

## THYROID DYSFUNCTION AND HEART CONDITIONS IN EXERCISING YOUNG PEOPLE

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**Abstract:** Thyroid hormones have a global effect on the whole body, the heart being particularly sensitive to their action. Both hypo- and hyperthyroidism cause various cardiac abnormalities and, therefore, the management of these diseases is very important. The aim of this study is to highlight the arrhythmic risk and the echocardiographic changes in the young patients (between 18 and 45 years old), with a high degree of physical activity, diagnosed with hypo- / hyperthyroidism. There have been enrolled 71 patients (60 women, 11 men), diagnosed with thyroid pathology, without known cardiovascular history. The group studied and categorized from the endocrine point of view in hypo- or hyperthyroidism was investigated by non-invasive methods regarding cardio-vascular parameters. Abnormal diastolic filling of the left ventricle (suggestive for the alteration of left ventricular relaxation and diastolic filling times) is a common manifestation in hypo- and hyperthyroidism, so the observed diastolic dysfunction may be the prelude to more severe limitations of cardiac function and physical performance. Thyroid pathology may be a major risk factor in the initiation of cardiovascular disorders. Taking into consideration the incidence of subclinical thyroid dysfunction, routine dosing of TSH in the presence of cardiovascular manifestations is required. In the current practice there is a general effort of increasing the awareness of the medical staff on the arrhythmic risk and on the special importance of this problem in the evaluation of the young sportsman by a multidisciplinary department.

**Keywords:** *hyperthyroidism, hypothyroidism, arrhythmic risk, exercising young people.*

### Introduction

Thyroid hormones have a global effect on the whole body, the heart being particularly sensitive to their action. Today, both the direct and indirect effects of these hormones on the myocardium are known, their action being based on three potential mechanisms: 1) the direct effect on the cell, 2) the interaction with the sympathetic nervous system, 3) the alteration of the peripheral circulation and the energy metabolism [1].

Thyroid dysfunction has been described to be linked to a variety of cardiovascular morbidities.

Hyperthyroidism is characterized by a left ventricular ejection fraction (LVEF) increased at rest, but, paradoxically, by a significant decrease in effort. The return to euthyroidism is accompanied by the anticipated increase of LVEF in effort at the same pregnancy and ventricular allure. This reversible "cardiomyopathy" could explain the reduction in effort tolerance of patients with hyperthyroidism. Although it appears to be an intermediate state between normal left ventricular function and left ventricular dysfunction at rest, the inability of LVEF to increase in effort should rather be seen as a consequence of the extra burden, post-pregnancy increase induced by effort on a heart that works almost to maximum capacity [2].

Actual manifestations of heart failure such as decreased ejection fraction, diastolic dysfunction and pulmonary congestion may be the consequences of severe chronic hyperthyroidism, tachycardia, and atrial fibrillation [3, 4].

The characteristic tachycardia is determined by a combination between the increase of the excitability of the sinus node by lowering the triggering point of phase 1 of depolarization and the shortening of the action potential of the sinus-atrial cells, especially its phase 0. The refractory period of atrial myocardial cells is also shortened, which could explain the well-known tendency towards atrial rhythm disturbances such as atrial fibrillation / flutter, in particular by promoting the occurrence of ectopic outbreaks of atrial depolarization [5].

Other clinical present signs are: strengthening of noise I, accentuation of pulmonary component of noise II, noise III, systolic breath along the left margin of the sternum (representative of hyperkinetic syndrome) and blowing of mitral valve prolapse. Hypertension in hyperthyroidism appears to be caused by hyporeninemia, which is a result of increased peripheral vascular resistance. Some authors [6] have also noticed an increase in total intracellular sodium, which could be considered as being part of the mechanisms of

hypertonia in hypertension. It has been demonstrated that the cardiovascular capacity is reduced in hyperthyroid patients, which might be related to a disturbed chronotropic regulation and can be restored by treatment with antithyroid medication [7].

In contrast to hyperthyroidism, low concentrations of thyroid hormones are associated with decreased cardiac flow, ventricular allure, beat volume, and increased peripheral vascular resistance manifested especially by increased diastolic blood pressure [8], altered lipid metabolism [9,10], endothelial dysfunction [11], and an overall increased atherosclerotic risk [12].

Hypothyroidism, through hyposecretion or lack of hormones, slows metabolism, affecting almost all body functions. Its manifestations are more severe in the heart, where cardiomegaly, sinus bradycardia, hypotension, deafening of the heart, edema and signs of congestive heart failure such as ascites or orthopnea and nocturnal paroxysmal dyspnea are noted. Currently, this clinical picture is no longer frequent, due to the diagnosis of the disease at an early stage.

#### Electrocardiogram(EKG)

The cardio-vascular system is very sensitive to increased serum levels of thyroid hormones. Increased cardiac flow and high heart rate are early clinical manifestations of the influence of thyroid hormones on the myocardium. The most common EKG changes found in thyrotoxicosis are simple sinus tachycardia, increased electrical amplitude of all waves, but especially the T wave and atrial fibrillation.

In the case of hypothyroidism, the most common electrocardiographic changes are: sinus bradycardia, QT interval prolongation and ischemic changes manifested by negative or flattened T waves, over- or under-leveled ST. The QT interval is often prolonged in hypothyroidism due to the extension of the action potential. This may draw attention to the increased risk of triggering the torsade of the extremities and implicitly the risk of ventricular fibrillation / sudden cardiac death [13]. Most hypothyroid patients have low or normal ventricular allure (50-70 beats / min). Patients with severe hypothyroidism and those with pre-existing heart disease may develop varying degrees of atrioventricular block or may have intermittent or permanent branch blocks, especially the right branch.

The physiological adaptations encountered in intense physical effort are known as the "athlete's heart" and generally serve to meet the increased oxygen requirement of the skeletal muscle during

rigorous physical activity. Numerous pathological conditions have been identified in young athletes, many of them with malignant potential, with an increased risk of sudden cardiac death (hypertrophic cardiomyopathy, arrhythmogenic cardiomyopathy, idiopathic ventricular tachycardia in the normal heart, long / short QT syndrome, WPW syndrome, Brugada syndrome, ventricular polymorphic catecholaminergic tachycardia, etc.). Therefore, the **purpose** of this study is to highlight the arrhythmic risk and the echocardiographic changes in the young patients (between 18 and 45 years old), with a high degree of physical activity, diagnosed with hypo / hyperthyroidism.

#### **Materials and method**

The subjects of the study were 71 patients (60 women, 11 men), diagnosed with thyroid pathology, without known cardiovascular history, admitted to the Endocrinology Clinic of the Craiova County Emergency Clinical Hospital between 2015 and 2016, aged between 18 and 45 years, athletes, then followed up cardiologically in the ambulatory.

The endocrine diagnosis was supported by the clinical, hormonal parameters (TSH, FT4) and by the thyroid para-clinical tests represented by: thyroid ultrasound (by appreciation of the volume and echogenicity of the parenchyma), radioiodocapture at 2 hours and thyroid scintigram. The complete lipidogram was also performed.

The group studied and categorized from the endocrine point of view in hypo- or hyperthyroidism was investigated by non-invasive methods regarding cardio-vascular parameters. Noninvasive methods consisted of: clinical examination, electrocardiographic route registration and M- and B-mode echocardiography combined with color Doppler, PW, CW technique. The cases with subclinical hypo- and hyperthyroidism included in the study are a special mention. Subclinical hypothyroidism is defined by the absence of clinical symptoms, increased TSH and normal FT4, and subclinical hyperthyroidism by low TSH and normal FT4 [14, 15].

Plasma evaluation of thyroid hormones was performed using the electrochemiluminescence method using an Elecsys 1010 device, and color Doppler echocardiography using a 3.5 MHz probe to assess systolic and diastolic performance.

Physical activity was assessed by individual assessment interview. Subjects who participated in physical training for at least one hour a week were classified as being physically active. The exercises were performed minimum twice a week.

The data were reported as mean and standard derivation. For all statistical tests were used the

SPSS statistical software 10. The threshold for statistical significance was set to  $p < 0.05$ .

**Results**

Of the 71 patients, 28 (39.4%) were diagnosed with hypothyroidism, and the rest (43 cases - 60.6%) with hyperthyroidism. The distribution by clinico-pathogenic forms was as follows: subclinical hyperthyroidism 5 cases (11.6%), hyperthyroidized goiter 21 cases (48.8%), Basedow disease 11 ca-ses (25.5%), multiheteronodular goiter 4 (9.3 %), toxic node 2 cases (4.6%).

In hypothyroidism, the surgical etiology (post-thyroidectomy) was present in 18 cases (64.28%), the autoimmune 6 cases (21.4%) and secondary hypothalamo-pituitary in 4 cases (14.28%); 4 patients with Hashimoto's thyroiditis had subclinical hypothyroidism.

Hyperthyroidism

In the hyperthyroid studied patients, we found the increase of ventricular allure, appreciated by measuring the central and peripheral pulse in the radial artery and the presence of rhythm disorders: atrial fibrillation and extrasystoles. The second cardiovascular parameter followed, the blood pressure, measured in the left brachial artery, showed initially elevated values in 16 patients (systolic pressure  $175.2 \pm 1.9$  mm Hg, diastolic pressure  $90.38 \pm 1.64$  mm Hg). The symptomatology of hyperdynamic circulatory syndrome in hyperthyroidism was remitted after 4-8 weeks of treatment with synthesis antithyroid (ATS) and beta-blockers.

Hypothyroidism

In the studied patients with hypothyroidism bradycardia was found, as well as the presence of atrioventricular block II degree Mobitz I in 3 cases (10.7%) and the association with HTA in 6 cases (21.4%).

Electrocardiography

In the cases with hyperthyroidism of this study, the electrocardiographic changes were re-presented by sinus tachycardia - 34 patients (79.06%), atrial fibrillation - 9 patients (20.9%), left ventricular hypertrophy - 9 patients (20,93%) and increased QRS voltage in 35 cases (81.39%). Six patients (13.95%) had ventricular extrasystoles and 3 (7%) had non-systemic atrial extrasystoles.

Non-specific ST-T changes were observed in 20 cases (46.5%).

The EKG manifestations listed and observed by us were restored following treatment with ATS, when the patients reached euthyroidism. From the patients with hyperthyroidism and atrial fibrillation, 78% returned to sinus rhythm spontaneously in less than 4 months of treatment. Cardioversion was required in the other patients. Hypothyroidism resulted in bradycardia and prolonged QT interval in 25 cases (89.2%), low voltage in 21 patients (75%), HVS in 12 patients (42.8%), flattening of the T wave in 15 patients (53.5%).

Echocardiography

The effect of hyper- and hypothyroidism on some hemodynamic parameters is varied and illustrated in Table I.

Size	Normal values	Values in hyperthyroidism	Values in hypothyroidism
Systemic vascular resistance (dyn * sec / cm)	1500-1700	700-1200	2100-2700
Ventricular allure (beats / min)	60-100	90-130	<70
Ejection fraction (%)	50-60	>60	≤60
Cardiac flow (L/min)	4-6	>7	<4,5
Isovolumetric relaxation time (m/sec)	60-80	25-40	>80
Blood volume (% of normal)	100	105,5	84,5

**Table I - Changes of cardiac function in thyroid disease [13]**

As a result of the data obtained through numerous invasive and non-invasive investigations, it is known that cardiac parameters such as heart rate, cardiac flow and peripheral vascular resistance are closely related to thyroid status.

In this context, the following have been found in hyperthyroidism:

- increased cardiac flow from  $6.13 \pm 0.25$  l / min to  $8.94 \pm 0.21$  l / min ( $p < 0.01$ );
- increase in ejection fraction at rest, but decrease in effort (from  $71.12 \pm 1.4$  to  $65.73 \pm 1.61$ );

- decrease of the isovolumetric relaxation time (E wave) and the ratio between cardiac cycle/ diastolic filling;

- increase of the mass index of the left ventricle, the dimensions of the interventricular septum and the posterior wall of the left ventricle (over 11 mm) in 9 cases.

In cases of hypothyroidism, when examining the resting heart by transthoracic echocardiography, the determination of cardiac parameters revealed the following:

- the ejection fraction of VS, although it was in the physiological range, was at its lower limit (60%). The correlation coefficient  $R = -0.62$  indicates an average dependence, its negative value indicates the decrease of the ejection fraction determined by the increase of TSH;

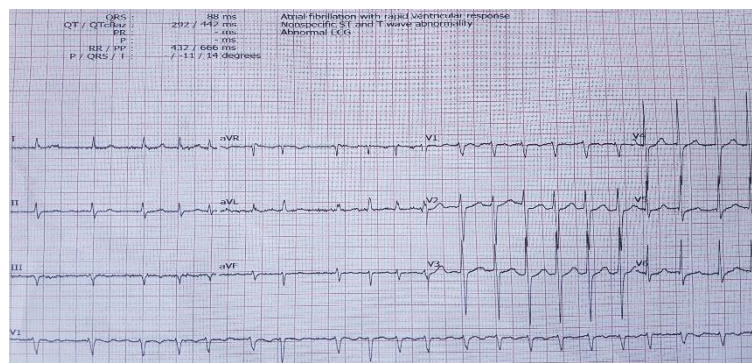
- the fraction of shortening of myocardial fibers (FS) registered low values (25%), being in

correlation with the high level of TSH; the correlation coefficient obtained  $R = 0.56$  shows an average dependence between the 2 parameters;

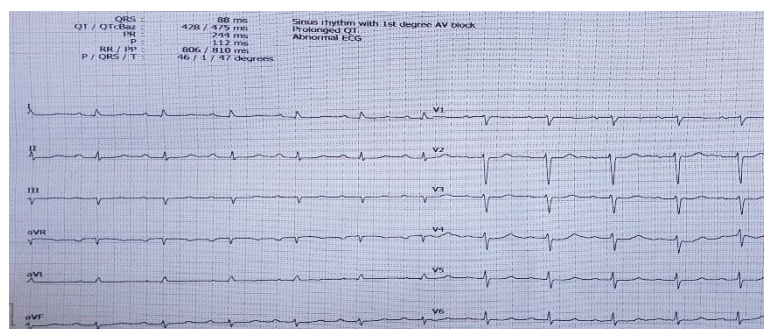
- indices of diastolic function obtained through Doppler showed a significant prolongation of the isovolumetric relaxation time (E wave) ( $94 \pm 13$  msec versus  $84 \pm 8$  msec), increased atrial filling (A wave) ( $55 \pm 13$  cm / sec compared to  $48 \pm 9$  cm / sec) and reduced E / A ratio ( $1.4 \pm 0.3$  compared to  $1.7 \pm 0.3$ );

- the beat volume, determined at rest, was at the lower limit of normal.

Below there are some EKG and echocardiographic aspects encountered in the studied patients (Fig.1, Fig.2, Fig.3, Fig.4, Fig.5, Fig.6, Fig.7, Fig.8).



**Fig.1 - Atrial fibrillation with rapid ventricular allure and HVS in a patient with hyperthyroidism**



**Fig.2 - BAV first degree and prolonged QT interval in a patient with hypothyroidism**

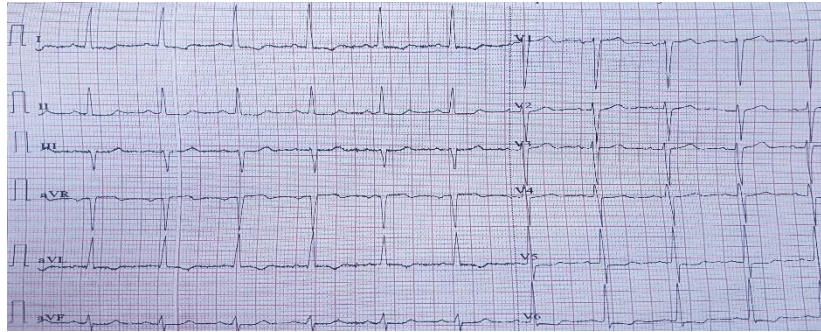


Fig.3 - Left ventricular hypertrophy with mixed repolarization changes in the patient with hyper-thyroidism

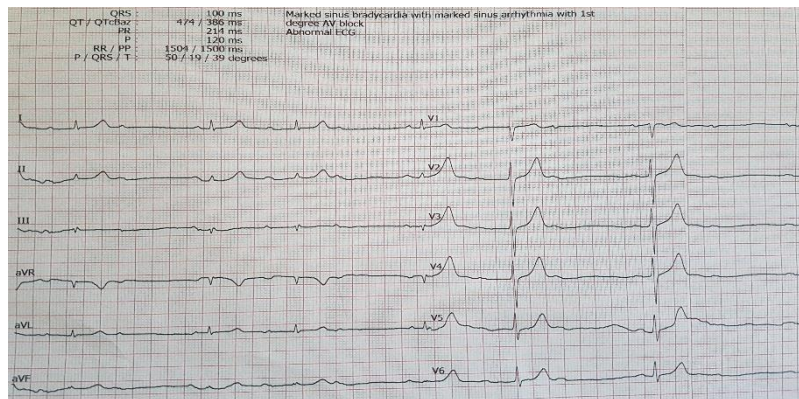


Fig.4 - BAV second degree Mobitz I in a patient with hypothyroidism

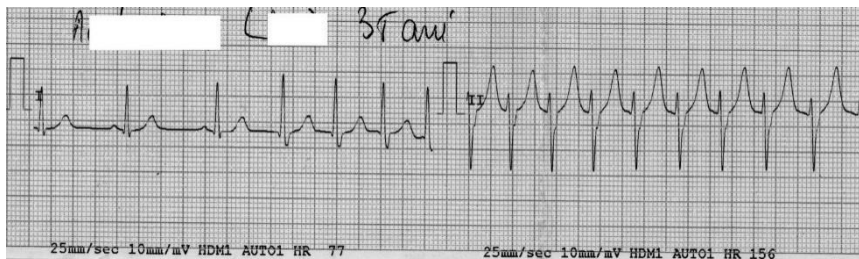


Fig.5 - Sinus rhythm, alternating with paroxysmal supraventricular tachycardia



Fig. 6 - Left ventricular hypertrophy in a patient with hyperthyroidism

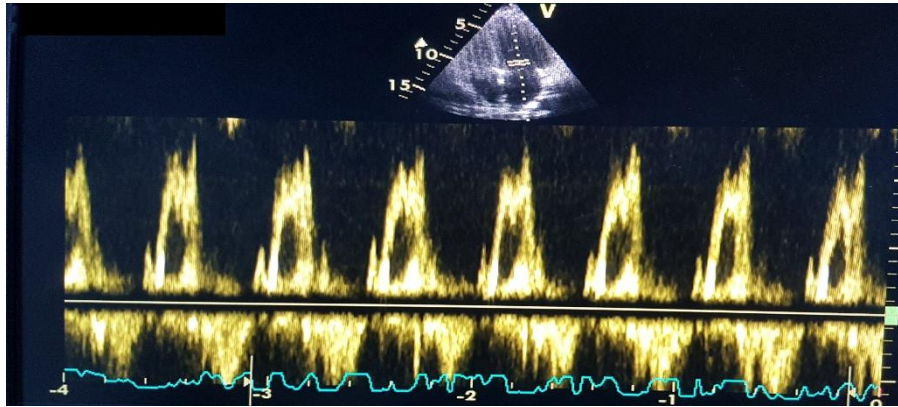


Fig.7 - Mitral pulsed Doppler - E wave with A wave fused in a tachycardic patient with hyperthyroidism

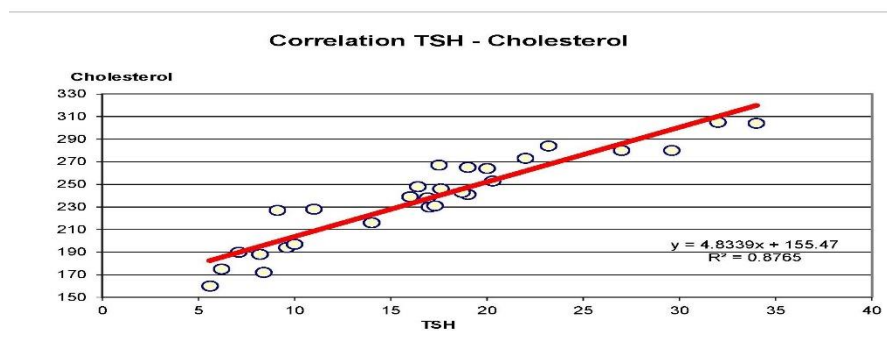


Fig.8 - TSH - Cholesterol Correlation

Due to the presence of changes in lipid metabolism, atherosclerotic risk is increased in patients with hypothyroidism. The increase of cholesterol and serum triglycerides and the alteration of the mobilization of free fatty acids are encountered in association with premature coronary artery disease. In addition, hypothyroid patients have an almost double frequency of coronary atherosclerosis compared to subjects of the same sex.

Although the cholesterol levels were not very high, there is a close connection of the two parameters. The regression coefficient R indicates that an increase in TSH with one unit increases total plasma cholesterol by 4.83 mg / dL.

The study of lipoprotein fractions in hypothyroid cases indicates important changes in serum levels:

- LDL-cholesterol increased in 67.8% of cases (19 patients) - an important factor in the genesis of atherosclerosis, especially coronary artery disease
- HDL-cholesterol decreased in 46.4% of cases (13 patients), the rest being at the lower limit of the normal ( $R = - 0.64$  - inverse proportionality relation, demonstrates its antiatherogenic role) - triglycerides (TG) showed an average level within normal limits ( $116 \pm 29.2$  mg/dL), indicating a reduced influence of TSH on their plasma concentration.

Patients with hypothyroidism have been shown to have an intrinsic deficit of receptor-mediated LDL catabolism, which is reversible under replacement therapy. Both symptomatic and subclinical hypothyroidism may be risk factors for premature appearance of coronary heart disease. Surprisingly, these patients have a reduced incidence of myocardial infarction and angina [6].

#### Discussions

Physical activity influences energy metabolism in human subjects by increasing activity-induced energy expenditure and resting metabolic rate for several hours after exercise. Effects of exercise on circulating thyroid hormone values remain controversial. [16]. When exercise is repeated at certain intervals, there is a pituitary-thyroid reaction that is properly coordinated by increasing turnover of thyroid hormones. Even gentle exercise such as walking, swimming, or yoga stimulates thyroid gland secretion and increases tissue sensitivity to thyroid hormones. [17].

Previous studies reported that intense exercise increases total serum T3 and T4 and a moderate-intensity level of exercise can increase T4 concentration in the blood. [18]. In hyperthyroidism myocardial contractility is increased as a result of a modification in the

synthesis of the myosin heavy chain protein from form  $\beta$  to form  $\alpha$ , of the increased transcription of the calcium ATP gene and of the increased calcium and glucose uptake. These changes make the contraction less efficient and increase the heat output. Post-pregnancy is reduced, and peripheral systemic vascular resistance decreases by up to 50-70%, cardiovascular consequences arise from the direct effects of T3 and the indirect effects of excessive lactate production (increased tissue thermogenesis) on smooth vascular musculature. Thus, the blood flow is much increased and redirected, especially to the skin, muscles and heart. Heart pressure increases too as a consequence of the increase of positive modulating blood volume by increasing the serum concentration of the angiotensin conversion enzyme and the high erythropoietin concentration, which have as immediate result the increase of renal uptake of sodium and of the erythrocyte mass [2].

There is a complex interaction between thyroid hormones and the adrenergic system and many of the clinical and paraclinical aspects of hyperthyroidism, such as resting sinus tachycardia, cardiac flow, beat volume, resting ejection fraction, increased pulse pressure and tremor, are similar to adrenergic beta status increased from pheochromocytoma [19].

Most patients with hyperthyroidism report palpitations and dyspnea at effort.

Pre-existing angina can get worse and only rarely is it de novo. Myocardial ischemia is thought to be caused by the increased needs of the thyroid toxic myocardium. However, coronary spasm may be an additional factor and myocardial heart attack may occur in the absence of significant atheromatosis. The electrocardiogram is usually normal, but in severe hyperthyroidism with cardiothyrosis, major changes of STT may be present in the absence of precordial pain. Typically, there is sinus tachycardia at about 120-140 beats/ minute, filiform pulse and wide pulse pressure. The apexian shock is strong, the cardiac breaths are common, mostly systolic. Moderate malleolar edema is common, but is rarely caused by heart failure, and is largely a manifestation of the reduced day / night ratio of urinary sodium excretion. Manifest cardiac insufficiency is not frequent in common hyperthyroidism and usually occurs only in the context of atrial fibrillation with rapid ventricular allure in an elderly patient with pre-existing ischemic or valvular disease [8].

Regarding hypothyroidism, the discrepancy in results among previous studies investigating associations between thyroid dysfunction and

exercise capacity is probably referred to the fact that all those studies were conducted in selected patient populations [7]. The effect of exercise on thyroid function is controversial, and it seems to depend on the severity and duration of the training protocol [20].

It is noticed that both hypo- and hyperthyroidism cause various cardiac abnormalities and, therefore, the management of these diseases is very important.

Cardiac manifestations of hypothyroidism include: bradycardia, pericardial fluid collection, congestive heart failure, and coronary atheromatosis.

Manifest hypothyroidism is associated with dyslipidemia and coronary heart disease. About 3% of patients with long-term hypothyroidism report typical angina and a similar proportion is reported during thyroxine treatment. In most patients angina does not change, decreases or disappears when thyroxine therapy is introduced. However, it can be aggravated, so up to 40% of these patients who present with hypothyroidism and angina cannot tolerate the correct substitution treatment due to its worsening. Moreover, myocardial infarction and sudden death are known complications at the beginning of treatment, even when patients receive only 25 mcg thyroxine daily [2].

Increased voltage is a common, but non-specific, EKG manifestation in young patients. Patients with thyrotoxicosis have a resting ventricular appearance of over 100 beats / minute. Atrial tachyarrhythmias are common, because the atria are very sensitive to T3 effects [ 21]. In severe cases of supraventricular tachycardia with very high ventricular allure, increased myocardial consumption and decreased diastolic filling may cause ischemic and electrocardiographic EKG (ST-T) changes by decreasing systolic function or even dilating the cardiac cavities (tachyarrhythmia cardiomyopathy). They often have a clinical correspondent (signs of heart failure, angina, etc.). Atrial fibrillation is the most common arrhythmia, occurring in about 20% of cases of thyrotoxicosis, is repetitive, sustained and resistant to antiarrhythmic and beta-blocker treatment, in the absence of antithyroid.

Most hypothyroid patients have low or normal ventricular allure (50-70 beats/min). Patients with severe hypothyroidism and those with pre-existing heart disease may develop varying degrees of atrioventricular block or may have intermittent or permanent branch blocks, especially the right branch. Among the echocardiographic structural changes were noted: left ventricular hypertrophy, slight increase in the volumes of the cardiac cavities and the index of ventricular mass. Electrocardiographic

changes may derive from ventricular remodeling and are characterized by increased QRS complex amplitude, suggestive of left ventricular hypertrophy, left or right axial deviation, T reversed waves, first degree atrioventricular block, and increased duration of QRS complex.

Changes in thyroid hormone levels in response to exercise, are in general, small and within the normal range. Increase, decrease, or no change in the levels of thyroid hormones has been reported, regardless of the type of exercise, duration, and intensity. These divergent findings might be attributed to several confounding factors, such as variations in body composition, nutritional status and the type of exercise training [22]

The study has some limitations: it did not have a control group without thyroid dysfunction, the patients didn't follow a standardized exercise schedule and they weren't ECG-monitored (Holter system) during the physical exercise.

Given the important role of thyroid hormone metabolism during and after exercise and physical activity, and in the initiation of cardiovascular disorders, is clearly still a need for further evaluation until the uncertainty is resolved.

### Conclusions

The results of this study show that there is an increased incidence of cardiovascular manifestations in both hyper- and hypothyroidism, including in young patients who perform intense physical activity on a regular basis.

Abnormal diastolic filling of the left ventricle (suggestive for the alteration of left ventricular relaxation and diastolic filling times) is a common manifestation in hypo- and hyperthyroidism, so the observed diastolic dysfunction may be the prelude to more severe limitations of cardiac function and physical performance.

The means of investigating the cardiovascular manifestations of thyroid disease are simple and, although they are only guidelines, they can effectively assess the condition of the heart and the response to the specific hormone therapy. Doppler echocardiography can be considered a reliable method for a complete and correct assessment of diastolic and systolic VS function, as well as for monitoring patients with wall dysfunction or those with pericardial fluid.

In the current practice there is a general effort of increasing the awareness of the medical staff on the arrhythmic risk and on the special importance of this problem in the evaluation of the young sportsman by a multidisciplinary department.

Thyroid pathology may be a major risk factor in the initiation of cardiovascular disorders. Taking into consideration the incidence of subclinical thyroid

dysfunction, routine dosing of TSH in the presence of cardiovascular manifestations is required.

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