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Psychosocial factors, anxiety and depressive disorders in patients with coronary artery disease: problems of comorbidity and prognosis

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Aim. To assess the significance of psychosocial factors, anxiety and depressive disorders in predicting the comorbidities in patients with coronary artery disease (CAD).

Material and methods. The study included 132 patients aged 37 to 66 years with CAD and anxiety-depressive disorders. Depression was found in 42% of patients, anxiety — in 25%; combination of anxiety, depression — in 33%. The assessment of the significance of cardiovascular and psychosocial factors in predicting comorbidities in patients with CAD was carried out using the logistic regression.

Results. The total prognosis percentage was 95,4% in the general group of patients (Somers'D — 0,910). In the group of men, it was 95,5% (Somers'D –0,912); in the group of women — 93,1% (Somers'D — 0,877). The predictors with a high significance level (p=0,0001) were following cardiovascular risk factors: patient age, hypertension, diabetes, dyslipidemia, left ventricular hypertrophy, arrhythmias, smoking, positive family history of cardiovascular diseases and others. Following psychosocial factors were also significant: stress and characteristics of stressors, active psychopathological syndrome with leading anxiety and/or depressive symptoms, the patient age at the onset of mental disorder diagnosis, duration of the mental disorder, and psychological characteristics of patients. The age of the mental disorder onset was found to be related to the previous stressful events (p=0,0001). A relationship was found between the age of patients with the onset of mental disorder and the severity of CAD (p=0,0001), as well as with the age of CAD onset and the sex of patients (p=0,0007). The contribution of stressful events before anxiety and depressive disorders to the development of predictors effecting the course and diagnosis of CAD was shown.

Conclusion. Logistic regression showed a relevant relationship of cardiovascular risk factors, psychosocial factors, anxiety and depressive disorders, included in the list of significant predictors of comorbidities and the progression of CAD. The results obtained serve as a guideline for an interdisciplinary approach to the treatment and prevention of comorbidities.

Key words: cardiovascular risk factors, coronary disease, psychosocial factors, stress, anxiety, depression, comorbidity.

Relationships and Activities: none.

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The modern model of total cardiovascular risk (CVR), based on the multifactoriality in the development of one or several socially significant diseases, with the introduction of new prevention strategies, is aimed at reducing the prevalence and correction of the leading controllable risk factors, primarily at reducing cardiovascular morbidity and mortality [1].

Scientific research over the past decades has demonstrated the pathogenicity of often unrecognized psychosocial factors. The concept of psychosocial factors includes a wide range of mental and behavioral disorders, social factors and psychological personality traits that increase the risk of cardiovascular diseases (CVD) and complications that worsen the prognosis and survival of patients with coronary artery disease (CAD), at the same time complicating clinical course, diagnosis, treatment, prevention of CVD and comorbid conditions [2, 3].

The 2016 European Guidelines and 2017 Russian National Guidelines on cardiovascular disease prevention are based on the principles of preventive interventions aimed at identifying, controlling and correcting both known CVD factors and psychosocial factors. Confirmed by the results of large clinical and epidemiological studies and meta-analyzes, the Guidelines present the following psychosocial factors: low or no social support, low socioeconomic status, stress at work and in the family, depression, anxiety, hostility, type D personality, post-traumatic stress disorder and other mental disorders [4, 5]. Psychosocial factors caused by the pathophysiological and psychophysiological mechanisms have a negative impact on behavioral factors (Figure 1) that reduce medical adherence [3, 6-8].

It should be emphasized that modern Guidelines on cardiovascular and psychosocial factors help physicians in acquiring experience and skills in identifying, assessing and interpreting symptoms of mental and psychological maladjustment, as well as mastering competencies in the diagnosis, treatment and correction of comorbidities in patients with CVD [9, 10].

The aim of the study was to assess the significance of psychosocial factors, anxiety and depressive disorders in predicting the comorbidities in patients with CAD.

Material and methods

The presented work belongs to interdisciplinary research on the problem of cardiovascular and mental comorbidities, in particular, the impact of psychosocial factors and mental disorders on the course of CVD and other diseases. The sample consisted of patients with CAD (n=132), including 92 men and 40 women aged 37 to 66 years, who were treated in a psychiatric department due to severe anxiety and depressive disorders. All patients with CAD, class II-III effort angina, progressive angina, including those with acute coronary events, were previously examined in a cardiology hospital to verify the diagnosis. Some patients (9,8%) had a previous myocardial infarction. In 83% of cases, CAD was associated with hypertension (HTN), in 22% — with type 2 diabetes (T2D), in 9,8% — with impaired glucose tolerance (IGT). In addition, 58% of patients had hypercholesterolemia/dyslipidemia (DLP), 36,4% — cardiac arrhythmias, 30,3% — left ventricular hypertrophy (LVH), 60% — overweight, in more than half of men — smoking.

The mental state was assessed by the clinical-psychopathological method. A psychological examination of stress response was carried out using the Minnesota Multiphasic Personality Inventory (MMPI). Symptoms of depression were observed in 42% of patients, anxiety — in 25%; combination of anxiety, depression with asthenia — in 33% of cases. Mental disorder in 53,6% of the surveyed met the criteria for neurotic stress-related disorders, including adjustment disorders (prolonged depressive reaction, mixed anxiety-depressive reaction, other reactions to severe stress); anxiety disorders (generalized anxiety disorder, panic disorder). In 13,6% of patients, the revealed affective disorders were classified as a depressive episode, dysthymia, recurrent depressive disorder; in 32,8% — organic (anxious, depressive, asthenic) disorder.

This study was performed in accordance with the Helsinki declaration and Good Clinical Practice standards. The medical ethics committee of approved this study. All patients signed informed consent.

Statistical analysis. Data analysis was carried out using the Statistica 8.0 software package (StatSoft Inc., USA). To study the relationship of traits, multivariate analysis was used, including analysis of variance and contingency tables. Statistical hypotheses were tested using nonparametric methods (Mann-Whitney and Kruskal-Wallis tests). Quantitative indicators are represented as mean and standard deviation (M±SD). Logistic regression and Wald test were used for creating predictive models and assessing the significance of cardiovascular and psychosocial factors. Out of 80 independent features, significant predictors were determined, which were included by stepwise inclusion in logistic models. Differences were considered significant at $p<0,05$.

Results and discussion

Stepwise logistic regression demonstrated the compatibility of CVR and psychosocial factors reflecting the somatic, mental and psychological state of patients with CAD. The predictors selected

by the algorithm in the amount from 9 to 22 were included in all logistic equations. As examples, this paper presents the results of some final models.

The most significant component of comorbid conditions of CAD was the presence in the patients' history of a psychological trauma, which was the main reason of psychopathological symptoms. Psychosocial stress factors, depending on the nature and duration of exposure to stress, were defined as important life events (serious illness or death of a significant other), medical problems in the patient, work and family stress.

To assess the characteristics of comorbid conditions, the age ratios of the duration of coronary and mental disorder were taken into account. The interrelationships were determined: the age of patients at the time of examination, CAD onset, identification of the leading psychopathological syndrome and the mental disorder. A relationship was found between the age of patients with the onset of the stress-related disorder, the severity of CAD (p=0,0001), the age of CAD onset, and the sex of patients (p=0,0007).

Thus, the age of patients at the onset of mental disorder in the general group was 47,4±8,4 years (in women — 51,4±6,9 years, in men — 45,6±8,4 years (p=0,0001)). The age of CAD onset in the general group was 50,1±7,0 years (in women — 54,2±5,6 years, in men — 48,3±6,8 years (p=0,0232)). So, manifestation of mental disorder symptoms precedes the CAD, regardless of its clinical manifestations and the sex of patients.

The development of comorbidities in men with CAD was observed up to 50 years of age, in women — over 50 years of age.

The diagnosis of CAD was made with already existing symptoms of psychological maladjustment caused by stress.

All qualitative and quantitative traits of the relationship between coronary and mental pathology were included in the logistic regression as predictors and had high values of the regression coefficients, indicating their prognostic significance.

The analysis performed may indicate the initiating role of psychosocial stress and the resulting mental disorders in the formation of the prerequisites for development or progression of CAD and comorbid conditions.

Early diagnosis of CAD in patients with severe clinical manifestations of anxiety and/or depression was difficult and was overlapped by neurotic, stress-related, affective and other disorders.

Table 1 reflects the results of one of stepwise analysis of predictors, where the concordant was 95,4%; Somers'D=0,910. For patients with CAD (regardless of sex) from the first step, the most significant predictor was the dyslipidemia, which was

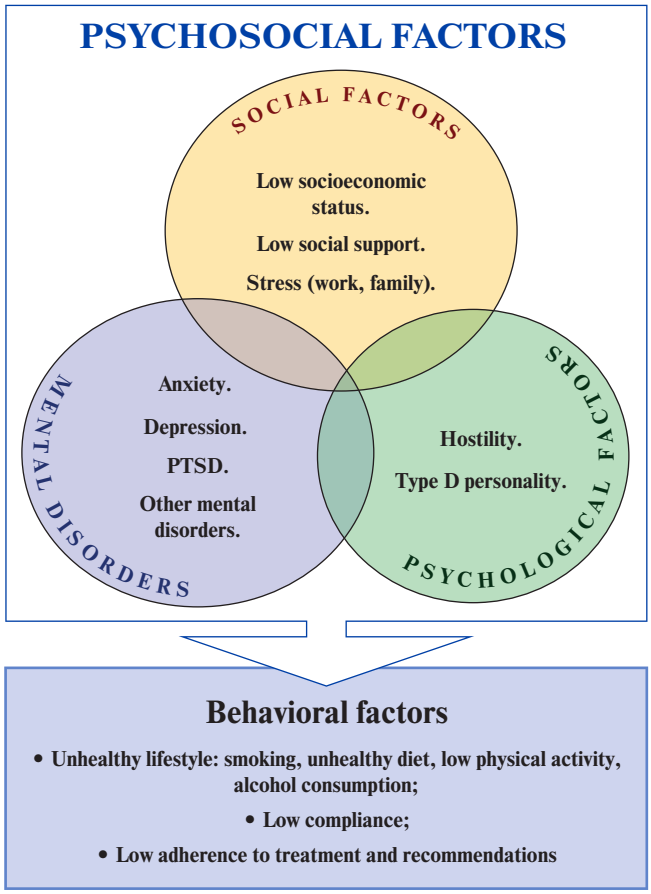

Figure 1. Psychosocial factors and their influence on behavioral factors of CVR.
Abbreviation: PTSD — post-traumatic stress disorder.

>50% of the prediction (p=0,0001). Then, the equation included other characteristic signs reflecting the progression of CVR: patient's age (p=0,0001), blood pressure level (p=0,0001), HTN (p=0,0240), cardiac arrhythmias (p=0,0001), T2D/IGT (p=0,0066), LVH (p=0,0490), family history of CVD (p=0,0371), along with a wide range of psychosocial factors. The mental condition and psychological characteristics of patients were characterized by the participation of such predictors as the mental disorder (p=0,0172), the leading psychopathological syndrome (p=0,0077), the patient's age at the onset of mental disorder (p=0,0322), severe anxiety (p=0,0379), fear of death (p=0,0108), introversion (p=0,0045), rigidity (p=0,0249), low activity (p=0,0475), impaired social adaptation (p=0,0238), previous stress (p=0,0184).

The analysis of the revealed cardiovascular and psychosocial factors in the groups of patients divided by sex revealed significant differences in the clinical manifestations of CAD in patients with anxiety and depressive disorders.

Table 1

Predictors of comorbid conditions in patients with CAD (stepwise logistic regression)

Step	Trait	(χ^2) Wald test	Accurate prediction (%)	p
1	Hyperlipidaemia, DLP	322,2	50,4	0,0001
2	Age	109,8	89,9	0,0001
3	Arrhythmias	45,2117	91,6	0,0001
4	Blood pressure level (mm Hg)	35,9287	93,3	0,0001
5	Introversion	8,0569	93,8	0,0045
6	Leading psychopathological syndrome (anxiety, depression)	7,1001	94,2	0,0077
7	T2D/IGT	7,3708	94,4	0,0066
8	Social maladaptation	5,1058	94,5	0,0238
9	Hypertension	5,0957	94,6	0,0240
10	Diagnosis of a mental disorder	5,6750	94,6	0,0172
11	Rigidity	5,0306	94,6	0,0249
12	Fear of death	6,5044	94,7	0,0108
13	Family history of CVD	4,3448	94,8	0,0371
14	LVH	3,8768	95,0	0,0490
15	Anxiety, various fears	4,3107	95,1	0,0379
16	Psychosocial stress (life events)	5,5620	95,1	0,0184
17	Family psychosocial stress	3,5495	95,2	0,0533
18	Age of onset of mental disorder	4,5870	95,2	0,0322
19	Hepato-biliary diseases (including hepatic steatosis)	3,3619	95,3	0,0667
20	Low activity	3,9265	95,4	0,0475
21	Non-cardiac manifestations	3,0661	95,4	0,0799
22	Emotiveness	2,9802	95,4	0,0843

Note: Concordant=95,4%; Somers'D=0,910.

Abbreviations: LVH — left ventricular hypertrophy, DLP — dyslipidemia, IGT — impaired glucose tolerance, CVD — cardiovascular diseases.

Table 2 presents the results of predicting comorbid conditions with CAD in men (n=92), where the concordant was 95,5%. The following predictors was significant: duration of mental disorder (p=0,0228), diagnosis of mental disorder (p=0,0318). Stress-related anxiety-depressive disorders preceded the CAD in men by an average of 2,7 years (p=0,0001). The age of the mental disorder onset was found to be related to the previous psychological trauma (p=0,0001).

For men, the stressors (p=0,0243) were significant life events (death or serious illness of a significant other), stress at work (dismissal, job loss), medical problems in the patient himself.

Clinically, there is a dependence of an acute coronary event (progressive/unstable angina, myocardial infarction), which developed with severe depressive episode in 11 patients who experienced extreme stress (death of a of a significant other), on average 4 months before the onset of acute cardiac symptoms.

In cases of comorbidity of CAD and anxiety disorders, angina attacks were associated with panic disorder with a severe leading thanatophobia (p=0,0111), accompanied by a tachycardia or tachyarrhythmia. Paroxysmal arrhythmias (paroxysmal supraventricular tachycardia, atrial fibrillation, frequent premature beats), as well as panic disorder, occurring in the form of sudden attacks of severe anxiety, fear of death, autonomic and somatic vegetative symptoms, hemodynamic disorders and

Table 2

Predictors of the severity of CAD and comorbid conditions in men (stepwise logistic regression)

Step	Traits	(χ^2) Wald test	Accurate prediction (%)	p
1	Age	117,9	86,7	0,0001
2	Hypercholesterolemia, DLP	45,5266	91,2	0,0001
3	Arrhythmias	21,4362	92,5	0,0001
4	Hypertension	15,2462	93,7	0,0001
5	LVH	7,4900	94,1	0,0062
6	Fear of death, panic disorder	6,4530	94,2	0,0111
7	T2D/IGT	6,2532	94,3	0,0124
8	Positive family history of cancer	6,1633	94,5	0,0130
9	Duration of mental disorder	5,1824	94,5	0,0228
10	Psychosocial stress (life events)	5,0734	94,7	0,0243
11	Social maladaptation	3,9340	94,9	0,0473
12	Diagnosis of a mental disorder	4,6102	95,2	0,0318
13	Hypochondriasis	4,0743	95,3	0,0435
14	Internal tension	3,7710	95,3	0,0521
15	Hepato-biliary diseases (including hepatic steatosis))	3,4940	95,5	0,0616

Note: Concordant=95,4%; Somers'D=0,910.
Abbreviations: LVH — left ventricular hypertrophy, DLP — dyslipidemia, IGT — impaired glucose tolerance.

cardiac arrhythmias, are psycho-traumatic events which leads to maladaptive response, depression, and hypochondriasis (p=0,0435).

In addition, the clinical manifestations of anxiety and depression were supplemented by low activity, sleep disorders, headache, aggressive outbursts, anger, irritability, internal tension, hypochondriasis, fear of death from heart disease.

The progression of CAD is accompanied by the severity and nature of psychosocial stress, symptoms of anxiety and depression, the predominance of depressive disorders, psychological characteristics leading to social maladaptation (p=0,0473), anosognosia and low medical adherence of men.

Positive family history of cancer (p=0,0130) was included in some of the final equations only in men with CAD.

Analysis of the CAD predictors in women also revealed some features. The analysis showed a high prediction percentage in a number of logistics models: Concordant=93,1%; Somers'D=0,877 and Concordant=95,0%; Somers'D=0,916. There were following predictors of CVR: DLP (p=0,0001), which provided 31,1-50% of the prognosis; LVH (p=0,0162), HTN (p=0,0002), T2D/IGT (p=0,0085), arrhythmias (p=0,0001), body mass index (p=0,0203).

For women, the most significant stressors were family stress and life events (p=0,0448).

In women, CAD was associated with postmenopausal period of age (p=0,0001), dyshormonal disorders (p=0,0027), thyroid diseases (p=0,0379), family history of endocrine disorders (p=0,0157). Women were characterized by non-cardiac manifestations (p=0,0447), autonomic dysfunctions (globus sensation, shortness of breath (p=0,0047), vegetative paroxysms (p=0,0466)), severe anxiety, and fears (p=0,0379)

Conclusion

The progression of CAD and predicting comorbid conditions in these patients are associated with combined effect of CVR and psychosocial factors.

Among psychosocial factors, mental and psychological components turned out to be significant predictors: history of stress and the nature of stress factors (death or serious illness of a significant other and other life events; family, industrial, and medical stress), the patient's age at the time of mental disorder

diagnosis, the duration of mental disorders, leading psychopathological syndrome (the severity of anxiety and/or depressive symptoms), some personal characteristics of patients, leading to a social maladaptation.

The development of a comorbid pathology that aggravates the CAD course is specified by the sex and age of patients, while in men at a younger age (<50 years) than in women (>50). Psychopathological symptoms precede the primary diagnosis of CAD, which is due to the impact of psychological trauma with a subsequent prolonged depressive reaction (adjustment disorders, anxiety, mixed anxiety and depressive disorder, depressive episode or dysthymia), complicating the clinical performance and diagnosis of CAD.

The analysis showed that psychosocial stress and the resulting anxiety-depressive disorders can be considered as significant predictors of the development or progression of CAD and comorbid conditions.

The revealed significant predictor "positive family history of cancer" in men requires additional study and follow-up of patients.

The results obtained serve as a guideline for an interdisciplinary approach to the treatment and prevention of combined cardiovascular and mental diseases.

Relationships and Activities: none.

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