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REVIEW ARTICLE

The Link between Major Depressive Disorder & Chronic Coronary Syndrome - A Literature Review

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Abstract:

Depression is prevalent among patients with coronary artery disease and has significant consequences. Occurrence of depression after a new diagnosis of stable angina is common and affects nearly 1 in 5 individuals. There have been several biological mechanisms by which depression may be related to coronary artery disease. As compared with nondepressed patients, those with depression have increased catecholamine levels,elevated resting heart rate, and decreased heart rate variability. . Behavioral characteristics of patients with depression include poor medication adherence, lower exercise tolerance,physical inactivity, poor dietary habits,and tobacco use. Although depression and its impact have been well documented in post-MI patients, much less is known about its significance in patients with chronic coronary syndrome(CCS).Despite the fact that CCS is the most common manifestation of coronary artery disease,sothere is a huge gap in the field of knowledge correlating CCS and depression.

Keywords: Depression, Heart Disease, Chest Pain, CCS

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Introduction:

In Bangladesh, coronary artery disease (CAD) is an increasing, important medical and public health problem and is the leading cause of mortality and morbidity. Most notable features of CAD in this population are extreme prematurity and severity, 2- 4 fold higher prevalence & incidence, 5- 10 fold higher rates of myocardial infarction and death before age of 40 years, 5 -10 years earlier onset of first myocardial infarction. Study showed the prevalence of CAD was 4.5% among 13,724 study subjects of 16 villages in a rural area[1,2]. The prevalence was slightly higher in male patients (6%), whereas in female it was 3.5%. Younger people also had a similar risk as aged people in that study. In a study CAD burden in the rural population of Bangladesh in 2007, information was sought on 447 adults (157 men and 290 women) aged above 20 years (mean 40years). CAD was defined by the presence of pathological Q wave on electrocardiogram or current medication for CAD. The prevalence of CAD was found 3.4%. Prevalence in men (4.6%) was almost twice than in women (2.7%).[3]

Major Depression,As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)[5], clinical depression, or major depression, is characterized by depressed mood or anhedonia (loss of interest or pleasure) for at least 2 weeks accompanied by significant functional impairment and additional somatic or cognitive symptoms(Figure 1).

The situation was even worse in the urban population[4], in which the prevalence of CAD in a sample of working professionals in Dhaka was found to be 19.6%. Cardiovascular diseases are becoming a significant burden on health care services in Bangladesh. From July,1995 to June,1997, analysis of 4410 cardiac patients admitted to 13 regional and tertiary hospitals revealed hospital admission due to CAD was 34%.

Many studies have shown a relationship between major depression or depressive symptoms, and CAD.[6]

In one of the relatively recent meta-analyses[7], which included 30 prospective cohort studies of individuals initially free of CAD, depression was associated with a 30% increased risk of future coronary events.. In community samples and in general practice clinics, the rate of depression is about, 10% but it goes up to about 15–30%in patients with CAD.[8]

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DSM-5 Diagnosis

- Major Depressive Episode Criteria (cont.)
  - Five or more of the following symptoms (at least one of which is either
    1) Depressed mood
    2) Diminished interest in activities
    3) Significant weight loss or gain
    4) Insomnia or hypersomnia
    5) Psychomotor agitation or retardation
    6) Fatigue/loss of energy
    7) Feelings of worthlessness/inappropriate guilt
    8) Diminished ability to think or concentrate/indecisiveness
    9) Suicidal ideation or suicide attempt

Ref: APA (2013)

Fig.-1 : *DSM V criteria for Major Depression according to APA (2013).*

Diagnostic tools for Chronic Coronary Syndrome: Application of the new Pre test probabilities has important consequences for the referral of patients for diagnostic testing.

In a patient with a high clinical likelihood of CAD, symptoms unresponsive to medical therapy or typical angina at a low level of exercise, and an initial clinical evaluation (including echocardiogram and, in selected patients, exercise ECG) that indicates a high event risk, proceeding directly to invasive coronary angiography (ICA) without further diagnostic testing is a reasonable option. In other patients in whom CAD cannot be excluded by clinical assessment alone, non-invasive diagnostic tests are recommended to establish the diagnosis and assess the event risk. The current Guidelines recommend the use of either noninvasive functional imaging of ischemia or anatomical imaging using coronary CT angiography (CTA) as the initial test for diagnosing CAD. These recommendations are summarized in the following figure.

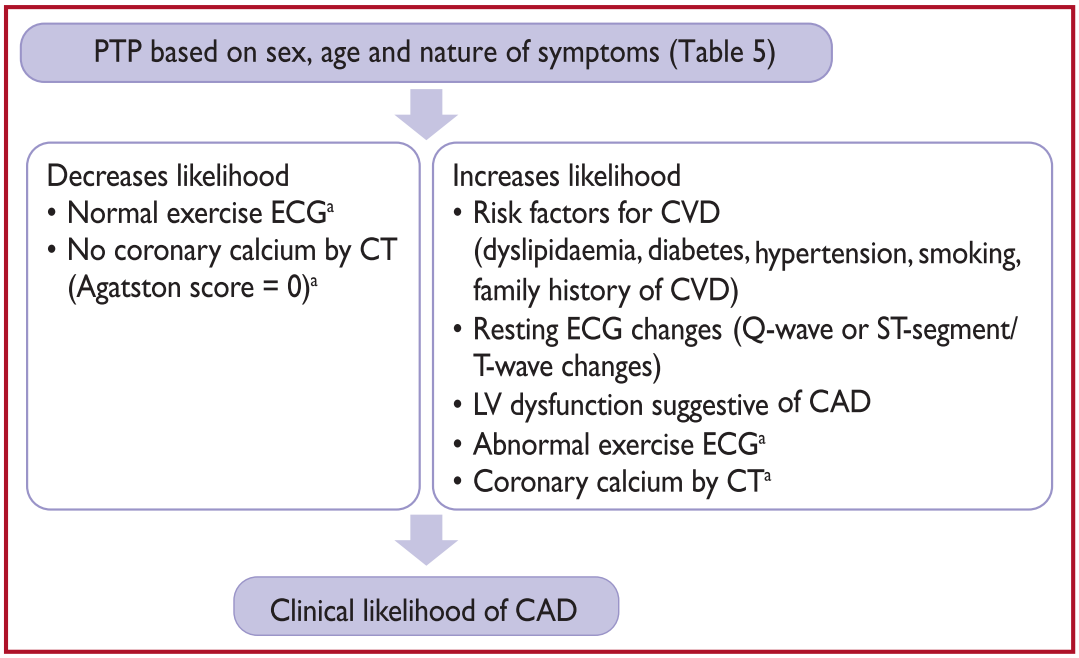

Fig.-2: *Clinical likelihood of CAD based on PTP & non-invasive testing.*

Functional non-invasive tests for the diagnosis of obstructive CAD are designed to detect myocardial ischemia through ECG changes, wall motion abnormalities by stress CMR or stress echocardiography, or perfusion changes by single-photon emission CT, (SPECT), positron emission tomography (PET), myocardial contrast echocardiography, or contrast CMR (Figure 2).

Dobutamine stress echocardiogram (DSE) is an alternative test for the diagnosis of chronic coronary syndrome which is available in our country. A recent study demonstrated good sensitivity and specificity of DSE. Some study found DSE had a sensitivity of 88% and a specificity of 83% for the diagnosis of significant CAD.[19]

The new ESC guideline on CCS 2019 has given a diagnostic approach & modalities depending upon clinical likelihood which is given below (Figure 3)

Mechanisms linking depression to coronary heart disease :

Neurobiological aspects of relevance to coronary heart disease –Dysregulation of stress-response pathways may contribute to CAD in vulnerable individuals by changes in sympathetic nervous system and neurohormonal function as well as alterations in central brain function.[9]

Neuroendocrine pathways –Endocrine changes associated with depression include alterations in corticotropin-releasing factor (CRF), dysregulated adrenocorticotropic hormone (ACTH) responses to CRF, enhanced adrenal responses to ACTH, and elevated circulating cortisol levels. Several of these changes may affect the immune system leading to excessive secretion of cytokines such as interleukin (IL)-1, IL-6, and tumour necrosis factor (TNF)-a. [10.]

Brain systems, autonomic function and cardiovascular physiology –Studies have shown that asymmetric brain responses to stress result in pro-arrhythmic sympathetic inputs to the heart. Brain areas involved in stress may modulate peripheral vascular and autonomic function,[11] which may mediate the effects of stress acting through the brain to cause myocardial ischemia in patients with CAD.

Depression & Inflammation – Depression has been associated with a sustained state of inflammation and increased concentrations of inflammatory molecules, including C-reactive protein and various cytokines, such as TNF-a, IL-1b, and IL-6 with known adverse effects on the heart and circulation. Depression has been also associated with elevated markers of oxidative stress. which is involved in the initiation, progression, and complications of atherosclerosis. [12]

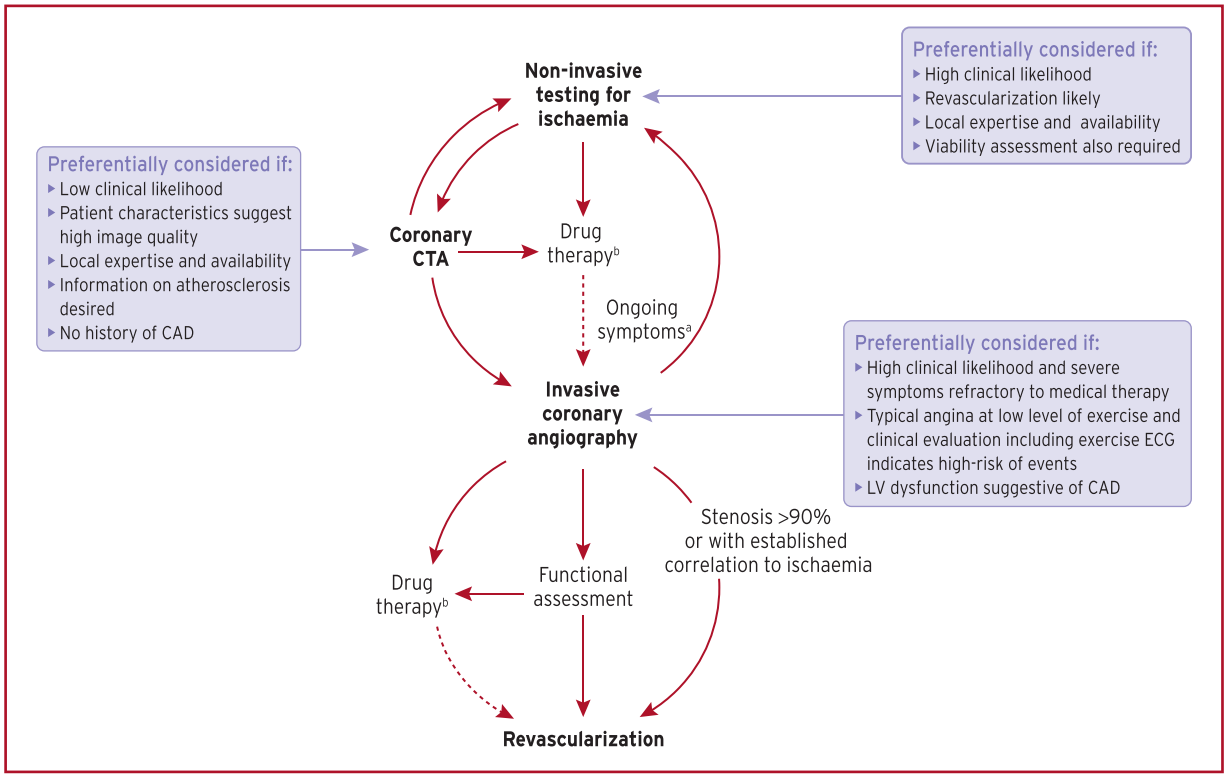

Fig.-3: *Selection of appropriate testing to diagnose CAD according to PTP & clinical likelihood, according to ESC guideline on CCS 2019*

Depression and endothelial dysfunction –The relationship between depression and endothelial dysfunction is likely due to reduced endothelium derived nitric oxide (NO). The metabolic syndrome is associated with depression and can contribute to the development of vascular endothelial dysfunction.[13]

Platelet activation and thrombosis –Several studies have shown increased platelet activity in major depression.[14] Of note, plasminogen activator inhibitor (PAI)-1, an anti-fibrinolytic factor, may also play a pivotal role, PAI-1 inhibits the formation of mature brain-derived neurotrophic factor (BDNF), and decreased BDNF levels have been described as a potential link between thrombosis and depression.

Depression and chest discomfort– Epidemiological evidence suggests a close relationship between depression and angina, with these two clinical entities frequently co-existing. Presence of depression is associated with increased reporting of shortness of breath and/or chest discomfort symptoms in patients with established CAD.[15] Not only is depression associated with everyday life angina independently of CAD severity, but it is a stronger predictor of angina than severity of coronary artery disease or other traditional risk indicators.[16] Over reporting of chest discomfort in depressed patients could be related to alterations in pain perception. Furthermore, patients with chronic pain, including angina, may develop depressive symptoms as a consequence of their symptom burden or disability[17]. Evidence also suggests that chest discomfort and depression share common neurohormonal pathways and a common genetic background,[18] which could explain their co-existence (Figure 4).

The links between depression and chest discomfort are summarized in following Figure :

Approach to a patient of Depression to detect cardiovascular disease: There is no specific guideline for the diagnostic approach to a patient of depression for the detection of cardiovascular disease. So the diagnosis is done according to recommended guideline for the diagnosis of CAD. It is done by 2 steps. 1st step is to diagnose & assess the severity of major depression. And the 2nd step is to diagnose CAD in patients with Major Depressive Disorder

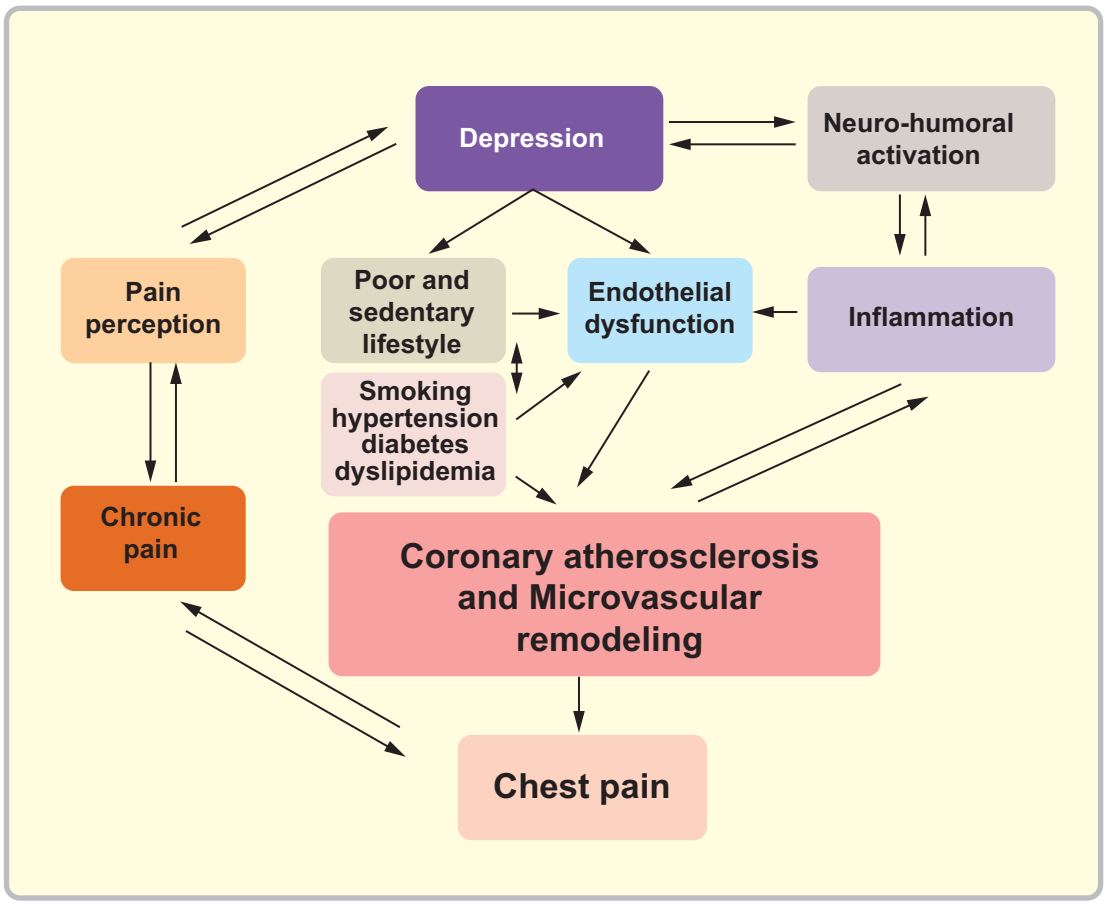

Fig.-4 : *Link between depression & chest discomfort in coronary heart disease.*

who present with chest discomfort. Diagnosis of Major Depressive Disorder is made by DSM V criteria.(see operational definition) which is widely accepted. Severity of major depression is assessed by several tools.

In 2008,AHA science advisory recommended that, at a minimum, the Patient Health Questionnaire (PHQ-2) provides 2 questions that are recommended for identifying currently depressed patients. . If the answer is "yes" to either or both questions, it is recommended that all 9 PHQ items be asked. The PHQ-9 is a brief depression screening instrument .Most patients are able to complete it without assistance in 5 minutes or less. It yields both a provisional depression diagnosis and a severity score that can be used for treatment selection and monitoring. The PHQ-9 has been shown to have reasonable sensitivity and specificity for patients with CHD .

Regarding the diagnosis of chronic coronary syndrome , European Society of Cardiology (ESC) established a guideline at 2019. They used a pretest probability (PTP) & Clinical likelihood to screen out the patients who may have Chronic Coronary Syndrome

Conclusion:

In summary, the high prevalence of depression in patients with CCSneedsincreased awareness and screening. Patients with positive screening results should be evaluated by a professional qualified in the diagnosis and management of depression. Patients with cardiac disease who under treatment for depression should be carefully monitored for adherence to their medical care, drug efficacy, and safety with respect to their cardiovascular as well as mental health. Coordination of care between healthcare providers is essential in patients with combined medical and mental health diagnoses

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