www.ThePharmaJournal.com

# The Pharma Innovation

**Pertseva NO**
State Establishment
Dnipropetrovsk Medical
Academy of MHC of Ukraine,
Dnipro, Ukraine

**Khrustaliova LO**
State Establishment
Dnipropetrovsk Medical
Academy of MHC of Ukraine,
Dnipro, Ukraine

# Influence of diabetes mellitus type 2 on manifestation of anxiety in patients with myocardial revascularization

## Pertseva NO and Khrustaliova LO

**Abstract**
Influence on diabetes mellitus type 2 on manifestation of anxiety in patients with myocardial revascularization has been studied. Three groups of patients were selected: patients with coronary artery bypass grafting; patients with stenting of coronary arteries; patients who received drug therapy. The research has shown that diabetes increases the risk for development of superficial wound infections, renal insufficiency after coronary artery bypass grafting, however patients with diabetes do not obligatory have the increased risk for development of severe complications and mortality after the surgery.

**Keywords:** Anxiety, diabetes mellitus, stable coronary artery disease

## Introduction

Ischemic heart disease (IHD) and diabetes mellitus (DM) type 2 are widespread pathologies which frequently combine and potentiate each other. Diabetes mellitus is the main factor in development of cardio-vascular diseases (CVD), and the patients who suffer from circulatory system diseases are more prone to diabetes [1].

At present the active implementation of surgical methods of treating patients with IHD, particularly patients with myocardial infarction (MI) with unstable angina pectoris is taking place in Ukraine [2].+

The presence of DM in patients with surgical restore of cardiac blood flow is a factor in development of unfavorable cardiologic and psychosomatic conditions. Insulin-dependent diabetes mellitus as well as insulin-independent diabetes are potential factors in the development of myocardial infarction and heart failure in patients with ischemic heart disease who survived cardio-surgical interventions [3].

Although a peripheral vascular disease does not affect early results of coronary artery bypass grafting, it has been proven that it is an independent predictor for a negative long-term survival among patients with myocardial revascularization [4].

The increased risk for cardio-vascular complications has also been associated with emotional disorders which are explained by behavioral and biological mechanisms [5]. The carried out biological examinations show that negative psychological conditions are connected with a higher body mass index, hypertonia, hypercholesterolemia and diabetes [6].

Anxiety symptoms are associated with the increased risk for ischemic heart disease, both in combination with depression disorders and independent of it [7].

Ukrainian researches have proven that the patients with DM 2 type with anxiety-depressive disorders have the diseases which are accompanied by more frequent appearance of atherosclerotic damages, including joint damage from different areas [8]. The course of the IHD, comorbid with the metabolic syndrome, is associated with a higher level of anxiety and depression, which correlates with such components of the metabolic syndrome as abdominal obesity, dyslipidemia and hyperglycemia [9].

A sufficient number of researches both in Ukraine and abroad have been focused on studies associated with IHD risk factors and comorbid pathologies [5, 6, 8-10]. At that the long-term estimation of the anxiety level in patients with IHD who had myocardial revascularization and its connection with the presence of DM 2 type have been insufficiently studied which enabled us to carry out the present research.

The purpose of the research is to study the influence of diabetes mellitus type 2 on manifestations of anxiety throughout a year in patients with surgical and conservative methods of IHD treatment.

**Correspondence**
**Pertseva NO**
State Establishment
Dnipropetrovsk Medical
Academy of MHC of Ukraine,
Dnipro, Ukraine

**Materials and methods:** 215 patients with IHD (165 males and 50 females) who underwent treatment in departments of cardiology, intervention cardiology, and cardio-surgery in SE "Dnipropetrovsk Regional Clinical Center of Cardiology and Cardiac Surgery of DRC" from 2010 to 2016 were included in the study. The age of the patients ranged from 39 to 82 years old, the average age was $59.81\pm0.66$ (9.61) years – M±m (SD).

Three groups of patients have been studied: I group (61 patients) – patients who had coronary artery bypass grafting (CABG); II group (85 patients) – patients who had stenting of coronary arteries (SCA) and III group (69 patients) – patients who received drug therapy. Depending on the presence or absence of diabetes mellitus 2 type, the patients in the groups were distributed to subgroups: subgroup "a" – patients with DM 2 type; subgroup "b" – patients without DM 2 type.

During the primary hospitalization, one month and one year after the received treatment, the level of personal and reactive (situational) anxiety of the patients was evaluated by questionnaires of Ch. Spilberger in the Russian edition – Y.L. Khanina. The scales of reactivity and personal anxiety (STAI – State-Trait Anxiety Inventory) consist of 40 questions-opinions, from them 1 - 20 are designed to determine the level of reactive anxiety and 21 - 40 – to determine the level of personal anxiety. To each question there are 4 possible options to answer. The total indicator by each scale can be within the range 20 – 80 points. According to the methodology, the determination of a reactive and personal anxiety is carried out separately. The level of anxiety equal or less than 30 points is considered as low, from 31 to 45 points – moderate (middle), from 46 points and more – high [11].

The analysis of the research results was carried out using descriptive and analytical biostatistics methods in accordance with the type of feature and determined type of character of distribution of quantitative variables with the help of the software STATISTICA 6.1 (StatSoftInc., serial number AGAR909E415822FA).

The check of the normal distribution hypothesis among the studied quantitative features was held by Shapiro-Wilk criterion, evenness of variance – by Fisher test. Depending on the results of the check, parametrical and non-parametrical methods of statistics were used. In case of a normal distribution of clinical signs, the descriptive statistics included arithmetical mean (M), its standard deviation (SD), and standard error of estimate (m). In case of distribution different from normal – median (Me) and interquartile range (25%; 75%). Respectively the estimation of significance of discrepancies in indicators: by Student's t-test for unbundled statistical sampling considering homo- and heteroscedasticity of dispersion and Student's t-test for the related samples or Mann-Whitney U-test (U) and Wilcoxon test (W) correspondingly відповідно. Determination of reliability in the discrepancy of qualitative parameters which were described in the form of relative indicators (%) was carried out using Pearson Chi-Square Test ($\chi^2$). For multiple comparison by parametric (ANOVA) and not-parametric Kruskal-Wallis one-way analysis of variance were carried out. Multiple comparisons were made considering Scheffe's method.

The presence and interconnection density between the studied parameters were determined by the results of the correlation analysis considering Spearman's rank correlation coefficient ($\rho$). Critical value for statistical significance (p) for all types of analysis were taken as <5% ($p<0.05$).

**Results and discussions:** The frequency of the studied patient with IHD and diabetes mellitus 2 type was on average 44.19% from the total sample. Though indicators ranged between 34.43% in the I studied group and 45.88% – in the II and 50.72% – in the III, there were no statistically significant differences by the presence of diabetes ($p=0.188$), which made possible to compare correctly subgroups by other indexes (Table 1).

There were no statistically significant differences in the studied groups and subgroups by age and gender structure (in all subgroups most of the subgroup were men); level of systolic blood pressure (SBP).

Subgroup 1-a was different from subgroup 1-b by indexes of diastolic blood pressure (DBP), which was lower in the subgroup of patients with coronary artery bypass graft without diabetes mellitus ($p<0.05$).

Differences between groups were determined by the heart rate (HR, per 1 minute), which was the highest in the II group 76.0 (68.0; 86.0) – Me (25%; 75%) and they were significantly different from indices in I and III groups ($p=0.022$ and $p=0.001$ respectively). There were no differences by HR in subgroups of one group ($p>0.05$).

**Table 1:** General characteristics of the subgroups of patients with IHD

| Characteristics | I group CABG (n=61) | | II group SKA (n=85) | | III group – drug treatment (n=69) | |
|---|---|---|---|---|---|---|
| | 1-a with DM | 1-b without DM | 2-a with DM | 2-b without DM | 3-a with DM | 3-b without DM |
| Number of patients, n (%) | 21 (9.77) | 40 (18.6) | 39 (18.14) | 46 (21.4) | 35 (16.28) | 34 (15.81) |
| Males, n (%) | 17 (80.95) | 36 (90) | 30 (76.92) | 37 (80.43) | 21 (60) | 24 (70.59) |
| Females, n (%) | 4 (19.05) | 4 (10) | 9 (23.08) | 9 (19.57) | 14 (40) | 10 (29.41) |
| Age, years M±m (SD) | 59.86±2.06 (9.46) | 57.95±1.3 (8.2) | 60.95±1.45 (9.03) | 59.26±1.62 (11) | 60.79±1.3 (7.59) | 60.41±2.02 (11.76) |
| BMI, kg/m$^2$ M±m (SD) | 31.26±0.71 (3.25) | 29.35±0,52 (3.32)* | 31.07±0.78 (4.87) | 28.37±0.47 (3.21)* | 31.74±0.84 (4.99) | 29.58±1.15 (6.71) |
| SBP, mm Hg; Me (25%; 75%) | 130 (130; 140) | 130 (120; 150) | 140 (130; 160) | 132.5 (120; 150) | 140 (130; 150) | 130 (130; 147,5) |
| DBP, mm Hg; Me (25%; 75%) | 90 (80; 90) | 80 (80; 90)* | 80 (80; 90) | 80 (80; 90) | 87.5 (80; 90) | 80.5 (80; 90) |
| HR per 1 min. Me (25%; 75%) | 68 (67.5; 80) | 69 (68; 76) | 78 (72; 87) | 72.5 (68; 80) | 70 (68; 76) | 68 (64; 73) |
| 6-minute walk test, m; Me (25%; 75%) | 200 (150; 350) | 250 (150; 400) | 175 (150; 200) | 250 (200; 300)* | 250 (200; 300) | 350 (300; 450)* |
| Glucose, mmol/l Me (25%;75%) | 7.5 (6.3; 9.7) | 4.7 (4; 4.9)* | 7.2 (6.1; 9.3) | 4.25 (4; 5)* | 8.4 (6.4; 11.5) | 4.4 (3.9; 4.8)* |

Note * – differences between subgroups "a" and "b" at the level of statistical significance $p<0.05$

Between groups with different treatment approaches no differences by body mass index (BMI) were revealed. At the same time statistically significant differences between subgroups I and II groups with revascularization of myocardium and BMI were revealed of, the former in the patients with diabetes mellitus type 2 was higher than that in the patients without diabetes ($p=0.036$ and $p=0.003$ respectively). In the group with drug treatment, patients with DM had on average higher BMI but without statistically significant differences ($p>0.05$).

By the distance of the 6-minute walk test the highest indicator was revealed in the group with drug treatment without diabetes mellitus ($p<0.05$ compared with the corresponding subgroup with DM type 2). Moreover diabetes influenced the functional condition of the patients in the group with stenting of the coronary arteries; in the latter the increase in the distance of the 6-minte test in patients without DM was observed. Nonetheless the same trend without statistically significant differences was determined in the CABG group.

By the level of glucose all subgroups without diabetes mellitus were statistically different ($p<0.05$) from the subgroup "a" with DM, there the level of glucose was significantly higher.

The essential characteristic of emotional disorders in patients with IHD is the presence and severity of expressing anxiety. The determination of anxiety (situational) and features of anxiety in the examined patients which was carried out using the Scales of Spielberg-Khanina (Fig. 1) revealed that the level of anxiety of patients with diabetes mellitus is higher (45.00±1.53 (8.25) points in case of reactive anxiety, 56.48±1.42 (7.66) points – in personal) in comparison with patients with IHD without DM (40.90±0.82 (8.45) points in case of reactive anxiety, 54.01±0.70 (7.23) points – in personal), for situational anxiety with statistically significant difference ($p<0.05$).

During the analysis of the level of anxiety in the studied groups depending on the level of presence of DM (Table 2), it was revealed that the level of anxiety in patient with CABG did not depend on the course of diabetes at the initial stage of treatment and in a short-term period after it, however, the level of both personal and reactive anxiety in the subgroups with DM was higher without statistically significant differences. In the long-term period one year after the surgery, patients of 1-a subgroup with diabetes mellitus showed reliably higher ($p<0.05$) indexes of both personal (46.19±1.21 versus 41.7±1.15), and reactive (35±1.36 versus 29.83±0.9) anxiety, which can be explained by the influence of manifestation of diabetes mellitus on psychological-emotional condition of the patients.
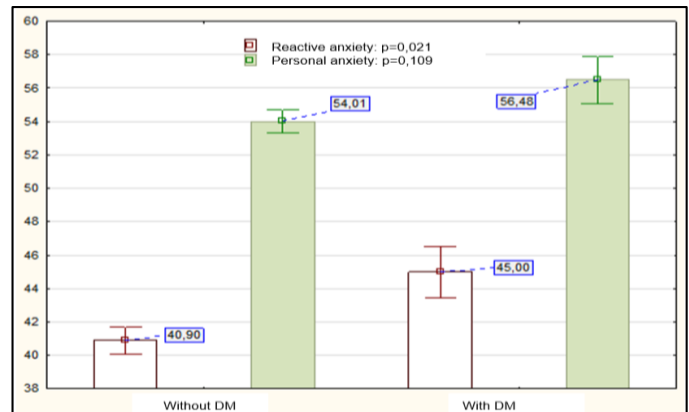


**Fig 1:** Average level of personal and reactive anxiety in the studied patients with IHD depending on the presence of diabetes mellitus type 2 (M±m, points)

In the group with stenting of the coronary arteries and in patients with drug treatment at the initial stage of the examination, the level of both personal and reactive anxiety in patients with diabetes mellitus was higher. In groups with myocardial revascularization the anxiety gradually decreased in dynamics during a year, unlike patients with drug treatment both in groups with IHD accompanied by DM and in comparison groups.

**Table 2:** Average indexes of anxiety in subgroups of the studied patients with IHD at different stages of treatment

| Level of anxiety M±m (SD) | Group 1 CABG (n=61) | | Group 2 SCA (n=85) | | Group 3 Drug treatment (n=69) | |
|---|---|---|---|---|---|---|
| | 1-a with DM (n=21) | 1-b without DM (n=40) | 2-a with DM (n=39) | 2-b without DM (n=46) | 3-a with DM (n=35) | 3-b without DM (n=34) |
| Personal anxiety | | | | | | |
| Visit 1 | 50.95±0.95 (4.36) | 49.93±0.86 (5.44) | 61.33±0.66 (4.1) | 52.57±0.93 (6.31)* | 61.54±0.26 (1.52) | 59.41±0.95 (5.54)* |
| Visit 2 | 48.95±1.14 (5.22) | 46.7±0.8 (5.08) | 45.18±0.91 (5.71) | 47.26±0.88 (5.94) | 62.69±0.18 (1.05) | 60.47±0.99 (5.75)* |
| Visit 3 | 46.19±1.21 (5.56) | 41.7±1.15 (7.27)* | 35.21±0.67 (4.21) | 43.13±1.22 (8.29)* | 63.49±0.4 (2.36) | 61.74±0.98 (5.71) |
| Discrepancies in dynamics | $p_{2-1}=0.166$ $p_{3-2}=0.068$ $p_{3-1}=0.005$ | $p_{2-1}=0.005$ $p_{3-2}<0.001$ $p_{3-1}<0.001$ | $p_{2-1}<0.001$ $p_{3-2}<0.001$ $p_{3-1}<0.001$ | $p_{2-1}<0.001$ $p_{3-2}<0.001$ $p_{3-1}<0.001$ | $p_{2-1}=0.002$ $p_{3-2}=0.069$ $p_{3-1}=0.001$ | $p_{2-1}=0.375$ $p_{3-2}=0.260$ $p_{3-1}=0.039$ |
| Reactive anxiety | | | | | | |
| Visit 1 | 39.05±0.97 (4.44) | 38.25±0.87 (5.48) | 48.92±0.72 (4.51) | 39.11±1.07 (7.23)* | 52.03±0.13 (0.75) | 45.38±1.64 (9.59)* |
| Visit 2 | 36.9±1.43 (6.53) | 36.45±0.84 (5.33) | 38.15±0.56 (3.47) | 36.04±0.95 (6.45) | 54.17±0.14 (0.82) | 46.53±1.48 (8.62)* |
| Visit 3 | 35±1.36 (6.24) | 29.83±0.9 (5.72)* | 27.62±0.53 (3.33) | 31.96±1.24 (8.44)* | 52.74±0.14 (0.85) | 46.21±1.58 (9.2)* |
| Discrepancies in dynamics | $p_{2-1}=0.108$ $p_{3-2}=0.140$ $p_{3-1}=0.023$ | $p_{2-1}=0.117$ $p_{3-2}<0.001$ $p_{3-1}<0.001$ | $p_{2-1}<0.001$ $p_{3-2}<0.001$ $p_{3-1}<0.001$ | $p_{2-1}=0.001$ $p_{3-2}=0.001$ $p_{3-1}<0.001$ | $p_{2-1}<0.001$ $p_{3-2}<0.001$ $p_{3-1}=0.001$ | $p_{2-1}=0.420$ $p_{3-2}=0.808$ $p_{3-1}=0.665$ |

Notes. Discrepancies in dynamics:
$p_{2-1}$ – between 2nd and 1st visits;
$p_{3-2}$ – between 3rd and 2nd visits;
$p_{3-1}$ – between 3rd and 1st visits;
* – discrepancies between subgroups "a" and "b" at the level of statistical significance $p<0,05$

The influence of diabetes mellitus on the increase in the level of both personal and reactive anxiety can be observed in patients with a surgical recovery of cardiac blood supply (both in case of CABG and stenting of the coronary arteries) at the initial stage of treatment and one year after the intervention, in patients with drug treatment – during the whole period of examination. At first examination which coincided with the assignment of the corresponding method of treatment (surgical or conservative) reactive anxiety as a reaction of a person to a stressful situation was the highest in IHD patients with diabetes mellitus who were prescribed drug treatment – 52.03±0.13 (0.75) points. One month later this subgroup showed the increase in the level of reactive anxiety ($p<0,001$), after one year it decreased ($p=0.001$), not reaching the initial level. In the subgroup of IHD patients without diabetes mellitus, who were prescribed conservative treatment, reactive anxiety in all stages of observation was significantly lower ($p<0.05$) and remained almost stable in dynamics ($p>0.05$).

The increased personal anxiety, which is considered as a relatively stable individual trait of a personality, is higher than the level of reactive anxiety in all studied subgroups. If a personal anxiety is a stable individual characteristic, the condition of the reactive anxiety can be rather dynamic both by time and the degree of expression [4].

Reactive (situational) anxiety – is a condition characterized by the level of a person's anxiety which develops in a certain stressful situation. If at the beginning of the treatment and in a short-term period or the surgical intervention if needed, the determination of the treatment approach is that stressful situation then one year later among stressful factors concomitant, comorbid pathologies are essential, they degrade the quality of life, in particular diabetes mellitus. This conclusion is confirmed by the results of the estimations in group 3 in which 1 year after basic drug treatment a high level of reactive anxiety (45 points and higher) was observed in all patients with DM unlike the patients with isolated IHD (Fig. 2).
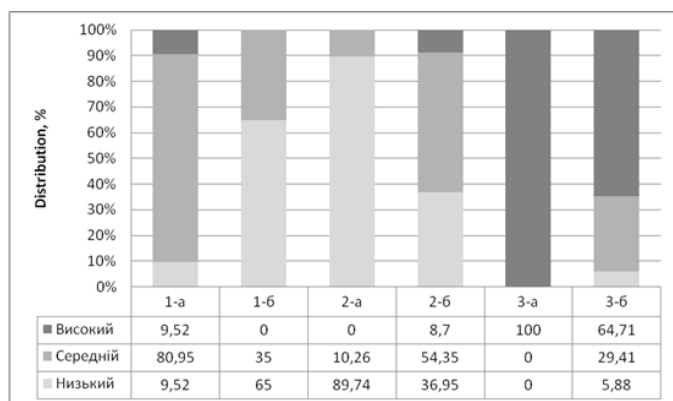


**Fig 2:** Distribution by the expression of reactive anxiety level in subgroups of patients with IHD 1 year after the beginning of treatment, n (%)

According to the rank correlation analysis it was determined that the presence of diabetes mellitus type 2 correlates in patients with IHD, who require myocardial vascularization, with BMI (Spearman's rank correlation coefficient – ρ=0.29; *p=0.001*); with SBP (ρ=0.15; *p=0.034*); with DBP (ρ=0.31; *p=0.018*); strong connection with the level of glucose (ρ=0.76; *p<0.001*) and inverse relationship with the results of 6-minute walk test (ρ=-0.33; *p<0.001*).

The presence or absence of DM in patients influences the level of reactive anxiety of the studied patients, which is significantly manifested at the primary level of treatment – statistically significant correlation connection was determined between the level of reactive anxiety and presence of DM (ρ=0.19; *p=0.022*), which is most manifested in the group which requires stenting of the coronary arteries (ρ=0.50; *p<0.001*).

**Conclusions:** As a result of the carried out research we can conclude that the patients who have severe forms of ischemic heart disease and require recovery cardiac blood supply with diabetes mellitus type 2 represent a group with a higher risk due to major vascular disorders. It has been confirmed by the direct connection between DM and the increased level of SBP (ρ=0.15; *p=0.034*) and DBP (ρ=0.31; *p=0.018*), inverse – with the distance of a 6-minute walk test (ρ=-0.33; *p<0.001*).
The course of IHD, comorbid with DM type 2 is associated with a higher level of reactive anxiety (ρ=0.19; *p=0.022*).
Diabetes mellitus considering a complicated regime of control and treatment as well as multiple somatic manifestations, acute and chronic complications, provides the increased influence on the emotional condition of patients, which is reflected in the increased level of anxiety, especially reactive anxiety which is the highest and provides no positive dynamics in the long-term prospect in the group of patients who are prescribed conservative treatment.
The presence of DM type 2 worsens the quality of life of patients with IHD due to the increased level of anxiety both in short-term and long-term periods therefore such patients should be rendered utmost care and thorough medical control and examination.
Prospects for further research can be considered in finding out whether drug treatment of anxiety disorders influences the psychological-emotional condition of patients with myocardial vascularization and the condition of their cardio-vascular system.

**References**
1. Bartnik N, Rydén L, Ferrari R *et al*. The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe. The Euro Heart Survey on diabetes and the heart. Eur. Heart J. 2004; 25:1880-1890.
2. Shulghai AG, Terenda NO. Myocardial revascularization – the leading technique in treatment of the ischemic heart disease and myocardial infarction. Hospital Surgery. 2016; 4:84-87.
3. Marcheix B, Vanden Eynden F, Demers P *et al*. Influence of diabetes mellitus on long-term survival in systematic off-pump coronary artery bypass surgery. Ann Thorac Surg. 2008; 86(4):1181-1189.
4. Chu D, Bakaeen FG, Wang XL *et al*. The impact of peripheral vascular disease on long-term survival after coronary artery bypass graft surgery. Ann Thorac Surg. 2008; 86(4):1175-1180.
5. Tully PJ, Baker RA. Depression, anxiety, and cardiac morbidity outcomes after coronary artery bypass surgery: a contemporary and practical review. J Geriatr Cardiol. 2012; 9:197-208.
6. Barger SD, Sydeman SJ. Does generalized anxiety disorder predict coronary heart disease risk factors independently of major depressive disorder? J Affect Disord. 2005; 88:87-91.
7. Celano CM, Daunis DJ, Lokko HN *et al*. Anxiety

Disorders and Cardiovascular Disease. Curr Psychiatry Rep. 2016; 18(11):101-121.

8. Khimion LV, Rybytska MO. Combined atherosclerotic damage in patients with diabetes mellitus type 2. International Endocrine Journal. 2016; 3(75):99-103.

9. Mikhailovskaya NS, Litvinenki VA, Melnik AI. Interconnection between anxiety-depressive disorders with the course of ischemic heart disease, comorbid and metabolic syndromes. Zaporozhskiy Meditsynskiy Journal. 2015; 5:23-27.

10. Korchina TY. Ischemic heart disease at diabetes mellitus. Issues of pathogenesis, diagnostics and surgical treatment. Tomsk STT. 2002; 1:352.

11. Sidorov PI. Psycho-somatic medicine: Guidelines for doctors. MED pressing form. 2006: 568.