# **Review Article**

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# The Impact of Major Depressive Disorder on Heart Failure Patients: A Literature Review

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#### **Abstract**

Cardiovascular diseases continue to pose a great threat to human beings worldwide. They are known to cause significant morbidity and mortality not just in one place, but throughout the world. The worst part about cardiovascular diseases is that if they are detected at an earlier stage, there is a lot that could be done to manage and intervene, and thus, prevent their complications. However, as the patient's condition keeps on progressing, it might become very difficult for the physicians to work on it and reverse the damage already done. Among the various types of cardiovascular diseases that are prevalent in society today, heart failure is among the leading ones. Or, it could better be said that it is the end point of all other cardiovascular diseases that either do not respond to treatment or have progressed to a stage from which any sort of control or reversal of the symptoms might not be easy. Once heart failure is ensured, there is little that can be done to extend the lifeline of the patient or to improve their prognosis. However, with the recent advancements in the field of cardiology and technology, there is hope that exists for everyone. It is expected that with the better prognosis of newer drugs that are safer and more effective than the existing ones, people can easily enjoy the benefits of such drugs and be saved from the atrocities of cardiovascular diseases and their unwanted complications. However, this review deals with the psychological aspect of cardiovascular diseases. It is a well-established fact that with the existence of any disease in the human body, things tend to take a mental toll on the patient's sanity and mode of living. Everything, be it intentionally or unintentionally, gets connected to the presence of illness, and people more often than not tend to react negatively to it. Depression, or major depressive disorder is one of the most prevalent psychological disorders that is diagnosed in people with heart failure, as per different studies. This review will reflect upon such studies and explore the various factors that are linked to the prevalence and development of depression in heart failure patients.

Keywords: Heart Failure, Major Depressive Disorder, Depression Symptoms, Cardiovascular Disease, Poor Prognosis.

# 1. Introduction

In a very literal sense, heart failure is a very talked-about condition in the world because of its complications and poor prognosis in the majority of individuals. Heart failure is indeed a very complicated and complex condition. It arises when the heart becomes incapable of efficiently pumping an adequate amount of blood to fulfill the body's ever-demanding needs. Such a state of affairs transpires due to a variety of disorders that hinder the heart's ability to either fill or eject blood into the systemic circulation [1].

Once heart failure has ensued in a patient's body, there are usually various indicators that indicate its presence. Fatigue and dyspnea, two major clinical symptoms, signal the heart's struggle to keep pace with the body's demands. Reduced exercise tolerance becomes another chapter in this narrative, leaving patients with an ever-diminishing capacity for physical exertion. The story's climax, often marked by the ominous presence of fluid retention, manifests as both pulmonary and peripheral edema. This excess fluid serves as a stark reminder of the heart's inability to maintain its vital duties, casting a shadow over the patient's well-being [2].

Heart failure is among those cardiovascular diseases that exert a significant toll on global health, and continues to afflict millions of individuals, bearing witness to a distressingly high morbidity and mortality rate. Its prevalence is seen to be increasing over time, with an estimated 26 million people worldwide currently

OA J Dis Glob Health, 2024 Volume 2 | Issue 1 | 1

affected by its burdensome consequences. The ripple effect extends to the realm of healthcare economics, as it engenders a substantial surge in healthcare costs worldwide. In many countries of the world, access to healthcare and the facilities that enhance the experience of patients is not that readily available to all [3].

The causes and origins of heart failure are diverse, stemming from a multitude of underlying conditions and diseases. The causative factors behind this ailment profoundly influence the course of treatment, and similarly, the majority of therapeutic recommendations primarily address the manifestations of heart failure itself, irrespective of its root cause [4].

Left-sided heart failure, often referred to as congestive heart failure (CHF), occurs when the left ventricle of the heart is unable to pump blood efficiently to meet the body's needs. This can result from various factors such as coronary artery disease, high blood pressure, or damage to the heart muscle. As the left ventricle struggles to pump blood, fluid can accumulate in the lungs, leading to symptoms like shortness of breath, coughing, and fatigue. Left-sided heart failure can ultimately affect the right side of the heart as well if left untreated.

Conversely, right-sided heart failure occurs when the right ventricle is unable to effectively pump blood to the lungs for oxygenation. It often develops as a consequence of left-sided heart failure, but it can also be caused by lung disease, pulmonary hypertension, or a condition known as right ventricular myocardial infarction. The result is that blood backs up into the body's veins, leading to symptoms such as swelling in the legs and ankles, abdominal discomfort due to fluid buildup, and liver congestion.

Both types of heart failure can coexist, and when they do, it's known as congestive heart failure (CHF) [5, 6].

Defining these categories involves establishing thresholds for ejection fraction (EF). HFrEF, for instance, is generally delineated by an EF of less than 40%. On the other hand, HFpEF is characterized by an EF exceeding 50%, marking a departure from the norm. Meanwhile, HFmrEF falls within the EF range of 40% to 50%, serving as a transitional zone within the spectrum of heart failure. These distinctions in EF and symptomatic presentation play a pivotal role in tailoring treatment strategies for patients grappling with this intricate ailment [7].

### 1.1. Clinical Presentation of Heart Failure

The clinical presentation of heart failure depends largely on the location of the primary dysfunction, whether it is on the left side, right side, or affecting both ventricles [8].

Left ventricular dysfunction, whether due to volume or pressure overload, results in elevated pulmonary pressure, a condition known as backward failure. This elevation in pulmonary capillary wedge pressure (PCWP) leads to pulmonary congestion, causing symptoms such as dyspnea and rapid breathing. This is attributed to the transudation of fluid into the lungs, which can be detected by the presence of pulmonary crackles [9].

Concurrently, as the forward flow of blood to the peripheral circulation diminishes, it triggers a cascade of complications. This includes renal dysfunction, inadequate peripheral perfusion, and impaired absorption of nutrients, eventually culminating in the development of cardiac cachexia.

Additionally, peripheral vasoconstriction leads to acrocyanosis or the bluish discoloration of extremities, an elevated resting and exercise heart rate, and a further deterioration of the cardiac and renal system. Anemia increases pulmonary pressure, and muscle fatigue affecting muscles including the diaphragm and peripheral muscles exacerbate the symptoms of dyspnea [10].

Heart overload, whether due to pressure or volume, causes the heart itself to enlarge. As a result, the cardiothoracic index increases, and the palpable cardiac pulsation shifts to the left. In situations where there are periodic increases in ventricular filling volume, a characteristic third or fourth heart sound may emerge, referred to as a proto-diastolic gallop. This phenomenon was once colloquially known as "the heart crying out for digitalis" during the era when digitalis was a common treatment for heart conditions [11].

In essence, heart failure is not confined solely to the heart itself; it intricately involves and affects nearly all organ systems. It can be aptly described as a systemic disease, manifesting as a syndrome with a wide-ranging clinical spectrum that encompasses various physiological systems throughout the body.

### 1.2. Outcomes and Prognosis of Heart Failure

As per the reports published in December 2015, the Centers for Disease Control and Prevention (CDC) revealed a profound analysis of heart failure-related mortality [12].

Their findings drew a complex picture of the evolving landscape of this medical condition. At the dawn of the new millennium in 2000, heart failure-related deaths were recorded at a rate of 103.1 per 100,000 population [13].

Over the course of a decade, these numbers exhibited a glimmer of hope, descending to 89.5 deaths per 100,000 by the year 2009. However, the optimism was short-lived as the tide shifted once again, witnessing an increase to 96.9 deaths per 100,000 by 2014 [14].

This fluctuating trend bore a notable correlation with a transformative shift in the underlying causes of heart failure-related deaths. Where once coronary heart disease stood as the predominant culprit, there emerged a new cast of characters—metabolic diseases and other non-cardiac factors. This troupe included obesity, diabetes, malignancies, chronic pulmonary diseases, and renal disease. These conditions, each with its own complex narrative, were now playing a more prominent role in the tale of heart failure mortality.

Beyond the statistical landscape, the CDC also sheds light on the somber journey that patients with heart failure must endure. The mortality rate following a hospitalization for heart failure was a sobering statistic to behold. At the 30-day mark, it stood at an estimated 10%, signaling the immediate challenges faced by these patients. The journey extended to the one-year mark, where the mortality rate rose to a somber 22%, casting a shadow over the longer-term prospects for those affected. Tragically, at the five-year milestone, the figure reached a disheartening 42%, painting a grim picture of the challenges faced by these individuals and their healthcare providers [15].

Yet, within this narrative of struggle, there were those who faced even greater odds. For patients classified under NYHA class IV, the final stage of heart failure known as stage D, the battle became even more daunting. Their mortality rate could soar beyond 50%, underscoring the immense challenges and complexities inherent to this advanced stage of heart failure [16].

This is indeed an alarming picture painted in the context of heart failure, for it signifies that once a patient has been diagnosed with heart failure, their condition only keeps on worsening if no further measures are taken to control it.

# 2. Understanding the Association between Cardiovascular Diseases and Psychological Illnesses

As stated earlier, there is always a strong link between the presence of an existing or ongoing illness in the body of an individual and the mental toll that it takes on the minds of these affected patients. It is quite an expected reaction as well, for people are likely to spend their time wondering about what could possibly go wrong with them or thinking about the unthinkable too, that is, their death [17].

Mental health issues are quite common, affecting about one in every eight people in 2019, according to the World Health Organization. Because they are so widespread, it is very likely that people might have both mental health problems and physical health problems at the same time. This is the reason why the whole spectrum of mental health and the underlying causes that give rise to them needs careful scientific study [18].

The connection between cardiovascular diseases and mental health is quite complicated, and it goes both ways. For instance, when someone is diagnosed with heart failure, it can be really stressful and make them feel down, increasing the chance of them developing a major depressive disorder. On the other hand, people with depression often have trouble sleeping, being active, and following healthy habits, which are all things that can raise the risk of heart problems [19].

There is solid evidence showing that the risks for mental and heart diseases go up together. However, there are some problems with the research that make it hard to draw strong conclusions. Some studies only look at people's health at one point in time, so it then becomes difficult to figure out if the heart or mental problem came first. Moreover, most of the research focuses on the relationship between heart health and depression or generalized anxiety, and not much attention has been given to other mental health conditions like psychosis or bipolar disorder.

In the context of cardiovascular diseases, there are several psychological conditions that could arise in a patient. A brief overview of all such conditions is given in the preceding section.

### 2.1. Generalized Anxiety Disorder (GAD)

Researchers have done a significant amount of work into extracting the complex relationship between anxiety and adverse cardiac events, aiming to unravel the potential implications for patients recovering from recent myocardial infarctions (MI) and grappling with reduced ejection fractions. In a study conducted by Iedinger and colleagues, anxiety emerged as a noteworthy and independent predictor of unfavorable cardiac outcomes in such patients. It seemed that the presence of anxiety could cast a shadow over the recovery process, raising concerns about the heart's ability to function optimally in the aftermath of an MI [20].

Additionally, a separate investigation uncovered intriguing insights into the physiological markers associated with anxiety. This study, which directly correlated anxiety with brain natriuretic peptide levels, suggested a potential link between anxiety and Congestive Heart Failure (CHF). This finding hinted at the possibility that anxiety might have far-reaching effects on cardiac health, reaching beyond the initial event of MI [21].

Epidemiological insights have consistently pointed to the potential benefits of addressing psychosocial factors, particularly anxiety, in the context of cardiovascular health. This body of evidence reinforces the connection between psychosocial risks and cardiovascular diseases, highlighting the significance of emotional well-being in heart-related outcomes [22].

One noteworthy milestone in this field was the Ischemic Heart Disease study, which marked an early success in interventions targeting psychosocial factors. This innovative study introduced a distinctive home-based stress reduction program aimed at improving the mental and emotional well-being of individuals at risk of cardiovascular issues. The results were compelling, demonstrating that this treatment approach was associated with a significant reduction in cardiac events [23].

# 2.2. Post-Traumatic Stress Disorder (PTSD)

In a very similar way, the presence of cardiovascular diseases is not immune to the far-reaching impacts of Post-Traumatic Stress Disorder (PTSD), as it weaves its presence into the lives of many patients.

PTSD symptoms and formal diagnoses are not uncommon within this patient population, shedding light on the intricate relationship between mental and cardiac well-being [24].

In a prospective cohort study, which followed the progress of 105 patients enrolled in cardiac rehabilitation, a significant 24% reported experiencing symptoms of PTSD. Similarly, a recent cohort study centered on veterans disclosed a PTSD prevalence rate of 6%. These findings emphasize that the influence of post-traumatic stress disorder is not confined to a specific subgroup but extends its reach across the diverse spectrum of cardiac patients [25].

Various studies have unveiled intriguing insights into the cardiovascular responses of individuals grappling with Post-Traumatic Stress Disorder (PTSD). These findings paint a picture of heightened heart rates during periods of rest and a decreased heart rate variability, characteristics that align with an uptick in sympathetic nervous system activity. One notable discovery stems from the observation that the baseline heart rate tends to be higher among veterans afflicted by PTSD in comparison to their counterparts without this condition. This finding suggests a sustained state of hyperstimulation within the autonomic nervous system, which governs our body's involuntary functions. However, it's crucial to consider an alternative perspective - that this elevated heart rate may be an artifact, a result of the research participants experiencing anxiety related to the impending psychophysiological assessments [26].

Nevertheless, another distinct study led by Gerardi et al. ventured into the heart health of Vietnam veterans. This particular research enlisted 32 individuals who had experienced combat-related PTSD and 26 Vietnam era veterans with no exposure to combat. The results of this study provided compelling evidence, as those afflicted by PTSD exhibited substantially higher heart rates, alongside elevated systolic and diastolic blood pressure levels, distinguishing them from their non-PTSD counterparts [27].

While the connection between PTSD and the development of cardiac diseases stands clear, the impact of PTSD on cardiac outcomes is more enigmatic. Among patients lacking preestablished CAD, PTSD has been linked to higher mortality rates. This association was held even among patients with implantable cardioverter-defibrillators, where elevated PTSD symptoms carried a more than threefold increase in the risk of mortality, a relationship that persisted even after accounting for relevant factors [28].

These findings emphasize the profound and multi-faceted nature of the connection between PTSD and cardiac health, warranting further exploration and understanding in the pursuit of holistic patient care.

### 2.3. Panic Disorder

Panic Disorder (PD), is yet another condition that finds its place among patients dealing with cardiac issues. Studies examining PD within the context of CAD have yielded a range of prevalence estimates, painting a somewhat uncertain picture. One review suggests a broad spectrum, with estimates fluctuating numbers of 10% to 50% among CAD patients [29].

However, a closer look reveals a more focused picture on this topic.

Panic disorder, a condition marked by intense episodes of fear and anxiety, is entangled with several cardiac abnormalities that warrant attention. When examining patients with panic disorder, a notable observation is their tendency to exhibit elevated resting heart rates, which is a clear indication of increased sympathetic activity. Furthermore, approximately 10% of individuals with panic disorder experience arrhythmias, adding another layer of

complexity to their cardiac health [30].

Interestingly, research has revealed that panic disorder is associated with specific structural changes in the heart. For instance, individuals with panic disorder tend to have increased left ventricular mass and diameter, suggesting a potential impact on the heart's functioning. Moreover, these patients exhibit poorer cardiovascular fitness, as evidenced by lower maximum oxygen consumption and reduced exercise tolerance [31].

Even in emergency department settings, where patients present with panic attacks, there are telltale signs of cardiac involvement, with increased levels of B-type natriuretic peptide being detected.

However, the relationship between panic disorder and cardiac conditions is not without controversy. Some studies have presented conflicting findings, particularly concerning an association with idiopathic cardiomyopathy [32].

As the research continues to unravel the interplay between Panic Disorder and cardiac diseases, it underscores the importance of addressing not only the physical aspects but also the psychological dimensions of heart health for a comprehensive approach to patient care.

# 3. Major Depressive Disorder in the Context of Heart Failure

For the purpose of convenience and staying relevant, the most prevalent and major of all psychological disorders, major depressive disorder has been discussed separately. It is also important to discuss the implications of depression in every aspect that might affect the people already suffering from heart failure amidst everything else.

Heart Failure (HF) and depression have always had an association, even before research was being done on this subject. An extensive meta-analysis, which meticulously reviewed 36 studies, uncovered a startling reality: clinically significant depressive symptoms affect a substantial 21.5% of individuals grappling with HF [33].

Furthermore, one-third of HF patients indicate elevated depressive symptoms when assessed through questionnaires, and an additional 19% meet the criteria for a depressive disorder upon undergoing a diagnostic interview. Typically, these disorders manifest as Major Depressive Disorder, although some studies have encompassed conditions like Dysthymia and Minor Depression within this spectrum [34].

It is also worth noting that these prevalence rates persist consistently across studies conducted in various settings, whether it be inpatient or outpatient care. Moreover, they stand at an alarmingly two to three times higher than the rates observed in the broader general population. This contrast underscores the profound impact of HF on the mental well-being of those living with the condition, highlighting the urgent need for comprehensive care that addresses not only the physical aspects but also the intricate emotional dimensions of HF patients'

health.

Depression casts a shadow over the landscape of cardiovascular health, leaving its mark on both the development and progression of Heart Failure (HF) and other heart-related conditions. Recent findings from a prospective observational study involving nearly 2 million healthy adults illuminate the intricate connection. In this study, depression, defined by either a billing diagnosis of depression or a prescription for an antidepressant, emerged as a harbinger of heart troubles [35].

It was prospectively associated with an 18% increased risk of developing HF over a subsequent seven-year period, even after meticulously accounting for other well-established cardiovascular risk factors.

The link between depression and HF does not end there. In another study, which focused on over 80,000 veterans free of pre-existing heart disease, a diagnosis of major depression was identified as a significant risk factor [36].

Major depression, as defined by one inpatient stay or two outpatient ICD-9 codes for major depressive disorder, was tied to a 21% heightened risk of developing HF over the course of the next 5.8 years. This relationship persisted even when accounting for various other medical factors, reinforcing the substantial impact of depression on heart health in HIV-negative veterans [37].

Yet, the story of depression's impact on HF is not limited to its role in the development of the condition. For those already diagnosed with HF, depression serves as a gloomy prognostic marker [38].

The presence of depression and anxiety can introduce significant challenges for individuals dealing with heart disease when it comes to following recommended health behaviors. These emotional states have a profound influence on a range of crucial lifestyle choices and treatment adherence.

For instance, patients with Heart Failure (HF) are already seen to be grappling with depression. Research has shown that they are less likely to maintain a healthy diet, engage in regular exercise, adhere to prescribed medications, or complete cardiac rehabilitation when compared to their non-depressed counterparts. This is quite evident from a layperson's perspective too, as people are more likely to engage in their misery rather than focus on what could be done to improve their condition. Similarly, individuals with depression often find it more difficult to effectively lower their cholesterol levels, further complicating their cardiovascular health management. The struggle extends to patients of every extent as they too are less likely to complete essential cardiac rehabilitation programs when depression is in the picture [39].

These disorders have been linked to smoking, physical inactivity, binge drinking, and heavy drinking. Notably, Post-Traumatic Stress Disorder (PTSD), a specific form of anxiety

disorder, has been associated with reduced physical activity and smoking, further complicating cardiovascular health [40]. Like depression, anxiety can hinder adherence to crucial health behaviors post-myocardial Infarction (MI), such as engaging in regular physical activity or quitting smoking [41].

Beyond behavioral aspects, physiological factors also come into play in the intricate relationship between psychiatric symptoms and adverse outcomes in Heart Failure (HF). Inflammation, for instance, is implicated in the pathogenesis of various HF subtypes and may contribute to ventricular remodeling, ultimately leading to increasing fibrosis and worsening cardiac function. Among patients already diagnosed with HF, elevated levels of interleukin-6 (IL-6), a marker of inflammation, have been linked to both short- and long-term cardiovascular mortality [42].

Furthermore, depression has been associated with elevated levels of inflammatory biomarkers, as indicated by recent metaanalyses. These biomarkers include C-reactive protein (CRP), interleukin-1 (IL-1), and IL-6. Other studies have identified connections between depression and inflammatory markers such as tumor necrosis factor-alpha (TNF-α) and monocyte chemoattractant protein-1 (MCP-1) [43, 44].

Even an analysis of data from the Cardiovascular Health Study revealed that depression was associated with higher levels of both inflammatory and fibrosis markers. Moreover, in individuals coping with both major depression and HF, depression was found to be linked to multiple inflammatory markers, further illustrating the complex interplay between mental health and cardiac health at the physiological level.

## 4. Conclusion

It is evident that there exists a strong link between the presence of cardiovascular diseases and psychological disorders. In the context of this study, heart failure (HF) and major depressive disorder were studied. Both disorders have a significant impact on worsening the prognosis of either one.

However, what is more concerning is the fact that patients were seen to have a negative impact linked with the presence of depression amidst their heart failure. This is indeed a fact that requires more exploration into it. Only if a person is able to successfully work their way out of either of these conditions, can they be able to live for a longer time.

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