

Impact of Hyperthyroidism on Heart Disease: A Systematic Review

ABSTRACT

Introduction: The cardiovascular consequences of hyperthyroidism are particularly worrying, as it is capable of causing and aggravating a variety of heart diseases, from arrhythmias to heart failure, which are important clinical concerns because they can cause high morbidity and mortality. **Objective:** To provide a comprehensive and up-to-date overview of the effects of hyperthyroidism on the cardiovascular system. **Methods:** This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (Simple Multi-Attribute Rating Technique using Exploiting Rankings) (MarquesAzzini VO, Castilho Lopes CC, Natascha SB, Eduardo BL, Lucas C). **Results:** A comprehensive systematic search of the literature yielded 4490 articles referring to the impact of hyperthyroidism on heart disease, of which 26 articles were eligible to be included in this systematic review. **Conclusion:** Hyperthyroidism has a significant impact on the cardiovascular system, contributing to the development and exacerbation of several heart diseases.

Keywords: Hyperthyroidism, Heart Diseases, Cardiovascular System, Thyroid Dysfunction

INTRODUCTION

The excessive production of thyroid hormones by the thyroid gland is known as hyperthyroidism, which is an endocrinological condition. These hormones are essential for regulating metabolism and keeping the body in homeostasis (BROWN et al., 2023; WANG et al., 2023). High levels can cause several systemic complications, including significant effects on the cardiovascular system (PINGITORE et al., 2023). The cardiovascular consequences of hyperthyroidism are particularly worrying, as it is capable of causing and aggravating a variety of heart diseases, from arrhythmias to heart failure, which are important clinical concerns because they can cause high morbidity and mortality (AHMAD et al., 2022; NAVARRO-NAVAJAS et al., 2022).

Sinus tachycardia, atrial fibrillation, left ventricular hypertrophy and thyrotoxic cardiomyopathy are widely documented cardiac manifestations of hyperthyroidism (CHU et al., 2024; IRIDA KECAJ et al., 2024; NAVARRO-NAVAJAS et al., 2022). The complex pathophysiological mechanisms involving

thyroid hormones and the cardiovascular system include a greater sensitivity of the myocardium to adrenergic stimulation, an increase in metabolic demand and changes in the contractile function of the heart (BARREIRO ARCOS, 2022; KRENTZ, 2023).

The suggested pathophysiological mechanisms that explain these cardiovascular complications include hyperactivity of the sympathetic system, greater metabolic demand and greater tissue sensitivity to thyroid hormones (LISCO et al., 2022). These effects can be particularly serious in the elderly or individuals with previous heart disease, who are more prone to the negative effects of thyroid dysfunction. In addition to increasing the risk of stroke and heart failure, these complications affect patients' quality of life. (CAPPOLA et al., 2019; CHAKER et al., 2024).

To create effective diagnosis, treatment and prevention methods, it is necessary to understand the relationship between hyperthyroidism and heart disease (IGLESIAS; DÍEZ, 2023). Although there are effective treatments for hyperthyroidism, such as antithyroid medications, radioactive iodine therapy and surgery, treating cardiac complications requires a multidisciplinary and individualized approach (COHEN et al., 2022). Furthermore, early identification of cardiac signs and symptoms in patients with hyperthyroidism is essential to avoid more serious complications and improve clinical results (WIERSINGA; POPPE; EFFRAIMIDIS, 2023). Scientific literature has improved our understanding of these connections. However, there are still large gaps that need to be filled through additional research.

In this context, this review article aims to provide a comprehensive and up-to-date overview of the effects of hyperthyroidism on the cardiovascular system, emphasizing the need for an integrated approach to the treatment of these conditions. By consolidating existing knowledge and highlighting areas that require further investigation, we hope to contribute to the improvement of clinical practices and the formulation of effective prevention and treatment strategies, aiming to improve cardiovascular health and quality of life for patients with hyperthyroidism.

METHODS

Comment [MS1]: These lines are repeated, kindly add citation (LISCO et al., 2022) to previous paragraph (with barreiro arcos)

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This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*). The work carried out is of a qualitative and quantitative nature. Qualitative data analysis was carried out intuitively and inductively during the survey of the theoretical framework. It is also quantitative through the use of the multi-criteria method. In addition, there is also a numerical experimental study in order to simulate an article selection situation based on the observed criteria.

The bibliographical research was carried out in the following databases: *Web of Science*; *Science Direct*; *Wiley*; *SpringerLink*; *Taylor and Francis* and *PubMed*. In addition, searches were carried out using bibliographical references of studies that relevantly addressed the topic on the *Google Scholar search platform*.

The search in the databases was carried out using the terminologies registered in the Health Sciences Descriptors created by the Virtual Health Library developed from the *Medical Subject Headings of the US National Library of Medicine*, which allows the use of common terminology in Portuguese, English and Spanish. The present study sought to investigate the literature on the impact of hyperthyroidism on heart disease. To this end, the descriptors “hyperthyroidism”, “heart diseases”, “cardiovascular system” and “thyroid dysfunction” were used, initially in English, and in a complementary way in Spanish and Portuguese.

As a tool to support decision-making in the selection and prioritization of articles, a set of criteria were considered essential to represent the state of the art of the topic under study. This method has the following characteristics: (i) rigorous logic allows the method to be accepted as a decision support tool; (ii) simple to understand and apply with easy-to-interpret results.

References from selected works were also searched for other documents of potential interest. Once qualified for full text in the evaluation, articles were included in the qualitative review if they met the following inclusion criteria: a) contained data on hyperthyroidism; b) contained data on the relationship between heart disease and hyperthyroidism. Articles were excluded if they were

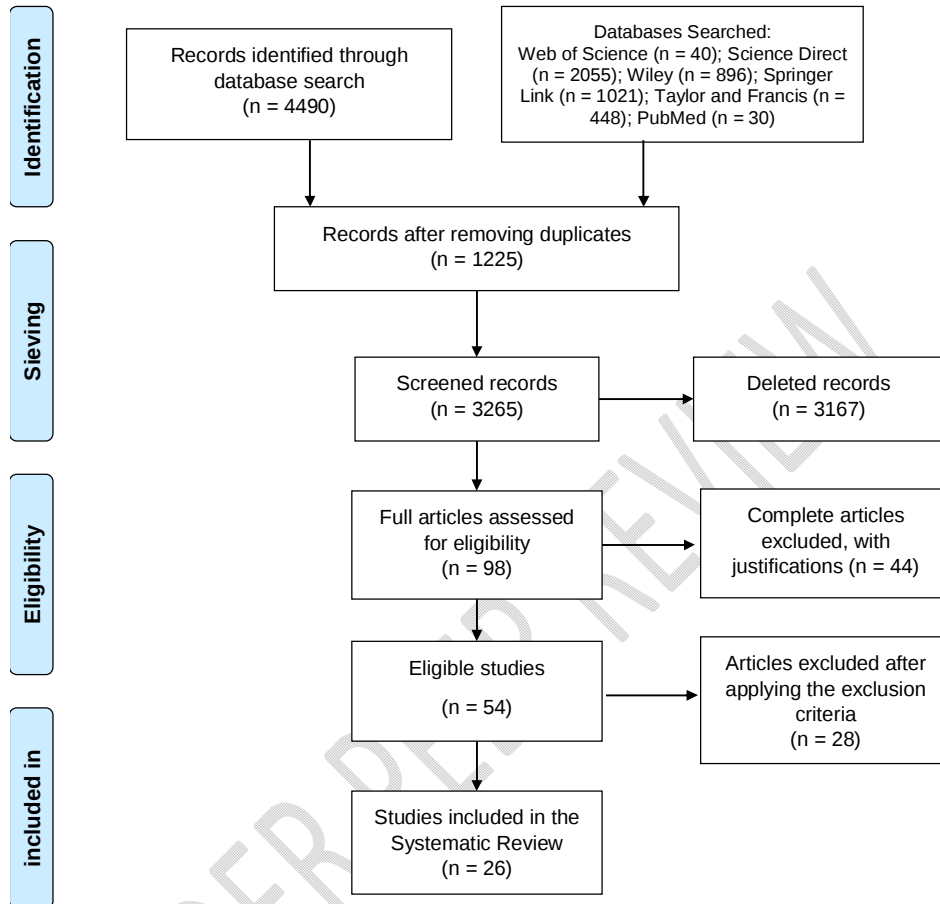
reports, banners or conference abstracts. There was no review of confidential health information and the study was non-interventional. Therefore, ethics committee approval was not necessary. In the end, the result obtained totaled 26 articles that covered the desired characteristics for the study.

Four independent researchers extracted data from articles that met the inclusion criteria and recorded them in a “data extraction form” generated in Microsoft Excel on the impact of hyperthyroidism on heart disease. From this form, the authors and year of publication, study summary, type of study, measured results, limitations and conclusions were included, which was demonstrated in table 1. (Marques Azzini VO, Castilho Lopes CC, Natascha SB, Eduardo BL, Lucas C)

RESULTS

A comprehensive systematic search of the literature yielded 4490 articles referring to the incidence of overweight and obesity in adolescents. Of these, 1225 studies were excluded due to data overlap. From this, the SMARTER method (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*) was chosen and 98 articles were selected that were suitable for full-text screening, of which 54 articles were included for data extraction, of which 28 were excluded by the exclusion criteria, making 26 articles eligible and included for systematic review. In Figure 1, we describe the strategy for selecting articles on the topic in question. (Marques Azzini VO, Castilho Lopes CC, Natascha SB, Eduardo BL, Lucas C)

Figure 1. Article search strategy



Source: Authors (2024)

Table 1. Selected studies and their main findings

Author/year	Abstract	Kind of study	Measured result	Limitations	Conclusions
Gelen; Şengül; Kükürt (2023); Paschou et al. (2022)	Hyperthyroidism, characterized by excessive production of thyroid hormones, significantly impacts the cardiovascular system.	Literature review	Cardiovascular changes associated with hyperthyroidism	Theoretical review, lack of direct experimental studies	Importance of understanding the cardiovascular consequences of hyperthyroidism.
Barreiro Arcos (2022); Ross et al. (2022)	Thyroid hormones such as T4 and T3 regulate basal metabolism and cardiac function.	Literature review	Impact of thyroid hormones on cardiac function	Dependence on secondary studies	Thyroid hormones are crucial for heart function.
Ghaemmaghami (2022); Stojković (2022)	Hyperthyroidism can increase the risk of cardiovascular complications.	Literature review	Cardiovascular risks associated with hyperthyroidism	Variability in study methods	Need for strict monitoring to prevent cardiovascular complications.
Fairuz et al. (2023); Pyvovar; Rudyk; Scherban (2024)	Thyroid hormones increase the expression of β -adrenergic receptors, altering hemodynamics.	Literature review	Hemodynamic changes induced by thyroid hormones	Theoretical review, lack of direct experimental evidence	Importance of thyroid hormones in the cardiac response to catecholamines.
Barreiro Arcos (2022); Murolo et al. (2022)	Thyroid hormones promote vasodilation and influence cardiac function.	Literature review	Impact on vascular resistance and stroke volume	Theoretical review, lack of direct experimental studies	Importance of modulation of thyroid hormones in cardiovascular hemodynamics.
Glivic et al. (2022)	Hyperthyroidism can increase lipid levels, increasing the risk of atherosclerosis.	Literature review	Cholesterol and triglyceride levels in patients with hyperthyroidism	Theoretical review, need for longitudinal studies	Regular monitoring of lipid levels is essential.
Danzi; Klein (2022); Rasool et al. (2023)	Prolonged exposure to thyroid hormones can cause ventricular hypertrophy.	Literature review	Structural changes in the heart due to hyperthyroidism	Theoretical review, lack of direct experimental evidence	Need for early treatment to prevent heart failure.
Davies (2022)	Studies by Martin Surks show that excess thyroid hormones increase cardiac sensitivity to catecholamines.	Literature review	Changes in heart rate and myocardial contractility induced by hyperthyroidism	Theoretical review, lack of direct experimental studies	Hyperthyroidism increases hemodynamic overload.

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Author/year	Abstract	Kind of study	Measured result	Limitations	Conclusions
Olanrewaju et al. (2024); Murolo et al. (2022)	Thyroid hormones affect cardiac function through genomic and non-genomic mechanisms.	Systematic review	Cardiovascular risks associated with hyperthyroidism	Variability in study methods, differences in populations studied	Timely treatment and monitoring reduce cardiovascular risks.
Duzen et al. (2021); Nel (2022)	Study on changes in left ventricular function in patients with hyperthyroidism.	Observational study	Changes in left ventricular function	Limitations in generalization due to patient characteristics	Direct impact of hyperthyroidism on cardiac structure and function.
BekturAykanat et al. (2021)	Investigation of the molecular mechanisms of cardiac hypertrophy induced by hyperthyroidism in animal models.	Animal experimental study	Molecular changes in the heart associated with hyperthyroidism	Limitations in translation to humans, need for additional clinical studies	Understanding molecular mechanisms for future therapies.
Corona et al. (2021)	Systematic review on the epidemiology of thyroid dysfunction and its cardiovascular implications.	Systematic review	Prevalence of thyroid dysfunction in patients with heart disease	Limitations due to heterogeneity in included studies	Importance of early treatment to reduce cardiac complications.
Nie et al. (2022)	Effects of CaMKII inhibition in the management of cardiac arrhythmias associated with hyperthyroidism in animal models.	Animal experimental study	Reduced incidence of arrhythmias and adverse myocardial remodeling	Limitations in translation to humans, need for additional clinical studies	Therapeutic potential of CaMKII inhibition in arrhythmias associated with hyperthyroidism.
Rahimi-Bashar et al. (2023)	Review of amiodarone-induced thyroid dysfunction in patients with heart disease.	Systematic review	Prevalence of amiodarone-induced thyroid dysfunction	Variability in study methods, limitations of retrospective data	Need for strict monitoring to manage adverse hormonal changes.
Lillevang-Johansen et al. (2019); Vrigkou et al. (2022)	Patients with hyperthyroidism should be evaluated for cardiovascular risk, considering various risk factors.	Systematic review	Cardiovascular risk assessment in patients with hyperthyroidism	Limitations in generalization due to different risk factors	An integrated approach is essential to reduce the cardiovascular impact of hyperthyroidism.
Wang et al. (2023); Liu et al. (2021)	Treatment of hyperthyroidism aims to normalize hormone levels and control symptoms to reduce cardiovascular risk.	Systematic review	Impact of hyperthyroidism treatment on cardiac function and cardiovascular risk	Theoretical review, lack of direct experimental studies	Individualized treatment improves cardiac function and reduces cardiovascular risk.

Source: Authors (2024)

DISCUSSION

Hyperthyroidism, a clinical condition characterized by excessive production of thyroid hormones by the thyroid gland, has profound implications for the cardiovascular system (GELEN; ŞENGÜL; KÜKÜRT, 2023; PASCHOU et al., 2022). These hormones, mainly thyroxine (T4) and triiodothyronine (T3), play a crucial role in regulating basal metabolism and directly influence cardiac function (BARREIRO ARCOS, 2022; GELEN; ŞENGÜL; KÜKÜRT, 2023; ROSS et al., 2022). The hypersecretion of these hormones can lead to a series of pathophysiological changes that affect the heart and blood vessels, contributing to a significant increase in the risk of cardiovascular complications (GHAEMMAGHAMI, 2022; STOJKOVIĆ, 2022).

The relationship between hyperthyroidism and heart disease is complex and multifactorial, involving pathophysiological mechanisms such as the activation of the sympathetic nervous system, the reduction in peripheral vascular resistance and the change in the sensitivity of cardiac adrenergic receptors (NAVARRO-NAVAJAS et al., 2022; PINGITORE et al., 2023).

Thyroid hormones have direct and indirect effects on the cardiovascular system (BARREIRO ARCOS, 2022). They increase the expression of β -adrenergic receptors in the heart, which results in greater sensitivity to circulating catecholamines, such as adrenaline and noradrenaline. This leads to a series of hemodynamic effects, including increased heart rate (tachycardia), increased strength of contraction of the heart muscle (positive inotropism), and greater cardiac output (FAIRUZ et al., 2023; PYVOVAR; RUDYK; SCHERBAN, 2024). Furthermore, thyroid hormones promote peripheral vasodilation, which can result in a reduction in systemic vascular resistance and an increase in venous return, contributing to an increase in the heart's ejection volume (MUROLO et al., 2022).

In addition to the direct effects on the heart, hyperthyroidism can also influence blood lipid levels, increasing the risk of atherosclerosis and coronary heart disease. Regular monitoring of cholesterol and triglyceride levels is important in these patients to prevent cardiovascular complications (GLUVIC et al., 2022).

Hypertrophy is another significant consequence of hyperthyroidism. Prolonged exposure to excess thyroid hormones can lead to abnormal growth

of the heart muscle, increasing left ventricular mass (DANZI; KLEIN, 2022) . The direct stimulation of thyroid hormones in myocytes and the activation of cell signaling pathways that promote cell growth and the synthesis of contractile proteins mediate this effect. This hypertrophy can be functionally beneficial in the short term, as it increases the heart's ability to pump blood. However, in the long term, it can predispose patients to arrhythmias, heart failure and other cardiovascular disorders (BARREIRO ARCOS, 2022; GELEN; ŞENGÜL; KÜKÜRT, 2023; RASOOL et al., 2023).

Martin Surks has been a central figure in research into the cardiovascular effects of hyperthyroidism. Surks has demonstrated in his studies that thyroid hormones have a significant impact on heart rate and myocardial contractility. He elucidated the mechanisms by which excess T3 increases the heart's sensitivity to catecholamines, resulting in tachycardia and, eventually, ventricular hypertrophy. Their studies have provided a solid foundation for understanding how hyperthyroidism can lead to hemodynamic overload and an increased risk of congestive heart failure and arrhythmias (DAVIES, 2022).

According to Olanrewaju et al. (2024), thyroid hormones affect cardiac function through genomic and non-genomic effects, leading to changes in heart rate, contractility, rhythm and output. Both overt and subclinical hyperthyroidism are associated with increased risks of ischemic heart disease, stroke and cardiovascular mortality, particularly in individuals without pre-existing cardiovascular conditions (MUROLO et al., 2022).

Untreated hyperthyroidism represents a greater cardiovascular risk compared to treated cases, with the duration of TSH decrease correlating with an increase in cardiovascular events (LILLEVANG-JOHANSEN et al., 2019). The mechanisms that drive cardiac dysfunction in hyperthyroidism may involve vascular changes, tachyarrhythmias or myocyte remodeling and fibrosis (KHAN et al., 2020). These findings emphasize the importance of timely treatment and careful monitoring of patients with hyperthyroidism to reduce cardiovascular risks.

The studies reviewed on the relationship between thyroid disease and cardiovascular disorders reveal a number of significant findings. A key point is the impact of hyperthyroidism on cardiac function, highlighted by Duzen et al. (2021), who found marked changes in left ventricular function in patients using

speckle-tracking echocardiography. These changes include interventricular septal thickness, left ventricular systolic diameter, ejection fraction, and global longitudinal and circumferential strain, offering crucial insights into how hyperthyroidism directly influences cardiac structure and function (NEL, 2022).

Furthermore, experimental studies in animal models, such as those carried out by Bektur Aykanat et al. (2021), investigated the molecular mechanisms underlying cardiac hypertrophy induced by hyperthyroidism. They identified that increased activation of ATF-6, IRE-1, and TRPC1 is associated with pathological changes in the heart, including calcium ion imbalance and adverse myocardial remodeling. These findings highlight the importance of understanding molecular mechanisms to develop effective therapeutic strategies.

Systematic reviews, such as those conducted by Corona et al. (2021), provide a comprehensive overview of the epidemiology of thyroid dysfunction and its cardiovascular implications. They not only document the prevalence of hypothyroidism and hyperthyroidism among patients with heart disease, but also explore the underlying pathophysiological mechanisms and the importance of early treatment to mitigate the risks of cardiac complications.

Experimental studies, such as that of Nie et al. (2022), investigated the effects of CaMKII inhibition in the management of cardiac arrhythmias associated with hyperthyroidism in animal models. Inhibition of CaMKII not only reduced the incidence of arrhythmias but also decreased adverse myocardial remodeling, suggesting promising therapeutic potential for patients with hyperthyroidism who experience arrhythmias.

The review by Rahimi-Bashar et al. (2023), on the prevalence of amiodarone-induced thyroid dysfunction in patients with heart disease highlights the need for strict monitoring of these patients to detect and early manage hormonal changes that can adversely affect cardiac function.

Taken together, these studies highlight the complexity of the interaction between thyroid disease and cardiovascular disorders. They provide valuable insights not only into the underlying pathophysiological mechanisms, but also into the importance of clinical surveillance and appropriate management to reduce the adverse impacts of these conditions on the heart. Study limitations, such as variability in study methods, small sample sizes, and differences in

populations studied, also highlight the continued need for robust research to better understand and manage these interconnected conditions.

Patients with hyperthyroidism should be evaluated for global cardiovascular risk, taking into account factors such as age, sex, smoking, family history of heart disease and the presence of comorbidities such as diabetes mellitus and obesity. This integrated approach is essential to reduce the impact of hyperthyroidism on the heart (LILLEVANG-JOHANSEN et al., 2019; VRIGKOU et al., 2022).

The treatment of hyperthyroidism aims to normalize thyroid hormone levels and control associated symptoms, which can contribute to improving cardiac function and reducing cardiovascular risk (WANG et al., 2023). Therapies such as the use of antithyroid drugs, radioactive iodine and surgery must be individualized according to the characteristics of each patient (LIU et al., 2021).

In addition to the specific treatment of hyperthyroidism, it is essential to adopt primary and secondary prevention measures for cardiovascular diseases, such as promoting healthy lifestyle habits, controlling body weight, practicing regular physical activity and stopping smoking. These interventions are crucial to reduce the morbidity and mortality associated with hyperthyroidism.

FINAL CONSIDERATIONS

Hyperthyroidism has a significant impact on the cardiovascular system, contributing to the development and exacerbation of several heart diseases. Among the main manifestations are tachycardia, arrhythmias, systolic hypertension and heart failure, with emphasis on atrial fibrillation, which is a common and worrying complication. Studies demonstrate that thyroid dysfunction can alter metabolism and cardiac function, increasing the risk of adverse events. Therefore, effective management of hyperthyroidism, through appropriate and individualized medical treatment, is crucial to minimize risks and improve patients' cardiac health.

Early diagnosis and continuous monitoring are essential to identify and treat cardiovascular complications in a timely manner, preventing consequences that are more serious. The interrelationship between thyroid and

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cardiovascular dysfunction highlights the importance of a multidisciplinary approach in the treatment of these patients, involving endocrinologists, cardiologists and other health professionals. This collaboration promotes a better quality of life and reduces mortality associated with heart disease in patients with hyperthyroidism, highlighting the need for constant surveillance and comprehensive therapeutic strategies.

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