Journal of Physiotherapy 70 (2024) 106–114

Journal of PHYSIOTHERAPY

journal homepage: www.elsevier.com/locate/jphys

Research

Some types of exercise interventions are more effective than others in people with coronary heart disease: systematic review and network meta-analysis

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KEY WORDS

Coronary heart disease
Exercise
Systematic review
Network meta-analysis
Physical therapy

ABSTRACT

Question: What are the effects of different types of exercise treatments on oxygen consumption, quality of life and mortality in people with coronary heart disease? **Design**: Systematic review with network meta-analysis of randomised controlled trials. **Participants**: Adults with coronary heart disease. **Intervention**: Exercise interventions including aerobic (continuous or high-intensity interval) training, resistance training, respiratory muscle exercises, water-based exercises, yoga, Tai chi, Qigong exercises and a combination of different types of exercise. **Outcome measures**: Oxygen consumption, quality of life and mortality. **Results**: This review included 178 randomised controlled trials with 19,143 participants. Several exercise interventions improved peak oxygen consumption (mL/kg/min): high-intensity interval training (MD 4.5, 95% CI 3.7 to 5.4); combined water-based exercises and moderate-intensity continuous training (MD 3.7, 95% CI 1.3 to 6.0); combined aerobic and resistance exercise (MD 3.4, 95% CI 2.5 to 4.3); water-based exercises (MD 3.4, 95% CI 0.6 to 6.2); combined respiratory muscle training and aerobic exercise (MD 3.2, 95% CI 0.6 to 5.8); Tai chi (MD 3.0, 95% CI 1.0 to 5.0); moderate-intensity continuous training (MD 3.0, 95% CI 2.3 to 3.6); high-intensity continuous training (MD 2.7, 95% CI 1.6 to 3.8); and resistance training (MD 2.2, 95% CI 0.6 to 3.7). Quality of life was improved by yoga (SMD 1.5, 95% CI 0.5 to 2.4), combined aerobic and resistance exercise (SMD 1.2, 95% CI 0.6 to 1.7), moderate-intensity continuous training (SMD 1.1, 95% CI 0.6 to 1.6) and high-intensity interval training (SMD 0.9, 95% CI 0.1 to 1.6). All-cause mortality was reduced by continuous aerobic exercise (RR 0.67, 95% CI 0.53 to 0.86) and combined aerobic and resistance exercise (RR 0.58, 95% CI 0.36 to 0.94). Continuous aerobic exercise also reduced cardiovascular mortality (RR 0.56, 95% CI 0.42 to 0.74). **Conclusion**: People with coronary heart disease may use a range of exercise modalities to improve oxygen consumption, quality of life and mortality. **Registration**: PROSPERO CRD42022344545. **[Gomes-Neto M, Durães AR, Conceição LSR, Saquetto MB, Alves IG, Smart NA, Carvalho VO (2024) Some types of exercise interventions are more effective than others in people with coronary heart disease: systematic review and network meta-analysis. *Journal of Physiotherapy* 70:106–114]**

Introduction

Coronary heart disease (CHD) is the most common cause of death globally.[1] People with CHD typically have reduced cardiorespiratory fitness and quality of life, which can negatively impact health outcomes and predict morbidity and mortality.[2–4] Therefore, efforts should be directed towards optimising exercise performance to improve the overall health of people with CHD.[5]

Exercise interventions are a safe and effective form of therapy to improve physical outcomes, quality of life and survival in people with CHD.[6,7] It is well established that exercise has quantifiable effects upon the structure and function of the cardiovascular system, and is considered a cornerstone of cardiac rehabilitation.[8] Thus, exercise training, regardless of type, is considered an important intervention for health promotion and rehabilitation for people with CHD.[9–15] Despite the unequivocal benefits, the most effective exercise intervention for CHD patients remains debatable.

Recently, Xia et al[16] conducted a network meta-analysis to comprehensively compare and rank the efficacy of centre-based, home-based and tele-based cardiac rehabilitation in patients with CHD and concluded that centre-based cardiac rehabilitation is the most effective therapeutic approach for people with CHD. Huang et al[17] also performed a network meta-analysis to evaluate the comparative effects of all major cardiac rehabilitation strategies across a broad array of mortality and cardiovascular outcomes for adults with CHD and concluded that cardiac rehabilitation programs

https://doi.org/10.1016/j.jphys.2024.02.018

containing exercise might provide broader cardiovascular benefits compared with those without exercise. Despite these benefits, these studies did not investigate the relative effect of different types of exercise.[16,17] Therefore, a better understanding of the effects of different types of exercise is important for decision-making. In addition, it is believed that there is no published systematic review incorporating a network meta-analysis on the effects of different exercise interventions in people with CHD. A network meta-analysis informs professionals and patients on the ranking of the effectiveness of different exercise interventions, as it provides detailed inference from different treatment options.[18] Therefore, the current study expanded on previous publications by performing a comprehensive systematic literature review with network meta-analysis of randomised controlled trials to investigate the effects of different types of exercise interventions in people with CHD. A systematic review and network meta-analysis was conducted to inform clinical practice by comparing the relative effects of different types of exercise interventions in people with CHD.

Therefore, the research question for this systematic review was:

What are the effects of different types of exercise on peak oxygen consumption (VO_2peak), health-related quality of life (HRQOL) and mortality in people with CHD?

Methods

Design

A prospectively registered systematic review with network meta-analysis was performed according to Cochrane recommendations.[19] The review was reported according to the Network Meta-Analysis extension of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) reporting guidelines.[20] The PRISMA-NMA checklist is presented in Appendix 1 on the eAddenda.

Identification and selection of studies

Eligibility criteria

Selection criteria related to study design, population, intervention, comparison and outcome characteristics are described (Box 1). Exercise interventions were categorised into the following types of exercise training: aerobic (continuous or interval training, at low, medium or high intensity), resistance training, water-based exercises, yoga, Tai chi, Qigong exercises, respiratory muscle training and combinations of these different types of exercise. The exercise modalities listed above could be compared with each other or compared with control, which was defined as no exercise or usual care only. Exercise-based cardiac rehabilitation studies were considered for inclusion if, during the rehabilitation program, the exercise lasted for ≥ 50% of the rehabilitation session. We excluded studies with multimodality interventions, encouragement to perform physical activity or exercise, telerehabilitation and interventions focusing only on lifestyle changes. Appendix 2 on the eAddenda presents the categories of individual exercise modalities used in this review and how each category was defined. The outcomes of interest were VO_2peak, HRQOL and mortality (all-cause mortality and cardiovascular mortality).

Search strategy

We screened MEDLINE via PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, the Physiotherapy Evidence Database (PEDro), Google Scholar and the Scientific Electronic Library Online (SciELO) for relevant randomised trials from inception to December 2022, without language restrictions. The search strategies for MEDLINE via PubMed, EMBASE and CENTRAL are presented in Appendix 3 on the eAddenda. Grey literature was searched via the databases Gray literature, Opengrey and Proquest. We also checked the reference lists of the included trials for additional eligible trials.

The identified titles and abstracts were independently evaluated by two reviewers. If at least one of the reviewers considered one reference to be eligible, the full text was obtained for complete assessment. Two reviewers (LR and MGN) independently assessed the full texts to verify whether they met the eligibility criteria. In case of any disagreement, the authors discussed the reasons for their decisions, and a consensual decision was made.

Assessment of characteristics of studies

Two reviewers independently extracted data from the published reports. All studies selected from the databases were exported in an appropriate file and were stored together in reference management software[a]. The exported files were then also added to the systematic review software[b] for evaluation, selection and data extraction independently by two reviewers.

Participants

We extracted data on the number of randomised participants, their mean age, sex, surgical procedure, duration of diagnosis, frequency of treatment, length of treatment and baseline VO_2peak.

Exercise treatments

Exercise treatments were categorised as outlined in Appendix 2.

Outcomes

The outcomes of interest were VO_2peak in mL/kg/min measured by cardiopulmonary exercise test, HRQOL assessed by validated instruments, and mortality (all-cause mortality and cardiovascular

Box 1. Inclusion criteria.

Design
- Randomised clinical trials

Participants
- People aged ≥ 18 years
- History of CHD with angina pectoris or myocardial infarction, diagnosed by American Heart Association standard criteria[21] or documented on angiography, and/or percutaneous coronary intervention

Intervention
- Any type of exercise intervention

Comparator
- Another exercise intervention or control (no exercise/usual care)

Outcomes measures
- VO_2peak
- HRQOL
- Mortality
  - o all causes
  - o cardiovascular

CHD = coronary heart disease, HRQOL = health-related quality of life, VO_2peak = peak oxygen consumption

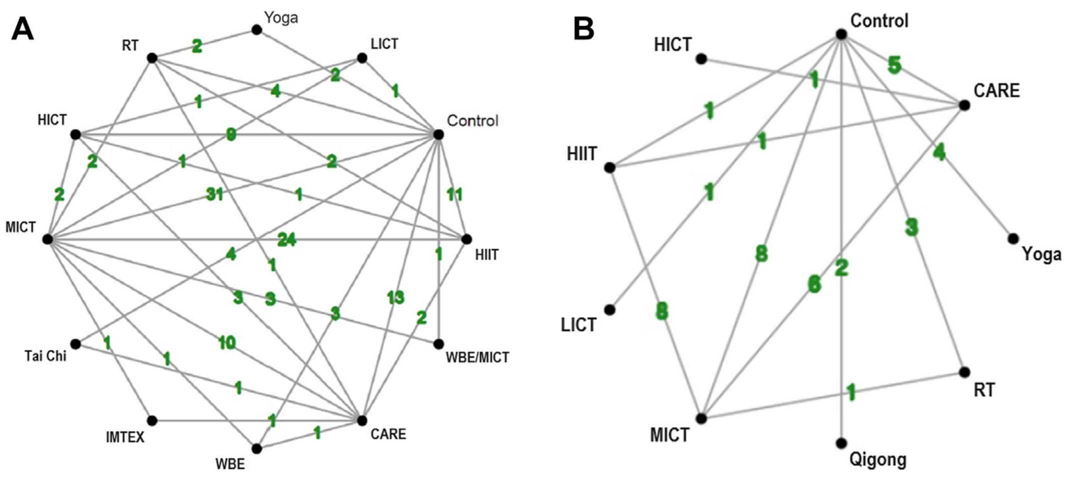

Figure 1. Network of eligible comparisons for outcomes. Network plot presenting the trial data contributing evidence comparing exercise treatment types. A. Peak VO_2: 12 interventions, 113 studies, 5,923 participants. B. HRQOL: 9 interventions, 38 studies, 6,915 participants. Numbers on the line indicate the number of trials conducted for the comparison.
CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, IMTEX = respiratory muscle training and aerobic training, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training, WBE = water-based exercise, WBEMICT = combined water-based exercises and moderate-intensity continuous training.

mortality). Regarding aerobic exercise intensity, the classification established by the European Association of Preventive Cardiology was followed: light ($<$ 40% maximal/VO_2peak, $<$ 55% maximum heart rate, $<$ 40% heart rate reserve); moderate (40 to 69% VO_2peak, 55 to 74% maximum heart rate, 40 to 69% heart rate reserve); and high ($>$ 70% VO_2peak, $>$ 75% maximum heart rate, $>$ 70% heart rate reserve).[6,22]

Risk of bias

The quality of studies included in this systematic review was scored by two reviewers using the PEDro scale.[24] The PEDro scale consists of 11 items. One item on the PEDro scale (eligibility criteria) is related to external validity and it is not included in the total score, making a score range of 0 to 10.[23]

Data analysis

Effectiveness of exercise types

In this systematic review, we performed random-effects pairwise and network meta-analysis using mean difference and/or standardised mean difference. A standardised mean difference of 0.2, 0.5 and 0.8 was interpreted as small, moderate and large effect size, respectively.[20]

First, the pairwise meta-analysis was conducted by comparing the mean change from baseline to endpoint for each group. Conversion of data to mean and standard deviation was based on recently established methods.[20,24,25] When the required outcome data were unavailable in the full text, but data were presented graphically, an attempt was made to digitise the graph[c].

Dichotomous outcomes for each comparison were expressed as risk ratios with 95% confidence intervals. Calculations were performed using a random-effects model. Statistical heterogeneity of the treatment effect among studies was assessed using Cochran's Q-test and the inconsistency I^2 test.[26]

If $>$ 10 studies were included in the meta-analysis, funnel plots of effect size (Hedge's g) against the standard error, Begg rank correlation test and Egger's regression test were used to assess publication bias.[20]

Network meta-analysis

A Bayesian and frequentist network meta-analysis was performed considering both a fixed-effect model and a model assuming random effects with homogeneous variability among studies. We presented the network meta-analyses of exercise interventions visually in a network plot.[27–29] The assessment of HRQOL in the included studies was performed using different instruments, so the SMD was used. Due to the limitation of the software to perform Bayesian analysis for SMD, only the frequentist model was used in the analysis of the HRQOL outcome.

Assessment of network transitivity

To assess transitivity, it was assumed that all exercise interventions included in the network meta-analysis were in-principle jointly randomisable, and we inspected the distribution of measures that could potentially modify effects (number of randomised participants, mean age, sex, surgical procedure, duration of diagnosis, frequency and length of treatment, and baseline VO_2peak) across the comparisons in the network.

Assessment of consistency

The consistency assumption was satisfied when the magnitude of the effect through direct and indirect comparisons was consistent.[27] The presence of inconsistency was assessed from indirect and direct evidence using node-split and the Bayesian *p*-values produced by the node splitting method.[27,28] To assess evidence consistency, a node-splitting analysis was performed separately for each of the comparisons in the treatment network on which both direct and indirect evidence was available. The objective was to identify whether the effect size was similar through direct and indirect comparisons.[27,28] In the case of inconsistency, the possible reasons were explored and the deviance information criterion was analysed.[27,28] Sensitivity analysis was performed by removing the studies that contributed to the inconsistency (deviance report $>$ 2).

To rank the different exercise treatments, the probability of each exercise intervention being the most effective, the second most effective, the third most effective and the fourth most effective was calculated. Surface under the cumulative ranking curves (SUCRA) on relevant outcomes were computed to rank the different exercise interventions in Bayesian analysis.[29,30] Thus, we used the SUCRA to infer an exercise interventions hierarchy: 0% (treatment is the worst for effectiveness) to 100% (treatment is the best for effectiveness). Pairwise and network meta-analyses were summarised in forest plots and league tables. All analyses were conducted using systematic review software[d] and the MetaInsight interactive web-based tool.[31]

Certainty of the evidence

The certainty of evidence produced by the synthesis for each outcome in network meta-analysis was evaluated using Confidence in

Table 1
Network meta-analysis mean difference results for exploratory analyses of all exercise types and all comparisons: VO_2peak.

HIIT	.	−0.3 (−3.3 to 2.6)		.	.	2.1 (1.2 to 3.0)	4.0 (−2.2 to 10.2)	1.1 (−1.9 to 4.0)	.		**4.5 (3.1 to 5.8)**
0.9 (−1.6 to 3.4)	**WBEMICT**			.	.	0.8 (−1.6 to 3.2)	.	.	.		**4.0 (0.1 to 8.0)**
1.2 (−1.8 to 4.1)	0.3 (−3.4 to 3.9)	**CARE**	0.0 (−6.3 to 6.3)	−2.0 (−5.5 to 1.5)	0.0 (−3.9 to 3.9)	1.2 (−0.3 to 2.7)	0.6 (−2.0 to 3.2)	0.0 (−3.5 to 3.5)	.		**3.0 (1.8 to 4.2)**
1.2 (0.1 to 2.3)	0.3 (−3.4 to 3.9)	−0.0 (−2.9 to 2.8)	**WBE**		−0.1 (−4.1 to 4.1)	−0.0 (−4.2 to 4.2)		.	.	.	**3.8 (0.7 to 7.0)**
1.4 (−1.2 to 4.0)	0.5 (−2.9 to 3.9)	0.2 (−2.3 to 2.7)	0.2 (−3.5 to 4.0)	**IMTEX**	.	−2.0 (−5.5 to 1.5)		.		.	.
1.6 (−0.6 to 3.8)	0.7 (−2.4 to 3.8)	0.4 (−1.8 to 2.5)	0.4 (−3.0 to 3.8)	0.2 (−3.1 to 3.4)	**Tai chi**	.		.			**2.9 (0.8 to 5.0)**
1.6 (0.8 to 2.4)	0.7 (−1.6 to 3.0)	0.4 (−0.5 to 1.3)	0.5 (−2.4 to 3.3)	0.2 (−2.3 to 2.8)	0.1 (−2.1 to 2.1)	**MICT**	−0.0 (−2.7 to 2.7)	0.5 (−2.5 to 3.5)		1.0 (−3.5 to 5.5)	**3.5 (2.7 to 4.20)**
1.9 (0.3 to 3.3)	1.0 (−1.6 to 3.6)	0.7 (−0.6 to 2.0)	0.8 (−2.2 to 3.7)	0.5 (−2.2 to 3.3)	0.4 (−1.9 to 2.6)	0.3 (−0.9 to 1.5)	**HICT**	.		1.0 (−2.5 to 4.5)	**2.8 (1.5 to 4.2)**
2.4 (0.8 to 4.0)	1.5 (−1.3 to 4.3)	1.2 (−0.5 to 2.9)	1.3 (−1.9 to 4.4)	1.0 (−1.9 to 4.0)	0.9 (−1.7 to 3.4)	0.8 (−0.8 to 2.4)	0.5 (−1.4 to 2.4)	**RT**	0.46 (−2.6 to 3.6)		1.8 (−0.3 to 3.7)
3.0 (0.6 to 5.5)	2.2 (−1.1 to 5.4)	1.9 (−0.6 to 4.3)	1.9 (−1.7 to 5.5)	1.7 (−1.7 to 5.0)	1.5 (−1.5 to 4.5)	1.5 (−0.9 to 3.8)	1.1 (−1.4 to 3.7)	0.6 (−1.6 to 2.9)	**Yoga**	.	1.3 (−1.8 to 4.4)
3.8 (1.4 to 6.2)	2.7 (−0.6 to 6.0)	2.4 (0.0 to 4.9)	2.5 (−1.2 to 6.1)	2.3 (−1.2 to 5.7)	2.1 (−1.0 to 5.2)	2.0 (−0.3 to 4.4)	1.7 (−0.7 to 4.1)	1.2 (−1.6 to 4.0)	0.6 (−2.7 to 3.8)	**LICT**	−1.0 (−5.2 to 3.2)
4.5 (3.7 to 5.4)	**3.7 (1.3 to 6.0)**	**3.4 (2.5 to 4.3)**	**3.4 (0.6 to 6.2)**	**3.2 (0.6 to 5.8)**	**3.0 (1.0 to 5.0)**	**3.0 (2.3 to 3.6)**	**2.7 (1.6 to 3.8)**	**2.2 (0.6 to 3.7)**	1.5 (−0.8 to 3.8)	0.9 (−1.4 to 3.3)	**Control**

Lower-left triangle presents the findings (MD with 95% CI) of the network meta-analysis. Upper-right triangle presents the findings (MD with 95% CI) of the pairwise meta-analyses. A positive MD favours the upper-left intervention, and a negative MD favours the lower-right intervention. Statistically significant findings are bolded. Blue indicates that the size of the treatment effect is likely to be compatible with a clinically important difference, whereas orange indicates that the intervention is not likely to be clinically relevant.
CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, IMTEX = respiratory muscle training + aerobic training, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training, WBE = water-based exercises, WBEMICT = combined water-based exercises and moderate-intensity continuous training.

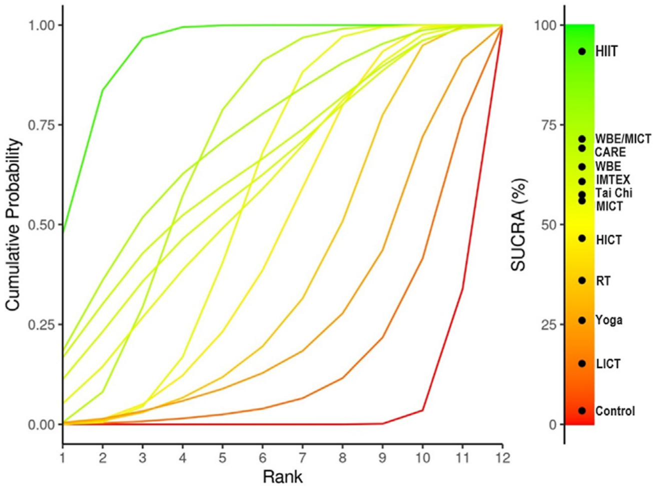

Figure 2. Ranking of treatments based on the surface under the cumulative ranking curves (SUCRA).
CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, IMTEX = respiratory muscle training and aerobic training, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training, WBE = water-based exercise, WBEMICT = combined water-based exercises and moderate-intensity continuous training.

Network Meta-analysis (CINeMA).[32] The risk of bias in the included studies was assessed by two reviewers independently using the revised Cochrane risk-of-bias tool for randomised trials (RoB 2).[33] To analyse imprecision and heterogeneity in relation to continuous outcomes, the CINeMA approach calls for the definition of the clinically important size of effect. The minimum clinically important difference in VO_2peak between exercise interventions was interpreted as 2 mL/kg/min. This was calculated as the smallest worthwhile effect based on a 10% improvement in VO_2peak from the average baseline VO_2peak (21 mL/kg/min, 95% CI 19 to 23) for the included trials. For the HRQOL outcome, SMD 0.5 was nominated as a clinically important effect, equating to a moderate effect size. Since it was not possible to perform network meta-analysis for the mortality outcome, Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) was used to assess the certainty of the evidence. Downgrade reasons were noted when the findings were summarised.

Results

The initial search led to the identification of 10,433 abstracts, from which 211 studies were considered to be potentially relevant and were retrieved for detailed analysis. After a complete reading of 211 studies, 33 were excluded; the reasons for exclusion are presented in Appendix 4 on the eAddenda. Finally, we included 178 randomised trials that evaluated exercise interventions (19,143 participants). Citations for the included studies are presented in Appendix 5 on the eAddenda. Appendix 6 on the eAddenda shows the PRISMA flow diagram of studies in this systematic review. A total of 100 trials compared exercise with usual care (non-exercise) and 78 trials compared groups receiving different exercise interventions.

Characteristics of included trials

The number of participants in the included trials ranged from 12 to 3,921, with a median sample size of 46 participants (IQR 26 to 73). The mean age of participants ranged from 49 to 79 years. Most studies included participants of both sexes, but there was an overall predominance of men. Participant age, the proportion of women and the baseline measures were balanced across comparisons. The baseline mean of VO_2peak of participants ranged 15 to 23 mL/kg/min. The baseline mean of VO_2peak for each exercise intervention is

Table 2
Network meta-analysis mean difference results for exploratory analyses of all exercise type and all comparison: HRQOL.

Yoga	.	.	.	.	.	.	.	**1.5 (0.5 to 2.4)**
0.3 (−0.8 to 1.4)	**CARE**	0.2 (−0.5 to 0.9)	.	.	0.3 (−1.51 to 2.1)	.	0.6 (−1.3 to 2.5)	**1.03 (0.3 to 1.8)**
0.4 (−0.7 to 1.5)	0.1 (−0.4 to 0.7)	**MICT**	.	−0.2 (−2.0 to 1.6)	0.3 (−0.33 to 0.9)	.	.	**1.14 (0.5 to 1.7)**
0.5 (−1.5 to 2.4)	0.2 (−1.2 to 2.0)	0.1 (−1.7 to 1.8)	**LICT**	.	.	.	.	1.00 (−0.7 to 2.7)
0.6 (−0.66 to 1.9)	0.3 (−0.7 to 1.4)	0.2 (−0.7 to 1.2)	0.2 (−1.7 to 2.1)	**RT**	.	.	.	0.69 (−0.3 to 1.7)
0.6 (−0.58 to 1.8)	0.3 (−0.4 to 1.1)	0.2 (−0.4 to 0.8)	0.1 (−1.7 to 2.0)	−0.03 (−1.1 to 1.1)	**HIIT**	.	.	**2.00 (0.3 to 3.7)**
0.8 (−0.72 to 2.3)	0.5 (−0.8 to 1.8)	0.4 (−0.9 to 1.7)	0.3 (−1.7 to 2.4)	0.18 (−1.3 to 1.7)	0.2 (−1.2 to 1.6)	**Qigong**	.	0.66 (−0.54 to 1.9)
0.9 (−1.25 to 3.1)	0.6 (−1.3 to 2.5)	0.5 (−1.4 to 2.5)	0.5 (−2.1 to 3.1)	0.30 (−1.9 to 2.5)	0.3 (−1.7 to 2.4)	0.1 (−2.2 to 2.4)	**HICT**	.
1.5 (0.5 to 2.4)	**1.2 (0.6 to 1.7)**	**1.1 (0.6 to 1.6)**	1.0 (−0.7 to 2.7)	0.8 (−0.1 to 1.7)	**0.9 (0.1 to 1.6)**	0.7 (−0.5 to 1.9)	0.5 (−1.4 to 2.5)	**Control**

Lower-left triangle presents the findings (SMD with 95% CI) of the network meta-analysis. Upper-right triangle presents the findings (SMD with 95% CI) of the pairwise meta-analyses A positive SMD favours the upper-left intervention, and a negative MD favours the lower-right intervention. Statistically significant findings are bolded. Blue indicates a large effect size of the treatment effect, whereas orange indicates a small effect size.
CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, HRQOL = health-related quality of life, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training.

summarised in Appendix 7 on the eAddenda. Parameters used in the application of exercise intervention were reported by most of the studies. Appendix 8 on the eAddenda describes summary characteristics of the included trials. Overall, the assumption of transitivity was considered to be valid. Participants' characteristics stratified by network, number of randomised participants, surgical procedure, duration of diagnosis, frequency and length of treatment in pairwise comparison are summarised in Appendix 9 on the eAddenda. Results of individual assessment using the PEDro scale are presented in Appendix 10 on the eAddenda.

Comparative effectiveness of exercise treatment types

VO_2peak (mL/kg/min)

Pairwise meta-analyses for all comparisons are provided with detailed individual trial-level information. Appendix 11 on the eAddenda shows the forest plot of change in VO_2peak in all pairwise meta-analyses. Most trials included a non-exercise group (usual care). A total of 113 studies were included in the network meta-analysis for VO_2peak, including a total of 5,923 participants with CHD. Figure 1A shows the network of eligible comparisons for VO_2peak.

Synthesis of VO_2peak results

A forest plot (Appendix 12 Figure A on the eAddenda) of the exercise interventions' effects demonstrated that, compared with no treatment (usual care), HIIT had the largest MD. Low-intensity continuous training (LICT) and yoga were not superior when compared with usual care. HIIT, CARE, MICT and HICT exercises had the narrowest confidence intervals, providing some certainty in the results for these exercise types.

The network was well connected, with 42% of comparisons having direct evidence (Figure 1A). The network consisted of 113 studies (5,923 participants) with 102 two-arm studies, 11 multi-arm studies and 66 possible pairwise comparisons. The league table (Table 1) shows the VO_2peak pooled estimates for the results of direct comparisons only (pairwise meta-analysis), and combination of direct and indirect-comparisons meta-analysis (network meta-analysis).

In the network meta-analysis, HIIT had great improvement in VO_2peak ($>$ 4 mL/kg/min). Water-based exercise (WBE)/MICT, WBE, CARE and IMTEX exercises also had great improvement in VO_2peak ($>$ 3 mL/kg/min). Tai chi, MICT, HICT and RT also improved VO_2peak ($>$ 2 mL/kg/min). LICT and yoga were not superior in VO_2peak improvement when compared with the usual care group. The figure with the ranking of treatments based on the SUCRA is presented in Figure 2.

This study identified some incoherence in node-split analysis for these comparisons: MICT versus usual care, MICT versus HIIT, CARE versus HIIT, CARE versus IMTEX, CARE versus MICT and LICT versus usual care. Appendix 13 on the eAddenda shows the global incoherence (node-split analysis) for primary models and sensitivity analyses. Due to the inconsistency found, we performed a sensitivity analysis. In the analyses performed, it was identified that the study by Benetti et al had a deviance report above 2. This study was removed from the analysis; however, the inconsistency remained. Appendix 14 on the eAddenda shows the sensitivity analysis (residual deviance from network model and unrelated mean effect inconsistency model for all studies, per-arm residual deviance for all studies, and leverage versus residual deviance).

HRQOL

Pairwise meta-analyses for all comparisons are provided with detailed individual trial-level information. Appendix 11 shows the forest plot of change in HRQOL in all pairwise meta-analyses. Most trials included a non-exercise group (usual care). Thirty-nine studies were included in the network meta-analysis for HRQOL, including a total of 7,118 participants with CHD. Figure 1B shows the network of eligible comparisons for HRQOL.

Synthesis of HRQOL results

A forest plot of the exercise interventions effects demonstrated that, compared with no treatment (usual care), yoga had the largest SMD (1.5, 95% CI 0.53 to 2.38). Other exercise interventions demonstrated similar SMDs: 1.2 (95% CI 0.6 to 1.7) for CARE, 1.1 (95% CI 0.6 to 1.6) for MICT and 0.9 (95% CI 0.1 to 1.6) for HIIT. HICT, LICT, RT and Qigong were not superior when compared with usual care (Appendix 12 Figure B). CARE and MICT exercises had the narrowest confidence intervals, providing some certainty in the results for these exercise types.

The network was well connected, with 33% of comparisons having direct evidence (Figure 1B). The network consisted of 39 studies (7,118 participants) with 38 two-arm studies, one multi-arm study and 38 possible pairwise comparisons. The league table (Table 2) show the HRQOL pooled estimates for the results of direct comparisons only (pairwise meta-analysis), and combination of direct and indirect-comparison meta-analysis (network meta-analysis). Comparing the various exercise types with each other, yoga had larger improvement in HRQOL compared with other exercise types. CARE, MICT and HIIT exercises also had larger improvement in HRQOL compared with other exercise interventions.

The inconsistency in the HRQOL outcome was assessed by using a design-by-treatment model, a loop inconsistency model and a node-splitting model. No evidence of inconsistency was found. Appendix 15 on the eAddenda presents the global incoherence (node-split analysis) for primary models (HRQOL).

Mortality

Due to the small number of studies that analysed mortality (all-cause mortality and/or cardiovascular mortality), it was not possible to perform a network meta-analysis comparing the different types of exercise. Most of the included studies were of continuous aerobic exercise. In addition to continuous aerobic exercise, other studies have tested the effect of CARE. Therefore, we performed only pairwise meta-analysis comparing the effect of exercise (in general) on mortality. When pooling all studies together we observed an RR of 0.74 (95% CI 0.62 to 0.89), indicating a moderate reduction in all-cause mortality risk in the exercise group compared with usual

Table 3
Evaluation of the certainty of evidence using Confidence in Network Meta-analysis (CINEMA) and Grading of Recommendations, Assessment, Development, and Evaluations (GRADE): VO_2peak.

Comparison	Studies *(n)*	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
CARE:HICT	3	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
CARE:HIIT	2	Major concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	Very low
CARE:IMTEX	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	Some concerns	Very low
CARE:MICT	11	Major concerns	Low risk	No concerns	No concerns	Major concerns	Some concerns	Very low
CARE:RT	2	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
CARE:Tai chi	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
CARE:UC	14	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
CARE:WBE	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:HIIT	1	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
HICT:LICT	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
HICT:MICT	2	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
HICT:UC	8	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
HIIT:MICT	24	Major concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Very low
HIIT:RT	2	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
HIIT:UC	11	Major concerns	Low risk	No concerns	No concerns	No concerns	No concerns	Low
IMTEX:MICT	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LICT:MICT	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
LICT:UC	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	Some concerns	Very low
MICT:RT	3	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
MICT:UC	33	Major concerns	Low risk	No concerns	No concerns	Some concerns	Some concerns	Very low
MICT:WBE	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
MICT:WBEMICT	3	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
RT:UC	5	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
RT:Yoga	2	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
Tai chi:UC	4	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
UC:WBE	3	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
UC:WBEMICT	1	Major concerns	Low risk	No concerns	No concerns	Some concerns	No concerns	Very low
UC:Yoga	2	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low

CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, IMTEX = respiratory muscle training and aerobic training, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training, UC = usual care, WBE = water-based exercise, WBEMICT = combined water-based exercises and moderate-intensity continuous training.

care, with low heterogeneity across studies (I^2 = 0%). In the 10 studies (2,605 participants) that reported cardiovascular mortality, we observed that the RR was 0.55 (95% CI 0.41 to 0.73), indicating a significant reduction in cardiovascular mortality risk in the exercise group compared with usual care, with low heterogeneity across studies (I^2 = 0%). Forest plots of all-cause and cardiovascular mortality risk in all pairwise meta-analyses are shown in Appendix 16 Figures A and B on the eAddenda.

A subgroup analysis was then performed with the two different types of exercise that were able to be grouped (continuous aerobic exercise and CARE). When pooling the 16 studies on continuous aerobic exercise, we observed an RR of 0.67 (95% CI 0.53 to 0.86) indicating a significant reduction in all-cause mortality risk in the continuous aerobic exercise group compared with usual care, with low heterogeneity across studies (I^2 = 0%). When we performed a subgroup analysis with nine studies of CARE, the meta-analyses showed a significant reduction in all-cause mortality risk with an RR of 0.58 (95% CI 0.36 to 0.94) in the CARE group compared with usual care, with low heterogeneity across studies (I^2 = 0%).

When pooling the seven studies on continuous aerobic exercise, we observed an RR of 0.56 (95% CI 0.42 to 0.74) indicating a large reduction in cardiovascular mortality risk in the continuous aerobic exercise group compared with usual care, with low heterogeneity across studies (I^2 = 0%). When a subgroup analysis was performed with three studies of CARE, the meta-analyses showed an unclear reduction in cardiovascular mortality risk (RR 0.33, 95% CI 0.07 to 1.61) in the CARE group compared with usual care, with low heterogeneity across studies (I^2 = 0%). Forest plots of all-cause and cardiovascular mortality risk in the subgroup analysis are presented in Appendix 16 Figures C and D.

As the studies differed in endpoint for mortality, a subgroup analysis was performed for mortality during the exercise training protocol and at follow-up (after completion of the exercise protocol). This is presented in Appendix 16 Figures E to H.

Certainty of the network meta-analysis evidence

The certainty of the evidence for the VO_2peak and HRQOL outcomes as measured with CINeMA varied from low to very low. Most of the comparisons were rated as very low. Full CINeMA information is presented in Table 3 for VO_2peak and Table 4 for HRQOL. The certainty of the evidence was rated as moderate for the all-cause mortality and cardiovascular mortality outcomes. The downgrade was performed for the risk of bias. Full information on GRADE is described in the Table 5.

Discussion

It is believed that this systematic review and network meta-analysis is the most comprehensive and largest data synthesis on different exercise interventions for adults with CHD. This study showed that exercise training has clear benefits for VO_2peak, HRQOL and mortality. Moreover, HIIT had the largest mean difference of change in VO_2peak followed by WBEMICT, CARE, WBE, IMTEX, Tai chi, MICT, HICT and RT. Regarding HRQOL, this study showed that yoga and CARE were the most efficient types of exercise intervention, followed by MICT and HIIT. In general, exercise training (continuous aerobic exercise and CARE) was also effective in reducing all-cause and continuous aerobic exercise in reducing cardiovascular mortality.

This study included a total of 178 randomised trials that enrolled 19,143 participants and demonstrated novelty in the exploration of the effect of different types of exercise for people with CHD. The findings with respect to VO_2peak are important, as this clinical marker is the gold standard method to assess cardiorespiratory fitness. In turn, cardiorespiratory fitness is considered by the American Heart Association and others as perhaps the strongest prognostic marker of survival and HRQOL.[34,35] The current results are therefore an important decision-making guide to both researchers and clinicians in the field of cardiovascular rehabilitation.

These data showed that any type of exercise is better than no exercise; however, HIIT may be optimal for improvements in VO_2peak in people with CHD. A previous meta-analysis showed that the potential superiority of HIIT over MICT disappeared when isocaloric protocols were compared in individuals with CHD[13] or heart failure.[36] Hence, it is still uncertain whether energy expenditure, exercise type or a combination of both predicts the optimal VO_2peak gain in patients with CHD. Future studies should investigate this topic.

Table 4
Evaluation of the certainty of evidence using Confidence in Network Meta-analysis (CINEMA) and Grading of Recommendations, Assessment, Development, and Evaluations (GRADE): HRQOL.

Comparison	Studies *(n)*	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
CARE:HICT	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
CARE:HIIT	1	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
CARE:MICT	6	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
CARE:UC	5	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
HIIT:MICT	8	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	Very low
HIIT:UC	1	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
LICT:UC	1	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
MICT:RT	1	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
MICT:UC	8	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
Qigong:UC	2	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
RT:UC	3	Major concerns	Low risk	No concerns	Some concerns	Some concerns	No concerns	High
UC:Yoga	4	Major concerns	Low risk	No concerns	No concerns	Major concerns	No concerns	Very low
CARE:LICT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
CARE:Qigong	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
CARE:RT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
CARE:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:HIIT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:LICT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:MICT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:Qigong	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:RT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:UC	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HICT:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HIIT:LICT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HIIT:Qigong	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HIIT:RT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
HIIT:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LICT:MICT	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LICT:Qigong	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LICT:RT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
LICT:Yoga	0	Some concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
MICT:Qigong	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
MICT:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Qigong:RT	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
Qigong:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low
RT:Yoga	0	Major concerns	Low risk	No concerns	Major concerns	No concerns	No concerns	Very low

CARE = combined aerobic and resistance training, HICT = high-intensity continuous training, HIIT = high-intensity interval training, HRQOL = health-related quality of life, LICT = light-intensity continuous training, MICT = moderate-intensity continuous training, RT = resistance training, UC = usual care.

The strengths of this study were the inclusion of a vast number of randomised trials and important clinical outcomes (VO_2peak, HRQOL and mortality). This network meta-analysis provides further support for different types of exercise training and guideline-recommended care. These findings are important because they support evidence-based decision-making in cardiovascular rehabilitation.

The results of this network meta-analysis should be interpreted with some caution for several reasons. Few trials have provided a direct comparison between different exercise interventions (most of the studies compared with a usual care group). Studies did not provide exercise total energy expenditure, which would be interesting to compare across different types of exercise, especially to confirm or reject the apparent superiority of an exercise type. Substantial risk of bias in studies was found in the primary analyses. Some inconsistencies (discrepancies between direct and indirect evidence) in some comparisons were observed. The certainty of the evidence for the VO_2peak and HRQOL outcomes ranged from low to very low. Nevertheless, these results ultimately reflect the body of evidence

Table 5
Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) summary of findings table for mortality.

Exercise compared with usual care for mortality in chronic heart disease

Patient or population: people with chronic heart disease
Setting: rehabilitation
Intervention: exercise training
Comparison: usual care

Outcomes	Anticipated absolute effects[a] (95% CI)		Relative effect (95% CI)	Participants *(n)* (studies *(n)*)	Certainty of the evidence (GRADE)
	Risk with usual care	Risk with exercise			
Mortality	81 per 1,000	60 per 1,000 (50 to 72)	RR 0.74 (0.62 to 0.89)	6,261 (27)	⊕⊕⊕○ Moderate[b]
Cardiovascular mortality	93 per 1,000	51 per 1,000 (38 to 68)	RR 0.55 (0.41 to 0.73)	2,605 (10)	⊕⊕⊕○ Moderate[b]

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a] The risk in the experimental group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
[b] Studies without allocation concealment, random allocation, intention-to-treat analysis, and/or sample size calculation.

about different types of exercise and relevant outcomes for adults with CHD.

Further research is required to investigate how to sustain the positive effects of different types of exercise over time and to determine the characteristics of exercise training (intensity, frequency and duration) for optimal effects on VO_2peak, HRQOL and mortality. In addition, more well-designed trials are necessary to determine the most appropriate types of exercise by directly comparing the different types.

In conclusion, this network meta-analysis showed that exercise training has clear benefits on VO_2peak, HRQOL and survival. HIIT was possibly the most effective type of exercise intervention to improve VO_2peak in adults with CHD. Regarding HRQOL improvements, this analysis showed that yoga and CARE were the most effective type of exercise intervention. In addition, exercise training (continuous aerobic exercise and CARE) was also effective in reducing all-cause and cardiovascular mortality (continuous aerobic exercise). The findings from this network meta-analysis represent the best evidence currently available to guide the decision-making in the field of cardiovascular rehabilitation for CHD patients.

What was already known on this topic: People with coronary heart disease typically have reduced cardiorespiratory fitness and quality of life, which can negatively impact health outcomes and predict morbidity and mortality. Exercise interventions are a safe and effective form of therapy to improve physical outcomes, quality of life and survival in people with coronary heart disease. However, there is limited evidence to support the use of one type of exercise or program characteristic over another.

What this study adds: Most exercise types were more effective than usual care for improving peak oxygen consumption, health-related quality of life and survival in people with coronary heart disease. High-intensity interval training, water-based exercise combined with moderate-intensity continuous training, combined aerobic and resistance exercise, and moderate-intensity continuous training were the most efficient types of exercise intervention to improve peak oxygen consumption, while yoga and combined aerobic and resistance exercise were best at improving health-related quality of life. Continuous aerobic exercise and combined aerobic and resistance exercise were effective in improving survival.

Footnotes: [a] EndNote X7.8, Clarivate, Philadelphia, USA.

[b] Rayyan software, Qatar Computing Research Institute, Ar Rayyan, Qatar.

eAddenda: Appendices 1 to 16 can be found online at https://doi.org/10.1016/j.jphys.2024.02.018.

Ethical approval: The study did not require Research Ethics Committee approval as it involved secondary analysis of published studies.

Competing interest: Nil.

Source of support: The study received funding support from the Conselho Nacional de Desenvolvimento Científico e Tecnológico – Brasil (CNPq). "Bolsista do CNPq – Brasil.

Provenance: Not invited. Peer reviewed.

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