



## Depressive Symptoms in Heart Failure: Pathophysiology and Diagnosis

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### ABSTRACT

Depression commonly affects individuals with heart failure and is associated with higher mortality rates, increased disability, healthcare costs, and reduced quality of life. Heart failure patients are more likely to experience depression. This study was aimed to describe pathophysiology and treatment of depression in heart failure patients. Both physiological and behavioral variables may influence the relationship between depression and the development and progression of heart failure, as well as increased rates of mortality. Because of the similarities between the symptoms of cardiac and mental illnesses, it may be difficult to make an appropriate diagnosis of depressive disorders in individuals who are suffering from heart failure. Further research is urgently needed to improve the diagnosis of these disorders and develop therapies that benefit patients with heart failure.

### 1. Introduction

Heart failure is a chronic decline in the functioning of the heart, marked by symptoms such as difficulty breathing, swelling, exhaustion, impaired overall well-being, and a diminished quality of life. More than 5 million people in US experience heart failure, with an annual occurrence of approximately 660,000 cases each year.<sup>1</sup> Heart failure is characterized by frequent hospitalizations and substantial healthcare expenses. According to the American Heart Association's Heart Disease and Strokes Statistics, the projected prevalence of heart disease and strokes in 2030 will grow by 3 million individuals.<sup>2,3</sup> Despite medical interventions, nearly 50% of individuals diagnosed with heart failure succumb within five years, indicating a substantial mortality rate. Psychological distress, encompassing conditions like despair, sorrow, dysphoria, and other types of psychological reactivity, has a connection to

the overall life satisfaction of individuals with heart failure.<sup>3,4</sup> Individuals suffering from chronic heart failure are at a higher risk of experiencing depression. This study was aimed to describe pathophysiology and treatment of depression in heart failure patients.

#### The pathophysiology of cardiac insufficiency

There are multiple interconnected elements in the pathophysiology of the connection between heart failure (HF) and depression. The concomitant elements include the initiation of an inflammatory cascade, dysregulation of neurohormones, the occurrence of arrhythmias, and the manifestation of behavioral impacts. In both depression and heart failure (HF), the body is under a lot of stress for a long time. This stress causes inflammatory markers like C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) to rise. An analysis of data from the Cardiovascular Health Study showed a link between

depression and elevated levels of inflammatory and fibrotic markers.<sup>5,6</sup>

The increased activation of neurohormones, along with the subsequent increase in autonomic activity, could worsen the dysfunction of the left ventricle. Activation of the sympathetic nervous system and the hypothalamic-adrenal-pituitary axis both lead to vasoconstriction and volume expansion. While this combination may have benefits in situations with low output, it also raises afterload and reduces cardiac output, potentially triggering the activation of the renin-angiotensin-aldosterone pathway and exacerbating heart disease. Initially, higher levels of inflammatory markers may be a healthy response to the stressors of the disease, as they help cardiac myocytes get bigger and protect them from apoptosis.<sup>6,7</sup>

However, if left unresolved, these markers can exacerbate the situation by triggering ventricular remodeling, which further impairs the contractility of the left ventricle. Both cardiac failure and depression are associated with decreased heart rate variability. The theorized cause is an imbalance in the autonomic nervous system between the sympathetic and parasympathetic branches. The sympathetic and parasympathetic systems control the functioning of the heart and blood vessels. The sympathetic nervous system increases heart rate and causes blood vessels to narrow, while the parasympathetic nervous system decreases heart rate and causes blood vessels to widen.<sup>8</sup>

Decreased heart rate variability indicates a decrease in parasympathetic activity due to excessive sympathetic stimulation. This unopposed sympathetic tone can provoke ventricular arrhythmias. Arrhythmias account for 25% to 50% of deaths caused by heart failure, and individuals with depression exhibit a higher incidence of arrhythmias. Endothelial function may also be of paramount importance. Endothelial function plays a crucial role in maintaining heart health by ensuring proper blood flow to the heart and other organs while also minimizing stress on the heart. Endothelial dysfunction is associated with a higher likelihood of HF-related events and overall mortality in individuals

diagnosed with heart failure. People who have heart failure and depressive symptoms are more likely to have a lower ratio of L-arginine to asymmetric-dimethylarginine (ADMA). This means that less nitric oxide is available and the endothelium isn't working properly. Individuals suffering from depression may exhibit a decrease in the adoption of health-promoting behaviors that can lower the likelihood of experiencing cardiovascular events in the future. These behaviors include engaging in physical activity, making dietary adjustments, quitting smoking, managing stress, and seeking treatment for substance abuse. By actively participating in these behaviors, individuals with depression can potentially alleviate the adverse cardiovascular health consequences associated with their condition. Empirical evidence has shown that engaging in physical activity can reduce symptoms of depression and enhance cardiovascular well-being.<sup>8,9</sup>

### **Diagnosing depression in individuals with heart failure**

Accurately diagnosing psychiatric conditions in patients with heart failure might present challenges due to the substantial similarity in symptoms exhibited by heart failure and serious depression. Physicians should do a comprehensive investigation of patients with heart failure to see if they meet all the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) for severe depression or anxiety disorder, considering the challenges associated with this diagnosis. The American Heart Association advises conducting a two-step depression screening for all individuals with heart disease. This screening process involves first administering the two-item Patient Health Questionnaire (PHQ-2) and then using the nine-item PHQ-9 for patients who receive a positive result on the initial test. The two-step approach demonstrates a low sensitivity rate of 52% but a high specificity rate of 91%, suggesting that it is an effective screening tool. Nevertheless, positive screenings necessitate a subsequent, comprehensive evaluation to validate the diagnosis. The PHQ-9 assesses depression comprehensively by examining each of the nine domains that characterize illness, with scores ranging

from 0 to 27. Participants rate each item on a scale of 0 to 3. When used as a screening tool in primary care settings, the PHQ-9 scores greater than 10 showed 88 percent sensitivity and 88 percent specificity for identifying major depression.<sup>9-11</sup>

Treating both heart failure and depression concurrently psychotherapy and medication treatments are both effective in treating depression and anxiety disorders in individuals with HF. Empirical psychotherapy, such as cognitive behavioral therapy (CBT), has demonstrated its superiority over conventional treatment in diminishing the intensity of depressive symptoms in patients with heart failure and depression. SSRIs are considered efficacious and secure in pharmacological therapy. In order to accurately assess the effect, it is necessary for a patient to adhere to a therapeutic dosage for a duration of 4 to 6 weeks.<sup>12</sup> The majority of adverse effects diminish after a period of 10 to 14 days after initiating the medication. The common side effects of selective serotonin reuptake inhibitors (SSRIs) include low blood pressure (hypotension), high blood pressure (hypertension), and disturbances in electrolyte levels.

For those suffering from heart failure, the primary treatment for depression may involve the use of selective serotonin reuptake inhibitors (SSRIs) or nonpharmacological interventions such as cognitive-behavioral therapy (CBT) or exercise. Cognitive behavioral therapy (CBT) and physical exercise may be the preferred treatment options for patients with heart failure due to the lack of well-established effectiveness of selective serotonin reuptake inhibitors (SSRIs). SSRIs are the preferred choice over SNRIs when it is necessary, as they carry a decreased risk of hypertension and tachycardia. Avoid monoamine oxidase inhibitors due to their considerable drug-drug interactions with some cardiovascular medications and heightened risk of hypertension. To effectively address depression in people with heart failure, it is advisable to use a multidisciplinary approach. Cardiologists may closely interact with psychiatrists for the initial management of mild to severe depression. Internists should employ the collaborative care approach to assist individuals in managing depression, provided that it is accessible.<sup>13,14</sup>

## 2. Conclusion

Depression frequently occurs in individuals with various cardiac problems, and it increases their vulnerability to negative cardiovascular outcomes in the short and long term, as well as increased healthcare costs and a worse quality of life. Screening for depression in heart failure aids in determining the course of patient care to ensure effective medication. Patients with heart failure and depression require a comprehensive approach to treatment, which includes psychotherapy, medication, and exercise.

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