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# DEPRESSION: AS A RISK FACTOR FOR CORONARY HEART DISEASE

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**Abstract:**

*We conducted a review to resolve whether there is relationship between depression and coronary heart disease or not. Depression is a mental health problem which is spread widely and most of physicians are well acquainted with this concept of depression. Diagnosis of depression disorder based on continuity of illness, etiology of illness and number of symptoms - all these discriminations should be reported during inspecting the link between depression and coronary heart disease. We review the mechanism of linking depression and coronary heart disease i.e. relationship between depression and inflammation, depression and autonomic dysfunction, CHD and autonomic dysfunction, depression and Sleep architecture disruption, depression and circadian rhythm disruption, CHD and circadian rhythm disruption, and depression and behavioural mechanism. There is bidirectional association between depression and coronary artery disease i.e. coronary artery disease can cause major depressive disorder and depression is risk factor for CAD and its complications. Major depression is a devastating comorbid disease that can make recovery difficult and increase risk of cardiac mortality and morbidity. We also go over the therapy options like Psychotherapy, Electroconvulsive therapy, Exercise etc. But there are some antidepressant medications also available for treating depression in patients associated with CAD. The antidepressant medications like SNRI e.g. mirtazapine, desvenlafaxine, venalafaxine etc. appears to be safe in individual with depression and concomitant CAD or unstable angina. However, some evidence suggests that SSRI like tricyclics, may increase risk cardiac events and death when taken for long time. New classes of antidepressants have dual reuptake inhibition for serotonin and nor-epinephrine. These medications are slightly more successful than SSRIs in treating depression*

***Keywords:*** *Coronary heart disease, Depression, CAD, SNRI, mirtazapine.*

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## INTRODUCTION:

Psychiatric depression is a precursor of major cardiac events. Approximately, 65% of patients report symptoms of depression along with myocardial infraction[1-3]. It has a great repercussion on health when co occurring with a chronic malady[4].

The pervasive of depression is 15-30% in patients with coronary heart disease[5] and it is roughly twofold high in women than men, chiefly affecting young women after consequences of acute myocardial infraction[6]. After an acute coronary syndrome (ACS), more than 17 million American adults are survived with 1.2 million new surviving cases are added per year[7]. Depressive manifestation have been reported more than two patients in five[8] and these symptoms of depression will remain long after discharge of patients[9]. Thus, considerably 7 million of Americans living with coronary heart disease are also distressed with clinically significant depression and half of a million new cases to this public health burden have been append by us annually. The comorbidity between depression and CHD is high and both causes occurrence of each other. Thus, the interrelation of depression and acute coronary syndrome is come up for study. For example, presence of depressive symptoms appears to be anticipating CHD recurrence and results in mortality[10,11]. Depression as a risk factor for coronary heart disease has been characterized from moderate depressive symptoms to clinical diagnosis of major depression. As per definition of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), depression is specified by depressed mood or anhedonia for about two weeks which was accompanied by functional ruination.[12] The exact mechanism of depression as risk factor for coronary heart disease is complicated and still incompletely understood[13.] The present paper summarizes aspects about linking of depression and coronary heart disease.

### What Is Depression?

Depression is a mental health problem which is spread widely and most of physicians are well acquainted with this concept of depression. It is usually difficult to analyze because there is not decisive laboratory test present till the date. The diagnosis of depression depends upon appraisal of severity and duration of symptoms. The universally accepted Symptom based criteria for diagnosis of depression and other psychiatric disorders are spotted in the Diagnostic and Statistical Manual of Mental Disorders. Categories of disease are started because some of dispute may enlighten depression-CHD association.

Depression as a psychiatric disorder: Diagnosis of depression disorder based on continuity of illness, etiology of illness and number of symptoms – all these discriminations should be reported during inspecting the link between depression and CHD. Impairment in five areas such as appetite or sleep that are remain for at least 2 weeks with addition of depressed mood or anhedonia during those 2 weeks are the chief characteristics of depression. In contrast, dysthymia is a condition that persisted for two years. Both dysthymia and major depressive disorder (MDD) are classified according to presence or absence of symptoms such as reactive mood, Polyphagia, Hypersomnia or leaden paralysis. The diagnosis of mood disorder describes disturbance in mood is directly connected with presence of medical condition known as depression. Hence, there must be proof that psychiatric symptoms are created by medical condition rather than a reaction to being ill. The example of this type of depressive disorder is the depression that develops from Parkinson's disease[14].

Depression authorizes the classification of less severe syndrome of depression having short duration of action (less than 2 weeks) that doesn't meet criteria of major depressive disorder. It encloses DSM-IV research categories such as minor depression and recurrent depressive disorder which is labelled as "Subthreshold" depression, a category that encloses syndromes of depression but fail to satisfy the criteria of major depressive disorders,[15] but it shows some impairment in social functioning[16]. Thus, assessment of depressive symptoms as well subthreshold depression levels should carried out carefully to determine if one or both are critical to ACS prognosis.

Depression as Self-Reported Distress Symptoms: In absence of trained interviewers for conduction of psychiatric diagnostic interview, reliance on self-report measures of depression for diagnostic classification has been common in studies of CHD patients. There are many measures, each having its own advantages, and some are available in modernize form. Designing of these self-report measures are used to identify depressive disorders in various population (such as primary care patients, or older adults, or Population based sample) and determine item consistency, split half reliability, and stability to varying, but generally satisfactory degrees17, 18.

**Mechanism Linking Depression and Coronary Heart Disease:**

There are many biological mechanisms have been suggested to explain relationship between the depression and coronary heart disease. Depression-CHD prognosis association comprises; inflammations, autonomic dysfunction, sleep architecture disruption, circadian rhythm disruption, behavioral mechanism etc.

1. Relationship of depression and inflammation: The chronic inflammation is risk factor which is responsible for increased risk of CHD associated with depression[19.] During depression, concentration of inflammatory molecules like C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-alpha), cytokines, soluble intercellular adhesion molecule 1 etc. are increased, which have direct impact on cardiovascular events[20-23]. Many studies demonstrate that elevated level of proinflammatory molecules increase a risk of cardiovascular event in depressed patients.

2. Relationship of depression and autonomic dysfunction: Autonomic dysfunction is described by disturbance in sympathetic and para sympathetic system which plays a key role in linking of depression to CHD.

The relation between activity of sympathetic nervous system and depression has long research history. Some studies suggest that during depression catecholamine levels has been increased but still there are some exceptions[24,25]. Veith and his colleagues explained that entry of nor-adrenaline into circulation is increase in depressed patients[26]. Increased heart rate, BP, CSF NE and plasma NE has been seen in severely depressed patients which was manifested by Gold et al[27].

3. Relationship of CHD and autonomic dysfunction: There are various evidences are available that shows that autonomic nervous system has key role in CHD recurrence. Experiment on animals suggests capacity of high level of cardiac vagal regulation to prevent sudden death after experimentally induced MI[28]. Alpha -2 receptor blockade by yohimbine reduced sympathetically-mediated effects like increase in platelet aggregation, it further indicates that sympathetic nervous system has major mole in atherosclerosis[29].

4. Relationship of depression and sleep architecture disruption: Depression and sleep architecture disruption are closely linked with each other. There is controversy in polysomnographic parameters of depression. In depressed patients, sleeping time is decrease and it leads to depressive episodes. Slow sleep wave in depressed patients is decreased which was evaluated from survey of 177 studies including details of 7151 patients[30-33]. In depressed patients, sleep cycle is reversed by use of antidepressant; it is possible by increasing total slow wave sleep and the slow wave sleep in first sleep cycle not in second cycle[34].

5. Relationship of depression and circadian rhythm disruption: Hormonal, psychological and physiological variables are regulated by endogenous circadian rhythm in acute coronary syndrome and depression[35]. Core temperature is defined as temperature of an organism. In evaluation of circadian rhythm, core temperature is good standard. In depressed patients, circadian abnormalities are measured by elevated body temperature[36-41]. Melatonin is derivative of serotonin and is an indicator of circadian rhythmicity. Concentration of melatonin is increased at night but negligible during the day. In 1979, a depression-related disturbance in melatonin circadian profile is present in form of decrease in nocturnal magnitude42-44.

6. Relationship of CHD and circadian rhythm disruption: Some evidences are available which suggest that majority of cardiovascular events shows circadian rhythmicity among peak incidence between 6 am and 2 pm[45,46]. Although, circadian dysfunction in depressed patients having general time for myocardial infarctions is 10 pm and 6 am[47.] Thus, circadian rhythm disruption in depressed patients helps to recognized increased risk of cardiovascular events.

7. Relationship of depression and behavioral mechanism: Effect of depression on patient's behaviors has major impact on ACS; such as constancy with prescribed medication[48,49] or to secondary prevention instruction after ACS[50]. Not only secondary prevention behaviors but also behaviors related to controlling ACS symptoms have impact on medical events in case of ACS. For example, delay in period from when patients have symptoms of chest pain to the period that they present for medical care is associated with worse Post-ACS prognosis[51.]

**Bidirectional Relationship of Depression and Cad:**

CAD can cause major depressive disorder: In study reports, a history of MI was linked to depressive symptoms while in the hospital. When contrasted to the 6.6 percent one-year prevalence of major

depressive disorder in a community sample, the findings of these studies with significant prevalence of depression in this cohort of CAD patients gain more importance[52].

Depression is risk factor for CAD and its complications: Patients with a history of dysphoria or depression, regardless of coronary artery risk factors, have 4.5 times the relative risk of developing an acute MI at follow up in the Baltimore Cohort of the Epidemiologic Catchments Area (ECA) Study[53]. Lesperance et al looked for depression in 222 patients who had been brought to the hospital for an acute MI. The depression was assessed in the patients by utilizing a tweaked version of the International Diagnostic Schedule (DIS). At the time of the initial MI hospitalisation, as well as one week, six months, and a year afterwards, depression ratings were completed. This research is regulated for the age of the patient and circulatory health. There are six, seven and eight deaths were reported at six months, six to twelve months and thirteen to eighteen months respectively (i.e.total 21 deaths) all of which were linked with depressive disorder.

Patients who had depression while in the hospital were also more likely to have had past depression and the state of being depressed after discharge[54].

Lauzon et al., tracked patients for a year in a multicenter experiment to measure the incidence and prognostic significance of depression after a heart attack. A nurse practitioner documented acute MI in recruited individuals within 2 to 3 days. The days after being admitted Patients had to finish their work. The Beck Depression Inventory (BDI) is a tool that can be used during their stay in the hospital and thereafter one year, six months, and thirty days post-MI. Patients who were depressed had an increased risk of cardiac problems, such as recurrent ischemia, infarction, or CHF. When they are admitted to the hospital for the first time or when they are discharged repeat readmission for angina MI, CHF, or arrhythmias (adjusted HR: 1.4, 95 percent confidence interval: 1.05–1.86) when compared to people who aren't depressed patients[55,56]. These studies add to the importance of the depression-coronary artery disease link by indicating that depression has an impact on CAD and its consequences.

**Treatment of Depression in Patients Associated with Coronary Artery Disease:**

This section discusses the relevance of treating depression in patients with coronary artery disease (CAD) and highlights many studies on pharmacological therapy of depression in CAD patients. For a variety of reasons, treating depression in people with CAD is crucial.

The CREATE (Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy) and ENRICHD studies found that psychotherapy, such as interpersonal psychotherapy and cognitive behavioural therapy, was ineffective in treating depression in CAD patients, emphasising the importance of antidepressants in this population. We looked at the Sequenced Treatment Alternatives to Relieve Depression (STAR* D) trial and offered antidepressant treatment methods. STAR*D is the largest study of its kind (4,041 participants) to evaluate antidepressant medication efficacy in patients with an average of three medical comorbidities and one psychological comorbidity. At eight weeks of treatment with selective serotonin reuptake inhibitor (SSRI) monotherapy, the study found that remission rates were around 47 percent[57]. Many cardiac patients are treated for depression, yet there is still concern about cardiotoxicity of antidepressants.

**Antidepressant medication:**

Antidepressant act on the serotonin, nor-adrenaline and dopamine neurotransmitters in the brain.

1. Selective serotonin reuptake inhibitor: SSRIs (selective serotonin reuptake inhibitors) block the transporter that transports serotonin back into the cell from the synapse. They have less or no anticholinergic and cardiac effects due to their differing mechanisms of action. As a result, they are the first line of treatment for patients with CHD.

SSRIs includes fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox), citalopram (Celexa) and escitalopram (Lexapro). Glassman et al[58] assessed the safety and efficacy of sertraline in major depressive disorder (MDD) treatment among patients who had previously been diagnosed with acute MI or an unstable angina in the well-known SAD HART trial. In a randomized, double-blind, placebo-controlled experiment, the researchers enrolled 369 individuals with MDD who had either a MI or unstable angina. After a two-week single-blind placebo run, patients were randomised to receive a flexible dose of sertraline (50– 200mg) or placebo for the next 24 weeks.

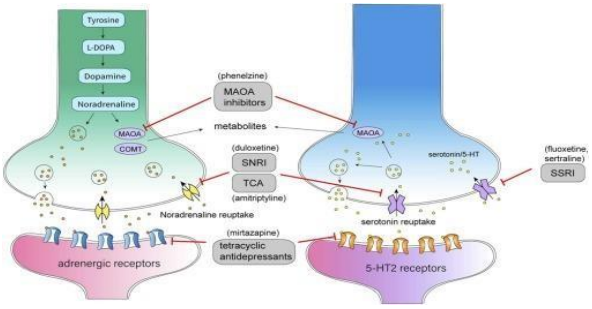
Various cardiac metrics, such as left ventricular ejection fraction (LVEF), extended QTc, and other cardiac measurements, showed no alterations.

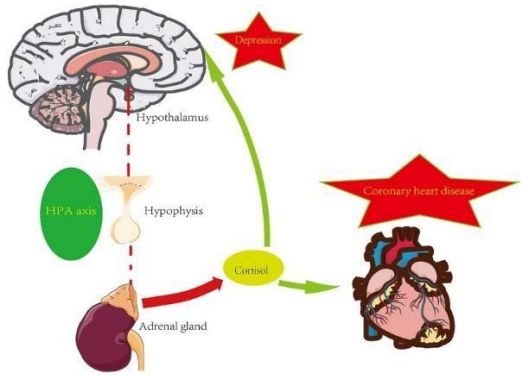
Sertraline appears to be safe in individuals with depression and concomitant CAD or unstable angina, according to this research. Sertraline, on the other hand, was not very effective in treating depression in this group of patients. Over the course of 24 weeks; it was statistically superior to placebo on Cognitive Global Impression (CGI) 1 scales, but not on HAM-D scores. On the other hand, sertraline was found to be more effective than placebo in both the CGI-1 and HAM-D scales (p=0.001) when studied in a designated sample of patients with severe depression[59]. However, some evidence suggests that SSRIs, like tricyclics, may raise the risk of cardiac events and death when taken long-term[60,61].

2. Serotonin and nor-adrenaline dual reuptake inhibitor:

Dual reuptake inhibition for serotonin and norepinephrine is found in the most recent generation of antidepressants. These medications are slightly more successful than SSRIs in treating depression, but they come with a higher risk of side effects. mirtazapine has been linked to a dose-dependent decrese in blood pressure, which is especially concerning for CHD patients, particularly those who already have hypotension. Furthermore, among all the antidepressants.

**Mechanisam of action of mirtazapine:**




Medications to be taken with extreme caution in people with CHD.

In the synapse, tricyclics raise the levels of norepinephrine and serotonin. The lengthening of the PR interval, QRS duration, and QT interval, as well as the flattening of the T wave on the ECG, has all been linked to these medicines. These drugs also have anticholinergic, antiadrenergic, and antihistamine effects. In the event of an overdose, these substances can be lethal. Side effects are possible in patients taking cardiac drugs like calcium channel blockers, alphaadrenergic antagonists, diuretics, and beta-blockers.

Selegiline in a transdermal form was recently licenced for the treatment of major depressive disorder (MDD). Oral selegiline at a low dose (5–10mg/day) does not require dietary restrictions, although it is not an effective antidepressant. When compared to oral selegiline, the Selegiline Transdermal System (STS) results in stable plasma levels of the drug, increased drug concentrations in the brain, and decreased metabolite synthesis. STS inhibits monoamine oxidase (MAO) A and B enzymes in the central nervous system with little effect on MAO A in the gastrointestinal and hepatic systems, lowering the risk of tyramine interactions[62].

Medication to be avoided in patients with CHD Physicians prescribe MAO inhibitors to treat depression and anxiety disorders. They are the oldest class of antidepressants. Because of the possibility of interactions with meals high in tyramine as well as other medications including cold cures and antidepressants, the use of these pharmaceuticals has decreased. This potentially lethal combination can trigger adrenergic crisis or postural hypotension[63]. In cardiac patients using diuretics or other antihypertensives, this side effect can be exacerbated. Beta adrenergic blockers are also generally contraindicated in patients who are on MAO inhibitors because their main clinical effect in these individuals is to increase vasoconstriction, which might lead to worsened hypertension. In CVD patients, MAO inhibitors are rarely used.

**Electroconvulsive therapy:**

In patients who have failed many rounds of psychotherapy and medication, electroconvulsive treatment (ECT) is used as a last resort to treat depression. Electroconvulsive therapy (ECT) has an overall response rate of 80% and is a safe operation, contrary to popular assumption. ECT generates

significant hemodynamic abnormalities, such as bradycardia, tachycardia, and hypertension, however these effects are temporary and usually disappear within 20 minutes. Complication rates have been linked to older age and pre-existing cardiovascular disorders, including as hypertension, CHD, congestive heart failure, aortic stenosis, implanted cardiac devices, and AF. Patients with hemodynamic instability or newly diagnosed or uncontrolled hypertension should have the surgery postponed. Medication can be continued through the morning of the procedure in patients with a stable CHD and managed hypertension. With the detection mode turned off during ECT and continuous electrocardiographic monitoring and life resuscitation equipment on hand, Electroconvulsive therapy appears to be safe in patients with an implanted cardioverter defibrillator.

**Exercise:**

Aerobic exercise appears to be the most effective treatment for mild-to-moderate depression at a dose commensurate with public health recommendations for CHD prevention. In depressed patients who do not respond to antidepressant drugs completely, exercise may help to enhance their effects. Finally, cardiac rehabilitation is particularly beneficial in improving mental health, such as depression, as well as physical health outcomes, such as additional CHD episodes and death, in patients with CHD[64]. When compared to regular cardiac rehabilitation, cardiac rehab augmented by stress management training has been demonstrated to be helpful in reducing stress and improving medical outcomes[65].

## CONCLUSION:

There is bidirectional relationship between depression and CHD, according to experimental and epidemiological research. The fundamental mechanisms that link the major depressive disorder and coronary heart disease are diverse and complicated. Depression is a risk factor for coronary heart disease (CHD). Due to the growing body of data linking depression to CHD, physicians are advised to check patients CHD for depressed symptoms.

Treatment is necessary and warranted for those patients who have a significant depressive episode. Because there is not enough research to back up the psychotherapy, we need to use antidepressant as a first line of treatment. The patients with CHD may be at high risk from older medicines such as tricyclic antidepressants and MAO inhibitors. Antidepressants from the new classes have been demonstrated to be safe and effective in the treatment of depressive symptoms in these patients. These classes of medication consist of SNRIs like mirtazpine are generally safe and effective for treatment of serious depression in patients with CHD.

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