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### **RESEARCH ARTICLE**

#### **DEPRESSION IN POST MYOCARDIAL INFARCTION PATIENTS: A REVIEW**

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ARTICLE INFO	ABSTRACT
Article History: Received 25 <sup>th</sup> March, 2022 Received in revised form 19 <sup>th</sup> April, 2022 Accepted 14 <sup>th</sup> May, 2022 Published online 30 <sup>th</sup> June, 2022	Myocardial infraction is characterized by necrosis of heart cells because it doesn't get enough blood flow to heart due to blockage of blood clots. Depression is one of the common, frequent complications occur after an attack of myocardial infraction, its impact affects long term quality of life to a higher incidence of mortality of myocardial infraction patients. Thus, the present consensus statement aims to provide an overview of the prevalence, risk factors associated with depression followed by a myocardial infraction, impact of depression in a myocardial infraction patient,
Key words:	diagnosis and its treatment options. Overall research studies show that patients with myocardial infarction have higher risk of all-cause mortality, cardiac mortality and recurrence of cardiac events if they have post-myocardial infraction depression. The patients with history of either myocardial
Cardiovascular Disease, Myocardial Infraction, Depression, Post Myocardial Depression.	infarction or depression, complication that occurs during hospitalization, patients with infirm social relationships, biological imbalance and physical illness are the contributing risk factors of depression among myocardial infarction patients. Future studies are required to find out the exact relationship
*Corresponding Author: Krishnaprabha	between depression and myocardial infraction. Selective Serotonin Receptor Inhibitors are the better drug of choice among all anti-depressive drugs. Cardiac rehabilitation is also very effective. Early diagnosis and management of depression after myocardial infarction attack take the edge of future complications.

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# **INTRODUCTION**

Cardiovascular disease (CVD) is that the leading reason behind death worldwide, accounting for 31% of all deaths. A myocardial infarct (often mentioned as a heart attack) could be a life-threatening disorder caused by a shortage of blood supply to the heart muscle. The foremost manifestation of CHD, myocardial infarction (MI), is characterised by cardiac cell necrosis because of substantial and prolonged ischaemia. Not only do MIs cause physiological reactions like extreme pain, but they also cause psychological reactions like depression.<sup>1</sup> Depression (major depressive disorder) is also a widespread and significant medical condition that features a negative impact on your mental activities like how you're thinking that, behave and feel, and is luckily treatable. Depression makes unhappiness and/or a loss of interest in previously appreciated activities. It can cause a slew of mental and physical issues, moreover as a reduction in your capacity to figure at work and reception. After an acute MI most of the patients are likely to develop depressive symptoms. It's related to a rise risk of fatal and non fatal cardiac events, hospital readmission and cardiac mortality.

Prevalence of depression in Myocardial Infarction: Depression is frequent after a myocardial infarction (MI), and it can affect not just long-term quality of life but also cause an increase in mortality in MI patients.<sup>2</sup> Depression is one of the most common psychological reactions following a MI, according to accumulated research, and it may not only damage long-term quality of life but also cause higher mortality among MI patients.<sup>3</sup> In a meta-analysis of the effects of post-MI depression on cardiovascular outcomes, it was discovered that patients with MI have a 2.25 times higher risk of all-cause mortality, 2.71 times higher risk of cardiac mortality, and 1.59 times higher risk of cardiac events within 24 months if they have post-MI depression.<sup>4</sup> The prevalence of depression among patients with MI has varied significantly over the last two decades, ranging from 13.5 percent to 41.6 percent, which could be explained by differences in sociodemographic characteristics such as sex, race, and marital status, as well as the tool used to detect depression. Thombs et al completed the most recent quantitative systematic investigation on depression in MI patients, which was published in March 2004. They discovered that the combined prevalence of depression identified by structured interview and Beck Depression Inventory (BDI) with a cut-off value of 10 was 19.8% and 31.1% respectively.5

According to a random effects model, the prevalence of depression among patients with MI ranged from 9.17% to 65.88% in the meta-analysis study conducted by Limin Feng, MD et al and the pooled prevalence of depression among patients with MI was 28.70%. More psychological resources, including early assessment and effective treatment of depression, should be allocated to patients with MI, given the high pooled prevalence of depression found in this study and the link between depression and subsequent adverse health outcomes, such as impaired quality of life and increased risk of mortality among patients with MI.6 In March 2004, a systematic search was done by Brett D Thombs et.al to find original research publications published since 1980 that assessed depression using a standardised interview or validated questionnaire. Structured interviews revealed major depression in 19.8% of patients. The prevalence of significant depressive symptoms was 31.1%, 15.5%, and 7.3% using a Hospital Anxiety and Depression Scale (HADS). Depression is common among AMI survivors and can last for years. The prevalence of somatic symptoms varies depending on the technique of assessment, which is likely due to treatment.<sup>7</sup>

In a cross-sectional study to determine the prevalence of major depressive disorder and subsyndromal depression in patients who had their first heart attack, undiagnosed and untreated major depressive illness and subsyndromal symptoms were common in MI patients. When compared to the no depressive symptom group, these groups had more established coronary factors. This underscores the importance of routine depression screening in our community following MI.<sup>8</sup>

Risk factor for post MI depression: Risk factors that lead to depression after a myocardial infraction will help to prevent the impact of depression among individual. Temporary feeling of depression and sadness usually occur in initial days of post cardiac surgery. The exact relationship between depression after a myocardial infraction not really well established. However, determining whether risk variables are triggers or early indicators of a depressive episode that existed before to or at the time of the MI, are linked phenomena, or are even disease outcomes, is difficult. After the myocardial infraction the occurrence of low heart rate variability and disturbance in cardiac autonomic tone will lead to depression. Depression also associated with dysfunction in hypothalamic pituitary thyroid axis and hypothalamic pituitary adrenal axis.<sup>9</sup> The patient with already had a history of depression also had a chance to reoccurrence of depression after MI.<sup>10</sup> In past If patients having arrhythmia before myocardial infraction will complicated after myocardial infraction will lead to depression.<sup>11</sup> The patients who had past medical history of MI are more prone to develop depressive symptoms after a MI event.<sup>12</sup> From all the studies conducted, can be categories the risk factors contributed to depression in to three such as psychological factors, biological factors, environmental factors. Biological factors include, during hospital stay, the usage of benzodiazepine derivatives, complications occurred during the time of disease, the patient with already had a history of depression in past, social history of smoking, and hypertension are also contributing for the depression after MI.<sup>12,13</sup> Psychological factors are such that complication occurs during the hospital stay will affect the patient mind set it considered as the psychological parameter that trigger depression. Fear, hostility, type D personality, social inhibition these of negative moods are also the psychological risk factors<sup>14</sup>.

Environmental or social factors include patients who lives alone and those who don't get support from family, friends, society or an owner of emotionally imbalanced life and social isolation<sup>15</sup> were more likely to be depressed after myocardial infraction. The available studies provide this much risk factors involve in the development of depression. The exact reason behind this is not revealed yet.

Impact of depression on recovery from MI: A large percentage of individuals with heart disease experience depression at some point during their illness.<sup>16,17</sup> According to the most reasonable estimate, 15-20% of hospitalized cardiac patients fulfil diagnostic criteria for major depressive disorder, with a far greater number (ranging from 25% to 65%) reporting at least one depressive symptom.<sup>18,19</sup> In comparison, the annual prevalence of serious depression in the overall adult population is roughly 5%, rising to 10% when taking the entire lifespan into account.<sup>20,21</sup> Depression makes people more susceptible to acquire cardiovascular disease and has a higher mortality rate than the general population. Patients with MI who are also depressed have a worse prognosis than patients without depression. The severity of depression is related to the eventual risk of death and other cardiovascular problems.<sup>23</sup> Greater levels of depression and severe depression (major versus mild) are associated with higher morbidity and death owing to cardiac events, which are primarily caused by arrhythmia. Second, the severity of a MI has no or even a negative relationship with the development of depression. Only 10% of sad MI patients are diagnosed as such, hence depression after MI typically remains unnoticed. This is due to depression's unique profile, clinicians' predisposition to perceive depressive symptoms as a temporary and 'normal' reaction to a life-threatening event, and a lack of knowledge of risk factors related with post-MI depression development. In the first 18 months after a myocardial infarction, depression co-occurring with ischemic heart disease has a significant detrimental influence on cardiovascular prognosis, increasing cardiac morbidity and mortality four to fivefold. Rehospitalization and recovery are more challenging for depressed post-MI patients. New cardiac events, such as angina pectoris and reinfarction, are also more common in depressed MI patients than in non-depressed MI patients. This increased risk can remain for up to five years following a heart attack.<sup>24</sup> Following a myocardial infarction (MI), depression should be considered a significant risk factor for poor cardiac prognosis. For both mortality and morbidity, the extra risk was determined to be 2-2.5 fold on average. Patients suffering from a myocardial infarction frequently experience major depression (MI). MI was found to be substantially linked to an elevated risk of suicide.<sup>25</sup> Because depression remains strongly correlated with mortality after correcting for left ventricular ejection fraction(LVEF), post-MI depression is linked to a poor cardiac prognosis, regardless of the severity of cardiac illness. Given the link between LVEF and cardiac prognosis in MI patients, a detailed research of the potential link between LVEF and depression is essential. Both the rate of depressive illness (3-12 months post-MI) and the severity of depressed symptoms were associated with LVEF (during hospitalisation and 3 months post-MI). As a result, the lower the LVEF, the greater the risk of post-MI depression and the severity of depressive symptoms.<sup>26</sup> In individuals with acute coronary syndromes, social isolation and depression are frequently associated, which may be significant. LVEF, measured shortly after MI, is likewise linked to the development of depression in the year following the MI.

The researchers discovered that the lower the LVEF, the higher the risk of post-MI depression. Even after controlling for important depression correlates, this link remained significant.<sup>27</sup> Two mechanisms, a psychological and a biological channel, may be involved in the substantial relationship between left ventricular function and both the rate and severity of depression. Increased cytokine levels in CHF, including as interleukin-1, interleukin-6, and tumour necrosis factor-alpha, are thought to play a mediating role in the development of depression.<sup>28</sup> The degree of CAD is another major indicator of heart disease severity in the post-MI context.<sup>29</sup>

**Diagnosis of depression following MI:** In people with cardiovascular disease, depression is commonly misdiagnosed and mistreated. Only about one-half of cardiac patients with significant depression are identified with depression, and only about a quarter of those patients receive therapy for depression.<sup>30</sup> Major reason why depression remain underdiagnosed and untreated among patients with MI or any other cardiovascular disease are as follows:

- Depression may be mistakenly thought to be a typical reaction to cardiovascular disease by doctors and patients.
- Patients may be hesitant to report depression symptoms.
- Physicians may be reluctant to inquire about depression in their patients, and also may be reluctant to prescribe antidepressant drugs to patients with cardiovascular disease due to potential side effects.<sup>31</sup>

Understanding the risk factors for depression in patients with myocardial infarction is necessary when assessing for depression. Female gender, a history of depression, a family history of depression, a lack of social support, and a loss of functionality or a main life role are among these factors. A thorough interview with the patient and his or her significant other can provide this information.<sup>32</sup> Anxiety, sleep disturbances, exhaustion, pain syndromes, weight loss, irritable bowel symptoms, peptic ulcer symptoms, and premenstrual symptoms without any biological reason are all common somatic complaints among depressed people.<sup>33</sup>

**Screening Tools:** The majority of studies have screened for MDD or used a cut-off score on a self-report scale to 'diagnose' MDD. The Patient Health Questionnaire (PHQ), Beck Depression Inventory (BDI), Hospital Anxiety Depression Scale (HADS), Cardiac Depression Scale (CDS), and the Center for Epidemiologic Studies Depression Scale-10 are examples of self-report questionnaires (CES-D)<sup>34,35,36,37</sup>. There are also other scales to detect depression such as General Health Questionnaire, Geriatric Depression Inventory & Zung Self-Rating Depression Scale.<sup>38,39</sup>

**Treatment of depression:** After an acute myocardial infarction (MI), depression is a risk factor for mortality, as well as a sluggish recovery and a poor quality of life.<sup>40</sup> Despite this, only a small percentage of individuals who become depressed following a MI obtain treatment. It is unknown whether treating depression can lessen the risk of morbidity and mortality in people recovering from a MI. Antidepressant medication treatment in individuals who have just undergone an acute MI is yet unknown in terms of safety and efficacy. SADHART is researching the effects of antidepressant medication given soon after a heart attack.<sup>41</sup> According to the available evidence, Selective Serotonin Receptor Inhibitors are

safer than Tricyclic Antidepressants in people with heart disease. Increased heart rate, orthostatic hypotension, altered intracardiac conduction, and susceptibility to ventricular arrythmia are all unfavourable cardiovascular outcomes in people with heart disease while taking TCAs.<sup>42</sup> TCAs should therefore be avoided in patients with ventricular arrythmias, according to the experts.<sup>43</sup> In a study, Fluoxetine resulted in improved depression symptoms, especially in individuals who had moderate depression at the start, without affecting heart function as measured by electrocardiography and echocardiography.<sup>44</sup> In another study when Sertraline was used, no significant changes in heart rate, pressure, cardiac conduction, left ventricular ejection fraction, or ventricular ectopy were seen throughout sertraline administration.<sup>41</sup> In comparison to TCAs, these trials show that SSRIs are the preferred class of antidepressant drugs in individuals with post-MI depression. Even though antidepressant medication is frequently necessary to adequately treat post-MI depression and avoid recurrence, cardiac rehabilitation is an important element of post-MI care for all patients, depressed or not. Cardiac rehabilitation improves several areas of psychological health, including depressive symptoms. Cardiovascular rehabilitation has been shown to lessen depressed symptoms and depression prevalence by 50% to 70%.<sup>45</sup> Exercise training has been observed to reduce depressive symptoms and the prevalence of depression by 50 percent to 70 percent in a recent randomised experiment. Exercise training reduced depressed symptoms as effectively as antidepressant medicines in a recent randomised experiment.46

# CONCLUSION

Depression after MI is prevalent, underdiagnosed, and has a significant prognostic influence. Only 10% of people with MI are diagnosed as depressed. This will increase morbidity, mortality and will decrease the quality of life in patients. Because the largest prevalence of depression is noticed in hospitals and in the first six months after a heart attack, it should be diagnosed at an early stage. SSRIs appear to be the primary line of treatment for depression following MI. Tricyclic anti-depressants are also used but less efficacious than SSRIs. They are less effective than SSRIs. Cardiac rehabilitation was also proven to be beneficial.

### REFERENCES

- 1. Gidron Y., Gilutz H., Berger R., *et al.* 2002. Molecular and cellular interface between behavior and acute coronary syndromes. *Cardiovascular research.* 56:15–21.
- 2. Kala P, Hudakova N, Jurajda M, *et al.*, 2016. Depression and anxiety after acute myocardial infarction treated by primary PCI. *PLoS One.*,11(4)
- Bush DE., Ziegelstein RC., Tayback M. *et al.*, 2001. Even minimal symptoms of depression increase mortality risk after acute myocardial infarction. *Am J Cardiol.*, 88:337– 41.
- 4. Meijer A, Conradi HJ, Bos EH, *et al.* 2011. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis of 25 years of research. *Gen Hosp Psychiatry.*, 33:203–16.
- 5. Thombs BD, Bass EB, Ford DE, *et al.*, 2006. Prevalence of depression in survivors of acute myocardial infarction. *J Gen Intern Med*.21:30.

- Feng L, Li L, Liu W, *et al.* 2019. Prevalence of depression in myocardial infarction: A PRISMA-compliant metaanalysis. Medicine (Baltimore).98.
- Thombs, Brett D et al. 2006. Prevalence of depression in survivors of acute myocardial infarction. Journal of general internal medicine.21:30-8.
- 8. M Agarwal, JK Trivedi *et al.* 2011. Depression in Patients of Myocardial Infarction: A Cross-sectional Study in Northern India. *Journal of the associations of physicians of India*.59.
- Carney RM, Blumenthal JA, Freedland KE, Stein PK, Howells WB, Berkman LF, *et al.* 2005. Low heart rate variability and the effect of depression on post-myocardial infarction mortality. *Arch Intern Med.*,165(13):1486-91.
- 10. Jacqueline JMH, 2001. Strik Adriaan Honig, Michael Maes. Depression and myocardial infarction: relationship between heart and mind. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 25(4):879-892.
- 11. Musselman DL, Evans DL, Nemeroff CB. 1998. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Arch Gen Psychiatry*. 55(7):580-592.
- Richard Fielding. 1991. Depression and acute myocardial infarction: A review and reinterpretation. Social Science & Medicine. 32(9):1017-1027.
- Wells KB, Stewart A, Hays RD, Burnam MA, Rogers W, Daniels M, *et al.*, 1989. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. JAMA. 262(7):914-919.
- 14. Erla Svansdottir, Hrobjartur D. Karlsson, Thorarinn Gudnason, Daniel T. Olason, Hordur Thorgilsson, Unnur Sigtryggsdottir *et al.* 2011. Validity of Type D personality in Iceland: Association with disease severity and risk markers in cardiac patients. *Journal of behavioral medicine.* 35:155-66.
- 15. Pincus, Theodore. 2001. Psychosocial influences and mortality. Advances in mind-body medicine. 17: 24-7.
- Carney R. M. and Freedland. K. E. 2008. Depression in patients with coronary heart disease. *American Journal of Medicine*. 121: S20–S27.
- 17. Koszycki, D.S. Lafontaine, N. Frasure-Smith, R. Swenson, and F. Lespérance. 2004. An open-label trial of interpersonal psychotherapy in depressed patients with coronary disease. *Psychosomatics*. 45:319–324.
- Robert M. Carney PH.D., Kenneth E. Freedland PH.D., Yvette I. Sheline M.D., Edward S. Weiss M.D. 1997. Depression and coronary heart disease: a review for cardiologists. *Clinical Cardiology*. 20: 196–200.
- 19. Richard V. Milani and Carl J. Lavie. 2007. Impact of cardiac rehabilitation on depression and its associated mortality. *American Journal of Medicine*. 120: 799–806.
- 20. Friedewald, V. E. L. W. Arnold, R. M. Carney, A. S. Jaffe, D. S. Sheps, and W. C. Roberts. 2007. The editor's roundtable: major depression in patients with coronary heart disease. *American Journal of Cardiology*. 99: 519– 529.
- Frasure-Smith, N., Lesperance, F. and Talajic. M. 1995. Depression and 18-month prognosis after myocardial infarction. Circulation. 91: 999–1005.
- 22. Ceccarini, M., Manzoni, G. M., Castelnuovo. G. 2014. Assessing Depression in Cardiac Patients: What Measures Should Be Considered?. Depression Research and Treatment. 2014:17 pages.

- Johansson P., Lesman-Leegte I., Lundgren J., Hillege HL., Hoes A., Sanderman R., van Veldhuisen DJ., Jaarsma T. 2013. Time-course of depressive symptoms in patients with heart failure. *Journal of Psychosomatic Research*, 74:238-43.
- Strik JJ., Honig A., Maes M. 2001. Depression and myocardial infarction: relationship between heart and mind. *Prog Neuro psychopharmacol Biol Psychiatry.*, 25(4):879-92.
- 25. Havik OE., Maeland JG. 1990. Patterns of emotional reactions after a myocardial infarction. *J Psychosom Res.*, 34(3):271-85.
- Larsen KK. 2013. Depression following myocardial infarction--an overseen complication with prognostic importance. *Danish Medical Journal*. Aug;60(8):B4689.
- 27. Strik JJ, Denollet J, Lousberg R, Honig A. Comparing symptoms of depression and anxiety as predictors of cardiac events and increased health care consumption after myocardial infarction. Journal of American College of Cardiology. 2003 Nov 19;42(10):1801-7.
- 28. van Melle JP., de Jonge P., Ormel J., Crijns HJ., van Veldhuisen DJ., Honig A. *et al.*, 2005. Relationship between left ventricular dysfunction and depression following myocardial infarction: data from the MIND-IT. *European Heart Journal*. ;26(24):2650-6.
- 29. van Melle JP., de Jonge P., Spijkerman TA., Tijssen JG., Ormel J., van Veldhuisen DJ. *et al.*, 2004. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis. *Psychosomatic Medicine*. Nov-Dec;66(6):814-22.
- 30. Musselman DL., Evans DL., Nemeroff CB. 1998. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. *Arch Gen Psychiatry.*, 55:580–92.
- Carney RM., Freedland KE., Sheline YI., Weiss ES. 1997. Depression and coronary heart disease: a review for cardiologists. *Clin Cardiol.*, 20:196–200.
- 32. Thomas P. Guck, Ph.d., Michael G., Kavan, Ph.d., Gary N. Elsasser, Pharm. D and Eugene J. Barone, M.D. Assessment and Treatment of Depression Following 14 Myocardial Infarction. Am Fam Physician. 2001 Aug 15;64(4):641-648.
- Montano, C.B. 1994. Recognition and treatment of depression in a primary care setting. Journal of Clinical Psychiatry. 1994;12:18-34.
- Beck AT., Ward CH., Mendelson M., Mock J., Erbaugh J. 1961. An inventory for measuring depression. Arch Gen Psychiatry. 4:561-571.
- 35. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67:361-370.
- 36. Shi WY., Stewart AG., Hare DL. 2010. Major depression in cardiac patients is accurately assessed using the Cardiac Depression Scale. *Psychother Psychosom.*, ;79:391-392.
- 37. Andresen EM., Malmgren JA., Carter WB., Patrick DL. 1994. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *Am J Prev Med.*, 10:77-84.
- Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychol Med. 1979;91:139–45.
- Yesavage JA., Brink TL., Rose TL., Lum O., Huang V., Adey M. *et al.*,1982. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res.*, 17(1):37–49.

- Frasure-Smith N., Lesperance F., Talajic M. 1993. Depression following myocardial infarction: Impact on 6month survival. JAMA. 270: 1819-1825.
- 41. Shapiro PA., Lesperance F., Frasure-Smith N., *et al.*, 1999. An open-label preliminary trial of sertraline for treatment of major depression after acute myocardial infarction (the SADHAT Trial): Sertraline Anti-Depressant Heart Attack Trial. *Am Heart J.*,137:1100-1106.
- 42. Roose SP., Glassman AH. 1989. Cardiovacsular effects of tricyclic antidepressants in depressed patients with and without heart disease. *J Clin Psychiatry.*, 50;(suppl): 1-18.
- 43. Roose SP., Glassman AH., Bigger JT., Jr. 1993. The safety tricyclic antidepressants in cardiac patients: risk-benefit reconsidered. JAMA.269:2673-2675.
- 44. Strik JJ., Honig A., Lousberg R. *et al.*, 2000. Efficacy and safety of fluoxetine in the treatment of patients with major depression after first myocardial infarction: findings from a double-blind, placebo-controlled trial. *Psychosom Med.*, 62:783-789.
- 45. Milani RV., Lavie CJ. 1998. Prevalence and effects of cardiac rehabilitation on depression in the elderly with coronary heart disease. *Am J Cardiol.*, 81(10):1233-1236.
- 46. Blumenthal JA., Babyak MA., Moore KA. *et al.* 1999. Effects of exercise training on older patients with major depression. *Arch Intern Med.*,159(19):2349-2356.

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