Which modes of cardiac rehabilitation are most effective in adults with heart failure? a Bayesian network meta-analysis

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Abstract

Objective Currently, the most effective exercise-based cardiac rehabilitation (CR) modality in adults with heart failure (HF) remains unknown. Thus, our network meta-analysis (NMA) aimed to evaluate the efficacy of different modalities of exercise-based CR in patients with HF.

Methods By searching PubMed, Cochrane Central Register of Controlled Studies (CENTRAL), and Embase, randomized controlled trials (RCTs) assessing the efficacy of various CR treatments on heart failure to May 2022 were obtained. Bayesian NMA was utilized for data analysis and compare the efficacy of various rehabilitation modalities. Assessment of risk of bias (ROB) utilizing the Cochrane Risk of Bias tool for included publications.

Results A total of 8,354 participants from 72 studies were included. Some of the included literature had a high risk of bias. These studies were published between 1990 and 2022, with participants aged 44-81 years and intervention durations ranging from 8 to 48 weeks. In accordance with the Bayesian NMA model, following CR methods have the highest ranking compared to usual care: cardiac telerehabilitation (CTR) for health-related quality of life (HR-QOL) [surface under the cumulative ranking (SUCRA)=84.48%; standard mean difference (SMD)=-0.82, Credible interval (CrI) -1.32, -0.33)], center-based cardiac rehabilitation (CBCR) for peak oxygen uptake (peakVO2)[SUCRA=78.46%; mean difference (MD)=2.48, CrI 1.73, 3.24], CBCR for 6-minute walk test (6-min WT) [SUCRA=99.99%; MD=39.89, CrI 29.62, 50.52].

Conclusion The results show that CTR is the most effective treatment for improving HR-QOL for patients with HF. The results need to be interpreted with care. This evidence could be considered by clinicians when recommending CR to patients with HF to achieve better outcomes.

Keywords Cardiac rehabilitation therapies, Heart failure, Adults, Bayesian network meta-analysis.

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Introduction

Heart failure (HF) is a syndrome in which the pumping function of the heart is impaired for multiple reasons, and the cardiac output cannot meet the basic metabolic requirements of the systemic tissue. Characterized by respiratory distress, activity limitation, and fluid retention, which limit patients' daily activities and social interactions, resulting in a poor quality of life. HF is also a public health problem with severe consequences. According to estimates, about 6 million Americans over 20 years of age suffered from HF during 2015-2018[1], and it is estimated that over 60 million people globally suffer from HF[2]. In addition, past research have demonstrated that mortality rates for people suffering from acute HF in European countries range from 21.6% to 36.5% and for those who have chronic HF from 6.9% to 15.5%[1]. Moreover, HF also burdens the healthcare system heavily regarding resource use and expenditures[3].

The conventional view is that medication therapy is an efficient method of treating patients with HF, and that patients with HF are regarded to be at risk from physical exercise and are generally prevented from engaging in physical activity. Several studies, on the other hand, have established the safety and advantages of physical activity for people with heart failure[4], and the negative consequences of long-term bed rest, they also confirmed that exercise-based cardiac rehabilitation (CR) is safe and effective in patients with HF[5]. Besides, studies found that CR combined with medication therapy can enhance life quality, decrease mortality and hospitalization rates compared to medication therapy alone[6, 7]. According to current guidelines for people with HF, regular exercise training has been given a recommendation level I and an evidence level A. Patients with ambulatory symptoms (stage C) with stable New York Heart Association (NYHA) cardiac functional class II or III HF symptoms should be considered for supervised CR based on guideline-guided medical therapy[8]. The above effects on patients with HF can be explained in several ways in terms of mechanisms, CR increases and improves oxygen uptake and utilization by skeletal muscle, increasing the body's maximal oxygen uptake and improving hemodynamics[9], it also increases muscle fiber strength and power, improves muscle perfusion and metabolism, and increases exercise endurance in patients[10]. Many studies have discovered that CR reverse left ventricular remodeling in patients with clinically stable heart failure, resulting in better aerobic capacity and peak oxygen uptake (peak VO2) improvement, and modification of cardiovascular disease risk factors[11]. Various CR modalities are currently available, CR is performed under medical supervision in the hospital and is called center-based cardiac rehabilitation (CBCR). In addition, home-based cardiac rehabilitation (HBCR), cardiac telerehabilitation (CTR), and hybrid cardiac rehabilitation (HCR), which combines short-term CBCR with HBCR have become increasingly popular in recent years[12-14].

Although some guidelines highly recommend early CR for patients with HF, the most effective rehabilitation modality is currently inconclusive. Moreover, the previous papers have the following limitations. First, a study published by Patterson K included randomised controlled trials (RCTs) comparing various CR modalities. However, the study population included patients with other cardiovascular diseases in addition to HF, the included diseases varied widely in homogeneity leading to unreliable conclusions[15]. Second, previously published articles on the effectiveness and safety of CTR were pairwise meta-analyses due to statistical methodology deficiencies. Presently, no studies can include all CR modes to compare the superiority of CR modalities simultaneously[16, 17]. Network meta-analysis (NMA) can analyzes the efficacy of various interventions by combining direct and indirect evidence from included studies. Finally, the database searched and the sample size included in the previous studies were inadequate. Thus, more evidence needs to be included to improve the stability of the results. Compared with pairwise meta-analysis, the accuracy of estimates of effect is improved. Therefore, the main aim of our study was to determine the optimal CR mode for treating patients with HF by summarizing and analyzing the available evidence.

Methods

This study was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) extended statement for systematic reviews that encompasses network meta-analysis of medical treatments[18]. None of the analyses required ethical approval or patient agreement, as they were all based on published studies.

Search strategy and study selection

An electronic search for "Randomised Controlled trial", "Heart failure", "Cardiac rehabilitation", "Rehabilitation", "Exercise", "Exercise therapy", "Physical exertion" and "Physical fitness" search terms was conducted using Medical Subject Headings (MeSH), searching PubMed, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) for studies published between the inception to May 2022. Additional searches included a review of the literature included in previously published meta-analyses. To ensure that no pertinent studies were missed, the proceedings of significant international conferences from 2000 to 2022 were also thoroughly searched. **Supplement table 1** contains a complete list of search terms.

J-WT and X-TF assessed titles and abstracts of studies according to inclusion and exclusion criteria while removing duplicate studies. Full text of the studies after initial screening were further screened independently by J-WT and X-TF. All citations were downloaded and managed using Endnote 20.2 (BLD 17373). To ensure the success of further analysis, J-WT evaluated the data's reliability and completeness. All disagreements were discussed and adjudicated by an experienced author (JJ).

Inclusion and exclusion criteria

All inclusion criteria follow the selection criteria of the Participants, Interventions, Comparators, Outcomes, and Study design framework (PICOS). The Adults (⩾18 years) with HF (reduced or preserved ejection fraction) who completed at least eight weeks of CR consisted the population of interest. The diagnostic criteria for heart failure are based on guidelines[8]. In terms of intervention and comparators, studies comparing HF patients using different CR modalities (CBCR, HBCR, CTR, or HCR) and usual control (UC) were included. The types of articles included were must RCT. The primary outcome was health-related quality of life (HR-QOL), other outcomes were cardiopulmonary function, and exercise tolerance. Professional scales measure HR-QOL, peak oxygen uptake (peak VO2) was used to determine cardiopulmonary function, and 6-minute walking test (6-min WT) was used to determine exercise tolerance.

Additional inclusion criteria required that RCTs must be published in English-language, scientific publications.

Data extraction

We analyzed the collected data and demographics of all research included, J-WT and X-TF independently extracted pertinent publication data (e.g., author, title, year, journal), patient numbers, patient characteristics (e.g., age and sex), interventions, and outcome measures (e.g., cardiopulmonary function, exercise tolerance, quality of life).

The mean and standard deviation (SD) of the pre and post-intervention were the extracted outcome data. To obtain standard data that can be evaluated, data expressed using the median or alternative approaches were changed to mean and SD.

Risk of bias assessment

Two investigators evaluated and classified the risk of bias (ROB) for each included trial using the Cochrane Risk of Bias tool[19], which examined potential selection bias (random sequence generation and allocation concealment), performance bias (blinding of patients and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting) and other bias. The risk of bias in studies was categorized as high, low, or unclear. ROB was assessed through Review Manager (version 5.4).

Statistical analysis

The homogeneity, transitivity, and consistency hypotheses are the three main hypotheses of the NMA[20]. We validated these hypotheses by assessing clinical aspects (e.g., patients' characteristics, follow-up time, and outcome indicators), methodology (similarity of trial design), and statistics (outcome effect size and accuracy) of the included studies[21, 22]. Network plots were created to describe and present the comparative relationships between different exercise modalities. Each intervention has a corresponding node, the size of the node is related to the number of participants for that intervention type, and the thickness of the line between interventions is related to the number of studies for that comparison. Based on a Bayesian framework and the Markov Chain Monte Carlo (MCMC) method, the NMA used a random effects model to extract descriptive data from each study and to simultaneously compare data from direct and indirect comparisons between multiple interventions. Since the effect indicators used were continuous variables, means and standard deviations (SDs) of the relevant groups for each study were used to calculate the standardized mean differences (SMDs) for each comparison [39]. The 95% Credibility Interval (CrI) and pooled SMDs were calculated as measures of estimated uncertainty and pooled effect sizes. A state is randomly selected, and three parallel Markov chains are initially created to simulate the exact estimation of the model. 50,000 iterations were generated for each chain, and the initial 10,000 iterations were discarded due to the aging period to ensure that the deviation from the initial value was minimized when the chain reached its target distribution[23]. The Brooks Gelman Rubin diagnostic method was used to evaluate the convergence of the model by visual trajectory plots combined with historical trajectories of density plots[24]. The surface cumulative ranking (SUCRA) was used to determine the superiority of the intervention. SUCRA ranges from 0% to 100%, with a SUCRA value of 100% indicating the best intervention and a value of 0% indicating the worst intervention[25]. We assessed the consistency hypothesis by using node-splitting method, the P value obtained by analysis is less than 0.05, and it was considered that there was significant inconsistency between the two interventions[25]. To check whether small studies lead to publication bias in the NMA, we generated network funnel plots and performed visual checks using symmetry criteria. The aforementioned analyses were conducted STATA software (version 14.2) and OpenBUGS (version 3.2.3 rev 1012, MRC, UK).

Results

Literature selection and study characteristics

7,149 records were identified after preliminary search, after filtering duplicates, the list contains 5,461 records. After reviewing the titles and abstracts, 391 studies were subjected to a complete full manuscript review. Ultimately, 72 studies were included in this review. The detailed process is illustrated in **Figure 1**. These studies consisted of participants across different interventions, providing adequate data published from 1990 to 2022, ranging from 44-81 years, and intervention duration range from 8 to 48 weeks. 4 studies did not report age, 9 studies did not report gender, while the remaining studies included both sexes. More than 80% of RCTs participants were from Europe and the United States with 7,191 participants. Key characteristics of participants and interventions for included studies (n=72) are presented in **Table 1**[26-97].

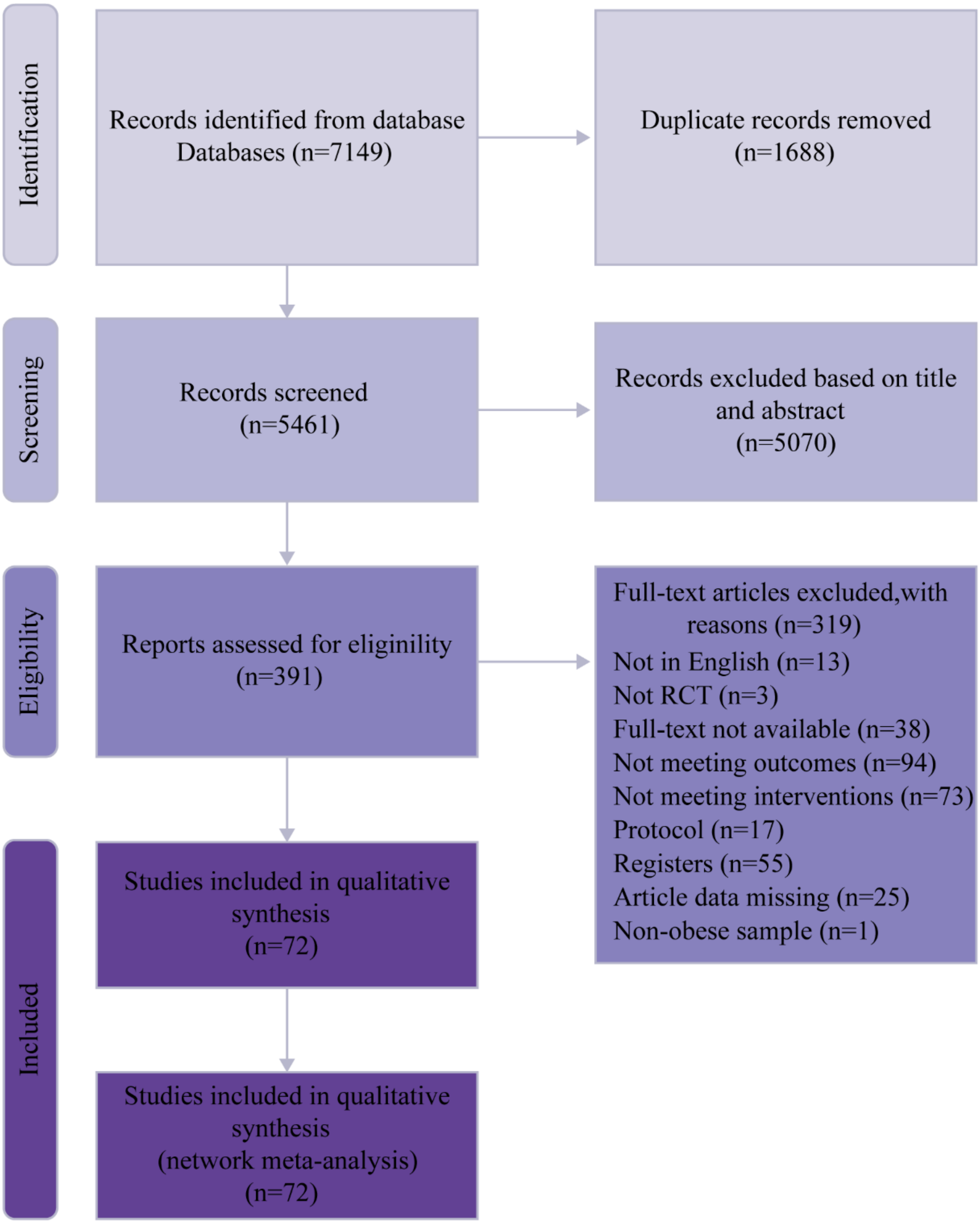

Figure 1. PRISMA flow diagram of the search process for studies examining the efficacy of exercise-based cardiac rehabilitation in patients with heart failure; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; RCT, randomised controlled trial.

Table2 Characteristics of included studies

	Rehabilitation modes	Duration (weeks)	Sample N/EG/CG	Age (years)	Outcome measures reported	Country
otrowicz 10	CTR HBCR	8	131/75/56	58.5±9.9	Peak VO2, 6-min WT, SF-36	Poland
Liu et	CTR HBCR	12	60/30/30	54.3±6.6	6-min WT, MLHFQ	China
wang et	CTR CBCR	12	53/24/29	67.5±12.5	6-min WT, MLHFQ	Australia
Karapolat 09	HBCR CBCR	8	68/36/32	44.6±12.5	Peak VO2, 6-min WT	Turkey
ento de e et	HBCR CBCR	12	23/11/12	60±6.0	Peak VO2, 6-min WT, MLHFQ	USA
otrowicz 20	CTR UC	9	850/425/425	62.4±10.5	Peak VO2, 6-min WT	Poland
en Peng 18	CTR UC	8	98/49/49	N	6-min WT, MLHFQ	China
otrowicz 15	CTR UC	8	69/46/23	57.4±11.1	Peak VO2	Poland
Maria es et	HBCR UC	12	28/17/11	52.4±9.0	Peak VO2, MLHFQ	Brazil
Selig et	HBCR UC	12	39/19/20	64.5±11.0	Peak VO2	Australia

o et	HBCR UC	36	90/71/19	62±2.0	Peak VO2	Italy
K.Oka 00	HBCR UC	12	40/20/20	N	Peak VO2	USA
eyu et	HBCR UC	12	78/40/38	77±3.8	6-min WT, MLHFQ	China
A et	HBCR UC	12	37/20/17	N	6-min WT, MLHFQ	USA
A et	HBCR UC	12	24/12/12	60±10.5	6-min WT, KCCQ	USA
h Fayazi 12	HBCR UC	8	60/30/30	61.3±9.0	6-min WT, MLHFQ	Iran
, KA et	HBCR UC	8	173/87/86	54.0±12.6	Peak VO2, 6-min WT, MLHFQ	USA
n M al,2019	HBCR UC	48	216/107/109	69.8±11.0	MLHFQ	UK
-Tinde 04	HBCR UC	12	79/42/37	62.6±10.6	Peak VO2, 6-min WT	USA
J.S et	HBCR UC	8	11/5/6	63.2±3.1	Peak VO2	UK
in Chien 11	HBCR UC	8	51/24/27	58±16.0	6-min WT, MLHFQ	China
n Chen 17	HBCR UC	12	37/19/18	60.5±13.5	Peak VO2, 6-min WT, MLHFQ	China

A et	HBCR UC	12	28/15/13	68±11.0	MLHFQ	USA
ista, e S et	HBCR UC	24	99/48/51	54±12.5	Peak VO2	USA
D. et al,	HCR UC	24	82/41/41	80.5±5.0	6-min WT	UK
F et	HCR UC	48	204/102/102	60.4±11.5	6-min WT, MLHFQ	USA
S. ie et	HCR UC	48	181/90/91	65.5±1.0	6-min WT, MLHFQ	Canada
Beckers 10	HBCR CBCR	12	36/18/18	60±10.0	Peak VO2	Belgium
D. , et	CTR UC	12	25/16/9	63.2±7.7	Peak VO2	USA
D. et	HCR UC	24	42/23/19	40.3±5.0	6-min WT	UK
P et		12	67/35/32	64±1.0	Peak VO2	The Neth
an den nons 03	HBCR UC	12	34/18/16	58.6±11.4	Peak VO2, 6-min WT, MLHFQ	The Neth
Visloff et	CBCR UC	12	18/9/9	75.0±12.5	Peak VO2	Norway

Tyni- et	CBCR UC	8	24/16/8	62.5±10.0	Peak VO2, 6-min WT	Sweden
ia Turri- al,2021	CBCR UC	12	16/8/8	58.5±9.7	Peak VO2	Brazil
pher M. hor et	HCR UC	12	2331/1159/1172	51.1-68.2	Peak VO2, 6-min WT	USA
Sturm 99	CBCR UC	12	26/13/13	54±9.0	Peak VO2	Austria
Spee et	CBCR UC	12	26/12/14	62.3±8.3	Peak VO2	The Neth
Smart et	CBCR UC	16	25/12/13	64.5±6.4	Peak VO2, MLHFQ	Australia
Maria es et	CBCR UC	12	37/18/19	54±8.5	Peak VO2, MLHFQ	Brazil
Senden 05	HCR UC	26	61/25/36	N	Peak VO2	The Neth
. Sabelis 04	HCR UC	26	29/16/13	N	Peak VO2	The Neth
Palevo 09	CBCR UC	8	16/10/6	67.5±12.5	6-min WT	USA
d et	CBCR UC	16	78/39/39	70.2±7.9	6-min WT, MLHFQ	Norway

F. n et	HCR UC	24	40/20/20	28±3.1	6-min WT, KCCQ	USA
R. et	HCR UC	12	27/15/12	72.3±10.0	6-min WT, KCCQ	USA
W. n et	HCR UC	12	349/175/174	72.7±8.1	6-min WT, KCCQ	USA
n Myers 12	CBCR UC	8	50/24/26	56±8.0	Peak VO2	USA
Maria et	CBCR UC	12	60/30/30	53±5.5	Peak VO2	Italy
Mandic 09	CBCR UC	12	27/14/13	62.5±12.0	Peak VO2, Macnew	Canada
R. Lan 19	CBCR UC	12	24/12/12	62.9±2.6	Peak VO2	Australia
Kulcu et	CBCR UC	8	44/23/21	59.4±10.8	Peak VO2, MLHFQ	Turkey
vou et	CBCR UC	24	26/16/10	52.6±9.9	MLHFQ	Greece
oppen et	CBCR UC	12	136/63/73	51-70	Peak VO2, KCCQ	Norway
Klecha et	CBCR UC	24	50/25/25	60.4±9.9	Peak VO2	Poland

avuori et	HCR UC	12	27/12/15	52±8.0	Peak VO2	Finland
J. **n et**	CBCR UC	24	29/15/14	54±11.5	Peak VO2	USA
J. **n et**	CBCR UC	24	43/21/22	56±12.0	Peak VO2, MLHFQ	USA
Jo´nsdo **l,2006**	CBCR UC	20	43/21/22	68.5±6.0	Peak VO2, 6-min WT, MLHFQ	Iceland
arsma et	HBCR UC	12	605/305/300	66.5±11.5	6-min WT	Sweden
o **zz et**	HCR UC	24	90/45/45	60.5±7.0	Peak VO2, 6-min WT	Italy
eng Fu **13**	CBCR UC	12	30/15/15	67.1±2.3	Peak VO2	China
ibeiro de **es et**	CBCR UC	24	30/15/15	N	Peak VO2	Brazil
M. **on et**	HCR UC	12	105/53/52	72.8	6-min WT, MLHFQ	Australia
na **hoou et**	CBCR UC	12	72/33/39	59.5±10.0	6-min WT, MLHFQ	Greece
A. **eld et**	HCR UC	12	17/11/6	N	6-min WT, MLHFQ	Australia

H. er et	CBCR UC	16	59/30/29	70.2±5.8	Peak VO2, MLHFQ	USA
Borland, al,2014	CBCR UC	12	48/25/23	70.5±7.5	6-min WT	Sweden
do nelli et	CBCR UC	48	99/50/49	54.5±8.0	Peak VO2	USA
celli et	HCR UC	24	343/170/173	76.9±5.6	6-min WT, MLHFQ	Italy
S et	CBCR UC	10	30/15/15	58.6±9.1	Peak VO2, 6-min WT	Turkey
jiboye et	CBCR UC	12	51/28/23	53.8±2.3	6-min WT	Nigeria
ico a et	CBCR UC	4	40/20/20	71±3.5	Peak VO2	Italy

Abbreviations: peak VO2, peak oxygen uptake; 6-min WT, 6-min walk test; SF-36, Medical Outcome Survey Short Form 36 questionnaire; MLHFQ, Minnesota Living With Heart Failure questionnaire; KCCQ, Kansas City Cardiomyopathy Questionaire Scale; UK, The United Kingdom of Great Britain and Northern Ireland; USA, The United States of America.

Results of ROB assessment

Supplement figure 1 and **Supplement figure 2** provides details of the ROB assessment for each study. All 72 included RCTs reported sufficient random sequence generation. Forty-one of the RCTs did not describe their randomization methods. Because the exercise intervention could not be blinded to patients, 71 studies were judged to be highly biased in terms of performance bias. 4 had detection bias. 11 RCTs were at high risk of bias due to attrition items. 1 had reporting bias.

32 RCTs with sample sizes⩽40 were judged to have other biases.

Primary outcome

HR-QOL

Twenty-six studies assessed HR-QOL. As shown in **Figure 2**, HBCR was the most prevalent intervention studied in 12 arms (n=418). The second most common treatments were CBCR comprising 10 arms (n=266), CTR containing 4 arms (n=178), and HCR involving 4 arms (n=324). The evidence shows that, compared to UC, CBCR (SMD=-0.72, CrI -1.04, -0.39), and CTR (SMD=-0.82, CrI -1.32, -0.33), HBCR (SMD=-0.55, CrI -0.83, -0.27) all improved post-intervention HR-QOL (**Figure 3**). **Table 3** demonstrates the rank of each intervention, which indicated that CTR got the highest probability (SUCRA: 86.90%) in adults with heart failure in terms of quality of life compared with other interventions, CBCR (SUCRA: 77.24%) also got a great ranking. Followed by HBCR (54.97%) and HCR (SUCRA: 28.03%) got an inferior ranking. UC (SUCRA: 2.97%) was most likely to be the least effective. Due to the fact that there was no statistically significant difference between direct and indirect estimates utilizing the node-splitting approach, it is used to conduct a valid comparison of the aforementioned treatments (UC vs. CBCR p value=0.90, UC vs. HBCR p value =0.66, UC vs. CTR p value=0.54, CBCR vs. HBCR p value =0.53, CBCR vs. CTR p value =0.646, HBCR vs. CTR p value =0.86).

Secondary outcomes

PeakVO2

Forty-six studies assessed peak VO2. **Figure 2** shows the NMA plots of peak VO2, CBCR was the most common intervention and was investigated in 28 arms (n=614). The second most common interventions were HBCR involving 13 arms (n=411), CTR involving 4 arms (n=562), and HCR involving 5 arms (n=1,257), four of the studies were direct studies. NMA results provided evidence that, compared to UC, CBCR [mean difference (MD)=2.48, CrI 1.73, 3.24), CTR (MD=2.45, CrI 0.46, 4.54), and HBCR (MD=1.97, CrI 0.85, 3.10) all improved post-intervention peakVO2 (**Figure 3**). As shown in **Table 3**, CBCR (SUCRA: 78.46%) was the best intervention for improving peakVO2, CTR (SUCRA: 72.35%) also got an outstanding ranking, HBCR (55%), and HCR (SUCRA: 42.80%) achieved an inferior ranking. UC (SUCRA: 1.39%) was most likely the least effective. There is no statistical difference between direct and indirect estimates (UC vs. CBCR p value =0.69, UC vs. HBCR p value =0.38, UC vs. CTR p value =0.57, CBCR vs. HBCR p value =0.38, CBCR vs. CTR p value =0.57, HBCR vs. CTR p value =0.76).

Thirty-seven studies assessed 6-min WT and were eligible for NMA of 6-min WT (**Figure 2**). HBCR was the most common intervention investigated in 13 arms (n=674). Both CBCR (n=316) and HCR (n=1,904) involved 12 arms, and CTR involved 5 arms (n=603), five of the studies were direct trials. NMA results provided evidence that, compared to UC, CBCR (MD=39.89, CrI 29.62, 50.52), CTR (MD=20.60, CrI 13.61, 27.58), HBCR (MD=8.59, CrI 0.34,16.78), HCR (MD=8.21, CrI 2.53, 14.01) all improved post-intervention 6-min WT. In addition, CBCR [vs. HBCR (MD=30.12, CrI -43.13, -17.07), vs. CTR (MD=-20.49, CrI -33.09, -7.858), HCR (MD=31.68, CrI 19.72, 43.68)] were significantly better than HBCR, CTR and HCR (**Figure 3**). CTR [vs. HBCR (MD=12.04, CrI 2.49, 21.57), HCR (MD=12.4, CrI 3.35, 21.32)] were significantly better than HBCR and HCR. As shown in **Table 3**, CBCR (SUCRA: 99.99%) was the best intervention to improve 6-min WT, CTR (SUCRA: 74.76%), HBCR (37.89%), and HCR (SUCRA: 36.79%) ranking behind CBCR, UC (SUCRA: 0.56%) was most likely the least effective. The results of compared direct and indirect estimates are as follows (UC vs. CBCR p value =0.40, UC vs. HBCR p value =0.47, UC vs. CTR p value =0.053, CBCR vs. HBCR p value =0.32, CBCR vs. CTR p value =0.96, HBCR vs. CTR p value =0.20).

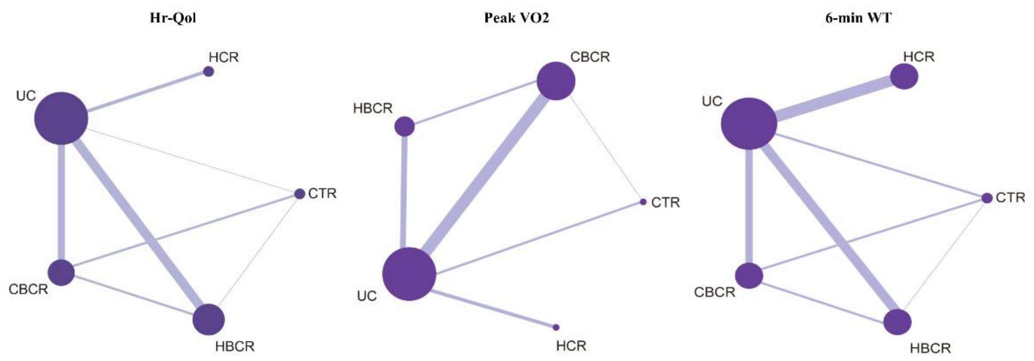

Figure 2. Network meta-analysis maps of studies examining the efficacy of exercise based cardiac rehabilitation on HR-QOL, Peak VO2, and 6-min WT in patients with heart failure.

Treatments | Significant pairwise comparisons

Peak VO2 (mL/min/kg)

CBCR				
0.03 (-2.09,2.07)	CTR			
0.52 (-0.76, 1.79)	0.49 (-1.78, 2.82)	HBCR		
0.95 (-1.02, 2.90)	0.92 (-1.77, 3.68)	0.44 (-1.69, 2.56)	HCR	
2.48 (1.73, 3.24)	2.45 (0.46, 4.54)	1.97 (0.85, 3.10)	1.53 (-0.27, 3.36)	UC

6-min WT (m)

CBCR				
19.28 (7.47, 31.33)	CTR			
31.3 (18.79, 44.02)	12.04 (2.49, 21.57)	HBCR		
31.68 (19.72, 43.68)	12.4 (3.35, 21.32)	0.39 (-9.61, 10.32)	HCR	
39.89 (29.62, 50.52)	20.6 (13.61, 27.58)	8.59 (0.34, 16.78)	8.21 (2.53, 14.01)	UC

Health-related quality of life

CTR				
-0.10 (-0.38, 0.59)	CBCR			
-0.27 (-0.79, 0.25)	-0.17 (-0.57, 0.24)	HBCR		
-0.55 (-1.23, 0.11)	-0.46 (-1.02, 0.10)	-0.28 (-0.82, 0.24)	HCR	
-0.82 (-1.32, -0.33)	-0.72 (-1.04, -0.39)	-0.55 (-0.83, -0.27)	-0.27 (-0.72, 0.19)	UC

Figure 3. Significant two-by-two comparisons are highlighted in orange, bold and underlined. Peak VO2, 6-min WT: clinically desirable outcome is an increased(+). Health-related quality of life: clinically desirable outcome is a decreased(-). Abbreviations: Peak VO2, peak oxygen uptake;

6-min WT, 6-minute walk test; CBCR, centre based cardiac rehabilitation; CTR, cardiac telerehabilitation; HBCR, home based cardiac rehabilitation; HCR, hybrid cardiac rehabilitation.

Table 3 Ranking of cardiac rehabilitation interventions in order of effectiveness

Ranking	HR-QOL	P score [a]	6-min WT	P score	Peak VO2	P score
1	CTR	0.869	CBCR	0.999	CBCR	0.784
2	CBCR	0.772	CTR	0.747	CTR	0.723
3	HBCR	0.549	HBCR	0.378	HBCR	0.550
4	HCR	0.280	HCR	0.367	HCR	0.428
5	UC	0.029	UC	0.005	UC	0.013

Abbreviations: peak VO2, peak oxygen uptake; 6-min WT, 6-min walk test; HR-QOL, Health-related quality of life; CBCR, centre based cardiac rehabilitation; CTR, cardiac telerehabilitation; HBCR, home based cardiac rehabilitation; HCR, hybrid cardiac rehabilitation; UC, usual care.

[a] P score ranges from 0 to 1, where 1 indicates best treatment with no uncertainty and 0 indicates worst treatment with no uncertainty.

Discussion

Our study summarized the available evidence to establish that CTR is the most effective strategy for enhancing the quality of life of patients (SUCRA: 86.9%). CBCR is the most effective in improving patients' cardiopulmonary function (SUCRA: 78.46%) and exercise tolerance (SUCRA: 99.99%). These promising therapies exhibit different effects due to their characteristics or specific technical differences and deserve further investigation.

The optimal cardiac rehabilitation mode is currently inconclusive, and implementing a practical treatment is critical. Our study concluded that three cardiac rehabilitation therapies (CTR, CBCR, and HBCR) had achieved statistically significant improvements in treating adults with heart failure compared with UC. Our results complement previous studies[98], expand on existing treatments. Furthermore, we found that CTR was most effective as a more comprehensive and safe approach to cardiac rehabilitation in HR-QOL, this result is in accordance with previous study[31], according to the study of Peng et al., patients with HF who participated in a telemedicine exercise rehabilitation program saw improvements in their HR-QOL and functional exercise capacity. The telehealth group did not report any adverse events, and the program's effects persisted at the 4-month post-test follow-up. We inferred that the more positive impact of CTR on quality of life could be related to several factors. First, exercise training may improve quality of life by ameliorating edema, fatigue, shortness of breath, and other uncomfortable symptoms in patients with HF[11]. Second, the increased exercise capacity positively impacted patients' self-perceived health status, which indirectly led to improved quality of life. Furthermore, CTR is performed outside hospital or CR center, using monitoring devices and remote communication with patients via modern communication technologies such as applications, the Internet, or video consultations. Personal health data (e.g., heart rate during exercise, daily physical activity) are monitored and fed back in real-time for personalized adjustment and education by healthcare professionals[99], which is a very novel therapy. Due to its monitoring and feedback function, improving patients' exercise adherence, make the patient's exercise situation better achieve the setup standard, which indirectly leads to quality of life enhanced. At last, CTR is carried out at home with the support of family members, with fewer time constraints and easier logistics, making patients feel more valuable and could be involved in managing their condition[16]. HF severely affects patients' daily life, besides the patient's symptoms, we should pay more attention to the patient's quality of life. We recommend that future cardiac rehabilitation research be more concerned with patients' quality of life. We also recommend using standardized assessment tools, as some studies included in this study assessed quality of life through different scales.

Our study also concluded that CBCR and CTR obviously enhanced peak VO2 and 6-min WT in patients with HF, and the difference between CTR and CBCR in peak VO2 were insignificant. These results are also consistent with previous studies. In a comparison of the effects of CTR and CBCR, Piotrowicz et al. [26] discovered that both CR programs significantly increased peak VO2 and 6-min WT, but the patients of CTR had better adherence than patients in CBCR. We considered that the improvement in cardiopulmonary function and exercise endurance is also owing to CTR monitoring the patient's exercise through a remote device and adjusting the exercise prescription promptly, increasing the patient's compliance and ensuring the exercise's length and strength. As for CBCR, a traditional exercise modality, is more effective because a professional physician is on hand to guide the patient through the exercise, thus ensuring that the patient's exercise meets the set goals in terms of precision, intensity, and frequency. However, CBCR is conducted only at in-hospital rehabilitation centers, and factors such as distance from the rehabilitation center, lack of transportation, increased costs, excessive time spent, and conflicts with work schedules may reduce cardiac rehabilitation compliance, and patients' daily life and work are adversely affected[100], which may result in less improvement than CTR in terms of quality of life. Thus, when patients have barriers to performing CBCR, CTR may be considered an ideal alternative. In the future, clinicians can refer to our findings when prescribing exercise training and cooperate with patients to identify a mode that meets the patient's requirements and matches the patient's abilities to maximize the benefit from treatment.

Strengths and limitations

Strengths of this study include the following, the search was not limited by publication date and was systematic and exhaustive, and we then included a large literatures (n=72) with a large sample size (n= 8,354), which enabled the detection of statistically significant mean differences. In addition, only RCT——the gold standard for assessing intervention effects was included in the study which strengthens the persuasiveness of the results of this study.

We also report several limitations. Although we employing tight inclusion and exclusion criteria, the research populations differed in a number of ways (age, country of recruitment, proportion of male and female participants, and the duration of the intervention), the variation in characteristics of the literature can cause some bias in the interpretation of the results of this paper. In addition, according to our statistics, CBCR was the most commonly used intervention, contributing more than 1/3 (35.7%) of the data on exercise intervention patterns for all NMAs. In contrast, CTR and HCR contributed only 10% and 21.4%, respectively. Because there are less directly comparable data for some interventions, which may reduce the reliability of the results. Finally, according to the ROB results, the quality of the literature we included was mixed, with high risks of selection bias and other bias present even after ignoring performance bias (CR cannot be blinded to patients).

Conclusions

Our NMA suggests that CTR is the ideal intervention, and UC is the least efficient treatment. Our work may give evidence that CTR can enhance the physical and mental health of individuals with HF, as well as insight for future research. Among the many exercise rehabilitation therapies available, CTR promises to solve the challenges that heart failure poses to patients and society.

Contribution JW-T served as the primary author and had complete access to all study data, assuming responsibility for the reliability of the data analysis and the data's quality. YY-Z and J-J contributed to the conception and design. XT-F, ZY-X, and M-W contributed to data acquisition and interpretation. JW-T contributed to the draft of the manuscript. YY-Z and J-J contributed to revise of the article and final approval.

Data Availability Some or all of the data generated during the study are contained in the data repositories listed herein or in the references.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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