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# Depression and Cardiovascular Diseases: Cause, Consequence or Comorbidity

*"Have a heart that never hardens, and a temper that never tires, and a touch that never hurts."*

Charles Dickens

**Introduction.** According to the World Health Organization (WHO) Report currently more than 350 million people in the world suffer from clinically significant anxiety and depressive disorders and this number is expected to grow [1]. Depression is the leading cause of disability worldwide.

The special attention should be given to the category of patients with the cardiovascular diseases, because the existence of depression greatly deteriorates the disease course. It is well-known that depression and anxiety are the risk-factors for the development of cardiovascular diseases [2]. Also depression is usually observed in patients in early post-myocardial infarction period, in patients with hypertension, especially with the heart failure syndrome. So what is the relationship of depression to cardiovascular diseases: is it a cause, consequence or just comorbidity?

The combination of depression and cardiovascular diseases is a well-known clinical fact, supported by the results of many clinical studies. Since the 90's more than 100 descriptive studies in this field assessing the relationship of depression with cardiovascular morbidity and mortality have been performed. Also more than 60 prospective studies were conducted to establish the connection between the presence of depression and coronary heart disease [3]. It is important to note that the negative impact on the prognosis has not only the so-called major depression, but also its mild form.

E.I. Chazov highlights an increase in mortality from cardiovascular diseases in the period from 1990 to 2003 and attributes this, in particular, to the high prevalence of depressive disorders in these patients [4]. Without a doubt, depression is an independent risk factor for cardiovascular diseases [5].

Brett D. Thombs identifies depression as an independent risk factor that increases mortality after myocardial infarction [6]. Patients with the clinical signs of depression have more than 7 % a year increase

of recurrent coronary events as well as the necessity for coronary arteries interventions [7].

According to the register of National Health Interview Survey (NHIS) including 30,801 participants the presence of depression was found in 9.3 % of patients affected by cardiovascular diseases and in 4.8 % of patients without them.

According to the EUROASPIRE III, that enrolled 8,580 patients from 22 European countries, who were followed for 6 months after hospitalization for coronary heart disease (CHD), the prevalence of depression ranged from 8.2 to 35.7 % among men and from 10.3 to 62.5 % among women. The prevalence of anxiety disorders ranged from 12.0 to 41.8 % among men and from 21.5 to 63.7 % among women [8].

In patients with coronary artery disease undergoing coronary angiography procedure, the symptoms of depression were identified in 17–27% of cases, and in post-myocardial infarction patients depression was found in 16–45 % of cases [9, 10]. Depression that develops in a few weeks after myocardial infarction results in 3.5-fold increased risk of dying. Also it was established that in patients with documented coronary artery disease according to the coronary angiography the presence of depressive disorder is a predictor of the development of acute coronary syndrome in the following 12 months.

A. B. Smulevich detected the prevalence of anxiety and depression in hypertensive patients as 40 % and 19 % respectively [11].

The prevalence of depression in patients with heart failure varies considerably from study to study. The wide range, from 77.5 % to 13 %, reflects both the assessment settings and the tools used [12].

Women are 1.7 times more likely to experience a significant depression than men. The majority of clinical studies of depression in patients with heart failure do not provide a separate data for men and women. One study analyzed the prevalence of depression in patients with heart failure only in out-of-hospital settings. The symptoms of depression were observed in 64 % of the women and 44 % of the men [12].

Interestingly, the hospitalization for treatment of acute heart failure usually exacerbates the symptoms of depression. Once the heart failure is under control, the depressive signs and symptoms may abate.

The problem of the combination of depression and heart diseases is particularly important for Ukraine, where the rates of morbidity and mortality from cardiovascular pathology are still the highest.

**Assessment and Diagnosis.** According to the Ukrainian laws and regulations the diagnosis of depressive disorder may be determined only by a psychiatrist.

According to the ICD-0, the presence of 2-3 of the following symptoms persisting for at least for 2 weeks is a typical evidence of the depressive episode:

- Low (depressed) mood, not peculiar to the earlier observed period and varying a little from the external circumstances;
- A clear decrease in interest and satisfaction of usually pleasurable activities, loss of the ability to rejoice, to enjoy life;
- Fatigue, decreased vitality, decreased work capacity;
- Low self-esteem and self-confidence;
- Unwarranted censure or excessive and inappropriate guilt;
- Thoughts of death, suicide or suicidal behavior;
- Gloomy and pessimistic vision of the future;
- Reduced ability to concentrate, absentmindedness, variations in decision-making, uncertainty, indecision;
- Lethargy or alarming fussiness (violations of psychomotor functions);
- Sleep disorders of any type;
- Changes in appetite (increase or decrease) with a corresponding change in body weight;
- A clear loss of libido.

Most of the patients don't agree to cooperate with psychiatrist or psychologist, so the signs of the depression are either ignored or marked but not treated adequately.

Depression in patients with cardiovascular diseases can be assessed in hospital or in the outpatient setting.

The clinical signs of depression are usually evaluated by interviewing the patient during the physical examination. Also there is a multitude of questionnaires that help to detect the depressive disorder and evaluate its severity.

In clinical practice it is recommended to use the Patient Health Questionnaire 2 and 9 (PHQ-2 and PHQ-9 respectively), that are valid and easy enough to be used in the clinical practice.

The PHQ-2 includes two questions that help to identify the patients with depression. If the patient gives a positive response to one or two questions, it is recommended to pass the following nine in the PHQ-9.

The survey of the patient PHQ-9 is a short questionnaire to identify depression. Most patients can freely complete it in 5 minutes or less. A profile allows to set a preliminary diagnosis, prescribing the patients' treatment and monitoring.

Patient health questionnaire 2 (PHQ-2)

• Have you experienced any of the following over the past two weeks?

1. Reduction of interest and pleasure in familiar events and actions.

2. The feeling of emptiness, hopelessness, worsening of mood.

If the patient answers "yes" to at least one question, the PHQ-9 should be used to establish an accurate diagnosis.

Patient health questionnaire 9 (PHQ-9)

• How often have you experienced the following over the last two weeks?

1. Reduction of interest and pleasure in familiar events and actions.

2. The feeling of emptiness, hopelessness, worsening of mood.

3. Sleep problems: insomnia or oversleeping.

4. Decreased or increased appetite.

5. Dissatisfaction.

6. Inability to concentrate.

7. Fatigue, lack of energy.

8. Confusion in the movements and conversation, noticed by other people.

9. Thoughts of death or of causing yourself pain.

Evaluation of the responses: no – 0 points, a few days – 1 point, more than half the days – 2 points, nearly every day – 3 points.

**Pathophysiology of depression and heart dysfunction.**

There are different pathological mechanisms of depression in cardiovascular diseases. The first is the psychological aspect associated with the development of life-threatening condition. The feeling of fear of death, anxiety about the future course of the disease, restrictions of physical activity, necessity of the invasive procedures usually cause anxiety and/or depression in patients in the acute phase of the disease. For the early post-myocardial infarction patients' depression substrate more often is due to the impossibility of returning to normal physically active life, reduced work capacity, social adjustment difficulties and the impact of myocardial infarction on sexual activity. At the same time, despite the psychological mechanisms of depression, the dysfunction of the heart muscle also attributes to the development of depression. Myocardial dysfunction is usually observed in cardiovascular diseases (coronary heart disease, arterial hypertension, cardiomyopathy, inflammatory heart diseases, valvular lesions). Also the myocardial dysfunction in the form of heart failure is the final link in the chain of cardiovascular continuum. Any damage to the heart muscle leads to the increasing of the filling pressure in the heart chambers and thereby stimulates the increased activity of neurohumoral systems: the rennin-aldosterone-angiotensin, sympathetic nervous system, vasopressin and natriuretic peptides systems. It is convenient to consider that the body's response to stress positions the Hans Selye's stress response concept.

The actual importance of stress as a component of the syndrome of heart failure and depression should also be noted. According to the teachings of Hans Selye the stress can be defined as non-specific total body reaction aimed at supporting homeostasis in response to the stressor. Heart failure is itself a condition of recurrent stress because it requires constant adaptation of the regulatory systems of the body to support homeostasis by rapid response activity of neurohumoral systems.

Activation of neurohumoral systems aims to support the adaptation processes and homeostasis in heart failure syndrome but often causes harm [13]. In the settings of the heart failure syndrome we should also mention the endogenous cannabinoid system, which as a system of the immediate response to stress, after the period of overstimulation becomes depleted causing a paradoxical effects (the third phase of the stress progresses according to the theory of Hans Selye). At the same time, depressive disorders are often accompanied by the hyperactivity of the hypothalamic-pituitary-adrenal axis, followed by increased excretion of cortisol in the bloodstream. Increased cortisol in this situation has a protective effect by mobilizing the body's reserves [14]. Interestingly, the higher levels of blood coagulation are observed in patients with cardiovascular disease and depression in comparison with patients without depression [15]. The exact cause of this phenomenon remains unclear. There are suggestions

that this might be due to the increasing number of serotonin receptors – HT2A on the surface of platelets. In addition, the increased levels of cytokines (IL-1, IL-6, TNF) also are more often observed in patients with cardiovascular diseases and depression that might be an explanation of the more rapid cardiac remodeling process in this category of patients [16].

One of the most important diagnostic procedures to detect the level of neurohumoral regulation in heart failure is the analysis of the heart rate variability. The persistence of depressive disorder in association with low rates of heart rate variability is a strong predictor of the high risk of death.

**Conclusions.** The depression in terms of cardiovascular diseases may act as a risk factor for their development, it can be a cause of the heart muscle dysfunction, as well as be caused by psychological problems in consequence of the disease .

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## Депресія і серцево-судинні захворювання: причина, наслідок чи супутнє захворювання

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Депресивні розлади у поєднанні з серцево-судинними захворюваннями нерідко трапляються у клінічній практиці. Доведено, що депресія є незалежним чинником ризику виникнення захворювань серця і судин, а також їх наслідком, зумовленим спільними патофізіологічними процесами виникнення цих станів. Приділено увагу методам діагностики депресії у цієї категорії пацієнтів.

**Ключові слова:** серцево-судинні захворювання, депресія, діагностика, перебіг.

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Depressive disorders in combination with cardiovascular diseases are frequently encountered in clinical practice. Depression is proved to be an independent risk factor for the heart and blood vessels diseases, as well as their consequence caused by common pathophysiological processes of the emergence of these states. Special attention is paid to the depression diagnostic methods in this category of patients.

**Keywords:** cardiovascular diseases, depression, diagnostics, course.