A systematic review of the cardiovascular benefits of resistance exercise training in patients with Heart Failure

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Abstract

Cardiovascular disorders are a significant worldwide health challenge. Out of them, congestive heart failure is the primary reason for death and illness globally. Based on the latest census data, heart failure results in a significant financial burden each year. Exercise therapy is a crucial component of the non-pharmacological treatment of heart failure. Prescribing a proper exercise program might be tough due to the availability of many exercise regimens and the quick developments in available research. While there is clear and indisputable evidence supporting the cardiovascular advantages of aerobic exercise, it is equally important to promote the inclusion of resistance training in exercise routines because of its impact on muscular endurance and improvement of skeletal myopathy in individuals with heart failure. This study employed a systematic literature review methodology to provide a comprehensive summary of the existing literature and emphasize the cardiovascular advantages of resistance training, either on its own or when combined with aerobic training. We conducted a comprehensive analysis by examining articles from reputable journals published from 2010 to 2023. Eventually, we picked nine studies for a detailed examination. The inclusion criteria consist of studies that focus on heart failure with reduced ejection fraction (HFrEF), weight training either alone or in conjunction with aerobic therapy, and research that are accessible for free in either the PubMed or PubMed Central databases. The systematic study found that the combination of resistance training and aerobic therapy yields superior cardiovascular benefits compared to either resistance or aerobic therapy alone. Periodic intermittent muscular exercise (PRIME) and super circuit training (SCT) were shown to enhance both cardiac and non-cardiac clinical results when compared to traditional exercise therapy. In addition, other variables, such as insufficient motivation and limited time availability, contribute to inadequate compliance with exercise therapy. Methods such as telerehabilitation and tailoring exercise programs to include activities that patients find enjoyable have resulted in enhanced long-term adherence rates. However, it is crucial to conduct larger-scale randomized controlled trials to thoroughly investigate the potential of resistance training in rehabilitating patients with heart failure and reduced ejection fraction. This will help in developing the most effective exercise therapy. **Keywords:**Heart failure, exercise, exercise therapy, resistance training, aerobic exercise, High interval intensity training.

Introduction

Heart failure is a multifaceted clinical illness that occurs when the heart is incapable of efficiently pumping blood to fulfill the body's metabolic requirements (1). It is a persistent condition that can arise from many cardiovascular disorders, such as coronary artery disease, hypertension, and myocardial infarction. The defining characteristics of heart failure encompass dyspnea, exhaustion, and edema. The condition can be classified into two distinct types: systolic heart failure, characterized by impaired myocardial contractility, and diastolic heart failure, characterized by poor myocardial relaxation. The worldwide prevalence of heart failure is significant, impacting millions of individuals globally. Based on a thorough examination of epidemiology, the frequency of heart failure has been consistently rising, presenting a notable public health obstacle(2). Based on the 2023 American Heart Association Statistical Update, the estimated prevalence of this condition in the United States is roughly 2.3% of the entire population(3).In 2012, the United States incurred an expenditure of approximately 31 billion dollars for healthcare financing. It is projected that by 2030, this amount will increase significantly to reach up to 70 billion dollars(4). In India, the precision and dependability of the prevalence and incidence estimates of HF are not available due to the insufficient surveillance strategies employed in the process of data acquisition(5). The industrialization, urbanization, and economic progress in India have resulted in changes that have increased the susceptibility to heart failure. Cardiovascular disease (CVD) is the primary cause of death in India, and its occurrence is expected to increase. By the year 2000, the prevalence of Coronary Artery Disease (CAD) in India was estimated to be over 30 million individuals. The prevalence of heart failure (HF) caused by coronary artery disease (CAD) ranges from 0.4% to 2.3% annually(5).

The increasing prevalence of heart failure is attributed to the aging population and the escalating occurrence of cardiovascular risk factors. Comprehending the extent of this illness is essential in order to effectively tackle its consequences on individuals and society. Heart failure not only diminishes the quality of life but also results in heightened morbidity and mortality. Heart failure patients frequently have repeated hospitalizations as a result of symptom exacerbations and consequences. Heart failure is linked to various negative health effects, including decreased ability to engage in physical activity, diminished cognitive abilities, and an increased likelihood of developing other health conditions such chronic kidney disease. Moreover, heart failure plays a substantial role in causing cardiovascular death on a worldwide scale(6).

The death rates for heart failure are contingent upon various factors, such as the severity of the ailment, comorbidities, and healthcare accessibility. Despite progress in medical interventions, heart failure continues to be a prominent factor contributing to mortality, underscoring the importance of sustained research and novel therapeutic approaches.

The economic ramifications of heart failure are significant, including both direct medical

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expenses, indirect expenses, and intangible expenses related to the diminished quality of life. Multiple studies have emphasized the economic hardship that heart failure imposes on both people and society.

Cost-of-illness studies highlight the growing financial impact of heart failure. These studies examine healthcare costs associated with hospital stays, drugs, and visits to healthcare facilities. The expenses increase in proportion to the seriousness of heart failure, highlighting the significance of efficient management and preventative measures. Heart failure incurs indirect expenses associated with reduced production, increased absenteeism, and disability. The workforce is greatly affected by heart failure, as individuals with this condition may encounter difficulties in retaining employment due to the chronic nature of the illness and the accompanying symptoms(7).The intangible expenses associated with heart failure are frequently disregarded, however they play a vital role in evaluating the entire impact. The intangible expenses associated with reduced quality of life, psychological discomfort, and the emotional burden on patients and their families are difficult to quantify(8). These factors emphasize the comprehensive influence of heart failure beyond conventional economic indicators. Gaining a comprehensive understanding of the underlying mechanisms that cause heart failure is crucial in order to devise specific therapies and enhance patient outcomes. The development of heart failure entails complex alterations in the anatomy and physiology of the heart. Long-term stress on the heart, frequently caused by illnesses such as hypertension or coronary artery disease, results in structural remodeling. This include myocardial hypertrophy, fibrosis, and changes in ventricular morphology. Over time, these alterations hinder the heart's capacity to efficiently circulate blood, hence contributing to the onset and advancement of heart failure. Heart failure is characterized by functional deficiencies, including decreased contractility and relaxation of the cardiac muscle. Systolic heart failure is defined by a reduced ejection fraction, which indicates a compromised ability to pump blood. Diastolic heart failure occurs when the heart's ability to relax is hindered, which leads to inadequate filling of the heart between beats.

The activation of neurohormones, specifically the renin-angiotensin-aldosterone system and sympathetic nervous system, is crucial in the progression of heart failure. Although initially providing compensation, chronic activation of these systems becomes harmful, leading to narrowing of blood vessels, excessive fluid accumulation, and worsening of heart function(9), The aforementioned factor continues to be the primary cause of death and illness on a global scale(10). Heart failure is a clinical syndrome characterized by symptoms like shortness of breath, swelling of anke, and exhaustion. These symptoms may be accompanied by indicators such as high jugular venous pressure, pulmonary crackles, and peripheral edema(11). HF has been categorized into discrete phenotypes according to the assessment of left ventricular ejection fraction (LVEF). Individuals whose left ventricular ejection fraction (LVEF) is less than 40% experience a notable decline in left ventricular systolic function and are classified as having heart failure with reduced ejection fraction (HFrEF). Individuals with a left ventricular ejection fraction (LVEF) ranging from 41% to 49% and displaying slightly diminished left ventricular systolic function are classified as having heart failure with mid-range ejection fraction (HFmrEF). On the other hand, individuals experiencing symptoms and signs of heart failure, along with evidence of structural and/or functional cardiac abnormalities and/or elevated levels of natriuretic peptides

(NPs), and possessing an LVEF greater than 50%, fall into the category of heart failure with preserved ejection fraction (HFpEF). Heart failure can be caused by various factors, including coronary heart disease, hypertension, valve disease, arrhythmias, cardiomyopathies, congenital heart disease, infections, drug-induced conditions, infiltrative disorders, storage disorders, endomyocardial diseases, pericardial disease, metabolic diseases, and neuromuscular disease(3).Coronary artery disease (CAD) and hypertension are the primary causal factors in Western and affluent countries(10). The management of heart failure involves both pharmaceutical and non-pharmacological approaches. Exercise therapy is a crucial component of non-pharmacological therapeutic methods. Most of the evidence indicates that incorporating exercise therapy into the treatment plan results in significant enhancement of the health of patients with stable HF in New York Heart Association (NYHA) functional classes II or III. However, no substantial advantage has been observed in NYHA functional class IV(12).The primary elements of exercise treatment in cardiac rehabilitation encompass aerobic therapy, which can be either high-intensity interval training (HIIT) or moderate continuous aerobic therapy (MCAT), resistance training (RT), and inspiratory muscle training (IMT). Exercise training restores balance by exerting neurohumoral and anti-inflammatory effects, while also enhancing endothelium and skeletal muscle function(13). Exercise training has positive effects on the nervous and hormonal systems. It can reverse autonomic dysfunction by increasing vagal activity and reducing sympathetic activity. Additionally, exercise training can decrease the levels of certain neurohormones such as angiotensin II, aldosterone, vasopressin, and natriuretic peptides in the bloodstream(14), (15). TThe anti-inflammatory properties of regular exercise training have been proven in experimental models. Exercise training has been shown to elevate the levels of anti-inflammatory cytokines and reduce the levels of inflammatory cytokines such as tumor necrosis factor (TNF) and interleukin-6 (IL-6). This is achieved by regulating the function of macrophages and lymphocytes(13). Moreover, empirical research indicates that exercise training enhances the activity of oxidative enzymes and the amount of mitochondria, thereby enhancing the usage of oxygen and diminishing oxidative stress(16). Nevertheless, the incorporation of exercise therapy has not exhibited a substantial enhancement in mortality or the frequency of hospitalization (17). Multiple pieces of evidence indicate that High-Intensity Interval Training (HIIT) is superior than Moderate Continuous Aerobic Training (MCAT) in terms of reversing left ventricular remodeling, enhancing cardiac output, improving endothelial function, increasing maximum oxygen consumption (VO2 max), and enhancing quality of life(18), (19).In addition, incorporating inspiratory muscle training into aerobic or resistance training resulted in enhanced inspiratory muscle strength, resting heart rate, heart rate reserve, and overall quality of life. This was demonstrated by the observed increase in the total score on the Minnesota Living with Heart Failure Questionnaire(20).

Despite the compelling evidence that supports the cardiovascular advantages of aerobic treatment in individuals with HFrEF, the rate of involvement

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among Medicare beneficiaries is lower than anticipated(21). Conversely, the impact of resistance training on the cardiovascular well-being of patients with HFrEF has been investigated to a comparatively lower degree. Given these circumstances, we aim to perform a meta-analysis to further investigate the cardiovascular advantages of resistance training in patients with heart failure with reduced ejection fraction (HFrEF), as well as their clinical and statistical relevance.

Methodology

This systematic review focuses on clinical trials investigating the effect of resistance training on the cardiovascular health of patients diagnosed with heart failure and reduced ejection fraction. We have excluded animal research and publications that solely focused on aerobic exercise training. This systematic review adheres to the principles outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)(22)as depicted in Figure 1.

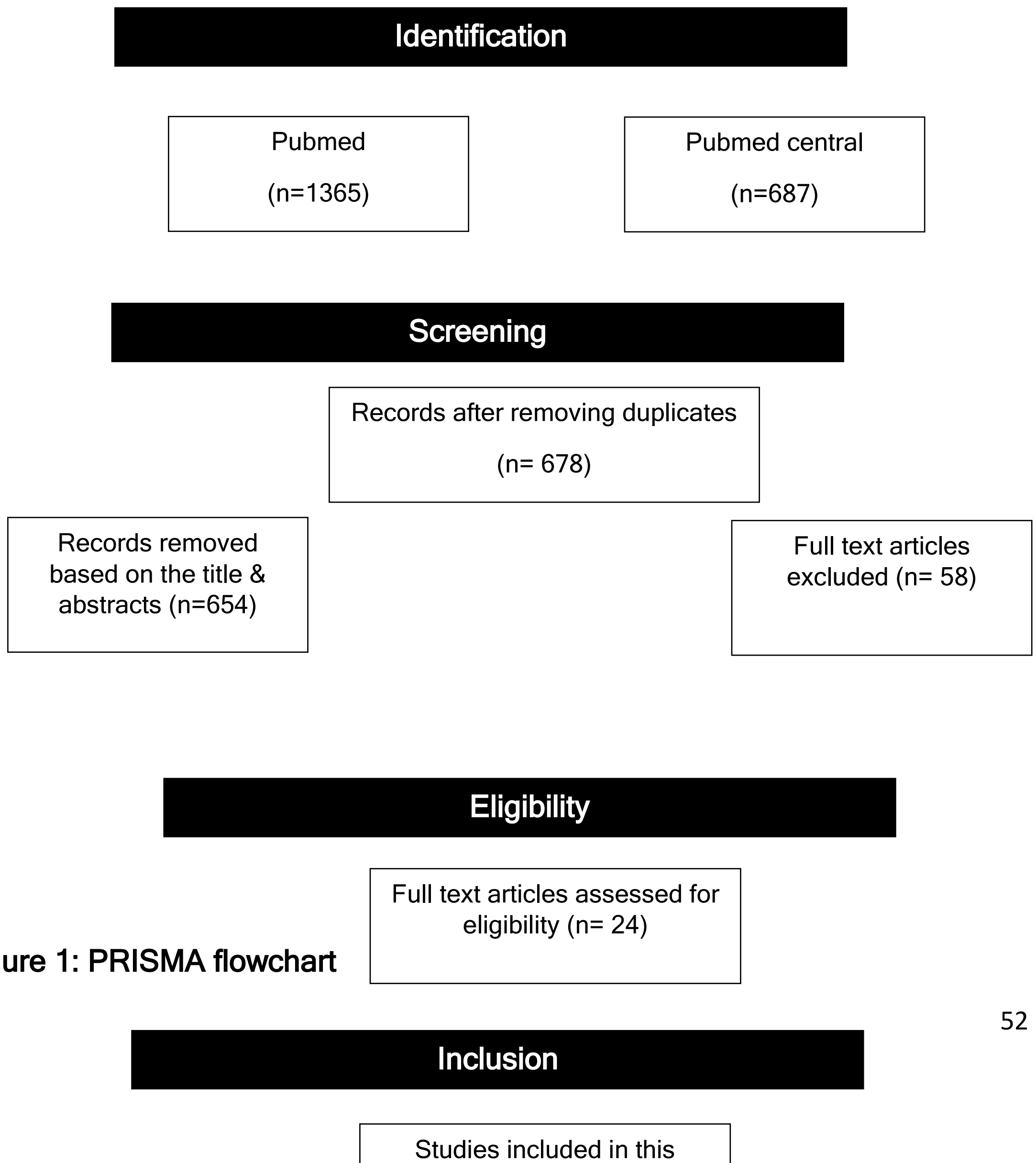

Figure 1: PRISMA flowchart

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Systematic literature search and study selection

We conducted a comprehensive search for pertinent publications utilizing PubMed and PubMed central. We conducted a targeted search for studies referenced in review papers, editorials, and commentaries on PubMed and PubMed Central. Nevertheless, we persisted in our pursuit of further papers that met our specific criteria for inclusion.

Search strategy

A comprehensive literature review was conducted using the PICO (Population, Intervention, Condition, and Outcome) criteria. The search was performed on databases including PubMed and PubMed Central, including relevant keywords such as "heart failure", "reduced ejection fraction", and "resistance training".

Quality appraisal

In order to ascertain the dependability of the chosen articles, we employed a range of quality evaluation instruments. We utilised the PRISMA checklist to conduct systematic reviews and meta-analyses, as well as the Cochrane bias tool to analyse randomised clinical trials. The Newcastle-Ottawa tool scale was used to assess non-randomized clinical studies. In order to eliminate any ambiguity in categorization, we employed the Scale for the Assessment of Narrative Review Articles (SANRA) to evaluate the quality of the article.

Results

The procedure commenced with the identification phase, wherein a comprehensive search is undertaken across multiple databases to locate relevant records. For this particular situation, searches were conducted in PubMed, resulting in 1,365 results, and in PubMed Central, resulting in 687 records. The records comprise a diverse range of studies, papers, and publications that are pertinent to the topic under evaluation. During the screening process, the identified records are combined, and any duplicates are eliminated, resulting in a total of 678 distinct records. Subsequently, the records undergo a screening process where their titles and abstracts are carefully examined. As a result, 654 records are excluded from the evaluation due to their failure to match the required requirements. The eligibility phase entails a comprehensive evaluation of the complete text articles. An additional 15 articles are excluded from the remaining 24. Exclusion at this stage typically based on more precise criteria, such as study design, population, irrelevant outcomes to the review topic, or the publication not being a research study.The inclusion phase involved selecting studies that completely satisfy the predetermined criteria and including them into the systematic review. Finally, total of 9 studies were deemed suitable and were incorporated into this systematic review.

Discussion

Physical activity plays key role in the recovery of HF patients and reduced ejection fraction. In congestive heart failure (CHF), intolerance to exercise, ventilatory insufficiency, and chronotropic incompetence occur due to the wasting of myofibrillar proteins in the diaphragm and quadriceps muscles, as well as different anti-oxidative and catabolic processes (23). Moreover, an increase in inflammatory cytokines in congestive heart failure (CHF) results in loss of appetite, as well as malnutrition, which exacerbates sarcopenia and exercise intolerance (23). Resistance training enhances the ability of blood vessels to dilate in response to the inner lining of the blood vessels, thus restoring blood flow to the muscles. This type of training also stimulates the growth of muscle fibres, increases the density of mitochondria (the energy-producing units of cells), and promotes the development of type-I muscle fibres. Additionally, it leads to a notable reduction in the resistance of blood vessels in the legs and the release of noradrenaline, while improving both muscular endurance and strength. As a result, exercise tolerance is increased (24), (25), (26). A study conducted in China found that combining resistance training with Simvastatin therapy for six months in patients with heart failure and reduced ejection fraction resulted in several positive outcomes. These included improved cardiac function, as indicated by reduced interventricular septal thickness, left ventricular diastolic diameter, and increased left ventricular ejection fraction. Additionally, the study observed improved mitochondrial function, specifically increased levels of Janus kinase/signal transducers and activators of transcription. Furthermore, the combination therapy led to decreased levels of inflammatory markers like C-reactive protein, galectin-3, and Interleukin-6. The patients also demonstrated increased six-minute walk distance and experienced a lower incidence of adverse cardiac events compared to those receiving simvastatin therapy alone(27). The most effective strategy to avoid sarcopenia in elderly individuals with heart failure with reduced ejection fraction is resistance training, maybe in combination with sufficient protein consumption (23).

The four primary categories of resistance training include isometric exercise, dynamic resistance exercise, combined isometric/dynamic exercise, and isokinetic exercise. Isometric exercise is a type of exercise where a muscle contracts without changing its length. This causes a significant increase in pressure within the muscle, which blocks the flow of blood to the contracting muscle. Isometric exercise also leads to a greater increase in mean arterial pressure compared to dynamic exercise, even when the amount of oxygen consumed is the same. Conversely, dynamic resistance training, which is highly recommended for heart failure patients, enables changes in muscle length without causing excessive intramuscular pressure or complete blockage of blood flow to the contracting muscle. As a result, the systolic blood pressure and the pressure exerted on the heart do not rise as significantly as they do during isometric exercise. The prescription of resistance exercise for people with heart failure must be determined based onNYHA classification. Patients classified as NYHA I are advised to perform four to five exercises. Each exercise should consist of one or two sets, with each set including six to 10 repetitions. The intensity of these exercises should be set at 50% to 60% of the patient's one repetition maximum (one RM). The recommended duration for these exercises is 15 to 20 minutes per day, with a frequency of two days per week. These exercises should be performed in addition to aerobic training. Patients with NYHA grade II-III should perform three to four exercises. Each exercise should consist of one to two sets, with four to six repetitions per set. The intensity of each set should be set at 40%-50% of their one rep maximum. The total duration of the exercise session should be 12-15 minutes per day, with a frequency of one to two days per week. These exercises should be done in addition to their regular aerobic training. Patients in NYHA grade I may be prescribed whole-body training only after successfully tolerating exclusive segmental training in the initial months. Whole-body training is not typically indicated for patients with NYHA grade II-III. Patients diagnosed with severe heart failure, specifically classified as NYHA grade IV, should avoid incorporating resistance training into their exercise routine(28).

However, in comparison to weight training, conventional aerobic therapy has demonstrated superior enhancement in VO2 max, which is the primary prognostic indicator in heart failure(13). Therefore, the strategy of integrating resistance therapy with aerobic therapy is currently being extensively researched to evaluate its superiority compared to standard resistance or aerobic therapy alone. There are multiple methods in which resistance therapy can be used with aerobic therapy. In a randomised controlled trial, the inclusion of resistance training alongside HIIT has shown comparable enhancements in resting oxygen consumption, peak oxygen consumption, predicted peak oxygen consumption, peak work rate, heart rate recovery, and work rate at anaerobic threshold compared to HIIT alone. However, the combined therapy has demonstrated superior improvements in the one repetition maximum (1 RM) test and muscular endurance of the chest muscles when compared to HIIT therapy alone(29).

Periodic intermittent muscular exercise is a form of resistance training that consists of eight specific exercises: chest press, leg press, seated row, triceps pushdown, latissimus dorsi pulldown, upright row, hack squat, and calf raises. Although traditional aerobic exercise was not included in the training programme, the utilisation of PRIME for a duration of four weeks, followed by four weeks of combination therapy, resulted in a more significant enhancement in VO2 max compared to eight weeks of combination therapy alone in older individuals (30). Dor-Haim, H., conducted a comparative analysis of the advantages between the continuous aerobic training (CAT) group and the SCT group. Each SCT set consisted of a single weight training set, followed by a three-minute session of aerobic exercise spanning from moderate to high intensity, and concluding with a period of rest. The sequence was iterated eight times. The resistance training regimen comprised eight distinct exercises, including horizontal rowing, chest press, leg press, shoulder press, leg extension, lateral pulldown, leg flexion, and aided squat. In contrast to the continuous aerobic therapy group, the super circuit training group showed a notable enhancement in E/e', which represents the ratio of the peak early mitral inflow velocity (E) to the early diastolic mitral annular velocity (e'). This ratio is a measure of the heart's diastolic function and ejection fraction. It is important to note that the continuous aerobic therapy group did not display a significant change in cardiac function. The super circuit training group shown superior improvement compared to continuous aerobic therapy in non-cardiac clinical outcomes, namely in metabolic equivalents, rate pressure product, and the physical component of the quality-of-life scale(31).

Although there is ample evidence supporting the cardiovascular advantages of exercise therapy in heart failure patients, a significant proportion (40%-91%) fail to engage in regular exercise. Furthermore, within the programme itself, dropout rates range from 33%-56% (32). Several factors that contribute to low adherence include advanced age, limited educational attainment, socio-economic disadvantage, lack of motivation for physical activity, time constraints, inertia, insufficient social support, compromised health status with more severe symptoms, rate of disease progression, presence of additional medical conditions, and limited access to healthcare(33). Conversely, aspects such as organising exercise sessions, drive, understanding of exercise, support from others, and enhancement of health condition all contributed to sustained commitment over time (32). Therefore, in order to apply the proven benefits of different combination exercise therapies to patients with heart failure and reduced ejection fraction in real-world clinical settings, it is important to consider the factors that contribute to low patient adherence. This will help in prescribing an exercise therapy that is tailored to the individual needs of the patient. A randomised control trial conducted on older individuals with heart failure found that the enjoyment of physical activity fully mediated the connection between motivation and exercise.

Therefore, it is important to create a workout routine that allows patients to derive pleasure from participating in activities such as walking, football, modified dancing, or medi-yoga(34).Home-based telerehabilitation proves to be a viable substitute for patients with limited access to facility-based cardiac rehabilitation, since it exhibits superior rates of adherence compared to control groups (35).

Conclusion

Our systematic review focuses on the advantages and wide-ranging use of resistance training in the cardiac rehabilitation of patients with heart failure and low ejection fraction. By incorporating resistance and aerobic training protocols into the exercise routine of individuals with HFrEF, it is possible to target both vascular reactivity and skeletal myopathy. This can result in enhancements in aerobic capacity and exercise tolerance. A group of researchers have devised combination therapies that have shown superior enhancement in clinical parameters compared to traditional exercise therapy. Furthermore, given the poor rates of long-term commitment to exercise therapy, it is crucial to prescribe a patient-specific exercise regimen that takes into account their individual preferences. However, conducting large-scale randomised controlled trials is essential in order to develop the most efficient exercise therapy for rehabilitating individuals with heart failure and low ejection fraction.

Limitations and future perspectives

There are constraints to our systematic review. We restricted our study to reports available in English that were published within the past decade. We exclusively examined complimentary publications, and our investigation was restricted to studies accessible solely in two databases, namely PubMed and PubMed Central. Further investigation with an extensive array of resources is necessary to get definite results.

References

1. Schwinger RHG. Pathophysiology of heart failure. Cardiovasc Diagn Ther. 2021 ;11(1):263–76.
2. Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global burden of heart failure: a comprehensive and updated review of epidemiology. Cardiovasc Res. 2023;118(17):3272–87.
3. Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation. 2023;147(8):e93–621.
4. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail. 2013;6(3):606–19.
5. Huffman MD, Prabhakaran D. Heart failure: epidemiology and prevention in India. Natl Med J India. 2010;23(5):283–8.
6. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019. J Am Coll Cardiol. 2020;76(25):2982–3021.
7. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. Int J Cardiol. 2014;171(3):368–76.
8. Essue BM, Iragorri N, Fitzgerald N, de Oliveira C. The psychosocial cost burden of cancer: A systematic literature review. Psychooncology. 2020;29(11):1746–60.
9. Hartupee J, Mann DL. Neurohormonal activation in heart failure with reduced ejection fraction. Nat Rev Cardiol. 2017;14(1):30–8.
10. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. Heart Br Card Soc. 2007 ;93(9):1137–46.
11. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599–726.
12. Remme WJ, Swedberg K, Task Force for the Diagnosis and Treatment of Chronic Heart Failure, European Society of Cardiology. Guidelines for the diagnosis and treatment of chronic heart failure. Eur Heart J. 2001;22(17):1527–60.

13. Piepoli MF, Conraads V, Corrà U, Dickstein K, Francis DP, Jaarsma T, et al. Exercise training in heart failure: from theory to practice. A consensus document of the Heart Failure Association and the European Association for Cardiovascular Prevention and Rehabilitation. Eur J Heart Fail. 2011;13(4):347–57.
14. Braith RW, Welsch MA, Feigenbaum MS, Kluess HA, Pepine CJ. Neuroendocrine activation in heart failure is modified by endurance exercise training. J Am Coll Cardiol. 1999;34(4):1170–5.
15. Leosco D, Parisi V, Femminella GD, Formisano R, Petraglia L, Allocca E, et al. Effects of exercise training on cardiovascular adrenergic system. Front Physiol. 2013 :28;4:348.
16. Hambrecht R, Niebauer J, Fiehn E, Kälberer B, Offner B, Hauer K, et al. Physical training in patients with stable chronic heart failure: effects on cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. J Am Coll Cardiol. 1995;25(6):1239–49.
17. Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of exercise-based cardiac rehabilitation in patients with heart failure (ExTraMATCH II) on mortality and hospitalisation: an individual patient data meta-analysis of randomised trials. Eur J Heart Fail. 2018;20(12):1735–43.
18. Fu TC, Wang CH, Lin PS, Hsu CC, Cherng WJ, Huang SC, et al. Aerobic interval training improves oxygen uptake efficiency by enhancing cerebral and muscular hemodynamics in patients with heart failure. Int J Cardiol. 2013;167(1):41–50.
19. Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognmo Ø, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. Circulation. 2007;115(24):3086–94.
20. Ahmad AM, Hassan MH. Effects of Addition of Inspiratory Muscle Training to Exercise-Based Cardiac Rehabilitation on Inspiratory Muscle Strength, Peak Oxygen Consumption, and Selected Hemodynamics in Chronic Heart Failure. Acta Cardiol Sin. 2022;38(4):485–94.
21. Ritchey MD, Maresh S, McNeely J, Shaffer T, Jackson SL, Keteyian SJ, et al. Tracking Cardiac Rehabilitation Participation and Completion Among Medicare Beneficiaries to Inform the Efforts of a National Initiative. Circ Cardiovasc Qual Outcomes. 2020 ;13(1):e005902.
22. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol. 2009;62(10):e1-34.
23. Springer J, Springer JI, Anker SD. Muscle wasting and sarcopenia in heart failure and beyond: update 2017. ESC Heart Fail. 2017;4(4):492–8.
24. Giuliano C, Karahalios A, Neil C, Allen J, Levinger I. The effects of resistance training on muscle strength, quality of life and aerobic capacity in patients with chronic heart failure - A meta-analysis. Int J Cardiol. 2017;227:413–23.
25. Esposito F, Mathieu-Costello O, Wagner PD, Richardson RS. Acute and chronic exercise in patients with heart failure with reduced ejection fraction: evidence of structural and functional plasticity and intact angiogenic signalling in skeletal muscle. J Physiol. 2018;596(21):5149–61.
26. Silva TOC, Sales ARK, Araujo GSM, Fonseca GWP, Braga PGS, Faria D, et al. Disturbed Blood Flow Acutely Increases Endothelial Microparticles and Decreases Flow Mediated Dilation in Patients With Heart Failure With Reduced Ejection Fraction. Front Physiol. 2021;12:629674.

27. Wang X, Yan K, Wen C, Wang J. Simvastatin Combined with Resistance Training Improves Outcomes in Patients with Chronic Heart Failure by Modulating Mitochondrial Membrane Potential and the Janus Kinase/Signal Transducer and Activator of Transcription 3 Signaling Pathways. Cardiovasc Ther;2022:8430733.
28. Volaklis KA, Tokmakidis SP. Resistance exercise training in patients with heart failure. Sports Med Auckl NZ. 2005;35(12):1085–103.
29. Alshamari M, Kourek C, Sanoudou D, Delis D, Dimopoulos S, Rovina N, et al. Does the Addition of Strength Training to a High-Intensity Interval Training Program Benefit More the Patients with Chronic Heart Failure? Rev Cardiovasc Med. 2023;24(1):29.
30. Giuliano C, Levinger I, Vogrin S, Neil CJ, Allen JD. PRIME-HF: Novel Exercise for Older Patients with Heart Failure. A Pilot Randomized Controlled Study. J Am Geriatr Soc. 2020;68(9):1954–61.
31. Dor-Haim H, Barak S, Horowitz M, Yaakobi E, Katzburg S, Swissa M, et al. Improvement in cardiac dysfunction with a novel circuit training method combining simultaneous aerobic-resistance exercises. A randomized trial. PloS One. 2018;13(1):e0188551.
32. Warehime S, Dinkel D, Alonso W, Pozehl B. Long-Term Exercise Adherence in Patients with Heart Failure: A Qualitative Study. Heart Lung J Crit Care. 2020;49(6):696–701.
33. Conraads VM, Deaton C, Piotrowicz E, Santaularia N, Tierney S, Piepoli MF, et al. Adherence of heart failure patients to exercise: barriers and possible solutions: a position statement of the Study Group on Exercise Training in Heart Failure of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2012;14(5):451–8.
34. Klompstra L, Deka P, Almenar L, Pathak D, Muñoz-Gómez E, López-Vilella R, et al. Physical activity enjoyment, exercise motivation, and physical activity in patients with heart failure: A mediation analysis. Clin Rehabil. 2022;36(10):1324–31.
35. Lundgren KM, Langlo KAR, Salvesen Ø, Zanaboni P, Cittanti E, Mo R, et al. Feasibility of telerehabilitation for heart failure patients inaccessible for outpatient rehabilitation. ESC Heart Fail. 2023;10(4):2406–17.