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Effects of Aerobic Exercise Alone on Lipids in Healthy East Asians: A Systematic Review and Meta-Analysis

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Aim: The purpose of the current work was to review the effects of regular aerobic exercise on serum lipid and lipoprotein levels in East Asians using meta-analysis.

Methods: The randomized controlled trials analyzed involved healthy adults who were East Asians with a mean age ≥40 years, an exercise group that only performed regular aerobic exercise, and a control group that did not carry out exercise-related intervention; the trials indicated mean high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), or triglyceride (TG). The mean difference (MD) was defined as the difference (mean value at post-intervention in the exercise group − mean value at baseline in the exercise group) − (mean value at post-intervention in the control group − mean value at baseline in the control group) in HDL-C, LDL-C, TC, and TG and was calculated for each trial. The weighted MD was calculated with a random-effects model.

Results: The meta-analysis examined 994 subjects in 25 studies. The weighted MD in HDL-C, TC, and TG improved significantly (HDL-C, 2.2 mg/dL; TC, −5.8 mg/dL; TG, −13.7 mg/dL). The weighted MD in HDL-C and TC contained significant heterogeneity (HDL-C, I^2=45.1%; TC, I^2=56.2%). When trials were limited to those involving moderate-intensity exercise (55%−69% of the maximum heart rate) or an exercise volume ≥150 min/week, the weighted MD in HDL-C, LDL-C, TC, and TG improved significantly and did not contain significant heterogeneity.

Conclusions: The findings suggest that the ideal form of exercise to improve lipid and lipoprotein levels in East Asians is exercise of moderate-intensity and in a volume ≥150 min/week.

Key words: Randomized controlled trial, Heterogeneity, Form of exercise

Introduction

In Japan, the Ministry of Health, Labor, and Welfare reported that national health-care costs related to cardiovascular disease amounted to 743 billion yen in 2014 and that costs for adults aged 45 or over accounted for approximately 98% of these health-care costs[1)]. In addition, the number of patients with dyslipidemia has tended to increase when Japanese are in their 40s[2)]. Several epidemiological studies involving East Asians have reported that dyslipidemia contributed to the incidence of arteriosclerosis or coronary heart disease[3-7)]. These results suggest that dyslipidemia is a major risk factor for cardiovascular disease in East Asians and that dyslipidemia has contributed to the growth of the national budget.

The major risk factors for dyslipidemia are known to depend heavily on lifestyle, and several meta-analyses have indicated that lifestyle modifications improve the lipid and lipoprotein levels[8-16)]. Physical activity is one way of improving these levels, and a number of previous studies have noted the beneficial effects of regular exercise on lipid and lipoprotein levels. According to previous meta-analyses, regular aerobic exercise resulted

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in changes in high-density lipoprotein cholesterol (HDL-C) of approximately 2 mg/dL, changes in low-density lipoprotein cholesterol (LDL-C) of approximately −4 mg/dL, changes in total cholesterol (TC) of approximately −4 mg/dL, and changes in triglyceride (TG) of approximately −2 mg/dL[11-16]. However, these meta-analyses involving mostly Western subjects[11-16], and several meta-analyses reported heterogeneity among randomized controlled trials in terms of changes in the lipid and lipoprotein levels[11, 14]. Meta-analyses of changes in blood pressure as a result of aerobic exercise suggested that heterogeneity was due to differences in ethnic groups, subjects' characteristics, form of exercise, and exercise volume[17, 18]. Therefore, taking these aspects into account should limit the influence of heterogeneity on the lipid and lipoprotein levels. Several meta-analyses of regular aerobic exercise reported that changes in lipid and lipoprotein levels were related to exercise volume[10, 11, 16], but these meta-analyses did not examine trials involving only East Asians.

On the basis of this hypothesis, the purpose of the current work was to perform a meta-analysis to evaluate the effects of regular aerobic exercise on the lipid and lipoprotein levels in East Asians.

Methods

The current work was performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement[19] and was registered in the International Prospective Register of Systematic Reviews (PROSPERO, registration number: CRD42018089749)[20].

Data Sources and Study Selection

MEDLINE via PubMed, EMBASE, SPORTDiscus, the Cochrane library, and Google Scholar were searched using terms such as dyslipidemia, hyperlipidemia, lipid, lipoprotein, cholesterol, exercise, exercise therapy, and physical fitness. The literature was searched using combinations of terms related to lipids or lipoproteins and exercise and/or by adding synonyms (**Table 1**). In addition to the references the current work cited (original articles, reviews, or textbooks), we also looked for other sources by searching Google and online articles. These searches were performed before April 2018. The inclusion criteria for this meta-analysis were as follows: (i) East Asian subjects (studies meeting one of the following three prerequisites: text described subjects as East Asians; all the researchers worked in East Asia; or the intervention was performed in East Asia); (ii) subjects with a mean age of 40 years or older and with no cardiovascular or other diseases (except for lifestyle-related diseases such as dyslipidemia, type 2 diabetes, hypertension, obesity, and metabolic syndrome); (iii) a randomized controlled trial, with the exercise group performing only regular aerobic exercise and the control group not exercising, and neither group receiving intervention such as improved diet or a change in lifestyle; (iv) intervention lasting 4 weeks or longer; (v) studies describing the mean HDL-C, LDL-C, TC, or TG level and its standard deviation (SD) in the exercise and control groups before and after the intervention. The identified articles were first screened by title and abstract, and the full text of the article was obtained if the studies included interventions involving exercise and those examining the effect of exercise on the lipid and lipoprotein levels in Asians. Once these studies were identified, two authors (Igarashi and Akazawa) determined whether the study should be included in this meta-analysis. If the two authors disagreed, the third author (Maeda) made a final decision on whether to include the study.

Data Extraction and Assessing the Risk of Bias

Data [mean HDL-C, LDL-C, TC, or TG, mean body mass index (BMI), and these SDs] and intervention details (number of subjects, type of aerobic exercise, intensity, time, frequency, and duration of the intervention) were ascertained from studies for meta-analysis. All the serum lipid and lipoprotein data were standardized to mg/dL. Data expressed in mmol/L were converted to mg/dL (for cholesterol, the level was multiplied by 38.7; for TG, the level was multiplied by 88.7). BMI was selected as a secondary outcome.

Two authors (Igarashi and Akazawa) used the Cochrane Collaboration tool, which consists of six domains, to assess the risk of bias in each trial[21]: (i) random sequence generation, (ii) allocation concealment, (iii) blinding, (iv) incomplete outcome data, (v) selective reporting, and (vi) other bias. Each domain was ranked in one of three categories: low risk, unclear, or high risk.

Statistical Analyses

The mean difference (MD) in HDL-C, LDL-C, TC, TG, and BMI was examined for each trial. MD was defined as follows: (mean value at post-intervention in the exercise group − mean value at baseline in the exercise group) − (mean value at post-intervention in the control group − mean value at baseline in the control group). The weighted MD (WMD), i.e., overall MD, was weighted by the inverse variance of differences from baseline to final assessment in each trial and calculated with a random-effects model using the DerSimonian−Laird method[22]. The correlation coefficient between the baseline and the final assessment was assumed to be 0.50[23]. Cochran Q statistics were

Table 1. Search strategy in a database

Source	Terms searched	Results (articles)
MEDLINE	(("Dyslipidemias/blood"[Mesh] OR "Dyslipidemias/metabolism"[Mesh] OR "Dyslipidemias/physiology"[Mesh] OR "Dyslipidemias/prevention and control"[Mesh] OR "Dyslipidemias/therapy"[Mesh]) OR ("Hyperlipidemias/blood"[Mesh] OR "Hyperlipidemias/physiopathology"[Mesh] OR "Hyperlipidemias/prevention and control"[Mesh] OR "Hyperlipidemias/therapy"[Mesh]) OR ("Lipoproteins/blood"[Mesh] OR "Lipoproteins/metabolism"[Mesh] OR "Lipoproteins/physiology"[Mesh]) OR ("Cholesterol/blood"[Mesh] OR "Cholesterol/metabolism"[Mesh] OR "Cholesterol/physiology"[Mesh]) OR ("Cholesterol, HDL/blood"[Mesh] OR "Cholesterol, HDL/metabolism"[Mesh] OR "Cholesterol, HDL/physiology"[Mesh]) OR ("Cholesterol, LDL/blood"[Mesh] OR "Cholesterol, LDL/metabolism"[Mesh] OR "Cholesterol, LDL/physiology"[Mesh]) OR ("Triglycerides/blood"[Mesh] OR "Triglycerides/metabolism"[Mesh] OR "Triglycerides/physiology"[Mesh]) OR ("Lipids/blood"[Mesh] OR "Lipids/metabolism"[Mesh] OR "Lipids/physiology"[Mesh]) OR ("Metabolic Syndrome/blood"[Mesh] OR "Metabolic Syndrome/metabolism"[Mesh] OR "Metabolic Syndrome/physiology"[Mesh])) AND (("Exercise/blood"[Mesh] OR "Exercise/metabolism"[Mesh] OR "Exercise/methods"[Mesh] OR "Exercise/physiology"[Mesh]) OR ("Exercise Therapy/methods"[Mesh] OR "Exercise Therapy/therapy"[Mesh]) OR "Physical Fitness/physiology"[Mesh] OR "Physical Fitness/physiology"[Mesh] OR "Walking/physiology"[Mesh] OR "Bicycling/physiology"[Mesh] OR "Running/physiology"[Mesh] OR "Jogging/physiology"[Mesh] OR ("Life Style/blood"[Mesh] OR "Life Style/metabolism"[Mesh] OR "Life Style/methods"[Mesh] OR "Life Style/physiology"[Mesh] OR "Life Style/therapy"[Mesh]))	1624
EMBASE	('exercise'/exp OR 'walking'/exp OR 'running'/exp OR 'bicycling'/exp OR 'physical fitness'/exp OR 'kinesiotherapy'/exp OR 'life style'/exp) AND ('dyslipidemia'/exp OR 'hyperlipidemia'/exp OR 'lipoprotein'/exp OR 'cholesterol'/exp OR 'high density lipoprotein'/exp OR 'low density lipoprotein'/exp OR 'lipid'/exp OR 'triacylglycerol'/exp OR 'metabolic syndrome x'/exp) AND [adult]/lim AND [humans]/lim AND [randomized controlled trial]/lim'	2181
SPORTDiscus	(DE "HYPERLIPIDEMIA" OR DE "HYPERCHOLESTEREMIA" OR DE "BLOOD lipoproteins" OR DE "BLOOD lipids" OR DE "BLOOD proteins" OR DE "LIPOPROTEINS" OR DE "HIGH density lipoproteins" OR DE "LOW density lipoproteins" OR DE "CHOLESTEROL") AND (DE "EXERCISE" OR DE "EXERCISE for men" OR DE "EXERCISE for women" OR DE "EXERCISE for middle-aged persons" OR DE "EXERCISE therapy" OR DE "EXERCISE therapy for older people" OR DE "AEROBIC exercises" OR DE "PHYSIOLOGICAL therapeutics" OR DE "WALKING" OR DE "CYCLING" OR DE "RUNNING" OR DE "PHYSICAL fitness")	955
The Cochrane library	#1 MeSH descriptor: [Dyslipidemias] explode all trees #2 MeSH descriptor: [Hyperlipidemias] explode all trees #3 MeSH descriptor: [Lipids] explode all trees #4 MeSH descriptor: [Lipoproteins] explode all trees #5 MeSH descriptor: [Cholesterol] explode all trees #6 MeSH descriptor: [Cholesterol HDL] explode all trees #7 MeSH descriptor: [Cholesterol LDL] explode all trees #8 MeSH descriptor: [Triglycerides] explode all trees #9 MeSH descriptor: [Metabolic Syndrome] explode all trees #10 MeSH descriptor: [Exercise] explode all trees #11 MeSH descriptor: [Exercise Therapy] explode all trees #12 MeSH descriptor: [Physical Fitness] explode all trees #13 MeSH descriptor: [Walking] explode all trees #14 MeSH descriptor: [Running] explode all trees #15 MeSH descriptor: [Bicycling] explode all trees #16 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9) AND (#10 OR #11 OR #12 OR #13 OR #14 OR #15)	2380
Google Scholar	(dyslipidemia OR hyperlipidemia OR lipid OR lipoprotein OR cholesterol) AND (exercise OR "exercise therapy" OR "physical fitness") AND (Japan OR Korea OR Taiwan OR China)	71

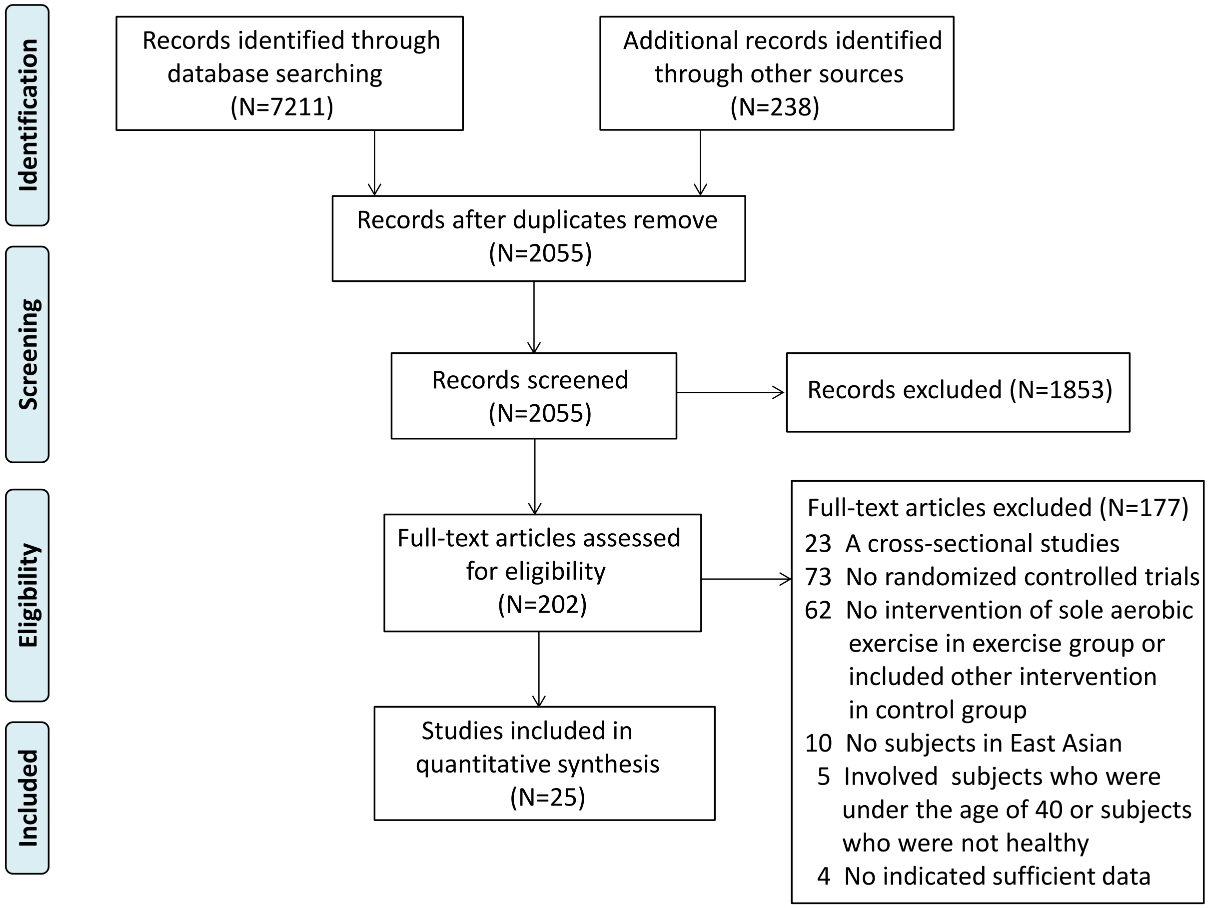

Fig. 1. PRISMA flow diagram regarding article selection for the meta-analysis.

calculated, and the heterogeneity of WMD was examined among trials. The I^2 statistic represented the level of heterogeneity. An I^2 of 25% or lower indicated a low risk, an I^2 of 25%−75% indicated a moderate risk, and an I^2 greater than 75% indicated a high risk[24)].

Subgroup analyses of WMD in the HDL-C, LDL-C, TC, and TG levels were performed by classifying trials. The study group was stratified into 14 categories: dyslipidemia, no dyslipidemia, no medication, overweight, not overweight, significant decrease in the MD in BMI, no significant decrease in the MD in BMI, walking, jogging, bicycle ergometer, moderate-intensity exercise, vigorous-intensity exercise, exercise volume ≥150 min/week, and exercise volume <150 min/week. Dyslipidemia was defined based on the Japan Atherosclerosis Society guidelines[25)], and trials with a mean HDL-C <40 mg/dL, mean LDL-C ≥140 mg/dL, or mean TG ≥150 mg/dL of subjects were designated as having dyslipidemic subjects. If none of the subjects in a trial was taking medication, then a trial was categorized as no medication. Overweight was defined in accordance with WHO[26)], and trials involving subjects with a mean BMI ≥25.0 kg/m^2 were designated as having overweight subjects. On the basis of the American College of Sports Medicine (ACSM) guidelines[27)], moderate-intensity exercise was defined as 55%−69% of the maximum heart rate (HR_{max}). Trials involving exercise at 70% or greater of HR_{max} were categorized as involving vigorous-intensity exercise. If a trial indicated exercise intensity as a percentage of maximum oxygen uptake, the value was converted to a percentage of HR_{max} using the equation of Londeree and Ames[28)]. Exercise volume was based on the exercise volume as recommended in the American Heart Association (AHA) and the ACSM guidelines[29)]. In addition, a sensitivity analysis was used to evaluate the influence of a risk of bias according to the Cochrane Risk of Bias tool[21)]. Trials falling into one or more domains of a high risk of bias were excluded, and the WMD in HDL-C, LDL-C, TC, and TG was then calculated.

Publication bias was evaluated by assessing the symmetry of funnel plots produced by the MD in serum lipids or lipoproteins (x-axis) and the inverse of

Table 2. Characteristics of the analyzed randomized controlled trials

Authors name	Number of Subjects (male/female)	Age (years)	Type	Intensity	Time (min)	Frequency (sessions/week)	Time × frequency (min)	Duration (weeks)
Sasaki *et al*[32], 1989, Japan	20 (8/12)	51.0 ± 9.5	B	LT level	60	3	180	10
Fukahori *et al*[33], 1999, Japan	101 (101/0)	48.9 ± 5.4	W	70-75% of HR_{max}	20	3	60	24
Higashi *et al*[34], 1999, Japan	17 (13/4)	46.9 ± 9.2	W	52% of $\dot{V}O_{2max}$	30	6	180	12
Higashi *et al*[35], 1999, Japan	27 (20/7)	52.5 ± 9.5	W	52% of $\dot{V}O_{2max}$	30	6	180	12
Sunami *et al*[36], 1999, Japan	40 (20/20)	67.5 ± 4.0	B	50% of $\dot{V}O_{2max}$	60	3	180	20
Tsai *et al*[37], 2002, Taiwan	23 (12/11)	48.0 ± 7.8	W/J	65% of HR_{max}	30	3	90	12
Tsai *et al*[38], 2002, Taiwan	42 (23/19)	41.3 ± 8.6	W/J	65% of HR_{max}	30	3	90	12
Tsuda *et al*[39], 2003, Japan	16 (16/0)	47.6 ± 10.6	W/J	AT level	50	2	100	24
Maeda *et al*[40], 2004, Japan	15 (0/15)	63.3 ± 4.0	B	VT level	30	5	150	12
Yoshizawa *et al*[41], 2009, Japan	24 (0/24)	48.0 ± 8.8	B	65% of $\dot{V}O_{2max}$	30	2	60	12
Uchikawa *et al*[42], 2010, Japan	37 (18/19)	52.9 ± 12.8	W	Instructed to walk briskly 10000 steps/day	N/A	N/A	N/A	8
Cho *et al*[43], 2011a, Republic of Korea	23 (0/23)	45.4 ± 7.3	W	40-50% of $\dot{V}O_{2max}$	N/A	3	N/A	12
Cho *et al*[43], 2011b, Republic of Korea	22 (0/22)	45.4 ± 7.3	W	70-75% of $\dot{V}O_{2max}$	N/A	3	N/A	12
Choi *et al*[44], 2012, Republic of Korea	75 (0/75)	54.4 ± 6.6	W	3.6-6.0 METs	60	5	300	12
Eguchi *et al*[45], 2012a, Japan	20 (0/20)	51.9 ± 8.4	B	60% of $\dot{V}O_{2max}$	30	3	90	12
Eguchi *et al*[45], 2012b, Japan	18 (0/18)	51.9 ± 10.5	B	50% of $\dot{V}O_{2max}$	30	3	90	12
Kim *et al*[46], 2012, Republic of Korea	30 (0/30)	54.5 ± 2.8	O	68% of HR_{max}	60	3	180	16
Lee *et al*[47], 2012a, Republic of Korea	14 (0/14)	40.0 ± 4.6	J	70% of $\dot{V}O_{2max}$	N/A	4.5	N/A	14
Lee *et al*[47], 2012b, Republic of Korea	15 (0/15)	40.1 ± 4.7	J	50% of $\dot{V}O_{2max}$	N/A	4.5	N/A	14
Miyaki *et al*[48], 2012, Japan	22 (0/22)	60.0 ± 6.5	W/B	70-75% of HR_{max}	38	4	152	8
Ohta *et al*[49], 2012, Japan	26 (0/26)	71.9 ± 6.0	O	LT level	15	3	140	12
Sugawara *et al*[50], 2012, Japan	27 (0/27)	59.0 ± 7.4	W/B	70-75% of HR_{max}	43	5	170	12
Uchikawa *et al*[51], 2012, Japan	44 (22/22)	55.0	W	Instructed to walk briskly 10000 steps/day	N/A	N/A	N/A	8
Kim *et al*[52], 2014, Republic of Korea	32 (0/32)	46.4 ± 3.2	W	50-60% of $\dot{V}O_{2max}$	30	3	90	12
Zhang *et al*[53], 2014, China	111 (0/111)	47.2 ± 4.9	W	100m within 60-70 second	30	3	90	12
Nishida *et al*[54], 2015, Japan	62 (0/62)	70.1 ± 6.2	O	LT level	15	3	140	12
Ohta *et al*[55], 2015, Japan	65 (26/39)	60.2 ± 9.4	W	Instructed to walk briskly 10000 steps/day	45	N/A	N/A	4
Tan *et al*[56], 2016, China	26 (0/26)	50.3 ± 6.6	W/J	Maximal fat oxidation HR	40	5	200	10

Age are expressed as weighted mean ± SD except that by a trial[51], which did not report the SD.
Abbreviations (exercise type): B, bicycle ergometer; J, jogging; O, other type of exercise; W, walking.
Abbreviation (exercise intensity): AT, anaerobic threshold; HR, heart rate; HR_{max}, maximum heart rate; LT, lactate threshold; METs, metabolic equivalents; N/A, not applicable; $\dot{V}O_{2max}$, maximum oxygen uptake; VT, ventilatory threshold.

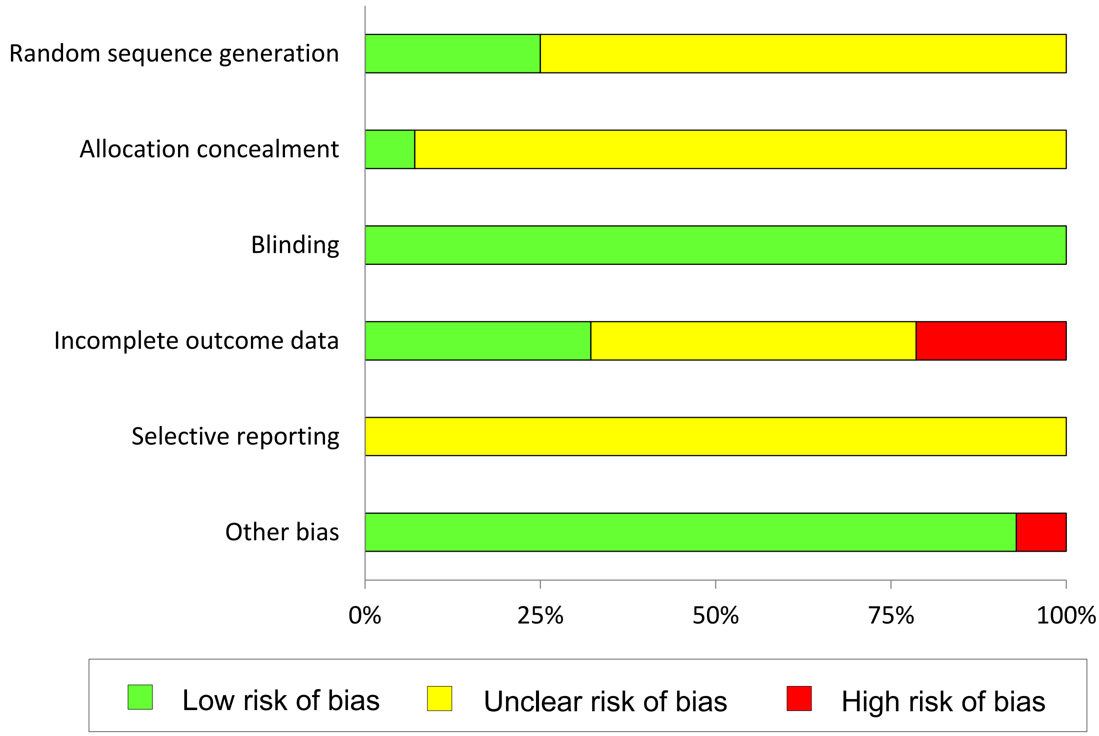

Fig. 2. Overall results for risk of bias.

the standard error (y-axis). First, Egger's regression test was used to evaluate the asymmetry of funnel plots[30]. Second, the trim and fill method of Duval and Tweedie was used to estimate the number of missing trials[31]. If the results suggested that trials were missing, then the WMD in lipids and lipoproteins was adjusted in light of the effect of these trials.

The results for baseline variables were expressed as the mean ± SD weighted by the number of subjects. In all the statistical tests, a P value <0.05 was considered to be statistically significant. The results of MD and WMD were expressed as the 95% confidence intervals (CI). The Comprehensive Meta-Analysis soft program (Version 2.2; Biostat, Inc., Englewood, NJ, USA) was used to perform the meta-analysis.

Results

Study Selection

Our literature search turned up 191 studies involving Asian subjects, an exercise intervention, and describing lipid and lipoprotein level data. Of these, 166 studies did not meet the selection criteria and were excluded from the meta-analysis (**Fig. 1**). As a result, 25 studies[32-56] (HDL-C in 28 trials, LDL-C in 19 trials, TC in 25 trials, and TG in 26 trials) were ultimately analyzed.

Characteristics of Studies

Twenty-three trials had a parallel study, and two trials had a cross-over study[42, 55]. **Table 2** shows the characteristics of the analyzed trials. The trials involved 994 subjects in total [509 subjects in exercise groups and 485 subjects in control groups, including 280 male (29.8%) and 714 female (70.2%) subjects] aged 53.6 ± 7.1 years. Seventeen trials were from Japan[32-36, 39-42, 45, 48, 51, 54, 55], seven were from the Republic of Korea[43, 44, 46, 47, 52, 53], two were from China[56], and two were from Taiwan[37, 38]. The baseline BMI was 24.2 ± 3.9 kg /m^2 (875 subjects in 25 trials[32-37, 39-43, 45-54, 56]).

Assessing the Risk of Bias

Fig. 2 shows the results for the assessed risk of bias. A random sequence was adequately generated in seven trials (25.0%)[36, 42-45], indicating a low risk of bias, but the method of randomization was unclear in the other trials. Allocation was adequately concealed in two trials (7.1%)[43], indicating a low risk of bias, but the method of allocation concealment was unclear in the other trials. Because blinding with regard to exercise intervention was not performed[57], all the trials were considered to have a low risk of bias. Outcome data were complete in nine trials (32.3%)[33, 38, 42, 44, 48, 49, 51, 54, 56], indicating a low risk of bias, but were incomplete in six trials (21.4%)[37, 43, 47, 53]; hence, these trials were considered to have a high risk of bias. Whether out-

Study name	n	Baseline	MD (95% CI)
		HDL-C (mg/dL)	
Sasaki *et al* [32], 1989	20	55.3 ± 10.8	7.4 (−3.0 to 17.8)
Fukahori *et al* [33], 1999	101	39.8 ± 5.9	−0.8 (−3.9 to 2.3)
Higashi *et al* [34], 1999	17	48.6 ± 6.6	5.9 (−2.5 to 14.3)
Higashi *et al* [35], 1999	27	52.6 ± 6.7	6.6 (−2.6 to 15.8)
Sunami *et al* [36], 1999	40	50.5 ± 9.1	6.5 (−0.9 to 13.9)
Tsai *et al* [37], 2002	23	50.7 ± 7.9	13.8 (1.5 to 26.1)
Tsai *et al* [38], 2002	42	50.8 ± 8.5	7.8 (−4.3 to 19.9)
Tsuda *et al* [39], 2003	16	50.0 ± 7.8	−4.0 (−10.8 to 2.8)
Maeda *et al* [40], 2004	15	52.9 ± 8.3	8.6 (−7.7 to 24.9)
Yoshizawa *et al* [41], 2009	24	63.6 ± 10.5	−7.1 (−18.9 to 4.7)
Uchikawa *et al* [42], 2010	37	55.4 ± 10.5	3.3 (0.4 to 6.2)
Cho *et al* [43], 2011a	23	38.9 ± 6.8	7.7 (1.6 to 13.8)
Cho *et al* [43], 2011b	22	42.8 ± 6.9	1.3 (−7.4 to 10.0)
Choi *et al* [44], 2012	75	46.2 ± 7.2	−2.0 (−7.6 to 3.6)
Eguchi *et al* [45], 2012a	18	63.4 ± 10.7	−1.4 (−13.2 to 10.4)
Eguchi *et al* [45], 2012b	20	60.2 ± 10.2	−0.7 (−9.9 to 8.4)
Kim *et al* [46], 2012	30	48.5 ± 9.0	5.5 (−1.7 to 12.8)
Lee *et al* [47], 2012a	14	53.0 ± 8.9	7.8 (−2.2 to 17.8)
Lee *et al* [47], 2012b	15	53.7 ± 8.6	3.4 (−6.5 to 13.3)
Miyaki *et al* [48], 2012	22	65.0 ± 12.1	7.0 (−3.8 to 17.8)
Ohta *et al* [49], 2012	26	72.6 ± 17.5	−1.2 (−7.8 to 5.4)
Sugawara *et al* [50], 2012	27	68.1 ± 12.2	3.0 (−4.5 to 10.5)
Uchikawa *et al* [51], 2012	44	56.2 ± 11.4	−0.7 (−6.6 to 5.2)
Kim *et al* [52], 2014	32	45.8 ± 11.9	8.5 (1.6 to 15.3)
Zhang *et al* [53], 2014	111	56.7 ± 11.1	1.5 (−1.7 to 4.7)
Nishida *et al* [54], 2015	62	66.5 ± 14.7	−0.9 (−5.6 to 3.8)
Ohta *et al* [55], 2015	65	56.0 ± 17.0	0.0 (−5.8 to 5.8)
Tan *et al* [56], 2016	26	52.5 ± 6.7	1.2 (−6.5 to 8.9)
Overall	**994**	**53.6 ± 10.5**	**2.2 (0.7 to 3.6)**

Q=19.3,P=0.02 for heterogeneity; I^2=45.1%

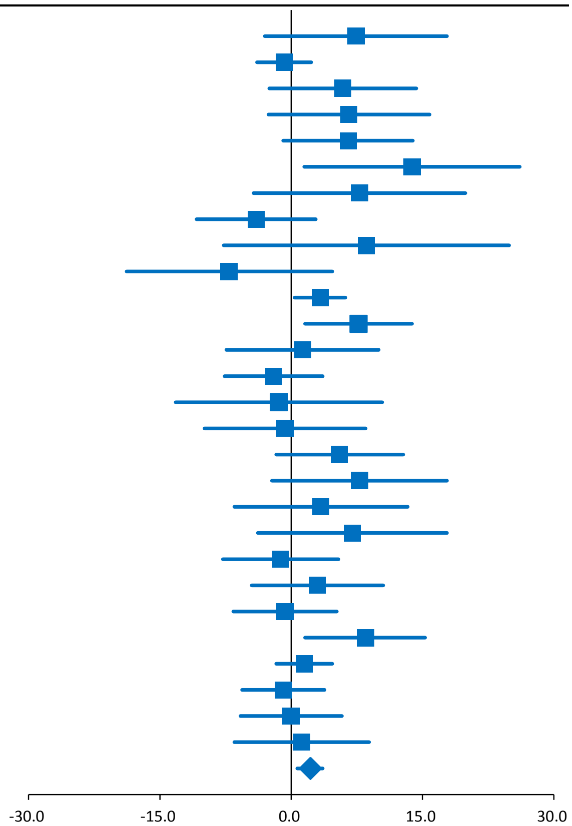

Fig. 3. Baseline HDL-C and forest plot for the MD in HDL-C. Each trial is represented by blue squares (MD) and widths (95% CI). The WMD (i.e., overall MD) is represented by blue rhombuses (WMD) and widths (95% CI).

Study name	n	Baseline	MD (95% CI)
		LDL-C (mg/dL)	
Sasaki *et al* [32], 1989	20	113.5 ± 27.9	8.0 (−24.4 to 40.4)
Higashi *et al* [34], 1999	17	133.2 ± 16.3	−28.2 (−51.1 to −5.3)
Higashi *et al* [35], 1999	27	140.6 ± 17.8	−17.7 (−40.6 to 5.2)
Sunami *et al* [36], 1999	40	134.1 ± 22.0	−1.9 (−18.3 to 14.5)
Tsai *et al* [37], 2002	23	129.5 ± 24.9	−23.0 (−48.8 to 2.8)
Tsai *et al* [38], 2002	42	128.0 ± 18.8	−16.4 (−30.3 to −2.5)
Maeda *et al* [40], 2004	15	126.2 ± 12.3	1.5 (−23.2 to 26.2)
Yoshizawa *et al* [41], 2009	24	119.4 ± 14.7	−5.6 (−22.4 to 11.2)
Eguchi *et al* [45], 2012a	18	129.9 ± 16.5	−2.8 (−27.3 to 21.7)
Eguchi *et al* [45], 2012b	20	128.7 ± 15.7	−7.5 (−32.3 to 17.3)
Kim *et al* [46], 2012	30	155.5 ± 19.6	−19.2 (−35.4 to −3.0)
Lee *et al* [47], 2012a	14	113.2 ± 20.6	8.9 (−15.4 to 33.2)
Lee *et al* [47], 2012b	15	106.1 ± 19.9	2.4 (−23.9 to 28.7)
Miyaki *et al* [48], 2012	22	136.2 ± 13.5	3.0 (−15.2 to 21.2)
Ohta *et al* [49], 2012	26	142.4 ± 27.6	7.0 (−11.2 to 25.6)
Sugawara *et al* [50], 2012	27	132.8 ± 15.7	−10.0 (−26.7 to 6.7)
Uchikawa *et al* [51], 2012	44	121.8 ± 35.9	−4.1 (−23.7 to 15.5)
Zhang *et al* [53], 2014	111	117.3 ± 16.6	0.8 (−6.5 to 8.1)
Nishida *et al* [55], 2015	62	140.0 ± 25.5	12.5 (−0.3 to 25.3)
Overall	**597**	**128.4 ± 22.7**	**−4.3 (−9.4 to 0.8)**

Q=26.7,P=0.09 for heterogeneity; I^2=32.6%

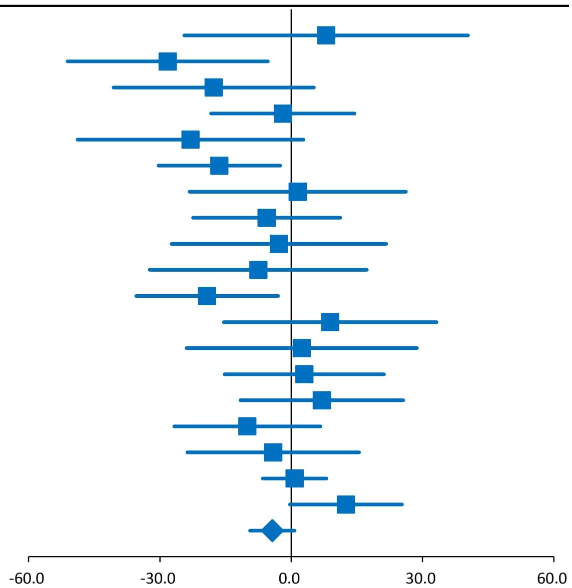

Fig. 4. Baseline LDL-C and forest plot for the MD in LDL-C. Each trial is represented by blue squares (MD) and widths (95% CI). The WMD (i.e., overall MD) is represented by blue rhombuses (WMD) and widths (95% CI).

Study name	n	Baseline	MD (95% CI)
		TC (mg/dL)	
Sasaki *et al* [32], 1989	20	209.5 ± 30.8	3.0 (−25.3 to 31.3)
Fukahori *et al* [33], 1999	101	230.7 ± 24.5	−5.3 (−16.2 to 5.6)
Higashi *et al* [34], 1999	17	195.0 ± 19.3	−22.5 (−48.2 to 3.2)
Higashi *et al* [35], 1999	27	199.2 ± 15.9	−10.8 (−29.9 to 8.3)
Sunami *et al* [36], 1999	40	205.4 ± 24.3	−2.0 (−20.3 to 16.3)
Tsai *et al* [37], 2002	23	202.3 ± 22.4	−17.1 (−50.2 to 16.0)
Tsai *et al* [38], 2002	42	193.6 ± 14.2	−14.5 (−24.2 to −4.8)
Tsuda *et al* [39], 2003	16	215.0 ± 33.7	12.0 (−24.8 to 48.8)
Maeda *et al* [40], 2004	15	221.0 ± 9.5	−8.1 (−25.4 to 9.2)
Yoshizawa *et al* [41], 2009	24	200.2 ± 20.2	−10.9 (−33.1 to 11.3)
Uchikawa *et al* [42], 2010	37	202.6 ± 33.3	−8.0 (−5.9 to 21.8)
Eguchi *et al* [45], 2012a	18	222.0 ± 25.2	−10.2 (−34.8 to 14.4)
Eguchi *et al* [45], 2012b	20	213.0 ± 23.9	−1.9 (−27.9 to 24.1)
Kim *et al* [46], 2012	30	209.5 ± 15.2	−26.5 (−38.9 to −14.0)
Lee *et al* [47], 2012a	14	190.0 ± 17.9	24.2 (0.2 to 48.2)
Lee *et al* [47], 2012b	15	187.7 ± 17.3	13.0 (−8.0 to 34.0)
Miyaki *et al* [48], 2012	22	222.8 ± 17.7	1.1 (−20.9 to 23.1)
Ohta *et al* [49], 2012	26	235.3 ± 28.4	2.5 (−16.5 to 21.5)
Sugawara *et al* [50], 2012	27	221.9 ± 19.3	−10.0 (−27.4 to 7.4)
Uchikawa *et al* [51], 2012	44	214.1 ± 44.2	−7.8 (−32.1 to 16.5)
Kim *et al* [52], 2014	32	205.8 ± 28.9	−9.3 (−26.6 to 8.0)
Zhang *et al* [53], 2014	111	197.5 ± 20.2	−24.0 (−33.0 to −15.7)
Nishida *et al* [54], 2015	62	226.5 ± 28.3	10.0 (−5.1 to 25.1)
Ohta *et al* [55], 2015	65	218.0 ± 23.0	1.0 (−9.7 to 11.7)
Tan *et al* [56], 2016	26	173.7 ± 16.5	−10.4 (−27.1 to 6.2)
Overall	**874**	**211.1 ± 25.7**	**−5.8 (−11.0 to −0.6)**

Q=54.7,P<0.01 for heterogeneity; I^2=56.2%

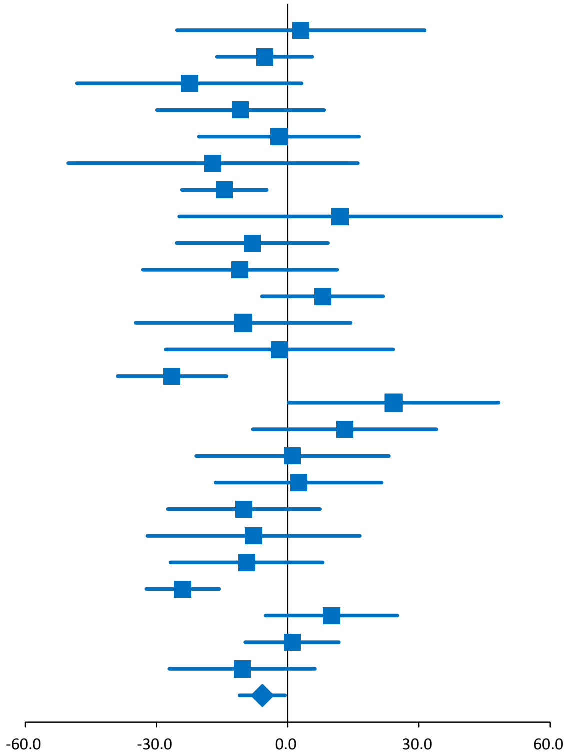

Fig. 5. Baseline TC and forest plot for the MD in TC. Each trial is represented by blue squares (MD) and widths (95% CI). The WMD (i.e., overall MD) is represented by blue rhombuses (WMD) and widths (95% CI).

comes were selectively reported was unclear in all trials. Some other form of bias was identified in two trials (7.1%)[51, 55]; hence, these trials were considered to have a high risk of bias.

Calculation of WMDs

Figs. 3−6 show forest plots of the MD in HDL-C, LDL-C, TC, and TG, respectively. The WMD in HDL-C, TC, and TG improved significantly. The WMD in HDL-C and TC contained significant heterogeneity (moderate risk). In addition, using 24 trials and 833 subjects[33-37, 39-43, 45-54, 56], the MD in BMI was calculated. The WMD in BMI was −0.5 kg/m^2 (95% CI, −0.6 to −0.3; Q=23.5; I^2=2.2%).

Table 3 shows the results of the subgroup analyses. Each category consisted of eight trials[33, 35, 43, 45, 46, 49, 51, 54] involving dyslipidemia, 20 trials[32, 34, 36-45, 47, 48, 50, 52, 53, 55, 56] involving no dyslipidemia, 9 trials[32, 36, 37, 40, 41, 46, 47, 50] involving subjects taking no medication, 11 trials[37, 39, 43-45, 47, 52] involving overweight subjects, 17 trials[32-36, 38, 40-42, 46, 48-51, 53-55] involving no overweight subjects, 5 trials[46, 49, 52, 54, 56] involving a significant decrease in the MD in BMI, 19 trials[33-37, 39-43, 45, 47, 48, 50, 51, 53] involving no significant decrease in the MD in BMI, 11 trials[33-35, 42-44, 51-53, 55] involving walking, 6 trials[37-39, 47, 56] involving jogging, 7 trials[32, 36, 40, 41, 45, 50] involving a bicycle ergometer, 8 trials[34-38, 43, 45, 47] involving moderate-intensity exercise, 8 trials[33, 41, 43, 45-48, 50] involving vigorous-intensity exercise, 10 trials[32, 34-36, 40, 44, 46, 48, 50, 56] involving exercise volume ≥150 min/week, and 11 trials[33, 37-39, 41, 45, 49, 52-54] involving exercise volume <150 min/week. The WMD in HDL-C, LDL-C, TC, and TG improved significantly in trials involving moderate-intensity exercise or an exercise volume ≥150 min/week and did not contain significant heterogeneity. In addition, the WMD in HDL-C improved significantly in trials involving no dyslipidemia, subjects taking no medication, no overweight subjects, no significant decrease in the MD in BMI, or walking. The WMD in TC also improved significantly in trials involving no overweight subjects or an exercise volume <150 min/week but contained significant heterogeneity. The WMD in TG improved significantly in trials except for those involving jogging or a bicycle ergometer. The WMD in HDL-C and TG did not contain significant heterogeneity in any of the categories.

When eight trials that included one or more domains with a high risk of bias were excluded, sensi-

TG (mg/dL)

Study name	n	Baseline	MD (95% CI)
Sasaki *et al* [32], 1989	20	117.0 ± 32.1	−7.0 (−62.6 to 48.6)
Fukahori *et al* [33], 1999	101	225.7 ± 188.7	−6.2 (−87.9 to 75.5)
Higashi *et al* [34], 1999	17	89.3 ± 38.0	−9.8 (−59.2 to 39.6)
Higashi *et al* [35], 1999	27	102.9 ± 12.9	−11.5 (−32.8 to 9.8)
Sunami *et al* [36], 1999	40	96.4 ± 32.0	−0.8 (−26.0 to 24.4)
Tsai *et al* [37], 2002	23	130.2 ± 30.0	−18.9 (−47.8 to 10.0)
Tsai *et al* [38], 2002	42	121.5 ± 42.5	−1.4 (−31.8 to 29.0)
Tsuda *et al* [39], 2003	16	120.0 ± 54.6	−0.0 (−61.2 to 61.2)
Maeda *et al* [40], 2004	15	118.5 ± 12.4	−33.2 (−69.5 to 3.1)
Uchikawa *et al* [42], 2010	37	130.2 ± 58.5	−4.8 (−29.6 to 20.0)
Cho *et al* [43], 2011a	23	142.7 ± 39.6	−56.8 (−111.6 to −2.0)
Cho *et al* [43], 2011b	22	118.0 ± 40.5	−30.9 (−77.6 to 15.8)
Eguchi *et al* [45], 2012a	18	164.0 ± 63.6	−72.8 (−215.9 to 70.3)
Eguchi *et al* [45], 2012b	20	144.6 ± 60.3	28.9 (−130.6 to 188.4)
Kim *et al* [46], 2012	30	110.7 ± 17.7	−13.8 (−31.2 to 3.5)
Lee *et al* [47], 2012a	14	119.5 ± 71.6	38.6 (−35.9 to 113.1)
Lee *et al* [47], 2012b	15	139.8 ± 69.1	36.2 (−82.5 to 154.9)
Miyaki *et al* [48], 2012	22	119.5 ± 71.6	−21.3 (−60.5 to 17.9)
Ohta *et al* [49], 2012	26	101.7 ± 28.0	−16.8 (−53.8 to 20.2)
Sugawara *et al* [50], 2012	27	105.1 ± 35.8	−14.0 (−46.3 to 18.3)
Uchikawa *et al* [51], 2012	44	181.5 ± 117.7	−32.8 (−110.1 to 44.5)
Kim *et al* [52], 2014	32	118.2 ± 35.9	−32.9 (−76.3 to 10.5)
Zhang *et al* [53], 2014	111	118.1 ± 53.3	−16.0 (−38.0 to 6.0)
Nishida *et al* [54], 2015	62	100.5 ± 29.8	−8.5 (−27.7 to 10.7)
Ohta *et al* [55], 2015	65	141.0 ± 43.2	−14.0 (−35.5 to 7.5)
Tan *et al* [56], 2016	26	121.7 ± 25.3	−29.3 (−58.8 to 0.2)
Overall	**895**	**137.3 ± 78.7**	**−13.7 (−20.0 to −7.9)**

Q=12.7,P=0.98 for heterogeneity; I^2=0.0%

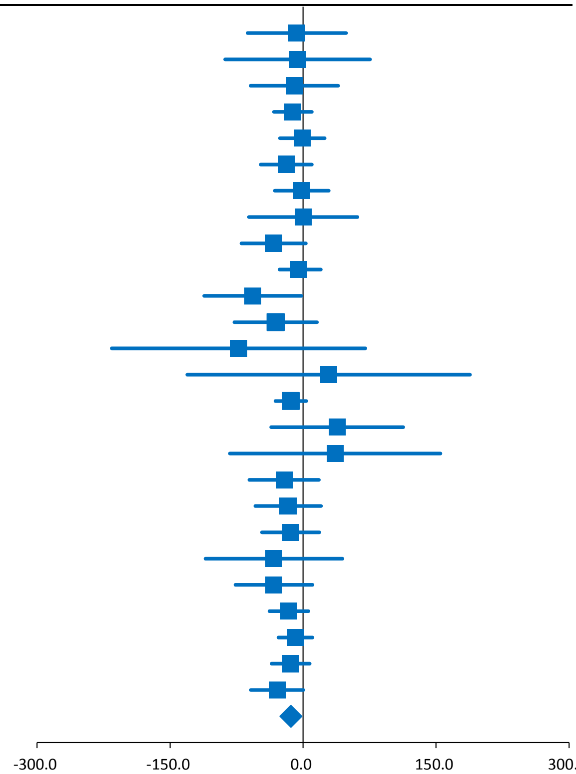

Fig. 6. Baseline TG and forest plot for the MD in TG. Each trial is represented by blue squares (MD) and widths (95% CI). The WMD (i.e., overall MD) is represented by blue rhombuses (WMD) and widths (95% CI).

tivity analysis indicated that the WMD in HDL-C, TC, and TG improved significantly (HDL-C: 1.9 mg/dL, 95% CI, 0.1 to 3.7; TC: −6.7 mg/dL, 95% CI, −11.6 to −1.8; TG: −12.4 mg/dL, 95% CI, −19.8 to −5.1), but the WMD in LDL-C did not improve significantly (−5.5 mg/dL, 95% CI, −12.0 to 1.1). All outcomes did not contain significant heterogeneity (HDL-C, 24.4%; LDL-C, 39.9%; TC, 32.3%; TG, 0.0%).

Publication Bias

Fig. 7 shows the funnel plots for publication bias with regard to HDL-C, LDL-C, TC, and TG. Egger's regression test indicated an intercept of 0.82 (P=0.09) for HDL-C, −0.79 (P=0.29) for LDL-C, 1.64 (P=0.04) for TC, and −0.12 (P=0.69) for TG. Duval and Tweedie's trim and fill method suggested that five trials were missing data for HDL-C, and three trials were missing data for TC. After adjusting for the effects of these missing trials, the WMD in HDL-C was estimated to be 1.5 mg/dL (95% CI, 0.01 to 3.1), and the WMD in TC was estimated to be −7.8 mmHg (95% CI, −13.0 to −2.5).

Discussion

The current work performed a meta-analysis of the effects of regular aerobic exercise on the lipid and lipoprotein levels in trials involving only East Asians. The results indicated that exercise resulted in a WMD in HDL-C of 2.2 mg/dL, a WMD in LDL-C of −4.3 mg/dL, a WMD in TC of −5.8 mg/dL, and a WMD in TG of −13.7 mg/dL. However, the WMD in LDL-C did not improve significantly, and the WMD in HDL-C and TC contained significant heterogeneity.

The current meta-analysis assumed that heterogeneity of the WMD in lipid and lipoprotein levels would be influenced by subjects' characteristics, form of exercise, or exercise volume. Accordingly, subgroup analyses were performed. First, this work focused on moderate-intensity exercise as recommended by the ACSM guidelines for promoting and maintaining health[27]. When trials were limited to those involving moderate-intensity exercise (55%−69% of HR_{max}), the WMD in HDL-C, LDL-C, TC, and TG improved significantly, and significant heterogeneity was not noted. When, however, trials were limited to those involving vigorous-intensity exercise (70% or greater than that

Table 3. Baseline and WMD in subgroup analyses

Category	Trials (n)	Changes in lipid and lipoprotein levels, mg/dL		Heterogeneity	
		Baseline	WMD (95% CI)	Q	I^2 %
HDL-C					
Dyslipidemia	8 (331)	53.0 ± 10.8	1.3 (−1.3 to 3.9)	10.5	33.0
No dyslipidemia	20 (663)	53.9 ± 10.3	2.7 (1.0 to 4.4)	22.4	15.2
No medication	9 (208)	55.0 ± 9.7	5.2 (2.1 to 8.3)	7.2	0.0
Overweight	11 (284)	49.3 ± 8.5	2.8 (−0.4 to 6.0)	17.1	41.7
No overweight	17 (710)	55.1 ± 11.1	1.8 (0.3 to 3.2)	17.5	8.3
Significant decrease in the MD in BMI	5 (176)	58.5 ± 12.9	2.2 (−1.5 to 6.0)	6.8	40.8
No significant decrease in the MD in BMI	19 (616)	52.8 ± 9.6	2.4 (0.6 to 4.2)	23.9	24.7
Walking	11 (554)	50.7 ± 10.1	2.1 (0.2 to 4.1)	15.9	37.2
Jogging	6 (136)	51.5 ± 8.0	3.7 (−1.4 to 8.8)	8.7	42.6
Bicycle ergometer	7 (164)	58.7 ± 10.3	2.7 (−0.9 to 6.3)	6.0	0.0
Moderate-intensity exercise	8 (205)	50.8 ± 8.2	6.4 (3.3 to 9.6)	3.7	0.0
Vigorous-intensity exercise	8 (260)	50.6 ± 8.9	1.3 (−1.4 to 4.0)	8.0	12.8
Exercise volume ≥ 150 min/week	10 (299)	52.6 ± 8.8	3.7 (1.1 to 6.2)	7.1	0.0
Exercise volume < 150 min/week	11 (475)	54.2 ± 10.8	0.7 (−1.8 to 3.1)	16.2	38.3
LDL-C					
Dyslipidemia	6 (207)	135.2 ± 28.0	−3.2 (−14.8 to 8.5)	12.0	58.3
No dyslipidemia	13 (390)	124.0 ± 18.5	−4.9 (−10.4 to 0.5)	14.4	16.4
No medication	9 (208)	128.8 ± 20.4	−6.5 (−13.2 to 0.3)	7.6	0.0
Overweight	5 (90)	123.0 ± 20.0	−4.2 (−15.4 to 7.1)	3.5	0.0
No overweight	14 (507)	129.3 ± 23.1	−4.5 (−10.5 to 1.5)	23.2*	44.0
Significant decrease in the MD in BMI	3 (118)	144.5 ± 24.6	0.3 (−19.4 to 20.1)	9.5*	78.9
No significant decrease in the MD in BMI	14 (417)	124.9 ± 22.3	−3.4 (−8.0 to 1.1)	12.1	0.0
Walking	4 (199)	122.7 ± 25.3	−9.4 (−22.7 to 3.9)	7.3	58.8
Jogging	4 (94)	122.7 ± 20.9	−8.6 (−22.5 to 5.4)	5.0	39.5
Bicycle ergometer	7 (164)	127.4 ± 18.9	−4.2 (−11.9 to 3.6)	1.4	0.0
Moderate-intensity exercise	7 (182)	130.3 ± 19.9	−12.4 (−20.3 to −4.5)	6.4	5.9
Vigorous-intensity exercise	6 (137)	133.4 ± 16.7	−6.7 (−14.5 to 1.0)	5.1	2.8
Exercise volume ≥ 150 min/week	8 (198)	135.5 ± 19.1	−8.9 (−16.9 to −0.9)	8.9	21.7
Exercise volume < 150 min/week	8 (362)	127.4 ± 20.4	−2.5 (−10.3 to 5.2)	13.3	47.3
TC					
Dyslipidemia	7 (308)	221.5 ± 30.4	−7.1 (−17.3 to 3.0)	15.4*	61.2
No dyslipidemia	18 (566)	205.3 ± 22.7	−5.2 (−11.5 to 1.2)	39.3*	56.7
No medication	9 (208)	206.4 ± 20.9	−4.9 (−15.7 to 6.0)	20.6*	60.2
Overweight	8 (164)	200.8 ± 24.1	−0.8 (−10.7 to 9.0)	10.0	30.0
No overweight	17 (710)	213.2 ± 26.0	−7.4 (−13.5 to −1.4)	41.5*	61.5
Significant decrease in the MD in BMI	5 (176)	213.3 ± 25.2	−7.3 (−21.0 to 6.5)	15.1*	73.5
No significant decrease in the MD in BMI	17 (571)	210.2 ± 26.8	−5.2 (−12.0 to 1.6)	34.5*	56.3
Walking	8 (434)	212.1 ± 28.0	−8.3 (−17.5 to 0.9)	23.1*	69.7
Jogging	6 (136)	192.8 ± 19.9	−0.5 (−14.5 to 1.3)	13.8*	63.8
Bicycle ergometer	7 (164)	212.0 ± 23.0	−6.5 (−14.4 to 1.4)	1.2	0.0
Moderate-intensity exercise	7 (182)	200.6 ± 20.0	−9.2 (−17.1 to −1.4)	7.2	17.2
Vigorous-intensity exercise	7 (238)	219.3 ± 21.5	− 7.0 (−18.1 to 4.0)	16.2*	63.0
Exercise volume ≥ 150 min/week	9 (224)	205.8 ± 19.8	−11.5 (−18.3 to −4.7)	9.7	17.4
Exercise volume < 150 min/week	11 (475)	213.2 ± 24.0	−8.0 (−15.6 to −0.5)	22.5*	55.6

(**Cont. Table 3**)

Category	Trials (n)	Changes in lipid and lipoprotein levels, mg/dL		Heterogeneity	
		Baseline	WMD (95% CI)	Q	I^2 %
TG					
Dyslipidemia	8 (331)	159.8 ± 115.6	− 14.0 (− 24.2 to − 3.9)	3.6	0.0
No dyslipidemia	18 (564)	123.1 ± 46.8	− 14.0 (− 21.6 to − 5.5)	9.0	0.0
No medication	8 (184)	113.6 ± 38.4	− 12.1 (− 23.0 to − 1.2)	4.8	0.0
Overweight	10 (209)	130.9 ± 48.3	− 23.3 (− 38.6 to − 8.0)	7.0	0.0
No overweight	16 (686)	138.3 ± 86.0	− 11.8 (− 18.7 to − 4.8)	3.8	0.0
Significant decrease in the MD in BMI	5 (176)	108.8 ± 28.5	− 15.7 (− 26.5 to − 4.8)	2.0	0.0
No significant decrease in the MD in BMI	18 (633)	145.3 ± 96.2	− 13.6 (− 22.3 to − 4.9)	9.8	0.0
Walking	10 (479)	151.2 ± 97.8	− 15.6 (− 25.5 to − 5.6)	4.4	0.0
Jogging	6 (136)	124.6 ± 47.3	− 12.2 (− 28.1 to 3.7)	4.5	0.0
Bicycle ergometer	6 (140)	119.0 ± 41.7	− 12.0 (− 28.5 to 4.4)	3.1	0.0
Moderate-intensity exercise	8 (205)	119.9 ± 41.1	− 10.8 (− 20.8 to − 1.8)	5.3	0.0
Vigorous-intensity exercise	7 (236)	164.2 ± 129.1	− 14.7 (− 27.9 to − 1.6)	3.2	0.0
Exercise volume ≥ 150 min/week	9 (224)	108.1 ± 34.5	− 14.5 (− 23.9 to − 5.2)	3.4	0.0
Exercise volume < 150 min/week	10 (451)	142.9 ± 97.9	− 12.8 (− 23.5 to − 2.2)	3.0	0.0

BMI: body mass index; CI: confidence intervals; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MD: mean difference; TC: total cholesterol; TG: triglyceride; WMD: weighted mean difference.
Trials are expressed as the number of trials (number of subjects)
Baseline lipids and lipoproteins are expressed as the mean ± SD
Trials with a mean HDL-C < 40 mg/dL, mean LDL-C ≥ 140 mg/dL, or mean TG ≥ 150 mg/dL of subjects were designated as having dyslipidemic subjects.
Trials involving subjects with a mean BMI ≥ 25.0 kg/m^2 were designated as having overweight subjects.
*Significant heterogeneity (P < 0.05)

of HR_{max}), the WMD in HDL-C, LDL-C, and TC did not improve significantly. Previous meta-analyses have not reported the relationship between exercise intensity and changes in the lipid and lipoprotein levels[10-16], but exercise at a moderate level of intensity is presumably sufficient to improve the lipid and lipoprotein levels in East Asians. Second, the current meta-analysis focused on exercise volume (a total of 150 min/week), as recommended by the AHA and the ACSM guidelines[29]. When trials were limited to those involving an exercise volume ≥ 150 min/week, the WMD in HDL-C, LDL-C, TC, and TG improved significantly, and significant heterogeneity was not noted. When, however, trials were limited to those involving exercise volume < 150 min/week, the WMD in TC and TG improved significantly, and significant heterogeneity in TC was noted. Thus, an improvement in lipid and lipoprotein levels is presumably related to exercise volume. Previous meta-analyses have yielded results similar to the current findings because HDL-C levels increased by 1.4 mg/dL for every 10 min an exercise session was prolonged[16] and because the HDL-C levels were related to calorie consumption (kcal/day)[11]. This relationship is also evident in blood pressure. A meta-analysis of trials involving East Asians reported that an exercise volume ≥ 150 min/week significantly lowered the systolic blood pressure more than trials involving an exercise volume < 150 min/week[18]. Findings suggest that the ideal exercise volume to prevent or alleviate lifestyle-related diseases in East Asians is more than 150 min/week.

The current meta-analysis focused on the relationship between changes in lipid and lipoprotein levels and BMI. Most previous meta-analyses indicated that lipid and lipoprotein levels improved significantly, and that BMI decreased significantly as a result of regular aerobic exercise[10-12, 14, 15]. In the current meta-analysis, the WMD in BMI also decreased significantly. When, however, trials were limited to those involving a significant decrease in the MD in BMI, the WMD in HDL-C, LDL-C, and TC did not improve significantly. This suggests that improvement in the lipoprotein levels as a result of regular aerobic exercise may be independent of weight loss in East Asians. A second focus of the current meta-analysis was on the WMD in TG. In subgroup analyses, the WMD in TG improved significantly in trials except for those involving jogging and a bicycle ergometer. Significant heterogeneity

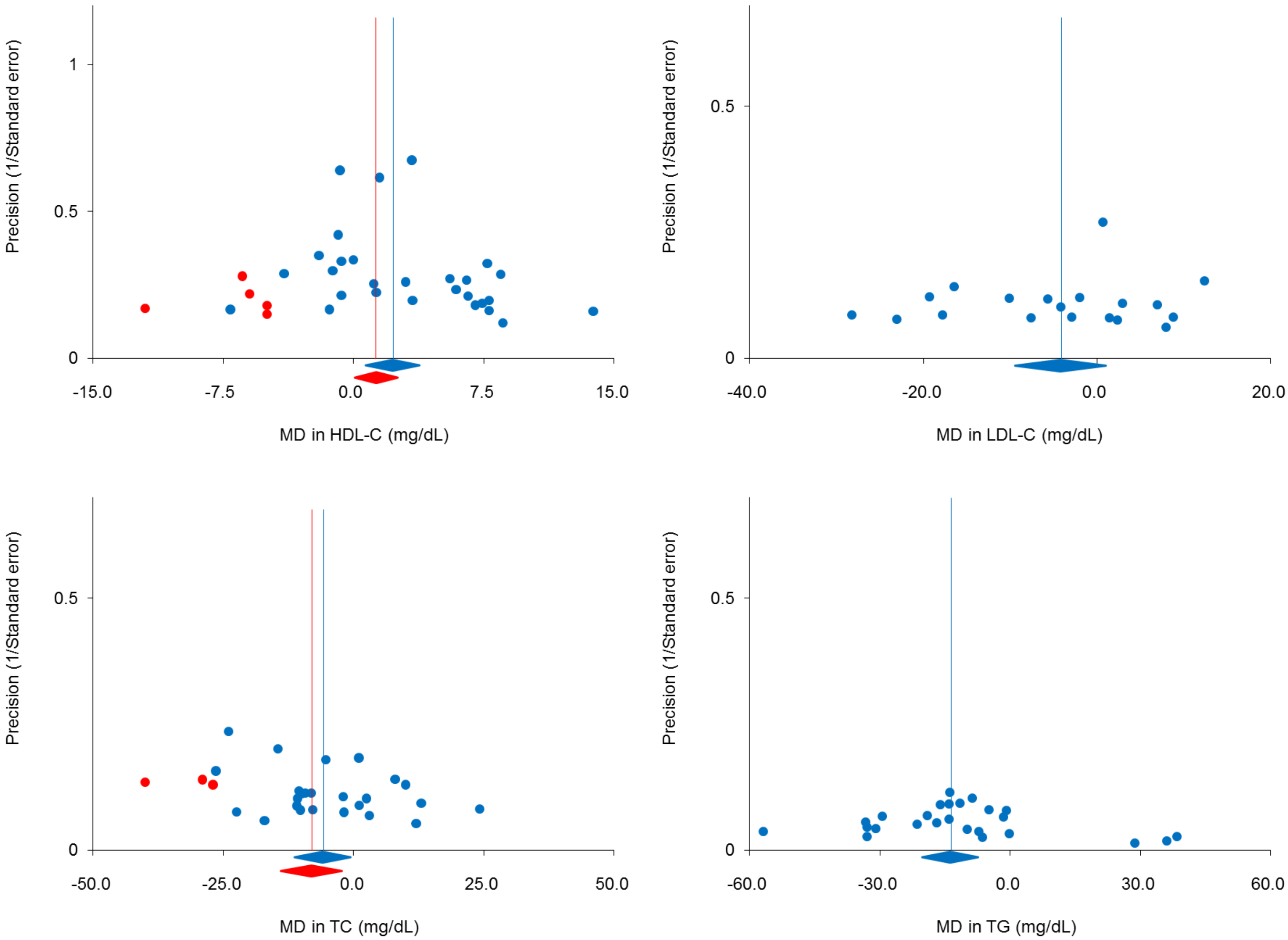

Fig. 7. Funnel plot of HDL-C, LDL-C, TC, and TG for each trial. Egger's test indicated that funnel plot of TC had significant asymmetry. Vertical blue lines and blue rhombuses indicate the WMD and 95% CI in HDL-C, LDL-C, TC, and TG. In the WMD in HDL-C and TC, the trim and fill method of Duval and Tweedie suggested that there were missing trials (red circles). Vertical red lines and red rhombuses indicate the WMD and 95% CI in these after adjusting for the missing trials.

was not noted in any of the categories. Previous meta-analyses reported a significant improvement in TG as a result of regular exercise, but the results contained significant heterogeneity[11, 14].

Looking specifically at East Asians in the current meta-analysis presumably alleviated heterogeneity and may indicate that improvement in the lipid and lipoprotein levels differs from that in other ethnicity groups. The WMD in HDL-C, LDL-C, and TC in the current meta-analysis was equivalent to values in previous meta-analyses, but improvement in the WMD in TG was greater in the current meta-analysis[11-16]. The mechanisms by which exercise improved the lipid and lipoprotein levels are still unclear, but several processes may account for these mechanisms. Insulin resistance may be related to dyslipidemia[58]. Because the incidence of type 2 diabetes differs among different ethnic groups, insulin resistance may differ among these groups[59]. Therefore, the mechanisms responsible for improvement in the lipid and lipoprotein levels as a result of exercise may differ among the different ethnic groups. Several trials cited in the current meta-analysis measured insulin-related outcomes. Nine trials[34, 35, 40, 42, 43, 46, 51, 55] measured serum insulin or homeostatic model assessment of insulin resistance (HOMA-IR)[60], but only three trials reported significant improvements in insulin-related outcomes and lipid and lipoprotein levels[43, 46]. In addition, the mechanism by which lipid and lipoprotein levels improved as a result of exercise may be associated with adipocytokines[61]. According to a large randomized controlled trial involving interventions to increase physical activity and reduce caloric intake, both the HDL-C and adiponectin levels increased, and changes in HDL-C levels were associated with changes in adiponectin levels as a result of these interventions[62]. A recent meta-analysis reported that aerobic exercise reduced serum leptin and increased adiponectin[63]. Four trials cited in the current meta-analysis measured the adipocytokine levels, and these trials reported that leptin or adiponectin levels improved significantly[42, 56] but that TNF-α did not improve significantly[47, 54]. Thus, the mechanisms for improvement in lipid and lipoprotein levels in East Asians may involve numerous factors, and identification of these factors is a topic for the future.

The current meta-analysis has several limitations. First, this meta-analysis may have been influenced by publication bias. Trials reporting HDL-C and TC may be missing. Even after adjusting for the influence of these missing trials, the WMD in HDL-C and TC still improved significantly. Trials indicating improvement in TC in particular were lacking. Therefore, including additional trials in the future will presumably indicate that aerobic exercise has a greater effect on TC in East Asians. Second, only a few trials involved subjects with dyslipidemia or subjects who were overweight. This limitation presumably influenced the results of the subgroup analysis of the WMD in HDL-C, LDL-C, and TC. When trials were limited to those involving subjects with dyslipidemia or overweight subjects, the WMD in HDL-C, LDL-C, and TC did not improve significantly. As mentioned earlier, the WMD in HDL-C, LDL-C, TC, and TG improved significantly when trials were limited to those involving moderate-intensity exercise or an exercise volume ≥150 min/week. Nonetheless, two of five trials that examined HR_{max} in subjects with dyslipidemia did not involve moderate-intensity exercise, and four of six trials that examined exercise volume in subjects with dyslipidemia did not involve an exercise volume ≥150 min/week. In addition, three of seven trials that examined HR_{max} in overweight subjects did not involve moderate-intensity exercise, and five of seven trials that examined exercise volume in overweight subjects did not involve an exercise volume ≥150 min/week. Thus, there may be issues with exercise intensity or volume in patients with dyslipidemia or in individuals who are overweight. In addition, few trials involved moderate-intensity exercise and an exercise volume ≥150 min/week[34-36]; hence, subgroup analysis was not possible in the current meta-analysis. Adding additional trials involving exercise of moderate-intensity and in a volume ≥150 min/week and performing analysis again may be a topic for the future.

Conclusion

Regular aerobic exercise improved the HDL-C, TC, and TG levels in East Asians. However, the results suggest that improvement depends on exercise intensity or exercise volume. The ideal form of exercise to improve lipid and lipoprotein levels is exercise of moderate-intensity and in a volume ≥150 min/week.

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Conflicts of Interests

None.

List of Abbreviations

HDL-C: high-density lipoprotein cholesterol
LDL-C: low-density lipoprotein cholesterol
TC: total cholesterol
TG: triglyceride
PRISMA: the Preferred Reporting Items for Systematic Reviews and Meta-analyses
PROSPERO: the International Prospective Register of Systematic Reviews
SD: standard deviation
BMI: body mass index
MD: mean difference
WMD: weighted mean difference
ACSM: the American College of Sports Medicine
HR_{max}: maximum heart rate
AHA: the American Heart Association
CI: confidence intervals
HOMA-IR: homeostatic model assessment of insulin resistance

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