

# Effect of Thyroid Hormones on Cardiovascular and Muscle Systems and on Exercise Tolerance: a Brief Review

Alexandre Gonçalves, Elmiro Santos Resende, Maria Luiza Mendonça Pereira Fernandes, Alberto Martins da Costa  
*Universidade Federal de Uberlândia - Uberlândia, MG*

Thyroid disorders (hypothyroidism and hyperthyroidism) have been the focus of studies in the most diverse areas of health sciences, because of their repercussion on various parts of the human body.

Among the many consequences of these disorders, decreased exercise tolerance, due to direct involvement of cardiovascular and muscle systems, is rarely reported in literature<sup>1-3</sup>.

This article addresses, through literature review, the cause-effect relationship of thyroid hormone actions on both systems and their implications for exercise capacity.

## THYROID HORMONES AND THE CARDIOVASCULAR SYSTEM

According to the classical literature on human physiology<sup>4</sup>, thyroid hormones – thyroxine (T4) and triiodothyronine (T3) – produce an overall increase in the basal metabolism of the human body. This is accompanied by greater tissue oxygen consumption, owing both to vasodilation and the concomitant increase in cardiac output, which are facilitated by enhanced chronotropism and inotropism.

Studies of hyperthyroid patients<sup>5-10</sup> have demonstrated that they show increased contractile force and cardiac output, with decreased peripheral resistance.

Cardiac ATPase consists of two heavy-chain proteins, alpha ( $\alpha$ ) and beta ( $\beta$ ), and is involved in energy production for cells of the entire body. The  $\alpha$ -chain has a high ability to dephosphorylate ATP, while the  $\beta$ -chain has a low ability. Thus, three different cardiac ATPase molecules may exist:  $\alpha\alpha$ ,  $\beta\beta$  and  $\alpha\beta$ . The expression of the  $\alpha$ -chain gene increases in the presence of the thyroid hormone, thereby improving myocardial contractility. However, this improvement in contractile force occurs only with slight elevations of thyroid hormone levels, because excessive levels of it enhance contractile protein catalysis. When it comes to hypothyroidism, the  $\alpha\beta$  molecule is converted to

$\beta\beta$ , reducing myocardial contractility<sup>11-13</sup>. In both cases, therefore, contractility is impaired. In hyperthyroidism, this is associated with excessive breakdown of contractile proteins. In hypothyroidism, the functional deficit is related to structural changes in the ATPase enzyme.

Both situations cause changes that may decrease physical fitness, because of reduced pump function.

With regard to thyroid hormone influence on hemodynamic parameters, during hormone replacement systolic blood pressure increases and diastolic blood pressure decreases, leading to wider pulse blood pressure. However, mean blood pressure remains unchanged<sup>4</sup>. Systolic pressure elevation is explained by the increment in blood flow induced by increased cardiac output. Diastolic pressure decrease is due to the peripheral vasodilation caused by greater relaxation of arterial smooth muscle. In hypothyroidism, the opposite is true.

Some studies<sup>14-16</sup> have demonstrated that thyroid hormones also increase venous return, contributing to greater cardiac output and systemic vascular resistance.

This understanding of reduced systemic vascular resistance, one of the postload components found in hyperthyroidism or hormone replacement, emerged with the discovery of the vasodilator role of T3 on the vascular smooth muscle<sup>17</sup>.

Thus, the effect of thyroid hormones on hemodynamic variables, such as heart rate, cardiac output, pre- and postload components, systolic pressure, diastolic pressure and pulse pressure, is a result of higher or lower peripheral metabolic demand associated with hyperthyroid or hypothyroid states, respectively.

Low exercise tolerance in hypothyroid patients is justified - among other factors - by the decrease in myocardial contractile force caused by structural changes in the ATPase enzyme described previously. This reduction in the heart's pumping function decreases cardiac output, an important factor in determining the degree of exercise tolerance. On the other hand, despite their high cardiac output, hyperthyroid patients also

## KEY WORDS

Thyroid, hyperthyroidism, hypothyroidism, exercise tolerance.

**Mailing Address:** Alexandre Gonçalves • Rua Delmira C. R. da Cunha, 1161/301 – 38408-208 – Uberlândia, MG, Brazil  
E-mail: profalexandre09@gmail.com

Received on 09/22/05 • Accepted on 11/11/05

have low exercise tolerance. This is caused by increased levels of circulating thyroid hormones over a long period, which keep the heart rate permanently elevated and, as a result, decrease the heart's capacity to work. This effect is enhanced by high catalysis of contractile proteins, as already mentioned<sup>18</sup>.

## THYROID HORMONES AND THE MUSCLE SYSTEM

Some studies<sup>19-21</sup> have related hypothyroidism to muscle dysfunction. The problem seems to lie in the lower activity of the enzymes involved in the aerobic and anaerobic glucose mechanism. Reduced mitochondrial activity also occurs, with abnormal muscle energy metabolism.

Therefore, in addition to deficits associated with decreased blood flow to tissues and oxygen delivery to muscles, there are also metabolic deficits that increase these patients' exercise intolerance.

This inference is supported by the fact that skeletal muscle is one of the primary targets for thyroid hormones<sup>22</sup>.

Furthermore, studies conducted by Ramsay<sup>23</sup> demonstrated that thyroid hormone action on skeletal muscles affects mainly type-I muscle fibers, which promote slow contractions and are most prevalent in the postural muscles recruited during prolonged effort.

Different metabolic changes, yet with similar consequences, may therefore be observed in both hypothyroid and hyperthyroid patients. In the first case, fatigue is directly related to deficient action of thyroid hormones. In the latter, however, the cause is mainly depletion of muscle energy substrate due to high metabolic demand.

As we may observe in the Everts' (Graphic 1), all these muscle dysfunctions may be exemplified by the Achilles tendon reflex test used to diagnose thyroid disorders prior to development of new methods<sup>22</sup>.

In the soleus muscle, which is composed predominantly of type I fibers and is involved in the reflex response already

described, fiber recruitment is faster in the hyperthyroid state and slower in the hypothyroid state.

## THYROID HORMONES AND EXERCISE TOLERANCE

One of the primary consequences of thyroid dysfunction is lower tolerance to physical exertion, because of its implications involving the muscle and cardiovascular systems. This interferes directly in the patient's ability to perform daily activities, thereby reducing his quality of life.

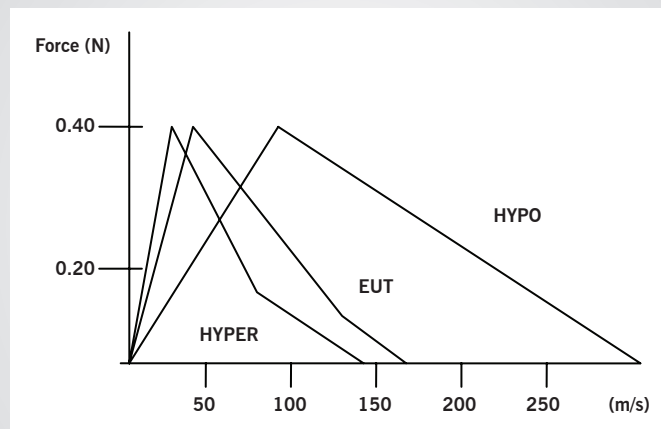
According to traditional studies in the field of exercise physiology<sup>24-28</sup>, one of the key parameters for measuring tolerance to high-intensity exercise is the anaerobic threshold, because it reflects the point of the body's maximal oxygen consumption.

Compared to those less fit, people with good cardiorespiratory fitness require higher-intensity exercise to reach the anaerobic threshold. That is why athletes show higher exercise tolerance.

The study performed by Kahaly et al<sup>3</sup> showed that subjects with thyroid dysfunction have reduced workload tolerance at the anaerobic threshold, compared to euthyroid subjects. According to these authors, in hyperthyroidism this exercise intolerance is caused by mitochondria oxidative dysfunction, and in hypothyroidism, by inadequate cardiovascular support.

## FINAL CONSIDERATIONS

Several studies demonstrate the effects of thyroid disorders on cardiovascular and muscle systems. Foremost among them are impaired cardiac function and decreased ability to perform daily activities, because of exercise intolerance. Further studies should be stimulated to evaluate disorders secondary to thyroid function variations and their implication, as well as therapeutic options for this highly prevalent disease.



Graphic 1 – Soleus muscle contraction in hypothyroid (HYPO) and hyperthyroid (HYPER) rats, compared to euthyroid (EUT) rats. (Adapted from Everts, 1983)

## REFERENCES

1. Everts ME. Effects of thyroid hormones on contractility and cation transport in skeletal muscle. *Acta Physiol Scand.* 1996; 156: 325-33.
2. Kahaly GJ. The thyroid and the heart. *Thyroid Internacional* 1998; 4: 1-21.
3. Kahaly GJ, Kampmann C, Mohr-Kahaly S. Cardiovascular hemodynamics and exercise tolerance in thyroid disease. *Thyroid.* 2002; 12, 6: 473-81.
4. Guyton AC, Hall, JE. *Tratado de Fisiologia Médica.* 10ª ed. Rio de Janeiro: Guanabara-Koogan; 2002.
5. Mintz G, Pizzarello R, Klein I. Enhance left diastolic function in hyperthyroidism: noninvasive assessment and response to treatment. *J Clin Endocrinol Metab.* 1991; 73: 146-50.
6. Rohrer DK, Hartong R, Dillmann WH. Influence of thyroid hormone and retinoic acid on slow sarcoplasmic reticulum Ca ATPase and myosin heavy chain alpha gene expression in cardiac myocytes. *J Biol Chem.* 1991; 266: 8638-46.
7. Klein I, Ojamaa K. Cardiovascular manifestations of endocrine disease. *J Clin Endocrinol Metab.* 1992; 75:339-42.
8. Polikar R, Burger AG, Scherrer U, Nicod P. The thyroid and the heart. *Circulation.* 1993; 87: 1435-41.
9. Ojamaa K, Balkam C, Klein I. Acute effects of t3 on vascular smooth muscle cells. *Ann Thorac Surg.* 1993; 56: 568.
10. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system: from theory to practice. *J Clin Endocrinol Metab.* 1994; 78: 1026-7.
11. Landenson PW, Sherman SI, Baughman KL, Ray PE, Feldman AM. Reversible alterations in myocardial gene expression in a young man with dilated cardiomyopathy and hypothyroidism. *Proc Natl Acad Sci.* 1992; 89: 5251-5.
12. Kahaly GJ, Kampmann C, Mohr-Kahaly S. Ineffective cardiorespiratory function in hyperthyroidism. *J Clin Endocrinol Metab.* 2000; 83, 11: 4075-78.
13. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism. *Thyroid.* 2000; 10: 665-79.
14. Woebler KA. Thyrotoxicosis and the heart. *N Engl J Med.* 1992; 327: 94-8.
15. Fadel BM, Ellahham S, Ringel MD, Lindsay J, Wartofsky L, Burman KD. Hyperthyroid heart disease. *Clin Cardiol.* 2000; 23: 402-8.
16. Toft AD, Boon NA. Thyroid disease and the heart. *Heart.* 2000; 84: 455-60.
17. Ojamaa K, Klemperer JD, Klein I. Acute effects of thyroid hormone on vascular smooth muscle. *Thyroid.* 1996; 6: 505-12.
18. Klein I, Ojamaa K. Thyrotoxicosis and the heart. *Endocrinol metab. Clin North Am.* 1998; 27: 51-62.
19. Argov Z, Renshaw PF, Boden B, Winkokur A, Bank WJ. Effects of thyroid hormones on skeletal muscle bioenergetics. *J Clin Invest.* 1988; 81: 1695-701.
20. Kaminsky P, Klein M, Robin-Lherbier B, et al. A 31p nmr study of different hypothyroid states in rat leg muscle. *Am J Physiol.* 1991; 261: 706-12.
21. Kaminsky P, Robin-Lherbier B, Brunotte F, et al. Energetic metabolism in hypothyroid skeletal muscle, as studied by phosphorus magnetic resonance spectroscopy. *J Clin Endocrinol Metab.* 1992; 74: 124-9.
22. Everts ME. Effects of the thyroid state on force development and metabolism in skeletal muscle of the rat. Thesis. State University Leiden. Leiden, Netherland, 1983.
23. Ramsay I. *Thyroid disease and muscle dysfunction.* London: Heinemann Medical Books Ltd.; 1974.
24. Weineck J. *Treinamento Ideal.* 9ª ed. São Paulo: Manole; 1999
25. Powers SK, Howley ET. *Fisiologia do Exercício: Teoria e Aplicação ao Condicionamento e ao Desempenho.* 3ª ed. São Paulo: Manole; 2000.
26. Wilmore JH, Costill DL. *Fisiologia do esporte e do exercício.* 2ª ed. São Paulo: Manole, 2001.
27. McArdle WD, Katch FI, Katch VL. *Fisiologia do Exercício: Energia, Nutrição e Desempenho Humano.* 4ª ed. Rio de Janeiro: Guanabara-Koogan; 1998.
28. Weineck J. *Biologia do Esporte.* 7ª ed. São Paulo: Manole, 2005.