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Human Kinetics
SCHOLARLY REVIEW

Are the Current Cardiac Rehabilitation Programs Optimized to Improve Cardiorespiratory Fitness in Patients? A Meta-Analysis

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Previous meta-analyses have shown that high-intensity interval training (HIIT) is more suitable than moderate continuous training (MCT) for improving peak oxygen uptake (VO_2peak) in patients with coronary artery disease. However, none of these meta-analyses have tried to explain the heterogeneity of the empirical studies in optimizing cardiac rehabilitation programs. Therefore, our aims were (a) to estimate the effect of MCT and HIIT on VO_2peak, and (b) to find the potential moderator variables. A search was conducted in PubMed, Scopus, and ScienceDirect. Out of the 3,110 references retrieved, 29 studies fulfilled the selection criteria to be included in our meta-analysis. The mean difference was used as the effect size index. Our results showed significant enhancements in VO_2peak after cardiac rehabilitation based on MCT and HIIT (mean difference = 3.23; 95% confidence interval [2.81, 3.65] $ml \cdot kg^{-1} \cdot min^{-1}$ and mean difference = 4.61; 95% confidence interval [4.02, 5.19] $ml \cdot kg^{-1} \cdot min^{-1}$, respectively), with greater increases after HIIT ($p < .001$). Heterogeneity analyses reached statistical significance with moderate heterogeneity for MCT ($p < .001$; $I^2 = 67.0\%$), whereas no heterogeneity was found for the effect of HIIT ($p = .220$; $I^2 = 22.0\%$). Subgroup analyses showed significant between-group heterogeneity of the MCT-induced effect based on the training mode ($p < .001$; $I^2 = 90.4\%$), the risk of a new event ($p = .010$; $I^2 = 77.4\%$), the type of cardiovascular event ($p = .009$; $I^2 = 84.8\%$), the wait time to start cardiac rehabilitation ($p = .010$; $I^2 = 76.6\%$), and participant allocation ($p = .002$; $I^2 = 89.9\%$). Meta-regressions revealed that the percentages of patients undergoing a revascularization procedure ($B = –0.022$; $p = .041$) and cardiorespiratory fitness at baseline ($B = –0.103$; $p = .025$) were inversely related to the MCT-induced effect on the VO_2peak.

Keywords: acute myocardial infarction, aerobic training, angina pectoris, coronary artery bypass grafting, percutaneous coronary intervention

According to the World Health Organization (2018), cardiovascular diseases continue to be the most prevalent cause of death worldwide. In 2015, more than 17 million people died from this cause, representing 31% of all deaths registered in the world. Of these deaths, 7.4 million were due to coronary artery disease (CAD). Exercise-based cardiac rehabilitation (CR) is an effective strategy for reducing total and cardiovascular mortality in patients with CAD (Anderson et al., 2016). Furthermore, cardiorespiratory fitness (CRF), which is measured directly as peak oxygen uptake (VO_2peak), has been deemed to be a strong predictor of mortality (Kodama et al., 2009). A traditional training methodology used in CR programs to increase VO_2peak is moderate continuous training (MCT). The MCT is characterized by long-term training periods (between 30 and 60 min) at 60–85% VO_2peak (Fletcher et al., 2001). More recently, high-intensity interval training (HIIT) emerged as an alternative to MCT to improve CRF. The main principle of HIIT is to perform brief periods of high-intensity exercise (e.g., >85% VO_2peak or above anaerobic threshold) interspersed by periods of low-intensity exercise (e.g., <60% VO_2peak or below aerobic threshold) or rest (Gayda, Ribeiro, Juneau, & Nigam, 2016). Previous meta-analyses have shown that HIIT is more effective than MCT for increasing VO_2peak in patients with CAD (Elliott, Rajopadhyaya, Bentley, Beltrame, & Aromataris, 2015; Gomes-Neto et al., 2017; Hannan et al., 2018; Liou, Ho, Fildes, & Ooi, 2016; Pattyn, Beulque, & Cornelissen, 2018; Pattyn, Coeckelberghs, Buys, Cornelissen, & Vanhees, 2014; Xie, Yan, Cai, & Li, 2017). However, the findings of these meta-analyses showed high heterogeneity. A cornerstone of the meta-analytic process is to analyze all the variables that could be related to the effect size (ES) magnitude to explain the heterogeneity of the results. None of these previous meta-analyses tried to analyze all these variables and, therefore, reach conclusive findings.

Despite the higher efficiency of HIIT in improving CRF, there is evidence that shows the relevance of managing training variables like frequency, intensity, time (duration), and type (modality) properly to increase the long-term effects of exercise training (Vanhees et al., 2012). As we can see, the training method used in CR is just a part of the training prescription, and the lack of control of the other training variables could explain part of the heterogeneity found in the results of the previous meta-analyses (Ballesta García, Rubio Arias, Ramos Campo, Martínez González-Moro, & Carrasco Poyatos, 2019; Conraads et al., 2015; Hannan et al., 2018). In addition, other potential moderator variables related to the pathology (i.e., type of cardiovascular event or revascularization), sample characteristics (i.e., age, sex, or physical fitness), or study design (i.e., study quality) could modify the effect of MCT and HIIT on CRF.

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Knowledge of the influence of all these variables when MCT and HIIT are performed in CR would allow CR programs to be designed and managed adequately, or at least limitations of the previous studies to be identified with a view to improving CR. Therefore, our aims were (a) to estimate the effect of MCT and HIIT on VO_2peak, and (b) to analyze, if heterogeneity was found, the potential moderator variables of the impact of MCT and HIIT on VO_2peak.

Method

The systematic review and meta-analysis were reported following the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Liberati et al., 2009).

Study Selection

Studies that enrolled adult patients (≥18 years), regardless of sex, who had experienced an acute myocardial infarction (AMI) or angina pectoris, who had undergone revascularization (percutaneous transluminal intervention or coronary artery bypass grafting), or who had experienced coronary heart disease documented by angiography were included. Exercise-based CR was delineated as a supervised outpatient intervention that included MCT or HIIT as aerobic training, either alone or in addition to psychosocial or educational interventions. Studies that applied CR, based on resistance training or combined resistance and aerobic training, as well as unsupervised interventions, were excluded. Randomized, nonrandomized, controlled, and uncontrolled trials were included. In the controlled studies, the control group (CG) could include usual care and psychosocial or educational interventions, but they did not include structured exercise training. Studies had to report direct measurements of VO_2peak, and they had to have been published between January 2000 and February 2020 to be included in this systematic review and meta-analysis.

Search Procedure

The following databases were consulted to select the studies that fulfilled the selection criteria: *PubMed*, *Scopus*, and *ScienceDirect*. We combined the following keywords for the electronic searches: ("Coronary artery disease" OR "Coronary heart disease" OR "Myocardial infarction" OR "Angina pectoris" OR "Cardiac disease" OR "Cardiovascular disease") AND ("Aerobic interval training" OR "High-intensity interval training" OR "High-intensity exercise" OR "Exercise rehabilitation" OR "Anaerobic interval training" OR "Moderate continuous training"). We restricted the search of the keywords to titles and abstracts. We also reviewed the references of nine previously published meta-analyses (Ballesta García et al., 2019; Elliott et al., 2015; Gomes-Neto et al., 2017; Hannan et al., 2018; Kraal, Vromen, Spee, Kemps, & Peek, 2017; Liou et al., 2016; Pattyn et al., 2014, 2018; Xie et al., 2017).

Coding Moderator Variables

Study characteristics that could be related to the ESs were extracted, with the purpose of examining the heterogeneity between the results of the analysis units. Moderator variables were classified as treatment, subject, methodological, and extrinsic variables.

The treatment characteristics coded were (a) the training mode (treadmill, cycle ergometer, or a combination of different exercises) and (b) the session duration (in minutes). In the analysis units of HIIT, the length of the training was calculated as *number of intervals × interval length*. As regards the training duration progression, the average weighted length was taken as the point of reference. In addition, in those interventions in which several training sessions were carried out over a day, the length of the training was calculated by adding them up; (c) the intensity percentage related to the maximum achieved. In those analysis units in which the intensity was prescribed as a range, we used the weighted average. When the intensity was not relative to the maximum, it was calculated using the maximum average values of the group; (d) the weekly training frequency (in days per week); (e) the treatment duration (in weeks); (f) the number of sessions; (g) the total time they were performing at target intensity during the intervention (in minutes); and (h) the wait time to start exercise-based CR (≤3, 4–12, or >12 weeks).

The subject characteristics coded for the samples of each analysis units were: (a) the number of patients; (b) the average age of the sample (in years); (c) the sex of the sample (male, female, or mixed); (d) the percentage of males; (e) the type of cardiovascular event; (f) the percentage of patients with AMI; (g) the percentage of patients who had undergone revascularization; (h) the type of revascularization surgery (percutaneous transluminal intervention, coronary artery bypass grafting, or mixed); and (i) The risk of a new event, that was established based on the VO_2peak and left ventricular ejection fraction (low: $VO_2\text{peak} > 24.5\ \text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and/or LVEF > 50%; moderate: $VO_2\text{peak} = 17.5\text{–}24.5\ \text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and/or LVEF 40–50%; high: $VO_2\text{peak} < 17.5\ \text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ and/or LVEF < 40%) (Leon et al., 2005).

Finally, we also coded methodological and extrinsic variables, assessing the methodological quality of the study taking each item of the PEDro scale (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003) as an independent categorical moderator variable. In addition, we analyzed the methodological quality score (on a scale from 0 to 10 points) as a continuous variable. We coded the publication year of the study as a continuous variable to analyze whether changes in the treatment and management of patients with CAD over the years could have influenced the CR-induced effect on the CRF.

Computation of ESs and Statistical Analysis

The literature search revealed the existence of studies that included a CG and studies without a CG. In order not to discard studies without a CG, we included all of them and, as a consequence, our analysis unit was the group, not the study. Thus, for each group (MCT, HIIT, and CG), the mean difference (MD) was used as the ES index. MD was defined as the difference between pre- and posttest means at VO_2peak. Although between-group ESs exhibit better internal validity than within-group ones, using one-group pre- and posttest ESs is recommended in the meta-analytic area when there are many studies without CGs (Borenstein, Hedges, Higgins, & Rothstein, 2011; Hunter & Schmidt, 2004). A random-effects model was applied to carry out statistical analyses, according to which its inverse variance weighted each MD index. The overall ES obtained was represented using MD_+. A first analysis consisted of calculating the mean ES with its 95% confidence interval (CI), the heterogeneity test, χ^2, and the I^2 index (Higgins & Thompson, 2002; Huedo-Medina, Sánchez-Meca, Marín-Martínez, & Botella, 2006; Sánchez-Meca & Marín-Martínez, 2008). Statistical analyses were considered significant at $p \leq .05$. Heterogeneity was interpreted depending on I^2 magnitude as no heterogeneity (<25%), low (25–49.9%), moderate (50–74.9%), and large heterogeneity (>75%) (Higgins & Thompson, 2002; Huedo-Medina et al., 2006). We carried out subgroup analyses to compare the overall ES of the MCT, the HIIT, and the CG. If heterogeneity was found, the influence of moderator variables on training effects was evaluated separately for the MCT and HIIT groups. The relationships between the ESs and the categorical and continuous moderator variables were investigated using analysis of variances (or subgroup analysis) and meta-regressions with Q_B and Z statistics, respectively, and assuming mixed-effects models (Cooper & Hedges, 1993). The abovementioned criteria were also applied to perform subgroup analyses.

We carried out sensitivity analyses to investigate the robustness of our results. We assessed the impact of including or excluding outliers. To determine outliers, we used the outlier-labeling rule (Tukey, 1977). In addition, we also analyzed the effect of including/excluding nonrandomized trials to discover the impact of the study design on our findings.

Given that this meta-analysis did not include any unpublished paper, we carried out an analysis of publication bias using a funnel plot, the Egger test, and the trim-and-fill method for imputing missing ESs. We performed statistical analyses using Review Manager (version 5.3, Copenhagen, Denmark), Comprehensive Meta-Analysis (version 3.3, Englewood, NJ), and macros for SPSS (Chicago, IL) elaborated by David B. Wilson.

Results

Search Procedure

The search strategy produced a total of 3,110 references. Out of all the studies revised, 29 articles fulfilled the selection criteria to be included in this meta-analysis. Although we attempted to localize nonpublished works, all the selected works were studies that had been published in peer-reviewed journals. Out of all the selected studies, one of them included CG, MCT, and HIIT groups; nine included MCT and HIIT groups; 13 included CG and MCT groups; three included only MCT groups; and three included only HIIT groups (one of them with two different HIIT groups). A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of our literature search and selection is presented in Figure 1.

Study Characteristics and Quality Analysis

The total sample size of the meta-analysis involved 1,417 patients, of which 703 patients formed the 26 MCT groups (mean ± *SD* sample size = 27.1 ± 18.0 patients), 350 patients formed the 14 HIIT groups (mean ± *SD* sample size = 25.0 ± 21.9 patients), and 364 patients formed the 14 CGs (mean ± *SD* sample size = 26.0 ± 12.8 patients). The average ± *SD* age of participants across groups was 58.7 ± 3.9 years for the MCT (min–max: 52–69 years), 58.1 ± 2.9 years for the HIIT (min–max: 53–63 years), and 58.8 ± 4.7 years for the CG (min–max: 52–68 years). Twenty-two MCT analysis units included patients of both sexes, three included only males, and one study did not report this. Thirteen HIIT analysis units included male and female patients, and one study included only males. In terms of the CG, 12 analysis units included patients of both sexes, and two included only males. The average ± *SD* CRF at baseline of participants across groups was 21.2 ± 5.3 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ for the MCT (min–max: 13.0–32.1 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$), 25.6 ± 5.2 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$ for the HIIT

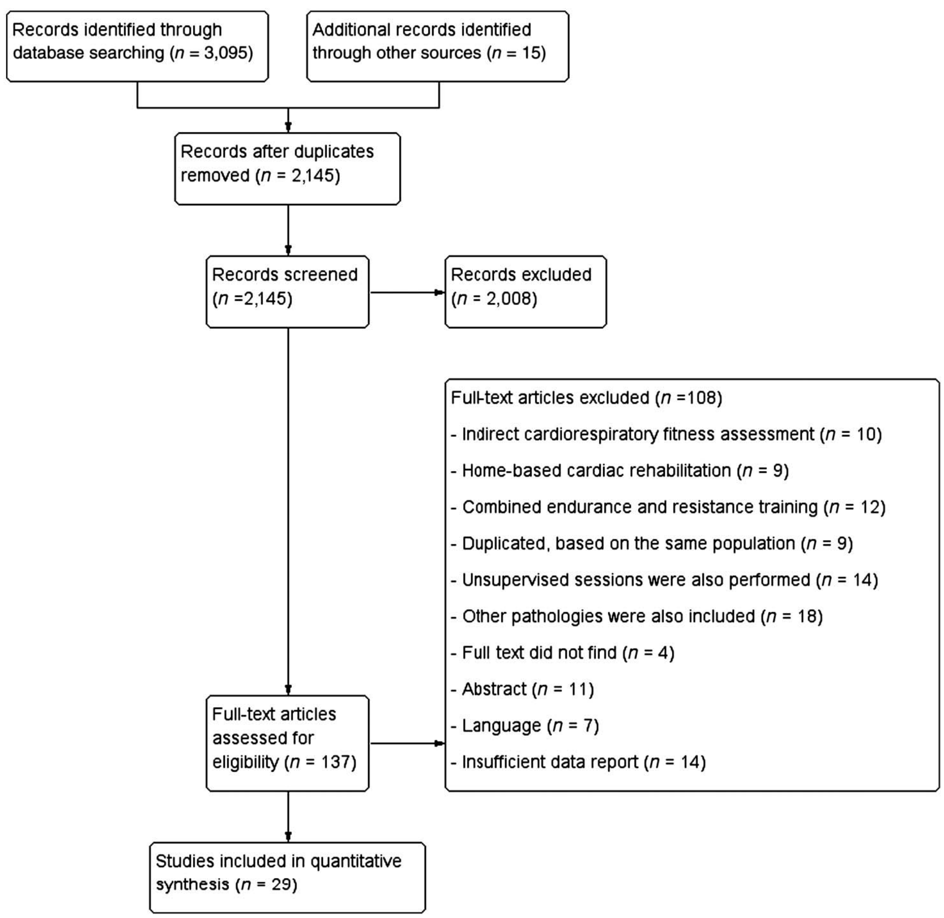

Figure 1 — Systematic review and meta-analysis flowchart.

(min–max: 18.9–34.7 ml·kg^{-1}·min^{-1}), and 19.5 ± 5.4 ml·kg^{-1}·min^{-1} for the CG (min–max: 13.7–32.6 ml·kg^{-1}·min^{-1}). The treatment length was between 2 and 26 weeks (mean = 11.7 weeks) for the MCT and between 5 and 16 weeks (mean = 11.3 weeks) for the HIIT. The training frequency varied between two and 14 weekly sessions (mean = 3.8 weeks) for the MCT and between two and three weekly sessions (mean = 2.6 weeks) for the HIIT, with a mean session length (without warm-up and cooldown) of 32 min for the MCT (min–max: 20–50 min) and 28.9 min for the HIIT (min–max: 20–42 min). The mode of exercise involved walking/jogging on a treadmill in nine studies, cycling in 15 studies, and a combination of exercises in four studies. One study did not report the training mode. The mean ± *SD* intensity was 63.9 ± 9.5% VO_2peak for the MCT (min–max: 46.1–81% VO_2peak) and –92.5 ± 8.2% VO_2peak for the HIIT (min–max: 84.1–117% VO_2peak). Out of the 14 HIIT groups, nine of them used length intervals ≥3 min, two groups combined long and short intervals throughout the CR program, and three used short intervals. Only one group used a training intensity above the peak power output (PPO) achieved during the cardiopulmonary exercise test throughout the whole intervention.

The main characteristics of the samples and training are shown in Tables 1 and 2, respectively. The results of the methodological quality analysis using the PEDro scale appear in Table 3.

Effect of Aerobic Training on VO_2Peak

Twenty-six and 14 groups applied MCT and HIIT, respectively. All these pre- and posttest ESs (MDs) together with those of the 14 CGs are presented in the forest plot in Figure 2. The meta-analyzed effects of both training methods showed statistical improvements ($p < .001$) in VO_2peak ($MD_+ = 3.36$; 95% CI [2.96, 3.76] ml·kg^{-1}·min^{-1} for MCT and $MD_+ = 4.61$; 95% CI [4.02, 5.19] ml·kg^{-1}·min^{-1} for HIIT). The change exhibited in the CG ($MD_+ = 0.12$; 95% CI [−0.31, 0.55] ml·kg^{-1}·min^{-1}) did not reach statistical significance ($p = .590$). However, tests for subgroup differences among the three average MDs did show statistical significance ($p < .001$) with large heterogeneity explained ($I^2 = 98.9\%$). Therefore, we carried out pairwise comparisons. We performed a Bonferroni correction to control the increase in Type I error (significant at $p \leq .017$). The comparison between the average MD of each training method with the average MD for the CG reached statistical significance ($p < .001$). In addition, the comparison between the average MDs of the MCT and HIIT groups also reached statistical significance in favor of the HIIT groups ($p < .001$). As regards heterogeneity analysis, the 26 ESs of MCT attained statistical significance with moderate heterogeneity ($p < .001$; $I^2 = 67\%$), while the 14 ESs of HIIT did not reach statistical significance and no heterogeneity was found ($p = .220$; $I^2 = 22\%$). Consequently, we examined the influence of the characteristics of the analysis units, which may explain part of the heterogeneity of the studies that carried out CR based on MCT.

Sensitivity Analysis

No outliers were found for MCT and HIIT ESs, indicating that there is no need to assess the overall effect without outlier analysis units. With a lower critical value (MD = −1.95) and an upper critical value (MD = 2.45), we found one outlier for the CG (MD = −3.30; Cardozo et al., 2015), and we carried out the analysis after removing it (see Supplementary Figure 1 [available online]). Although the overall ES of the CG increased (from $MD_+ = 0.12$; 95% CI [−0.31, 0.55] ml·kg^{-1}·min^{-1} to $MD_+ = 0.25$; 95% CI [−0.13, 0.62] ml·kg^{-1}·min^{-1}) and the heterogeneity diminished (from 72% to 62%), the conclusions were similar to those before removing the outlier, which confirms the validity of our findings. We included two nonrandomized trials in our meta-analysis (Subiela et al., 2018; Takagi et al., 2016). Removing these two studies, the pooled ES and heterogeneity were unchanged for the CG, while the overall ES decreased (from $MD_+ = 3.36$; 95% CI [2.96, 3.76] ml·kg^{-1}·min^{-1} to $MD_+ = 3.23$; 95% CI [2.81, 3.65] ml·kg^{-1}·min^{-1}) and the heterogeneity was unchanged for the MCT (Supplementary Figure 2 [available online]). The conclusions were similar to before removing nonrandomized studies. All patients were randomly allocated in studies that used HIIT protocols to carry out CR. Therefore, our findings were robust to the decision of the inclusion of nonrandomized trials.

Publication Bias

There was no evidence of asymmetry in the funnel plot for MCT and HIIT (Figure 3). However, the Egger test applied for MCT was statistically significant, $t(25) = −2.46$, $p = .022$, but not for HIIT, $t(13) = .63$, $p = .529$. Although the Egger test for the MCT groups reached statistical significance, the trim-and-fill method did not impute missing ESs to symmetrize the funnel plot. Therefore, on a reasonable basis, publication bias can be discarded as a threat against the results of the meta-analysis both for the MCT and the HIIT groups.

Analysis of Moderator Variables on the ESs of MCT

Table 4 shows the results of analyzing the influence of categorical moderator variables on the effect of MCT. Our subgroup analyses showed significant between-group heterogeneity with high inconsistency for the training mode ($p < .001$; $I^2 = 90.4\%$), the risk of a new event ($p = .010$; $I^2 = 77.4\%$), the type of cardiovascular event ($p = .009$; $I^2 = 84.8\%$), and the wait time to start CR ($p = .010$; $I^2 = 76.6\%$). There were greater CRF increases for patients who carried out CR on a bicycle ($n = 469$ patients; $MD_+ = 3.71$ ml·kg^{-1}·min^{-1}) or by combining a bicycle and treadmill ($n = 84$ patients; $MD_+ = 3.42$ ml·kg^{-1}·min^{-1}) compared with a treadmill alone ($n = 129$ patients; $MD_+ = 1.63$ ml·kg^{-1}·min^{-1}). With regard to the risk of a new event, our findings showed higher CRF increases after CR as the risk of a new event increased (low: $n = 111$ patients; $MD_+ = 2.40$ ml·kg^{-1}·min^{-1}, moderate: $n = 433$ patients; $MD_+ = 3.04$ ml·kg^{-1}·min^{-1}, and high: $n = 159$ patients; $MD_+ = 3.96$ ml·kg^{-1}·min^{-1}). There were greater improvements for patients with AMI ($n = 363$ patients; $MD_+ = 3.82$ ml·kg^{-1}·min^{-1}) than in the mixed category ($n = 287$ patients; $MD_+ = 2.60$ ml·kg^{-1}·min^{-1}). In addition, patients who started to receive CR within the first 3 weeks after the event showed a higher increase ($n = 243$ patients; $MD_+ = 4.05$ ml·kg^{-1}·min^{-1}) than those who had to wait between 4 and 12 weeks ($n = 284$ patients; $MD_+ = 3.10$ ml·kg^{-1}·min^{-1}) or >12 weeks ($n = 63$ patients; $MD_+ = 2.04$ ml·kg^{-1}·min^{-1}). As regards the study quality, a statistically significant relationship with the ESs was found for Item 2 of the PEDro scale ($p = .002$; $I^2 = 89.9\%$). MCT groups belonging to studies in which participants were randomly assigned to the groups exhibited an average MD lower ($n = 676$ patients; $MD_+ = 3.23$ ml·kg^{-1}·min^{-1}) than that of the MCT groups that did not belong to studies that applied an experimental design ($n = 27$ patients; $MD_+ = 4.58$ ml·kg^{-1}·min^{-1}). Table 5 presents the results of the simple meta-regressions for the continuous moderator variables. The meta-regression findings revealed that the percentage of patients undergoing revascularization ($n = 614$;

Table 1 Sample Characteristics

Study	Group	Sample size	Male (%)	Age (years ± *SD*)	Time from the event (weeks)	AMI (%)	CRF at baseline (ml·kg^{-1}·min^{-1})	Risk of a new event	Revascularization procedure	Undergoing an intervention (%)
Prado et al. (2016)	MCT	18	77.8	61.3 ± 9.3	NR	26.0	18.8	Moderate	Mixed	100
	HIIT	17	82.4	56.5 ± 11.1		17.0	19.9			100
Oliveira et al. (2014)	MCT	47	85.1	54.8 ± 10.6	4–12	100	27.6	Low	PCI	93.6
	CG	45	82.2	58.6 ± 10.7		100	26.9			86.7
Aamot et al. (2014)	HIIT	32	84.4	56.0 ± 9.0	NR	67.6	34.7	Low	CABG	26.5
Conraads et al. (2015)	MCT	89	89.9	59.9 ± 9.2	4–12	48.0	22.4	Moderate	Mixed	52.0
	HIIT	85	95.3	57.0 ± 8.8		67.0	23.5			33.0
Blumenthal et al. (2005)	MCT	48	64.6	62.0 ± 10.5	NR	50.0	19.1	Moderate	NR	NR
	CG	42	76.2	63.0 ± 9.0		60.0	20.2			
Cardozo, Oliveira, and Farinatti (2015)	MCT	24	66.7	62.0 ± 12.0	>12	62.0	21.8	Moderate	NR	NR
	HIIT	23	65.2	56.0 ± 12.0		43.0	20.6			
	CG	24	76.0	64.0 ± 12.0		62.0	21.9			
Choi, Han, Choi, Jung, and Joa (2018)	MCT	21	85.7	57.3 ± 12.6	≤3	100	28.0	Moderate	PCI	100
	HIIT	23	91.3	53.0 ± 6.84		100	31.9			100
Currie, Bailey, Jung, McKelvie, and MacDonald (2015)	MCT	10	90.0	66.0 ± 8.0	>12	66.7	19.8	Moderate	Mixed	100
	HIIT	9	100	63.0 ± 8.0		60.0	21.1			88.9
Eto et al. (2004)	MCT	18	94.4	58.4 ± 4.5	≤3	100	17.0	High	PCI	70.0
	CG	18	100	60.0 ± 7.9		100	16.2			67.0
Ghroubi et al. (2013)	MCT	16	NR	59.0 ± 5.9	4–12	100	20.4	Moderate	CABG	100
Giallauria, De Lorenzo, et al. (2006)	MCT	22	86.4	55.0 ± 2.0	≤3	100	16.3	High	PCI	90.0
	CG	22	90.9	54.0 ± 3.0		100	17.0			90.0
Giallauria, Lucci, et al. (2006b)	MCT	20	80.0	68.6 ± 2.3	≤3	100	16.3	High	PCI	90.0
	CG	20	85.0	68.2 ± 2.6		100	15.7			95.0
Giallauria et al. (2011)	MCT	37	75.7	61.0 ± 7.0	≤3	100	16.4	High	PCI	55.0
	CG	38	84.0	60.0 ± 8.0		100	16.7			61.0
Giallauria et al. (2012)	MCT	24	95.8	54.0 ± 7.0	≤3	100	13.0	High	PCI	100
	CG	26	84.0	52.0 ± 10.0		100	14.0			100
Giallauria et al. (2013)	MCT	25	88.0	54.0 ± 7.0	≤3	100	14.0	High	PCI	100
	CG	21	86.0	54.0 ± 9.0		100	14.0			100
Heber et al. (2020)	MCT	42	100	61.7 ± 9.8	4–12	62	22.9	Moderate	PCI	100
Helgerud et al. (2011)	HIIT	8	75.0	61.4 ± 3.7	NR	30.0	27.2	Low	Mixed	70.0
Jayo-Montoya et al. (2020)	HIIT-LV	21	85.7	58.9 ± 9.6	NR	100	23.2	Moderate	Mixed	100
	HIIT-HV	23	82.1	58.9 ± 8.0		100	23.2			100
Keteyian et al. (2014)	MCT	13	92.3	58.0 ± 9.0	NR	69.0	21.8	Moderate	Mixed	93.0
	HIIT	15	73.3	60.0 ± 7.0		53.0	22.4			93.0

(continued)

Table 1 ***(continued)***

Study	Group	Sample size	Male (%)	Age (years ± *SD*)	Time from the event (weeks)	AMI (%)	CRF at baseline (ml·kg^{-1}·min^{-1})	Risk of a new event	Revascularization procedure	Undergoing an intervention (%)
Kim, Choi, and Lim (2015)	MCT	14	71.4	60.2 ± 13.6	≤3	100	27.1	Low	PCI	100
	HIIT	14	93.3	57.0 ± 11.6		100	29.2			100
Lee et al. (2009)	MCT	20	100	52.0 ± NR	>12	100	22.2	Moderate	PCI	100
	CG	19	100	52.0 ± NR		100	22.7			100
Madssen et al. (2014)	MCT	21	71.4	60.5 ± NR	NR	NR	29.8	Low	PCI	100
	HIIT	15	93.3	55.5 ± NR			31.2			100
Ribeiro et al. (2012)	MCT	20	90.0	54.3 ± 10.8	4–12	100	30.8	Low	PCI	85.0
	CG	18	72.2	57.0 ± 7.6		100	32.6			72.2
Rognmo, Hetland, Helgerud, Hoff, and Slørdahl (2004)	MCT	9	88.9	61.2 ± 7.3	>12	44.4	32.1	Low	Mixed	55.6
	HIIT	8	75.0	62.9 ± 11.2		50.0	31.8			37.5
Subiela, Torres, De Sanctis, and Hernández (2018)	MCT	17	100	53.9 ± 8.0	4–12	100	21.2	Moderate	NR	NR
Takagi et al. (2016)	MCT	10	80.0	59.0 ± 10.0	≤3	100	18.1	Moderate	PCI	100
	CG	6	83.3	61.0 ± 9.0		100	18.6			100
Takeyama et al. (2000)	MCT	13	100	58.8 ± 6.3	NR	76.9	13.1	High	CABG	100
	CG	15	86.7	61.7 ± 8.7		66.7	13.7			100
Villelabeitia-Jaureguizar et al. (2019)	MCT	53	79.2	58.3 ± 9.5	4–12	NR	18.9	Moderate	Mixed	90.6
	HIIT	57	87.7	57.6 ± 9.8			19.5			91.1
Vona et al. (2009)	MCT	52	75.0	56.0± 6.0	≤3	100	22.0	Moderate	PCI	73
	CG	50	74.0	58.0 ± 7.0		100	22.3			76

Note. AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; CG = control group; CRF = cardiorespiratory fitness; HIIT = high-intensity interval training; HV = high volume; LV = low volume; MCT = moderate continuous training; NR = no reported; PCI = percutaneous coronary intervention.

Table 2 Training Characteristics

Study	Group	Mode	Duration, frequency	MCT exercise program	MCT intensity (%VO_2peak)	HIIT exercise program	HIIT intensity (%VO_2peak) W	HIIT intensity (%VO_2peak) R
Prado et al. (2016)	MCT HIIT	Treadmill	13 weeks 3×/week	5 min WU + 50 min (AT) + 5 min CD	NR	5 min WU + 3 × 7 × 3 min (RCP)/3 min (AT) + 5 min CD	NR	NR
Oliveira et al. (2014)	MCT	Mixed	8 weeks 3×/week	10 min WU + 30 min (70–85% HRm) + 10 min CD	65.1			
Aamot et al. (2014)	HIIT	Treadmill	12 weeks 2×/week			10 min (50–70% HRp) WU + 4 × 4 min (85–95% HRp)/4 min (70% HRp) + 3–5 min (70% HRp) CD	84.1	53.7
Conraads et al. (2015)	MCT HIIT	Bicycle	12 weeks 3×/week	5 min (60–70% HRp) WU + 37 min (70–75% HRp) + 5 min (60–70% HRp) CD	57.5	5 min (60–70% HRp) WU + 4 × 4 min (90–95% HRp)/3 min (50–70% HRp)	87.9	38.5
Blumenthal et al. (2005)	MCT	Treadmill	16 weeks 3×/week	10 min (50–70% HRr) WU + 35 min (70–85% HRr)	77.5			
Cardozo et al. (2015)	MCT HIIT	Treadmill	16 weeks 3×/week	5 min WU + 30 min (70–75% HRp) + 5 min CD	57.5	5 min WU + 7 × 2 min (90% HRp)/2 min (60% HRp) + 5 min CD	84.1	38.5
Choi et al. (2018)	MCT HIIT	NR	9 weeks 2×/week	5 min (40–50% HRm) WU + 28 min (60–70% HRm) + 5 min (40–50% HRm) CD	46.1	5 min (40–50% HRm) WU + 4 × 4 min (85–100% HRm)/3 min (50–60% HRm) + 5 min (40–50% HRm) CD	87.9	31
Currie et al. (2015)	MCT HIIT	Bicycle	13 weeks 2×/week	30 – 50 min (51–65% PPO)	57	10 × 1 min (85% PPO, Month 1), (100% PPO, Month 2), (108% PPO, Month 3)/ 1 min (10% PPO)	100	10
Eto et al. (2004)	MCT	Bicycle	2 weeks 14×/week	30 min (AT)	75			
Ghroubi et al. (2013)	MCT	Bicycle	8 weeks 3×/week	10 min WU + 2 × 10 min (70% HRr)/5 min + 10 min CD	70			
Giallauria, De Lorenzo, et al. (2006)	MCT	Bicycle	13 weeks 3×/week	5 min WU + 30 min (60% VO_2peak) + 5 min CD	70			
Giallauria, Lucci, et al. (2006)	MCT	Bicycle	13 weeks 3×/week	5 min WU + 30 min (70% VO_2peak) + 5 min CD	60			
Giallauria et al. (2011)	MCT	Bicycle	26 weeks 3×/week	5 min WU + 30 min (60–70% VO_2peak) + 5 min CD	65			
Giallauria et al. (2012)	MCT	Bicycle	26 weeks 3×/week	5 min WU + 30 min (60–70% VO_2peak) + 5 min CD	65			
Giallauria et al. (2013)	MCT	Bicycle	26 weeks 3×/week	5 min WU + 30 min (60–70% VO_2peak) + 5 min CD	65			
Heber et al. (2020)	MCT	Bicycle	6 weeks 4×/week	5 min (40% PPO) WU + 20–30 min (60% PPO) + 5 min (30% PPO) CD	60			
Helgerud et al. (2011)	HIIT	Treadmill	NR NR			5 min WU + 4 × 4 min (85–95% HRp)/ 3 min (60–70% HRp) + 5 min CD	84.1	46.1

(continued)

Table 2 *(continued)*

Study	Group	Mode	Duration, frequency	MCT exercise program	MCT intensity ($\%VO_2$peak)	HIIT exercise program	HIIT intensity ($\%VO_2$peak) W	HIIT intensity ($\%VO_2$peak) R
Jayo-Montoya et al. (2020)	HIIT-LV HIIT-HV	Mixed	16 weeks 2×/week			Treadmill: 5–10 min (65–75% HRr) WU + 2 × 4 min (HIIT-LV); 2 – 4 × 4 min (HIIT-HV) (85–95% HRr)/3 min (65–75% HRr) + 4 min (65–75% HRr) CD Bicycle: 5 – 10 min WU + 4 – 8 × 30 s (HIIT-LV); 4 – 16 × 30 s (HIIT-HV) (85–95% HRr)/3 min (65–75% HRr) + 4 – 7 min (65–75% HRr) CD	90 90	70 70
Keteyian et al. (2014)	MCT HIIT	Treadmill	10 weeks 3×/week	5 min WU + 30 min (60–80% HRr) + 5 min CD	70	5 min WU + 4 × 4 min (80–90% HRr)/ 3 min (60–70% HRr) + 5 min CD	85	65
Kim et al. (2015)	MCT HIIT	Treadmill	6 weeks 3×/week	10 min (50–70% HRr) WU + 25 min (70–85% HRr) + 10 min (50–70% HRr)	77.5	10 min (50–70% HRr) WU + 4 × 4 min (85–95% HRr)/3 min (50–70% HRr) + 10 min (50–70% HRr)	90	60
Lee et al. (2009)	MCT	Bicycle	13 weeks 3×/week	5 min WU + 20 min (55–70% VO_2peak) + 5 min CD	62.5			
Madssen et al. (2014)	MCT HIIT	Treadmill	12 weeks 3×/week	46 min (70% HRm)	53.7	10 min WU + 4 × 4 min (85–95% HRp)/ 3 min (70% HRp)	84.1	53.7
Ribeiro et al. (2012)	MCT	Mixed	8 weeks 3×/week	10 min WU + 35 min (65–75% HRm) + 10 min CD	53.7			
Rognmo et al. (2004)	MCT HIIT	Treadmill	10 weeks 3×/week	41 min (50–60% VO_2peak)	55	5 min (50–60% VO_2peak) WU + 4 × 4 min (80–90% VO_2peak)/3 min (50–60% VO_2peak) + 3 min (50–60% VO_2peak)	85	55
Subiela et al. (2018)	MCT	Mixed	12 weeks 3×/week	20 – 30 min (60–80% VO_2peak)	77.5			
Takagi et al. (2016)	MCT	Bicycle	12 weeks 2×/week	30 min (AT – 10 W)	47			
Takeyama et al. (2000)	MCT	Bicycle	12 weeks 2×/week	30 min (AT)	81			
Villelabeitia-Jaureguizar et al. (2019)	MCT HIIT	Bicycle	8 weeks 3×/week	12 – 5 min WU + 15 – 30 min (AT – AT + 10%) + 13–5 min CD	NR	12 – 5 min WU + 15 – 30 × 20 s (108–126% PPO)/40 s (22% PPO) + 13 – 5 min CD	117	22
Vona et al. (2009)	MCT	Bicycle	4 weeks 4×/week	10 min WU + 40 min (75% HRp) + 10 min CD	61.3			

Note. AT = aerobic threshold; CD = cooldown; HIIT = high-intensity interval training; HRm = heart rate maximal; HRp = heart rate peak; HRr = heart rate reserve; HV = high volume; LV = low volume; MCT = moderate continuous training; NR = not reported; PPO = peak power output achieved in cardiopulmonary exercise test; R = recovery; RCP = respiratory compensation point; VO_2peak = peak oxygen uptake; W = work; WU = warm-up.

Table 3 Quality Analysis Using PEDro Scale

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	MQS
Prado et al. (2016)	N	Y	N	Y	N	N	N	N	N	Y	Y	4
Oliveira et al. (2014)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Aamot et al. (2014)	N	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Conraads et al. (2015)	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Blumenthal et al. (2005)	N	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Cardozo et al. (2015)	N	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Choi et al. (2018)	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Currie et al. (2015)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Eto et al. (2004)	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Ghroubi et al. (2013)	N	Y	N	Y	N	N	N	N	N	Y	Y	4
Giallauria, De Lorenzo, et al. (2006)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Giallauria, Lucci, et al. (2006)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Giallauria et al. (2011)	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Giallauria et al. (2012)	Y	Y	N	Y	N	N	Y	N	N	Y	Y	5
Giallauria et al. (2013)	Y	Y	N	Y	N	N	Y	N	N	Y	Y	5
Heber et al. (2020)	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Helgerud et al. (2011)	N	Y	N	Y	N	N	N	Y	N	Y	Y	5
Jayo-Montoya et al. (2020)	N	Y	N	Y	N	N	Y	N	Y	Y	Y	6
Keteyian et al. (2014)	N	Y	Y	Y	N	N	Y	N	N	Y	Y	6
Kim et al. (2015)	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Lee et al. (2009)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Madssen et al. (2014)	N	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Ribeiro et al. (2012)	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Rognmo et al. (2004)	Y	Y	Y	Y	N	N	N	N	N	Y	Y	5
Subiela et al. (2018)	N	N	N	Y	N	N	N	N	N	Y	Y	3
Takagi et al. (2016)	Y	N	N	Y	N	N	N	N	N	Y	Y	3
Takeyama et al. (2000)	N	Y	N	Y	N	N	N	N	N	Y	Y	4
Villelabeitia-Jaureguizar et al. (2019)	N	Y	N	Y	N	N	N	N	N	Y	Y	4
Vona et al. (2009)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4

Note. MQS = methodological quality score; N = no; Y = yes; Item 1 = eligibility criteria were specified (not included in total score, MQS); Item 2 = subjects randomly assigned to groups; Item 3 = allocation concealed; Item 4 = equivalence of groups at baseline in most important prognostic variables; Item 5 = blinding of all participants; Item 6 = therapists who administered the treatment were blinded; Item 7 = assessors were blinded for at least one key outcome; Item 8 = data were obtained from at least 85% of the participants initially assigned to the groups; Item 9 = there were no attrition or, where it was not the case, data for at least one key outcome were analyzed by intention to treat; Item 10 = results of between-group comparisons were reported for at least one key outcome; Item 11 = the study reports point estimates and variability statistics for at least one key outcome.

$B = -0.022$; $p = .041$) and CRF at baseline ($n = 703$; $B = -0.103$; $p = .025$) were inversely related to the CR-induced effect on the CRF.

Discussion

According to our findings, both training methods are appropriate for increasing the VO_2peak in patients with CAD. This finding is in line with previous meta-analyses that found a significant effect of HIIT (Ballesta García et al., 2019) and MCT (Kraal et al., 2017) in improving VO_2peak. CRF improvement after aerobic training in patients with CAD could be related to changes in cardiovascular structure and function (Lee et al., 2009).

Although MCT and HIIT seem to be suitable for improving CRF, HIIT seems to be more effective than MCT for improving CRF. This finding is in line with all previous meta-analyses that compared the effect of both training methods on the VO_2peak (Elliott et al., 2015; Gomes-Neto et al., 2017; Hannan et al., 2018; Liou et al., 2016; Pattyn et al., 2014, 2018; Xie et al., 2017). There is some evidence that could explain this superiority. High intensity induces a larger improvement in contractility and hypertrophy of the cardiomyocyte than moderate intensity, which contributes to increasing the contractile cardiac pump function (Kemi et al., 2005). In addition, it also produces an increased activation of the peroxisome proliferator-activated receptor gamma coactivator 1-alpha, which improves mitochondrial function and reduces skeletal muscle fatigue (Tjønna et al., 2008). HIIT allows the accumulation of more time performing at high intensity and, therefore, produces a greater stimulus for cardiovascular and muscular adaptations (Wisløff, Ellingsen, & Kemi, 2009).

Due to the high variability observed in the MCT-induced effect on the CRF ($I^2 = 67\%$), we carried out heterogeneity analyses to explain at least part of it. In terms of the characteristics of the

Study or subgroup	MD	*SE*	Weight	Mean difference IV, Random, 95% CI
1.15.1 Moderate continuous training				
Blumenthal et al. (2005)	1.9	0.65	4.2%	1.90 [0.63, 3.17]
Cardozo et al. (2015)	0.1	0.95	2.8%	0.10 [−1.76, 1.96]
Choi et al. (2018)	2.42	1.44	1.6%	2.42 [−0.40, 5.24]
Conraads et al. (2015)	4.4	0.52	5.0%	4.40 [3.38, 5.42]
Currie et al. (2015)	3.4	1.8	1.1%	3.40 [−0.13, 6.93]
Eto et al. (2004)	3.1	0.52	5.0%	3.10 [2.08, 4.12]
Ghroubi et al. (2013)	1.7	0.77	3.6%	1.70 [0.19, 3.21]
Giallauria, De Lorenzo, et al. (2006)	4.2	0.35	6.1%	4.20 [3.51, 4.89]
Giallauria, Lucci, et al. (2006)	4.5	0.39	5.9%	4.50 [3.74, 5.26]
Giallauria et al. (2011)	4.6	0.28	6.5%	4.60 [4.05, 5.15]
Giallauria et al. (2012)	4	0.58	4.6%	4.00 [2.86, 5.14]
Giallauria et al. (2013)	4	0.57	4.7%	4.00 [2.88, 5.12]
Heber et al. (2020)	2.1	0.71	3.9%	2.10 [0.71, 3.49]
Keteyian et al. (2014)	1.7	0.94	2.9%	1.70 [−0.14, 3.54]
Kim et al. (2015)	2.47	1.75	1.1%	2.47 [−0.96, 5.90]
Lee et al. (2009)	2.8	0.8	3.5%	2.80 [1.23, 4.37]
Madssen et al. (2014)	2	1.49	1.5%	2.00 [−0.92, 4.92]
Oliveira et al. (2014)	2.1	0.93	2.9%	2.10 [0.28, 3.92]
Prado et al. (2016)	4.2	0.97	2.8%	4.20 [2.30, 6.10]
Ribeiro et al. (2012)	3.1	1.4	1.6%	3.10 [0.36, 5.84]
Rognmo et al. (2004)	2.7	1.43	1.6%	2.70 [−0.10, 5.50]
Subiela et al. (2018)	4.5	0.44	5.5%	4.50 [3.64, 5.36]
Takagi et al. (2016)	4.8	0.71	3.9%	4.80 [3.41, 6.19]
Takeyama et al. (2000)	3	0.4	5.8%	3.00 [2.22, 3.78]
Villelabeitia-Jaureguizar et al. (2019)	2.97	0.59	4.6%	2.97 [1.81, 4.13]
Vona et al. (2009)	3.7	0.16	7.1%	3.70 [3.39, 4.01]
Subtotal (95% CI)			**100.0%**	**3.36 [2.96, 3.76]**
Heterogeneity: $\tau^2 = 0.55$; $\chi^2 = 76.72$, df = 25 ($p < .00001$); $I^2 = 67\%$				
Test for overall effect: $Z = 16.52$ ($p < .00001$)				
1.15.2 High intensity interval training				
Aamot et al. (2014)	4.3	1.05	6.6%	4.30 [2.24, 6.36]
Cardozo et al. (2015)	3.8	0.81	9.8%	3.80 [2.21, 5.39]
Choi et al. (2018)	7.58	1.05	6.6%	7.58 [5.52, 9.64]
Conraads et al. (2015)	5.1	0.54	16.3%	5.10 [4.04, 6.16]
Currie et al. (2015)	5.3	1.24	5.0%	5.30 [2.87, 7.73]
Helgerud et al. (2011)	4.6	1.31	4.5%	4.60 [2.03, 7.17]
Jayo-Montoya et al. (2020) HV	5	1.15	5.6%	5.00 [2.75, 7.25]
Jayo-Montoya et al. (2020) LV	3.5	1.29	4.6%	3.50 [0.97, 6.03]
Keteyian et al. (2014)	3.6	1.09	6.2%	3.60 [1.46, 5.74]
Kim et al. (2015)	6.46	1.47	3.7%	6.46 [3.58, 9.34]
Madssen et al. (2014)	3.3	1.26	4.8%	3.30 [0.83, 5.77]
Prado et al. (2016)	4.4	0.82	9.6%	4.40 [2.79, 6.01]
Rognmo et al. (2004)	6	3.14	0.9%	6.00 [−0.15, 12.15]
Villelabeitia-Jaureguizar et al. (2019)	3.88	0.55	16.0%	3.88 [2.80, 4.96]
Subtotal (95% CI)			**100.0%**	**4.61 [4.02, 5.19]**
Heterogeneity: $\tau^2 = 0.25$; $\chi^2 = 16.61$, df = 13 ($p = .22$); $I^2 = 22\%$				
Test for overall effect: $Z = 15.46$ ($p < .00001$)				
1.15.3 Control group				
Blumenthal et al. (2005)	−0.8	0.58	6.8%	−0.80 [−1.94, 0.34]
Cardozo et al. (2015)	−3.3	0.95	3.8%	−3.30 [−5.16, −1.44]
Eto et al. (2004)	0.7	0.61	6.5%	0.70 [−0.50, 1.90]
Giallauria, De Lorenzo, et al. (2006)	0.8	0.21	11.7%	0.80 [0.39, 1.21]
Giallauria, Lucci, et al. (2006)	−0.4	0.27	11.0%	−0.40 [−0.93, 0.13]
Giallauria et al. (2011)	−0.4	0.26	11.1%	−0.40 [−0.91, 0.11]
Giallauria et al. (2012)	1	0.61	6.5%	1.00 [−0.20, 2.20]
Giallauria et al. (2013)	1	0.85	4.4%	1.00 [−0.67, 2.67]
Lee et al. (2009)	−0.3	0.54	7.3%	−0.30 [−1.36, 0.76]
Oliveira et al. (2014)	−0.1	0.68	5.8%	−0.10 [−1.43, 1.23]
Ribeiro et al. (2012)	0.3	1.25	2.5%	0.30 [−2.15, 2.75]
Takagi et al. (2016)	0.3	1.36	2.2%	0.30 [−2.37, 2.97]
Takeyama et al. (2000)	1.1	0.48	8.1%	1.10 [0.16, 2.04]
Vona et al. (2009)	0.5	0.16	12.3%	0.50 [0.19, 0.81]
Subtotal (95% CI)			**100.0%**	**0.12 [-0.31, 0.55]**
Heterogeneity: $\tau^2 = 0.37$; $\chi^2 = 45.83$, *df* = 13 ($p < .0001$); $I^2 = 72\%$				
Test for overall effect: $Z = 0.53$ ($p = .59$)				

Test for subgroup differences: $\chi^2 = 185.56$, df = 2 ($p < .00001$), $I^2 = 98.9\%$

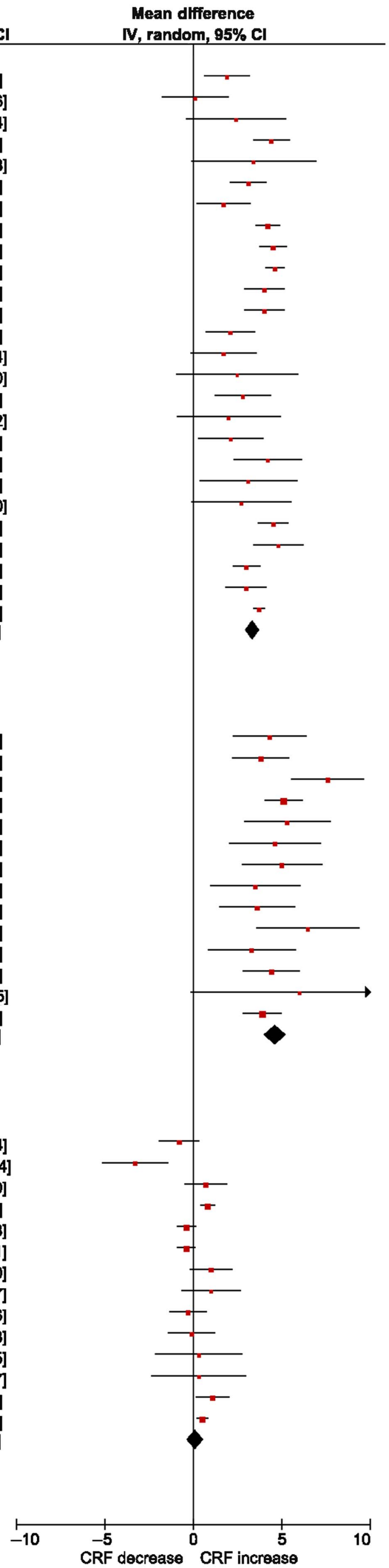

Figure 2 — Forest plot grouping the MD indices for VO_2peak in moderate continuous training, high-intensity interval training, and control group. MD = mean difference; VO_2peak = peak oxygen uptake; 95% CI = 95% confidence interval around mean difference; HV = high volume; LV = low volume.

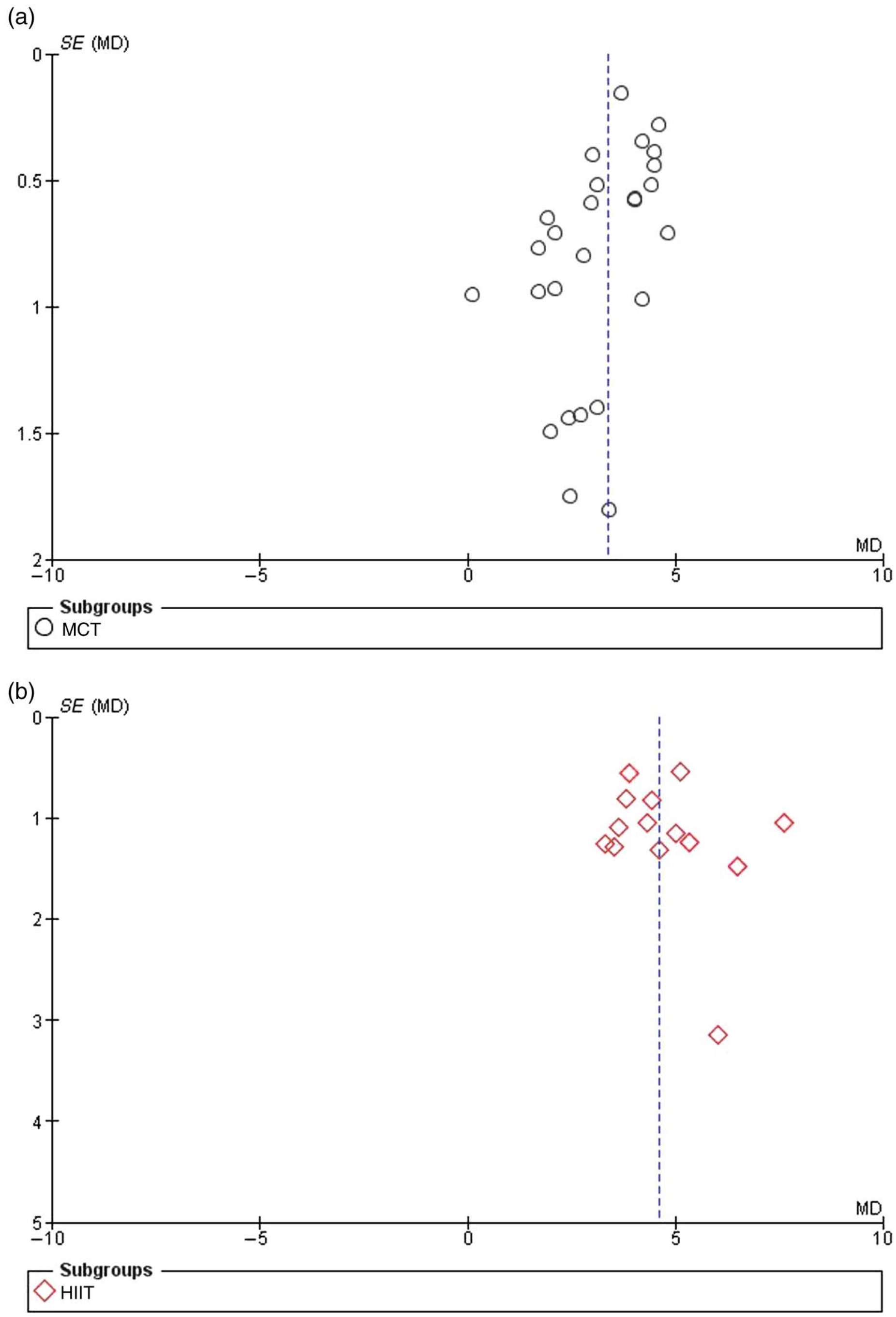

Figure 3 — Funnel plot of (a) the 26 MD indices of MCT and (b) the 14 MD indices of HIIT. MD = mean difference; MCT = moderate continuous training; HIIT = high-intensity interval training.

subjects, our findings showed the relevance of the type of cardiovascular event, the percentage of patients undergoing revascularization, the preintervention CRF, and the risk of a new event when MCT is applied. These four variables are related to some extent to the health state of the patient just before they began CR.

In regard to the type of cardiovascular event, CRF improvement was greater when the study sample was constituted by patients who had experienced an AMI. The severity of both diagnostics, AMI and angina, is different. While unstable angina is due to a transitory lack of oxygen, in AMI there is a necrosis of the myocardial cells, which affects the myocardial function directly. Thus, patients with AMI had a worse prognosis than patients with angina pectoris (Dudas et al., 2013). Similarly, CRF improvement was higher when the study sample was constituted by patients who had been revascularized. The combined effect of surgical manipulation of the heart and anesthesia can produce a worse heart condition for several weeks after surgery (Kalisnik et al., 2006). We also found that the effect of MCT is larger when this training method is applied in patients with low CRF or with a high risk of experiencing a new event. Previous studies have also reported that people in poor physical condition experience a higher exercise training effect on CRF (Støren et al., 2017). As we can see,

Table 4 Results of Analyzing the Influence of Categorical Moderator Variables on the Effect of MCT

Moderator variable	Category	*k*	MD [95% CI]	χ^2	*p*	I^2 (%)
(a) Treatment characteristics						
Training mode	Treadmill	6	1.63 [0.82, 2.44]	20.75	<.001	90.4
	Cycling	16	3.71 [3.32, 4.09]			
	Mixed	3	3.42 [1.72, 5.11]			
Wait time	≤3 weeks	10	4.05 [3.68, 4.42]	8.55	.010	76.6
	4–12 weeks	7	3.10 [2.16, 4.04]			
	>12 weeks	4	2.04 [0.46, 3.62]			
(b) Subject characteristics						
Type of revascularization procedure	CABG	2	3.26 [0.23, 6.30]	0.85	.650	0
	PCI	15	3.74 [3.32, 4.15]			
	Mixed	6	3.28 [2.36, 4.20]			
Risk of a new event	Low	5	2.40 [1.26, 3.54]	8.86	.010	77.4
	Moderate	14	3.04 [2.40, 3.67]			
	High	7	3.96 [3.46, 4.46]			
Type of cardiovascular event	AMI	15	3.82 [3.42, 4.22]	6.56	.009	84.8
	Mixed	10	2.60 [1.76, 3.44]			
Sex of the sample	Male	5	3.34 [2.42, 4.26]	0.01	.920	0
	Mixed	20	3.39 [2.94, 3.84]			
(c) Methodological quality						
Item 2	Yes	24	3.23 [2.81, 3.65]	9.91	.002	89.9
	No	2	4.58 [3.85, 5.32]			
Item 3	Yes	7	2.66 [1.62, 3.70]	2.36	.120	57.7
	No	19	3.54 [3.11, 3.96]			
Item 7	Yes	8	3.13 [2.19, 4.08]	0.28	.600	0
	No	18	3.42 [2.96, 3.76]			
Item 8	Yes	11	2.72 [1.77, 3.66]	3.36	.070	70.3
	No	15	3.67 [3.27, 4.07]			
Item 9	Yes	7	2.76 [1.61, 3.91]	1.91	.170	47.7
	No	19	3.61 [3.23, 3.99]			

Note. 95% CI = 95% confidence interval around MD; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; χ^2 = between-categories *Q* statistic for testing the significance of the moderator variable; I^2 = heterogeneity index; *k* = number of studies; MD = mean difference; MCT = moderate continuous training; *p* = probability level associated to the χ^2 statistic; PCI = percutaneous coronary intervention. Item 2 = subjects randomly assigned to groups; Item 3 = allocation concealed; Item 7 = assessors were blinded for at least one key outcome; Item 8 = data were obtained from at least 85% of the participants initially assigned to the groups; Item 9 = there were no attrition or, where it was not the case, data for at least one key outcome were analyzed by intention to treat.

these findings show an increased impact of CR when it is applied to patients with a worse prognosis or in a worse physical condition, and this reinforces the recommendation that all patients with CAD should be included in a CR program.

The wait time to start CR was also related to CRF improvement when CMT was used to carry out CR. We found that the highest gain appeared when CR began within 3 weeks after the event. If the wait time is longer, the increase in VO_2peak is smaller. Despite this variable being a continuous variable, due to the descriptive limitations of empirical studies, we could not analyze it in that way. However, our results are similar to the findings of Collins, Suskin, Aggarwal, and Grace (2015) who found a positive effect on functional capacity when CR initiation occurred within 3 months after the event. More considerable CRF improvement when CR starts early could be explained by an increased exercise training effect on cardiac function in the acute phase of the recovery. Haykowsky et al. (2011) reported that CR has a beneficial impact on left ventricular remodeling after AMI, but the most significant changes were found when CR began ~1 week after the event. Repair of the infarcted myocardium can be described in three phases: inflammatory (in hours), proliferative (in days), and maturation phase (in weeks). Early stimulation of inflammatory signaling is essential for the clearance of dead cells from the infarcted area (Frangogiannis, 2014). Exercise training could help to decrease the inflammatory response and allow higher adaptations in these acute phases. Therefore, from a clinical point of view, delays in starting CR should be minimized so that patients with CAD can obtain the maximum benefits.

As we have commented previously, it seems that the intensity could explain the difference between MCT and HIIT effect on VO_2peak. Surprisingly, when we carried out heterogeneity analyses to study the heterogeneity across the MCT groups, no other exercise training variables were related to the MCT effect. The only variable that showed differences was the training mode, which showed that the increase in CRF is higher when MCT is carried out on a bicycle. We hypothesized that this could be due to a lower

Table 5 Results of Analyzing the Influence of Continuous Moderator Variables on the MCT Effect

Moderator variable	*k*	*B*	*Z*	*p*
(a) Treatment characteristics				
Intensity	25	−0.0140	−0.569	.569
Session duration	26	0.0001	0.045	.964
Treatment duration	26	0.0497	1.747	.081
Number of sessions	26	0.0174	1.572	.116
Total volume	26	0.0001	0.888	.374
Frequency	26	−0.0364	−0.610	.542
(b) Subject characteristics				
Age	26	−0.0191	−0.349	.727
Sample size	26	0.0045	0.398	.691
Patients with AMI (%)	24	0.0169	1.802	.072
Undergoing an intervention (%)	23	−0.0215	−2.047	.041
Male (%)	25	0.0154	0.767	.443
CRF at baseline (ml·kg^{-1}·min^{-1})	26	−0.1029	−2.241	.025
(c) Extrinsic and methodological characteristics				
Publication year	26	−0.0124	−0.272	.786
Methodological quality score	26	−0.2733	−1.907	.057

Note. AMI = acute myocardial infarction; *B* = regression coefficient; CRF = cardiorespiratory fitness; *k* = number of studies; MCT = moderate continuous training; *p* = probability level associated to the *Z* statistic; *Z* = statistic for testing the significance of the moderator variable.

previous adaptation to this training mode in patients with CAD, which limits the muscular capacity of the patients to reach their maximum at baseline in the cardiopulmonary exercise test. Therefore, to know the true effect of CR, a previous adaptation period to baseline assessment should be performed when CR is carried out on a bicycle.

As regards the methodological quality of the studies that used MCT, our findings showed that quasi-experimental studies exhibited larger CRF improvements than experimental studies. The greater CRF improvement found in quasi-experimental studies could be due to selection bias (allocation and concealment), and therefore, their results should be interpreted with caution. In addition, we also found a residual statistical relationship between the methodological quality score and the effect of MCT ($p = .057$). In light of both these findings, it may be relevant to only examine randomized studies with higher methodological quality as a means of estimating the confidence-accuracy effect (Cooper, Hedges, & Valentine, 2019). The overestimation of the CRF improvement exhibited by the MCT group from nonrandomized studies leads us to conclude that a better estimate of the real CRF improvement of MCT is that based on randomized studies only, that is, $MD_+ = 3.23$ ml·kg^{-1}·min^{-1} in place of the overall estimate reported in Figure 2, $MD_+ = 3.36$ ml·kg^{-1}·min^{-1}. In addition, future research on this topic should routinely use randomized designs, as it seems that nonrandomized ones overestimate the true effect.

The CR-induced effects on the CRF found in studies that carried out aerobic training based on HIIT produced homogeneous findings ($p = .220$; $I^2 = 22\%$), showing no influence of the potential moderator variables. However, it should be highlighted that our systematic review showed low heterogeneity between HIIT protocols and participant characteristics in the studies that carried out CR based on HIIT. For instance, 65% of the studies ($n = 9$) that applied HIIT used long intervals (mainly 4-min intervals with 3-min rest between them) to carry out CR, 14% ($n = 2$) combined long and short intervals, and 21% ($n = 3$) used short intervals. In addition, only one of the studies that applied short intervals used an intensity above the PPO achieved in the cardiopulmonary exercise test. The low heterogeneity between HIIT protocols implemented in the included studies does not allow us to know the influence of different exercise exposures (e.g., long or short intervals, below or above the PPO). This justifies future research to study the effect of short intervals and intensities above the PPO on the CRF in patients with CAD.

As for patient characteristics, even though the mean age is similar in the MCT and HIIT groups (58.7 vs. 58.1 years, respectively), the age and preintervention CRF for the HIIT groups are more homogeneous than in the MCT groups (min–max: 53–63 years and 18.9–34.7 ml·kg^{-1}·min^{-1}; min–max: 52–69 years and 13.0–32.1 ml·kg^{-1}·min^{-1}, respectively). The greater homogeneity of these patients' characteristics in HIIT groups could also allow us to explain the absence of heterogeneity found in the results of studies that carried out CR based on HIIT. Moreover, HIIT protocols were only applied in patients with a low-to-moderate risk of a new event. We suppose that the HIIT protocols were not used with high-risk patients for fear that the patient would experience complications. However, this fear seems unjustified because a high intensity above the PPO with short intervals has proven to be less stressful on the heart and severe patients tolerated this high intensity better than moderate continuous efforts (Meyer et al., 1997; Vogiatzis et al., 2005). Therefore, future studies should focus on the effect of HIIT on high-risk older patients with low CRF at baseline.

As we have commented previously, our findings revealed that the MCT-induced effect on the CRF was inversely related to the preintervention VO_2peak, showing a lower CR-induced impact in patients with a higher level of physical fitness. However, despite the fact that the mean CRF at baseline of the included studies that applied HIIT protocols was higher than in the MCT studies (25.6 vs. 21.2 ml·kg^{-1}·min^{-1}, respectively), CR based on HIIT was more effective for improving VO_2peak. Therefore, it seems that, in patients with better physical fitness, HIIT protocols should be applied to reach a higher CR-induced effect on the CRF.

Although our findings show a lack of relevance of the exercise training characteristics for the effect of MCT or HIIT, previous studies have reported that proper management of the frequency, intensity, type, and time of training is important to increase the long-term effect of exercise training (Vanhees et al., 2012). Although the aim of our meta-analysis was not to analyze the application of exercise training principles in CR programs, such as individualization, overload, or progression, none of the included studies except one carried out a progression of the training load, even though the duration of this program was 26 weeks. Readjustment of work rates would have ensured that relative exercise intensity and metabolic stress remained unchanged throughout the training program (Meyer et al., 1997), thereby suggesting continuity in the CRF improvement. The lack of control of treatment variables and the incorrect manipulation or nonapplication of the exercise training principles could be the reason why the treatment variables were not related to the effect of both training methods on the CRF improvement.

Conclusion

Based on our findings, although current CR programs are sufficient to improve the CRF in patients with CAD, they are not optimized, and the training principles should be reviewed in order to achieve better short- and long-term effects. In addition, some variables should be taken into account when individualizing and applying an aerobic training program in CR correctly. MCT seems to be more useful for improving CRF in patients with CAD the sooner it starts. In addition, its effectivity is higher in patients with a worse prognosis revealed by lower CRF at baseline, or a higher risk of a new event, and in patients who had experienced AMI or had undergone revascularization. On the other hand, in patients with a better prognosis and a higher level of physical fitness, HIIT protocols should be applied to achieve a more significant CRF improvement as they seem to be more effective in this kind of patient. When carrying out the CR using a cycloergometer, clinicians should consider including an adaptation period and evaluate the performance after this adaptation period to avoid a possible misinterpretation of CRF changes.

Future studies should control and describe the wait time to start CR, the type of event and revascularization, and the risk of a new event to increase our knowledge about the effect of different aerobic training methods in this population. In addition, as the homogeneity of the training programs applied is remarkable, future studies should analyze the impact of varying HIIT setups (i.e., intensity above 100% PPO and short intervals) on different types of patients.

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