

## IMPACT OF HYPOTHYROIDISM ON CARDIOVASCULAR DISEASE: A REVIEW

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### ABSTRACT

Hypothyroidism a common condition characterized by thyroid hormone deficiency, has significant implications for cardiovascular health. If left untreated, it can lead to severe, potentially fatal outcomes. The relationship between hypothyroidism and cardiovascular disease (CVD) is intricate, involving multiple mechanisms such as disrupted lipid metabolism, endothelial dysfunction, and direct effects on the myocardium. This review synthesizes evidence from key studies to explore the pathophysiological mechanisms by which hypothyroidism contributes to cardiovascular disease. It highlights the clinical manifestations of these interactions and emphasizes the importance of understanding this relationship for the effective diagnosis and management of cardiovascular complications in patients with hypothyroidism. Early detection and intervention, particularly in populations at risk for cardiovascular disease, are crucial to prevent the progression of cardiovascular issues associated with hypothyroidism. Thyroid hormone replacement therapy, typically with levothyroxine, plays a central role in cardiovascular risks by normalizing thyroid hormone levels and improving lipid profiles. Understanding the complex interplay between hypothyroidism and cardiovascular health is essential for optimizing patient outcomes. Future research should focus on refining screening and treatment strategies, particularly for high-risk individuals, to enhance the management of cardiovascular risks in hypothyroid patients.

**KEYWORDS:** Hypothyroidism, cardiovascular health, Thyroid dysfunction, cardiovascular disease (CVD), Lipid metabolism.

## INTRODUCTION

Hypothyroidism is an insufficient production of thyroid hormones, it is interconnected with various metabolic and physiological changes, particularly affecting the cardiovascular system. One of the primary organs that thyroid hormones directly affect is the cardiovascular system.  $T_4$  thyroxine is primarily responsible for producing  $T_3$ , or triiodothyronine, which is a thyroid hormone that is vital for cardiomyocytes. It has both genomic and non-genomic effects on cardiomyocytes.  $T_3$  binds to thyroid hormone-responsive elements (TREs) found in target gene regulatory areas after attaching to thyroid hormone receptors (TRs) in the nucleus. This process controls transcription. Thyroid hormone signaling, alterations in thyroid hormone levels, and thyroid hormone receptors are among the non-genomic functions of  $T_3$ . The thyroid hormone receptor ( $TR\alpha 1$ ) has been shown to regulate genes linked to contractile proteins, pacemaker activity and conduction, cell proliferation, differentiation, and metabolism. It can also lessen myocardial damage and post-ischemic cardiac remodeling through  $T_3$  binding.<sup>[1]</sup> Both overt and subclinical forms of hypothyroidism have been associated with an increased risk of CVD, including coronary artery disease CAD, heart failure, and arrhythmias. This review expresses the relationship between hypothyroidism and CVD by analyzing findings from several key studies, focusing on the implications for clinical practice.

## PATHOPHYSIOLOGY OF HYPOTHYROIDISM AND CARDIOVASCULAR DISEASE

Thyroid stimulating hormone (TSH) levels that are increased due to low thyroid hormone levels are indicative of hypothyroidism, which can be primary or secondary. Overt hypothyroidism is defined as TSH elevation and  $T_4$  reduction, while subclinical hypothyroidism (SCH) is defined as TSH values beyond upper limit of assay reference range with normal thyroid hormone levels.<sup>[2]</sup> Because myocardial and vascular endothelial cells have thyroid hormone receptors, which change heart rate, cardiac contractility, vascular smooth muscle, and endothelial function, hypothyroidism raises the risk of CVD. In proportion to the rise in blood TSH levels, it also raises LDL and total cholesterol.<sup>[3]</sup> In women, thyroid dysfunction is very common and raises the risk of coronary heart disease overall. Women with hypothyroidism have been found to have microvascular endothelial impairment.<sup>[4]</sup> Reduced ventricular contractility, higher vascular resistance, and delayed diastolic filling are all consequences of low  $T_3$ . Low  $T_3$  syndrome is a hormonal imbalance that has been identified as a powerful predictive predictor of death in patients with cardiac disease. It may have a major impact on the pathophysiological mechanism and CV hemodynamics.<sup>[5]</sup> Additionally, people with heart disease who have a mildly changed thyroid state have a higher risk of dying.<sup>[6]</sup> Meta-analyses of individual participant data revealed that SCH was linked to a higher risk of heart failure<sup>[7]</sup> and coronary heart disease (CHD) events and mortality.<sup>[8]</sup> This association was particularly evident in patients whose blood TSH level was greater than 10 mU/L. Accordingly, SCH is linked to a greater risk of CVD events and mortality in people with higher TSH levels, especially in those with a TSH > 10mU/L.<sup>[8]</sup>

## THYROID HORMONES AND CARDIOVASCULAR FUNCTION

Thyroid hormones, the triiodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ) are essential in cardiovascular function. They influence heart rate, myocardial contractility, and vascular resistance. Hypothyroidism results in reduced cardiac output, increased systemic vascular resistance, and diastolic dysfunction.<sup>[9]</sup> Emphasized that these cardiovascular alterations are direct consequences of thyroid hormone deficiency, leading to significant clinical implications.<sup>[10]</sup>

### LIPID METABOLISM AND ATHEROSCLEROSIS

Hypothyroidism, particularly in its subclinical form, is strongly associated with dyslipidemia, and characterized by elevated levels of LDL cholesterol and triglycerides. This dyslipidemia profile promotes atherosclerosis, thereby increasing the risk of cardiovascular events such as myocardial infarction and stroke.<sup>[11]</sup> The persistent lipid abnormalities in hypothyroid patients underscore the need for early detection and management.<sup>[12]</sup>

### MYOCARDIAL EFFECTS AND HEART FAILURE

Hypothyroidism directly affects the myocardium, leading to decreased myocardial contractility and altered calcium handling. These changes can precipitate heart failure, particularly in patients with pre-existing cardiovascular conditions. Noted that hypothyroidism is also associated with an increased risk of pericardial effusion and diastolic dysfunction, both of which contribute to the development and worsening of heart failure.<sup>[2]</sup>

### CLINICAL MANIFESTATIONS OF CORONARY ARTERY DISEASE IN HYPOTHYROIDISM

Hypothyroidism, through its effects on lipid metabolism and endothelial function, increases the risk of CAD. It is conducted a meta-analysis that confirmed the heightened risk of CAD in patients with subclinical hypothyroidism, particularly those with elevated thyroid-stimulating hormone (TSH) levels. This association underscores the importance of managing thyroid function in patients at risk for CAD.<sup>[13]</sup> Heart failure is a common complication in hypothyroid patients, resulting from both direct myocardial effects and secondary factors such as hypertension and atherosclerosis.<sup>[14]</sup> The arrhythmogenic potential of hypothyroidism is well-documented, with common manifestations including bradycardia and QT interval prolongation. It is highlighted that these electrophysiological disturbances can lead to life-threatening arrhythmias, particularly in the context of severe or untreated hypothyroidism.<sup>[15]</sup>

### DIAGNOSIS AND MANAGEMENT OF CARDIOVASCULAR RISK IN HYPOTHYROIDISM

Regular screening for thyroid function is recommended, especially in patients with known cardiovascular disease, dyslipidemia, or heart failure.<sup>[16]</sup> Identifying subclinical hypothyroidism in at-risk individuals is particularly important for preventing the progression of overt disease and associated cardiovascular complications. Thyroid hormone replacement, typically with levothyroxine, is the standard treatment for hypothyroidism. This therapy normalizes thyroid hormone levels, improves lipid profiles, reduces atherosclerosis progression, and enhances cardiac function. It is demonstrated that Thyroid hormone replacement effectively reduces cardiovascular risk, particularly when initiated early in the disease course.<sup>[17]</sup>

**Table 1.**

Reference	Design and methods	Sample size	Population characteristics	Variables studied	Key findings
Udovcic et al., (2017) <sup>[2]</sup>	Review; Focus on hypothyroidism's impact on the heart	N/A	Patients with hypothyroidism	Heart function, myocardial contractility, heart failure risk	Hypothyroidism reduces myocardial contractility, increases the risk of heart failure, and may lead to pericardial effusion.
Chaker et al., (2017) <sup>[9]</sup>	Systematic review; Analysis of clinical studies on hypothyroidism		Cardiovascular outcomes, thyroid hormone levels	Cardiovascular outcomes, thyroid hormone levels	Hypothyroidism is associated with increased systemic vascular resistance, diastolic dysfunction, and reduced cardiac output. Thyroid hormone replacement improves cardiac function

					and reduces cardiovascular risk.
Jabbar et al., (2017) <sup>[10]</sup>	Review of literature on thyroid hormones and cardiovascular disease	N/A	Patients with thyroid dysfunction	Thyroid hormone levels, cardiovascular disease incidence	Thyroid hormones play a critical role in cardiovascular health; deficiency leads to a higher risk of cardiovascular disease, including heart failure and atherosclerosis
Delitala et al., (2017) <sup>[11]</sup>	Systematic review on subclinical hypothyroidism	N/A	Patients with subclinical hypothyroidism	Lipid metabolism, cardiovascular disease risk	Subclinical hypothyroidism is associated with altered lipid metabolism, which increases the risk of cardiovascular disease, particularly coronary artery disease.
Paschou et al., (2022) <sup>[12]</sup>	Review; Analysis of recent studies on thyroid disorders	N/A	The general population with thyroid disorders	Cardiovascular manifestations, lipid levels, atherosclerosis	Thyroid disorders, including hypothyroidism, contribute to dyslipidemia and atherosclerosis, increasing the risk of coronary artery disease.
Moon et al., (2018) <sup>[13]</sup>	Meta-analysis of prospective cohort studies	25,977	Patients with subclinical hypothyroidism	Cardiovascular disease incidence, all-cause mortality	Subclinical hypothyroidism increases the risk of cardiovascular disease and all-cause mortality, particularly in individuals with higher TSH levels
Ro et al., (2018) <sup>[14]</sup>	Observational study on hypothyroidism and heart failure	1,115	Patients with hypothyroidism and heart failure	Hospitalization risk, heart failure incidence	Hypothyroidism exacerbates heart failure, leading to an increased risk of hospitalization. Effective thyroid hormone replacement therapy is essential in reducing this risk.
Guerri et al., (2019) <sup>[15]</sup>	Review of clinical cases and studies on thyroid dysfunction	N/A	Patients with hypothyroidism and hyperthyroidism	Thyroid function, arrhythmias, cardiac complications	Hypothyroidism is linked to bradycardia and QT interval prolongation, leading to an increased risk of arrhythmias and cardiac complications.
Decandia, (2018) <sup>[16]</sup>	Review on cardiovascular risk factors in subclinical hypothyroidism	N/A	Patients with subclinical hypothyroidism	Cardiovascular risk factors, thyroid function	Subclinical hypothyroidism is associated with increased cardiovascular risk, including hypertension, dyslipidemia, and atherosclerosis
Razvi et al., (2018) <sup>[17]</sup>	Review; Analysis of thyroid hormones and cardiovascular function	N/A	Patients with thyroid dysfunction and cardiovascular disease	Thyroid hormone levels, cardiovascular outcomes	Thyroid hormone replacement is effective in improving cardiovascular outcomes in patients with hypothyroidism, reducing the risk of heart failure and atherosclerosis progression.

## CONCLUSION

The relationship between hypothyroidism and cardiovascular disease is complex and with significant implications for patient outcomes. Understanding the underlying mechanisms and clinical manifestations is crucial for the effective management of cardiovascular risk in patients with hypothyroidism. Early diagnosis, appropriate thyroid hormone replacement therapy, and management of associated cardiovascular risk factors are essential strategies to improve

outcomes in this population. Future research should continue to explore optimal screening and treatment approaches, particularly in high-risk groups.

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