DEPRESSION AS A RISK FACTOR FOR CARDIAC EVENTS IN ESTABLISHED CORONARY HEART DISEASE: A REVIEW OF POSSIBLE MECHANISMS

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ABSTRACT

Depression is highly prevalent in patients with coronary heart disease (CHD) and is associated with excess medical morbidity and mortality. This article reviews the mechanisms which may mediate the relationship between depression and cardiac events in these patients. Research in this area is at an early stage of development. However, there is evidence that altered autonomic tone, smoking, hyperension, and, at least in older patients, poor adherence to the cardiac treatment regimen may be responsible for the adverse cardiac effects of depression.


INTRODUCTION

Over 4.5 million Americans have coronary heart disease (CHD), one of the leading causes of disability, morbidity, and mortality among adults in the United States. There are approximately 1.5 million myocardial infarctions (MI) and over one-half million deaths related to MI each year (1). In addition to living with the fear of having a heart attack, many patients with CHD experience angina pectoris, fatigue, or other debilitating symptoms.

Perhaps it is not surprising that many patients with CHD become depressed. It may be surprising to some, however, that depression increases the risks of cardiac morbidity and mortality in patients with CHD.

Although it has been suspected for more than fifty years that depression increases the risk of myocardial infarction (2), the possibility that depression may be a risk factor for MI as well as for other cardiac events has only recently attracted the attention of behavioral and medical scientists. The purpose of this article is to summarize what has been learned so far about the prevalence, course, and medical significance of depression in patients with CHD, and to examine the possible mechanisms which may mediate the relationship between depression and cardiac morbidity and mortality in this population.

PREVALENCE AND CHARACTERISTICS OF DEPRESSION IN PATIENTS WITH CORONARY HEART DISEASE

The point prevalence of clinically significant depression is estimated to be between 40% and 65% in patients who have recently had an acute MI (3-6). The combined prevalence of major and minor depression, as defined by the Research Diagnostic Criteria (RDC), is an estimated 45% among post-MI patients (7). Major depression alone, as defined by RDC,Diagnostic and Statistical Manual III-Revised (DSM-III-R) (8) or modified DSM-III-R criteria, affects 16% to 22% of these patients (7,9-11) and 18% of patients with no history of MI but with angiographically proven coronary artery disease (CAD) (12).

Relatively little is known about the characteristics of depression in patients with CHD. However, it is known that approximately half of the patients who are depressed at the time that their coronary artery disease is initially diagnosed have had one or more prior episodes of depression. In the majority of these cases, the first episode of depression occurred years before there were any clinical manifestations of coronary disease (13).

Although there have been few follow-up studies of depression in patients with CHD, there is evidence that clinically significant depression usually follows a chronic course during the first year after MI (7,14-16), and that it tends to recur (17). However, one study found that although major depression tends to be chronic, minor depression tends to remit within a few months (7). These findings suggest that minor depression may be a transitory adjustment reaction to CHD, but that major depression, if left untreated, tends to be quite persistent in this patient population. Furthermore, patients who have never experienced a psychiatric disorder before their first MI tend to have a shorter duration of clinically significant depressive symptoms than those who do have a prior psychiatric history (16).

ADVERSE MEDICAL EFFECTS OF DEPRESSION

A wide range of methods have been used to define, detect, and measure depression in cardiac patients. Many studies have utilized structured or semistructured interviews that have not been adequately validated (18), or self-report questionnaires that do not differentiate between the symptoms of depression and those of a medical illness (e.g. fatigue). Unfortunately, such methodological issues have impeded the acceptance of depression as a cardiac risk factor (19).

Nevertheless, many recent studies using standardized methods of assessing depression have found that it has a wide range of adverse effects on the course and outcome of CHD. The presence of major depression at the time of coronary angiography in patients with CHD more than doubles the risk that a major cardiac event will occur within one year (20). This effect...
is independent of the severity of the CHD and of other potential confounds (20). Depression also increases the risks of reinfarction and mortality following MI (10,14,21-28), and the risk of mortality in patients with ventricular arrhythmias (29) and in cardiac surgery patients (30,31).

Depression may be a more important risk factor for women than for men. The prevalence of depression is at least twice as high among women as men with CHD (9,32), and depressed or bereaved women may be particularly vulnerable to sudden cardiac death (33-35). The differential prevalence of depression may help to explain why the mortality rate following MI is higher in women than in men (36).

Clearly, there is much evidence that depression is a significant and independent risk factor for cardiac events, including myocardial infarction and sudden cardiac death. However, even the most rigorously designed studies have left many questions unanswered. One of the more important is whether the cardiac risks that are attributable to depression are confined to certain severity levels or subtypes. We do not know whether it is only major depression that affects the course and outcome of coronary disease, or whether minor or subclinical depression, grief reactions, or even transient demoralization do so as well.

At the present time, this question cannot be easily answered. For example, in a 12-month follow-up study of patients with angiographically documented CHD, we found that only those with major depression at baseline were at greater risk for cardiac events (20). Unfortunately, no one in our sample met the Research Diagnostic Criteria for minor depression. Neither mild depression as defined by Beck Depression Inventory scores nor subclinical clusters of depressive symptoms as reported during the interview were predictive. However, this study was based on a relatively small sample, so the power to detect the effects of milder forms of depression may have been inadequate.

Studies which have defined depression by cutoff scores on standardized self-report inventories, or which have required fewer or less persistent symptoms than does DSM-III-R, have not helped to clarify this question. If, indeed, major depression is the only form of depression that is associated with worse medical outcomes in patients with CHD, its effect may be obscured in studies that fail to stratify heterogeneous samples by depression severity or subtype. Clarification of this question is of critical importance to the design of future intervention studies, the improvement of cardiac care, and the study of possible mediating mechanisms.

MECHANISMS

Studies of the mechanism(s) which may link depression to adverse medical outcomes inevitably rest on the investigator's assumptions about how depression should be defined. There are at least two compelling reasons to focus on major depression in mechanistic studies rather than on other subtypes. First, the cardiac effects of this comparatively severe form of depression are likely to be stronger than those of minor or subclinical depressions. Thus, the underlying mechanisms are probably easier to study. Second, unlike other forms of unipolar depression, there is an extensive literature on the behavioral and neuroendocrine features of major depression. This serves as a rich source of hypotheses about the potential mechanistic links between depression and cardiac morbidity and mortality. Table 1 lists the possible mechanisms which will be considered in the remainder of this review.

Severity of Coronary Disease

Even if a relatively narrow definition of depression is employed, there are still a number of plausible explanations for its effect on cardiac morbidity and mortality. First, it is possible that the patients who become depressed are also the ones who have the most severe heart disease. That is, perhaps the disabling effects of relatively severe heart disease cause vulnerable patients to become depressed.