



## TREATMENT OF COMORBID PATHOLOGY OF CHRONIC HEART FAILURE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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### ANNOTATION:

The article presents data from a scientific study on the role of the influence of comorbid pathologies such as: diabetes mellitus (DM) in patients with chronic heart failure (CHF), pathogenetic mechanisms for the development of heart failure in patients with DM, risk factors for developing CHF (hyperglycemia, increased body mass index, age, coronary heart disease, nephropathy, proteinuria, duration of diabetes, etc.). The results of the analysis of mortality in patients with or without DM depending on the ejection fraction are shown. The characteristics of various drugs for the treatment of CHF, including in patients with DM, are given, promising directions for the treatment of this group of patients are highlighted. Treatment has been shown to be effective with lifestyle changes: weight loss, exercise, diet, etc. in obese patients with and without DM.

**Relevance.** The relevance of studying chronic heart failure (CHF) in patients with diabetes mellitus (DM) is due to the prevalence of these diseases. The continuing rapid increase in the number of patients with DM is becoming an alarming non-infectious epidemic [1,2,10,13]. The association of DM and CHF is not accidental and is due to mutually aggravating multisystem disorders [3,6,9,11,12]. The relationship between DM and CHF is based on such common pathophysiological processes as neurohumoral activation, endothelial dysfunction, and oxidative stress [4,5,7,8,9]. Both in CHF and DM, the heart, liver, and kidneys are the main target organs that determine the prognosis and progression of both diseases. And the presence of specific metabolic disorders inherent in DM: hyperglycemia, insulin resistance (IR), dysregulation of lipid metabolism, increased levels of circulating free fatty

acids (FFA), as well as pronounced microcirculatory disorders, contribute to the rapid and irreversible progression of target organ damage.

**Purpose of the study:** based on the data of a retrospective analysis of the case histories of patients suffering from coronary artery disease, with type 2 diabetes and with normal carbohydrate metabolism and a prospective study involving patients with ischemic heart disease and chronic heart failure with type 2 diabetes and with normal carbohydrate metabolism, to study the severity of CHF depending on the presence of disorders of carbohydrate metabolism.

**Materials and research methods.** A retrospective analysis of 86 case histories of patients who were treated in the emergency departments of the RRCEMMP in Bukhara in the period from 2021 to 2022 was carried out. The case histories of men and women aged 55 to 75 years who were discharged from the hospital with diagnoses of unstable angina pectoris were analyzed, acute myocardial infarction (AMI) Q-, AMI Q+. In 1417 case histories, patients had normal carbohydrate metabolism (the first group, 41 men and 15 women) and in 30 cases they had T2DM (the second group, 14 men and 16 women). The groups were comparable in terms of age and BMI. We studied the prevalence of CHF II-IV FC according to NYHA, postinfarction cardiosclerosis (PICS), AMI Q-, AMI Q+, chronic LV aneurysm, permanent and paroxysmal forms of atrial fibrillation.

The prospective study involved 102 patients aged 60-80 years who were treated in the emergency cardiology departments of the RRCEMMP in Bukhara in the period from 2021 to 2022. The main group consisted of 65 patients with DM lasting 5 years or more, complicated by DACH (diagnosis of DACH were set on the basis of the results of the Ewing tests) in combination with CHF II-III FC according to NYHA and IHD. It has been established that with duration of DM2 for more than 5 years, the frequency of DACH increases statistically significantly [8], therefore, such patients are a group with a high probability of having DACH. The control group included 37 patients with CHF II-III FC according to NYHA and coronary artery disease, who did not have carbohydrate metabolism disorders. All patients underwent a general clinical examination, a 6-minute walk test (TSW), echocardiography, an assessment of the severity of pain in the region of the heart and dyspnea after exercise using the VAS, Holter ECG monitoring. Statistical processing of the obtained data was performed using the Statistica StatSoft Inc. software package (USA), version 6.0. Differences were considered significant at  $p < 0.05$ .

**Research results.** According to the results of this study, we found out in patients of both groups the severity of their anamnesis, bad habits, lifestyle, eating habits, which is not unimportant for determining the tactics of treating this comorbid condition. At the same time, it was found that, in the first group of 65 patients, 21 had a aggravated anamnesis, while in the second, 6. Bad habits in the form of smoking were recorded in 35 patients of the first and 7 from the second group. Alcohol intake was emphasized once a month in 15 of the first and 8 of the second group, more than 2 times a month in 9 patients of the first and 4 of the second group. Walking more than 1 km per day was noted by 31 patients of the first and 19 of the second group, more than 3 km by 12 in the first and 6 in the second group. A healthy lifestyle is currently supported by 27 patients in the first and 28 patients in the second group. The stress state was noted once a week by 28 from the first and 7 from the second group, while once a month 15 and 8 were noted in both groups of patients, respectively. The reception of semi-finished products once a week was noted by 9 of the first and 5 of the second group. All of the above data are shown in Table 1. See Table 1 below.

**Table 1. Lifestyle supported by patients in both groups.**

Name	First group (n=65)	Second group (n=37)
Burdened history	21	6
Smoking	35	7
Drinking alcohol once a month	15	8
Drinking alcohol more than 2 times a month	9	4
Walking more than 1 km per day	31	19
Walking more than 3 km per day	12	6
Maintaining a healthy lifestyle	27	28
Stress once a week	28	7
Stress condition once a week once a month	15	8
Reception of semi-finished products once a week	9	5

This table shows the etiological factors that could serve to worsen or worsen the condition of patients. In the first study group, bad habits and stress, a sedentary lifestyle dominates the indicators of the second group. On the one hand, this explains the deterioration in the performance of these patients.

Patients in both groups underwent ECG, Holter monitoring. Patients in both groups took  $\beta$ -blockers and hypoglycemic drugs in the form of metformin. During ECG Holter monitoring, we revealed a statistically significantly higher average heart rate and a higher incidence of ventricular extrasystoles in the main group ( $p < 0.05$ ). According to the results of our study, patients of the main group needed higher doses of  $\beta$ -blockers to control their heart rate. The average dose of bisoprolol in the main group was  $6.42 \pm 1.9$  mg, in the control group —  $3.92 \pm 1.5$  mg ( $p < 0.05$ ).

A retrospective analysis showed a statistically significant ( $p < 0.01$ ) increase in the incidence of PICS, Q+ AMI, chronic LV aneurysm, CHF II–IV FC according to NYHA, paroxysmal and permanent forms of atrial fibrillation in T2DM compared with patients without carbohydrate metabolism disorders. Thus, we confirmed the existing opinion about the effect of chronic hyperglycemia on the development of macroangiopathy with manifestations in the form of AMI complicated by LV aneurysm and the formation of CHF.

According to our study, in patients with CHF and DACH, there are more pronounced clinical manifestations of CHF during TSH, less tolerance to physical activity compared with patients with CHF who do not suffer from carbohydrate metabolism disorders. The distance covered during TST was statistically significantly less in the main group ( $p < 0.01$ ) than in the control group:  $304.0 \pm 54.3$  m versus  $371.51 \pm 41.48$  m. groups were forced to make statistically significantly more stops due to the appearance of severe dyspnea and chest pain than participants in the control group.

With the use of metformin at a dose of 500 mg in patients of the first group, the blood sugar level reached an average of 8.7 mmol/l, in the second group at the same dosage, 6.95 mmol/l was noted when analyzed on an empty stomach. Whereas outside the intake of metformin it was 10.1 mmol/l, and in the second group it was 8.75 mmol/l. The initial arterial pressure in the first group was 175/100 mm Hg, while in the second it was noted at the level of 165/90 mm Hg. After treatment with  $\beta$ -blockers and hypoglycemic drugs in combination, these indicators decreased to the level of 155/90 mm Hg. in the first and 150/85 mm Hg. in the second one, respectively. These indicators are shown in table 2.

**Table 2. Blood pressure and blood sugar levels before and after treatment in the compared groups.**

Parameters under study	First group		Second group	
	Before treatment	After treatment	Before treatment	After treatment
Arterial pressure, mm Hg	175/100	155/90	165/90	150/85
Blood sugar level, mmol/l	10,1	8,7	8,75	6,95

From the above indicators it can be seen that, in the first group, both the initial and post-treatment indicators were significantly higher than in the first group. Reliability of indicators  $p \leq 0.05$ .

Using a simple and demonstrative method for characterizing the clinical manifestations of CHF-VAS-subjective manifestations of CHF after exercise were assessed. The severity of dyspnea and chest pain was significantly higher in the main group ( $p < 0.05$  for both parameters). Thus, according to our data, the subjective manifestations of CHF in patients with coronary heart disease suffering from type 2 diabetes were stronger after exercise than in patients with normal carbohydrate metabolism. The parameters obtained during the echocardiography did not have significant differences between the groups ( $p > 0.05$ ). Both in the main and in the control group deviations from the norm were observed.

It should be noted that rest tachycardia is an early symptom of DACH, its development is associated with damage primarily to the vagus nerve with a relative predominance of the tone of the sympathetic division of the autonomic nervous system. The same opinion is shared by a number of researchers who studied the causes of resting tachycardia in patients with type 2 diabetes complicated by DACH. Without a doubt, increased activity of the sympathetic and reduced activity of the parasympathetic nervous system reduce the threshold for ventricular fibrillation, and the use of  $\beta$ -blockers in an adequate dose, selected taking into account individual characteristics, can achieve a decrease in heart rate and thereby improve the condition of patients, which was achieved in our study.

There was a statistically significant increase in the incidence of PICS, Q+ AMI, chronic LV aneurysm, CHF II-IV FC according to NYHA, paroxysmal and permanent forms of atrial fibrillation in T2DM compared with patients with normal carbohydrate metabolism ( $p < 0.01$  for all parameters). It has been established that the development and course of CHF is significantly affected by the presence of a history of previous myocardial infarction, cardiac

arrhythmias, and chronic LV aneurysm. This should be taken into account when studying the characteristics of the course of CHF in a particular cohort of patients.

According to our study, in patients with CHF and T2DM, more pronounced clinical manifestations of CHF were noted during TSH, less tolerance to physical activity compared to patients with CHF who did not suffer from carbohydrate metabolism disorders.

**Conclusion.** Based on the data of a retrospective analysis of the case histories of patients with coronary artery disease suffering from type 2 diabetes mellitus (DM2), a significant increase in the incidence of postinfarction cardiosclerosis, acute myocardial infarction Q+, chronic LV aneurysm, paroxysmal and permanent forms of atrial fibrillation was established in comparison with patients with coronary artery disease with normal carbohydrate metabolism, which determines more pronounced clinical manifestations of CHF. In patients with IHD and T2DM, CHF III FC occurs approximately 3 times, and IV FC - 2 times more often than in patients with IHD with normal carbohydrate metabolism. In patients with coronary artery disease suffering from type 2 diabetes, according to ECG Holter monitoring, the average heart rate is higher, ventricular extrasystoles are more often detected, which requires the appointment of higher doses of  $\beta$ -blockers to achieve target heart rates.

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## DIAGNOSTIC MARKERS OF OSTEOPOROSIS IN WOMEN IN MENOPAUSE

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### ANNOTATION:

Osteoporosis is a skeletal disease characterized by low bone mass, structural destruction of bone tissue and reduced bone strength, resulting in increased the risk of fractures [1,2,9]. It is one of the most common metabolic diseases and the main cause of morbidity and mortality among postmenopausal women [3,10]. Previous studies have shown that several conditions such as aging, amenorrhea, parental history of fractures, [4,5] dietary calcium intake, low body mass index (BMI) [6,7,8], decreased physical activity have been suggested as associated factors in changes in bone mineral density in elderly patients.

**Relevance.** Prior to menopause, the level of bone loss tissue in men and women is almost the same. But after the patients enter this phase of their life, they have an almost 1.5-fold increase in the chance of spontaneous fractures in comparison with the opposite sex. This is explained by the decline in estrogen levels as a consequence of menopause [1,2,4,5]. Since, it maintains a balance between resorption and bone formation. In the present study, we hoped to assess the prevalence of osteoporosis in postmenopausal women in urban and rural areas of Bukhara city, as well as to determine the risks of osteoporosis in all participants. We also analyzed the relationship between BMD (bone mineral density) and biochemical markers.



**The aim of the study** was to determine the criteria for diagnosing menopausal osteoporosis in different periods of menopause to prevent complications and improve the quality of life of women in this period.

**Materials and methods of research.** The material for our research was women living in the Bukhara region. Patients who applied to the Republican Scientific Center for Emergency Medical Aid of the Bukhara branch in different departments under different diagnoses: such as dysfunctional uterine bleeding, anovulatory uterine bleeding, climacteric syndrome, arterial hypertension, hypertensive crisis. These patients were studied from 2019 to 2020 at this center. Postmenopausal women were defined as women who reported menopause in the survey. Only those participants who provided written informed consent and were willing to provide blood samples were included. Finally, 121 perimenopausal women were included in the analysis. The following participants were excluded: individuals whose clinical data were incomplete, postmenopausal women who underwent hormone replacement therapy, with serious chronic kidney disease, chronic liver disease or osteogenesis imperfecta, with the presence of a tumor, women who had a hysterectomy, which is known to increase risk of early menopause. All participants were interviewed using a standardized questionnaire to collect data on: age, gender, menopause status, age at menopause, year after menopause, educational level, physical activity. Statistical analysis was carried out by the Fisher-Student method using the Statistica package. Significance was set at  $p < 0.05$ .

**Study results.** According to the results of our study, the average age of menopause was  $44.05 \pm 1.1$ . It is reliably suitable for the age of menopause in the Republic of Uzbekistan. According to the results of the study, the level of estradiol in the blood serum in the group remained almost unchanged in the first group. Decreased by 3.5 pg / ml in the second group. And in the third group, it increased by 16.5 pg / ml, which indicates a significant increase in this hormone. ALP also remained slightly changed in the first and second groups, while in the third it increased by 39 U/L. The situation with calcium also correlated with the above two data and changed only in a positive direction in the third group. The mean T and Z values were lower in the third group after treatment than in the other two groups. All data are shown in table 1.

**Table No. 1.**

**Comparative data of analyzes of perimenopausal women in the**

**dynamics of treatment,  $M \pm m$**

Parameters	Group 1, n = 15		Group 2, n = 15		Group 3, n = 15	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Estradiol, pmol / l	42,4±3,4	44,9±3,4	40,4±3,8	39,6±5,2	44,4±3,4	60,9±3,4
AP units / L	224	221	220	213	219	258
Calcium dg / ml	2,1	2,0	1,9	1,84	1,68	2,14
Ultrasound densitometry (T-criteria)	1,6	1,6	2,1	2,2	2,2	1,8

**Note: reliability of the results  $p < 0.05$**

As a result of the study, it was found that the use of Lenzetto in the combined treatment of women with blood pressure in the perimenopausal period, according to daily monitoring of blood pressure, led to a significant decrease in blood pressure with its stable normalization in 76 % of patients taking only pharmacadipine, this figure was 52%. Thus, the effectiveness of antihypertensive therapy in the main group was 24% higher than in the control group ( $p < 0.01$ ).

Normalization of the daily blood pressure profile and restoration of physiological decrease in blood pressure at night were achieved in 70% of patients in the main group and in 46% in the control group (the difference between the groups is significant,  $p < 0.01$ ). In the group of patients who additionally took Lenzetto, there was a significant decrease in the average heart rate, in contrast to the control group, which was associated with a decrease in the reactivity of the sympathetic system and an improvement in the adaptive capabilities of the body (Table 2).

**Table 2. Comparative indices of hemodynamic parameters in women in the perimenopausal period before and after treatment  $M \pm m$**

Indices	Control group		Main group	
	Before treatment	After treatment	Before treatment	After treatment
24 hours				
SBP, mmHg	160,4±5,2	141,5±2,8	157,6±2,3	138,5±2,5
DBP, mmHg	97,3±3,2	89,4±3,0	95,6±2,4	84,4±2,2
HR,beats/min	77,2±2,5	74,9±2,5	79,3±2,2	65,2±2,0
Daytime				
SBP, mmHg	163,6±5,6	144,2±3,4	167,4±2,5	138,3±2,4
DBP, mmHg	99,4±3,7	89,5±3,2	101,2±2,3	86,3±2,2
HR,beats/min	82,2±2,3	76,4±2,4	83,5±2,5	68,2±2,6
Night period				
SBP, mmHg	152,5±4,2	138,4±4,3	155,4±3,2	130,2±2,5
DBP, mmHg	92,3±2,4	88,2±3,0	93,5±2,4	82,5±2,4
HR,beats/min	74,2±2,3	72,2±2,5	72,2±2,5	62,4±2,3

Thus, the inclusion of Lenzetto in the complex treatment of patients with hypertension in the perimenopausal period favorably affects the daily blood pressure profile, hemodynamic parameters and increases the standard of living of women.

**Conclusions:** Based on the results of the study, we can say that the level of estradiol and biochemical markers of bone metabolism decreased with age. Timely menopausal hormone therapy, osteotropic drugs can reduce the level of bone resorption and reduce the symptoms of menopause, which significantly impair a woman's quality of life. Further research is needed to examine bone-related research to establish better statistics among women in the Bukhara region.

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