FEATURES OF HEART FAILURE IN PATIENTS WITH CORONARY HEART DISEASE AND THYROTOXICOSIS

Yarmatov Suvon Tatlibayevich
Assistant of the Department of Propaedeutics of Internal Diseases, Samarkand State Medical University
Muzaffarova Malika Sho'hratovna
Assistant at the ABU ALI IBN SINO SIAB COLLEGE OF PUBLIC HEALTH (Samarkand)
Jurayev Javohir
Samarkand State Medical University Faculty of treatment student group 511
Meyliyev Lazizbek
Samarkand State Medical University Faculty of treatment student group 511
Samarkand State Medical University, Samarkand, Uzbekistan

Abstract *Goal. To evaluate the diagnostic significance of criteria for chronic heart failure (CHF) and to study the features of structural and functional remodeling of the left heart in patients with coronary heart disease (CHD) and thyrotoxicosis.*

Material and methods. 131 patients aged 45-65 years with coronary heart disease were examined, CHF and/or thyrotoxicosis. The clinical condition of patients and exercise tolerance were assessed, and the level of N-terminal stress was determined. A fragment of the precursor of the cerebral natriuretic peptide (NTproBNP), Holter electrocardiogram monitoring and echocardiographic examination (EchoCG) with Dopplerography were performed.

Results. Cardiac arrhythmias were detected more often in patients with coronary heart disease, CHF and thyrotoxicosis than in patients with coronary heart disease and CHF without thyrotoxicosis (atrial fibrillation, sinus tachycardia, supraventricular extrasystole), a more pronounced autonomic imbalance with a predominance of activity of the sympathetic link of the autonomic nervous system. Elevated levels of NT-proBNP (>125 pg/ml) were detected in both patients with CHF and patients with thyrotoxicosis, regardless of the presence of cardiovascular

diseases. Concentration of NT-proBNP in patients with coronary heart disease and thyrotoxicosis without CHF exceeded the threshold value by 2.8 times (p=0.001). The highest level of NT-proBNP in patients with coronary heart disease, CHF and thyrotoxicosis is due to The effect on its secretion is not only remodeling of the left ventricle (LV), but also hyperfunction of the thyroid gland. A higher threshold

value of NT-proBNP was determined (according to the results of this study — 556.4 pg/ml) for the diagnosis of CHF with preserved and intermediate LV ejection fraction (LVEF) in patients with coronary heart disease and thyrotoxicosis. The analysis of echocardiography parameters in patients with coronary heart disease, CHF and thyrotoxicosis revealed significantly lower values of linear and volumetric LV indices, LV type I diastolic dysfunction

in 100% of cases, an intermediate type of LV ejection fraction (48%), more the frequent occurrence of concentric LV hypertrophy (84% of cases).

Keywords: *chronic heart failure, coronary heart disease, thyrotoxicosis, vegetative imbalance, threshold level NT-proBNP, left ventricular remodeling.*

Conclusion. To diagnose HF in patients with coronary heart disease and thyrotoxicosis, it is necessary to take into account the features of the clinical picture, heart rate variability, L V remodeling, and use a higher threshold level of NT-proBNP.

INTRODUCTION

The prevalence of chronic heart failure (CHF) in Uzbekistan is 7-10%, and in recent years the number of patients with preserved and intermediate left ventricular ejection fraction (LVEF) has increased. In this regard, in modern recommendations

for the diagnosis and treatment of CHF, in addition to assessing clinical symptoms and signs, performing echocardiographic examination (EchoCG), much attention is paid to determining the concentration of natriuretic peptides (NPS). However, the results of a number of studies indicate that, that with increased secretion of thyroid hormones, there is also an increase in the concentration of sodium-uretic peptides (NPS). According to the data available in the available literature, there is no consensus on whether the level of NPS increases in response to structural and functional changes in the myocardium with hyperfunction of the thyroid gland, or whether thyroid hormones have a direct stimulating effect on the secretion of NPS. The frequency of occurrence of thyrotoxicosis and cardiovascular diseases (CVD) in elderly patients determines the need to study the features of the diagnosis of-

heart failure in polymorbid patients with hyperthyroidism.

The aim of the study was to evaluate the diagnostic significance of CHF criteria and to study the features of structural and functional remodeling of the left heart in patients with coronary heart disease (CHD) and thyrotoxicosis.

MATERIALS AND METHODS OF RESEARCH

The open comparative clinical study included 131 patients (average age 58.3±5.6 years), who were divided into 4 groups: the main group consisted of 30 patients with thyrotoxicosis, coronary heart disease and CHF of functional class II-III (FC) and 3 comparison groups (group 1 — 35 patients with coronary heart disease

and CHF II-III FC, without thyroid pathology; Group 2 — 35 patients with thyrotoxicosis without CVD; Group 3 — 31 patients with thyrotoxicosis and coronary heart disease, without clinical symptoms and signs of CHF). The control group consisted of 15 people without signs of CVD and thyroid pathology. The 2nd, 3rd and main groups included patients with manifest thyrotoxicosis on the background of diffuse toxic goiter or nodular/multi -nodular goiter with functional autonomy. All patients with coronary heart disease had II-III FC of angina pectoris. Diagnosis and treatment of coronary heart disease, CHF and thyrotoxicosis were carried out in accordance with modern recommendations.

To assess the clinical symptoms and signs of CHF, the clinical condition assessment scale (SHOCK), tolerance to physical activity were used The load was assessed according to the

data of the 6-minute walk test (6MTH). The concentration of NT-proBNP in blood serum was determined using reagents (Biomedica, Austria) on the automatic enzyme immunoassay analyzer “Lapis Lazuli” (Dynex Technologies, USA). Holter ECG monitoring (XM ECG) was performed using a wearable eight-channel cardiomonitor “Kardiotechnika-04” (Incart CJSC, St. Petersburg), echocardiographic examination (EchoCG)was performed on a MyLab70 ultrasound machine ("Esaote", Italy) in B and M modes, pulse-wave Doppler mode. All studies were performed before the appointment

of thyrostatic therapy.Exclusion criteria from the study: hemodynamically significant heart defects; myocardial infarction or acute cerebrovascular accident <6 months old; unstable angina pectoris; severe pathology of the liver, kidneys; presence of an artificial pacemaker; inflammatory and infectious diseases; malignant neoplasms; other thyroid diseases, including iatrogenic thyrotoxicosis.

The study was performed in accordance with the standards of good clinical practice (Good Clinical Practice) and the principles of the Helsinki Declaration. The study protocol was approved by the local independent ethics committee, and all patients signed an informed consent to participate in the study. Statistical processing was performed using the Staistica 10.0 program (StatSoft, USA). Qualitative variables described absolute (n) and relative values (%), compared by Pearson's chi-squared criterion. The reliability of the differences in independent values between several groups was determined by the Kraskell-Wallis criterion, taking into account the number of groups, $p<0.0085$ was considered reliable. The pairwise comparison of the groups was performed using the nonparametric Mann-Whitney criterion. The correlation analysis was carried out using the Spearman method. The new threshold value of NT-proBNP was calculated using ROC analysis. Differences in values in pairwise comparison, as well as correlations, were recognized significant at a significance level of $p<0.05$.

THE RESULTS AND THEIR DISCUSSION

Assessment of clinical symptoms of CHF on a scale The SHOCK did not reveal significant differences between the patients of the main and the 1st comparison group (with coronary heart disease and CHF without hyperthyroidism), however, exercise tolerance in the patients of the main group was significantly lower - by 15.4% ($p=0.01$). Analysis of the results of XM ECG showed that patients in the main group were more likely than patients in group 1 to have cardiac arrhythmias (LDC): atrial fibrillation (32% vs 20%, $p=0.01$), sinus tachycardia (36% vs 22%, $p=0.01$), supraventricular extrasystole (31% vs 18%, respectively, $p=0.01$). The highest heart rate (HR) per day was observed in 2 groups of patients: 43.2% higher than in patients of the main group ($p=0.0002$), 60.7% higher than in patients of group 1 ($p=0.0001$). The patients of the main group showed the lowest value of the median circadian index (CI), the absence of a significant decrease in heart rate during the night hours. Assessing the parameters of heart rate variability (HRV),

the lowest time values were revealed in the patients of the main group.- The indicators are SDNN, rMSSD, pNN50 ($p<0.05$), the name value of the total power of the spectrum is TP ($p<0.05$), especially due to a decrease in HF ($p<0.05$), and the highest LF/HF ratio compared with the result in comparison groups 1, 2 and 3 ($p<0.05$), which indicates a decrease in the

activity of the parasympathetic link and hyperactivation of the sympathetic link of the autonomic nervous system (VNS).

In patients of the main group, reliable correlations were established: between the level of St.T4 and the HF indicator, characterizing a decrease in parasympathetic activity against the background of concomitant thyrotoxicosis (r=-0.41, p=0.045); between the level of NT-proBNP and SHOCK data (r=0.39; p=0.001) and 6MTH (r=-0.45; p=0.001). The analysis of echocardiography parameters revealed significantly lower values of linear and volumetric LV indices in patients of the main group. Thus, in patients with coronary heart disease, CHF and thyrotoxicosis compared with the results of patients with coronary heart disease

and CHF without hyperthyroidism index The final diastolic LV size (ICDR) was

10.9% smaller (p=0.03), the indices of the final systolic (ICSO) and diastolic (ICDO) volumes-LV MOV is less by 15.03% (p=0.01) and 5.92% (p=0.03), respectively. It should be noted that in patients with CHF(main and 1 comparison groups), two types of LV remodeling were identified: concentric (KGLJ) and eccentric (EGLJ) LV hypertrophy, and KGLJ was significantly more often determined in the main group (84% vs 70%, p=0.03), and EGLJ — in the 1st comparison group (16% vs 30%, p=0.01). Analysis of the parameters of the transmittal blood flow showed that in group 2 In 90% of patients, normal LV diastolic function was determined, and in 10% of cases, LV diastolic dysfunction (LVD) Type I (relaxation slowdown). In patients of group 3, type I BPH occurred in 65.4% of cases. In the main group of 100% cases were determined by type I DL. In group 1, type I DL occurred in 86.7% of cases, type II DL (pseudonormalization) — in 10% of cases, type III DL (restrictive relaxation) — in 3.3% of cases. The highest LVEF index was determined in patients of the 2nd comparison group. It is important It should be noted that in patients of the main and group 1, the LVEF values did not significantly differ (p= 0.1) and corresponded to an intermediate type of CHF, which indicates the need to determine NT-proBNP for the diagnosis of HF in polymorbid patients with concomitant thyroid hyperfunction. A comparative analysis of the concentration of NT-proBNP revealed an increased level of the indicator (>125 pg/ml, according to current recommendations) in all studied groups of patients, including those with

thyroid toxicosis without CVD. The level of NT-proBNP in patients with coronary heart disease and thyrotoxicosis without CHF exceeded- the threshold value was 2.8 times higher (p=0.001), in patients with thyrotoxicosis without CVD - 2.04 times (p=0.001). There were no significant differences between the values of NT-proBNP in comparison groups 1 and 3 (p=0.88), and the highest level of NT-proBNP was determined in polymorbid patients with coronary heart disease, CHF

and thyrotoxicosis — 2.2 times higher than in patients with coronary heart disease and CHF without hyperthyroidism (p=0.0001). During further follow-up, against the background of therapy with the inclusion of thyrostatics and the achievement of persistent euthyroidism, significant correlations were revealed- There are significant relationships between the dynamics of TSH and NTproBNP concentrations (r=-0.53; p=0.000), St.T4 and NT-proBNP (r=0.43; p=0.001), St.T3 and NT-proBNP (r=0.35; p=0.01). The data obtained allowed us to judge the low

diagnostic significance of the recommended level NUP for the detection of CHF with preserved and intermediate LVEF in conditions of hyperfunction This led to a revision of the threshold value for this category of patients. Using ROC analysis, based on the determination of the maximum sum of the values of diagnostic sensitivity and specificity (DH+DS),- The cut-off threshold was divided, which was 556.4 pg/ml. Thus, according to our data, in patients with thyrotoxicosis and coronary heart disease at the level of NTproBNP >556.4 pg/ml, a decision is made in favor of the presence of CHF with DH 72%, DS 100%, diagnostic accuracy of 87.2% ($p<0.001$), whereas the values of NTproBNP <556.4 pg/ml do not allow to confirm the presence of check heart failure using this criterion. The area under

The ROC curve was 0.942±0.0298 ($p<0.001$), which indicates the excellent quality of the model, and the obtained indicator can be recommended for use in clinical practice. The results obtained made it possible to identify the peculiarities of the clinical picture in patients with CHF of ischemic origin in combination with hyperfunctionality of the thyroid gland. Lower exercise tolerance and more frequent occurrence of cardiac arrhythmias in this category of patients are obviously due to the additional effect of thyroid hormones on the cardiovascular system. When evaluating the results of spectral and temporal analysis of HRV indicators in patients with coronary heart disease, CHF and thyrotoxicosis revealed a more pronounced the predominance of the sympathetic link of the ANS in the regulation of heart rhythm compared with the indicators in patients with coronary heart disease and CHF without hyperfunction of the thyroid gland, which indicates an increase in vegetative imbalance with the development of concomitant-acute thyrotoxicosis. The hyperactivation of the sympathetic link of the ANS can also be judged by the features of the daily heart rate profile in patients of the main group: higher values of the maximum daily and maximum daily heart rate, as well as the absence of a significant decrease in heart rate at night, which is-It is a sign of diurnal desynchronosis. The literature describes in sufficient detail the following-

the effect of thyroid hormones on the structural and functional parameters of the heart in hyperthyroidism, however , the study of the features of cardiac remodeling

in polymorbid patients with thyrotoxicosis remains relevant. In this study , the features of structural and functional remodeling of the left heart in the presence of concomitant thyrotoxicosis in patients with CHF of ischemic origin were determined: significantly lower values of indexed linear and volumetric LV parameters, the development of type I BPH in 100% of cases, a more frequent

occurrence of BPH compared with those in patients with CHF without thyroid pathology , due to the influence of an excess of thyroid hormones and, above all, hyperactivation of the sympathetic link of the ANS. Elevated levels of NT-proBNP (>125 pg/ml) were detected both in patients with CHF and in all patients with thyrotoxicosis, regardless of the presence of CVD, which is consistent with the results of previously published studies indicating the stimulating effect of excess thyroid hormones on secretion NPS. Comparative analysis of NT-proBNP results

He showed the absence of a significant difference between the indicators in patients with coronary heart disease and CHF without hyperthyroidism and in patients with coronary heart disease and thyrotoxicosis without clinical manifestations of CHF, which allows us to think

about a comparable contribution to the increase in the level of NUP of both LV remodeling in CHF and hypersecretion of thyroid hormones. The revealed highest level of NT-proBNP in

polymorphic patients with coronary heart disease, CHF and thyrotoxicosis, apparently, reflects the combined effect of LV morpho-functional changes on the secretion of NPS and hyperthyroidism. The obtained reliable correlations between the dynamics of TSH and thyroid hormones and the concentration of NT-proBNP against the background of therapy with the inclusion of thyrostatics in patients of the main group indicate the stimulating effect of thyroid hyperfunction on the secretion of NPS. In addition, the revealed correlations between the value of NT-proBNP and the indicators of SHOCK and 6MTH, as well as the absence of significant differences when comparing the clinical manifestations of CHF in patients of the main group and the 1st comparison group, allowed-It can be argued that the higher level of NTproBNP in patients with CHF of ischemic genesis and thyrotoxicosis is due precisely to the influence of an increased concentration of thyroid hormones. It is important to note that for the diagnosis of CHF with preserved and intermediate LVEF in patients with coronary heart disease and thyrotoxicosis, it is necessary to use a higher threshold level of NT-proBNP, according to this study - 556.4 pg/ml. Determining the NTproBNP value above the specified in polymorbid patients with a combination of CVD and hyperthyroidism will make it possible to diagnose CH (DH 72%, DS 100%). However, the results of NTproBNP below the calculated threshold level do not allow us to confirm the development of CHF using this criterion, but also do not exclude its presence. Apparently, in such cases, a more thorough assessment of clinical symptoms and signs, as well as structural and functional parameters of LV, taking into account the features of remodeling in conditions of polymorbidity, is necessary.

CONCLUSIONS:

Thus, the work revealed the features of the clinical picture, the daily heart rate profile, HRV indicators, LV remodeling in patients with ischemic heart disease and thyrotoxicosis, a new threshold level of NTproBNP was calculated and proposed for the diagnosis of CHF with preserved andintermediate LV LV in polymorbid patients with thyroid hyperfunction, which will optimize the management of such patients and improve the prognosis.

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