Depression and Cardiovascular Disease

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Abstract: Depressive disorder occurs frequently in response to the onset of several cardiovascular diseases, particularly in the post-myocardial infarction period, and can become an important determinant of prognosis or recovery. In patients whose heart disease or hypertension is managed by a cardiologist or primary care physician, depressive disorder is apt to go undiagnosed and therefore untreated. The Self-rating Depression Scale (SDS) and/or Mini-International Neuropsychiatric Interview (MINI) have been proposed as simple, useful diagnostic questionnaires for use in such patients. In the relationship between depressive disorder and cardiovascular diseases, the “physical or mental exhaustion” that can occur under depression seems to bear a great deal of responsibility for the onset or prognosis of cardiovascular diseases, because the pathophysiological features of depressive disorder closely resemble those of an exhausted human or animal. Selective serotonin reuptake inhibitors (SSRIs) appear to be a safe form of treatment for depressive disorder, especially in patients with preexisting cardiovascular diseases. However, the prevention of depressive disorder might be even more important, by preventing patients from falling into the exhausted state.

Key words: Depressive disorder; Heart disease/hypertension (cardiovascular disease); Selye's stress theory; Selective serotonin reuptake inhibitor (SSRI)

Introduction

In recent years, major and minor depression has been cited as a risk factor for heart diseases such as myocardial infarction. It has also attracted attention as the cause of white-coat hypertension and the white-coat effect found among hypertensive patients on therapy, thereby directing attention to the relation between depression and various cardiovascular diseases. This points to the importance of addressing depressive disorder in patients with cardiovascular diseases, even among primary care physicians and cardiologists, who generally are not trained in psychiatry.

The need to deal with depressive disorder in
the clinical treatment of patients with cardiovascular diseases is also important for the following reasons. First, most patients in Japan with depressive disorder (80% of mild cases in particular) visit non-psychiatric departments, e.g., departments of general internal medicine or cardiology, complaining of physical symptoms. Second, 15% of patients with depressive disorder have considered suicide.

It should always be considered, particularly in cases of life-threatening cardiac or other diseases, that having the disease itself may cause a depressed mood or induce depression.

This paper describes the importance of addressing depressive disorder in the clinical treatment of heart diseases and hypertension and examines treatment options.

Relation between Heart Disease or Hypertension and Depressive Disorder

It is apparent from a number of reports that depression has a great influence on the development, course, and prognosis of heart disease and hypertension. It has also been documented that myocardial infarction occurs frequently among patients with depressive disorder, and that the incidence of depression and the mortality of patients with depressive disorder are high after the onset of myocardial infarction.

Schleifer et al. have reported that major or minor depression occurring 8–10 days after the onset of myocardial infarction was found in 45% of patients as a whole. Alpert and Rippe noted that CCU patients with myocardial infarction often manifest a depressive state, depending on the speech, behavior, and attitude of the care staff and the CCU environment, as well as on the type of disease, and pointed out the importance of taking into account the patient’s mental status. They also reported that depression persisted after the patient’s release from hospital, a condition referred to as “homecoming depression,” and advocated active support by a medical care team and encouragement of patients’ participation in social activities.

Depression and lack of social engagement following the onset of myocardial infarction are known to be associated with increased mortality. According to Frasure-Smith, among 222 patients with myocardial infarction, mortality at 6 months was markedly higher in those who remained in a depressive state after onset (17%) than in those without depression.

On the other hand, a number of reports have documented that myocardial infarction, arrhythmia, and sudden death occur at high frequencies in patients with depressive disorder. Furberg et al. of the Cardiovascular Health Study Collaborative Research Group reported on 4,493 persons of advanced age who had no cardiovascular disease and were followed for 6 years. They found that, the higher the mean depression score, the higher the incidence of heart disease. In addition, Engel analyzed many patients in whom sudden death occurred possibly because of psychological stress. He found among these patients many cases of sudden death occurring probably under a depressive state caused by a sad event or severely damaged self-esteem, and presumed that the deaths were caused by arrhythmia. Thus, dealing with depression is important both from the aspect of the prevention of heart disease and from that of treatment and control.

The importance of attention to major and minor depression in terms of their relation to hypertension has also been widely noted. Patients with depression or anxiety are frequently hypertensive. In this context, an important issue is white-coat hypertension in depressed patients and a white-coat effect on blood pressure in hypertensive patients on antihypertensive drug therapy. If antihypertensive drug therapy is initiated or increased only on the basis of blood pressure readings obtained in a doctor’s office or clinic in patients with unstable blood pressure under a depressive state, organs such as the brain, heart, and kidneys may be harmed, a result that would be
antithetical to the true purpose of antihypertensive therapy. Therefore, comparisons with home blood pressure and 24-h ambulatory blood pressure monitoring are important.

Another issue is that the depressive state causes decreased blood flow in organs, resulting in injury to the brain, heart, and kidneys. Therefore, organ deterioration in depressive patients on antihypertensive therapy, especially with excessive doses or inadequate antihypertensive drug, must be prevented.

In addition, the depressive state is associated with decreased physical activity and increased drinking and smoking, i.e., failure to carry out lifestyle modifications prescribed in guidelines for the treatment of hypertension. The prevention of depression is also important in this regard.

**Mechanism of Depression as a Risk Factor for Heart Disease and Hypertension: Biological Reactions under Stress**

Various hypotheses have been put forth as to the mechanism by which depression acts as a risk factor for heart disease and hypertension. Among these are 1) involvement of the sympathetic and parasympathetic activity; 2) changes in platelet function; 3) injury to vascular endothelial cells; 4) vascular occlusion owing to plaque formation; and 5) increase in free radicals and fatty acids. Apart from these hypotheses, one factor to be noted is that most animal models of depression used in experimental studies or in the development of antidepressant drugs employ small animals that have undergone continuous stress loading (exhausted animals). This is done because specific features of an exhausted animal, e.g., serotonin and catecholamine metabolism and various biological functions, are considered to closely resemble those of depression in humans. This suggests that the exhausted condition resembles depression in humans as well as in animals.

It is important here to refer to Selye’s stress theory, which is useful for considering the process, mechanisms, and biological reactions of an individual under stress who lapses into a depressive state.

According to Selye’s theory, when stress is imposed, the living body exhibits the following three reactive phases as stress persists:

1. **Reactions in the alarm stage**: In the initial stage of stress stimulation, the body does not respond to the stimulation because it is not ready to do so, or if the stimulation is strong, it may exhibit decreased vital functions, i.e., decreases in blood pressure, body temperature, and blood glucose levels, in some cases, resulting in a state of shock.

2. **Reactions in the resistance stage**: Subsequent reactions include blood pressure elevation, increased heart rate, and enhancement of blood flow (decreases in blood flow in organs may occur due to peripheral vasoconstriction), all of which are commonly called stress reactions.

3. **Reactions in the exhaustion stage**: If stress persists for a prolonged period, the body becomes exhausted, and thus exhibit deteriorated functions. Figure 1 shows the results of our previous experiment on stress loading in rats. When stress stimulation persisted, the heart rate and myocardial norepinephrine level continued to decrease over time, while exercise...
tolerance also showed a prominent decline. Sudden death and heart disease or various other diseases can occur in this state of exhaustion. We previously investigated the life situation during one week before onset in patients with myocardial infarction who were treated in CCU. About half of the patients were exhausted by the stressors of work or domestic affairs and developed the infarct under a situation similar to that of the depressive state, e.g., complaining of inability to sleep. Kubo at Kyushu University enumerated decreases in immunological function under various types of stress, as shown in Table 1. These stressors often corresponded to those of the exhaustion stage of chronic stress. Decreased immunological function in the exhaustion stage or in a depressive state seems to greatly affect the course and prognosis of illness.

Thus, when they are exhausted owing to conditions of continuous stress, humans, as well as animals, show deteriorated biological functions and declines in behavior and volition, similar to the clinical symptoms of major and minor depression. Therefore, one of the basic factors in controlling depression seems to be that of preventing patients from being mentally and physically exhausted from stress.

### Overview of the Diagnosis of Depression in Clinical Cases of Cardiovascular Disease

Patients with major or minor depression generally present mental and physical symptoms such as those listed in Table 2. In the clinical setting, depressive state is often recognized by its characteristic features, including melancholic mood, decreased ability to think and act, sleep disturbance, and sickness in the morning that improves by evening.

The psychiatric diagnosis of depression is based on established criteria such as those of the DSM-IV or ICD-10. However, these criteria are complicated and unfamiliar to primary care physicians and cardiologists, who are not specialists in psychiatry.

Therefore, a self-rating depression scale (SDS) consisting of 20 items has long been used as a simple method of diagnosing depression, particularly in mild cases. In addition, an even simpler diagnostic tool, the Mini-International...
Neuropsychiatric Interview (MINI) has been available since 1998. The MINI consists of a group of simple questions beginning with those to determine whether the subject has been feeling unhappy much of the time and whether he or she has lost interest in various things.

Most patients with depressive disorder who attend the department of internal medicine or cardiology seem to have mild psychogenic disease owing to extreme psychosomatic wasting. Therefore, it is important to make good use of SDS and MINI so as not to overlook mild depression.

**Treatment of Depression and SSRIs**

1. **Drug treatment**

   Although tricyclic and tetracyclic antidepressant drugs have been widely used for some time, in recent years, selective serotonin reuptake inhibitors (SSRIs), which are associated with fewer side effects and thus easier to use, have been developed and become commonly used. Tricyclic antidepressant drugs are known to have certain side effects, such as those derived from their anticholinergic action (thirst, urinary disturbance, constipation) and α₁ block-
ade (dizziness, feeling lightheaded on standing up), as well as side effects on the cardiac conduction system and cardiac rhythm. On the other hand, tetracyclic antidepressant drugs, which appeared in the 1980s, are known to cause fatigability and sleepiness because of their antihistaminic action. Therefore, tricyclic and tetracyclic antidepressant drugs have been difficult for primary care physicians and cardiologists to use in patients with heart disease. In this regard, the recently developed SSRIs such as fluvoxamine and paroxetine heighten the decreased activity of the serotonin system to exert an antidepressant effect, while presenting fewer side effects related to anticholinergic, antihistaminic, and adrenaline α-blocking actions than tricyclic and tetracyclic antidepressants (Fig. 2). They also have hardly any cardiac toxicity. In addition, SSRIs prevent myocardial infarction through their inhibition of platelet function. In a double-blind comparative study with a tricyclic antidepressant drug in patients with myocardial infarction who had concomitant depressive disorder, discontinuance of therapy owing to the development of arrhythmia or other adverse reactions was markedly less frequent with SSRI therapy. Thus, SSRIs are regarded as easier to use for patients who have depression and heart disease.

2. Psychotherapy
Brief psychotherapy and counseling can be implemented by primary care physicians. Relevant monographs should be referred to for details.

3. Life style modification
(1) Patients should be encouraged to rest, find enjoyable activities, sleep soundly, and engage in light exercise that does not make them too tired, in order to prevent depression from exhaustion and anxiety about disease and the stress of daily life. Analysis of their life histories is indispensable to determine what has caused the depressive state.

(2) A healthy, robust body capable of withstanding stress is important. In this regard, patients should be instructed in how to reduce risk factors and how to maintain a healthy body.

Conclusion
This communication has examined the significance of depressive disorder and procedures for dealing with it when treating patients with heart disease or hypertension. It is strongly recommended that physicians pay attention to the psychological status of the patients with heart disease or hypertension in order not to overlook mild cases of depressive disorder.

REFERENCES