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REVIEW ARTICLE

The Role of Thyroid Hormones in Heart Failure

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Abstract
Cardiovascular diseases are the leading cause of death worldwide. Heart failure is the terminal manifestation of cardiovascular diseases, and its morbidity and mortality remain high. The prevalence of heart failure with preserved ejection fraction (HFpEF) among heart failure patients remains uncertain. However, recent studies have found that it ranged from 40 to 71%. There is still no effective treatment for HFpEF. Thyroid hormones (TH) have central regulatory actions in the cardiovascular system, particularly in the heart. Changes in plasmatic or tissue thyroid hormone levels are associated with significant alterations in cardiovascular function. A significant proportion of patients with heart failure presents some form of thyroid dysfunction including hypothyroidism, hyperthyroidism, and low T3 syndrome. Furthermore, thyroid hormones can vary at a local level independently of the serum TH levels. This may lead to local cardiac hypothyroidism in heart failure. Based on these findings and the role that TH play in cardiovascular regulation, they were proposed as a potential target for heart failure therapy. Several clinical and experimental studies have shown beneficial effects of TH supplementation. Data from epidemiological studies supports a higher risk of heart failure and a worse prognosis in heart failure patients with low levels of TH. In addition, animal studies and small clinical studies suggest that TH supplementation may improve cardiac function in heart failure. Although further studies are needed to evaluate the safety and efficacy of TH in this context, the available evidence suggests that TH modulation is a promising therapeutic approach to heart failure.

Keywords Thyroid hormones · Heart failure · Heart failure with preserved ejection fraction · Euthyroid sick syndrome · Type 3 deiodinase

Introduction

Heart failure is the terminal manifestation of cardiovascular diseases. Cardiovascular diseases are the leading cause of death worldwide [1]. Even though preventative measures, earlier detection, and better treatment have improved the prognosis of this threatening condition, heart failure remains a disease with high morbidity and mortality [2].

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Heart failure is a clinical syndrome caused by structural or functional cardiac dysfunction resulting in impairment of ventricular filling or ejection of blood. Heart failure can be divided in two different syndromes according to ejection fraction: heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). Although the prevalence of HFpEF among heart failure patients remains uncertain, recent studies' estimates ranged from 40 to 71% [3–12]. While in HFrEF the main abnormality is systolic dysfunction (impairment of contractile function), in HFpEF the main cardiac abnormality is diastolic dysfunction (abnormal cardiac relaxation or stiffness) [2, 13].

Thyroid hormones have central regulatory actions in the cardiovascular system, particularly in the heart. Changes in plasmatic or tissue thyroid hormone levels are associated with significant alterations in cardiovascular function. A significant proportion of patients with heart failure presents some form of

thyroid dysfunction including hypothyroidism, hyperthyroidism, and low T3 syndrome.

Given the central role of thyroid hormones in the cardiovascular system, it is important to study their role as a pathophysiological player in heart failure and as a potential therapeutic target in this group of patients.

Thyroid Hormone Physiology and Its Effects in the Cardiac Function

The thyroid gland synthesizes two tyrosine-based hormones—thyroxine (T4) and triiodothyronine (T3). The gland produces T4 in larger quantity than T3 [14]. T4 has a longer half-life while T3 is the more biologically active hormone [15, 16]. Most of T3 is produced in peripheral tissues by deiodinases [17]. There are three different iodothyronine deiodinases: type 1 deiodinase (D1), type 2 deiodinase (D2), and type 3 deiodinase (D3). D1, predominantly expressed in the liver and kidney [18], mainly converts T4 into T3 peripherally, being the major source of circulating T3. D2, expressed in several tissues including the heart [19], also converts T4 into T3, but it is more relevant at a local level [20]. D3 inactivates T4 and T3, converting them into reverse T3 (rT3) and 3,3-diiodothyronine (T2), respectively [21].

The thyroid gland is part of a classic endocrine axis—the hypothalamus–pituitary–thyroid gland axis—that regulates thyroid function. The hypothalamus produces thyrotropin-releasing hormone (TRH), which stimulates the thyrotrophic cells of the hypophysis to produce thyroid-stimulating hormone (TSH), which in turn stimulates the thyroid gland to produce and release T4 and T3 into the blood stream [22].

Thyroid hormones have both direct and indirect effects on cardiac function. These effects are mediated through genomic and nongenomic mechanisms. T3 binds to a specific nuclear receptor which regulates the transcription of various genes with important roles in cardiovascular function [23]. The nongenomic effects are mainly related to cell membrane transport of calcium and other ions [23]. In addition to the heart, T3 also has effects on the peripheral circulation. These impact cardiovascular hemodynamics, cardiac filling, and myocardial contractility [24, 25].

Thyroid hormones upregulate the expression of genes encoding sodium/potassium-transporting ATPases [26–28], increase the transcription of myosin heavy chain (MHC) α gene, and decrease that of MHC β gene, resulting in an increased velocity of contraction (Table 1) [26–28]. They also increase the transcription of calcium ATPase protein of the sarcoplasmic reticulum (SERCA2a) and downregulate the transcription of phospholamban (PLN), increasing the velocity of diastolic relaxation (Table 1) [26–28]. T3 decreases cardiac fibrosis through repression of collagen gene expression and induction of metalloproteinase expression (Table 1) [29, 30]. Thyroid hormones also possess positive inotropic properties through increased expression of β1-adrenergic receptors and modulation of ionic channels (Table 1) [25].

Regarding indirect effects, thyroid hormones activate sodium, potassium, and calcium membrane channels [25], have effects on the mitochondrial membrane and mitochondriogenesis [31], and are involved in several signaling pathways of cardiomyocytes and vascular smooth muscle cells [32]. Thyroid hormones induce production of endothelial nitric oxide and subsequent vasodilatation through the activation of phosphatidylinositol 3kinase (PI3K)/serine/threonine protein kinase (AKT) signaling pathways [33, 34]. By increasing calcium reuptake within the arterioles, thyroid hormones also promote smooth muscle relaxation [33]. Both these effects and the direct repression of PLN expression lead to a reduction in systemic vascular resistance [34, 35].

In sum, thyroid hormones decrease systemic vascular resistance through vasodilation and increase cardiac output through positive inotropic and chronotropic effects. Both hyperthyroidism and hypothyroidism result in hypertension. In hyperthyroidism, systolic arterial pressure is preferentially increased. In contrast, hypothyroidism leads to increased diastolic/median arterial pressure [36].

Through the aforementioned molecular effects, thyroid hormones improve systolic and diastolic function, being essential for proper cardiovascular function [37].

Hyperthyroidism and Heart Failure

Patients with even mildly altered thyroid function have a worse prognosis in heart disease, particularly heart failure [38]. Both hypothyroidism and hyperthyroidism can lead to heart failure [38].

Overt hyperthyroidism increases the risk of atrial fibrillation (AF) and is associated with a hyperdynamic state (Table 2) [24]. Cardiac output increases substantially due to reduced systemic vascular resistance and increased preload, contractility and heart rate (Table 2) [24]. When left untreated, hyperthyroidism may lead to heart failure owing to cardiac hypertrophy, arrhythmias, and increased preload (Table 2) [39]. Moreover, in a population-based study of individuals with hyperthyroidism, those who did not receive definitive therapy had a higher long-term cardiovascular mortality [40].

Studies on subclinical hyperthyroidism and intima–media thickness have reached contradictory conclusions. Some authors have reported a lack of association between the two [41], and others have found that subclinical hyperthyroidism presents with increased carotid intima–media thickness (Table 2) [42]. Delitala et al. have shown that high levels of free T4 have a detrimental effect on aortic stiffness and therefore may contribute to the aging process

Table 1 Genomic effects of thyroid hormones

Gene	Transcription	Effect
Myosin heavy chain α (MHC α)	↑	↑ velocity of contraction
Myosin heavy chain β (MHC β)	↓	
SERCA 2	↑	↑ velocity of diastolic relaxation
Phospholamban (PLN)	↓	
Collagen	↓	↓ cardiac fibrosis
Metalloproteinase	↑	
β1 adrenergic receptor	↑	↑ velocity of contraction
		↑ heart rate

Thyroid hormones (TH) increase the transcription of myosin heavy chain α (MHC α) gene and decrease the transcription of myosin heavy chain β (MHC β) gene, leading to an increased contraction velocity. By increasing the expression of SERCA 2 gene and decreasing the expression of phospholamban (PLN) gene, TH increase the velocity of diastolic relaxation. Cardiac fibrosis is suppressed owing to the decreased collagen gene transcription and to the increased metalloproteinase gene expression. The increased transcription of β1 adrenergic receptor gene causes both contraction velocity and heart rate to increase

of the vascular system [43]. One study reported an absence of changes in blood pressure or pulse pressure in subclinical hyperthyroidism as well as an absence of incident hypertension [44]. Low serum TSH is also associated with high plasma fibrinogen [45], which may contribute to the higher risk for cardiovascular events [45].

Subclinical hyperthyroidism has been consistently associated with cardiovascular diseases and adverse outcomes [46, 47], including coronary artery disease [48], AF [48–52], heart failure [53, 54], and cardiovascular mortality [48]. Even though studies of subclinical hyperthyroidism and cardiovascular events have many limitations (variable and inconsistent methodologies, different TSH cut-off levels, distinct cardivascular disease definitions, heterogeneity of populations, and absence of randomized, controlled trials), treatment is still recommended by international guidelines, particularly in older patients and in those with TSH < 0.1 mU/l [55].

Hypothyroidism and Heart Failure

Hypothyroidism has many cardiac effects opposite to those seen in hyperthyroidism. Hypothyroidism and subclinical hypothyroidism produce similar qualitative cardiovascular alterations that only differ in their extent [14].

Kisso et al. induced overt hypothyroidism in hypertensive rats by treating them with propylthiouracil (PTU). They found that LV diameters in systole and diastole were increased, while wall thickness, ejection fraction, heart rate, and systolic blood pressure were decreased in these rats. Furthermore, thyroid hormone dysfunction—hypothyroidism—in previously hypertensive rats led to systolic dysfunction and left ventricular (LV) dilation [56]. In hypothyroidism, heart rate and contractility are reduced, and peripheral vascular resistance is increased, leading to a reduction in cardiac output (Table 2) [57]. Much like in hyperthyroidism, overt hypothyroidism is

Table 2 Cardiovascular effects of hyperthyroidism and hypothyroidism

Hyperthyroidism and subclinical hyperthyroidism	Hypothyroidism and subclinical hypothyroidism
↑ cardiac output	↓ cardiac output
↑ heart rate	↓ heart rate
↑ contractility	↓ contractility
↓ systemic vascular resistance (↑ NO)	↑ systemic vascular resistance (↓ NO)
↑ carotid intima–media thickness	↑ carotid intima–media thickness
↑ systolic blood pressure	↑ diastolic blood pressure
Cardiac hypertrophy	Cardiac fibrosis
Heart failure	Heart failure
Increased arrhythmic risk	Hypercholesterolemia

Hyperthyroidism increases cardiac output, heart rate, and contractility and decreases systemic vascular resistance. Hypothyroidism has the opposite effects. Carotid intima–media thickness is increased in both diseases. Hyperthyroidism raises systolic blood pressure and is associated with cardiac hypertrophy. On the other hand, hypothyroidism raises diastolic blood pressure and favors cardiac fibrosis. Both disorders can lead to heart failure. There is an increased arrhythmic risk in hyperthyroidism. Hypercholesterolemia is another cardiovascular effect of hypothyroidism

accompanied by carotid intima–media thickening (Table 2). It is also associated with other atherosclerotic risk factors such as hypercholesterolemia, diastolic hypertension, and reduced production of nitric oxide (Table 2) [58]. These effects are reversible with thyroid hormone supplementation [58].

Subclinical hypothyroidism (SCH) is most frequently associated with diastolic dysfunction due to impaired ventricular filling and relaxation [59, 60]. Nevertheless, SCH is also associated with systolic dysfunction, which is reversed with thyroid hormone replacement therapy [61]. Similarly to overt hypothyroidism, SCH increases systemic vascular resistance (Table 2) and arterial stiffness by impairing relaxation of vascular smooth muscle cells [24] and by reducing nitric oxide availability [62]. Patients with SCH present with increased systolic and diastolic blood pressures and total cholesterol concentrations. Peixoto de Miranda et al. have found an association between SCH and increased carotid intima–media thickness [63]. Moreover, a study reported increased arterial stiffness in women with higher TSH levels [64] and Wang et al. found that free T4 levels were inversely associated with arterial stiffness in euthyroid subjects [65].

Population studies have found conflicting evidence concerning the association between SCH and cardiovascular morbidity and mortality [23]. Some studies concluded that SCH does not increase cardiovascular mortality [66, 67], while others suggested it does [68–70]. One metaanalysis found that SCH is associated with a higher risk of cardiovascular events and death in patients with high serum TSH levels (particularly TSH levels > 10 mU/l) [71]. Nonetheless, there are no randomized clinical trials to show whether or not thyroid hormone replacement therapy improves cardiovascular morbidity and mortality in SCH patients. Several levothyroxine supplementation therapy studies in SCH individuals showed improvements in cardiovascular function (improved LV function, vascular endothelial function, and decreased atherogenic lipid particles, among others) [24, 59–61, 72]. One study found that patients (aged < 70 years) with high TSH levels treated with levothyroxine had fewer cardiovascular events when compared with untreated patients [73]. Improvement in cardiac mitochondrial function with levothyroxine treatment has also been reported [74]. Due to the aforementioned lack of evidence and according to international guidelines, treatment should solely be considered in patients with more severe disease (TSH levels > 10 mU/l), or aged < 70 years, or that present with symptoms of hypothyroidism [75].

Low T3 Syndrome in Heart Failure

Low T3 syndrome, euthyroid sick syndrome, or nonthyroidal illness syndrome is characterized by normal serum TSH levels, low serum T3 levels, and high serum rT3 levels (Fig. 1a) [76]. These alterations in thyroid hormones have been well described in patients with acute illness and no history of thyroid disease [77–83]. This syndrome is also common in hospitalized patients or patients with critical illness. Even though the underlying cause of these changes is still unknown, these may be due to alterations in TSH and TRH secretion, thyroid hormone binding to plasma proteins, transport of thyroid hormone into peripheral tissues, iodothyronine deiodinase activity, and nuclear thyroid hormone receptor activity [76]. Particularly in heart failure, low T3 syndrome may be due to an activation of D3 causing T3 levels to fall and rT3 levels to rise (Fig. 1a) [21]. Low T3 syndrome should not be viewed as an isolated pathologic event as it is often associated with alterations of other endocrine systems [80]. It should be thought of as a coordinated systemic reaction to illness, in several different conditions. Given the positive association between low T3 syndrome and poor prognosis in various diseases, TH replacement treatment in this syndrome has been advocated.

Both patients with chronic and acute heart failure frequently present with low serum T3 levels [84]. Even in the absence of TSH abnormalities, low T3 levels have been associated with increased risk of mortality in patients with acute heart failure [85] and chronic heart failure [86–88]. Chronic heart failure patients treated with short-term infusion of dobutamine showed improvement of serum T3 levels and of cardiac function [89]. Consequently, thyroid hormone replacement therapy was postulated as a treatment for chronic heart failure. Small studies treating chronic heart failure with T3 [90, 91] have shown improvement in cardiac output and decrease in systemic vascular resistance. However, more studies are needed to prove that thyroid hormone supplementation is effective in the treatment of chronic heart failure [76].

Fruhwald et al. reported that, out of a series of 61 idiopathic dilated cardiomyopathy patients with no clinical evidence of thyroid disease, only 2 patients had completely normal thyroid morphology and function [92]. Hamilton et al. showed that 29% of patients in a series of 84 patients with NYHA class III and IV heart failure had a low serum T3 index [93]. Increased reverse triiodothyronine (rT3) levels were found in 38% of cases [93]. Fifty-eight percent of patients had decreased free T3 index to rT3 ratio [93].

Low T3 syndrome has been associated with several hemodynamic abnormalities. In a study of patients with chronic heart failure, those with low T3 levels presented lower cardiac index, higher pulmonary wedge pressure, and higher right atrial pressure [94]. In a prospective study enrolling patients with HFpEF, low T3 levels were associated with higher grade diastolic dysfunction, higher mitral E velocity and shorter deceleration time in echocardiographic evaluation [95].

Low T3 syndrome is also associated with important clinical consequences. Pantos et al. showed that, in patients with HFrEF, lower T3 levels were strongly associated with lower

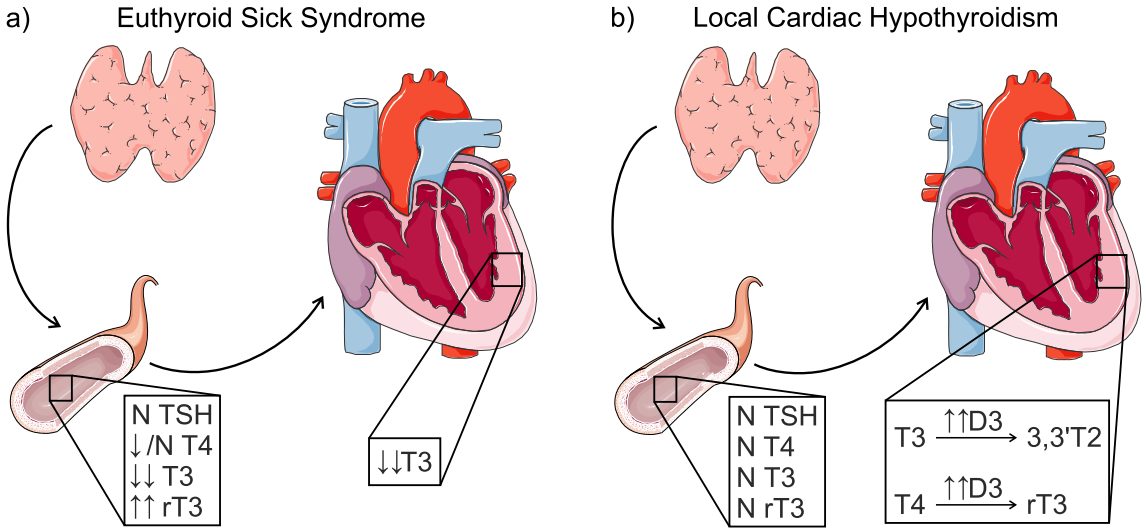

Fig. 1 Systemic and local cardiac thyroid function in euthyroid sick syndrome (**a**) and local cardiac hypothyroidism (**b**). **a** Euthyroid sick syndrome presenting with its key features: low T3 and high rT3 serum levels as well as normal TSH and low to normal T4 serum levels. Local cardiac T3 levels are decreased. **b** Local cardiac hypothyroidism presenting with a normal systemic thyroid function and increased D3 activity in the cardiac tissue leading to decreased local T3 and T4 levels (images obtained from Servier Medical Art)

exercise capacity as measured by peak oxygen consumption (VO_{2max}) [96]. Hamilton et al. and Ascheim et al. showed that the prevalence of low T3 syndrome increased with the severity of heart failure in the study population [93, 97]. Opasich et al. reported that low T3 levels were significantly more prevalent among more symptomatic patients. In this study, 31% of patients with NYHA class III–IV had low T3 levels whereas only 7% of patients with NYHA class I–II had low T3 syndrome [94]. Furthermore, mortality was significantly higher in the low T3 level group [94].

Local Cardiac Hypothyroidism in Heart Failure

Thyroid hormones can vary at a local level independently of serum thyroid hormone levels (Fig. 1b). D3 can decrease thyroid hormone signaling specifically in the cardiac tissue and may contribute to the regulation of cardiac thyroid function during heart failure progression (Fig. 1b) [21]. Heart failure is also associated with downregulated thyroid hormone nuclear receptors [98, 99], which may worsen cardiac function even further [20]. Wassen et al. demonstrated that rats with right ventricular hypertrophy have increased D3 activity in the RV but equal D3 activity in the LV when compared with controls. Moreover, rats with right ventricular hypertrophy that progressed to heart failure had even higher D3 activity when compared to rats with compensatory hypertrophy. The authors only found changes in serum thyroid function (decreased levels of T3) in rats that progressed to heart failure. The increase in D3 activity may represent a maladaptive process, as stable cardiac hypertrophy has less D3 activity than decompensated right ventricular hypertrophy [21].

Besides upregulation of D3, there are other altered processes that can contribute to locally impaired thyroid function in cardiac tissue: decrease in TH uptake, changes in the expression of TH receptors in cardiomyocytes [20, 21], altered peripheral T4 to T3 conversion [21], reduced T3 production by inhibition of D2, and changes in TH membrane transporters [20].

Thyroid Hormones as a Treatment for Heart Failure

Based on the above described findings and the role thyroid hormones play in cardiovascular regulation, thyroid hormones were proposed as a potential treatment for heart failure. Several studies, clinical and experimental, have shown beneficial effects of thyroid hormone supplementation [21].

Henderson et al. demonstrated that in rats with myocardial infarction–induced heart failure treatment with T3 improves systolic function and tends to improve diastolic function [100].

Contrary to patients with hypothyroidism where T4 supplementation is the recommended treatment, it seems illogical to supplement with T4 instead of T3 when peripheral conversion of thyroid hormones is impaired. In animal studies, treatment of cardiomyopathy and subclinical hypothyroidism with thyroid hormones prevented progression of fibrosis and necrosis, loss of cardiac cells, and dilation and dysfunction of the LV [20, 101]. Weltman et al. have demonstrated that chronic hypertension is associated with impaired cardiac function and decreased levels of T3 both in serum and in cardiac tissue. This leads to heart failure. Treatment with supplementation of T3 restored serum and cardiac T3 levels, improved cardiac function, and promoted remodeling benefits without causing any symptoms or signs of hyperthyroidism. Although

hypertension was still present, this therapy seemed to attenuate dysfunction and provide important cardiac benefits [102].

A locally decreased cardiac thyroid function may worsen heart failure progression, and treatment with thyroid hormone supplementation may improve it. LV function appears to be more closely related to thyroid hormone cardiac levels than to thyroid hormone serum levels [20]. Even though the cardiac tissue locally converts T4 into T3 [20], the heart is vulnerable to reductions in the levels of serum T3. Moreover, when serum T3 levels drop, the heart may become hypothyroid to a moderate extent [20]. Trivieri et al. studied the effects of a targeted cardiac increase of D2 activity in preventing cardiac dysfunction. Cardiac T3 levels were increased, and contractility was enhanced. Moreover, expression of Na^+/Ca^{2+} exchanger, β-MHC and sarcolipin was downregulated and expression of SERCA2a was increased. Increased D2 activity may have an important role in preserving cardiac function and normalizing gene expression that would be altered in pathological remodeling. The authors suggest that targeted thyroid hormone delivery to the heart may be an effective treatment in heart disease [103].

Rats with hypertensive heart failure, approaching dilated HF, showed improvement in chamber diameter and wall thickness when supplemented with T3 and T4. These improvements were dose-related [104, 105]. Another study showed that treatment with thyroid hormones was able to reinstate the expression of both Ca^{2+} signaling and its handling proteins and also myocyte contractile function [106]. When the heart muscle is stimulated with T3, an increased rate of contraction and relaxation is observed as well as changes in the expression of phospholamban, myosin heavy chains, and SERCA2. Treatment with thyroid hormones improved LV function by increasing cardiac output and exercise capacity and decreasing systemic vascular resistance [20].

Thyroid dysfunction is a cause of heart failure, and it is reversible with supplementation of thyroid hormones. The effects of this treatment on prognosis and mortality remain unknown. However, every patient with heart failure should have his/her thyroid function studied [107]. Evidence from animal studies suggests that treatment of thyroid dysfunction may improve the prognosis in heart failure. Zhang et al. found that rats with heart failure treated with T4 had improved cardiac function and decreased left atrial and ventricular internal diameters. Treatment with T4 also reduced AF susceptibility [108]. Khalife et al. found that treating subclinical hypothyroid cardiomyopathic rats with thyroid hormones restored coronary blood flow, preventing LV dysfunction and loss of myocytes [109].

Hamilton et al. reported safe acute intravenous administration of triiodothyronine in patients with advanced heart failure [91]. Pingitore et al. showed that T3 supplementation in patients with ventricular dysfunction and low T3 syndrome reduced activation of the neuroendocrine system and improved left ventricle stroke volume [90]. Other authors found that long-term oral T3 treatment in patients with chronic and stable systolic heart failure with low serum T3 levels did not improve or deteriorate heart function or neurohormonal stimulation [110].

Gaps and Limitations

Although thyroid hormone therapy has been advocated for treating heart failure, a clear benefit is yet to be established. There are a few unresolved issues concerning the treatment of subclinical hypothyroidism with supplementation of thyroid hormones namely the dosage and timing for initiating and suspending the treatment [20]. If thyroid hormone treatment proves to be beneficial, there will still be many questions to be answered. There is no clear evidence as to what form of thyroid hormone is most beneficial in heart failure. Both TH, T3 and T4, can be administrated solely or in association. There is no way of knowing whether thyroid hormone levels have normalized in the cardiac tissue without obtaining a biopsy. Some have proposed using TSH levels (feedback inhibition) as a guide. However, this may be insufficient as alterations in a specific tissue such as the heart may not be noticed systemically when observing TSH levels [111]. The existence of a biomarker of intracardiac thyroid hormone signaling would be most helpful. However, one has not been identified yet [20]. Moreover, the long-term effects of this treatment would need to be thoroughly studied [111].

Few studies have evaluated the role of thyroid hormones in patients with HFpEF and in animal models of HFpEF. There is currently no effective treatment for this disease, and thyroid hormones have been shown to be beneficial for diastolic function. Therefore, understanding the potential role of thyroid hormones in the treatment of HFpEF is also an important gap in this field [102]. One important limitation of the treatment with thyroid hormones is its potential harmful effects, namely, the risk of iatrogenic hyperthyroidism [112] with adverse cardiovascular effects (shortening of systolic time intervals, increased frequency of atrial premature beats and left ventricular hypertrophy) [113] and bone changes (reduced bone density and bone mass [114], and accelerated osteoporosis [112]). The most concerning adverse effects are arrhythmias, both AF and ventricular arrhythmias [115]. Studies testing T3 treatment in patients with heart failure found that T3 was well tolerated and no undesirable effects such as arrhythmias, myocardial ischemia, or hemodynamic instability were reported [20]. Nevertheless, it remains uncertain whether the use of physiological doses of thyroid hormones is associated with increased risk of arrhythmias.

Most studies of thyroid hormone replacement therapy have been performed in animal models. Further research in humans is needed to evaluate whether the same beneficial effects can be observed.

Conclusions

Thyroid dysfunction is common in patients with heart failure. Even when serum thyroid hormones are normal, patients with heart failure may have local cardiac hypothyroidism. As thyroid hormones are essential for cardiovascular function, thyroid hormone supplementation has been evaluated for the treatment of heart failure. Data from epidemiological studies supports a higher risk of heart failure and a worse prognosis in heart failure in patients with low levels of thyroid hormones. In addition, animal studies and small clinical studies suggest that thyroid hormone supplementation may improve cardiac function in heart failure. Although further studies are needed to evaluate the safety and efficacy of thyroid hormones in this context, the available evidence suggests that thyroid hormone modulation is a promising therapeutic approach to heart failure.

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