



## Review

## Psychological sequelae of myocardial infarction

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## ABSTRACT

Patient with myocardial infarction (MI) are often affected by psychological disorders such as depression, anxiety, and post-traumatic stress disorder. Psychological disorders are disabling and have a negative influence on recovery, reduce the quality of life and causes high mortality rate in MI patients. Despite tremendous advancement in technologies, screening scales, and treatment strategies, psychological sequelae of MI are currently understudied, underestimated, underdiagnosed, and undertreated. Depression is highly prevalent in MI patients followed by anxiety and post-traumatic stress disorder. Pathophysiological factors involved in psychopathologies observed in patients with MI are sympathetic over-activity, hypothalamic–pituitary–adrenal axis dysfunction, and inflammation. Numerous preclinical and clinical studies evidenced a positive association between MI and psychopathologies with a common molecular pathophysiology. This review provides an update on diagnostic feature, prevalence, pathophysiology, clinical outcomes, and management strategies of psychopathologies associated with MI. Moreover, preclinical research findings on molecular mechanisms involved in post-MI psychopathologies and future therapeutic strategies have been outlined in the review.

## 1. Introduction

Myocardial Infarction and psychological disorders are the two major cause of death and disability worldwide [1,2]. MI is the irreversible injury of myocardial tissue due to prolonged ischemia and hypoxia, and manifested by the cardinal symptoms of varying degree of chest pain, sweating, lethargy, and difficulty in breathing [3]. Psychological disorders particularly depression, anxiety, and post-traumatic stress disorders (PTSD) are caused due to abnormality in the central nervous system (CNS) activity and manifested by behavioral or psychological symptoms that impact multiple life areas and create distress in person experiencing these symptoms [4,5]. According to Diagnostic and Statistical Manual of Mental Disorders (DSM-5), psychological disorders are defined as “a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behavior that reflects a dysfunction in the psychological, biological, or developmental process underlying mental functioning” [6,7]. The Global Burden of Disease study launched by the World Health Organization (WHO) predicts coronary heart disease (including MI) and depression will be two of the three most disabling disorders worldwide by 2030 [8].

Over the past 20 years, it has been found that depressed MI patients have a high risk of cardiac morbidity and mortality independent of traditional risk factors [9–11] and a poor prognosis of further adverse cardiac events [12,13]. A great body of literature found that the MI

survivors are more prone to psychological disorders [14–18]. However, the precise neurobiological mechanisms underlying this association have not been fully described [19]. With the advancement in therapeutic strategy, health-care professionals are becoming more aware of the prevalence and relevance of psychological sequelae of MI, but the complications of MI are understudied, underestimated, underdiagnosed, and undertreated [20–23]. The acute treatment strategy of MI has improved noticeably in the past few decades with the use of pharmacological interventions such as thrombolytic agents and thrombectomy, and by patient awareness. As a result, the mortality rate associated with acute MI has decreased, but on the other hand, psychological sequelae of MI have increased [24]. The post-MI psychopathology causes significant reduction in the quality of life; increase in stress and exhaustion, and often precipitate hospitalization of the patient. Unfortunately, there is no effective treatment strategy available, which can treat both MI and psychological sequelae of MI.

This review provides an update on the acute and long-term psychopathologies associated with MI, with an emphasis on the diagnostic feature, prevalence, pathophysiology, clinical outcomes, and management strategies of psychopathologies associated with MI. Moreover, we have also discussed the possible mechanisms (Fig. 2) involved in post-MI psychopathologies and therapeutic strategies.

All of the relevant databases (PubMed, Science Direct and Google Scholar) were searched for the terms “myocardial infarction”, “post-MI psychopathologies”, post-MI depression, post-MI anxiety and “post-MI

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**Table 1**  
Common post-MI psychopathologies.

Disorder	Prevalence in MI patients (%)	Clinical characteristics	Treatment options	References
Depression	31–45	<ul style="list-style-type: none"> <li>• Anhedonia</li> <li>• Loss of energy</li> <li>• Decreased concentration</li> <li>• Social isolation</li> <li>• Decreased appetite</li> <li>• Suicidal thoughts</li> <li>• Insomnia</li> <li>• Guilt</li> </ul>	<ul style="list-style-type: none"> <li>• Antidepressants (SSRIs)</li> <li>• Cognitive-behavioral therapy</li> <li>• Psychotherapy</li> <li>• Exercise programs</li> </ul>	[25,88,89,92]
Anxiety	24–37	<ul style="list-style-type: none"> <li>• Worry</li> <li>• Pain</li> <li>• Nervousness</li> <li>• Restlessness</li> <li>• Fatigue</li> <li>• Irritation</li> <li>• Decreased appetite</li> <li>• Insomnia</li> </ul>	<ul style="list-style-type: none"> <li>• Anti-anxiety (BDZs)</li> <li>• Supportive therapy</li> <li>• Cognitive-behavioral therapy</li> <li>• Internet-based cognitive behavior therapy</li> </ul>	[113,128–130]
PTSD	4–8.7	<ul style="list-style-type: none"> <li>• Negative mood</li> <li>• Unpleasant and uncontrollable re-experiences of MI</li> <li>• Nightmares and flashbacks of MI attack</li> <li>• Extreme negative emotions</li> <li>• Poor social interaction</li> <li>• Persistent avoidance of stimuli associated with the MI</li> </ul>	<ul style="list-style-type: none"> <li>• Cognitive-behavioral therapy</li> <li>• Social support</li> <li>• Emotionally Focused Therapy</li> </ul>	[20,158,160]

PTSD” from 1980 to 30th March 2017. Clinical studies including clinical trials, meta-analysis and systematic reviews, and preclinical studies were selected for review. Reference lists of selected studies and review articles were hand searched to identify additional studies that met selection criteria.

## 2. Depressive disorders

### 2.1. Diagnostic features

MI is a sudden and intense stressor condition, which causes feelings of extreme sadness and despair. Most of the patients with MI develop a prominent and persistent depressed mood and loss of interest in daily activities (anhedonia) [25,26] (Table 1). Depressed mood and anhedonia are the two core symptoms of post-MI depression along with commonly associated symptoms such as social withdrawal, loss of energy and decreased concentration [27,28]. Other symptoms such as feelings of worthlessness or excessive guilt and frequent thoughts of suicide are less occurring symptoms [28,29].

An increasing number of studies have found that there is a strong association between adverse cardiovascular outcomes and depression [30]. The biopsychosocial model proposed that biological, psychological, and social factors altogether responsible for etiology of depression [31,32]. There are accumulated evidence on high cardiac morbidity and mortality independent of traditional risk factors (high cholesterol, atherosclerotic plaque, etc.) [11,24,33] and poor prognosis of further cardiac events [34], in depressed MI patients. Researchers are focusing on the bidirectional association between depression and MI but the precise neurobiological mechanism underlying this association remains unclear [19].

In clinical settings, diagnosis of depression in MI patients is a very crucial step that requires sound clinical judgment and expertise. The use of validated questionnaires and different screening scales provide insights on the depressive symptoms. The health care practitioners assess MI-related depressive symptoms by using a variety of screening scales that includes the Montgomery and Asberg Depression Rating Scale (MADRS) [35], the Hamilton Depression Rating Scale (HDRS) [36], the Hospital Anxiety and Depression Scale (HADS) [37], the Beck Depression Inventory (BDI) [38], and the Mini International Neuropsychiatric Interview (M.I.N.I.) [39]. To harmonize the detection and management of post-MI depression in clinical settings, the American

Academy of Family Physicians (AAFP) publishes guidelines that includes evidence-based recommendations [40].

### 2.2. Prevalence

Depressive disorders are much more common in MI patients and increases the risk of an acute MI attack by 4.5-fold, compared with non-depressed patients [41–43]. In a recent nationwide population-based cohort study, Feng et al. reported a high prevalence of anxiety and depressive disorders in MI patients [44]. The comorbid depression with MI is an independent predictor of mortality and rehospitalizations in MI patients.

In a systematic review of data more than 14,000 patient-based structured interviews, the prevalence of major depressive disorder (MDD) was found to be 19.8% [45]. Based on the Beck Depression Inventory (BDI) score and Hospital Anxiety and Depression Scale (HADS), the score of MDD in MI patients was found to be 31.1% and 15.5% respectively [45]. In another meta-analysis, Wu and Cling found 2.1% cases of MI due to depression and depression also increases 31% risk of MI in depressed patients [46]. In a longitudinal study, the post-MI depressive symptoms were assessed by BDI score and the prevalence of depressive symptoms during hospitalization was reported as 26%, and after 4 and 12 months it was increased up to 38% and 37% respectively [14].

Suicidal thoughts or attempts of suicide are one of the diagnostic symptoms of MDD [6]. Previous studies have reported suicidal ideation in post-MI depressed patients [47–49]. In a study, 886 cardiovascular patients were screened for depression according to American Heart Association (AHA) and American Psychiatric Association (APA) guidelines in which 12% of patients were found to have suicidal ideation [50]. In this context, Larsen et al. performed a population-based case-control study in which a total of 19,857 patients were recorded with suicide and among 19,857 patients who committed suicide, 851 (4.3%) had a history of MI compared with 5537 controls (2.9%) [51]. The study reported that the depressive symptoms had increased the suicidal risk 64 times during the month following MI and suicidality risk was highest within the first month after discharge and associated with younger age group patients [51].

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