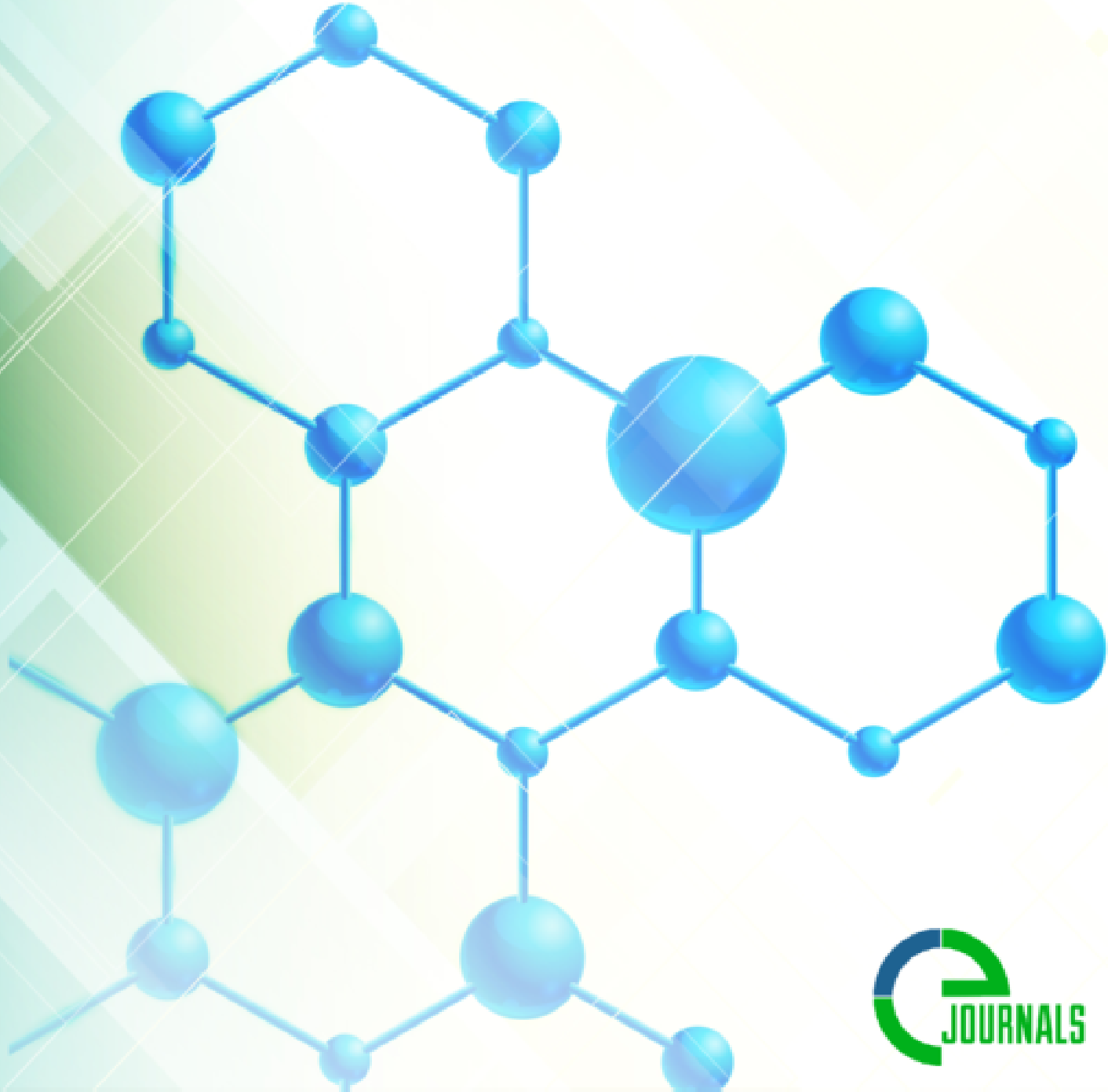
EUROPEAN JOURNAL OF

# MOLECULAR MEDICINE



JOURNALS

# European Journal of Molecular medicine

## Volume 4, No.5, October 2024

**Internet address:** ttp://ejournals.id/index.php/EJMM/issue/archive
**E-mail:** info@ejournals.id
Published by ejournals PVT LTD
DOI prefix: 10.52325
Issued Bimonthly
Potsdamer Straße 170, 10784 Berlin, Germany

*Requirements for the authors.*

*The manuscript authors must provide reliable results of the work done, as well as anobjective judgment on the significance of the study. The data underlying the work shouldbe presented accurately, without errors. The work should contain enough details andbibliographic references for possible reproduction. False or knowingly erroneous statementsare perceived as unethical behavior and unacceptable.*

*Authors should make sure that the original work is submitted and, if other authors'works or claims are used, provide appropriate bibliographic references or citations. Plagiarismcan exist in many forms - from representing someone else's work as copyright to copying orparaphrasing significant parts of another's work without attribution, as well as claimingone's rights to the results of another's research. Plagiarism in all forms constitutes unethicalacts and is unacceptable. Responsibility for plagiarism is entirely on the shoulders of theauthors.*

*Significant errors in published works. If the author detects significant errors or inaccuraciesin the publication, the author must inform the editor of the journal or the publisher aboutthis and interact with them in order to remove the publication as soon as possible or correcterrors. If the editor or publisher has received information from a third party that thepublication contains significant errors, the author must withdraw the work or correct theerrors as soon as possible.*

# CHIEF EDITOR



# EDITORIAL BOARD

# THE EFFECT OF TRIIODOTHYRONINE T3 ON HEART FAILURE

**Rasulova Mokhidil Tursunaliyevna**
Fergana Medical Institute of Public Health

*Abstract: Thyroid hormones have various impacts on the heart and peripheral vascular system. It is widely documented that they increase heart rate and cardiac contractility, enhance systolic and diastolic function, and lower systemic vascular resistance (SVR) under resting conditions. In this review, we summarize the effects of TH on the heart and the clinical symptoms of thyroid dysfunction from the viewpoint of the cardiology.*

*Keywords: Triiodothyronine T3 Nonthyroidal illness Cardiac Thyroid hormone Low T3 syndrome, Cardiovascular*

Thyroid hormones (THs) are produced in the thyroid gland and circulate in the bloodstream to control cells, tissues, and organs in the body. They have a significant impact on the cardiovascular system. THs are widely known for increasing heart rate and cardiac contractility, improving systolic and diastolic function of the heart, and decreasing systemic vascular resistance. Some researchers have spent the last 30 years studying the molecular pathways that mediate the role of TH in the cardiovascular system in order to better understand its methods of action.

Thyroid hormones have various impacts on the heart and peripheral vascular system. It is widely documented that they increase heart rate and cardiac contractility, enhance systolic and diastolic function, and lower systemic vascular resistance (SVR) under resting conditions . In this review, we summarize the effects of TH on the heart and the clinical symptoms of thyroid dysfunction from the viewpoint of the cardiology.

Hypothyroidism and Heart Failure. It is thought that TH deficiency raises the risk of developing and exacerbates Heart Failure . Basic experiments have reported that hypothyroidism suppresses myosin heavy chain 6 protein expression and enhances myosin heavy chain 7 protein expression and that hypothyroidism induces cardiac atrophy as a result. In addition, hypothyroidism is associated with the increased dilation of ventricular chambers and reduced myocardial perfusion . Congestive HF and myxedema have been recognized in patients with hypothyroidism , and their Heart Failure and myxedema symptoms improved with treatment for hypothyroidism. More recently, it was reported that patients with hypothyroidism were among patients with reversible dilated cardiomyopathy. Recent clinical studies have reported that patients with cardiovascular disease who have reduced T3 levels have a higher risk of death from heart failure.

It is interesting that the metabolism and serum levels of THs are changed by conditions of Heart Failure, myocardial infarction, and cardiac surgery. In these situations, the conversion of T4 to T3 decreases. Diseases with normal serum levels of TSH and no symptoms suggestive of hypothyroidism despite a decrease in blood thyroid hormone are called euthyroid sick syndrome or non-thyroidal illness. Among them, those with only low T3 levels are called low T3 syndrome.

Thyroid hormone metabolism changes in chronic heart failure, after a myocardial infarction, after cardiac surgery, and during acute and chronic disease. Low T3 levels due to abnormal thyroid hormone metabolism may have comparable negative effects as classical hypothyroidism, leading to a low T3 syndrome or nonthyroidal illness. Low T3 syndrome is a powerful, independent predictor of mortality in individuals with acute and chronic cardiac disease. T 3 controls several key genes in cardiac myocytes. Low T3 conditions, which accompany heart illness, change gene expression in a manner similar

to hypothyroidism.

Thyroid illness is typically caused by a hereditary susceptibility to autoimmune conditions, such as Graves or Hashimoto disease. Hypothyroidism is the most prevalent kind of thyroid malfunction, and its frequency rises with age. Hyperthyroidism is less prevalent and mostly affects women throughout their reproductive years. Thyroid dysfunction is five to seven times more frequent in women than males, which is understandable given the autoimmune nature of both illnesses. Thyroid function tests are sensitive and specific enough to accurately diagnose hyperthyroidism or hypothyroidism. Most societies urge that doctors conduct routine laboratory tests (e.g., thyroid-stimulating hormone [TSH]) to support aggressive case seeking . Thyroid function testing is often supported by International Classification of Diseases-10 codes, making it particularly useful in cardiology practice.1-3. Thyroid hormone metabolism. Thyroid Hormone Regulation The thyroid gland produces both tetraiodothyronine (T4) and triiodothyronine (T3).

T3 Effects on Cardiovascular Haemodynamics Thyroid hormone has direct and indirect effects on the heart and vasculature, influencing cardiovascular haemodynamics. Thyroid hormone activity leads to increased contractility and lower vascular resistance. Conversely, insufficient thyroid hormone leads to decreased contractility and increased resistance. T3 has direct effects on tissue thermogenesis, system vascular resistance, and cardiac chronotropy and inotropy, leading to changes in blood volume and cardiac output. Hyperthyroidism leads to increased cardiac contractility, output, and resting heart rate. Reduced system vascular resistance leads to improved systolic and diastolic functions and lower afterload. Improved cardiovascular haemodynamics leads to higher blood flow and tissue perfusion. Hyperthyroidism can cause atrial arrhythmias in elderly adults, as well as tachycardia, elevated pulse pressure, and dyspnoea during exercise. Hypothyroidism can cause modest indications such as bradycardia, diastolic hypertension, and constricted pulse pressure, which differ from hyperthyroidism. Cardiac contractility is reduced, but systemic vascular resistance is raised. The distinctive haemodynamic profile of heart failure, like that of clinically hypothyroid patients, involves a decreased cardiac output due to impaired cardiac contractility and a raised systemic vascular resistance . T3 seems to lower systemic vascular resistance by directly acting on vascular smooth muscle cells and altering the vascular endothelium. Nongenomic activities affect membrane ion channels and endothelial nitric oxide synthase. Increased endothelial nitric oxide generation may be due in part to T3-mediated effects on the protein kinase akt pathway, which can occur through nongenomic or genomic processes. Endothelial cells produce nitric oxide, which subsequently works in a paracrine way on nearby vascular smooth muscle cells to promote vascular relaxation.

Relaxation of vascular smooth muscle reduces arterial resistance and pressure, increasing cardiac output. Non-thyroidal Disease Over the last 30 years, it has been recognised that nonthyroidal illness states might affect thyroid function, in contrast to primary thyroid disease. Euthyroid ill states were once defined as having normal TSH levels despite low T3 levels. Low T3 levels have been linked to deleterious effects akin to classical hypothyroidism, resulting in the alternative term "nonthyroidal illnesses" (NTI).

Thyroid hormone metabolism, especially deiodination of T4, decreases in chronic heart failure, myocardial infarction, cardiac surgery, and acute and chronic illnesses. Recent investigations have shown alterations in thyroid hormone metabolism associated with various cardiovascular diseases. Serum T3 concentrations in heart failure patients fall in proportion to the severity of the illness, as determined by the New York Heart Association functional classification. Cytokines block the conversion of T4 to active T3

in the liver, contributing to the low T3 syndrome or NTI.

Thyroid Hormone-Based Treatment for Heart Failure Heart failure treatment often involves various medicines, such as b-adrenergic blockers, angiotensin-converting enzyme inhibitors, aldosterone antagonists, digitalis, and diuretics. In the past two years, two new FDA-approved drugs have hit the market. New therapy options for symptomatic heart failure include Entresto, a combination of sacubitril and valsartan, and Corlanor, a sinoatrial node channel inhibitor. Despite extensive medical care, significant death rates persist, prompting the search for new therapeutic options. Gene therapy involves delivering viral vectors that encode specific cardiac regulatory and structural proteins to damaged myocytes. Studies of the molecular processes of thyroid hormone action on the cardiac myocyte have previously shown that, like the hypothyroid myocardium, treating the failing heart with T3 generates a comparable and favourable alteration in the cardiac phenotype. Other thyroid hormone sensitive genes that may contribute to better cardiac contractile performance include the b1-adrenergic receptor, stimulatory guanine nucleotide binding proteins (Gs), a-MHC, sodium-calcium exchanger, and maybe voltage-gated potassium channels (Kv). Because the majority of heart failure deaths are caused by ventricular arrhythmias, a favourable effect on Kv expression that results in a shortening of the QT interval on the ECG is therapeutically desirable.

Perhaps most crucially, multiple studies have shown that T3 therapy has no adverse effects when given in either physiologic or short-term pharmacologic dosages to patients with concurrent cardiac illness.41 There have been no documented incidences of supraventricular arrhythmias, changes in heart rate, or worsening of cardiac ischaemia in any of the reported series thus far. To return serum T3 levels to normal, researchers employed short-term intravenous medication treatment. Although possibly effective in acute investigations, this ignores the more important subject of long-term treatment. Thus, any long-term trials conducted to determine the safety and efficacy of T3 therapy for heart failure must employ a T3 formulation that is not currently accessible.The clinical reality that such patients will already be treated with b-adrenergic blockade provides a combination of treatments with therapeutic synergy.

Conclusion. In this manuscript, we discussed how TH plays an important role in cardiovascular disease at the molecular level via genomic and non-genomic pathways. Serious cardiac complications such as arrythmia, congestive HF, and angina pectoris might arise in patients with hyperthyroidism or hypothyroidism, and their treatment requires control of the underlying TH levels. Judging from previous clinical observational studies and small-scale intervention studies, which have evaluated the association between THs and risk factors for CVD, it can be concluded that among patients who should be treated for thyroid function, those with severe CVD should be given priority thyroid treatment

**References:**

1.Klein I, Danzi S. Thyroid disease and the heart. CurrProbl Cardiol 2016;41:65-92.

2.Klein I. Endocrine disorders and cardiovascular disease. In: Bonow RO, Mann DL, Zipes DP, et al, editors. Braunwald's heart disease. 10th edition. St.Louis, MO: WB Saunders and Company; 2014. p. 1793-808 [Chapter 81].

3.Klein I, Danzi S. Thyroid disease and the heart. Circulation 2007;116(15):1725-35.

4.Ascheim DD, Hryniewicz K. Thyroid hormone metabolism in patients with congestive heart failure: the low triiodothyronine state. Thyroid 2002;12(6):511-5.

5.Hennessey JV, Klein I, Woeber K, et al. Aggressive case finding: a clinical strategy for the documentation of thyroid dysfunction. Ann InternMed 2015;163(4):311-2.

6.Danzi S, Ojamaa K, Klein I. Triiodothyronine-mediated myosin heavy chain gene transcription in the heart.Am J Physiol Heart Circ Physiol 2003;284:H2255-62.

7.Danzi S, Klein I. Thyroid hormone and the cardiovascular system. Med Clin North Am 2012;96:257-68.

8.Dumitrescu AM, Liao XH, Weiss RE, et al. Tissuespecific thyroid hormone deprivation and excess in monocarboxylate transporter (Mct) 8-deficient mice. Endocrinology 2009;150:4450-8.

9.Dillmann WH. Cellular action of thyroid hormone on the heart. Thyroid 2002;12:447-52.

10.Davis PJ, Davis FB. Nongenomic actions of thyroid hormone on the heart. Thyroid 2002;12:459-66.