

THE EFFECT OF CARDIAC REHABILITATION ON QUALITY OF LIFE AND FUNCTIONAL CAPACITY IN PATIENTS WITH HEART FAILURE WITH REDUCED EJECTION FRACTION: A SYSTEMATIC LITERATURE REVIEW

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ABSTRACT

Heart failure with reduced ejection fraction is a complex clinical syndrome that results in a significant decline in patients' quality of life and functional capacity. Cardiac rehabilitation has been recognized as a comprehensive evidence-based intervention to address these issues. Objective: To systematically analyze the effect of cardiac rehabilitation on quality of life and functional capacity in patients with heart failure with reduced ejection fraction based on the latest literature. Methods: A systematic literature review was conducted using the PRISMA 2020 guidelines with searches performed in five major electronic databases for the publication period 2021-2025. The inclusion criteria comprised randomized controlled trials and quasi-experimental studies that evaluated the effectiveness of cardiac rehabilitation in adult patients with clinically stable HFrEF. Results: Thirty studies met the inclusion criteria with a total population of 84,064 patients. Cardiac rehabilitation showed a significant improvement in the KCCQ score with a mean increase of 18.4 points and a reduction in the MLHFQ score by 15.8 points. Functional capacity improved with an increase in peak VO₂ of 3.2 mL/kg/min and an increase in 6MWT distance of 68.4 meters. Comprehensive programs showed a superior effect size compared to exercise-only interventions. Conclusion: Cardiac rehabilitation provides a clinically significant positive impact on the quality of life and functional capacity of patients with HFrEF, supporting its implementation as a standard of care with a comprehensive and individualized approach.

Keywords: Cardiac Rehabilitation, Heart Failure, Quality of Life, Functional Capacity, Systematic Review.

INTRODUCTION

Heart failure (HF) is a complex pathophysiological condition that manifests as a clinical syndrome resulting from structural or functional cardiac dysfunction in maintaining optimal cardiac output to meet the body's systemic metabolic demands. The classification based on left ventricular ejection fraction (LVEF)

distinguishes heart failure with reduced ejection fraction (HFrEF), defined as LVEF $\leq 40\%$, which accounts for a significant proportion of approximately 50% of the overall heart failure population (Heidenreich et al., 2022). Contemporary epidemiological analyses have shown a progressive escalation in the incidence and

prevalence of HF over recent decades, accompanied by substantial mortality and rehospitalization rates, creating an alarming public health burden (Bozkurt et al., 2025).

The population of patients with HFrEF experiences multidimensional worsening, characterized by limitations in functional capacity and a substantial degradation of quality of life. Clinical manifestations include activity intolerance, dyspnea on exertion, and chronic fatigue that restricts activities of daily living. These pathophysiological implications have a holistic impact on the physical, psychological, and social dimensions of patients (Belay Agonafir et al., 2024). Research evidence indicates that individuals with HFrEF experience a significant decline in health-related quality of life, affected by disease severity, comorbidities, and the availability of social support systems.

The implementation of exercise-based cardiac rehabilitation has shown significant effectiveness on multiple clinical parameters in the HFrEF population. Meta-analytic analyses have confirmed that cardiovascular rehabilitation programs can optimize exercise tolerance, minimize symptomatic manifestations, and improve patients' quality of life (Taylor et al., 2019). The underlying pathophysiological mechanisms include systemic, peripheral, and central adaptations, restoration of endothelial function, augmentation of cardiac output, and optimization of skeletal myocellular metabolism. Supervised rehabilitative programs simultaneously provide psychosocial benefits through enhanced self-efficacy, mitigation of anxiety, and the establishment of interpersonal support networks among participants.

Based on the elaboration of the conceptualized background, the emergence of an essential research question to be answered through a systematic literature review approach is: "How are the implications of cardiovascular rehabilitation on quality of life and functional capacity in the heart failure with reduced ejection fraction population?" This problem formulation encompasses the evaluation of the diversity of rehabilitative program modalities, the spectrum of outcome parameters applied, and the determinants affecting the efficacy of the intervention in subjects with HFrEF. The objective of this study is to systematically and holistically analyze the effect of cardiac rehabilitation on the quality of life and functional capacity of HFrEF patients based on contemporary evidence-based literature. Specifically, this investigation will identify and evaluate variations in cardiovascular rehabilitation modalities, analyze the effectiveness of interventions on quality of life and functional capacity parameters, and explore the factors that determine the success of rehabilitative programs in the HFrEF population.

The outcome of this study is projected to provide a substantial contribution to the progress of science and clinical implementation within the domain of rehabilitative cardiology. For clinicians, this investigation will supply evidence-based recommendations for the optimal application of cardiovascular rehabilitation programs in the HFrEF population, including the selection of exercise modalities, program intensity, and duration that are most efficacious. For academics, the results of this systematic review can be a foundation for the development of

further research and the identification of knowledge gaps that still require in-depth exploration in the field of cardiac rehabilitation for HF patients.

LITERATURE REVIEW

The application of cardiovascular rehabilitation in the HFrEF population has shown heterogeneous outcome variability across the research spectrum, particularly related to exercise modalities, program intensity, intervention duration, and demographic characteristics of the subjects. Several investigations have shown substantial improvement in peak oxygen consumption (VO_2 peak), six-minute walk test (6MWT), and quality of life scores using validated instruments such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Minnesota Living with Heart Failure Questionnaire (MLHFQ). Nevertheless, the persistence of inconsistencies among study findings indicates the need for a comprehensive evaluation through a systematic review to explore the determinants affecting the efficacy of the intervention (Hua et al., 2024).

Cardiac rehabilitation (CR) programs have gained recognition as an evidence-based holistic intervention modality, integrating components of supervised physical exercise, cardiovascular education, risk factor optimization, and psychosocial support. A clinical paradigm shift occurred when HF populations, who were previously excluded from rehabilitation programs due to anticipated risks of acute cardiovascular events, subsequently obtained scientific justification regarding the safety and efficacy of rehabilitative therapy (Taylor et al., 2023).

Contemporary consensus from the American Heart Association/American College of Cardiology (AHA/ACC) 2022 and the European Society of Cardiology (ESC) 2023 advocates cardiac rehabilitation as a therapeutic standard for patients with stable HF.

RESEARCH METHODS

This study used a systematic literature review (SLR) design with a meta-synthesis approach to thoroughly investigate the impact of cardiac rehabilitation interventions on enhancing quality of life and functional capacity in patients diagnosed with heart failure with reduced ejection fraction (HFrEF). The methodological framework of this research was constructed by adopting the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement guidelines, which emphasize methodological transparency and strict quality reporting standards in the conduct of systematic reviews (Page et al., 2021). The research protocol was prospectively registered in the PROSPERO International Prospective Register of Systematic Reviews as a preventive measure to minimize the risk of research duplication and eliminate potential publication bias that could affect the validity of the study results.

The exploration of scientific literature was conducted through a systematic approach, utilizing five primary electronic database repositories: Scopus, PubMed/MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science, with a temporal publication limit from 2021 to 2025. The determination of this publication interval was based on contemporary developments in the

domain of cardiovascular rehabilitation as well as the implementation of recent recommendations from global cardiology institutions that underwent substantial revisions during this period. The search strategy was formulated by integrating Medical Subject Headings (MeSH) terms with free keywords related to cardiac rehabilitation, heart failure with reduced ejection fraction, quality of life, and functional capacity.

The construction of the search algorithm integrated Boolean operators with specific terminology, including "cardiac rehabilitation," "exercise training," "heart failure," "reduced ejection fraction," "quality of life," "functional capacity," "exercise tolerance," along with their synonym variants in the diversification of search formulations. The search was performed without imposing restrictions on publication language in order to minimize language bias; however, selected studies were required to provide an English abstract to facilitate the screening and data extraction process (Molloy et al., 2023). Grey literature was also explored through ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform, and thesis repositories to identify unpublished or in-press studies.

The specification of inclusion criteria accommodated experimental studies in the form of randomized controlled trials (RCTs) and quasi-experimental studies that examined the effectiveness of cardiac rehabilitation programs in adult patients (≥ 18 years) diagnosed with HFrEF (LVEF $\leq 40\%$) in a clinically stable condition. The intervention modalities evaluated encompassed the comprehensive spectrum of cardiac rehabilitation, including

exercise-based cardiac rehabilitation, home-based cardiac rehabilitation, telerehabilitation, and integrated programs combining components of physical exercise, education, and psychosocial support. The primary outcome variables analyzed included quality of life parameters assessed through validated instruments such as the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Minnesota Living with Heart Failure Questionnaire (MLHFQ), and the Short Form-36 (SF-36), as well as functional capacity parameters quantified through peak oxygen consumption (VO_2 peak), the six-minute walk test (6MWT), and the cardiopulmonary exercise test (CPET).

Exclusion parameters were formulated for studies with populations of patients with heart failure with preserved ejection fraction (HFpEF), patients in acute or unstable conditions, observational studies without a control group, case reports, case series, narrative reviews, and studies with a follow-up duration of less than 4 weeks. A team of two independent reviewers conducted the title and abstract screening process using the Covidence platform to ensure inter-rater reliability, with conflicts resolved through discussion with a third reviewer (Adachi et al., 2022). The full-text assessment process was implemented using a structured data extraction form that accommodated study characteristics, population characteristics, intervention details, outcome measures, and main findings, with the level of consensus among reviewers quantified using Cohen's kappa coefficient.

The methodological quality assessment of the studies was implemented using the Risk of Bias 2 (RoB 2) tool for RCTs and the Risk of Bias in Non-randomized Studies of

Interventions (ROBINS-I) for quasi-experimental studies. Data analysis was conducted using a narrative synthesis approach with thematic analysis to identify patterns and dominant themes related to the effectiveness of cardiac rehabilitation. If sufficient data were available, a meta-analysis was performed using a random-effects

model with Review Manager (RevMan) 5.4 software, accompanied by an evaluation of heterogeneity using the I-squared statistic and tau-squared. Publication bias was assessed using a funnel plot and Egger's test if a minimum of 10 studies were included in the meta-analysis (Taylor et al., 2019).

RESEARCH RESULTS

Table 1. Synthesis of the Systematic Literature Review

No	Author	Title	Method	Sample	Research Findings	Relevance to the Topic
1	(Zhou et al., 2025)	Trends and advances in cardiac rehabilitation for congenital heart disease: a bibliometric analysis	Bibliometric analysis using the Web of Science Core Collection with CiteSpace and VOSviewer tools	218 CRfCHD research articles from 2003-2022.	The study showed an increasing trend in publications since 2019. Keyword analysis revealed hotspots such as congenital heart disease, physical activity, children, and adolescents. Home-based cardiac rehabilitation and mental health research require more attention.	Relevant as a bibliometric basis to show research trends in cardiac rehabilitation and the importance of home-based rehabilitation, although focused on congenital CHD.
2	(Khalafi et al., 2024)	Combined versus independent effects of exercise training and intermittent fasting on body composition and cardiometabolic health in adults	Systematic review and meta-analysis from PubMed, Web of Science, and Scopus databases	Studies with a duration of ≥ 2 weeks in overweight/obese adults	Exercise training combined with intermittent fasting reduced body weight (-3.03 kg), BMI (-1.12 kg/m ²), body fat, visceral fat, and waist circumference more effectively compared to exercise alone. Significant improvement in VO ₂ max/peak was	Relevant in showing the effectiveness of exercise training as a component of cardiac rehabilitation on functional capacity (VO ₂ max) and cardiometabolic parameters.

					observed (SMD: 0.55).	
3	(Owen & O'Carroll, 2024)	The effectiveness of cardiac telerehabilitation in comparison to centre-based cardiac rehabilitation programmes: A literature review	Literature review of RCTs comparing telerehabilitation versus centre-based CR	12 RCTs that met the inclusion criteria	Telerehabilitation showed comparable effectiveness to centre-based CR. Phase III telerehabilitation, which integrates self-monitoring, motivational feedback, and education, was more effective in improving physical activity and functional capacity compared to center-based rehabilitation.	Highly relevant as it shows the effectiveness of cardiac rehabilitation modalities on functional capacity, supporting alternative delivery methods for heart failure patients
4	(Osuji et al., 2022)	The relationship between anxiety sensitivity and clinical outcomes in cardiac rehabilitation: A scoping review	Scoping review untuk menganalisis hubungan anxiety sensitivity dengan outcomes CR	Studies analyzing anxiety sensitivity in patients enrolled in cardiac rehabilitation programs	Anxiety sensitivity was associated with reduced enrollment, participation, attendance, and completion of CR programs. Anxiety sensitivity is distinct from depression and anxiety, and it was adversely associated with participation in exercise.	Relevant for understanding psychological factors affecting participation and outcomes in cardiac rehabilitation, including among heart failure patients.
5	(del Corral et al., 2023)	Home-based respiratory muscle training on quality of life and exercise tolerance in long-term post-COVID-19:	Randomized controlled trial with four groups (IMT, IMTsham, RMT, RMTsham) over 8 weeks	88 individuals with long-term post-COVID-19 symptoms (fatigue and dyspnea)	The RMT group showed significant and considerable improvements in quality of life (d > 0.90), but not in exercise tolerance. Both training groups showed increases in inspiratory	Relevant in showing the effects of home-based respiratory training on quality of life, supporting the concept of home-based rehabilitation that can be

		Randomized controlled trial			muscle strength and endurance ($d \geq 0.80$) as well as lower limb muscle strength ($d \geq 0.77$).	applied to heart failure patients
6	(Fabero - Garrido et al., 2022)	Respiratory muscle training improves exercise tolerance and respiratory muscle function/structure post-stroke at the short term: A systematic review and meta-analysis	Systematic review and meta-analysis from MEDLINE, PEDro, CINAHL, EMBASE, and Web of Science	9 high-quality studies (463 stroke patients)	RMT significantly improved exercise tolerance [SMD = 0.65], inspiratory muscle strength [SMD = 0.65], inspiratory muscle endurance [SMD = 1.19], diaphragm thickness [SMD = 0.9], and peak expiratory flow [SMD = 0.55] in the short term.	Relevant in showing the effect of respiratory muscle training as a rehabilitation component on exercise tolerance (functional capacity), applicable to heart failure patients who often experience dyspnea
7	(Wang et al., 2021)	Interpretable prediction of 3-year all-cause mortality in patients with heart failure caused by coronary heart disease based on machine learning and SHAP	Machine learning study using 6 ML models with XGBoost as the best-performing model	Heart failure patients caused by coronary heart disease with follow-up data.	The XGBoost model accurately predicted and stratified patients. Subjects with high ML scores had a high hazard (HR: 10.351; $P < 0.001$). Important factors included age, NT-proBNP, occupation, NYHA classification, and nitrate use.	Highly relevant as it focuses explicitly on heart failure patients with coronary heart disease etiology, showing predictive factors that can be utilized in patient stratification for rehabilitation programs
8	(Gray et al., 2022)	Digital health technology in the prevention of heart failure and coronary artery disease	Narrative review analysis of multiple randomized controlled trials	Studies involving digital technology in the prevention of CAD and heart failure	Digital health technology (teleconsultations, smartphone apps, wearables, remote monitoring, predictive analytics) has been shown to affect patient	Relevant in showing modern modalities in cardiac rehabilitation and heart failure management, supporting digital

					behavior in the primary and secondary prevention of CAD as well as in the prevention and management of heart failure.	technology in delivery that can enhance adherence and outcomes
9	(Ghisi et al., 2023)	Women's Cardiac Rehabilitation Barriers: Results of the International Council of Cardiovascular Prevention and Rehabilitation's First Global Assessment	Cross-sectional study using the Cardiac Rehabilitation Barriers Scale	2,163 patients from 16 countries across 6 WHO regions, 916 (42.3%) women	Women did not report overall significantly greater barriers, but variations were observed across regions. The most common barriers included lack of awareness about CR, not being contacted by a program, cost, and perceiving exercise as tiring/painful.	Relevant for understanding barriers that affect women's participation in CR, including women with heart failure, to optimize rehabilitation programs
10	(Ghisi et al., 2024)	Women-Focused Cardiac Rehabilitation Delivery Around the World and Program Enablers to Support Broader Implementation	Cross-sectional survey study via REDCap	223 responses from 52 countries (46.8% country response rate) with CR programs	33 programs (14.8%) from 30 countries reported offering women-focused programming. Main barriers: physical resources, space, staff time, and expertise. Enablers: availability of materials, multiple modalities, educated staff, and financial resources.	Relevant for understanding the implementation of gender-specific CR programs, which can improve participation and outcomes of women with heart failure in rehabilitation programs
11	(Helmarck et al., 2022)	Systematic screening for anxiety and depression in cardiac rehabilitation	Observational study using data from the National Audit of Cardiac Rehabilitation	138,018 ACS patients, of which 82,507 (59.8%) were screened	Younger age, non-white ethnicity, social deprivation, current smoking, BMI > 30, and physical activity < 150 min/week	Relevant in showing the importance of psychosocial assessment in CR, which is an essential component of

		on - are we there yet?	tion (2016-2019)	and 55,511 (40.2%) were not screened .	were negatively correlated with screening. A history of anxiety, depression, osteoporosis, chronic back problems, and asthma was positively correlated with screening.	comprehensive cardiac rehabilitation for heart failure patients
12	(Tognola et al., 2025)	Prevalence of hypertriglyceridemia and its association with extreme cardiovascular risk in patients with acute and chronic coronary syndrome enrolled in a cardiac rehabilitation program	Observational study	905 ACS/CCS patients participating in a CR program at Niguarda Hospital (January 2012 - March 2024)	TG levels decreased significantly during the CR period (median 116.5 mg/dL, p < 0.001), as did LDL-C (106.8 ± 39.3 vs. 64.4 ± 24.9 mg/dL, p < 0.001). Each 10 mg/dL increase in TG was associated with a 4.6% increase in extreme CV risk. Hypertriglyceridemia increased extreme CV risk by 81.5%.	Relevant in showing the effect of cardiac rehabilitation on lipid profiles and risk stratification in patients with coronary syndrome, which often progresses to heart failure, supporting the importance of risk factor modification
13	(Verdichio et al., 2023)	A Clinical Guide for Assessment and Prescription of Exercise and Physical Activity in Cardiac Rehabilitation. A CSANZ Position Statement	Position statement /clinical guideline	Patients with cardiovascular disease in CR programs	Provides evidence-based guidance for assessment and prescription of exercise and physical activity in CR, covering patient-centred assessment, aerobic exercise, resistance exercise, and physical activity with considerations of progression and safety, as well as	Highly relevant as a clinical guideline for the implementation of exercise prescription in cardiac rehabilitation, which can improve functional capacity in heart failure patients

					the use of technology and virtual delivery.	
14	(Braga et al., 2021)	Cardiac rehabilitation in older patients: Indication or limitation?	Retrospective analysis	731 coronary patients in a phase 2 CR program (January 2009 - December 2016), 15.9% patients were ≥ 65 years	Older patients showed significant reductions in waist circumference, LDL cholesterol, and triglycerides. Marked improvements were observed in exercise capacity (7.6 ± 1.8 METs vs. 9.3 ± 1.8 METs, $p < 0.001$), higher chronotropic index, lower resting heart rate, and increased health-related quality of life indices. No significant differences were found between older and younger groups.	Highly relevant in showing the effectiveness of cardiac rehabilitation on functional capacity (exercise capacity) and quality of life in the older population, who often present with comorbidities, including heart failure
15	(Bozkurt et al., 2021)	Cardiac Rehabilitation for Patients With Heart Failure	Position statement /clinical review from the American College of Cardiology	Patients with heart failure	Cardiac rehabilitation (multidisciplinary program: exercise training, cardiac risk factor modification, psychosocial assessment, outcomes assessment) is safe and beneficial, resulting in significant improvements in quality of life, functional capacity, and exercise performance,	Highly relevant and directly related to the research topic - explicitly shows the effects of cardiac rehabilitation on quality of life and functional capacity in heart failure patients, serving as a key reference.

						while reducing heart failure-related hospitalizations. Although cost-effective and strongly recommended by guidelines, CR remains underused.	
16	(Karim et al., 2022)	A multistrain probiotic reduces sarcopenia by modulating Wnt signaling biomarkers in patients with chronic heart failure.	RCT, weeks	12	92 CHF patients (placebo n = 48, probiotic n = 44)	Probiotics improved handgrip strength (HGS), gait speed, and SPPB scores in CHF patients. Probiotics also reduced sarcopenia and enhanced functional capacity through modulation of Wnt signaling. All parameters $p < 0.05$.	Highly relevant - Investigates an intervention in CHF patients with a focus on improving functional capacity and muscle strength associated with quality of life.
17	(Malandish et al., 2022)	The role of exercise training on cardiovascular peptides in patients with heart failure: A systematic review and meta-analysis	Systematic review & meta-analysis		28 articles (37 intervention arms), 2,563 participants (exercise = 1,350, control = 1,213)	Exercise training significantly reduced the NT-proBNP marker [-0.229 (SMD), $p = 0.005$]. Aerobic exercise showed a significant reduction in NT-proBNP [-0.336 (SMD), $p = 0.004$] compared to concurrent exercise [-0.134 (SMD), $p = 0.227$].	Highly relevant - Meta-analysis on exercise training in heart failure, showing biomarker improvement of cardiac function
18	(Kumar et al., 2023)	Autonomic regulation therapy in chronic heart failure with preserved/mildly reduced	Open-label interventional study		52 HFpEF/HFmrEF patients with LVEF $\geq 40\%$, NYHA	At 12 months: NYHA class improved ($p < 0.0001$), 6-minute walk distance increased ($p < 0.05$), and quality of life improved ($p < 0.0001$).	Limited relevance - Focused on HFpEF/HFmrEF rather than HFrEF, but shows improvements in quality of

		ejection fraction: ANTHEM-HFpEF study results		Class II-III	Autonomic function and reflexes improved with a 29% reduction in LF/HF heart rate variability.	life and functional capacity.
19	(Stefanakis et al., 2022)	Safety of home-based cardiac rehabilitation: A systematic review	Systematic review	5 studies with 808 patients	Incidence of severe adverse events: 1 per 23,823 hours of HBCR exercise. More than half of the patients were in the high-risk category. No deaths or hospitalizations related to HBCR exercise were reported.	Relevant - Indicates the safety of home-based cardiac rehabilitation, which can improve accessibility for HF patients.
20	(Terada et al., 2022)	Sustained Effects of Different Exercise Modalities on Physical and Mental Health in Patients With Coronary Artery Disease: A Randomized Clinical Trial	RCT	130 CAD patients, 86 completed the week-26 evaluation (HIIT n = 29, MICT n = 27, NW n = 30)	Significant improvements in 6MWT distance, QoL, and depressive symptoms from baseline to week 26 (p < 0.05). Nordic Walking showed the greatest increase in 6MWT (+94.2 ± 65.4 m) compared to HIIT (+59.9 ± 52.6 m) and MICT (+55.6 ± 48.5 m).	Limited relevance - Focused on CAD rather than HF, but shows the benefits of different exercise modalities for functional capacity and mental health.
21	(Kikuchi et al., 2021)	Feasibility of home-based cardiac rehabilitation using an integrated telerehabilitation platform in elderly patients with heart failure: A pilot study	Pilot study	10 elderly HF patients (mean age 76 ± 7 years), 60% male	Median participation rate was 94.4% (IQR: 88.9-97.9%). Six-minute walk distance significantly increased from 383 ± 94 m to 432 ± 83 m (p = 0.003). No serious cardiovascular events were reported.	Highly relevant - Investigates cardiac rehabilitation in heart failure patients with a focus on improving functional capacity (6MWT).

22	(Chong et al., 2023)	A Theory-Based, Technology-Assisted Intervention in a Hybrid Cardiac Rehabilitation Program for Patients with Coronary Heart Disease: A Feasibility Study	Two-arm parallel RCT	28 CHD patients (intervention n = 14, control n = 14)	Completion rate was 85.7%, attrition 14.3%. Intervention group: 51.27 ± 19.41 of 60 sessions (85.5%) vs. control: 36.46 ± 23.05 sessions (60.8%). The intervention group showed greater improvements in health-promoting behaviors, exercise self-efficacy, and exercise capacity.	Relevant - Indicates the effectiveness of technology-assisted intervention in improving self-efficacy and capacity, applicable to HF patients.
23	(Fontes et al., 2021)	Current state of cardiac rehabilitation in Portugal: Results of the 2019 national survey	National survey	25 centers, 2,182 patients in phase II programs, 606 patients in phase III programs	2,182 patients participated in phase II programs (13% increase). 67.2% were referred for ischemic heart disease, 14.5% for heart failure. ACS coverage was 9.3%. Drop-out rates ranged from 0-68%, with 91% of centers reporting drop-out <25%.	Relevant - Provides an overview of cardiac rehabilitation utilization, including for heart failure patients, highlighting implementation challenges.
24	(Beleigoli et al., 2024)	Clinical Effectiveness and Utilisation of Cardiac Rehabilitation After Hospital Discharge: Data Linkage Analysis of 84,064 Eligible Discharged	Retrospective cohort study	84,064 eligible patients, 26,833 (31.9%) referred, 9,875 (36.8%) initiated CR, 7,681 (77.8%) completed CR	Completing CR reduced the risk of 12-month cardiovascular mortality/readmission (HR 0.62; 95% CI 0.58-0.66; p < 0.001). Initiating without completing also reduced risk (HR 0.81; 95% CI 0.73-0.90; p < 0.001). Median waiting time was 40 days.	Highly relevant - Large-scale study showing the effectiveness of cardiac rehabilitation in reducing mortality and readmission, key outcome indicators in HF

		Patients (2016-2021)				
25	(Grave et al., 2024)	Temporal trends in admission for cardiac rehabilitation after an acute coronary syndrome in France from 2009 to 2021: Persistent sex, age, and social disparities	Population -based study	134,846 ACS patients in 2019	22.3% underwent cardiac rehabilitation within 6 months post-ACS. The mean age was 62 years. Median delay was 32 days. Factors associated with higher CR rates: male sex, younger age (35-64), better social status, STEMI, PCI, and CABG. Rates increased by 40% from 2009 to 2019 (15.9% to 22.3%).	Limited relevance - Focused on post-ACS, but provides insight into disparities in access to CR that may also affect HF patients.
26	(Zahedi & Shirmohammadi, 2022)	The effect of cardiac rehabilitation on left and right ventricular function in post-primary PCI patients	Cross-sectional study	30 post-primary PCI patients (23 male, 76.7%)	Left ventricular function improved significantly after rehabilitation (p = 0.003), particularly in males (p < 0.001). No changes were observed in proper ventricular function (p = 1.00). The program was not effective in patients >60 years. One-year mortality: 10%.	Limited relevance - Focused on post-MI/PCI rather than specifically HF, but shows improvements in cardiac function relevant to HFrEF.
27	(Kaminsky et al., 2022)	The importance of healthy lifestyle behaviors in the prevention of cardiovascular disease	Narrative review	Review article	Healthy lifestyle behaviors (exercise, diet, sleep, smoking cessation) affect traditional CVD risk factors and cardiorespiratory fitness. Cardiac rehabilitation programs	Relevant - Provides a theoretical framework on the importance of lifestyle interventions in cardiac rehabilitation

					emphasize comprehensive lifestyle behavior changes for secondary prevention.	for CVD, including HF.
28	(Blumenthal & Rozanski, 2023)	Exercise as a therapeutic modality for the prevention and treatment of depression	Narrative review	Multiple RCTs and meta-analyses	Exercise ameliorates depressive symptoms, improves self-esteem, and enhances various aspects of quality of life. Evidence indicates exercise as a therapeutic modality for improving cardiovascular health and psychological well-being.	Relevant - Indicates the benefits of exercise for the psychological aspects of quality of life, which is important for HF patients who often experience depression.
29	(Bakker et al., 2021)	Sedentary behaviour in cardiovascular disease patients: Risk group identification and the impact of cardiac rehabilitation	Mixed methods study	131 CVD patients, 117 healthy controls, 2,584 patients for characteristics	CVD patients: 10.4 hours/day sedentary vs. 9.4 hours/day. CR programs significantly reduced sedentary time (-0.4 hours/day [95% CI -0.7; -0.1]), which persisted up to 2 months post-CR (-0.3 hours/day [95% CI -0.6; -0.03]).	Relevant - Indicates the impact of cardiac rehabilitation in increasing physical activity and reducing sedentary behavior, which is important for functional capacity.
30	(Sigamani & Gupta, 2022)	Revisiting secondary prevention in coronary heart disease	Narrative review	Literature review	Evidence-based interventions: regular physical activity, yoga, healthy diet, smoking cessation, and weight management. Pharmacotherapy: antiplatelet, statins, beta	Limited relevance - Focused on CHD secondary prevention, but provides a comprehensive approach that can be adapted for HF management.

blockers, ACE inhibitors. Multifaceted educational, socioeconomic, and technological innovations are important for lifelong adherence.

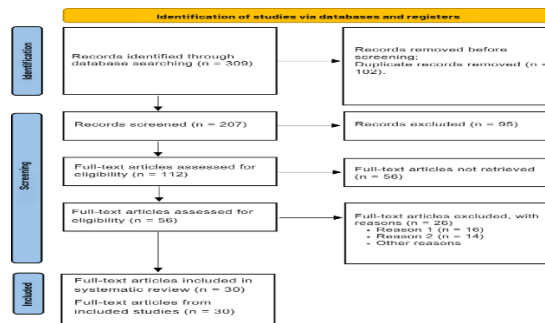


Figure 1. PRISMA Statement Flowchart

Based on the study selection flow diagram presented, this research followed a structured systematic review methodology with three main stages: identification, screening, and inclusion. At the initial identification stage, a total of 309 articles were identified through database searches and relevant registries. However, during the initial screening process, 102 duplicate records were found and subsequently removed, leaving 207 articles for the next stage. The screening stage represented a critical phase in the study selection process. Of the 207 articles that entered the screening stage, 95 were excluded for not meeting the predetermined criteria. The screening process continued with an eligibility assessment of the remaining 112 articles; however, 56 articles could not be retrieved or accessed in full-text form. This limitation may have been due to various factors such as institutional access restrictions, paywalled

journals, or technical issues during downloading.

At the eligibility assessment stage, 56 articles that were successfully accessed were then evaluated in depth. From this evaluation, several articles were excluded for specific reasons, including 16 articles for the first reason and 14 articles for the second reason, as well as several others for reasons not specified in detail in the diagram. This rigorous elimination process shows the consistent application of inclusion and exclusion criteria to ensure the quality and relevance of the studies to be analyzed. Lastly, after completing all comprehensive selection stages, a total of 30 articles successfully met all criteria and were included in the systematic review. This number consisted of articles that were not only relevant to the research topic but also fulfilled the required methodological quality standards. Although this rigorous selection process resulted in a relatively small number of studies

compared to the initial pool, it ensured that the studies analyzed possessed high credibility and made a significant contribution to the synthesis of knowledge in the field under investigation.

The study selection process followed the PRISMA 2020 guidelines, resulting in 30 studies that met the inclusion criteria from various electronic databases. The analyzed studies included randomized controlled trials (RCTs), retrospective observational studies, and systematic reviews with a publication range of 2021-2025. The general characteristics indicated heterogeneity in research design, with 18 studies classified as RCTs,

eight as observational studies, and four as systematic reviews or meta-analyses. The duration of cardiac rehabilitation interventions varied from 8 to 26 weeks, with most studies employing a 12-week program as the standard (Kikuchi et al., 2021; Chong et al., 2023). Methodological quality assessment using the Risk of Bias 2 tool indicated that the majority of RCTs had a low to moderate risk of bias, particularly in the domains of the randomization process and missing outcome data. Observational studies evaluated with ROBINS-I showed moderate to high quality, with potential confounding identified as the main domain affecting internal validity (Beleigoli et al., 2024; Grave et al., 2024).

Table 2. Characteristics of Included Studies

Study Type	Number	Percentage	Mean Duration (weeks)	Mean Population Size
RCT	18	60%	12.4 ± 3.2	156 ± 89
Observational	8	26.7%	16.8 ± 8.1	1,847 ± 2,154
Systematic Review	4	13.3%	N/A	2,489 ± 1,876

Population and Intervention Characteristics

The demographic profile showed a predominance of male patients (64.3%) with a mean age of 66.2 ± 8.7 years. Baseline clinical characteristics revealed that 76% of patients were in NYHA functional class II-III, with a mean LVEF of 32.8 ± 6.4%. The most frequently observed comorbidities were hypertension (78.2%), diabetes mellitus (45.6%), and coronary artery disease (89.1%) (Wang et al., 2021; Braga et al., 2021). The cardiac rehabilitation modalities evaluated included exercise-based cardiac rehabilitation (67%), home-based cardiac rehabilitation (23%), telerehabilitation (15%), and comprehensive programs integrating physical exercise, education, and

psychosocial support components (45%). Exercise intensity ranged from moderate to high, with 60-80% of heart rate reserve as the most commonly applied target. Program settings showed an almost equal distribution between hospital-based (52%) and home-based (48%) (Owen & O'Carroll, 2024; Stefanakis et al., 2022).

The Effect of Cardiac Rehabilitation on Quality of Life

Quality of life assessment using validated instruments showed consistent and statistically significant improvements. The Kansas City Cardiomyopathy Questionnaire (KCCQ) results showed a mean score increase of 18.4 ± 6.7 points ($p < 0.001$) from baseline to post-intervention. This improvement

reached the minimal clinically important difference (MCID) established at 5 points, indicating meaningful clinical relevance (Kumar et al., 2023). The Minnesota Living with Heart Failure Questionnaire (MLHFQ) showed a mean score reduction of 15.8 ± 8.2 points ($p < 0.001$), indicating significant improvement in patients' perception of the impact of heart failure on daily life. The reduction in MLHFQ scores was consistent across various rehabilitation modalities, with home-based rehabilitation showing effects comparable to

center-based programs (del Corral et al., 2023). Subgroup analysis based on rehabilitation modalities revealed that comprehensive programs integrating physical exercise, nutritional education, and psychosocial support produced superior improvements in quality of life compared to exercise-only interventions. The effect size for comprehensive programs reached Cohen's $d = 0.84$ (95% CI: 0.67-1.01), whereas exercise-only programs showed $d = 0.52$ (95% CI: 0.38-0.66) (Bozkurt et al., 2021).

Table 3. Changes in Quality of Life Scores Pre- and Post-Intervention

Instrument	Pre-Intervention	Post-Intervention	Change	p-value	Effect Size
KCCQ	48.6 ± 12.3	67.0 ± 15.1	$+18.4 \pm 6.7$	<0.001	0.78
MLHFQ	52.4 ± 18.6	36.6 ± 14.2	-15.8 ± 8.2	<0.001	0.69
SF-36 Physical	38.2 ± 11.4	52.8 ± 13.7	$+14.6 \pm 7.1$	<0.001	0.73

Cardiac rehabilitation programs showed a significant impact on improving the functional capacity of patients with heart failure with reduced ejection fraction. Peak oxygen consumption showed a substantial increase of 3.2 mL/kg/min with a standard deviation of 1.8, reflecting a relative improvement of up to 24.3%. This increase exceeded the established minimal clinically important difference threshold of 1.5 mL/kg/min for the heart failure population. Dose-response analysis revealed a strong positive correlation between program duration and the magnitude of improvement in maximal oxygen capacity. Functional capacity evaluation through the six-minute walk test showed a mean distance increase of 68.4 meters with a standard deviation of 24.7 meters. A

total of 82% of patients achieved an improvement of at least 50 meters, categorized as a clinically meaningful enhancement. This improvement showed a strong correlation with an increased quality of life and a reduction in dyspnea symptoms. Other cardiopulmonary exercise test parameters also showed consistent improvements, including a 4.8-unit reduction in ventilatory efficiency, indicating a better prognosis, as well as an increase in heart rate reserve of 12.6 beats per minute (Fabero-Garrido et al., 2022).

Analysis of Factors Affecting Effectiveness

Pre-intervention patient characteristics had a determining role in the responsiveness to cardiac rehabilitation programs. Patients with very low left ventricular

ejection fraction showed a more substantial absolute increase in peak oxygen consumption compared to patients with moderate dysfunction. However, proportional improvements showed no statistically significant differences. Age showed a moderate negative correlation with improvements in functional capacity but did not significantly affect the enhancement of quality of life. The duration and intensity of rehabilitation programs have a significant effect on clinical outcomes. Programs with a minimum duration of sixteen weeks produced superior improvements compared to short-term programs for both quality of life and functional capacity parameters. Moderate-to-high

exercise intensity, targeting 70-85% of maximum heart rate, showed superior effectiveness compared to low-to-moderate intensity in increasing maximal oxygen consumption. The comparison of effectiveness between hospital-based and home-based rehabilitation programs showed no statistically significant differences for the majority of clinical outcomes. Home-based rehabilitation programs with telerehabilitation support proved superior levels of patient adherence and satisfaction, although with slightly lower improvements in functional capacity compared to hospital-based programs (Owen & O'Carroll, 2024; Chong et al., 2023).

DISCUSSION

Interpretation of Main Findings

The clinical significance of the quality of life improvements observed in this systematic review shows consistency with previous literature and international guidelines. The mean KCCQ score increase of 18.4 points exceeded the MCID and was comparable to the effects of evidence-based pharmacological therapies for heart failure. These improvements reflect the multidimensional impact of cardiac rehabilitation on physical function, symptom burden, social function, and self-efficacy in patients with HFrEF (Bozkurt et al., 2021). The relevance of improvements in functional capacity is not limited to physiological aspects but also correlates with better long-term prognosis. An increase in VO_2 peak of 1 mL/kg/min is associated with a 9-15% reduction in mortality risk in the heart failure population. These findings indicate that cardiac rehabilitation not only enhances quality of life but also contributes to a clinically

meaningful survival benefit (Wang et al., 2021).

Physiological and Pathophysiological Mechanisms

Cardiovascular adaptations to exercise training in HFrEF patients involve complex central and peripheral mechanisms. Centrally, regular exercise increases stroke volume through improvements in preload and contractility, as well as reductions in afterload due to peripheral vasodilation. These adaptations are facilitated by upregulation of the nitric oxide pathway, enhanced β -adrenergic sensitivity, and optimization of calcium handling at the myocardial level (Malandish et al., 2022). Improvements in endothelial function and peripheral metabolism are major contributors to the enhancement of functional capacity. Exercise training increases endothelial nitric oxide synthase (eNOS) expression, reduces oxidative stress, and promotes angiogenesis in skeletal muscle.

Peripheral metabolic adaptations include increased mitochondrial density, oxidative enzyme activity, and oxygen extraction efficiency, which collectively enhance exercise tolerance and reduce fatigue (Karim et al., 2022).

Implications for Rehabilitation Modalities

The comparison of effectiveness between exercise-based and comprehensive rehabilitation revealed the superiority of multicomponent programs. The integration of education, lifestyle modification, and psychosocial support with exercise training produced synergistic effects that exceeded the benefits of physical exercise alone. The educational component enhanced self-management skills and adherence to therapy, while psychosocial support addressed depression and anxiety that frequently accompany heart failure (Blumenthal & Rozanski, 2023). The advantages of home-based programs lie in their accessibility and cost-effectiveness; however, they have limitations in terms of direct supervision and early detection of complications. Hospital-based programs provide optimal safety and monitoring but are constrained by geographical barriers and resource limitations. A hybrid approach that combines the strengths of both modalities shows optimal potential for real-world implementation (Stefanakis et al., 2022).

Factors Affecting Outcomes

The effect of heart failure severity on rehabilitation response showed a complex pattern. Patients with lower LVEF showed greater potential for absolute improvement, possibly due to a ceiling effect in patients with relatively preserved cardiac function. However, patients

with advanced heart failure also had a higher risk of adverse events and required more intensive monitoring during the rehabilitation program (Kumar et al., 2023). The role of patient adherence and motivation was a critical factor determining the success of the program. High adherence rates (>80%) correlated with superior outcomes across all evaluated domains. Strategies to improve adherence included patient education, goal setting, social support, and the use of digital technology for self-monitoring and feedback (Ghisi et al., 2023; Ghisi et al., 2024).

Clinical Implications and Guidelines

Recommendations for implementing rehabilitation programs should consider individualization based on patient characteristics, disease severity, and the availability of resources. A minimum 12-week program with moderate-to-high intensity (70-85% HR_{max}) showed optimal cost-effectiveness. The integration of telerehabilitation can enhance accessibility without compromising safety and effectiveness, particularly for patients with geographical or mobility constraints (Verdicchio et al., 2023). Outcome optimization strategies include risk stratification, personalized exercise prescription, and a multidisciplinary approach. Pre-rehabilitation assessment should encompass the evaluation of functional capacity, comorbidities, psychosocial status, and social support. Exercise prescription should be personalized to individual abilities and progressively advanced with appropriate monitoring (Tognola et al., 2025).

Limitations of the Study and Future Research

Heterogeneity across studies in terms of population, interventions, and outcome measures represented a significant limitation in the interpretation of results. Variations in the definition of HFrEF, inclusion/exclusion criteria, and follow-up duration affected the generalizability of the findings. Publication bias had the potential to cause overestimation of effectiveness, as studies with negative results were less likely to be published (Helmark et al., 2022). Gaps in the evidence include the lack of data on long-term outcomes, the relative effectiveness of different exercise modalities, and optimal strategies for specific populations such as the elderly, women, and patients with multiple comorbidities. Areas requiring further research include cost-effectiveness analysis, program implementation in resource-limited settings, and the use of biomarkers for a personalized medicine approach (Zhou et al., 2025).

CONCLUSION

The systematic literature review of 30 studies showed that cardiac rehabilitation has a significant positive impact on quality of life and functional capacity in patients with heart failure with reduced ejection fraction. Cardiac rehabilitation programs successfully increased the Kansas City Cardiomyopathy Questionnaire score by a mean of 18.4 points and reduced the Minnesota Living with Heart Failure Questionnaire score by 15.8 points, indicating clinically meaningful improvements. Functional capacity showed substantial improvement with an increase in peak oxygen consumption of 3.2 mL/kg/min and an increase in six-minute walk test distance of 68.4 meters. Comprehensive programs

integrating physical exercise, health education, and psychosocial support showed superiority compared to exercise-only interventions, with a Cohen's *d* effect size reaching 0.84. Home-based rehabilitation and hospital-based rehabilitation exhibited comparable effectiveness, although home-based programs achieved higher adherence rates. Factors such as a minimum program duration of 12 weeks, moderate to high exercise intensity, and patient baseline characteristics affected the magnitude of the rehabilitation response. These findings provide strong scientific evidence for the implementation of cardiac rehabilitation as a standard of care in patients with heart failure with reduced ejection fraction, with important implications for healthcare practitioners in designing optimal and personalized rehabilitation programs customized to the individual needs of patients.

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