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Literature review

Relationship of heart failure and major depression disorder and the role of physical exercise

Relação da insuficiência cardíaca e transtorno de depressão maior e o papel do exercício físico

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ABSTRACT

Introduction: Heart Failure (HF) and Major Depressive Disorder (MDD) are diseases with high incidence, leading to high rates of morbidity and mortality. After the COVID-19 pandemic, around 11.5 million Brazilians were diagnosed with MDD, and in 2022, 192,852 emergency hospitalizations were registered in Brazil due to HF. The correlation between these two diseases is so significant that one is considered a risk factor for the other, negatively impacting the patients' quality of life. **Objective:** To conduct a literature review of the physiological mechanisms associated with HF and MDD, as well as the effect of physical exercise in alleviating the symptoms. **Methods:** Narrative literature review with a search in the databases PubMed, Scientific Electronic Library Online (SciELO), and Google Scholar. **Results:** Among observational studies and clinical trials, seven articles were selected. The main compensatory mechanisms related to these diseases are autonomic nervous system dysfunction, elevation of inflammatory cytokines, reduction of nitric oxide synthesis, and decreased cerebral blood flow. Aerobic training was responsible for improving depression symptoms and cognitive function, without significant changes in inflammatory biomarkers. **Conclusion:** There is a strong association between HF and MDD. Strategies to mitigate the symptoms of these diseases should be encouraged to improve the clinical outcomes of patients. Physical exercise is important for the treatment of symptoms in patients with HF affected by MDD, as it promotes improvements in clinical outcomes related to both diseases.

Keywords: cardiovascular disease; depression; physical activity; aerobic training

RESUMO

Introdução: A Insuficiência Cardíaca (IC) e o Transtorno Depressão Maior (TDM) são doenças de elevada incidência, que geram altas taxas de morbidade e mortalidade. Após a pandemia de COVID-19, cerca de 11,5 milhões de brasileiros foram diagnosticados com TDM e, em 2022, foram registradas 192.852 internações de emergência no Brasil por IC. A correlação entre essas duas doenças é tão significativa que uma é considerada fator de risco para a outra, gerando impacto negativo na qualidade de vida dos pacientes. **Objetivo:** Realizar uma revisão bibliográfica dos mecanismos fisiológicos associados à IC e ao TDM, bem como o efeito do exercício físico na atenuação dos sintomas. **Métodos:** Revisão bibliográfica narrativa com busca nas bases de dados PubMed, Scientific Electronic Library Online (SciELO) e Google Acadêmico. **Resultados:** Entre estudos observacionais e ensaios clínicos, foram selecionados 7 artigos. Os principais mecanismos compensatórios correlatos dessas doenças são a disfunção do sistema nervoso autonômico, a elevação de citocinas inflamatórias, diminuição da síntese de óxido nítrico e a redução do fluxo sanguíneo cerebral. O treinamento aeróbico foi responsável por melhorar os sintomas de depressão e a função cognitiva, sem alteração significativa dos biomarcadores inflamatórios. **Conclusão:** Existe uma forte associação entre IC e TDM. Estratégias para mitigação dos sintomas dessas doenças devem ser estimuladas para melhorar o desfecho clínico dos pacientes. O exercício físico é importante para o tratamento dos sintomas de pacientes com IC acometidos por TDM, pois promove melhorias nos desfechos clínicos relacionados a ambas as doenças.

Palavras-chave: doença cardiovascular; depressão; atividade física; treinamento aeróbico

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Introduction

Heart failure (HF) can be defined as a complex clinical syndrome in which the heart is unable to pump blood to the rest of the body efficiently to meet tissue demand or does so under high filling pressure. This condition is caused by structural or functional dysfunctions with signs and symptoms of low cardiac output and high cardiac filling pressure during exercise and rest [1].

Epidemiological data show that, in 2022, 192,852 emergency hospital admissions were performed for the treatment of HF in Brazil [2], and the number of deaths among hospitalized patients was 23,855 in the same year [3]. In addition, HF is associated with other adverse mental health outcomes, such as depression and anxiety, which affect the individual's quality of life [4].

Major Depressive Disorder (MDD) is characterized by the continuation of five or more symptoms for at least two weeks, such as depressed mood, lack of pleasure in activities that were previously pleasurable, fatigue, thoughts of death, feelings of guilt, changes in sleep behavior, weight loss or gain, difficulty concentrating, and psychomotor agitation [5].

MDD symptoms cause difficulty in social interaction and interfere in areas of work, personal relationships, or other relationships in which the individual is involved, causing suffering in personal life. When performing their tasks, the person with a depressive episode makes an excessive effort to maintain their functional and autonomic capacity [6].

Worldwide, the number of MDD cases continues to rise. Before the COVID-19 pandemic, it was estimated that 193 million people had been diagnosed with this disease; after the pandemic, this number reached 246 million. Brazil leads the ranking of South American countries with approximately 11.5 million diagnosed cases [7].

Given this scenario of increasing illness from HF and MDD, it is important to understand the physiological mechanisms that are associated with these two pathologies and the strategies to alleviate the symptoms of these diseases to obtain a better clinical outcome. Among the non-pharmacological strategies to control the symptoms of both HF and MDD, physical exercise is quite notable [8,9]. Thus, the main objective of this study is to review the pathophysiological mechanisms of HF and MDD and their interrelationship, in addition to demonstrating the effect of physical exercise on mental health, that is, on improving mood, cognitive capacity, reducing depressive symptoms, psychomotor speed and independence in performing tasks in patients with HF affected by MDD

Methods

The research design used in this study was a narrative bibliographic review with searches in the PubMed, Scientific Electronic Library Online (SciELO), and Google Scholar databases, using the following keywords: heart failure; depression; phy-

sical exercise; physical activity; strength training; aerobic training and combined training. The search took place from May 29, 2023, to June 2, 2023, and articles in Portuguese and English published in the last 5 years were included.

Results

Seven articles were selected, including observational studies and clinical trials (Table I).

Table I – Summary of articles selected for review

Author	Year	Sample characteristic	Intervention	Result
Ducan *et al.* [10]	2014	39 patients with LVEF <40% and stable medication for 30 days were divided into a control group (20) and a group with physical exercise intervention (22).	Both groups received educational guidance on HF for 12 weeks. The intervention group performed 24 weeks of aerobic exercise for 30 minutes 3 days a week and strength exercises 2 days a week. During the first 12 weeks, the exercise group received weekly goals, and the remaining sessions were performed independently.	The results indicated that the group that performed exercise improved their self-efficacy in performing physical exercise and improved their mood.
Pressleer *et al.* [11]	2010a	414 participants divided into 3 groups: HF, chronic degenerative disease without HF and control group.	All groups underwent a battery of neuropsychological tests and assessment of comorbidity, blood pressure, oxygen saturation, depressive symptoms and sociodemographic interview.	The group with HF showed low results in executive function, psychomotor speed and memory. The severity of HF was associated with greater cognitive deficit.
Pressleer *et al.* [12]	2010b	166 patients with chronic systolic HF and LVEF of 40%	Tests were applied to assess the patients' cognitive function, such as: working memory, global cognitive function, language proficiency, visual-spatial ability and executive function. Telephone calls were made 12 months after the start of the study to monitor the sample.	The results indicated that lower LVEF and worse memory results were predictors of mortality. Lower SBP and DBP and worse results in executive function, working memory and psychomotor speed also had predictive results of mortality.

Table I – Continuation

Author	Year	Sample characteristic	Intervention	Result
Abdelbasset *et al.* [13]	2019	69 patients with mild to moderate depression and systolic HF NYHA II and III with reduced ejection fraction <40% divided into 3 groups: Group I low to moderate intensity exercises; Group II continuous moderate intensity exercises, and Group III did not perform exercises.	Group I – 3x a week, lasting 20 to 30 minutes and intensity 40% to 50% of HR_{max} in the first 6 weeks and 30 to 40 minutes of 50% to 70% of HR_{max} in the last 6 weeks. Group II – 3x a week, lasting 40 to 50 minutes of moderate aerobic exercise and intensity of 60 to 70% of HR_{max} for 12 weeks. Group III - did not perform exercise. The PHQ-9 questionnaire was applied to the groups at the beginning of the study, after 6 months of the intervention and at the end.	The results showed that both groups I and II that performed physical exercise reduced their depression levels without any significant difference between them.
Bandeira *et al.* [14]	2020	79 elderly patients with HF	Cross-sectional study that evaluated the cognitive function of patients with HF through the Mini Mental State Examination (MMSE)	39.2% of patients had impaired cognitive function.
Abdelbasset & Alqahtani [15]	2019	46 participants with NYHA II and III HF, and mild to moderate depression divided into 2 groups: a control group and the other performed moderate aerobic exercise.	3 x a week, lasting 30 minutes at 60 to 70% of HR_{max} for 12 weeks.	The group that exercised had a greater decrease in depression.
Redwine *et al.* [16]	2020	69 patients with symptomatic stage C HF and a mean age of 65 years	Patients were divided into 3 intervention groups: Tai Chi Chuan, resistance exercise, and control group.	The groups that performed Tai Chi Chuan and resistance exercises showed greater effectiveness in improving cognitive function.

HR_{max} = maximum heart rate; LVEF = left ventricular ejection fraction; HF = heart failure; SBP = systolic blood pressure; DBP = diastolic blood pressure; PHQ-9 = Patient Health Questionnaire; NYHA = New York Heart Association

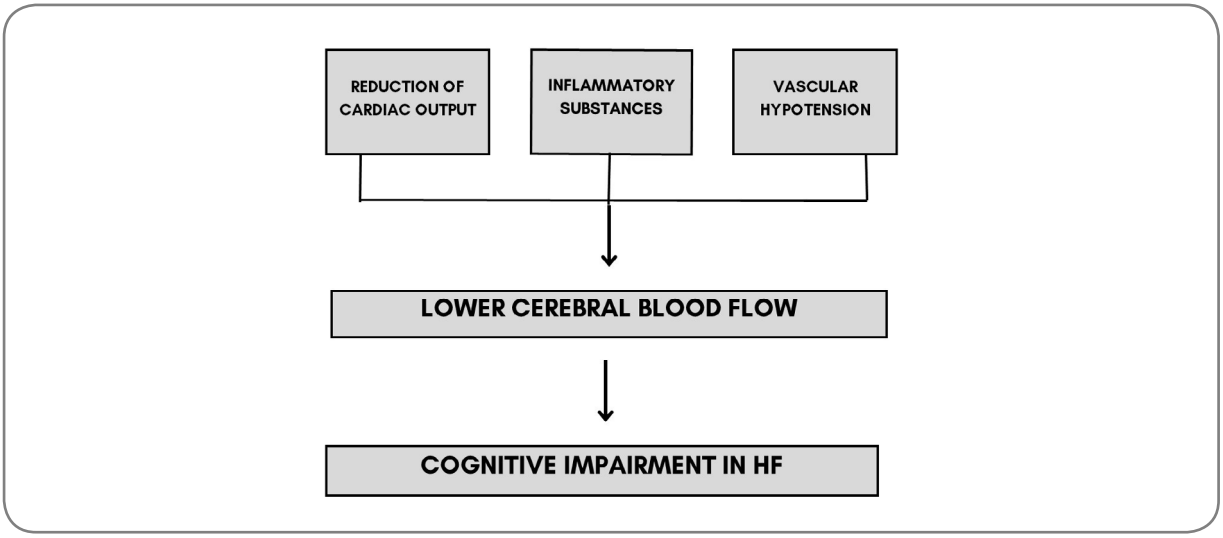
Discussion

The impairment in HF goes beyond the heart, since cognitive damage is present in a large proportion of these patients [14]. With cognitive impairment, the patient's perception of self-care is impaired, which directly affects their independence: maintaining a balanced diet, taking medication correctly, and independently perceiving the worsening of their health status. As age and HF increase, the performance

of executive function worsens, causing impairments in memory, psychomotor speed, and visual memory [11].

The cognitive deficit of individuals with HF, when compared to a healthy group and with other comorbidities, showed worse results in memory, psychomotor speed, and executive function [11]. The severity of HF and advanced age are risk factors for cognitive deterioration, as is the male gender [12].

Low cardiac output, production of inflammatory substances, and vascular hypotension are factors that reduce cerebral blood flow and compromise cognitive areas (Figure 1).



Adapted from Leto & Feola, 2014 [17]
Figure 1 – Physiological mechanisms contributing to cognitive impairment in heart failure

The increase in inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), brain natriuretic peptide (BNP), and asymmetric dimethylarginine (ADMA), present in individuals with MDD, increases the risk of endothelial injury, development of thrombi and increased risk of stroke [18]. Another change in MDD is the reduction in the bioavailability of nitric oxide, which may be associated with the formation of atherosclerosis due to the increase in nitric oxide inhibitors and the cell reduction that contributes to endothelial repair and angiogenesis [19].

The association of cognitive impairment with severe HF presents a higher risk of mortality [11]. Regarding the severity of the disease, MDD is associated with a greater number of hospitalizations and mortality, regardless of the LVEF condition. In patients with depressive symptoms and HF with reduced LVEF, the mortality rate and hospitalizations related to heart disease were 55% higher compared to other patients with the same condition of HF with reduced LVEF without depressive symptoms [20].

Physical exercise is indicated for both the prevention and treatment of HF and MDD. Participation in a regular physical exercise program positively impacts the lives of patients with these comorbidities, improving well-being and self-care [21]. Treatment with physical exercise in MDD is recommended because it reduces stress

levels, improves sympathovagal balance, stimulates new synapses, increases the hippocampus, and synthesizes Brain-Derived Neurotrophic Factor (BDNF), which acts on the brain and stimulates neurogenesis [22].

BDNF is an important marker for heart and brain health. It plays a role in endothelial health, in addition to generating a positive effect on angiogenesis. In the brain, BDNF contributes positively to brain plasticity, associated with a lower risk of neurodegenerative diseases. Physical exercise is capable of increasing BDNF levels, protecting the brain from possible cognitive damage. In cardiac function, increased BDNF reduces cardiovascular risk associated with physical activity and cardiorespiratory fitness [23].

The practice of physical exercise is important for psychological responses in patients with HF. Ducan *et al*. [10] evaluated the psychological responses generated by physical exercise, combining aerobic training and muscular resistance, and observed improvements in self-efficacy for physical exercise in the first three weeks of exercise. Those who performed more physical exercise over 24 weeks showed better results in levels of depression, self-efficacy, and confusion.

Abdelbasset & Alqahtani [15] evaluated the effect of continuous moderate--intensity aerobic training on symptoms of depression in individuals with HF. For 12 weeks, the intervention group performed three sessions of 40 to 50 minutes of walking between 60 and 70% of HR_{max}; the control group received recommendations for performing home activities, relaxation, and self-care. There was a reduction in the depression scale in both groups, but the group that performed physical exercise reduced it by 81% compared to 46% in the control group.

When comparing the effect of different intensities of aerobic exercise on the level of depressive disorders in patients with HF, Abdelbasset *et al*. [13] divided the sample into three groups: Group 1: Started with 6 weeks of low-intensity aerobic training (40 to 50% HR_{max}) and progressed to another 6 weeks of moderate-intensity aerobic training (50 to 70% of HR_{max}) lasting 20 to 30 minutes. Group 2: Performed 12 weeks of continuous moderate-intensity aerobic training (60 to 70% of HR_{max}). Group 3 received only guidance on home activities and self-care. The groups that performed physical exercise, regardless of intensity, presented similar positive results, with no significant difference in depression rates.

The effect of physical exercise on MDD symptoms and cognitive function in patients with HF was assessed in groups that performed physical exercise for 16 weeks, with two weekly 60-minute sessions of Tai Chi Chuan training, elastic resistance training, or the control group (no exercise). The results found reinforce the positive effect of physical exercise on cognitive function and symptoms of depression without altering inflammatory levels [16]. The main limitation of this study was the scarcity of articles that evaluated different types of physical exercise on MDD symptoms in patients with HF. For example, the benefit of strength training in improving functional capacity, increasing muscle strength, improving quality of life, and reducing the risk of mortality in patients with HF is well established [24]. However, studies using

this type of training to evaluate the attenuation of depressive symptoms in patients with HF are incipient.

Conclusion

HF and MDD are strongly correlated, and their deleterious effects negatively impact the quality of life, hinder treatment adherence, and contribute to the high mortality resulting from these diseases. The main correlated pathophysiological mechanisms are dysfunction of the autonomic nervous system, reduction of nitric oxide, and blood flow, which may contribute to the worsening of HF and the development of MDD.

Low and moderate-intensity aerobic exercise is beneficial for reducing MDD symptoms in patients with HF. In addition to aerobic training, exercises such as Tai Chi Chuan and elastic resistance have shown positive results in reducing symptoms of depression. The use of these exercises as a non-pharmacological treatment has been shown to be effective for individuals with HF and MDD. Further studies with different training modalities (e.g., strength training) are needed to evaluate MDD symptoms in patients with HF.

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Authors' contributions
Conception and design of the research: Florentino JO, Souza WMM; Obtaining data: Florentino JO, Souza WMM; Data analysis and interpretation: Florentino JO, Souza WMM; Manuscript writing: Florentino JO, Souza WMM; Critical revision of the manuscript for important intellectual content: Begni RM

References

1. Rohde LEP, Montera MW, Bocchi EA, Clausell NO, Albuquerque DC, Rassi S, *et al*. Diretriz brasileira de insuficiência cardíaca crônica e aguda. Arq Bras Cardiol. 10 de setembro de 2018;111(3):436–539. doi: 10.5935/abc.20180190

2. DATASUS. Procedimentos hospitalares do SUS - por local de internação - Brasil [Internet]. tabnet.datasus.gov.br. [cited 2024 May 15]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/qiuf.def

3. DATASUS. Procedimentos hospitalares do SUS - por local de internação, óbitos segundo procedimento - Brasil [Internet]. tabnet.datasus.gov.br. [cited 2024 May 15]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/qiuf.def

4. Dekker RL, Lennie TA, Doering L V, Chung ML, Wu JR, Moser DK. Coexisting anxiety and depressive symptoms in patients with heart failure. Eur J Cardiovasc Nurs. 2014;13(2):168–76. doi: 10.1016/j.pcad.2021.10.003

5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-5). 5th ed. American Psychiatric Publishing; 2013.

6. Laks J, Deslandes AC, Helena M. Exercício físico, envelhecimento e saúde mental. Rio de Janeiro: Instituto Vital Brazil, Centro de Estudo e Pesquisa do Envelhecimento (CEPE), Instituto de Psiquiatria UFRJ FAPERJ; 2014

7. World Health Organization. Depression and Other Common Mental Disorders Global Health Estimates [Internet]. 2017. [cited 2024 May 15]. Disponível em: https://iris.who.int/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf?sequence=1

8. Wheat HL, Fedson S, Bozkurt B, Josephson RA. Cardiac rehabilitation in heart failure: Indications for exercise training based on heart failure phenotype. Prog Cardiovasc Dis. 2022;70:16–21. doi: 10.1016/j.pcad.2021.10.003

9. Zhao J, Jiang W, Wang X, Cai Z, Liu Z, Liu G. Exercise, brain plasticity, and depression. CNS Neurosci Ther. 2020;26(9):885–95. doi 10.1111/cns.13385

10. Duncan K, Pozehl B, Hertzog M, Norman JF. Psychological responses and adherence to exercise in heart failure. Rehabil Nurs. 2014;39(3):130–9. doi: 10.1002/rnj.106

11. Pressler SJ, Subramanian U, Kareken D, Perkins SM, Gradus-Pizlo I, Sauvé MJ, *et al*. Cognitive deficits in chronic heart failure. Nurs Res. 2010;59(2):127–39. doi: 10.1097/NNR.0b013e3181d1a747

12. Pressler SJ, Kim J, Riley P, Ronis DL, Gradus-Pizlo I. Memory dysfunction, psychomotor slowing, and decreased executive function predict mortality in patients with heart failure and low ejection fraction. J Card Fail. 2010;16(9):750–60. doi: 10.1016/j.cardfail.2010.04.007

13. Abdelbasset WK, Alqahtani BA, Alrawaili SM, Ahmed AS, Elnegamy TE, Ibrahim AA, *et al*. Similar effects of low to moderate-intensity exercise program vs moderate-intensity continuous exercise program on depressive disorder in heart failure patients: A 12-week randomized controlled trial. Medicine (United States). 2019;98(32). doi: 10.1097/MD.0000000000016820

14. Bandeira GMS, Flores PVP, Alencar PC, Jardim PP, Tinoco JMVP, Cavalcanti ACD. Avaliação da função cognitiva de pacientes com insuficiência cardíaca crônica: estudo transversal. Online Braz J Nurs 22 de junho de 2020;18(4). doi: 10.17665/1676-4285.20196327

15. Abdelbasset WK, Alqahtani BA. A randomized controlled trial on the impact of moderate-intensity continuous aerobic exercise on the depression status of middle-aged patients with congestive heart failure. Medicine (United States). 2019;98(17). doi: 10.1097/MD.0000000000015344

16. Redwine LS, Pung MA, Wilson K, Bangen KJ, Delano-Wood L, Hurwitz B. An exploratory randomized sub-study of light-to-moderate intensity exercise on cognitive function, depression symptoms and inflammation in older adults with heart failure. J Psychosom Res. 2020;128. doi: 10.1016/j.jpsychores.2019.109883

17. Leto L, Feola M. Cognitive impairment in heart failure patients. Vol. 11, J Geriatric Cardiol. 2014(11):316–28. doi: 10.11909/j.issn.1671-5411.2014.04.007

18. Sbolli M, Fiuzat M, Cani D, O'Connor CM. Depression and heart failure: the lonely comorbidity. Eur J Heart Fail. 2020;22(11):2007–17. doi 10.1002/ejhf.1865

19. Rashid S, Qureshi AG, Noor TA, Yaseen K, Sheikh MAA, Malik M, *et al*. Anxiety and depression in heart failure: an updated review. Curr Probl Cardiol. 2023;48(11):101987. doi: 10.1016/j.cpcardiol.2023.101987

20. Newhouse A, Jiang W. Heart failure and depression. Heart Fail Clin. 2014;10(2):295–304. doi: 10.1016/j.hfc.2013.10.004

21. Cardoso G, Trancas B, Luengo A, Reis D. Insuficiência cardíaca e depressão: uma associação com relevância clínica [8] [Internet]. [citado 2024 Out 30]. Disponível em: https://repositorio.hff.min-saude.pt/bitstream/10400.10/162/1/Cardoso.pdf

22. Sanches A, Costa R, Marcondes FK, Cunha TS. Relationship among stress, depression, cardiovascular and metabolic changes and physical exercise. Fisioter Mov. 2016;29(1):23–36. doi: 10.1590/0103-5150.029.001.AO02

23. Trombetta IC, DeMoura JR, Alves CR, Carbonari-Brito R, Cepeda FX, Lemos JR. Níveis Séricos do BDNF na Proteção Cardiovascular e em Resposta ao Exercício. Arq Bras Cardiol. 2020;115(2):263–9. doi: 10.36660/abc.20190368

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. doi: 10.1016/j.ijcard.2016.11.023