ATRIAL FIBRILLATION IN THYROTOXICOSIS –DETERMINANTS OF DEVELOPMENT AND CONSERVATION

Khusainova Munira Alisherovna Assistant of Samarkand State Medical University Salimova Dildora Erkinovna Assistant of Samarkand State Medical University Xamrayeva Madinabonu Yazdonkulovna Student of Samarkand State Medical University Chuliyeva Ma'mura Zafarovna Student of Samarkand State Medical University Samarkand State Medical University

ABSTRACT

Atrial fibrillation is a frequent rhythm disorder in thyrotoxicosis and can lead to the development of serious complications (thromboembolism, stroke) and death. The study of factors that increase the risk of atrial fibrillation in thyrotoxicosis has been going on for many years, but the introduction of new methods of examination and mathematical analysis allows us to identify new determinants of the occurrence of fibrillation and its preservation after the restoration of euthyroidism. In the presented work, an echocardiography examination of 127 patients with Graves' disease and 55 people was performed with subclinical thyrotoxicosis. The analysis revealed a number of new determinants of the development and preservation of atrial fibrillation. This is primarily the duration of thyrotoxicosis, a concentric type of left ventricular hypertrophy. The contribution of various factors to the formation of atrial fibrillation has been determined.

Key words: thyrotoxicosis, atrial fibrillation, myocardial remodeling.

INTRODUCTION

Currently, it has been established that even radically treated thyrotoxicosis leads to a deterioration in the life prognosis. Thus, mortality from cardiovascular diseases, hypertension, valvular defects, rhythm disorders, heart failure and, to a lesser extent, coronary heart disease (CHD) increased in this cohort by 1.2 times, and cerebrovascular mortality by 1.4 times compared with the general population. The obvious reason for the increase in mortality is the development of persistent changes in the cardiovascular system during thyrotoxicosis, which determines the relevance of their detection and correction. The most typical manifestations of thyrotoxic heart disease are: left ventricular hypertrophy (LVH), atrial fibrillation (AF), dilation of the heart cavities and the development of heart failure (HF), pulmonary hypertension,

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diastolic dysfunction. The most significant factor in increasing mortality is the formation of AF, which often persists even after the elimination of thyrotoxicosis (TT). AF is the second most common heart rhythm disorder after sinus tachycardia in TT. Its frequency in TT, according to various authors, varies from 2 to 25%, while the prevalence in the general adult population is only 0.4%. The variability of prevalence is determined by significant differences in the surveyed samples. Thus, in studies involving patients without concomitant heart disease, the frequency of AF It amounted to 14 and 14.9%, respectively. At the same time, in a study involving women with cardiopathies of various etiologies, AF was present in 67% of patients with thyrotoxicosis. Such significant differences in prevalence have drawn attention to the issue of studying the factors influencing the likelihood of developing AF in TT. The results of the conducted studies revealed the following factors: age, male gender, and the presence of concomitant cardiovascular pathology. However, the contribution of each of them to the development of AF has not been studied enough. Only age is indicated as a reliable predictor, and there are only isolated reports on the significance of other factors (gender, duration of the disease). A few studies are devoted to the effect of cardiac remodeling on the risk of AF, and they studied only the effect of atrial remodeling. There are few works devoted to the study of the nature of left ventricular (LV) remodeling in thyrotoxicosis, and their results are contradictory. So, to date, the relationship of various LV remodeling options and other factors with the development of atrial fibrillation has not been clarified. At the same time, the identification These factors will make it possible to develop effective measures for the prevention and treatment of thyrotoxic cardiomyopathy, which in turn will improve the cardiovascular prognosis in patients with thyrotoxicosis. Thus, the purpose of this study was to assess the prevalence of atrial fibrillation in thyrotoxicosis of various genesis and severity, to study its relationship with other manifestations of thyrotoxic heart disease, in particular with the nature of LV remodeling.

MATERIALS AND METHODS OF RESEARCH

The criteria for inclusion in the study for patients with obvious thyrotoxicosis were: 1) the presence of obvious thyrotoxicosis (sv. T3 and/or sv. T4 above normal, TSH below 0.1 mEd / 1); 2) men and women aged 18-55 years; 3) informed consent of the patient to participate in this study; 4) Satisfactory image quality when Echocardiography research. Criteria for non-inclusion in the study:

1) concomitant diseases that could affect the structural and functional state of the heart (coronary heart disease, hypertension, valvular lesions, cardiomyopathy of non-thyrotoxic origin, diabetes mellitus, obstructive pulmonary diseases, heart failure and hemodynamically significant rhythm disturbances of non-thyrotoxic origin); 2) conditions that are a contraindication for long-term thyrostatic therapy:

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liver pathology (increased transaminases more than 5 times higher than the upper limit of the norm, liver failure), chronic renal failure, data on intolerance to thyrostatics in the anamnesis; 3) intoxication (alcoholism, substance abuse);4) Pregnancy and pregnancy planning. According to the specified criteria, the study

127 patients with clinical thyroidism were included The toxicosis of Graves' disease. The criteria for inclusion in the study for patients with subclinical thyrotoxicosis were: 1) the presence of subclinical thyrotoxicosis (the TSH level is below the lower limit of the norm of 0.1 mEd/l according to the results of two measurements with an interval of at least 3 weeks, the normal level of St. T3 and St. T4) of the following genesis:

• exogenous CT against the background of suppressive therapy L T4 with suppression of TSH levels < 0.1 mEd/l (after extirpation of the thyroid gland About you co-differentiated carcinomas); • CT of autoimmune origin (subclinical

stage of Graves' disease); • CT with nodular autonomy of the thyroid gland (pretoxic adenoma of the thyroid gland, multi-nodular toxic goiter in the CT stage);

2) men and women aged 18-59 years; 3) informed consent of the patient to participate thie in this study; 4) Satisfactory image quality when Echocardiography. Criteria for non-inclusion: 1) concomitant diseases that could have an impact on the structural and functional state of the heart (coronary heart disease, hypertension disease, valvular lesions, cardiomyopathiesof non-thyrotoxic origin, diabetes mellitus, obstructive pulmonary diseases, liver pathology (increased transaminases more than 5 times higher than the upper limit of normal), chronic renal failure, heart failure and hemodynamically significant disorders of non-thyrotoxic origin); 2) intoxication (alcoholism, substance abuse); 3) pregnancy; 4) obvious thyrotoxicosis; 5) destructive thyrotoxicosis. According to the specified criteria, the study 55 patients with subclinical thyrotoxicosis were included. The control group was represented by 27 healthy people (25 women, 2 men). The levels of free triiodothyronine (sv. T3), free thyroxine (sv. T4), thyrotropin (TSH), antibodies to thyroid peroxidase (AT TPO) and antibodies to the TSH receptor (AT RTG) were determined by the enzyme method on an automatic immunochemical analyzer. According to the data Ultrasound assessed the volume of the thyroid gland. If necessary, to clarify the genesis of thyroiditis

sycosis was evaluated by the absorption of radioac iodine deficiency (I123) by the thyroid gland (excluded treatment of destructive thyrotoxicosis) and scintigra thyroid gland pathology. Blood pressure was determined by a mercury sphygmomanometer with an accuracy of 2 mmHg three times with an interval of 5 minutes. Then the average of the last two measurements was calculated. The heart rate was determined by the pulse in 60 seconds. The thickness of the walls of the left ventricle and the size of the cavity were determined from the parasternal position of the long axis of the LV. Measurements were made in the M mode with an ultrasound beam parallel to the short axis of the left ventricle. The mass of the myocardium was calculated based on its

length and thickness along the short axis from the parasternal access. Evaluation of the left ventricular myocardial mass index (LVMM) was carried out according to the recommendations ASE 2005. All measurements were carried out for at least three cardiac cycles, and then averaged. The study did not include patients with segmental impairment of contractility.

MMLJ = $0.8 \times M0 + 0.6$, where LVMM is the mass of the myocardium of the left ventricle; $M0 = 1.04({TIL + TPWLV + KDLV }3) - {FDSLV }3)$, where 1.04 is the density coefficient of cardiac muscle; TIL – the thickness of the interventricular ligament; TPWLV – the thickness of the posterior wall of the left ventricle; FDSLV– the final diastolic size of the left ventricle (LV diameter). LVMM was calculated using the formula: MMLV = MMLJ/PPT, where PPT is the body surface area determined by the formula D. Dubois (1975). The threshold for The IMLJ was chosen according to the criteria proposed in the ASE 2005 recommendations. For men, it was 115 g/m², for women -95 g/m². The relative wall thickness (RWT) of the left ventricle was determined in the following way:

RWT = (TMJP + TSSLJ)/KDLJ RWT was considered to be increased at values of 0.42 or more. A sign of asymmetry For severe septal hypertrophy, the ratio of TMJ/TSLJ was considered to be more than 1.5. Both of the above quantitative indicators (LVMI and OTC) wereused to determine left ventricular hypertrophy and a specific type of LV geometry. When evaluating the type of LV remodeling geometry, threshold values for LVL were used and OTS. The parameters of diastolic function were estimated: the maximum blood flow rate of peak E (E), the maximum blood flow rate of peak A (A), their ratio (E/A), the time of slowing down of blood flow Peak E, the time of isovolemic relaxation (TIR) – the time from the closure of the aortic valve to the opening of the mitral valve. Signs of impaired diastolic function (the "classic" type of crisis) were considered: • VIVR of more than 100 ms; • E/A less than 1.0; • The deceleration time of peak E is more than 240 ms. For the differential diagnosis of naru To improve diastolic function, blood flow in the pulmonary veins was types monitored. The echocardiography method was also used to assess pulmonary artery pressure (PA) and diagnose pulmonary hypertension (PH). Systolic pulmonary artery pressure up to 25 mmHg at rest and up to 30 mmHg during physical activity was taken as normal. PH was diagnosed with systolic pulmonary artery pressure of 35 mmHg and above.

To increase the reliability and accuracy of the results, dynamics studies for the same patient were conducted by the same researcher. Statistical processing of the obtained data was performed using statistical software packages Statistica 6.0 and Exel 6.0. Methods of multidimensional statistics were used – factorial, cluster and discriminant analyses, multiple regression analysis. To assess the differences in

quantitative characteristics between groups, the Student's criterion was used for large samples with a distribution close to normal. The differences were considered significant at p < 0.05.

THE RESULTS AND THEIR DISCUSSION

The factors that can influence the development of remodeling of the heart chambers, the formation of "endpoints" were analyzed (LVH, DLP, AF, LH, CH), and their interrelationships. Ananalysis of 20 factors was carried out: demographic (gender, age) characterizing the clinical course of the disease (duration of preservation of obvious thyrotoxicosis (elevated levels of St. T3 and/or St. T4 at low, below 0.1 mEd/l, TSH), duration of preservation of subclinical thyrotoxicosis (normal level of sv. T3 and/or sv. T4 at low, below 0.1 mEd/l, TSH), heart rate, systolic level and diastolic blood pressure (BP) and laboratory parameters (St. T3 and St. T4 levels, TSH, titer of antibodies to the TSH receptor). To assess the effect of remodeling of various chambers of the heart and functional parameters, the parameters of echocardiography (absolute and relative wall thickness, diameter of the heart cavities: left atrium, left and right ventricles); pulmonary artery pressure, diastolic parameters (time of isovolumic relaxation and the ratio of peaks of E/A transmittal blood flow) were analyzed and systolic (ejection fraction by To Simpson, the shortening fraction) of the function. To compare the effect of various remodeling options on the development of AF, the nature of remodeling in the examined patients was evaluated new TT. In patients with obvious thyrotoxicosis, an hour total LVH was 22.1% (56 patients, of whom 44 (20.2%) were women and 12 (33.3%) men); at the same time, 46 (18.2%) patients had an eccentric LVH and only 10 (3.9%) have concentric LVH. Concentric LV re-modeling was noted in 20 (8.0%) patients. Thus, the frequency of the LVH in men turned out to be significantly higher than in women (OR = 3.6; DI; p < 0.05). Atrial fibrillation (AF) was one of the factors that influenced the development of thie HLV. In the group of patients with LVH, atrial fibrillation was 2 times more common than in patients without it. Conversely, the number of patients with AF who had LVH was 2 times higher than the number of patients without LVH. In dynamics (one -year control) in patients with AF and without it, the LVMI did not significantly change, although in some patients (14people) the sinus rhythm was restored. The prevalence of atrial fibrillation was It was analyzed in groups with different types of LV geometry. The prevalence of AF was maximal in groups with concentric LV remodeling variants (KGLJ and KRLJ), and was low in patients with LVH. There was a significant correlation between due to LP and AF dilation (r = 0.4, p < 0.0001). In patients who did not have AF, LP dilation occurred only in 35% of cases. In contrast, only 25% of patients with AF did not have LP dilation (p < 0.0001). In the examined sample at the stage of inclusion of she was in 42 patients with Graves' disease. OP statis It developed significantly more often in men: 13 out of 39 (33.3%) than in women -29 out of 214 (13.5%) (p = 0.001). Taking

into account the large number of factors influencing the development of AF, an analysis of multiple correlations and multivariate regression analysis was carried out. To assess the relationship of quantitative indicators of left ventricular remodeling, clinical and demographic parameters, the choice (age, gender, duration of TT, thyroid hormone levels and AT RTG levels) with the risk of developmentFP used the multiple step-bystep method regression analysis. Using a discretionary analysis, it was found that, of the clinical anamnetic and demographic parameters, the duration of thyrotoxicosis made the greatest contribution to the development of atrial fibrillation (clinically go and subclinical), heart rate and gender (male), from echocardiography – the diameter of the cavities (LP and LV) and mass LV myocardium. When taking into account all indicators (p < 0.0001) the probability of correct classification was 91.2%. In subclinical thyrotoxicosis, LVH was detected in 18.2% of patients. At the same time, there was a LVH in 7 cases of JAST (14%), and among patients with endogenous 25.7% of patients with autoimmune ST had LVH (9 out of 35). A fairly close indicator was obtained in the group of patients with nonimmune CT – LVH was observed in 20% (5 out of 25). LP dilation was detected in 16 cases of (32%) and 8 cases of ENST (32%), however, the highest the highest frequency of dilation was recorded at EFT – in 42.9% of cases (in 15 out of 35 people), which would be significantly more than in the other two groups (p < 0.05). The frequency of AF in the CT group was 7% (3 men (50%), 5 women (5%), p < 0.005), while it It turned out to be higher in the YAST and ENST groups – 8% (4 and 2 people, respectively), with EAST its frequency was 5.7% (2 people), but the differences were unreliable. All patients with AF were older 45 years old, all had LVH: in 62.5% of cases (5 people) – KGLJ, the rest – EGLJ (37.5%), dilatation LP infection was present in all patients with AF. Thus, the frequency of AF in the examined sample was significantly higher with an obvious TT compared to CT. For development AF in subclinical thyrotoxicosis was influenced by the same factors as in overt ones – age, gender, the concentric nature of LVH, the presence of DLP. The duration of CT had no significant effect on the development of AF in the examined patients CT, which may be due to the small number of patients with a long duration of the disease in the examined sample. The obtained datademonstrated that the presence of both left ventricular hypertrophy and concentric variants of left ventricular remodeling was associated with an increase in the frequency of AF formation. These data echo similar results obtained earlier in patients with arterial hypertension. In this subpopulation, the presence of LVH was also associated with a significant deterioration in cardiovascular prognosis. The development of atrial fibrillation was significantly more common in men, and according to the discriminant analysis, male gender was one of the most significant predictors of its development, along with the duration of thyrotoxicosis and heart rate there are no abbreviations. The nature of left ventricular remodeling was also important for the development of atrial fibrillation, and with

concentric hypertrophy, the frequency of its occurrence was significantly higher. Thus, the conducted analysis confirms the data obtained in other studieson the importance of gender, age and increased LP for the development of AF in TT were analyzed. A number of new determinants of the development of AF were also identified - this is the concentric nature of LVH, the degree of increase in the level of sv. T3. It was found that the duration of thyroidism was the most significant factor for the development of AF toxicosis. The following are important in terms of the degree of contribution my predictors of the development of fibrillation are these were the severity of tachycardia on the background of thyroidism toxicosis and male gender. The presence of concentricity coy LV hypertrophy, which is with high frequency It was found in men at any age, and in women after the age of 44, it was also a serious predictor of the development of AF. It should be noted that concentricity this variant of LVH is a risk factor for the development of not only AF, but also disorders of the functional state of the myocardium and systolic and diastolic functions, which was reflected in our earlier works. Special attention should be paid to the fact that a number of identified predictors of AF development are modifiable. This is primarily the duration of the disease, which is determined by how timely it is the patient will be referred for radical treatment, as well as heart rate, normalization of TSH levels during treatment. Timely correction of these factors will significantly reduce the risk of developing and storing AF.

CONCLUSIONS:

Based on the results of the analysis of the data obtained, members of the high and low risk groups of AF are identified:

1. Low-risk group: age less than 44 years, female, normal LV and LP geometry according to EchoCG data.

2. High-risk group: age over 44 years, male, presence of FGM and DLP according to the data Echocardiography.

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