

Depression and Heart Failure: A Narrative Review of Their Complex Relationship and Clinical Implications

Pemma Sai Sarath Kumar¹ , Venkata Anirudh Chunchu¹ , Pathan Mayur Srinivas¹ , Ben Walters² 
Nanki Singh³ , Anamika Pilaniya⁴ 

¹. Avalon University School of Medicine, Curacao

². Penn State College of Medicine, Pennsylvania, United States

³. School of medical sciences and research, Greater Noida, India

⁴. University College of Medical Sciences, New Delhi, India

ABSTRACT

Depression is a prevalent and debilitating comorbidity that affects heart failure (HF) patients worldwide, with significant social and economic impacts. The multifaceted, bidirectional relationship between depression and HF involves shared pathophysiological mechanisms such as hypercoagulability, inflammation, and neurohormonal and autonomic dysregulation. Furthermore, behavioural factors such as smoking, physical inactivity, and medication non-adherence exacerbate the association between depression and HF. These complex pathways not only contribute to the development of heart failure in depressed people but also increase depressive symptoms in heart failure patients, creating a vicious cycle that affects overall well-being. Treatment of depression in heart failure patients requires an integrated approach, including non-pharmacological and pharmaceutical interventions. Despite the low efficacy of existing antidepressant medicines, there is a need for novel treatment techniques, and current research studies provide optimism for improving the overall prognosis and management of depression in this susceptible population. This review focuses on providing comprehensive care strategies that address both physical and mental health requirements as necessary, along with the importance of diagnosis and treatment of depression impacting heart failure to improve the overall prognosis and quality of life.

Turk J Int Med 2025;7(2):44-51

DOI: 10.46310/tjim.1515390

Keywords: Depression, Heart Failure, Comorbidity, Quality Of life

INTRODUCTION

Depression is a leading global mental illness, affecting 280 million people worldwide. It affects 21% of women and 11%–13% of men in the United States, resulting in 15 million physician office visits and 12.5% of emergency

department visits, costing over \$200 billion annually.¹⁻⁴ Depression is a complex and multifactorial mood disorder, involving genetic, socioeconomic, environmental, and lifestyle factors with dysregulation of homeostatic

Received: July 25, 2024 Accepted: April 10, 2025 Published: April 29, 2025

How to cite this article: Kumar PSS, Chunchu VA, Srinivas PM, Walters B, Singh N, Pilaniya A. Depression and Heart Failure: A Narrative Review of Their Complex Relationship and Clinical Implications, *Turk J Int Med* 2025;7(2):44-51. DOI: 10.46310/tjim.1515390

Address for Correspondence:

Pemma Sai Sarath Kumar, Avalon University School of medicine WTC, Piscaderaweg z/n, Willemstad, Curaçao
Email: saisarath.pemma@gmail.com



systems. According to The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) criteria, depression commonly features persistent sadness, emptiness, irritability, and somatic and cognitive changes that impair functioning.^{5,6} In addition to cognitive impairment and overall decline in somatic function, depression poses a significant risk factor for other major medical conditions like stroke, autoimmune disease, diabetes, and cardiovascular disease, particularly heart failure (HF).¹ HF has been associated with a mortality rate of 15% within the first year and 53% within five years of diagnosis.⁷⁻⁸ In addition to traditional risk factors for HF, such as hypertension, diabetes, smoking, obesity and past myocardial infarction, non-traditional risk factors such as anxiety, depression, low level of education, high psychosocial stress, and low-grade inflammation may also contribute to the development of HF.⁹⁻¹¹ Depression is common in HF patients as their condition worsens, with prevalence rates of 11% in New York Heart Association (NYHA) class I patients and 42% in NYHA class IV patients.¹² It acts as both a risk factor for developing heart failure (HF) and a common comorbidity in HF patients.

A meta-analysis of 28 studies revealed that depressed individuals have a 46% higher risk of cardiovascular disease, and 20-30% of HF patients experience depression, creating a vicious cycle.¹³ The Nord-Trøndelag Health Study (HUNT 2) revealed that severe depressive symptoms were linked with diastolic dysfunction and left ventricular hypertrophy, which significantly increased the risk of HF with an adjusted hazard ratio of 1.41. This highlights depression as an independent risk factor for HF, particularly in the elderly population, women, and those with isolated systolic hypertension or coronary heart disease.¹⁴ Studies have also shown that patients with HF and comorbid depression have increased emergency department visits and are 4.1 times more likely to be hospitalized compared to those without depression.¹⁵ Emotional impairment during hospitalization is often seen as a normal response to illness, making depression a challenging diagnosis in patients hospitalized with cardiovascular diseases.¹⁶ The American Heart Association (AHA) advises a two-step depression screening for heart disease patients, starting with the PHQ-2 and using the Patient Health Questionnaire (PHQ-9) for those who screen positive, reflecting the long-recognized link between emotions and heart health noted as early as 1937 by Malzberg.^{17,18} In this narrative, we review the strong link between HF and comorbid depression, as well as how the psychological aspects of

cardiovascular patients are often overlooked, leading to inadequate treatment and gaps in comprehensive care. This oversight can exacerbate patient outcomes and negatively impact overall health.¹⁴

PATHOPHYSIOLOGY

Depression and HF often coexist and have a bidirectional relationship, with many pathophysiological processes such as hypercoagulability, inflammation, neurohormonal dysregulation, autonomic dysfunction, and behavioural factors.^{14,19} Patients with coronary heart disease (CHD) who have depression have increased platelet activation, causing thrombogenesis by interacting with the vascular endothelium and coagulation factors.²⁰ People with depression are at increased risk of blood clots because their platelets become more active. This happens due to altered serotonin levels, which promote platelet activation and, thus, promote clot formation.²¹ These changes may be the mediating factors behind the increased risk of ischemic events in these individuals, potentially contributing to the development of heart failure.²²

Individuals with depression often have reduced parasympathetic nerve activity, leading to lower vagal nerve stimulation. This can interfere with the body's ability to regulate immune responses through the cholinergic anti-inflammatory system (CAIS). As a result, the body produces more inflammation-related proteins, such as C-reactive protein (CRP) and cytokines like interleukin-1-beta, tumour necrosis factor-alpha, and interleukin-6.²³⁻²⁵ Increased levels of these inflammatory markers can lead to chronic inflammation, which may cause changes in the heart's structure and weaken the heart muscle, eventually leading to HF.¹⁹

The association between depression and outcomes in HF is impacted by neuro-hormonal and autonomic dysregulation.²² Individuals with depression often have an overactive stress response. This occurs secondary to hyperactivity of the hypothalamic-pituitary-adrenal axis. As a result, stress hormones like cortisol and catecholamine (epinephrine and norepinephrine) rise in the bloodstream. Cortisol increases blood clotting by releasing factor VIII and von Willebrand factor, while catecholamines reduce the body's ability to break down clots, promoting hypercoagulability. Also, these elevated catecholamine levels in depression impair the heart's overall responsiveness to adrenergic stimuli. This diminished sensitivity contributes to myocardial remodelling, cardiac damage, and an increased risk of arrhythmias, which may eventually precipitate the

development of heart failure (HF).²⁴ Changes in the body's autonomic stress response in depression are closely linked to heart rate variability (HRV), which reflects the heart's ability to adapt to different conditions. A reduced HRV has been positively correlated with depression severity.²⁵

Furthermore, various behavioural factors play a role in the association between depression and HF. High-risk behaviours in depressed individuals, including smoking, physical inactivity, poor diet, inadequate stress management, and noncompliance with cardiac rehabilitation programs after a CHD, can increase the risk of HF in patients who are depressed.²⁶ Individuals with heart failure who take antidepressants are more likely to discontinue their prescription drugs on time (BW3) and are less likely to obtain heart failure medical care that meets guidelines, resulting in worsening cardiac symptoms.²⁷ Marital status, also a significant predictor of depression in HF patients, is linked with social isolation, exacerbating depressive symptoms and contributing to poorer outcomes (BW4).¹⁴ This suggests that depression-related behavioural changes may be connected to poor cardiac outcomes and the progression of coronary artery disease (CAD) in individuals with and without preexisting cardiovascular disease (CVD), eventually leading to HF.²²(Figure 1)

DISCUSSION

In the United States, HF affects approximately 1.9%

to 2.6% of adults, while major depressive disorder (MDD) has a lifetime prevalence of 20.6%. Given the high prevalence of both conditions, their interplay presents a pressing public health concern.^{28,29} The bidirectional relationship between HF and MDD is well-established. Evidence suggests that MDD serves both as a contributing factor to HF development and as a frequent comorbidity following an HF diagnosis.²⁸ Given the significant burden of both conditions, addressing this comorbidity is crucial for improving patient outcomes and quality of life. Further research is needed to explore effective interventions and strategies to manage both HF and MDD simultaneously.

A 2022 meta-analysis of prospective cohorts found that patients with MDD had a 23% higher risk of developing HF (pooled HR: 1.23; 95% CI: 1.08-1.41), identifying MDD as a significant risk factor.³⁰ Another meta-analysis examining psychological health and cardiovascular disease further linked MDD to increased HF incidence and mortality, highlighting its negative impact on survival rates.³¹ Furthermore, a retrospective cohort study of veterans found that individuals diagnosed with MDD were more likely to develop HF than those without MDD (HR: 1.11; 95% CI: 1.04-1.18).³² However, while these findings are compelling, many of the included studies rely on observational designs, which limit the ability to establish causal relations. Additional factors warrant further evaluation, such as residual confounding and potential biases in patient selection.

Conversely, other analyses had the goal of determining

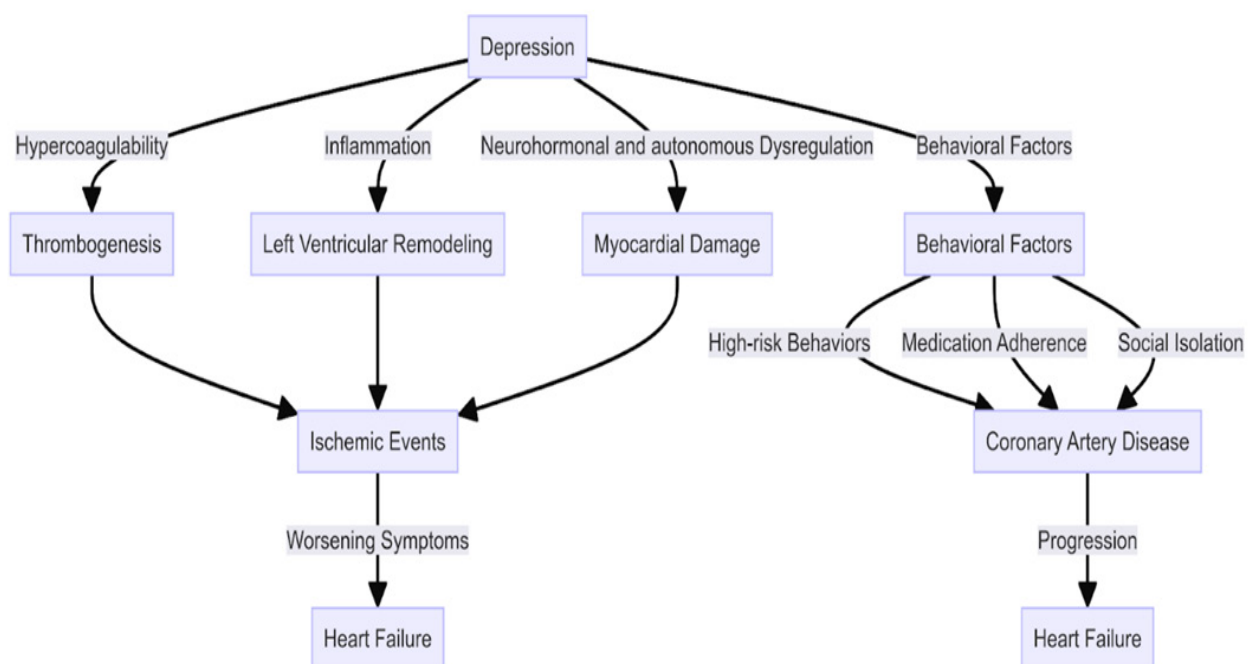


Figure 1. Flowchart on the pathophysiological association between depression and heart failure.

if there was a relationship present in patients with a diagnosis of HF and the development of MDD in these patients. One such cross-sectional study found that 22% of patients with congestive HF for more than six months developed MDD. This study also highlighted predictors of depression in HF patients, including higher NYHA classifications, previous acute coronary syndrome, lack of social support, and a sedentary lifestyle.³³ While the study highlights key factors linked to depression in HF patients, its cross-sectional design and certain limitations make it difficult to generalize the findings. Also, a review from 2020 found that 30% of patients with a diagnosis of HF concurrently experienced clinical depression, and an even higher number of these patients had experienced some degree of depressive symptoms.¹⁴ Interestingly, socioeconomic status also plays a significant role. In a systematic review from 2022, patients with heart failure were identified and pooled according to the concurrent diagnosis of depression and the socioeconomic status of the country in which they resided. It was found that, in almost half of the patients with HF, those who resided in low and middle-income countries were more likely to have a diagnosis of MDD. This suggests that economic disparities may substantially influence the psychological burden of HF.³⁴ These findings highlight the multifaceted nature of depression in HF, influenced by biological, psychological, and social determinants. Future research should prioritize prospective cohort studies to clarify causality and explore interventions targeting both socioeconomic disparities and modifiable risk factors (e.g., social support and physical activity).

In addition to the previously described connection between HF and MDD, there have also been studies that have described the negative impacts associated with these diagnoses when they are found together. One such study performed in 2001 found that patients diagnosed with both MDD and HF had nearly twice the risk of in-hospital mortality. Additionally, these patients faced a higher likelihood of hospital readmission within one year.³⁵ Further research on prognosis in HF patients with depression revealed a significant correlation with poor outcomes, including increased all-cause mortality (HR 1.31, $p < 0.001$) and higher hospital readmission rates (HR: 1.16, $p < 0.001$).³⁶

Another topic of research for this population of patients is regarding the treatment strategies and associated outcomes. In a systematic review of 27 studies of patients with HF and MDD, treatment strategies were evaluated to identify effectiveness in addressing the underlying MDD in these patients. Through interventions of

pharmacotherapy, psychotherapy, exercise, education, and non-pharmacological interventions, it was found that psychotherapy and cognitive behavioural therapy (CBT) led to significant clinical improvement. This conclusion may offer insight into the treatment of patients with HF and concomitant MDD.¹⁵ In the same vein, the Heart Failure - A Controlled Investigating Outcomes of Exercise Training (HF-ACTION) trial performed a similar study regarding the treatment of MDD in patients with HF. This trial found that exercise was significantly associated with a reduction in depressive symptoms at 3 and 12 months,^{37,38} which is important to this review as it identifies further positive interventions to clinically address these patients. However, the study's small sample size, limited number of women, and short follow-up period may limit the generalizability of the results and make it difficult to assess the long-term effects of the exercise intervention on mental and physical health. Additionally, the retrospective design of the secondary analysis, reliance on non-randomized exercise volumes, and issues with unplanned crossover and non-compliance among participants further complicate the results, reducing the strength of the conclusions that can be drawn.

Another concept important to the patient with HF and MDD is the negative effects that these two diagnoses can have on one another, which in turn can exacerbate either condition. For instance, untreated MDD in a patient with HF can lead to a worsened ability to care for oneself, and this, in turn, may result in increased morbidity and mortality.³⁹ Moreover, a systematic review explored the connection between the severity of MDD symptoms in HF patients and their adherence to their treatment regimen. It was found in this study that worsening depression symptoms significantly hinder medication adherence and lifestyle changes in HF patients, which are crucial for managing the condition and may lead to poor prognosis and increased morbidity.⁴⁰ On the other hand, a randomized controlled trial in 2021 discovered that patients with HF and MDD who increased their levels of self-care had an improvement in depressive symptoms.⁴¹

FUTURE DIRECTIONS AND LIMITATIONS

While the current literature offers valuable insights into the HF-MDD relationship, key gaps remain. Many studies rely on observational data, limiting the ability to establish causation. Future research should prioritise well-designed randomized controlled trials to assess intervention efficacy. Standardizing diagnostic criteria

Table 1. Studies on depression and heart failure: study designs, parameters studied, and conclusions.

Study	Study design	Parameter studied	Outcomes
Cao ³⁰	Meta-analysis of 6 prospective cohort studies with 4,727 HF events among 131,282 participants	Depression is a risk factor for developing heart failure.	Participants with depression had a 23% higher risk of developing HF compared to those without depression.
Krittana Wong ³¹	Meta-analysis of 26 studies with 1,957,621 participants	Association of HF and depression	Depression was associated with an increased risk of developing congestive HF (HR: 1.04; 95% CI: 1.00-1.09) and congestive HF mortality (HR: 3.20; 95% CI: 1.29-7.94).
Lee ³⁶	Systematic review and meta-analysis of 39 studies	Relationship between comorbidity and health outcomes in patients with HF.	HF with depression had negative prognostic outcomes: all-cause mortality (HR: 1.31; 95% CI: 1.18-1.45), all-cause readmission (HR: 1.16; 95% CI: 1.09-1.23), HF-related readmission (HR: 1.13; 95% CI: 1.05-1.23), and non-HF-related readmission (HR: 1.17; 95% CI: 1.07-1.27).
Jiang ³⁵	Logistic regression analyses	Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive HF.	Major depression was associated with increased mortality in patients with HF at 3 months (odds ratio: 2.5 vs no depression; p=0.08) and at 1 year (odds ratio: 2.23; p=0.04) and readmission at 3 months (odds ratio: 1.90; p=0.04) and at 1 year (odds ratio: 3.07; p=0.005).
Sherwood ⁴²	Cox proportional hazards regression analyses	Relationship of depression to death or hospitalization in patients with HF.	Patients with depression (BDI score ≥ 10) were associated with a HR of 1.56 (95% CI: 1.07-2.29) for the combined endpoint of death or cardiovascular hospitalization.
Ying ⁴⁴	Bibliometric	Overview of studies on HF comorbid with depression from 2002 to 2021	Research progress, hotspots, and trends in the field of HF with depression were illustrated.
Ishak ¹⁵	Analysis of 4846 papers published from January 2002 to December 2021	To identify the tools used to measure depression in HF and assess the impact of various treatment interventions on depression in HF.	BDI, PHQ, and HADS were more commonly used than clinician-rated questionnaires. Psychotherapy demonstrated the most significant impact, leading to notable reductions in BDI II and HAM-D scores, followed by collaborative care and education.
Peng ⁴³	Systematic Review and Meta-analysis	Efficacy of CBT to alleviate depression in patients with HF.	CBT can substantially decrease depression scale (Std. MD = -0.27; 95% CI: -0.47 to -0.06; p=0.01) but has no substantial influence on the quality of life, self-care scores, and 6-minute walk test distance.
Poletti ⁴⁰	Systematic review and Meta-analysis	The association between depressive symptoms and medication adherence in HF patients	HF patients with depression or depressive symptoms are less likely to adhere to their prescribed medication regimen compared to non-depressed patients.
Johansson ⁴¹	Systematic Review	The impact of internet-based CBT and depressive symptoms on self-care behaviour in patients with heart failure	No significant differences were found in self-care between the patients on the internet-based CBT and those in the online discussion group at the three- and nine-week follow-up.
Zambrano ⁴⁵	Secondary analysis of RCT	Psychiatric and psychological interventions for depression in patients with heart disease	SSRIs like sertraline did not show any significant reduction in depression scores in patients with HF.
Sbolli ¹⁴	Narrative Review	The relationship between depression and heart failure, and the role of SSRIs in the treatment of depression in patients with HF.	Pooled analysis of SADHART-CHF and MOOD-HF trials showed that SSRI treatment had a neutral effect on mortality (risk ratio 1.25, 95% CI 0.78-2.0) and cardiovascular death (risk ratio 1.38, 95% CI 0.77-2.45).

HR: hazard ratio, CI: confidence interval, BDI: Beck depression inventory, CBT: cognitive behavioural therapy, SSRIs: selective serotonin reuptake inhibitors, HF: heart failure.

for depression in HF patients would enhance consistency across studies. Additionally, examining socioeconomic factors and disparities in mental health care access could provide a more comprehensive understanding of this complex interaction.

Given the significant burden of HF and MDD, a multidisciplinary approach incorporating cardiology, psychiatry, and behavioural health strategies is essential. Early screening for depression in HF patients, combined with targeted interventions, may improve both mental health and cardiovascular outcomes. This approach

enhances quality of life and reduces healthcare utilization.

CONCLUSIONS

Depression and heart failure often coexist. Numerous studies suggest that it has a significant impact on the prognosis of heart failure, leading to higher rates of morbidity and mortality. Despite the substantial association between heart failure and depression, these are often under-recognized and under-treated. Several pathways, such as inflammation, neurohormonal activation, autonomic dysfunction, and behavioural

variables, mediate the bidirectional association between depression and heart failure. These complex pathways not only contribute to the development of heart failure in depressed people, but they also increase depressive symptoms in heart failure patients, creating an endless cycle that affects overall well-being. Treatment of depression in heart failure requires an integrated approach, including non-pharmacological and pharmaceutical interventions. Traditional antidepressant medications have proven to be little successful in this population, which highlights the need for new approaches to treatments; while psychotherapy and cognitive behavioural therapy show potential in treating depressed symptoms, there are still obstacles in the way of their broader acceptance. Ongoing research into new therapies like N-methyl-D-aspartate receptor antagonists, repeated transcranial magnetic stimulation, and omega-3 supplements offers hope for improving depression management and overall prognosis in this vulnerable population. Also, collaboration between cardiologists, psychiatrists, and healthcare professionals is essential to bridge the gap between depression and cardiovascular care by integrating routine depression screening into heart failure management protocols. Recognizing and addressing the complicated relationship between depression and heart failure is vital for offering effective treatment, while focusing on mental health alongside cardiovascular health to enhance patient well-being, quality of life, and prognosis.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding Sources

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: PMS, PSSK, NS, VAC; Study Design: PMS, PSSK, NS, VAC; Literature Review: VAC, PSSK, PMS; Critical Review: BW; Writer: PMS, PSSK, VAC, NS.

REFERENCES

1. Beurel E, Toups M, Nemeroff CB. The Bidirectional Relationship of Depression and Inflammation: Double Trouble. *Neuron*. 2020 Jul 22;107(2):234-256. doi: 10.1016/j.neuron.2020.06.002.
2. Slavich GM, Sacher J. Stress, Sex Hormones, Inflammation, and Major Depressive Disorder: Extending Social Signal Transduction Theory of Depression to Account for Sex Differences in Mood Disorders. *Psychopharmacology (Berl)*. 2019 Oct;236(10):3063-3079. doi: 10.1007/s00213-019-05326-9.
3. Moradi M, Doostkami M, Behnamfar N, Rafiemanesh H, Behzadmehr R. Global Prevalence of Depression among Heart Failure Patients: A Systematic Review and Meta-Analysis. *Curr Probl Cardiol*. 2022 Jun;47(6):100848. doi: 10.1016/j.cpcardiol.2021.100848.
4. Centers for Disease Control and Prevention. Depression. National Center for Health Statistics. Available from: <https://www.cdc.gov/nchs/fastats/depression.htm>. Accessed April 10, 2025.
5. Chand SP, Arif H. Depression. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK430847/>.
6. Chen C, Beaunoyer E, Guittion MJ, Wang J. Physical Activity as a Clinical Tool against Depression: Opportunities and Challenges. *J Integr Neurosci*. 2022 Sep 30;21(5):132. doi: 10.31083/j.jin2105132.
7. Okorare O, Ubokudum D, Jumbo U, Gbgbaje O, Ogunleye O, Ather K. Recent Trends in Heart Failure and Concomitant Depression: A Retrospective Study. *Curr Probl Cardiol*. 2024 Jan;49(1 Pt C):102122. doi: 10.1016/j.cpcardiol.2023.102122.
8. Pressler SJ, Jung M, Giordani B, Oommen S, Berkooz M, Bidwell JT, Fauer A, Ronis DL. Evaluating Depressive Symptoms, BDNF Val66Met, and APOE-ε4 as Moderators of Response to Computerized Cognitive Training in Heart Failure. *Heart Lung*. 2023 May-Jun;59:146-156. doi: 10.1016/j.hrtlng.2023.02.002.
9. Tromp J, Paniagua SMA, Lau ES, Allen NB, Blaha MJ, Cushman M, Desai AS, Deswal A, Erqou S, Finegold JA, Gansevoort RT, Guzman NJ, Ho JE, Khera A, Lam CSP, Lloyd-Jones DM, Psaty BM, Vasan RS, Yancy CW, Shah SJ. Age Dependent Associations of Risk Factors with Heart Failure: Pooled Population Based Cohort Study. *BMJ*. 2021 Mar 23;372:n461. doi: 10.1136/bmj.n461.
10. Näslund-Koch C, Vedel-Krogh S, Bojesen SE, Skov L. Traditional and Non-traditional Cardiovascular Risk Factors and Cardiovascular Disease in Women with Psoriasis. *Acta Derm Venereol*. 2022 Oct 11;102:adv00789. doi: 10.2340/actadv.v102.2244.
11. Kasireddy TR, Yukselen Z, Muthyala A, Kaur M, Goyal A, Bhandari S, Pradhan N, Subramaniam AV, Khullar V, Desai R. Association of Psychosocial Risk Factors and Outcomes in Heart Failure: Does COVID-19 Affect Outcomes? *Curr Probl Cardiol*. 2023 Oct;48(10):101795. doi: 10.1016/j.cpcardiol.2023.101795.
12. Gale SE, Mardis A, Plazak ME, Kukin A, Reed BN.

- Management of Noncardiovascular Comorbidities in Patients with Heart Failure with Reduced Ejection Fraction. *Pharmacotherapy*. 2021 Jun;41(6):537-545. doi: 10.1002/phar.2528.
13. von Haehling S, Arzt M, Doehner W, Edelmann F, Evertz R, Ebner N, Garfias Macedo T, Grabs V, Halle M, Herrmann-Lingen C, Hoendermis ES, Jankowska EA, Jansa P, Javaheri S, Kielstein JT, Kotecha D, Krüger T, Lainscak M, Leschke M, Masip J, Müller-Werdan U, Pieske B, Poole-Wilson P, Prondzinsky R, Scherer M, Störk S, Wachter R, Anker SD. Improving Exercise Capacity and Quality of Life Using Non-invasive Heart Failure Treatments: Evidence from Clinical Trials. *Eur J Heart Fail*. 2021 Jan;23(1):92-113. doi: 10.1002/ehjhf.1838.
14. Sbolli M, Fiuzat M, Cani D, O'Connor CM. Depression and Heart Failure: The Lonely Comorbidity. *Eur J Heart Fail*. 2020 Nov;22(11):2007-2017. doi: 10.1002/ehjhf.1865.
15. Ishak WW, Edwards G, Herrera N, Lin P, Kasckow J, Francis A, Balayan K. Depression in Heart Failure: A Systematic Review. *Innov Clin Neurosci*. 2020 Apr-Jun;17(4-6):27-38.
16. Bucciarelli V, Caterino AL, Bianco F, Capuano A, Salvatore M, Di Palma A, Di Tommaso MR, Viggiano A, Iovino P, Quagliariello V, Marsico S, Bimonte S, Cascella M. Depression and cardiovascular disease: The deep blue sea of women's hearts. *Trends Cardiovasc Med*. 2020 Apr;30(3):170-176. doi: 10.1016/j.tcm.2019.05.001.
17. Goyal P, Zainul O, Marshall D, Kitzman DW. Geriatric Domains in Patients with Heart Failure with Preserved Ejection Fraction. *Cardiol Clin*. 2022 Nov;40(4):517-532. doi: 10.1016/j.ccl.2022.06.006.
18. Basile C, Parlati ALM, Paolillo S, Iacoviello M, D'Andrea A, Trimarco B, Bossone E, De Luca G, Gargiulo P, Sarullo FM, Cice G, Agostoni P, Cleland JG, Piepoli MF. Depression in Heart Failure with Reduced Ejection Fraction, an Undervalued Comorbidity: An Up-To-Date Review. *Medicina (Kaunas)*. 2023 May 15;59(5):948. doi: 10.3390/medicina59050948.
19. Thomas SA, Chapa D, Friedmann E, Durden C, Ross A, Lee HJ, Jones K, Harris M, Mavromatis K. Depression in Patients with Heart Failure: Prevalence, Pathophysiological Mechanisms, and Treatment. *Crit Care Nurse*. 2008 Apr;28(2):40-55.
20. Varghese TP, Kumar AV, Varghese NM, Chand S. Depression Related Pathophysiological Mechanisms Relevant in Heart Disease: Insights into the Mechanism Based on Pharmacological Treatments. *Curr Cardiol Rev*. 2020;16(2):125-131. doi: 10.2174/1573403X15666191127104520.
21. Arora RC, Meltzer HY. Increased serotonin 2 (5-HT₂) receptor binding as measured by 3H-lysergic acid diethylamide (3H-LSD) in the blood platelets of depressed patients. *Life Sci*. 1989;44(11):725-734. doi: 10.1016/0024-3205(89)90384-6.
22. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and diagnosis. *Cardiovasc Psychiatry Neurol*. 2013;2013:695925. doi: 10.1155/2013/695925.
23. Ramos-Martínez IE, Rodríguez MC, Cerbón M, Camacho-Arroyo I, González-Arenas A, Morales-Montor J. Role of the Cholinergic Anti-Inflammatory Reflex in Central Nervous System Diseases. *Int J Mol Sci*. 2021 Dec 14;22(24):13427. doi: 10.3390/ijms222413427.
24. Shear FE. Depression in patients with heart failure: A review article. *Int J Med Res Health Sci*. 2020;9(9):31-9.
25. Kemp AH, Quintana DS, Gray MA, Felmingham KL, Brown K, Gatt JM. Impact of depression and antidepressant treatment on heart rate variability: a review and meta-analysis. *Biol Psychiatry*. 2010 Jun 1;67(11):1067-1074. doi: 10.1016/j.biopsych.2009.12.012.
26. Whooley MA, de Jonge P, Vittinghoff E, Otte C, Moos R, Carney RM, Ali S, Dowray S, Na B, Seeman TE. Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease. *JAMA*. 2008 Nov 26;300(20):2379-2388. doi: 10.1001/jama.2008.711.
27. Wu JR, Lennie TA, Dekker RL, Biddle MJ, Moser DK. Medication adherence, depressive symptoms, and cardiac event-free survival in patients with heart failure. *J Card Fail*. 2013 May;19(5):317-324. doi: 10.1016/j.cardfail.2013.03.010.
28. Bozkurt B, Ahmad T, Alexander KM, Bhatt DL, Bretherton K, Butler J, Drazner MH, Fonarow GC, Givertz MM, Hernandez AF, Jessup M, Kirklin JK, Maddox TM, Mann DL, Piña IL, Rosano GMC, Teerlink JR, Yancy CW. Heart Failure Epidemiology and Outcomes Statistics: A Report of the Heart Failure Society of America. *J Card Fail*. 2023 Oct;29(10):1412-1451. doi: 10.1016/j.cardfail.2023.07.006.
29. Hasin DS, Sarvet AL, Meyers JL, Saha TD, Ruan WJ, Stohl M, Grant BF. Epidemiology of Adult DSM-5 Major Depressive Disorder and Its Specifiers in the United States. *JAMA Psychiatry*. 2018 Apr 1;75(4):336-346. doi: 10.1001/jamapsychiatry.2017.4602.
30. Cao L, Sheng C, Luo G, Ou J. Depression as a Risk Factor for Developing Heart Failure: A Meta-Analysis of Prospective Cohort Studies. *J Cardiovasc Nurs*. 2022 Mar-Apr 1;37(2):112-121. doi: 10.1097/JCN.0000000000000760.
31. Krittanawong C, Maitra NS, Qadeer YK, Wang Z, Fogg S, Storch EA, Celano CM, Huffman JC, Jha M, Charney DS, Lavie CJ. Association of Depression and Cardiovascular Disease. *Am J Med*. 2023 Sep;136(9):881-895. doi: 10.1016/j.amjmed.2023.04.036.
32. Garfield LD, Scherrer JF, Hauptman PJ, Freedland KE, Buchholz KK, Boden JM, Balasubramanian S, Lawler EV, Lustman PJ. Association of anxiety disorders and depression with incident heart failure. *Psychosom Med*. 2014 Feb-Mar;76(2):128-136. doi: 10.1097/PSY.0000000000000027.

33. Zahid I, Baig MA, Ahmed Gilani J, Waseem N, Ather S, Farooq AS, Ghouri A, Siddiqui SN, Kumar R, Sahil, Suman, Kumar R, Kumar R, Mulla AA, Siddiqi R, Fatima K. Frequency and predictors of depression in congestive heart failure. *Indian Heart J.* 2018 Dec;70 Suppl 3:S199-S203. doi: 10.1016/j.ihj.2018.10.410.
34. Mulugeta H, Sinclair PM, Wilson A. Prevalence of depression and its association with health-related quality of life in people with heart failure in low- and middle-income countries: A systematic review and meta-analysis. *PLoS One.* 2023 Mar 23;18(3):e0283146. doi: 10.1371/journal.pone.0283146.
35. Jiang W, Alexander J, Christopher E, Kuchibhatla M, Gaulden LH, Cuffe MS, Blazing MA, Davenport C, Califf RM, Krishnan RKR, O'Connor CM. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. *Arch Intern Med.* 2001 Aug 13-27;161(15):1849-1856. doi: 10.1001/archinte.161.15.1849.
36. Lee KS, Park DI, Lee J, Oh O, Kim N, Nam G. Relationship between comorbidity and health outcomes in patients with heart failure: a systematic review and meta-analysis. *BMC Cardiovasc Disord.* 2023 Oct 10;23(1):498. doi: 10.1186/s12872-023-03527-x.
37. Redwine LS, Wilson K, Pung MA, Chinh K, Rutledge T, Mills PJ, Smith B. A Randomized Study Examining the Effects of Mild-to-Moderate Group Exercises on Cardiovascular, Physical, and Psychological Well-being in Patients With Heart Failure. *J Cardiopulm Rehabil Prev.* 2019 Nov;39(6):403-408. doi: 10.1097/HCR.0000000000000430.
38. Blumenthal JA, Babyak MA, O'Connor C, Keteyian S, Landzberg J, Howlett J, Kraus WE, Whellan DJ, Ellis SJ, Gottlieb SS, Forman DE, Saval MA, Christopher EJ, Gaulden LH, Koch GG, Pina IL. Effects of exercise training on depressive symptoms in patients with chronic heart failure: the HF-ACTION randomized trial. *JAMA.* 2012 Aug 1;308(5):465-474. doi: 10.1001/jama.2012.8720.
39. Wick LL. Depression and Heart Failure: Assessment, Treatment, and Interventions to Improve Self-Care Behaviors. *Crit Care Nurs Clin North Am.* 2022 Jun;34(2):157-164. doi: 10.1016/j.cnc.2022.02.005.
40. Poletti V, Pagnini F, Banfi P, Volpato E. The Role of Depression on Treatment Adherence in Patients with Heart Failure—a Systematic Review of the Literature. *Curr Cardiol Rep.* 2022 Dec;24(12):1995-2008. doi: 10.1007/s11886-022-01815-0.
41. Johansson P, Jaarsma T, Andersson G, Lundgren J. The impact of internet-based cognitive behavioral therapy and depressive symptoms on self-care behavior in patients with heart failure: A secondary analysis of a randomized controlled trial. *Int J Nurs Stud.* 2021 Apr;116:103454. doi: 10.1016/j.ijnurstu.2019.103454.
42. Sherwood A, Blumenthal JA, Trivedi R, Johnson KS, O'Connor CM, Adams KF Jr, Dupree CS, Waugh RA, Bensimhon DR, Gaulden L, Christenson RH, Koch GG, Hinderliter AL. Relationship of depression to death or hospitalization in patients with heart failure. *Arch Intern Med.* 2007 Feb 26;167(4):367-373. doi: 10.1001/archinte.167.4.367.
43. Peng Y, Fang J, Huang W, Qin S. Efficacy of Cognitive Behavioral Therapy for Heart Failure. *Int Heart J.* 2019 May 30;60(3):665-670. doi: 10.1536/ihj.18-408.
44. Ying H, Zhang X, He T, Feng Q, Wang R, Yang L, Duan J. A bibliometric analysis of research on heart failure comorbid with depression from 2002 to 2021. *Heliyon.* 2023 Jan 16;9(2):e13054. doi: 10.1016/j.heliyon.2023.e13054.
45. Zambrano J, Celano CM, Januzzi JL, Massey CN, Chung WJ, Millstein RA, Huffman JC. Psychiatric and Psychological Interventions for Depression in Patients With Heart Disease: A Scoping Review. *J Am Heart Assoc.* 2020 Nov 17;9(22):e018686. doi: 10.1161/JAHA.120.018686.



This is an open access article distributed under the terms of [Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License](https://creativecommons.org/licenses/by-nc-nd/4.0/).