Effects of muscle strength training combined with aerobic training versus aerobic training alone on cardiovascular disease risk indicators in patients with coronary artery disease: a systematic review and meta-analysis of randomised clinical trials

Tasuku Terada [1,2] Robert Pap,[3] Abby Thomas,[4] Roger Wei,[5] Takumi Noda,[6,7] Sarah Visintini,[8] Jennifer L Reed[2,9,10]

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For numbered affiliations see end of article.

Correspondence to
Dr Tasuku Terada; tasuku.terada@nottingham.ac.uk

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ABSTRACT

Objective To compare the effects of aerobic training combined with muscle strength training (hereafter referred to as combined training) to aerobic training alone on cardiovascular disease risk indicators in patients with coronary artery disease (CAD).
Design Systematic review with meta-analysis.
Data sources MEDLINE, Embase, CINAHL, SPORTDiscus, Scopus, trial registries and grey literature sources were searched in February 2024.
Eligibility criteria Randomised clinical trials comparing the effects of ≥4 weeks of combined training and aerobic training alone on at least one of the following outcomes: cardiorespiratory fitness (CRF), anthropometric and haemodynamic measures and cardiometabolic blood biomarkers in patients with CAD.
Results Of 13 246 studies screened, 23 were included (N=916). Combined training was more effective in increasing CRF (standard mean difference (SMD) 0.26, 95% CI 0.02 to 0.49, p=0.03) and lean body mass (mean difference (MD) 0.78 kg, 95% CI 0.39 kg to 1.17 kg, p<0.001), and reducing per cent body fat (MD −2.2%, 95% CI −3.5% to −0.9%, p=0.001) compared with aerobic training alone. There were no differences in the cardiometabolic biomarkers between the groups. Our subgroup analyses showed that combined training increases CRF more than aerobic training alone when muscle strength training was added to aerobic training without compromising aerobic training volume (SMD 0.36, 95% CI 0.05 to 0.68, p=0.02).
Conclusion Combined training had greater effects on CRF and body composition than aerobic training alone in patients with CAD. To promote an increase in CRF in patients with CAD, muscle strength training should be added to aerobic training without reducing aerobic exercise volume.

WHAT IS ALREADY KNOWN

⇒ Cardiorespiratory fitness is an important predictor of morbidity and mortality in patients with coronary artery disease (CAD).
⇒ Aerobic exercise training and muscle strength training can independently increase cardiorespiratory fitness in patients with CAD.

WHAT ARE THE NEW FINDINGS

⇒ Our systematic review of randomised clinical trials showed that combining aerobic and muscle strength exercise training increases cardiorespiratory fitness more than aerobic training alone in patients with CAD.
⇒ Our subgroup analyses showed that combined training has greater effects on cardiorespiratory fitness when muscle strength training is added to aerobic training without compromising aerobic training volume.
⇒ When aerobic exercise training volume was reduced to add muscle strength training, the change in cardiorespiratory fitness did not differ between combined and aerobic training alone but combined training improved body composition more than aerobic training alone.

BACKGROUND

Coronary artery disease (CAD) is the leading cause of death globally.[1] Although acute medical treatment, such as percutaneous coronary intervention, has reduced the number of deaths in patients with CAD,[2] such treatment does not improve pre-existing atherosclerotic risks. One in five patients discharged with myocardial infarction (MI) experience a subsequent cardiovascular event within 1 year (eg, stroke, MI or cardiovascular death), and the risk remains similarly high in those who survived the first year.[3] Secondary prevention guidelines highlight the importance of managing cardiovascular disease risk indicators (eg, obesity, hypertension, hyperlipidaemia and type 2 diabetes) in patients with CAD.[4 5]

Exercise-based cardiovascular rehabilitation (CR) involving continuous aerobic training (rhythmic cardiorespiratory endurance exercises, such as walking, jogging, running and cycling[6]) is a class IA recommendation for patients with CAD.[4] Continuous aerobic training improves cardiovascular disease risk indicators associated with secondary cardiovascular events, including cardiorespiratory fitness (CRF),[7] body mass,[8] triglycerides[9] and low-density lipoprotein cholesterol (LDL-C) concentrations[9] and reduces the risks of MI, hospitalisation and mortality.[10] Compared with continuous aerobic training, an increasing number of studies have

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shown that CR involving aerobic interval training (AIT, repetition of brief bouts of aerobic exercise interspersed by lower intensity recovery periods) elicits superior improvements in CRF,[11 12] body mass,[13] waist circumference,[13 14] per cent body fat,[14] abdominal fat,[14] lean mass,[13] fasting blood glucose,[13] triglycerides,[13 14] LDL-C[14] and diastolic blood pressure[13] in patients with CAD.

In addition to aerobic training, emerging evidence suggests that muscle strength training (strength-developing exercise that encompasses-free weights, machines, body weight, bands/tubing or any other objects that require one to exert force against a resistance[6]) can independently improve cardiovascular disease risk indicators.[15] Although its evidence on patients with CAD is limited, studies in non-CAD populations have shown that muscle strength training improves cardiovascular disease risk indicators associated with secondary cardiovascular events, including CRF,[16] body composition,[16 17] blood pressure,[16 17] glycated haemoglobin A1C (A1C),[17] LDL-C,[18 19] triglycerides[16] and total cholesterol,[18 19] independent of aerobic exercise. The European Society of Cardiology and the American Heart Association recommend muscle strength training as an adjunct therapy to aerobic training in patients with CAD.[20 21]

Meeting either aerobic or muscle strength training guidelines is associated with an approximately 20–35% reduced risk of cardiovascular disease mortality, whereas meeting both guidelines is associated with a 50% reduced risk of cardiovascular disease mortality.[15] The lower mortality risk in those who engage in combined training may be explained by a greater total volume of physical activity[15] and consequent improvements in cardiovascular disease risk indicators.[22–24] However, in patients with CAD, the effect of combined training compared with aerobic training alone on cardiovascular disease risk indicators remains unclear. Several randomised clinical trials in patients with CAD had small sample sizes (ie, n≤20 in each arm) and compared the effects of combined and aerobic training alone on selected cardiovascular disease risk indicators.[25–31] Further, existing reviews comparing combined training and aerobic training alone in patients with CAD have focused on physical performance[32–34] and body composition.[32 33] No study has systematically reviewed the effects of combined training on more comprehensive cardiovascular disease risk indicators in patients with CAD.

The primary purpose of this study was to systematically review randomised clinical trials, the gold standard of evidence for the research question, comparing the effects of combined training and aerobic training alone on cardiovascular disease risk indicators. The secondary purpose was to compare the effects of AIT combined with muscle strength training and AIT alone on cardiovascular disease risk indicators. It was hypothesised that combined training would be more effective in improving cardiovascular disease risk indicators.

METHODS

Study design

The protocol for this systematic review was prospectively registered with the international Prospective Register of Systematic Reviews (PROSPERO) on 23 July 2022 (registration #: CRD42022345938). The protocol was described in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) Protocols checklist.[35] This systematic review adhered to the most updated reporting guidelines of the PRISMA 2020 statement[36] and PRISMA in Exercise, Rehabilitation, Sport medicine and SporTs science, a guidance specific for the context of sport and exercise medicine, musculoskeletal rehabilitation and sports science.[37]

Eligibility criteria

Participants

Studies including adult patients (≥18 years old) with CAD with or without other cardiovascular or medical conditions were eligible.

Interventions

To address our study purpose (ie, to compare the effects of combined training and aerobic training alone on cardiovascular disease risk indicators), randomised clinical trials assigning participants into combined training or aerobic training alone with a duration of at least 4 weeks were included. Four weeks were chosen as a required period for physiological adaptations to occur in patients with CAD.[38 39] Exercise training could be combined with other interventions, such as nutritional counselling, stress management, smoking cessation, vocational counselling, psychological counselling and social work counselling. Aerobic training was defined as any structured, purposeful activity involving large muscle groups in a continuous and rhythmic manner.[6] Muscle strength training was defined as any structured exercise that required force to be applied against an external resistance using any major muscle group (eg, machine-based weight training, free-weight training or bodyweight exercise). AIT was defined as repeated bouts of relatively intense exercise interspersed by short periods of recovery.[40] When possible, exercise intensity was classified according to the American College of Sports Medicine (ACSM) guidelines.[6]

Comparators

Aerobic training alone was used as a comparator.

Outcomes

Eligible studies reported at least one of the following cardiovascular disease risk indicators: directly measured CRF, body mass index (BMI), lean mass, fat mass, waist circumference, waist-to-hip ratio, blood pressure, high-density lipoprotein cholesterol (HDL-C), LDL-C, triglycerides, total cholesterol, fasting glucose, A1C, insulin concentration or sensitivity. Due to its limitations,[6] body compositions assessed by skinfolds were excluded. We also explored additional outcomes including adherence as defined by the number of sessions attended by participants, dropouts and their reasons and adverse events.

Publication status and information sources

A peer-reviewed[41] search strategy was conducted on 11 August 2021 and updated on 5–12 February 2024, in MEDLINE, Embase, Cochrane Central Register of Controlled Trials, CINAHL, SPORTDiscus and Scopus (see online supplemental tables 1–6 for full search details). No limits to language or publication date were applied, but a search filter for randomised controlled trials was employed where applicable.[42 43] The main search concepts comprised of terms related to resistance-based exercise and CAD, and was informed by previously conducted systematic searches.[44]

For grey literature, we searched ProQuest Dissertations and Theses, Europe PubMed Central (PMC) for pre-prints published within the previous 2 years, and ClinicalTrials.gov and the WHO's International Clinical Trials Registry Platform in 2021. The search was updated in February 2024 (online supplemental tables 7–10). Conference abstract results in Embase were limited by publication date within 2 years of the searches, and a supplemental hand search was conducted in October 2021 and updated in February 2024 on a short list of relevant conferences (see online supplemental table 11 for full list) for any content not already indexed in Embase.

Selection process

Titles and abstracts of studies identified in our search strategies were uploaded into the Covidence Systematic Review Software (Veritas Health Innovation, Melbourne, Australia). Duplicate articles were automatically removed by the software. The title and abstract of each identified study were independently reviewed by two of the five authors (TT, AT, RW, TN and RP). Disagreements on study eligibility were resolved by discussion involving TT. Full texts of selected studies were uploaded to the Covidence Software. Each full text was independently reviewed by two of the five authors (TT, AT, RW, TN and RP) for eligibility. Any disagreement was resolved by consensus among the authors.

Data synthesis

A data extraction form was created using an Excel spreadsheet (Microsoft, USA). For each study, two of the five authors (TT, AT, RW, TN and RP) independently extracted: general study information (author, country, publication year); participants characteristics (sex, cardiac diagnoses, revascularisation procedures and medical conditions); study design; sample size; characteristics of combined and aerobic training alone (exercise frequency, intensity, time, type and progression); cardiovascular disease risk indicators and their assessment protocols. Adherence to the prescribed training, dropout rate and the number and types of adverse events during the study period were extracted by three separate authors (TT, TN and RP). All extracted data were verified for consistency by TT. Any inconsistencies between the two forms were resolved by discussion.

For continuous variables, the mean and SD at baseline, follow-up and changes from baseline were extracted. When not reported, mean changes were calculated by subtracting the pre-intervention value from the post-intervention values. The SD of change scores were calculated from pre-SD and post-SD values using a mean correlation coefficient calculated from studies reporting the mean and SD of pre, post and change as described in the Cochrane handbook.[45] The correlation coefficient of 0.5 was used for outcomes when it was not possible to calculate the correlation coefficient. In one study where post-SD was unavailable,[46] we used pre-SD for post-SD to estimate the SD of the change value. Multiple treatment groups from a single study were combined to create a single pairwise comparison.[45] Data presented in visual formats (ie, figures) were extracted using WebPlotDigitizer.[47] In one study that only reported a single pre and post CRF measure combining both training groups,[27] data were extracted from a previously published systematic review.[32]

Study risk of bias assessment

Study quality and reporting were assessed by the Tool for the assEssment of Study qualiTy and reporting in Exercise (TESTEX), a reliable tool specifically designed to facilitate a comprehensive review of exercise training trials.[48] The TESTEX is a 15-point scale; 5 points for study quality and 10 points for study reporting. The quality of the studies was classified as high (≥12 points), good (7–11 points) or low (≤6 points).[49] Two of five reviewers (TT, AT, RW, TN and RP) independently scored each domain. Agreement was reached by consensus.

Assessment of the certainty and strength of evidence

The certainty and strength of the evidence were assessed using a Grading of Recommendations, Assessment, Development and Evaluation approach.[50] Evidence was downgraded from high certainty when there was high risk of bias in: study limitations (risk of bias), inconsistency of results, indirectness of evidence and imprecision. Publication bias was only assessed for CRF by visually inspecting funnel plots as fewer than ten studies were included in the other meta-analyses.[51 52] One reviewer (TT) assessed the certainty of the evidence, and a second reviewer (RP) verified the assessment for accuracy. Any disagreement was resolved by discussion.

Statistical analysis

Statistical analyses were performed with Review Manager Software (RevMan Web, Cochrane Collaboration, Copenhagen, Denmark) using an inverse variance method. Because of heterogeneity in the methodology of the included studies, a random effects model was used for pooled analyses. The level of significance was set at $p<0.05$. Heterogeneity was assessed using the I^2 statistics with the estimates of <50% and ≥50% representing below moderate and substantial heterogeneity, respectively.[45]

Continuous outcomes were analysed using weighted mean differences with a 95% CI or standardised mean differences with 95% CI if different measurement scales were used. Because total exercise volume could emphasise the effects of combined training (ie, combined training group performing a greater total volume of exercise and thus more beneficial), when ≥2 studies were available for both subgroups, subgroup analyses were performed to assess the effects of combined training without reducing aerobic training volume and with reduced aerobic training volume when compared with aerobic training alone.

Equity, diversity and inclusion statement

Our research team is gender balanced (four men and three women) and included researchers from different career stages. Our study population included both women and men from various geographical locations (eg, Canada, seven European countries, Iran, Israel, Japan and the USA). Studies published in different languages (ie, French and Japanese) were included.

RESULTS

Study selection

Our search identified 17 438 studies. The full text was screened for 57 studies, of which 34 studies were excluded. One study was excluded because it reported median and IQRs due to non-normally distributed data.[53] As a result, 23 studies (N=916 patients with CAD) were included in this review. The process of study selection is summarised in figure 1.

Description of the included studies

A total of 23 single-centre randomised clinical trials published between 1995 and 2023 were included (online supplemental table 12). Three studies by Kambic *et al* were based on the same trial but reported CRF,[54] anthropometric measures[55] and biomarkers[56] in separate articles. Adherence and safety of the trial was extracted from another study.[57] The included patients were from Canada (n=268, 29.3%),[26–28 46 58 59] the USA (n=77, 8.4%),[29 60 61] European countries (n=413, 45.0%),[54 62–67] Israel (n=29, 3.2%),[25] Iran (n=88, 9.6%)[68] and Japan (n=41, 4.5%).[69] This included 59 patients from two studies reported in French[63] and Japanese.[69] Two studies included exclusively women[27 46] whereas seven included only men.[25 26 28 30 58 61 63]

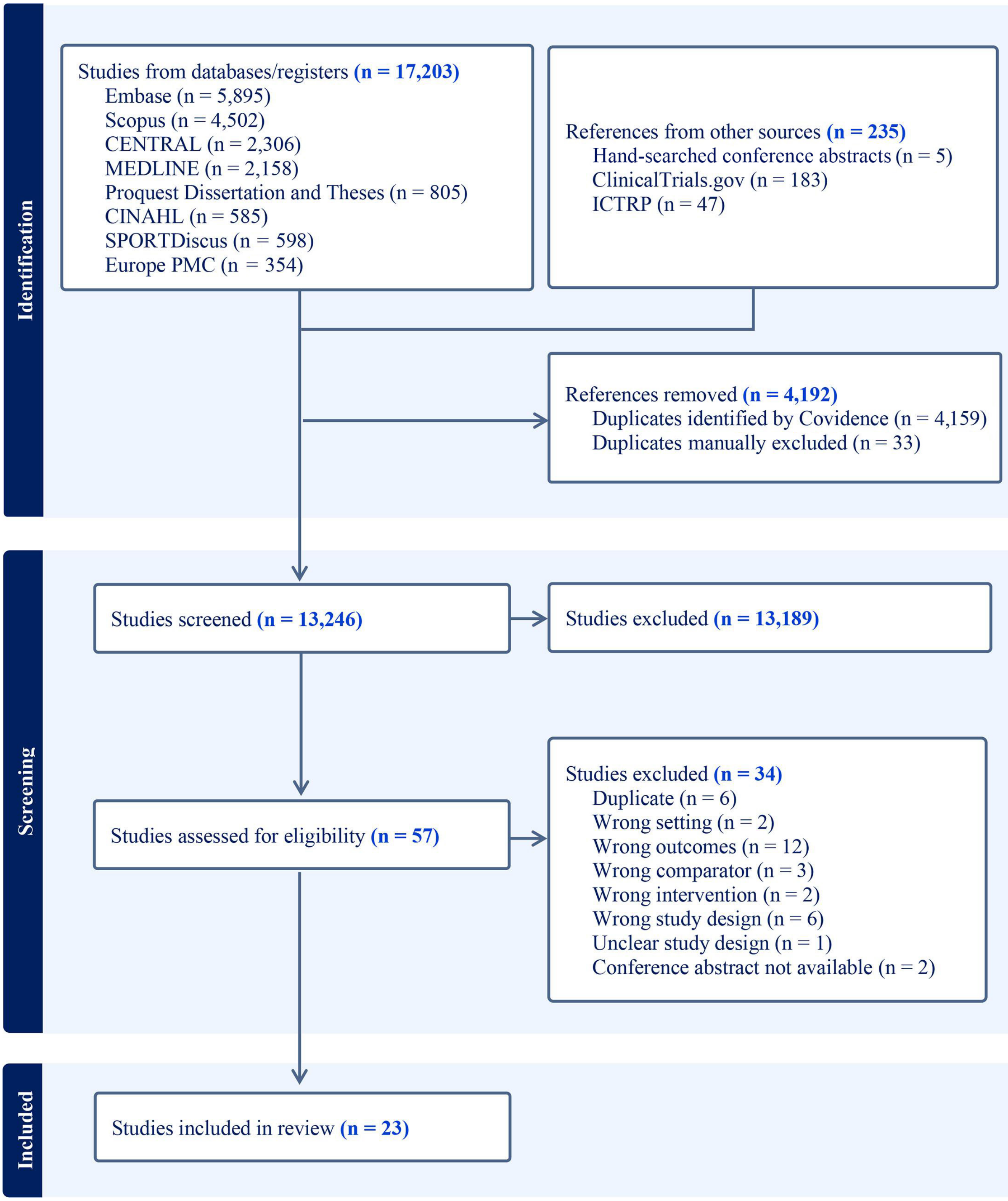

Figure 1 Preferred Reporting Items for Systematic Review and Meta-Analysis flow diagram with the number of included and excluded studies. ICTRP, International Clinical Trials Registry Platform; PMC, PubMed Central.

The sex distribution of participants was unclear in one study.[31] Among studies reporting the number of women, there were 264 women (29%) altogether. 18 studies excluded patients with contraindications to exercise (eg, uncontrolled blood pressure, diabetes, unstable angina, uncontrolled arrhythmia, acute heart failure, musculoskeletal problems).[25 26 29–31 46 54–56 58 59 62–66 68]

Most studies (n=20, 87%) conducted exercise sessions in hospitals or CR centres.[25–29 46 55–59 61 62 64–70] In two studies, exercise was performed at a university exercise gym[30 31] and the exercise setting was unclear in another.[63] Prescribed aerobic continuous exercise intensity varied among the studies, ranging from light-intensity,[68] light-to-moderate intensity,[30 31] moderate-intensity,[26 28 46 62 63 67] moderate-to-vigorous intensity[27 29 58 59 61 66 70] and vigorous-intensity.[64] The intensity could not be categorised in four studies[54–56 69] according to the ACSM guidelines.[6] Eight studies (including three from Kambic *et al*[54–56]) used AIT, of which two used high-volume (10-min intervals), light-to-moderate intensity intervals;[30 31] two used high-volume (≥5 min intervals), moderate-to-vigorous intensity intervals;[29 65] three used high-volume (5-min intervals), uncategorised exercise intensity;[54–56] and one used moderate-intensity intervals with the duration of intervals unclear.[46] The duration of exercise training ranged from 4 weeks to 8 months (mean and SD: 20±16 weeks). In general, studies with shorter durations involved more frequent exercise sessions (eg, 5 days/week). Studies with longer training durations were more likely to adjust exercise intensity as participants adapted to the exercise intensity.

For the combined exercise training, 12 of the included studies (including three by Kambic *et al*[54–56]) added muscle strength training to aerobic training (ie, the same aerobic exercise volume between combined and aerobic alone),[26–29 54–56 64 65 68–70] resulting in greater total exercise volume. The other studies[25 30 31 46 58 59 61–63 66 67] reduced the volume of aerobic training to add muscle strength training.

Study quality and risk of bias of included trials

Overall, the quality of the included randomised clinical trials was good (median TESTEX score of 10 (IQR 8.0–12; range 7–15). Six studies were classified as high quality (ie, TESTEX score ≥12 points) and 17 as good (ie, TESTEX score 7–11 points). Of the 23 studies included, 18 studies reported the eligibility criteria (78%); 11 studies reported a description of the method used to randomise participants (48%); 20 studies concealed allocation (87%); 22 studies reported similar participants characteristics at baseline between the groups (96%); and 11 studies included an unambiguous statement indicating that an assessor was blinded to group allocation (48%).

For study reporting, 19 studies reported adverse effects (83%) and 10 reported exercise attendance (43%). 18 studies reported that >85% of participants completed the study (78%). Point measures, measures of variability and between-group comparison were reported in most studies (n=22, 96%). However, only two studies clearly stated that they conducted an intention-to-treat analysis (9%). Exercise intensity was adjusted to maintain the same relative exercise intensity in 18 studies (78%), and exercise volume was available in all studies (n=23, 100%).

Certainty and strength of evidence

The overall risk of bias in included trials was judged to be serious or very serious (online supplemental table 13). For CRF, one study did not perform an intention-to-treat analysis.[54] Further, while patient blinding is often not feasible in exercise intervention studies, some studies lacked blinding of assessors.[58 66 69] The certainty of evidence on CRF was downgraded by two levels for combined training with aerobic exercise volume not reduced and combined training with reduced aerobic exercise volume. For lean body mass and per cent body fat, the certainty of the body of evidence was moderate. The funnel plot for CRF showed no publication bias (online supplemental figure 1).

Adherence, dropout and adverse events

Of the 23 studies included, 8 reported adherence to combined and aerobic training alone.[27 29 54–56 59 64 65] Adherence was >84% for both combined and aerobic training alone in seven studies that prescribed three exercise sessions per week for 7–24 weeks.[27 29 54–56 64 65] In one study that reported adherence only for combined training (performed 5 days per week, 3 days of aerobic and 2 days of muscle strength training, for 29 weeks), adherence was 84% when one set of muscle strength training was combined with aerobic exercise, whereas it decreased to 63% when three sets of muscle strength training was combined with aerobic training.[59]

The group-specific dropout ratios were reported in 14 studies.[25–29 31 46 59 62–67] Seven studies had no dropouts in either groups.[26 28 31 63 65 67] The dropout rates were particularly high for combined training in four studies,[29 59 64 66] ranging from 24% to 37%, and in four studies for aerobic training alone, ranging from 17% to 30%.[27 29 59 64] In the combined training group, three studies with the same aerobic training volume[29 65 70] and three with reduced aerobic training volume[30 62 66] compared with aerobic training alone reported a small number of joint or muscular pain (one to two cases per study except for one that reported occasional muscle pain[65]).

17 studies reported adverse events,[25 27 29 30 46 54–56 59 62 64–70] of which 15 reported group-specific adverse events.[25 27 29 46 54–56 59 62 64 65 67–70] 10 studies reported no adverse events from participating in aerobic training;[29 46 54–56 59 62 67–69] one study reported re-stenosis and injury outside of training;[64] and another study reported one case of worsening asthma.[27] Combined training programmes resulted in no adverse events in 10 studies,[27 46 54–56 59 67–69] one case of muscular pain that resolved by discontinuing muscle strength training in one study,[62] one case of exacerbating arthritis knee pain,[70] occasional muscle pain (case number unspecified),[65] one case of re-stenosis, pneumonia and cardiac event and two cases of infection in one study,[64] and four cases of low back pain, one case of elbow tendonitis and one case of shoulder pain in another study.[29]

Cardiovascular disease risk indicators

CRF was measured in 16 of the 23 studies.[26–29 31 46 54 58 59 61–64 66 67 69] Overall, CRF increased significantly more in combined training when compared with aerobic training alone (standard mean difference (SMD) 0.26, 95% CI 0.02 to 0.49, p=0.03, figure 2A). However, the heterogeneity was significant (I^2: 53%, p=0.007). Subgroup comparisons showed a greater increase in CRF following combined training when the aerobic training volume was the same between combined training and aerobic training alone (SMD 0.36, 95% CI 0.05 to 0.68, p=0.02). The heterogeneity was not significant in this subgroup (I^2: 36%, p=0.14). When the volume of aerobic training was reduced in combined training when compared with aerobic training alone, there was no difference between the groups (p=0.39) and there was a significant heterogeneity (I^2: 65%, p=0.005).

Body composition was assessed using bioelectrical impedance analysis (BIA)[55] and dual-energy X-ray absorptiometry (DXA).[29 59 70] Meta-analyses including body composition assessed by BIA and DXA showed that combined training was more effective in increasing lean body mass (mean difference (MD)=0.8 kg, 95% CI 0.4 kg to 1.2 kg, p<0.001) and reducing per cent body fat (MD=−2.2%, 95% CI −3.5% to −0.9%, p=0.001) compared with aerobic training alone (figure 2B,C). Subgroup analyses were not performed because there was only one study that reduced aerobic exercise volume in the combined training group. There were no differences in BMI, waist circumference, waist-to-hip ratio or blood pressure between the groups (online supplemental figure 2).

Few studies compared blood cardiometabolic biomarkers between combined and aerobic training alone. Overall, there were no differences in the cardiometabolic biomarkers between combined and aerobic training alone (ie, A1C, fasting blood glucose, insulin and lipids concentrations, online supplemental figure 2). However, subgroup analysis showed that combined training without reducing aerobic training volume resulted in a significantly greater increase in HDL-C compared with aerobic training alone (SMD 0.61, 95% CI 0.21 to 1.02, p=0.003, online supplemental figure 2).

Of the eight studies that compared the effects of muscle strength training combined with AIT and AIT alone, meta-analysis was

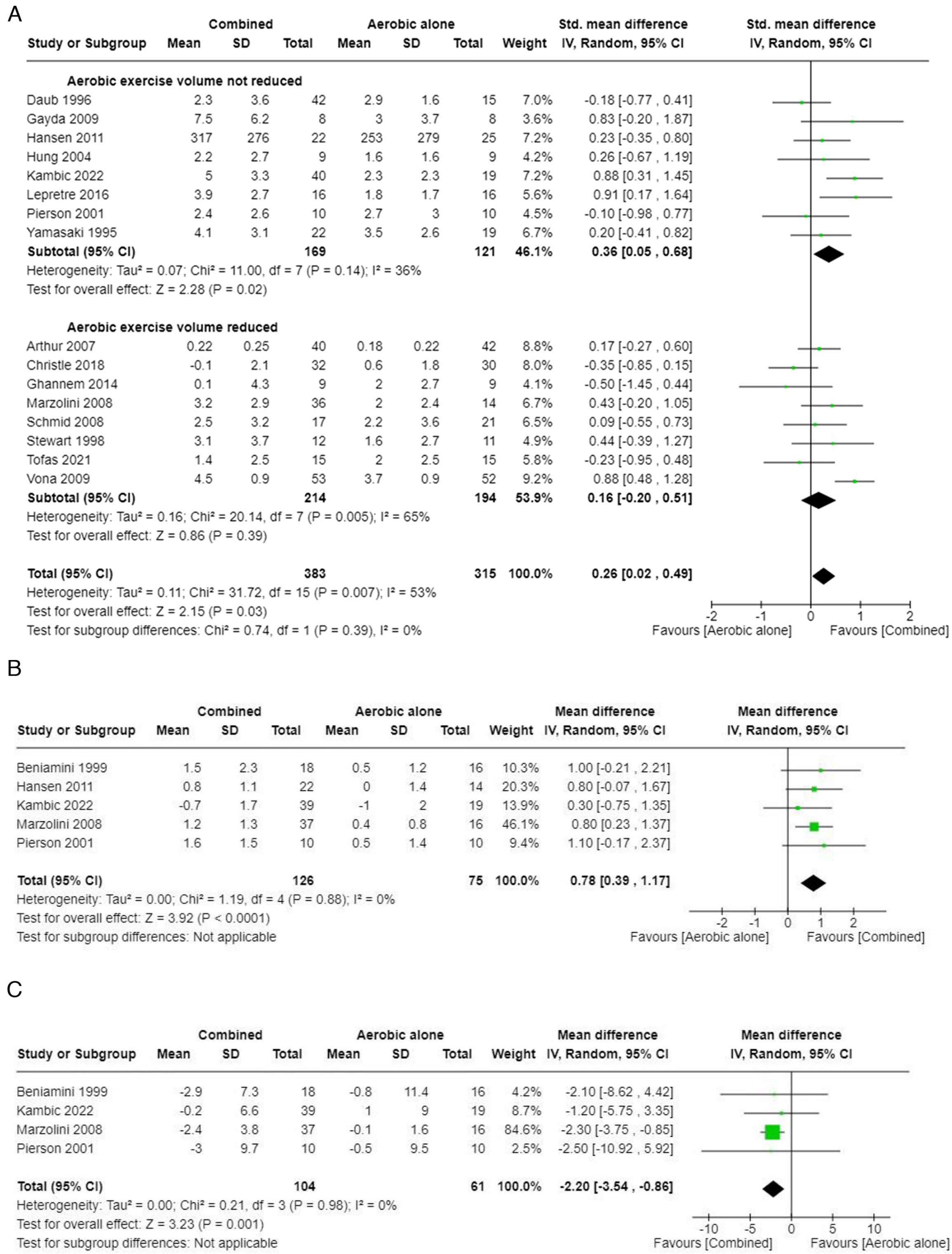

Figure 2 Changes in (A) cardiorespiratory fitness, (B) lean body mass and (C) per cent body fat following combined training and aerobic training alone. IV, inverse variance.

performed for CRF, lean body mass, per cent body fat, waist circumference, diastolic blood pressure and lipid concentrations. There were no differences between the groups (online supplemental figure 3).

DISCUSSION

This review included 23 studies involving 916 patients with CAD randomised into combined or aerobic training alone. Compared with previous systematic reviews completed in 2012 (12 studies, N=504),[32] our study included nearly twice as many studies and participants. Our analyses are different from the previous review in that we explored the effects of muscle strength training combined with AIT, included more comprehensive measures of cardiovascular disease risk indicators and accounted for different aerobic exercise volumes used in combined training. Consistent with the previous review,[32] our results showed that combined training increases lean body mass (certainty of evidence: moderate) and reduces per cent body fat (certainty of evidence: moderate) measured by BIA and DXA more than aerobic training alone. Higher per cent body fat is independently associated with future cardiovascular events,[71] and lower lean body mass predicts higher cardiovascular mortality in patients with CAD.[72] Combined training may confer additional cardioprotective benefits compared with aerobic training alone by further improving the body composition of patients with CAD.

It has been proposed that aerobic and muscle strength training have additive or synergistic benefits on CRF.[73] This is the first systematic review of randomised clinical trials to support this statement as the previous systematic reviews on randomised trials did not show a significant difference in CRF between combined and aerobic training alone.[32 34] A prospective cohort study using data from the National Health Interview Surveys from 1997 to 2013 demonstrated that muscle-strengthening activity at least twice per week is associated with 10% lower hazards of all-cause mortality, whereas those meeting both aerobic and muscle-strengthening recommendations had 47% lower hazards for cardiovascular disease mortality.[74] Because high or improved CRF is a strong predictor of lower cardiovascular disease mortality,[75] it is possible that lower mortality risk in those who engage in both muscle strength training and aerobic training is at least partly mediated by higher CRF. The ACSM[6] and WHO[76] physical activity guidelines recommend 3–5 days of aerobic training and two to three non-consecutive days of muscle strength training per week. Our results highlight the additive benefits of engaging in both muscle strength training and aerobic training for further increases in CRF in those with CAD.

Our subgroup analysis showed that the change in CRF following combined training was significantly greater than aerobic training alone when muscle strength training was added to aerobic training (the certainty of evidence: low). A progressive muscle strength training alone has been shown to improve CRF to a similar extent to aerobic training in patients with CAD,[34] which may be one of the reasons that muscle strength training independently improves mortality.[15] Because both muscle strength training and aerobic training independently increase CRF,[34] the combined group may have improved the CRF more than aerobic training alone. This also suggests that, regardless of exercise types, total exercise volume is a crucial determinant of changes in CRF in patients with CAD. Studies that reduced aerobic training volume to add muscle strength training showed significant heterogeneity and no significant changes in CRF when compared with aerobic training alone. It is important to note that substituting aerobic training with muscle strength training did not compromise the increase in CRF. Taken together, our results highlight the importance of performing both muscle strength training and aerobic training in patients with CAD. If possible, muscle strength exercise should be added without compromising aerobic exercise volume to further increase CRF.

Despite the significantly greater improvements in body compositions following combined training, our results showed no significant overall differences in changes in the other cardiovascular disease risk indicators, such as blood glucose or lipids concentrations. Blood glucose and lipids concentrations of included studies at baseline were either in the desirable or close to desirable range.[6] It is possible that medically well-controlled cardiometabolic biomarkers before participating in exercise training left little room for improvement, resulting in no changes in either group. Our results are similar to a recent randomised clinical trial involving 406 adults living with overweight or obesity showing that aerobic training alone and time-matched combined training are equally effective in improving composite cardiovascular disease risk profiles (ie, systolic blood pressure, LDL-C and fasting glucose).[77] Interestingly, our subgroup analysis showed that combined training can increase HDL-C more than aerobic training alone when muscle strength training was added to aerobic training. This highlights another potential benefit of adding (not substituting) muscle strength training to aerobic training. However, considering a relatively small number of studies included, further research is needed to elucidate the effects of combined training on cardiometabolic blood biomarkers.

Regardless of its known benefits, fewer adults meet muscle-strengthening activity recommendations compared with aerobic exercise recommendations (~30%vs ~50%)[78] and its long-term adherence is low.[79] In this systematic review, we found that overall adherence to combined training was comparable to aerobic training alone. However, one study showed deteriorated adherence as the sets of muscle strength training were increased from 2 (84%) to 3 (63%).[59] Of 23 studies, 14 reported group-specific dropout rates. In one study that prescribed five exercise sessions per week, the dropout rates were equally high in both combined (25%) and aerobic training alone (30%).[59] Contrarily, higher dropout rates in combined compared with aerobic training alone were reported in a few studies (37% vs 24%,[29] 27% vs 17%[64] and 23% vs 5%[66]). Because these studies added muscle strength training to aerobic training without reducing aerobic training volume, it is possible that greater time commitment resulted in the higher dropout rates.[79] Given the benefits of adding muscle strength training to aerobic training on CRF, strategies to increase adherence while reducing the dropout rates are warranted. The risk of adverse events was low, with muscular and joint incidences reported most frequently in the combined training group.

Despite the steep increase in the publication of studies examining the effects of AIT in cardiovascular disease populations, our systematic search resulted in only eight studies (including three studies from the same trial[54–56]) comparing the effects of AIT combined with muscle strength training. A previous randomised trial showed that AIT combined with muscle strength training improves BMI, per cent body fat and waist circumference more than conventional medical treatment.[80] In this review, we saw no additional benefits of combining muscle strength training with AIT on selected cardiovascular disease risk indicators. Six of the eight AIT studies included in this review used very high-volume (10-min intervals)[29–31] or high-volume (5-min intervals),[54–56 65] and one study did not specify the interval duration.[46] The intensity of intervals was light-to-moderate in two,[30 31] moderate in one,[46] moderate-to-vigorous in two studies[29 65] and could not be categorised in three studies.[54–56] Consequently, the interval characteristics of AIT included in our review is different from recent literature that focuses on shorter and/or higher intensity intervals. Since low volume, high-intensity interval training may be a time-effective approach to improve CRF in CAD,[81] it may offset the greater time commitment of combined training. More studies are needed to understand the effects of high-intensity interval training combined with muscle strength training on cardiovascular disease risk indicators.

This review has several strengths. For example, the included studies had robust study designs (randomised clinical trials) and represented various geographical locations (eg, Canada, seven European countries, Iran, Israel, Japan and the USA). Their quality scores ranged from good to high. There are also several limitations to this review. First, for some variables, the meta-analyses included a small number of studies. This precluded us from conducting subgroup analyses and drawing robust conclusions regarding the effects of combined training. Second, a high degree of heterogeneity was observed for some variables (eg, overall CRF). Third, adherence, dropout and adverse events were reported by 8 (35%), 14 (61%) and 17 (74%) studies, respectively. Because several studies failed to collect or report these important measures, it is difficult to clearly interpret how they affected the outcomes. Future studies should assess and report adherence, dropout and adverse events. Last, several studies required the imputation of variance estimation. While we adopted recommended approaches[45] to address this limitation, their effects on our outcomes cannot be overlooked.

CONCLUSION

This review showed the benefits of combining muscle strength training with aerobic training in improving body composition in patients with CAD. Additionally, when muscle strength training was added, not substituted, to aerobic training, combined training improved CRF, an important predictor of mortality in patients with CAD,[75] to a greater extent than aerobic training alone. Considering that the combination of increased time constraints, the need for access to equipment and facilities and the perceived complexity of muscle strength training may contribute to low participation rates,[73] CR addressing these barriers to promote participation in muscle strength training may further improve the health of patients with CAD.

Author affiliations
[1]Physiology, Pharmacology and Neuroscience, School of Life Sciences, University of Nottingham, Nottingham, UK
[2]Exercise Physiology and Cardiovascular Health Lab, Division of Cardiac Prevention and Rehabilitation, University of Ottawa Heart Institute, Ottawa, ON, Canada
[3]University of Alberta Faculty of Medicine & Dentistry, Edmonton, AB, Canada
[4]Department of Community Health Sciences, University of Calgary, Calgary, AB, Canada
[5]Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[6]Graduate School of Medical Sciences, Department of Rehabilitation Sciences, Kitasato University, Sagamihara, Japan
[7]Department of Cardiovascular Rehabilitation, National Cerebral and Cardiovascular Center, Suita, Japan
[8]Berkman Library, University of Ottawa Heart Institute, Ottawa, ON, Canada
[9]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
[10]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, ON, Canada

X Tasuku Terada @TasukuTerada

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ORCID iD
Tasuku Terada http://orcid.org/0000-0002-6623-6994

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