NS
			0/19	10	42.80 (2.69)	9	44.22 (3.63)	HIIE	Treadmill walk/ running	47 min	3	60%–70% HR_{max}	12 wk	NS
Ghardashi-Afousi et al[53]	Iran	T2DM	41/28	30	55.10 (6.07)	29	54.10 (5.68)	HIIE	Cycling	—	3	85%–90% HR_{max}	12 wk	Decrease
Glodzik et al[20]	Poland	Healthy adults	31/14	31	44.3 (5.57)	14	45.0 (3.41)	Aerobic	Cycling	40–60 min	3	40%–65% HRR	12 wk	Decrease
Hafner et al[35]	United States	Healthy adults	—	14	20.4 (1.6)	11	19.4 (1.1)	ET	Marathon	—	4	—	16 wk	NS
Kadoglou et al[38]	Sweden	T2DM	13/32	21	58.3 (5.4)	24	57.9 (7.2)	Aerobic	Walking/ cycling	60 min	4	60%–75% HR_{max}	6 mo	Decrease
			14/33	23	56.1 (5.3)	24	57.9 (7.2)	Resistance	—	60 min	4	60%–80% 1 RM	6 mo	Decrease
			12/34	22	57.9 (6.5)	24	57.9 (7.2)	Aerobic and resistance	Walking/ cycling	60 min	4	60%–75% HR_{max} /60%–80% 1 RM	6 mo	Decrease
Kim et al[46]	Korea	Abdominal obese	0/62	32	41.1 (5.5)	30	40.8 (6.2)	Aerobic and resistance	Walking/ elastic band	50–80 min	5	60%–70% HR_{max} / RPE 13–15	12 wk	Decrease
Kim et al[34]	Korea	Older adults	—	14	65 (1)	11	63 (2)	HIIE	Treadmill	40 min	4	90% HR_{peak}	8 wk	NS
			—	13	65 (2)	11	63 (2)	MICE	Treadmill	47 min	4	70% HR_{peak}	8 wk	NS
Kitzman et al[40]	United States	HFPEF	15/48	32	70 (7)	31	70 (7)	ET	Walking/ cycling	60 min	3	70% HR_{max}	16 wk	NS
Lee et al[50]	United States	Breast cancer	30/0	15	49.1 (7.9)	15	44.7 (11.2)	HIIE	Cycling	45 min	3	90% VO_2peak	8 wk	NS
Magalhães et al[47]	Portugal	T2DM	18/20	16	60.4 (6.8)	22	60.8 (7.5)	MICE	Cycling	45 (7.1) min	3	40%–60% HRR	1 y	Decrease
		T2DM	20/15	13	58.9 (7.5)	22	60.8 (7.5)	HIIE	Cycling	33.1 (64) min	3	70%–90% HRR	1 y	Decrease

(continued)

Table 1 (continued)

Studies	Country	Health status	Male/female	Exercise		Control		Types	Forms	Session duration	Frequency (times/wk)	Intensity	Duration	Effect
				n	Age	n	Age							
Miyachi et al[55]	Japan	Healthy adults	28/0	14	22 (1)	14	22 (1)	Resistance	—	45 min	3	80% 1 RM	4 mo	NS
Olson et al[54]	United States	Overweight	0/30	15	38 (1)	15	38 (2)	Resistance	—	—	2	—	12 mo	NS
Park[44]	Korea	Healthy older adults	30/0	15	73.1 (3.0)	15	70.9 (3.9)	Resistance	Elastic bands	30–50 min	3	—	24 wk	NS
Park et al[43]	Korea	Obese older	0/50	25	73.5 (7.1)	25	74.7 (5.1)	CARE	Elastic bands/ walking	50–80 min	5	RPE ≥ 15	24 wk	Decrease
Park et al[39]	Japan	Obese older	0/20	10	66.1 (3.1)	10	67.7 (5.2)	CARE	Walking/ elastic bands	70 min	3	RPE 12–13	12 wk	NS
Park et al[43]	Korea	Obese older	0/41	21	68.4 (2.6)	20	70.4 (4.5)	CARE	Elastic bands	40–80 min	5	RPE 5–6	6 mo	Decrease
Park et al[45]	Korea	Obese older adults	0/20	10	70.7 (0.7)	10	71.3 (0.6)	CARE	Walking/ dance	45 min	3	60%–70% HR_{max}	12 wk	Decrease
Rahbar et al[37]	Iran	T2DM	—	13	48.31 (5.02)	15	48.60 (4.80)	Aerobic	Treadmill	30 min	3	50%–70% HR_{max}	8 wk	Decrease
Saboo et al[41]	India	Prediabetes	85/165	125	—	125	—	Aerobic	Yoga	46 min	6	—	6 mo	Decrease
Shin et al[36]	Korea	Rheumatoid arthritis	0/43	29	64.0 (5.4)	14	62.7 (5.9)	Aerobic	Tai chi	60 min	1	—	3 mo	NS
Tanahashi et al[32]	Japan	Postmenopausal	0/30	10	62 (6)	20	61 (7)	Aerobic	Cycling	40–60 min	3	65%–80% HR_{max}	12 wk	NS

Abbreviations: CARE, combined aerobic and resistance exercise; DB, dumbbell; ET, endurance exercise; HFPEF, have preserved left ventricular ejection fraction; HIIE, high-intensity interval exercise; HR_{max}, maximal heart rate; HR_{peak}, peak heart rate; HRR, heart rate reserve; MICE, moderate-intensity continuous exercise; NS, no significant; RM, repetition maximum; RPE, rated perceived exertion; T2DM, type 2 diabetes mellitus; TCS, testicular cancer survivors; VO_2peak, peak aerobic fitness.

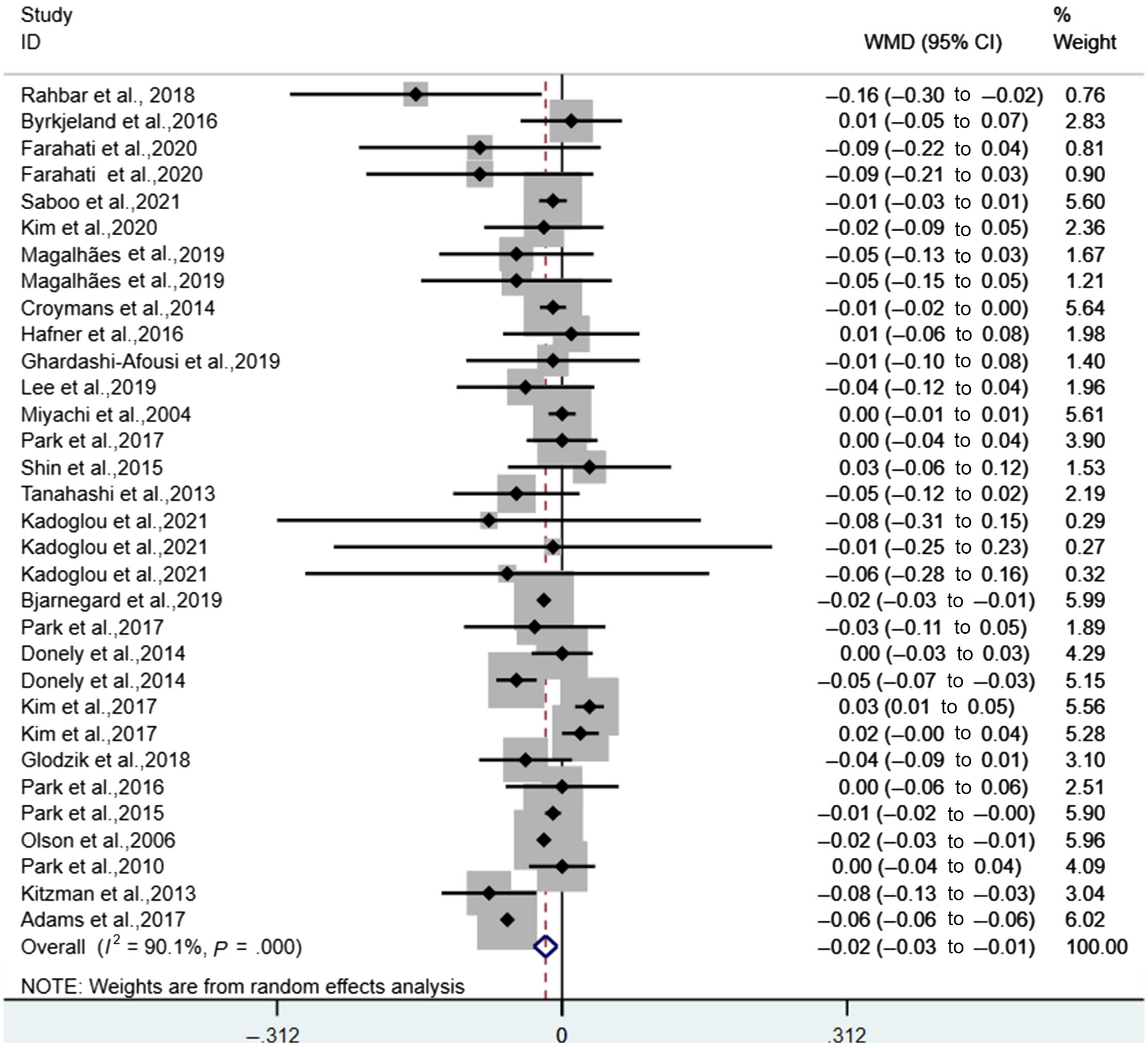

Figure 2 — Forest plot of included studies. CI indicates confidence interval; WMD, weighted mean difference.

Participant Characteristics. Subgroup analyses were used to explore the impact of study location, participant health status, age, and mean cIMT at baseline in the intervention group. cIMT ≥0.7 mm is reportedly associated with an increased risk for cardiac events; therefore, we selected 0.7 mm as the cut-off value.[13,20,56–58] A detailed description of the characteristics of each participant is provided in Table 2.

Sensitivity Analysis

A sensitivity analysis was performed by sequentially excluding each study to test the reliability of the results. We found that the combined results were not affected by the exclusion of any single data set (Figure S1, see Supplementary Material [available online]).

Risk of Publication Bias

We used a funnel plot to assess publication bias, which showed no apparent asymmetry (Figure S2, see Supplementary Material [available online]). Egger test ($P = .246$) provided evidence of no publication bias (Figure S3, see Supplementary Material [available online]).

Discussion

This systematic review and meta-analysis included 26 studies with 1396 participants. The pooled effects of the included studies demonstrated the beneficial effect of exercise on cIMT. However, a significant heterogeneity was observed among the included studies. We used subgroup analysis and a random-effects model to examine the effect of exercise prescription variables on the population. The studies included in this review included various types of exercise (eg, aerobic and resistance exercise), and a more detailed discussion of each factor is beyond the scope of this review.

Exercise Prescription Variables

Duration of Exercise. Our meta-analysis demonstrated interesting findings regarding the duration of exercise as follows: exercise

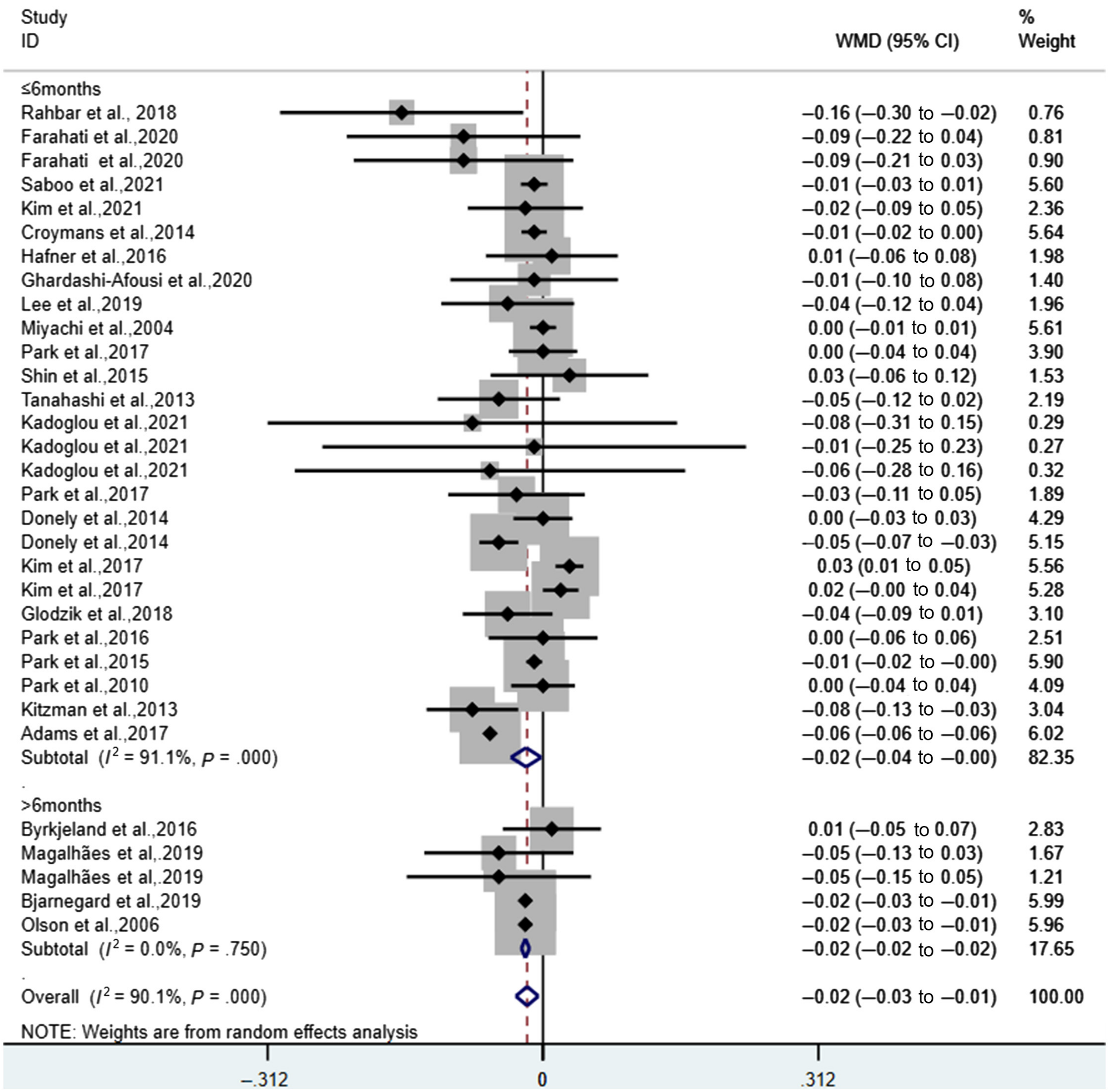

Figure 3 — Forest plot according to duration of intervention. CI indicates confidence interval; WMD, weighted mean difference.

for >6 months was associated with a greater decline in cIMT than exercise for ≤6 months in adults. Similarly, Elitok et al[59] reported that changes in cIMT were related to exercise duration. One possible reason for this is that cIMT is slowly modified, and the effects do not appear until the exercise intervention has continued for a prolonged period. Additionally, a previous study demonstrated that the effect of exercise on cIMT does not persist after the exercise is terminated[60]; therefore, exercise must be continued for sustained benefit. In general, changes in cIMT were correlated with the duration of exercise, suggesting that focusing on the temporal inflection point of the exercise effect is important for determining the optimal duration of exercise prescriptions.

Exercise Types. We also examined the effect of exercise type on cIMT. The results showed that aerobic exercise, resistance exercise, and CARE were associated with a reduction in cIMT; however, the magnitude of the reduction was more pronounced with aerobic exercise. A possible explanation for this is that aerobic exercise reduces age-related arterial inflammation and the production of tumor necrosis factor and interleukin.[61,62] Aerobic exercise also normalizes blood pressure and lipid levels, which are crucial factors in the development of cIMT.[63,64]

Regular resistance exercise increases the incidence of arteriosclerosis and blood pressure, although endothelial function remains intact.[65–67] Our results showed that resistance exercise improved cIMT, although the effect was not as significant as that of aerobic exercise. A previous meta-analysis showed that high-intensity resistance exercise was associated with increased arterial stiffness in younger participants with low baseline levels of arterial stiffness.[23,65–67] The results of the current review demonstrated that resistance exercise may not be suitable for all populations.

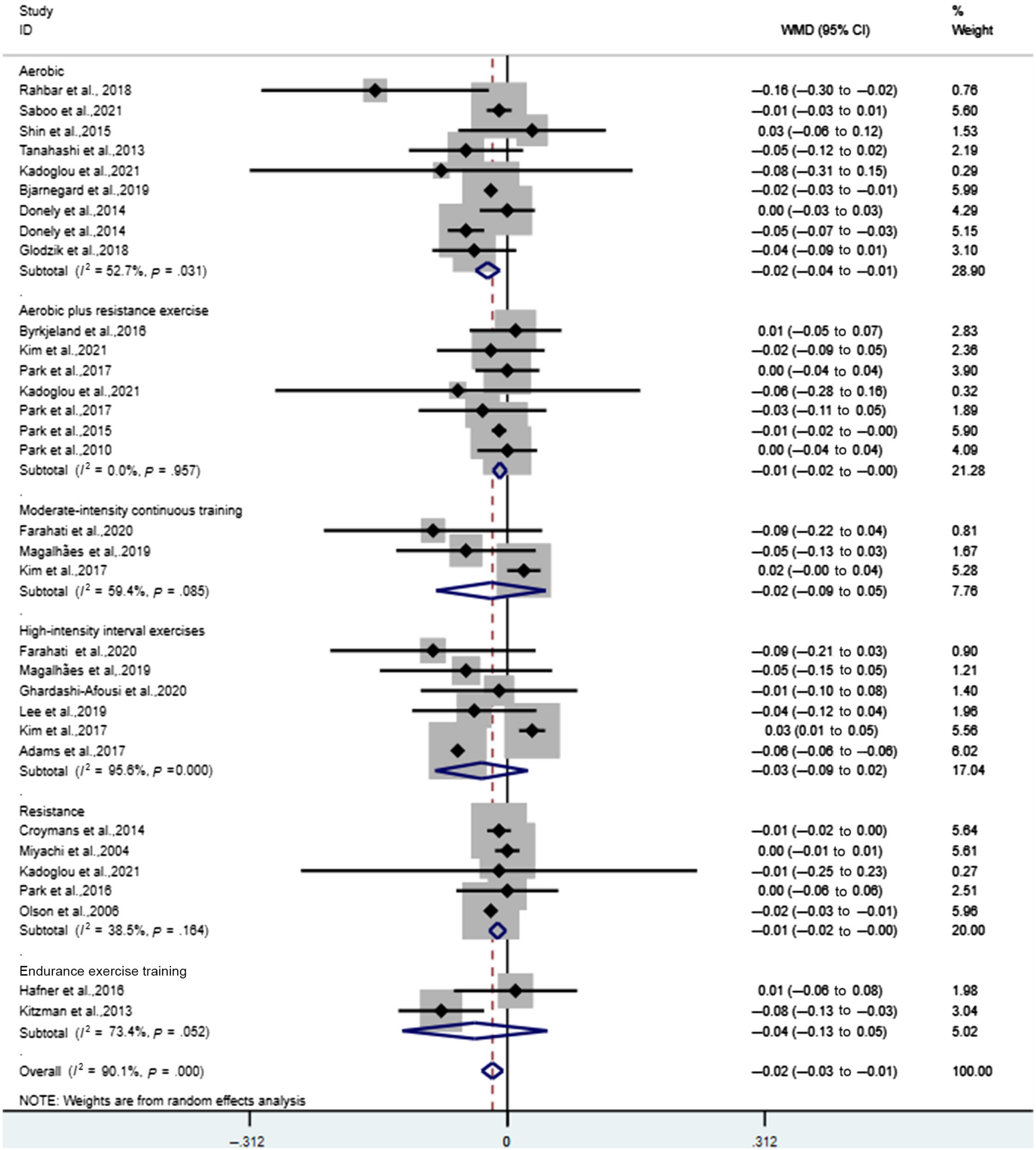

Figure 4 — Forest plot according to physical activity types. CI indicates confidence interval; WMD, weighted mean difference.

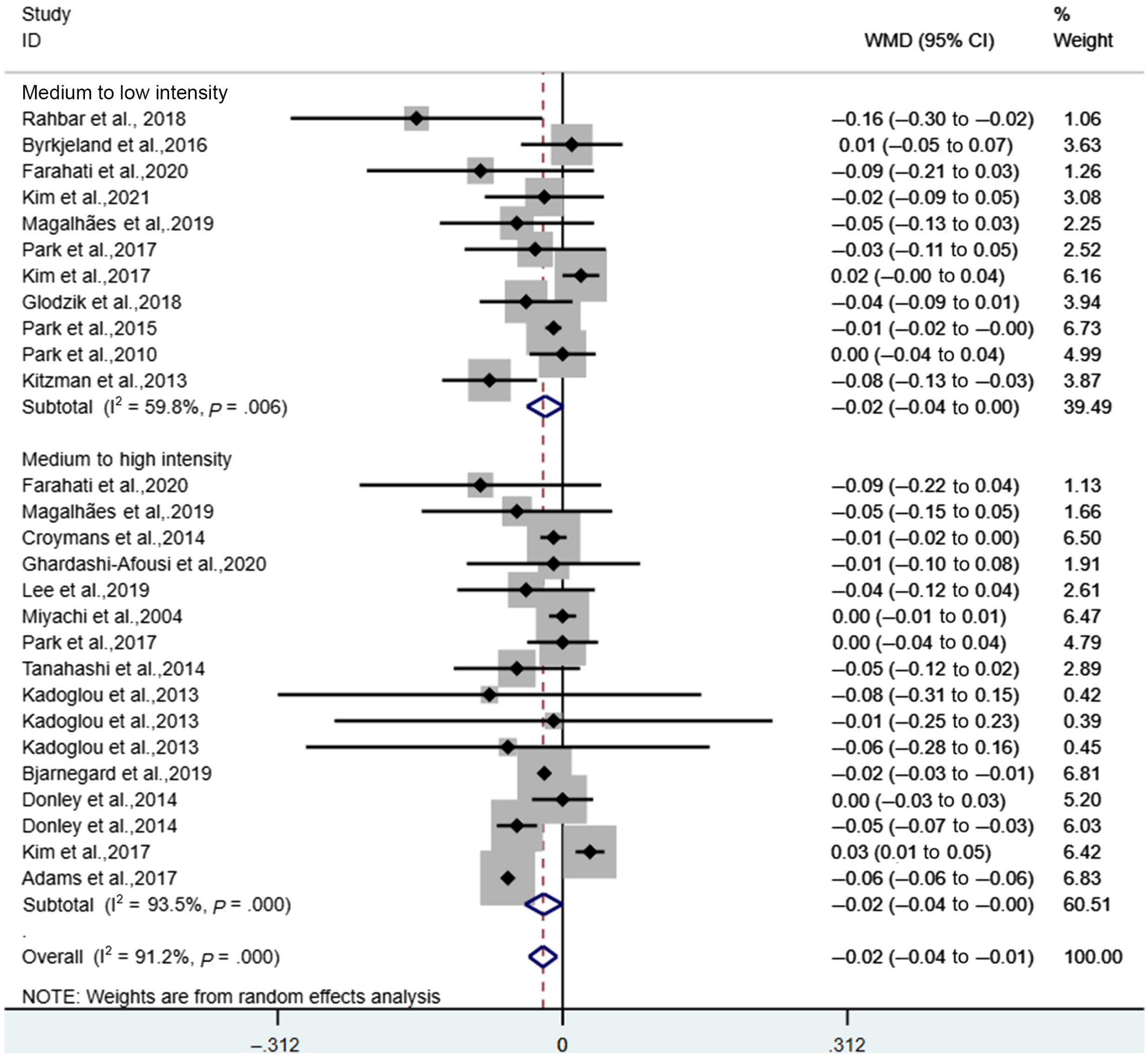

Figure 5 — Forest plot according to the intensity of intervention. CI indicates confidence interval; WMD, weighted mean difference.

Another interesting finding from our study is that CARE did not reduce cIMT to a greater extent than resistance exercise. However, Kawano et al[68] showed that synchronized aerobic exercise prevented carotid arteriosclerosis caused by resistance exercise in healthy young men. These results should be interpreted with caution, as there are relatively fewer studies on the various exercise types, except for aerobic exercise.

Exercise Intensity. Although some studies have suggested that high-intensity exercise for cardiac rehabilitation produces better results,[69–71] our findings did not demonstrate substantial declines in cIMT with high-intensity exercise.

Previously, researchers believed that high-intensity exercise generally involved lower training volumes than traditional aerobic and resistance exercises, making it a time-saving strategy.[70] However, Quindry et al[72] reviewed previous studies and found that high-intensity activities were not better than moderate-intensity activities in reducing risk factors for cardiovascular disease. Our results are consistent with these findings. This may be due to the fact that although the intensity of moderate-intensity exercise is low and its effect is not as strong as that of high-intensity exercise over a short period of time, moderate-intensity exercise often requires a longer period of activity to achieve effects similar to those of high-intensity exercise.[73,74] Despite the similar effects of the different exercise intensities, there are differences in exercise compliance and safety.[75,76] Therefore, when selecting exercise intensity, it is necessary to consider the health status of the individual.

Participant Characteristics

The results of our study showed that exercise may not be effective in reducing cIMT in a relatively healthy population with a well-preserved physiological and cardiovascular status. Similar to our results, a nonrandomized controlled trial of lifestyle intervention in Germany showed significant differences in subgroup analyses of

Table 2 Subgroup Analysis According to Study Characteristics

Subgroups	Study groups, n	Effects model	Overall effect, WMD (95% CI)	Heterogeneity	
				I^2, %	*P*
All	32	Random	−0.02 (−0.03 to −0.01)	90.1	.006
Study location					
Asia	16	Random	−0.00 (−0.01 to 0.01)	58.9	.788
Europe	8	Random	−0.02 (−0.03 to −0.01)	0.0	.000
North America	8	Random	−0.03 (−0.05 to −0.01)	93.9	.005
Participant's health status					
Participants with diseases	24	Random	−0.02 (−0.04 to −0.01)	88.0	.003
Healthy participants	8	Random	−0.01 (−0.03 to 0.01)	88.2	.575
Mean/median age, y					
<60	20	Random	−0.03 (−0.04 to −0.01)	90.2	.001
≥60	12	Random	−0.00 (−0.02 to 0.01)	69.7	.692
Mean cIMT at baseline of exercise group, mm					
<0.7	19	Random	−0.01 (−0.03 to 0.00)	93.9	.000
≥0.7	13	Random	−0.03 (−0.04 to −0.01)	32.5	.122

Abbreviations: CI, confidence interval; cIMT, carotid intima–media thickness; I^2, *I* square; WMD, weighted mean difference.

participants with a higher baseline mean cIMT.[56] This beneficial effect of exercise was more pronounced in participants with a high baseline cIMT. This may be because certain diseases (such as diabetes and hypertension) are risk factors for the progression of cIMT,[77] while the cIMT of healthy individuals does not increase beyond the normal level. However, this population could benefit from exercise in other aspects such as improved physical fitness, body composition, lipid profiles, and fasting blood glucose levels.[78,79]

Exercise was less effective in improving cIMT in the older subgroup, which may be because exercise does not reduce age-related increases in cIMT.[33,80] Therefore, the older adults' population may require a combination of drug therapy and exercise to achieve a positive effect on cIMT.

Limitations and Strengths

The strength of this meta-analysis is that we analyzed the independent effect of exercise on cIMT, after excluding interference from other interventions (eg, drugs and diet). However, owing to the heterogeneity of exercise regimens, such as varying duration and intensity, it was difficult to definitively identify the most appropriate and effective exercise type, duration, and intensity that will reduce cIMT.

In addition, our meta-analysis has some limitations. First, the included studies did not report the safety indicators with exercise. The choice of exercise type was guided by its effectiveness and safety. Second, this meta-analysis only included publicly available documents and excluded unpublished documents, which may have affected the comprehensiveness of the data. Third, in the subgroup analysis, some subgroups included fewer studies and had higher heterogeneity; therefore, our findings should be interpreted with caution.

Future studies should further evaluate the details of the optimal exercise prescription, the inflection point of the intervention time, and differences in the optimal interventions for the older and young populations. Additional research is needed to verify the results of this meta-analysis.

Conclusions

The results of this systematic review and meta-analysis suggest that aerobic exercise with a minimum duration of 6 months should be an effective method of improving the state of atherosclerosis markers in adults. However, our findings were limited by the mixed risk of bias among the significant studies. Evidence supporting the effectiveness of exercise as an additional health measure remains ambiguous. Additional atherosclerosis biomarkers are required as the outcome of trials to confirm the effectiveness of exercise.

Acknowledgments

The study was funded by the Nature Science Foundation of China (No. 71904127). All data supporting the results of this study are included in this article (and its Supplementary Material [available online]). **Author Contributions:** Y. Wang, X. Wu, and J. Wu were responsible for this study's conception, design, and hypothesis. Y. Wang, H. Wu, Sun, and J. Wu performed the systematic search, data extraction, and risk of bias assessment. Y. Wang, Sun, J. Wang, and Li completed all statistical analyses and wrote the first draft of this manuscript. All authors discussed the study results and drafted the manuscript and its revision.

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