Ischemic Heart Disease and Neurotic Psychological Disorders

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ABSTRACT

Recently, there has been a great scientific and practical interest in psychosomatic relationships in cardiology, in connection with the unfavorable dynamics of two clinical forms predicted by WHO experts for the coming decades - coronary heart disease and depression with a reduction in the duration of a working, socially fulfilling life.

Keywords: Psychosomatics, cardiac complications, ischemic heart disease

Introduction . The study of risk factors for the development and adverse outcome of coronary heart disease (CHD) made it possible, in addition to the "traditional" and thoroughly studied factors, to identify a number of psychosocial factors: the impact of stress, personality and psychological disorders, social isolation, etc. The INTERHEART study in 52 countries of the world confirmed the significant role psychological factors during heart disease, almost 90% of cases of primary myocardial infarction were associated with the cumulative influence of nine modifiable risk factors, among which psychosocial factors follow after smoking, arterial hypertension (AH), diabetes mellitus (DM) [1]. The study of the psychological aspects of cardiovascular diseases (CVD) seems to be especially relevant in the light of the data of the last decade on a significant increase in cardiovascular mortality in patients with anxiety-depressive disorders (ADD) in patients with coronary heart disease [2]. In this aspect, clinical studies devoted to the mutual influence and relationships between coronary artery disease and the most common psychopathological disorders [3], which in the future will allow the accumulation of unique and significant scientific, practical and theoretical material for the further implementation of multicomponent prevention, timely diagnosis and treatment in order to reduce disability and mortality from CVD.

The aim of the study was to study the frequency and structure of psychological disorders of the neurotic level (PND) and their relationship with the clinical course in patients with the main forms of coronary artery disease. The study of the clinical efficacy, feasibility and safety of the use of drugs with a wide spectrum of psychotropic action, as well as the relationship between the psychotropic efficacy of the studied drugs and the clinical course of the main forms of IBS with the prediction of the most optimal methods of psychopharmacological correction of the identified psychopathological disorders of the anxiety- phobic and depressive range.

Material and Methods . 297 patients of both sexes (192 men and 105 women) with various forms of coronary artery disease aged 28 to 70 years (mean age 58.3±6.4) were examined. The initial clinical characteristics of patients are presented in Table 1.

Table 1. Initial characteristics of the examined patients

Analyzed feature	Abs . number	%
Men	192	64.6
Women	105	35.4
Average age, years	58.3±6.4	
Acute myocardial infarction, including: - AMI of ST ST - Heart failure according to Killip II - Early post-infarction angina pectoris	104 64 (61.5%) 13 (12.5%) 24 (23.1%)	35.0 21.5 4.4 8.1
Unstable angina	92	31.0
Stable exertional angina, including: – Functional class II – Functional class III – Functional class IV with vasospastic component	101 53 (52.5%) 31 (30.7%) 17 (16.8%) 6 (5.94%)	34.0 17.8 10.4 5.7 2.0
History of myocardial infarction	78	26.3
arterial hypertension	119	40.1
Dyslipidemia	116	39.1
Smoking	97	32.7
Age >60 years	107	36.0
Body mass index >30	69	23.2
Type 2 diabetes	60	20.2
Left ventricular hypertrophy	103	34.7
Blockade of the left leg of the bundle of His	7	2.4
HPC requiring antiarrhythmic drugs	34	11.4
Left ventricular systolic dysfunction (EF <40%)	50	16.8
Total patients	297	100.0

The study program included three independent blocks: myocardial infarction (MI, n =104), unstable angina (UA, n=92), stable exertional angina (SSI, n=101). In each block, groups of patients without psychopathological disorders, with psychopathological disorders who did not receive and received psychopharmacotherapy (PFT) were formed. The latter were randomized into separate groups of patients taking tofisopam , sulpiride , sertraline . By the end of the three-month follow-up period, using the primary endpoints, patients were divided into groups: with a favorable and unfavorable course, followed by intergroup analysis and screening for predictors of adverse outcomes. More than 100 features were retrospectively analyzed.

In the course of the work, clinical methods and laboratory clinical and biochemical studies were used in accordance with the standards for managing patients with coronary artery disease, incl . electrocardiogram (ECG) registration, echocardiographic (EchoCG) study, 24-hour Holter ECG monitoring (CM) , bicycle ergometric (VEM) test.

In order to diagnose the severity of psychopathological disorders and dynamic control over changes, a set of psychodiagnostic tests of various target orientations was used [4–9].

1. Semi-structured clinical conversation-interview based on the criteria for diagnosing psychosomatic disorders (ICD-10);
2. Holmes-Rey questionnaire;
3. Clinical scale for assessing the psychological state of patients with coronary artery disease and arterial hypertension Zaitseva V.P.;

Spielberger -Khanin anxiety self-assessment scale ;

5. Beck Depression Self-Assessment Scale;
6. Hamilton Depression Rating Scale.
7. SMOL-1 (abbreviated multidisciplinary questionnaire for personality research).

All patients received basic drug therapy, in accordance with the Recommendations of international communities [10-14], for the correction of psychopathological disorders were used: "daytime" anxiolytic tofisopam at a dose of 50 mg 2 times a day for 4-6 weeks; atypical antipsychotic sulpiride 50 mg 2-3 times a day for 6-8 weeks, a balanced antidepressant from the group of selective serotonin reuptake inhibitors (SSRIs) sertraline 50 mg per day during the entire observation period. These drugs were administered to patients randomly.

Results . According to the results of psychological testing in the initial state in the surveyed sample of patients with coronary artery disease, PRNU was detected in 84.85% of cases (Table 2). To a greater extent, PRNU was registered among patients with acute myocardial infarction (AMI) and unstable angina pectoris (UA) than with stable exertional angina (SHF), the revealed differences became statistically significant when comparing patients with SHF with a pooled group of patients with acute coronary syndrome (ACS) (x2=6.8; p =0.009).

The data obtained can be explained by the high initial level of stress in this category of patients. When analyzing the average values of the level of stress in patients with coronary artery disease without PRNU (n = 45), they were significantly lower than in the whole group of patients with PRNU (n = 252), respectively, 221.9 ± 7.3 points versus 283.1 ± 8, 1 point (1=3.7; p<0.001).

Table 2. The structure of psychological disorders of the neurotic level in patients with various forms of coronary heart disease in the initial state

Form ischemic heart disease	Without PRNU (n=45)	With PRNS (n=252)			
		Total (n=252)	TFR (n=90)	DR (n=61)	TDR (n=101)
AMI (n=104)	12 (11.5%)	92 (88.5%)	29 (27.9%)	24 (23.1%)	39 (37.5%)
NA (n=92)	11 (12.1%)	81 (87.9%)	42 (45.7%)	14 (15.2%)	25 (27.2%)
CCH (n=101)	22 (21.8%)	79 (78.2%)	19 (18.8%)	23 (22.8%)	37 (36.6%)
χ^2 (*p*) MI–NS		0.11 (*p* =0.9)	5.92 (*p* =0.015)	1.5 (*p* =0.227)	1.92 (*p* =0.166)
χ^2 (*p*) MI–SSN		3.181 (*p* =0.07)	1.81 (*p* =0.17)	0.013 (*p* =0.91)	0.001 (*p* =0.987)
χ^2 (*p*) HC–SCH		2.623 (*p* =0.11)	14.8 (*p* <0.001)	1.32 (*p* =0.25)	1.566 (*p* =0.21)
Note - Percentages of the total number of patients with a separate form of coronary artery disease are given in brackets.					

The average values of the level of stress in patients with PRNU in acute forms of coronary artery disease were higher than in chronic ones, but the differences were not statistically significant. At the same time, the average values of the stress level of each separately analyzed form of coronary artery disease were significantly higher than the corresponding indicators of patients without PRNU (in relation to AMI: 1=3.56; p =0.003; in relation to NS: 1=3.18; p= 0.002; relative to CCH: 1=2.32; p=0.022). The highest level of stress was found in AMI patients with psychopathological disorders with an unfavorable course of the disease.

In patients with acute myocardial infarction, comorbid psychopathological disorders were diagnosed in 92 (88.5%) cases, including anxiety- phobic disorders (PDI) - in 29 (27.9%), depressive disorders (DR) - in 24 (23 .1%), TDR - in 39 (37.5%). Only in 12 (11.5%) patients the psychological state was assessed as adequate to the emerging clinical situation. In unstable angina pectoris, psychopathological disorders were detected in 81 (87.9%) patients, but their structure was somewhat different; disorders in 14 (15.2%). The course of stable exertional angina was complicated by psychopathological disorders in 79 (78.2%) cases, i.e. significantly less than with AMI (p = 0.028) and ACS (p = 0.046), but in this case, the proportion of TDR was the highest in 37 patients (36.6%), against TFR in

19 (18.8%) and depressive disorders in 23 (22.8%).

In order to study the influence of psychopathological disorders on the clinical course of coronary artery disease, to determine the role of psychopharmacological correction, the frequency of occurrence of these disorders in people with a favorable and unfavorable course of the disease, which is presented in Table 3, was compared. It was found that among people without psychopathological disorders, almost two and a half times more often there was a favorable course of coronary artery disease compared with an unfavorable course - 71.1%, versus 28.9%. On the contrary, in patients with psychopathological disorders who did not receive PFT, the nature of this ratio turned out to be almost the opposite - 32.4% versus 67.6%. Moreover, the differences between these categories of patients were statistically significant (x 2 =10.7; p <0.001).

Table 3. Clinical course of various forms of coronary heart disease in patients who received and did not receive psychopharmacotherapy

Form ischemic heart disease	CFT-free PRNR(1)		PRNU+CFT (3)		Without PRNR (3)		(1) vs (2)		(1) vs (3)		(2) vs (3)	
	good.	unfavorable .	good.	unfavorable .	good.	unfavorable .	χ^2	R	χ^2	R	χ^2	R
AMI n=104	4 (33.3 %)	8 (66.7%)	55 (68.8 %)	25 (31.2%)	9 (75%)	3 (25%)	4.2	0.04	2.7	0.1	0.0 1	0.9
NA n=92	3 (30%)	7 (70%)	49 (69.0 %)	22 (30.9%)	7 (63.6 %)	4 (36.4%)	4.2	0.04	1.2 9	0.3	0.1 3	0.9
SSN n=101	5 (33.3 %)	10 (66.7%)	47 (73.4 %)	17 (26.6%)	16 (72.7 %)	6 (27.3%)	6.9	<0.0 1	4.1 5	0.04	0.0 65	0.7 8
All patients	12 (32.4 %)	25 (67.6%)	151 (70.2 %)	64 (29.8%)	32 (71.1 %)	13 (28.9%)	18. 1	<0.0 01	10. 7	<0.0 01	0.0 04	0.9 5
in % of the total number of patients in the subgroup is given in brackets												

A similar picture was found when comparing the results of observation of patients with psychopathological disorders who underwent and did not undergo psychopharmacotherapy . So, out of 215 patients who received psychotropic drugs (tofisopam , sulpiride , sertraline), in the whole group, a favorable course of coronary artery disease occurred in 70.2%, unfavorable - in 29.8%. This ratio was close to that observed in persons who did not have psychopathological disorders (x2=0.004; p =0.95) and differed significantly from the corresponding indicator in patients who had PRNU but did not receive psychotropic drugs (x2=18.1; p <0.001) .

The assessment of dynamic changes in the structure of PRNU against the background of ongoing PFT showed that patients with a favorable course of coronary artery disease had a more frequent positive psychotropic effect of the drugs used, which is clearly shown in Figure 1. From the data presented, it can be seen that the percentage of patients who stopped clinically significant psychological disorders levels against the background of ongoing psychopharmacotherapy was significantly higher among those with a favorable course of coronary artery disease. On the contrary, in patients who did not receive psychotropic drugs, the structure of PRNU did

not change significantly, which was associated with a low incidence of a favorable course of coronary artery disease.

The results of the study showed that PRNU are more often combined with an unfavorable course of any form of coronary artery disease, which allows us to think about their contribution to the formation of an unfavorable course of coronary insufficiency. The obtained data are consistent with the results of studies of recent years, indicating the role of PrNy as an aggravating factor in the course of somatic diseases, as well as the fundamental possibility of influencing the nature of the course by supplementing basic therapy with means of psychopharmacological correction [15].

An analysis of dynamic changes in the structure of PRNU against the background of PFT showed their decrease against the background of taking each of the studied drugs. The most pronounced effect was exerted by sertraline in patients with depressive disorders and TDD, tofisopam was most effective in patients with TFR and somewhat less frequently in depressive disorders. Sulpiride acted approximately equally effectively in depressive and TDD. When using tofisopam, a clear positive trend was observed in relation to TFR, which was expressed in an almost 4.5-fold decrease in their frequency by the time the effectiveness of therapy was assessed, a less pronounced positive effect of the drug was manifested in TDD (2.8 times) and somewhat less often in depressive disorders (2.13 times). When using sulpiride, the most pronounced effects were observed in relation to DR (4.5 times), somewhat less pronounced - with TDR (more than 3.9 times) and significantly less often - in patients with TFR (2.5 times). The study of sertraline showed the most pronounced positive effect in patients with depressive disorders, which manifested itself in a decrease in their frequency while taking the drug by 6 times, a less pronounced effect was manifested in TDD (more than 3.86 times) and a slightly smaller effect in TFD (in 2.6 times).

It should be noted that the psychotropic drugs used by us have a minimal potential for behavioral toxicity and have a relatively wide spectrum of psychotropic effects. Common to these drugs is not only the absence of a cardiotoxic effect, but also the positive clinical experience of their use in cardiological practice [16-23]. Data on the safety of these drugs in patients with CVD, demonstrated in other studies, were also confirmed in our work. The analysis showed a low frequency of side effects of the ongoing PFT (4.39%), which did not require discontinuation of the studied drugs in any case.

The obtained data on the positive clinical course of IHD in a significant proportion of patients with achieved correction of PRNU with psychotropic drugs substantiates the feasibility of a more detailed study of the ratios of PRNU, their psychopharmacological correction with the clinical course of IHD and somatic indicators characterizing the severity of coronary insufficiency. For this, an intergroup comparative analysis of the clinical parameters of patients with AMI, NS, CHF was carried out, which revealed the most informative signs that differentiate patients with or without a positive effect of the therapy with a favorable and unfavorable course of each form of coronary artery disease. In accordance with the methodology used, the diagnostic table is a set of selected features, with the corresponding diagnostic coefficients (DC). DC is a quantitative measure (weight) of the information content of each analyzed feature, which affects the formation of a conclusion for assigning the patient to one of the alternative groups - with a favorable or unfavorable course of the disease. These data were the basis for the development of a mathematical model in the form of diagnostic tables for predicting clinical efficacy of PFT [24].

The proposed algorithm is a series of sequential steps with the identification of PRNU, the achievement of optimal basic drug therapy for coronary artery disease, the inclusion of psychopharmacotherapy , a clinical assessment of the significance of the achieved correction of psychopathological disorders, the stratification of the risk of an unfavorable somatic course of the disease (with fixation and calculation of the total DC and the use of

developed diagnostic tables, depending on on the form of coronary artery disease) and the conclusion about the advisability of continuing anti-ischemic therapy with enhanced PFT or the need for invasive and/or cardiac surgery.

Conclusion _ Psychological disorders of the neurotic level are more often combined with an unfavorable course of coronary artery disease and, in the absence of timely correction, tend to worsen, having a significant negative impact on the clinical course of all major forms of the disease. Subject to the achievement of positive psychotropic effects of the studied drugs (monotherapy tofisopam , sertraline or sulpiride in medium therapeutic doses) the effect of potentiation of basic therapy is manifested in most patients with coronary artery disease, which can significantly increase the proportion of people with a favorable clinical course of the disease.

This pattern, reflecting the fundamental possibility of potentiating anti-ischemic therapy through psychopharmacological correction, manifests itself regardless of the form of the disease and is explained by the elimination of the negative impact of neurotic psychological disorders on its course.

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