How Does the Thyroid Function Affect the Sport?

Healthcare

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Abstract

Some authors have speculated that the symptomatic chain of the thyroid function was linked to the alteration of basal metabolism that occurs during the dysthyroidism. Other researchers, though, suggest that changes of the cardiovascular apparatus ought to be put in relation to a direct action of thyroid hormones on the heart. However, it can be stated that in the determination of the heart phenomenology, during the thyroid disease, are implicated both direct and indirect effects.

Introduction

The disorders affecting the cardiovascular apparatus are certainly the most common among the clinical manifestations found in thyroid diseases; these ones have a high incidence in the various statistics, variable between 75 to 85%.

Is a common frequently experience that the heart rhythm disorders, primarily those ones of hyperkinetic type, such as the sinusal tachycardia or the atrial fibrillation, in asymptomatic or mildly symptomatic patients, are related to hyperactivity of the thyroid gland (see tables I and II).

Table 1. Most common signs and symptoms in hyperthyroidism

Palpitation	Increased Appetite
Tachycardia	Weight Loss
Increase of Dif. Blood pressure	Diarrhea
Anxiety	Intolerance to heat
Insomnia	Perfuse perspiration
Restlessness	Warm and clammy skin
Hyperreflexia	The GAEF sign
Trembling	Fixed gaze
Emotional lability	Exophthalmos
Asthenia	Gozo Infiltrative dermopathy

Table 2. Most common signs and symptoms in hypothyroidism

Asthenia	Facies Amimicia
Bradycardia	Weight Increase
Dyastolic Hypertension	Constipation
Anxiety	Intolerance to cold
Snoring	Hypothermia
Voca rauca	Dry hair and skin
Hyporflexia	Menorrhagia
Paresthesia	Fixed gaze
Emotional lability	Periorbital edema
Muscular cramps	Palpebral ptosis

In fact, thyroid hormones can potentially affect the cardiac activity through:

- Direct effects at the cellular level;
- Interaction of thyroid hormones with the autonomic nervous system (sympathetic);
- Indirect effects correlated to hemodynamic and metabolic adjustments.

In turn, these three mechanisms are capable of influencing all the cardiac kinetic and in particular, the contractility and the myocardial chronotropism.

Thyroid Hormone Direct Effects on the Heart

T3 exerts its effects on myocardial cell substantially via two systems. The first, that can be defined as the "nuclear effect" is expressed at the cellular level after the binding of the hormone with specific nuclear receptors and the subsequent activation of RNA for the encoding of specific proteins. The second, defined as the "extra-nuclear effect" does not require, instead, the bond with the nuclear receptor and is expressed without the activation of protein synthesis (3).

Nuclear receptors for thyroid hormones belong to C-erb – A related supergene family (4).

T3 effects are complex and various: some are the stimulant type, other of inhibitory type; many of them express their action in concert with other hormones or factors.

The binding of T3 to its own receptor leads to the activation (or deactivation) of protein synthesis, in particular of contractile proteins, thus determining thyroid - induced myocardial alteration. The most studied and ascertained modifications of the myocardial protein synthesis include increase of *alpha myosin* heavy chain and that of sarcoplasmic reticulum Ca^{++}-ATPase, while the synthesis of *beta myosin* heavy chain decreased. Moreover, has been shown that in the myocardium of some animal species T3 can also change the spectrum of myosin heavy chains and of $Na.^{+}K^{+}$-ATPase isoforms. Thus, is proved that the thyroid hormone increases the myosin synthesis and alters its structures, hence increasing the contractile properties and in particular by increasing the more movable isozyme of V1 myosin (See fig.1).

Fig 1. Isoforms of myosin heavy chains

ATPase	
Overloading	Training
Hypothyroidism	Hypothyroidism
Sedentary lifestyle	Catecholamines

Since it is believed that the active level of ATPase regulates the turnover rate of cross-links between actin and myosin, the increase of this enzyme seems to contribute to greater contractile response of a hyperthyroid heart. Besides the alteration of protein synthesis in hypothyroidism, as described above, there was also evidence of a transient increase in *alpha-actin* (5).

In addition, many other proteins that mediate the ($Na.^{+}$ K^{+}-ATPase) ionic flow, the $Ca.^{++}$ flow of channels and the leakage of $Ca-^{++}$ from the sarcoplasmic reticulum, are strongly influenced by the administration of thyroid hormones. The altered utilization of intercellular Calcium, specifically correlated to the recycling of Calcium from the sarcoplasmic reticulum, helps explain the changes in the myocardial contractile functions that are induced by thyroid hormones. This effect appears mostly noticeable only in the ventricular myocardium since the atriuml isozymes are poorly sensitive to thyroid hormones (6). In addition to their receptor-mediated nuclear effect, these hormones have been shown to activate extra nuclear sites which, as already mentioned, do not require activation of the protein synthesis to manifests its effects (see tab. III).

The exposure of cells or cardiac membranes isolated to thyroid hormones may cause very rapid effects that become obviously even when the protein synthesis is completely inhibited. It appears that these effects are mediated through a way which does not require receptors for thyroid hormones, thus representing the co-called "extra-nuclear effects".

Inter alia, these would consist in rapid changes in flow of the $Ca.^{++,}$ amino acids, sugars and mitochondrial oxidation (see fig.2). Also, the $Ca.^{++}$- ATPase of the sarcolemma is stimulated by thyroid hormones in vitro (isolated membranes of heart cells).

Interaction of Thyroid Hormones with the Sympathetic Nervous System

Many clinical manifestations of hyperthyroidism such as the tremor, tachycardia, anxiety, mimic a hyper - adrenergic state; also, the events related to hypothyroidism such as the bradycardia are subjective to a reduction in the sympathetic tone.

Table 3. Thyroid hormones and their action

Increase	
	Protein Synthesis
Thyroxine	Intracellular enzymes
Triiodothyronine	Number and volume of mitochondria
	Glucose uptake
	Mobilization of fatty acids
Calcitonin	Parathyroid hormone antagonist

Fig 2.

Alpha-agonist	$Ca.^{++}$	Dependent-Voltage Channel
	$Ca.^{++}$ Calmodulin	
$Ca.^{++}$	Kinase myositis	
Activated channels	actin-myosin interaction-vasoconstriction	$Ca.^{++}$
by receptors		cellular membrane

The assumptions concerning the interconnections between thyroid activity and the sympathetic nervous system, are numerous and sometimes in contrast with each other. This can be explained either by the difficulty of finding homogeneous groups of subjects to be studied, or by an insufficient direct experimentation on humans.

It is hypothesized that the thyroid hormone alters the intercurrent relationships between the sympathetic nervous system and cardiovascular system, either for the increased validity of the sympathetic adrenergic system, or for the high response of cardiac tissue to a normal adrenergic stimulation (7). It has also been speculated that the sympathetic stimulus exerts simply a direct additive effect on cardiovascular function in addition to thyroid hormone stimulus on its own.

However, these clinical effects suggestive of an altered sympathetic tone are not supported by a correlated rate of circulating catecholamines that, as is known is normal or reduced in hyperthyroidism and higher in hypothyroidism (8).

These results suggest that sympathomimetic aspects of hyperthyroidism cannot be explained simply by an excessive increase in adrenergic activity but rather as a secondary phenomenon to alterations in the affinity of catecholamines for their receptors or to a modification of a post-receptor mechanism.

The Effects on Myocardial Contractility

In 1967 Buccino and coll. (9) studied through myocardial biopsies the effects of thyroid hormones on the intrinsic contractile properties and on the energy deposits of phosphate in isolated papillary muscles of the cat. They correlated these results with hemodynamic measurements in intact animals. Compared to euthyroid animal's muscles, the muscles of hyperthyroid cats showed a significant increase in both shortening velocity and contraction force. Obviously, opposite modifications occur in the isolated muscles of hypothyroid animals. Moreover, it is proved that these changes were not related to the heart rate, with abnormal catecholamine cardiac deposits and/or of high energy phosphate compounds. These results have been confirmed in humans through the determination of systolic intervals, cardiac performance and oxygen consumption. As previously described, the biochemical substrate of thyroid hormones impacts on the heart is important because in hypothyroidism the myosin isoenzymes are present predominantly in *beta* slow forms, while the T3 induces an increase of *alpha* faster forms (10). Furthermore, thyroid hormones are one of the factors capable of stimulating $Ca.^{++}$ATPase of the heart's sarcoplasmic reticulum, which markedly influences the rate of diastolic relaxation (11).

The Effects on Diastolic Properties of the Left Ventricle

The left ventricular filling is influenced by various factors such as ventricular hypertrophy, the diastolic relaxation and reload, all elements influenced by thyroid hormones. Left ventricular hypertrophy, usually detectable in hyperthyroidism, can be put in relation either via the T3 direct stimulation on myocardial protein synthesis or with increased cardiac workload (10-11).

The Effects on the Peripheral Circulation

Thyroid hormones, in addition to the direct effects on the myocardium, may influence the cardiac function by changing the pre- and post- reload. In this sense, the most obvious actions are responsible of the venous return (pre-reload) and systemic arteria pressure (post-reload).

The effects of thyroid hormones on the venous "compliance" and circulating blood volume are still uncertain, and basically there are no recent and reliable studies, at least regarding humans, although it appears that the blood volume is increased in hyperthyroidism and decreased in hypothyroidism (12).

Conversely, there are numerous studies used to assess the effects of thyroid hormones on peripheral resistance.

Generally, the hyperthyroidism has only minor effects on mean arterial pressure, since although it determines an increase in the systolic blood pressure - secondary to an increase in stroke volume – it also causes a decrease in diastolic blood pressure due to peripheral vasodilatation (a classic example of systolic hypertension with wide differential). On the contrary, the hypothyroidism is correlated to a high diastolic blood pressure. Generally, in both situations it occurs a normalization of the pressure state with euthyroidism return (13,14).

Some peculiar characteristics have been observed within the research framework on this type of secondary hypertension.

The hormonal profile of hypothyroid hypertension patients has found that more than half of these presents a low plasma renin activity and were found as well low levels of angiotensin (15,16). This would demonstrate that the renin-angiotensin system plays a secondary role in this type of hypertension.

The Atrial Natriuretic Factor has been considerably diminished in hypothyroid patients and vice versa in hyperthyroid ones (17). This increase may be related to the T3 direct effect on the mRNA transcription for the ANF's and its synthesis (18).

The Chronotropic Effect

Although the positive chronotropic effect of thyroid hormones is well known and incontrovertible, the tachycardia isn't clearly explained in all studies; for the most part it would seem due to the combination of a speed increase in diastolic depolarization with a decreased duration of the action potential in cells of the sinoatrial node.

Studies results and Marcus and coll. research (19) also Valente and coll. research (20) would tend towards a direct effect of thyroid hormones on the heart rate. This interpretation is confirmed by three criteria:

- First, in vitro studies performed by using sinoatrial nodes' preparations and rabbit atrial muscles fibers have shown that thyroid hormones reduce the duration of repolarization phase of membrane action potential and increase the diastolic depolarization rate and therefore the contraction speed (21);
- Second, studies that have used isolated and perfused hearts have shown that the organs of animals rendered hyperthyroid present an increased heart rate and an absolute refractory period on average shorter than the euthyroid animals' hearts (22).
- Third, in isolated heart of euthyroid animals the addition of T3 via perfusion accelerates the heart rate and shortens the refractory period. The mechanisms by which thyroid hormones induce these electrophysiological changes are not yet fully understood, although it may be correlated to an increased density of the $Na.^{+}$ pump (23) and with an increased in permeability of the cell membrane to $Na.^{+}$ and K^{+} (23,24).

Cardiovascular Manifestations During Hyperthyroidism

In the thyroid disease the heart appears to be the most sensitive organ and the symptomatic chains constitutes an important clinical feature of hyperthyroidism.

It can be identified, chronotropic alterations that occur with sinus tachycardia, atrial fibrillation, shortening of the PR interval, and inotropic alterations that reflect changes in the contractile mechanism of the heart, such as increments in the cardiac index and the shortening velocity of the wall, the shortening of the ejection period and, clinically, systolic hypertension (26). Despite the high frequency of cardiac manifestations during hyperthyroidism it cannot be detected pathognomonic alterations from an anatomopathological point of view, even though there have been identified several anatomopathological alterations such as isolated

myocyte necrosis, small areas of fibrosis, individual myocytes with increased dimensions and containing a large number of mitochondria (26,27).

The main symptoms referable to the cardiac apparatus are palpitations – denounced as sub continuous, with particularly intense acute stage, sometimes accompanied to a sense of respiratory distress, and dyspnea, sometimes present even after modest efforts. Throughout the inspection it is found a hyperkinetic itto and during the cardiac auscultation a first high tone, an accentuation of the pulmonary component of the second tone and a third heart sound; occasionally it is appreciable a systolic click by ejection. Along the left costal margin are frequent the meso-systolic murmurs and, at times, during expiration it is possible to perceive on the second left intercostal space a systolic scratch known as "Means-Lerman scratch". Presumably, this last finding is secondary to the scratch of pericardial and/or pleural sheets, however normal but enhanced by the cardiac hyper dynamic.

The radiographic and electro radiographic changes are common in hyperthyroidism, but not specific; so the left ventricle, the aorta and the pulmonary artery appear prominent and in some cases it may be observe a generalized enlargement of the heart that can be accompanied by signs and symptoms of congestive heart failure.

The Heart Rate

In patients with sinus rhythm the extent of tachycardia is generally parallel to the severity of the disease. The sinus tachycardia (frequency greater than 100 beats per minute) is present in 40% of patients with hyperthyroidism, and occurs more frequently in younger subjects, and often at night. Approximately 15-25% of patients with hyperthyroidism have a chronic atrial fibrillation, which is often preceded by one or more paroxysmal episodes (28).

Conduction Disturbances

The disturbance of AV conduction is not clear, since the laboratory animals demonstrate a refractory period and a shortened conduction time (29). The most common intra-ventricular conduction disturbance is the right bundle branch block (RBBB), which occurs in 15% of patients with hyperthyroidism without associated or past heart disease (30). The paroxysmal supraventricular tachycardia and atrial flutter are rare in hyperthyroidism.

Rhythm Disorders

The impaired cardiac excitability may induce arrhythmias. The atriums are more sensitive to thyroid hyper stimulus than the ventricle (31). In fact, the arrhythmias typically found in hyperthyroidism are the supraventricular extra-systole and the atrial fibrillation. The ventricular extra-systole, instead, is quite rare, whereas the tachycardia and the ventricular fibrillation are exceptional and usually are correlated to a preexisting cardiopathy or to a severe heart failure. The preferential arrhythmogenic towards atrium could be explained by the highest density of *beta*-adrenergic receptors in the atrium and by the different autonomic innervation between the atrium and ventricles or, also by a different response of atrial and ventricular myocardium to thyroid stimulus.

Coronary Insufficiency

Both the angina pectoris and congestive heart failure occur in patients affected by hyperthyroidism, but for many years it was considered that these affections were observed only in the presence of a concomitant cardiovascular disease. This hypothesis is mainly supported by the fact that these symptoms are rare in the hyperthyroid young subject. However, it should be emphasized that when thyrotoxicosis is quite severe may overload even the normal heart, although in most cases the development of clinical manifestations of damage or myocardial ischemia in hyperthyroid patients subtends the presence of cardiopathy or a preexisting disease of the coronary vessels.

The systolic and cardiac index, the average speed of systolic ejection, the speed and contraction peak and coronary flow, as it might be expected, are all increased, the systolic ejection time and the time of pre ejection are abbreviated, the pulse is wider, and the systemic vascular resistances are diminished.

It has been hypothesized that many of the changes in cardiac function are secondary to the increased metabolic needs of peripheral tissues. Many hyperthyroid patients manifest dyspnea after moderate effort and easy tiredness even in the absence of heart failure. These symptoms may also have an extra cardiac genesis since hyperthyroidism implies a weakening of the skeletal musculature, including the respiratory muscles (32).

Treatment of Cardiovascular Manifestations of Hyperthyroidism

In hyperthyroid patients it is of paramount importance the rapid achievement of euthyroidism. This goal can be pursued with the use of drugs belonging to the family of thionamides; there are currently in use the Methymazole and Propylthiouracil (not yet in use in the Italian market). Depending on the necessity of having to reach as soon as possible the euthyroidism, the choice between Methymazole and Propylthiouracil should fall on the latter since this drug, besides the inhibition of T4 formation; it inhibits the peripheral conversion of T4 to T3. Other therapeutic modes employ more time to reach the euthyroidism. Generally, the concomitant administration of beta-blockers drugs leads to a considerable benefit in hyperthyroid; especially when there are no signs of heart failure. Some beta blockers, such as propanol, although they do not affect directly the action and/or the incretion of thyroid hormones, inhibit moderately the peripheral conversion of T4 to T3. In any case, beta blockers should never be used as the only therapeutic presidium.
The propanol can be administered orally at a dose of 120-160 mg/day divided into 3 or 4 doses. In patients, with acute problems related to an increased heart rate, can be achieved rapid effects with the administration of intravenous propanol (1 mg every 5-10 minutes) until rapid achievement of an adequate heart rate. In patients, where a deterioration of angina pectoris is manifested, can be successfully used calcium antagonist drugs.
Hyperthyroid patients (see table IV), who show a severe heart failure, can be treated with digital, whose effectiveness – in these conditions - is related to its negative chronotropic action. However, this drug should be administered with caution, as the hyperthyroid patients can have a marked sensibility to digoxin and the therapeutic range, in these cases, is much more limited (33).
About half of patients with concomitant onset of hyperthyroidism and angina pectoris have presented, after the treatment for hyperthyroidism, a complete remission of symptoms. Furthermore, the 62% of the 163 thyrotoxic patients with persistent atrial fibrillation, since more than one week, have submitted a spontaneous recovery of the sinus rhythm with the euthyroidism return (34).

Table 4. Examination that explores the thyroid function

Dosage of circulating T3 and T4 thyroid hormones	
Titration of TSH	
Specific Antibodies Research	
Iodine protidemia	
Determination of basal metabolism	
Ultrasound	
Iodine uptake and scintigraphy	
Needle aspiration	
Biopsy	
Thyroid Scintigraphy	
Cold air	Hot air
Needle aspiration- Ultrasonography	Diffuse-circumscribed
	Hyperthyroidism - Gozo

This shows how important it is to establish promptly if hyperthyroidism is present in patients with cardiovascular problems, since the treatment in this case causes a rapid improvement.

Cardiovascular Manifestations During Hypothyroidism

The first description of cardiovascular manifestations during hypothyroidism has been provided by Zondek in 1918 who coined the term “myxedematous heart” (35). In general, for serious cardiac problems to occur it is required a long period of hypothyroidism. The pathophysiological basis of cardiac modifications, are opposite to those described for hyperthyroidism. Are called into question, besides the effects caused by a decreased direct effect of thyroid hormones on myocytes, even indirect effects linked to a decreased oxygen consumption and changes in hemodynamic parameters. Therefore, it is possible that an important role is played by the reduced sensitivity of the sympathetic system. However, it is not possible to identify specific changes in the myxedematous heart (36).
In addition to an accumulation of mucopolysaccharides, during histologic examination can be observed myofibrillar swelling with loss of the normal striation and interstitial fibrosis of varying degrees. In addition to a dismemberment and a loss of the cristae, the mitochondria in the electron microscope show intracorpuscolari lipid inclusions (36).
The cardiac silhouette is generally increased due to the presence of pericardial effusion, since the weight of the heart is substantially normal, even if it is zoomed macroscopically; it also appears pale and floppy.
Actually, the hypothyroidism diagnosis is increasingly early; this makes it more infrequent the acclaimed framework of myxedematous cardiopathy, characterized by exertional dyspnea and easy tiredness, significant edema of the face and extremities, significant bradycardia, hypotension, paraphonic heart sound, congestive heart failure manifestations, such as orthopnea, paroxysmal dyspnea and ascites.

The myxedema is associated with an increased capillary permeability and consequent passage of proteins in the interstitial spaces and virtual cavities; this occur mainly in the pericardial space, that is why the detection of pericardial effusion is very frequent (about 1/3 of the cases), as it seldom gets complicated with cardiac tamponade (37).
The diagnostic hypothesis must still be confirmed by echocardiography, since the radiological cardiac silhouette and low ventricular electrocardiographic complexes are unreliable indicators for the diagnosis of pericardia effusion.

The electromyographic changes, observed in hyperthyroid patients, are many but not specific. Sinus bradycardia is often found. It may be present a lengthened Q-T interval, but since the amplitude of T wave is low, the precise measurement of the interval can be difficult. Even the amplitude of P wave is often low and in some cases is not distinguishable. It is possible that the hypothermia can facilitate reentrant ventricular arrhythmias due to the slowing down of the heart rate and the increase in duration of the QRS and QT events (38).

The incidence of atrioventricular and intraventricular conduction disturbances is about three times higher in patients with myxedema than in the general population.

The frequency of hypertension in hypothyroid population is differently estimated, depending on the various statistics, even though it may be really increased if the patients with severe myxedema are excluded. Anyway, the hypotension treatment should be initiated only after the normalization of thyroid hormones rates since, only with the euthyroidism return, in most patients, the values return to normal. The atherosclerotic risk is particularly high in the hypothyroid patient considering that he is often hyper hyperlipidemic. The documentation that arteriosclerosis of the coronary arteries occurs with a frequency two times higher in patients with myxedema compared to the control group supports this hypothesis (40).

In fact, the angina pectoris incidence and myocardial infraction in these patients is low. This discrepancy is probably due to low oxygen consumption by the myxedematous myocardium.

The Treatment of Cardiovascular Manifestations During Hypothyroidism

The substitution therapy offers significant benefits to hypothyroid patients with heart problems, since much of the alterations in this organ, are solved only by the return to euthyroidism. However, the presence of a severe symptomatic coronary artery disease (angina pectoris) may require greater caution during therapeutic approach, especially when it comes to elderly patients. Initially these patients should be treated with low doses of thyroid hormones (ex. 12.5 nanograms of thyroxine) with incremental adjustments every 4-6 weeks. During this period the cardiovascular status of the patient must be frequently monitored and the dose should be reduced if it occurs any unfavorable effect. With regard to a very severe form of angina pectoris the increments of the drug should be further procrastinated and, in the case that the achievement of a therapeutically effective dosage was not possible because of the ischemic cardiopathy is essential a coronarographic study in order to assess a surgical solution, bypass or angioplasty, that in moderately hypothyroid patients is always feasible (41,42).

The treatment of hypothyroid patient is particularly difficult both for the effect of thyroid hormone on the heart and for the altered response of the heart to cardiac glycosides (43).

Conclusions

The ailments correlated to thyroid function in Sport Medicine are frequently observations, especially among women. There are recent papers showing that physical activity in general and sports activities in particular may affect the activity of this gland especially by increasing the secretion of TSH hormone.

Hypothyroid subjects have lower performance capacity and concentration skills than those possessed by euthyroid subjects.

On the other hand, the continuous muscular work (training) not only can aggravate the induced conditions by a hypo- or hyperthyroidism on the various organs and systems, but also may underline a disorder of this type.

In conclusion, it may therefore be emphasized that an early diagnosis and an accurate and prompt therapeutic treatment of these subjects (with a thyroid both hypo then hyper functioning) allows, in the vast majority of the cases, to avoid coarser organic manifestations induced by dysthyroidism and, that such dysfunction once revealed, may, in a short time, be traced within the normal range. With regard to medical sports evaluation and the suitability assessment the Authors agree that, if the subjects are under constant surveillance, the whips forms or the mild ones do not cause problems of any kind. In the forms of medium severity, but treated with specific therapy, are required periodic and contiguous clinical monitoring, either instrumental or laboratory; to persons belonging to this class must be recommended sport and moderate cardiac engagement. Subjects suffering of overt

hyperthyroidism, instead, must stop the activity until the main parameters have return within the normal values and until the therapeutic dosage has been found.

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