



CLINICAL, PATHOGENETIC, AND DIAGNOSTIC FEATURES OF HEART FAILURE IN PATIENTS WITH CORONARY HEART DISEASE AND THYROTOXICOSIS

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<https://www.doi.org/10.5281/zenodo.7807749>

ARTICLE INFO

Received: 28th March 2023

Accepted: 06th April 2023

Online: 07th April 2023

KEY WORDS

Chronic heart failure, coronary artery disease, thyrotoxicosis, vegetative imbalance, threshold level of NT-proBNP, left ventricular remodeling.

ABSTRACT

Aim. To assess the diagnostic significance of chronic heart failure (CHF) criteria and to study the features of structural and functional remodeling of the left heart in patients with coronary artery disease (CAD) and thyrotoxicosis. Material and methods. We examined 131 patients aged 45-65 years with CAD, CHF and/or thyrotoxicosis. The clinical state of patients, exercise tolerance, NTproBNP level were evaluated. Holter ECG monitoring and Doppler echocardiography (echo) were performed. Results. Heart rhythm disturbances (atrial fibrillation, sinus tachycardia, supraventricular extrasystole), more severe vegetative imbalance with sympathetic predominance in patients with CAD, CHF and thyrotoxicosis were determined more often than in patients with CAD and CHF without thyrotoxicosis. Elevated levels of NT-proBNP (more than 125 pg/ml) were found in both patients with CHF and patients with thyrotoxicosis, regardless of the presence of cardiovascular disease. NT-proBNP levels in patients with CAD and thyrotoxicosis without CHF has exceeded the threshold value of 2,8 times ($p=0,001$). The highest level of NTproBNP was found in patients with CAD, CHF and thyrotoxicosis. A higher threshold value of NT-proBNP (556,4 pg/ml according to the results of this study) in HFpEF and HFmrEF patients with CAD and thyrotoxicosis was determined. Analysis of echo parameters in patients with CAD, CHF and thyrotoxicosis revealed significantly lower values of linear and volumetric LV parameters, type I LV diastolic dysfunction (100%), HFmrEF (48%), more frequent occurrence of LV concentric hypertrophy (84%). Conclusion. For HF diagnosis in patients with CAD and thyrotoxicosis, it is necessary to take into account the clinical features, heart rate variability, LV remodeling, as well as to use a higher threshold level of NT-proBNP.

Goal. To evaluate the diagnostic significance of the criteria of 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, CHF and/or thyrotoxicosis were examined. The clinical condition of patients and exercise tolerance were assessed, the level of the I-terminal fragment of the precursor of the brain natriuretic peptide (N1-rgoVIR) was determined, Holter monitoring of the electrocardiogram and echocardiographic examination (EchoCG) with Dopplerography were performed. Results. In patients with coronary heart disease, CHF and thyrotoxicosis, cardiac arrhythmias (atrial fibrillation, sinus tachycardia, supraventricular extra-systole), more pronounced autonomic imbalance with predominance of sympathetic activity of the autonomic nervous system were detected more often than in patients with coronary heart disease and CHF without thyrotoxicosis.

The prevalence of chronic heart failure (CHF) in the Russian Federation is 7-10%, and in recent years the number of patients with preserved and intermediate left ventricular ejection fraction (LVEF) has been increasing. 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) [1-6]. At the same time, the results of a number of studies indicate 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 whether the level of NUP increases in response to structural and functional changes in the myocardium with thyroid hyperfunction, or thyroid hormones have a direct stimulating effect on the secretion of NUP [7-10]. Frequency of occurrence of thyrotoxicosis and cardio.

Material and methods. The open comparative clinical study included 131 patients (mean age 58.3 ± 5.6 years), who were divided into 4 groups: the main group — 30 patients with thyrotoxicosis, coronary heart disease and CHF II-III functional class (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 clinical characteristics of patients are presented in Table 1. 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 [1, 2, 12, 13]

To assess the clinical symptoms and signs of CHF, a clinical condition assessment scale (SHOCK) was used, exercise tolerance was assessed according to the 6-minute walk test (6MTH). The concentration of NT-proBNP in blood serum was determined using reagents (Biomedica, Austria) on an automatic enzyme analyzer "Lapis Lazuli" (Dynex Technologies, USA). Holter ECG monitoring (XM ECG) was performed using a wearable eight-channel cardiomonitor "Kar-diotechnika-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; severe pathology of the liver, kidneys.

Declarations. The protocol of the study was approved by the local independent ethics committee, all patients signed an informed consent to participate in the study. Statistical processing was carried out using the Statistica 10.0 program (StatSoft, USA). The mean and standard deviation ($M \pm SD$) were determined with a normal distribution of quantitative features, and the median and quartiles ($Me [LQ; UQ]$) were determined with an abnormal distribution. The normality test was carried out using the Kolmogorov-Smirnov criterion. Qualitative variables were described by absolute (n) and relative values (%), compared by Pearson's chi-squared criterion. The reliability of the differences of 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. Pairwise comparison of groups was performed using the nonparametric Mann-Whitney criterion. Correlation analysis was carried out using Spearman's method. The new threshold value of NT-proBNP was calculated using ROC-an.

Results. Assessment of clinical symptoms of CHF on the SHOCK scale did not reveal significant differences between patients of the main and 1 comparison groups (with coronary heart disease and CHF without hyperthyroidism), however, exercise tolerance in 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%, 20%, $p = 0.01$), sinus tachycardia (36%, 22%, $p = 0.01$), supraventricular extrasystole (31% uz 18%, respectively, $p = 0.01$). The highest heart rate (HR) per day was observed in group 2 patients: 43.2% higher than in patients of the main group ($p = 0.0002$), 60.7% higher than in patients of group 1 ($p = 0.0001$) (Table 2). In patients of the main group, the lowest value was revealed median circadian index (CI), the absence of a significant decrease in heart rate at night. Evaluating the parameters of heart rate variability heart rate (HRV), the patients of the main group revealed the lowest values of time indicators - SDNN, rMSSD, RKSH0 ($p < 0.05$), the lowest value of the total power of the spectrum — TP ($p < 0.05$), especially due to a decrease in IR ($p < 0.05$), and the highest ratio of BP/IR 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 the patients of the main group, reliable correlations were established: between the level of SV.T4 and the IR indicator characterizing a decrease in parasympathetic activity against the background of concomitant thyrotoxicosis ($g = -0.41$, $p = 0.045$); between the level of ET-rgoBOT and the SHOCK data ($g = 0.39$; $p = 0.001$) and 6MTH ($g = -0.45$; $p = 0.001$).

Thus, in patients with coronary heart disease, CHF and thyrotoxicosis, compared with the results of patients with coronary heart disease and CHF without thyroid hyperfunction, the index of the final diastolic LV size (ICDR) was less by 10.9% ($p = 0.03$), the indices of the final systolic (ICSO) and diastolic (ICDO) LV volumes were less by 15.03% ($p = 0.01$) and 5.92% ($p = 0.03$), respectively. Types of LV remodeling in patients of the studied groups are also presented in Table 3. It should be noted that two types of LV remodeling were identified



in patients with CHF (main and 1 comparison groups): concentric (KGLJ) and eccentric (EGLJ) LV hypertrophy.

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 transmittal blood flow showed that in group 2 of patients, normal LV diastolic function was determined in 90% of cases, and in 10% of cases, LV diastolic dysfunction (LVD) Type I (relaxation slowdown). In patients of group 3, type I LDL occurred in 65.4% of cases. In the main group, in 100% of cases, type I DL was determined. 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 comparison group 2 (Fig. 1). It is important to note that in patients of the main and group 1, the LVEF values did not significantly differ ($p=0.1$) and corresponded to the intermediate type of CHF, which indicates the need to determine NT-proBNP for the diagnosis of HF in polymorbid patients with concomitant hyperfunction of the thyroid gland. 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 thyrotoxicosis without CVD (Fig. 2). The level of NT-proBNP in patients with coronary heart disease and thyrotoxicosis without CHF exceeded the threshold value by 2.8 times ($p=0.001$), in patients with thyrotoxicosis without CVD — by 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 thyroid hyperfunction ($p=0.0001$). During further observation, against the background of therapy with the inclusion of thyrostatics and the achievement of persistent euthyroidism, significant correlations were revealed between the dynamics of the concentration of TSH and SHH-proBNP ($g=-0.53$; $p=0.000$).

Using the JOS analysis, based on the determination of the maximum sum of the values of diagnostic sensitivity and specificity (DH+DS), the cut-off threshold (si^I) was determined, which was 556.4 pg/ml [14]. Thus, according to our data, in patients with thyrotoxicosis and coronary heart disease at the level of NT-pgoBNP >556.4 pg/ml, a decision is made in favor of the presence of CHF with 72% DC, 100% DC, 87.2% diagnostic accuracy (<0.001), while the values of NT-pgoBNP <556.4 pg/ml do not allow confirm the presence of CHF using this criterion. The area under the SS curve was 0.942 ± 0.0298 ($p<0.001$), which indicates the excellent quality of the model, and the resulting indicator can be recommended for use in clinical practice with an accuracy of 87.2% ($f<0.001$), while the values of NT-pgoBNP <556.4 pg/ml do not allow to confirm the presence of CHF using this criterion. The area under the SS curve was 0.942 ± 0.0298 ($p<0.001$), which indicates the excellent quality of the model, and the resulting indicator can be recommended for use in clinical practice.

Discussion. The obtained results allowed us to identify the features of the clinical picture in patients with CHF of ischemic genesis in combination with hyperthyroidism. 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, a more pronounced predominance of the sympathetic link of the ANS in the regulation of heart rhythm was revealed compared with those in patients with coronary heart disease and CHF without thyroid hyperfunction, which indicates an increase in vegetative imbalance with the development of concomitant thyrotoxicosis. 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 a sign of daily desynchronization.

The influence of thyroid hormones on the structural and functional parameters of the heart in hyperfunction is described in sufficient detail in the literature. However, the study of the features of heart remodeling in polymorbid patients with thyrotoxicosis remains relevant [15]. 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 genesis 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 to those in patients with CHF without thyroid pathology, which is 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 a stimulating effect of excess thyroid hormones on the secretion of NUP [6-10, 14].

A comparative analysis of the results of NT-proBNP showed no 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 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 and thyroid hyperfunction on NUP secretion.

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 and thyroid hyperfunction on NUP secretion. 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 NUP.

Conclusion: Thus, the paper revealed the features of the clinical picture, the daily heart rate profile, HRV indicators, LV remodeling in patients with ischemic heart failure and thyrotoxicosis, calculated and proposed a new threshold level of NT-pgoBNP for the diagnosis of CHF with preserved and intermediate LV LV in polymorbid patients with thyroid



hyperfunction, which will optimize the management of such patients and improve the forecast.

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