Review Article

Heart and the mind : depression and cardiovascular disease

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Depression is highly prevalent in patients with cardiovascular disease (CVD) and is associated with poor quality of life, poor medication adherence and higher cardiovascular morbidity and mortality. Though the American Heart Association (AHA) association recommends universal screening, there is currently no evidence to suggest that universal screening improves cardiovascular outcomes. That being said, physicians must be aware of risk of depression in this vulnerable population and screen when depression is suspected. To be effective, screening must be paired with appropriate referral or collaborative care. Patients with a positive screen, may be monitored and treated by a mental health professional. Treatment of depression improves mood and quality of life, though more research is needed to determine if treatment of depression in CVD improves cardiovascular outcomes.

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Mr S, a 65 year old man with a history of hypertension, type 2 diabetes and cigarette smoking came in to clinic with chest pain and shortness of breath upon exertion. Upon taking a history, his doctor found that Mr. S had been non-adherent to his medications for diabetes and hypertension. His electrocardiogram (EKG) was unremarkable but a stress test revealed signs of ischemia. His echocardiography showed normal left ventricular function with no wall motion abnormalities. Coronary angiography revealed a significant lesion at the proximal left anterior descending artery (LAD). Mr S underwent coronary angioplasty and received a stent to LAD. His discharge medications included aspirin, atenolol, lisinopril, atorvastatin and metformin. His doctor also recommended secondary prevention measures such as diet and exercise interventions and smoking cessation. Upon discharge, Mr S followed up intermittently but disappeared from follow up for several years, until one day he presented to the emergency department with acute onset chest pain and shortness of breath. On admission to the hospital his troponin I was elevated and EKG was suggestive of Anterior wall ST segment myocardial infarction (STEMI). This time coronary angiogram revealed critical stenosis at the left main coronary artery and a stent was placed. At one month follow up he revealed symptoms of low mood, loss of interest in life and fatigue that began 2 years prior to his diagnosis of heart disease. A diagnosis of major depression was made and Mr S was referred to a psychiatrist.

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Is Depression A Risk Factor For Recurring Cardiac Events ?

Depression is present in one in 5 patients with CVD a prevalence that is at least 3 times greater than in the general population(1).Though the prevalence of depression in CVD is higher in women, cardiac prognosis in worse for men[2]. Patients with depression and CVD are more likely to have physical limitations and poor quality of life, which are independent of measures of cardiac function such as left ventricular ejection fraction[1]. Patients with CVD and co-morbid depression are at increased risk for adverse cardiovascular outcomes independent of traditional risk factors such as diabetes, hypertension, cigarette smoking, obesity, hypercholesterolemia and left ventricular ejection fraction[3].

For example after one attack of myocardial infarction (MI), depressed patients have double the risk of cardiovascular events over the next 1-2 years, after accounting for traditional risk factors[4].

In terms of the course of illness, depression in CVD is often chronic and recurrent, in hospitalized patients with CVD approximately 50-70% of patients developed symptoms of depression prior to their cardiac event[5]. Symptoms of depression post MI might be viewed as a normal reaction to stress and be expected to remit spontaneously. In fact, spontaneous remission occurs in about half of cases of post-MI depression, while the other half will either persist or remit only to relapse within a year[6].

Is Depression A Risk Factor of New Onset CVD ?

Yes. There is also evidence to suggest that depression alone is a risk factor for new onset CVD. One meta-analysis of 30 prospective cohort studies (N=8,93850) found that individuals with depression compared with non depressed individuals experience a significantly increased risk of 30% for CVD[7].Another meta-analysis of prospective studies found that depression was associated with a 31% increase in risk for myocardial infarction (MI) and a 36% increase in coronary death compared with non depressed persons[8].

What is the Link Between Depression and CVD?

Both physiological and behavioral factors have been explored in the relationship between depression and heart disease.

With respect to behavioral factors, we already know that medication non-adherence and low physical fitness are associated with adverse cardiovascular outcomes. Depressed patients are less likely to engage in preventative behaviors such as smoking cessation, physical exercise and adherence to medications. One study found that depression is an independent predictor of medication non-adherence in patients with CVD[9]. In another study of depressed patients it has been shown that while they were hospitalized for cardiac conditions, adherence to diet, exercise and medication improved if their depression did improve[10].This may suggest that treating depression may promote preventative behaviors as well.

Numerous inter-related physiological factors have been proposed. While the role of inflammation in atherosclerosis has been well studied, depression has also been associated with increased inflammatory cytokines (such as IL-6, IL-1, CRP) Inflammation along with other mechanisms promote endothelial dysfunction which may contribute to myocardial ischemia[2]. Platelet dysfunction and abnormal blood serotonin levels are known to occur independently in patients with depression and in those with CVD. It is well known that serotonin binds to 5 Hydroxy Tryptamine (5-HT) receptors and leads to platelet aggregation. By depleting platelet serotonin stores antidepressants like selective serotonin reuptake inhibitors (SSRI) (antidepressants) have been shown to decrease platelet aggregation in vitro[2].This raises a fascinating question of whether antidepressants may be helpful to prevent myocardial damage.

Many more mechanisms exploring the link between CVD and depression have been postulated (Fig 1).

Diagnosis of Depression In Cardiovascular Disease : To Screen Or Not To Screen ?

Due to the high prevalence of depression in patients with CHD, the American Heart Association (AHA) supports a strategy of routine screening in various settings including hospitals and clinics[4] (Fig 2). Screening may be performed by the Patient Health Questionnaires (PHQ), a self-administered tool, that takes less than 2 minutes to complete, it is free of cost and available in multiple different languages online. At a minimum the PHQ-2 (consisting of 2 screening questions) is recommended to identify current depression (Table 1). A negative PHQ-2 ends the screening process. A positive PHQ-2, should be followed by a PHQ-9 (Table 2). A PHQ-9 yields a provisional diagnosis of major depression and a severity score that can used to guide monitoring and treatment. Critics however, remain skeptical about universal screening guidelines, due to concerns of misallocation of limited resources, misdiagnosis and improper delivery of care in those diagnosed with depression.

There is evidence to suggest that routine screening performed in the setting of collaborative care models may improve symptoms of depression, reduce cardiac symp-

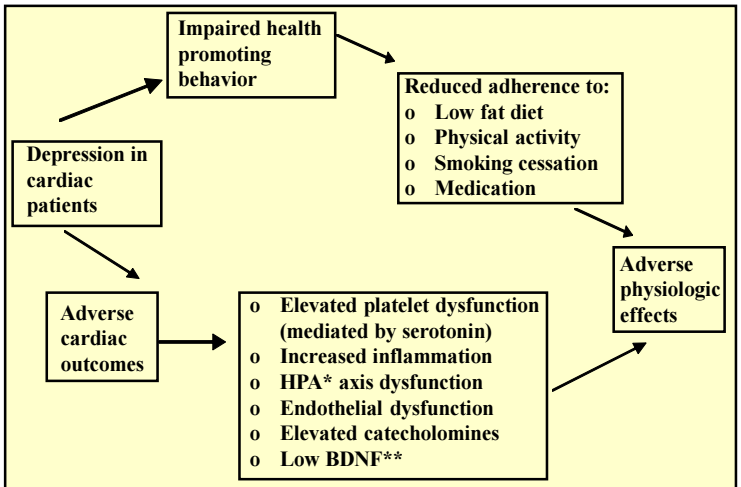

Fig 1 — Mechanisms by which depression may impact cardiac outcomes

Table 1 — *Patient Health Questionnaire: 2 Items**

Over the past 2 weeks, how often have you been bothered by any of the following problems?
(1) Little interest or pleasure in doing things.
(2) Feeling down, depressed, or hopeless.
*If the answer is "yes" to either question, then refer for more comprehensive clinical evaluation by a professional qualified in the diagnosis and management of depression or screen with PHQ-9.

Table 2 — *Patient Health Questionnaire-9 (PHQ-9)* Depression*

Screening Scales
Over the past 2 weeks, how often have you been bothered by any of the following problems?
(1) Little interest or pleasure in doing things.
(2) Feeling down, depressed, or hopeless.
(3) Trouble falling asleep, staying asleep, or sleeping too much.
(4) Feeling tired or having little energy.
(5) Poor appetite or overeating.
(6) Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down.
(7) Trouble concentrating on things such as reading the newspaper or watching television.
(8) Moving or speaking so slowly that other people could have noticed. Or being so fidgety or restless that you have been moving around a lot more than usual.
(9) Thinking that you would be better off dead or that you want to hurt yourself in some way.
*Questions are scored: not at all=0; several days=1; more than half the days=2; and nearly every day=3. Add together the item scores to get a total score for depression severity.

toms and reduce cardiac events, though more studies are needed to corroborate these findings[2,11,12]. Therefore, if screening is performed, it is to be paired with some management protocol such as referral to a trusted psychiatrist or better still establishing collaborative care between the patients' general practitioner, cardiologist, psychiatrist and other psychosocial supports[2].

Treatment of Depression In Cardiovascular Disease : Will It Prevent Future Cardiovascular Events ?

Treatment of depression in heart disease includes antidepressant medications and psychotherapy based on patient preference and available resources. Before referral to a psychiatrist, patients must be provided psychoeducation on depression, as the diagnosis is often associated with stigma and denial. SSRIs remain first line in the treatment of depression all of which are equal in efficacy. Out of psychotherapy modalities, cognitive behavioral therapy

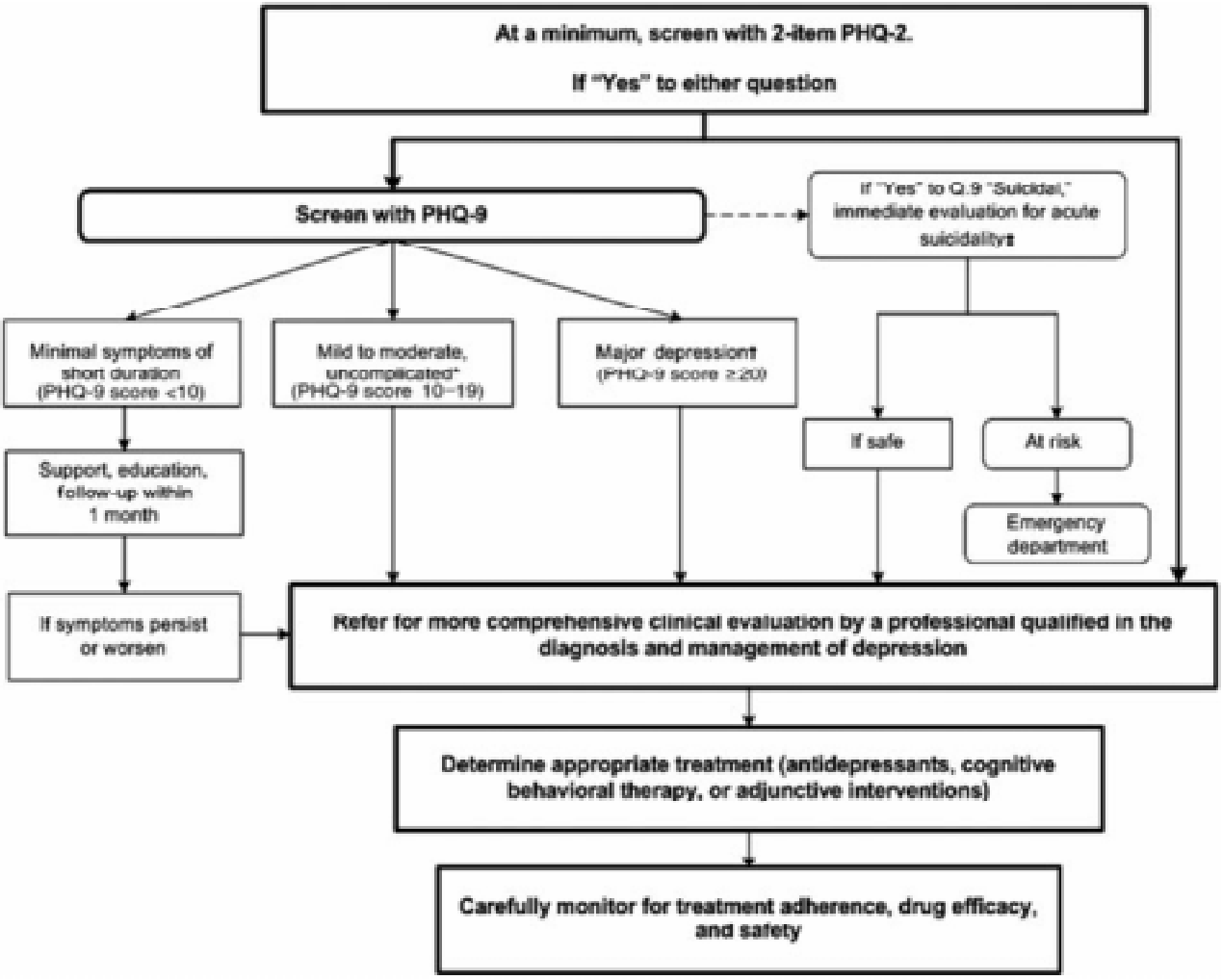

Fig 2 — Screening for depression in patients with CVD. AHA recommendations[4].

(CBT) is considered to be the most effective in treating depression. Treatment of depression requires time, antidepressants take 3-4 weeks to start working and CBT requires regular attendance for at least 12 weeks. Depression must be treated as it improves mood and quality of life. Patients recovering from depression are more likely to adhere to medications, diet and exercise regimens and more likely to enlist the support of family and friends[13].

Whether treatment of depression improves cardiovascular outcomes is unknown at this time. To date, there are few randomized control trials comparing antidepressants vs. placebo and their impact on long term cardiovascular outcomes. Though the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) was designed the test the safety and efficacy of Sertraline in post ACS depression, it did find a statistically non-significant reduction in adverse cardiovascular events in the Sertraline group[6]. A Korean study comparing Escitalopram vs. Placebo in post ACS depression found a statistically significant reduction in adverse cardiovascular events after 8.1 median years of follow up. This is the first randomized control trial that proves a causal association between CVD and depression[14]. These results are intriguing as SSRIs are known to reduce platelet activation. We need more randomized control trials to generalize these findings. In terms of psychotherapy, the Enhancing Recovery in Coronary Heart Disease (ENRICHD) was a randomized control trial that studied the effects of CBT vs. usual care in patients with post ACS depression. While investigators showed that 12 weeks of CBT allowed remission of moderate to severe depression, there was no difference in event free survival between the 2 study groups[15]. It is important to note that all the above trials were conducted in the post MI period where somatic symptoms may make diagnosis of depression more challenging. In order to fully understand whether treatment of depression improves cardiovascular outcomes there is need for more randomized control trials at different points on the spectrum of CVD.

In the above case, Mr. S's depression was present 2 years prior to the presentation of his CVD and depression was diagnosed only after he had an MI. Was depression a risk factor for his MI? If yes; would diagnosing and treating his depression earlier could have prevented his heart attack? We do not know that yet. What we do know is that treating depression would have improved his symptoms and quality of life. Physicians therefore, should consider mind disorders as important components while treating heart patients.

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