

FEATURES AND SEVERITY OF THYROTOXIC ATRIAL FIBRILLATION

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ABSTRACT

Atrial fibrillation (AF) is called the most serious complication of thyrotoxicosis, since it develops quite often (in 10–15% of cases) and is associated with an increased risk of mortality [1, 2]. There is evidence that patients with AF and hyperthyroidism differ from patients with AF and normal thyroid function, both clinically [3] and pathophysiologically[4]. However, there is a paucity of data describing the characteristics and outcomes of patients with thyrotoxic AF (TAF). It is also important to note the paucity of recommendations regarding treatment strategies for this group of patients [3]. Studying the features of the course of TAF and identifying predictors of its unfavorable course will provide a deeper understanding of the differences between DFT and AF of other etiologies and will help in creating more detailed recommendations for patients with TAF. When analyzing the literature, a number of studies were found that studied the relationship between clinical types of TFT, the results of which are contradictory. Some studies demonstrate the predominance of the paroxysmal type [5, 6], others - the persistent one [7, 8]. One study also examined factors associated with type of TFT: duration of thyrotoxicosis less than 1 year (odds ratio (OR) 4.3, 95% confidence interval (CI) 1.1–16.6) and lower levels of free tetraiodothyronine (OR 0.97, 95% CI 0.95–0.99) were associated with paroxysmal AF [6]. From our point of view, the characteristics of the course of TAF, in addition to the clinical type, can also include the severity of symptoms of AF and developed heart failure (HF) against the background of AF, and the ventricular contraction frequency (VFR) against the background of AF. No studies were found in the literature describing these characteristics in patients with TFT. Thus, the characteristics of the severity of TPP and the factors associated with them have not been studied enough, but their study seems important both for understanding the mechanisms of development of TPP and from a practical point of view. Among other things, this may be useful for optimizing the prevention of severe complications of this rhythm disorder.

Keywords: thyrotoxicosis, hyperthyroidism, atrial fibrillation, thyrotoxic atrial fibrillation, Graves' disease.

Purpose of the study: to establish factors associated with the severity of TPP.

MATERIAL AND METHODS

The study included patients who were undergoing inpatient treatment in the departments of endocrinology or cardiology, as well as those who were observed on an outpatient basis by an endocrinologist or cardiologist at the SFRSNPTSE in the period from 2015 to 2023. All patients had manifest thyrotoxicosis and TPP in the anamnesis or at the time of inclusion in the study. Data on the course of the disease were obtained from medical records and during anamnesis collection during a personal/telephone interview. All participants had at least one face-to-face visit to collect a medical history and sign an informed consent form to participate in the study.

Patient inclusion criteria:

- men and women aged 18 to 80 years;
- a history of manifest thyrotoxicosis caused by Graves' disease, toxic adenoma or multinodular toxic goiter;
- the presence of AF (at the time of inclusion in the study or in history), first recorded against the background of thyrotoxicosis.

Criteria for non-inclusion of patients:

- subclinical thyrotoxicosis without a period of manifest thyrotoxicosis;
- a history of AF before the onset of thyrotoxicosis;
- hemodynamically significant valvular lesions and heart defects, cardiomyopathies of non-thyrotoxic and non-ischemic origin;
- severe obstructive pulmonary diseases, severe blood diseases, severe organ failure;
- chronic intoxication (alcoholism, drug addiction, substance abuse);
- pregnancy during thyrotoxicosis.

To study the effect on the course of TPP, the following data were assessed (factors potentially associated with the severity of the course):

1. Gender and age.
2. Characteristics of the course of thyrotoxicosis: levels of thyroid-stimulating and thyroid hormones, duration of manifest (months) and subclinical (more or less 1 year) thyrotoxicosis, presence of periods of hypothyroidism, number of relapses of thyrotoxicosis, genesis of thyrotoxicosis.
3. Metabolic parameters and concomitant diseases: body mass index (BMI), smoking status, carbohydrate metabolism disorders (diabetes mellitus (DM), impaired fasting glycemia, impaired glucose tolerance), arterial hypertension (AH), coronary heart disease (CHD).

4. Parameters of echocardiography (EchoCG) against the background of AF: left ventricular myocardial mass index (LVMI), left ventricular end-diastolic size (LVED), left ventricular (LV) hypertrophy (presence/absence), ejection fraction (EF) according to Simpson, the nature of LV remodeling (normal geometry, concentric remodeling, concentric hypertrophy, eccentric hypertrophy), left atrium (LA) diameter, LA volume index, LA dilatation (presence/absence), pulmonary artery (PA) pressure.

5. Duration of AF.

The course of TPP was assessed using the following parameters:

1. Type of AF: paroxysmal, persistent, long-term persistent, permanent.

2. Severity of symptoms of HF against the background of AF (I–IV functional classes (FC)): no symptoms, I–II FC, III FC, IV FC.

3. Severity of symptoms associated with AF according to the European Heart Rhythm Association score of atrial fibrillation (EHRA): no symptoms; mild symptoms, normal daily activities are not affected; severe symptoms, normal daily activities are impaired; disabling symptoms, normal daily activities stopped.

4. Heart rate against the background of AF (assessed during echocardiography).

The presence of manifest thyrotoxicosis in a patient was confirmed when the level of thyroid-stimulating hormone decreased below the reference interval and the levels of triiodothyronine and/or tetraiodothyronine increased above the reference interval. Levels of free thyroid hormones at different times were measured using different sets of reagents, and therefore their reference intervals differed. Therefore, the excess of the upper limit of normal (how many times the hormone level exceeds the upper limit of normal) was calculated for tetraiodothyronine and triiodothyronine. The duration of thyrotoxicosis was established in months from the moment of the first clinical manifestations until the achievement of euthyroidism. The presence of TAF was determined either by the presence of this pathology in the diagnosis, or by the presence in the medical documentation of a standard electrocardiogram (ECG) or the results of Holter monitoring with AF first recorded against the background of thyrotoxicosis. If it was not possible to accurately establish the occurrence of AF on the background of thyrotoxicosis, patients were not included in the study. Atrial fibrillation and atrial flutter were not differentiated: “patients with AF” meant patients with both atrial fibrillation and atrial flutter. The duration of AF was assessed based on medical history data. The duration of AF in the case of paroxysmal type was determined as the entire period of time during which paroxysms were observed, and not as the total duration of paroxysms. The clinical type of AF was established in accordance with the recommendations for AF [9]. The severity of AF was assessed based on the effect on myocardial contractility (severity of HF according to the New York Heart Association (NYHA) classification and Simpson EF according to echocardiography against the

background of AF); severity of symptoms associated with AF (EHRA scale); Heart rate against the background of AF during echocardiography. Several metabolic parameters and comorbidities were assessed. Body mass index was calculated using the formula: body weight (kg) / (height (m))². Disorders of carbohydrate metabolism were established in the case of the presence of pathology in the diagnosis and/or taking glucose-lowering therapy, and/or the presence of criteria for the corresponding pathology established in the “Algorithms for specialized medical care for patients with diabetes mellitus” 2019 [10]. The presence of hypertension was confirmed in the presence of essential and/or secondary hypertension in the diagnosis and/or use of antihypertensive drugs, and/or if systolic blood pressure (BP) ≥ 140 mmHg. Art. and/or diastolic blood pressure) ≥ 90 mm Hg. Art. were found at least twice in medical records. The basis for noting the presence of coronary artery disease was the presence in the medical documentation of data on: clinical angina pectoris in combination with the presence of ischemic changes on the ECG or EchoCG; silent myocardial ischemia, recorded during Holter monitoring; positive result of stress echocardiography or treadmill test; documented myocardial infarction; hemodynamically significant stenoses of the coronary arteries identified during coronary angiography. EchoCG data. The myocardial mass index and the relative thickness of the LV walls, necessary to determine the type of geometry, were calculated using the formulas recommended by the American Society of Echocardiography in 2005 [11]. To describe the geometry of the LV, the G. Ganau classification was used [12]. LA dilatation was established when the LA diameter was more than 38 mm, LV hypertrophy was determined when the LV IMM was more than 115 g/m² for men and more than 95 g/m² for women [11]. SPSS Statistics v23 programs were used for statistical analysis.

RESEARCH RESULTS

Characteristics of patients. The study included 70 patients, of which 44 (62.9%) were women, aged from 24 to 70 years.

Factors associated with severe FFT

Patients with different severity scores were compared according to the characteristics presented in Table 1. Comparisons were made between the following groups:

1. Paroxysmal or persistent type of AF.
2. There are no FC I–II or FC III–IV HF due to AF.
3. EF (Simpson) $\geq 50\%$ or EF (Simpson) $< 50\%$.
4. EHRA 2 or EHRA 3, 4.
5. Heart rate against the background of AF < 90 per 1 min or ≥ 90 per 1 min.

Severe course of TAF was defined as: persistent type, class III–IV HF on the background of AF, EF $< 50\%$, EHRA 3–4, heart rate ≥ 90 per minute.

Gender was statistically significantly associated with all indicators of the severity of FFT, except for heart rate. The percentage of male patients was significantly higher in the group of persistent AF compared with paroxysmal AF (48.8% and 20.7%, respectively, $p = 0.017$), among patients with FC III–IV HF compared with FC I–II (48, 8% and 25.7%, respectively, $p=0.048$), in the group with EF below 50% compared with the group with preserved EF (63.3% and 26.7%, respectively, $p=0.002$) and among patients with severe symptoms AF: more in EHRA 3 and 4 than in EHRA 2 (52.5% and 16.7%, respectively, $p=0.003$).

To confirm the effect of gender on the severity of TPP, a logistic regression analysis was performed with only age and gender included in the list of independent variables.

DISCUSSION

The studied sample of patients was distinguished by a rather severe course of AF: half of the patients had HF class III–IV and had symptoms of AF corresponding to EHRA 3–4; One third of participants had a decrease in EF of less than 50%. Persistent type of AF was observed more often (58.6%) than paroxysmal (41.4%), which is consistent with the data of previous studies [2, 3, 7, 8, 13]. When analyzing the literature, no studies were found that described the above characteristics of the course of TAF, which, in our opinion, characterize the severity of AF. However, our data on the incidence of severe FTP cannot be extrapolated to all patients with FTP, since most of the study participants were hospitalized patients with severe thyrotoxicosis or its complications, which is due to the specifics of the medical institutions where patients were recruited. According to the results of this study, the only reliable predictor of a severe course of TAF was male gender: it is associated with the persistence of AF, the development of HF class III–IV, a decrease in EF below 50% and with severe symptoms of AF - 3 and 4 on the EHRA scale. In contrast to other studies that examined the influence of clinical and anamnestic parameters and other factors on the type of TFP [6], we did not find an association between the duration of thyrotoxicosis and the level of thyroid hormones with the severity of TFP. Thus, male patients with thyrotoxicosis should be given special attention in order to prevent AF, and men with already developed TAF need adequate pulse-lowering therapy, thyrostatic therapy to achieve normal levels of not only thyroid hormones, but also TSH, optimally early radical treatment of thyrotoxicosis (thyroidectomy or radioiodine therapy). In addition, several echocardiographic parameters were associated with the severity of TAF. In the severe AF groups, LV IMM and LA diameter were higher. This may be important for determining the prognosis of patients with these changes detected by echocardiography.

CONCLUSION

The results of the present study demonstrated that male gender is associated with a more severe course of TAF, manifested in the persistence of AF, the development of HF III-IV class, a decrease in EF below 50% and the presence of severe symptoms of AF - 3 and 4 on the EHRA scale. This fact makes it appropriate to focus special attention on male patients with other factors that increase the risk of developing TFP. In addition, the present study found that several echocardiographic parameters were associated with the severity of AF: LA diameter was associated with the type of AF, LV IMM was associated with the severity of AF symptoms according to the EHRA scale, and both of these parameters were associated with the FC of HF and EF at background of TFP. The present study provides important information about patients with TFP that can be used to further understand how to clinically manage this important group of patients. Given the small sample size of this study, further research is required to confirm and expand the results obtained, to create a risk stratification tool for severe FFT and to develop approaches to treatment and prevention in this group of patients.

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