

Advances in the Study of Thyroid Hormones and Atrial Fibrillation

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Abstract: Atrial fibrillation (AF) is a common cardiac arrhythmia characterized by irregular, rapid and ineffective contractions of the atrial rhythm. The relationship between thyroid hormones and AF has been of interest because past studies have identified that thyroid hormones play an important role in the cardiovascular system and that there is a strong link between abnormal thyroid function and AF. Hyperthyroidism is often accompanied by symptoms of arrhythmia such as increased heart rate and arrhythmia, whereas hypothyroidism patients may exhibit abnormalities such as slowed heart rate and enlarged atria. Thyroid hormones are involved in the onset and development of AF through several pathways. First, thyroid hormone may affect the electrophysiological properties of cardiomyocytes, altering the excitability and repolarization process of atrial cells. Second, thyroid hormones may also affect the structure and function of the atria, leading to atrial enlargement and fibrosis, thereby increasing susceptibility to AF. In addition, thyroid hormones may alter the maintenance and regression of AF by affecting the autonomic regulation of the cardiovascular system. This suggests that thyroid hormones play a key role in the pathophysiologic mechanisms of AF. In recent years, an increasing number of studies have focused on the relationship between thyroid hormones and AF and have attempted to reveal their specific mechanisms of action. Some studies have suggested that modulation of thyroid function may be a new strategy for the treatment of atrial fibrillation. In this article, we present a review of the latest research progress on thyroid hormones and atrial fibrillation.

Keywords: Atrial Fibrillation; Thyroid Hormones; Treatment; Progress.

1. Introduction

1.1. Physiological Role of Thyroid Hormones

Thyroid hormones are a class of important hormones secreted by the thyroid gland, mainly including thyroxine (T4) and triiodothyronine (T3) [1]. These two hormones play key physiologic roles in the body and are of particular interest for their effects on the cardiovascular system. In the cardiovascular system, thyroid hormones are involved in cardiac regulation through multiple pathways, and a close relationship exists between them and atrial fibrillation [2]. Thyroid hormone synthesis is a complex and sophisticated process that occurs mainly in the thyroid tissue. First, thyrotropin-releasing hormone (TSH) induces thyroid hormone synthesis by stimulating thyroid follicular cells in thyroid tissue. This process involves the uptake of iodide ions, iodination, synthesis of thyroglobulin, and production of T4 and T3. Thyroid hormones are widely distributed through the blood circulation to tissues throughout the body, including the heart. In the heart, thyroid hormones bind to thyroxine receptors and mediate a range of physiologic effects. Thyroxine receptors in the heart mainly include thyroxine α -receptors and β -receptors, which are expressed in different regions of the heart and regulate the systolic and diastolic functions of the heart [3]. The electrophysiologic activity of the heart is directly regulated by thyroid hormones. Thyroid hormones regulate the membrane potential of cardiomyocytes by affecting the opening and closing of ion channels. This has a direct effect on cardiac excitability and the rate of excitation conduction, which in turn affects cardiac rhythm and contractility [4]. These regulatory effects maintain normal cardiac function under normal physiological conditions, but when thyroid hormone levels are abnormal, they may lead to

disturbances in cardiac electrophysiology and increase the risk of atrial fibrillation.

1.2. Definition and Mechanisms of Atrial Fibrillation

Atrial Fibrillation (AF) is a common cardiac arrhythmia, the incidence of which increases significantly with age [5]. It is estimated that about 5% to 15% of people over 60 years of age suffer from AF. With the increasing trend of aging population, the burden of AF is gradually increasing. In addition to age factors, chronic diseases such as hypertension, diabetes, and heart disease are important risk factors for AF [6]. The characteristic feature of AF is the uncoordinated contraction of atrial muscle fibers, resulting in rapid and irregular beating of the atria. This irregular atrial activity may interfere with the normal contraction of the ventricles, leading to a decrease in the heart's pumping function and increasing the patient's risk of ischemic heart disease, stroke, and other serious complications. The mechanisms involved in the development of AF involve a variety of factors, including electrophysiologic, structural, and metabolic factors. Among them, abnormalities in electrophysiology are one of the most critical mechanisms for the development of AF.

First, AF is associated with abnormalities in atrial muscle electrophysiology. In patients with AF, abnormal depolarization and repolarization processes in atrial myocytes lead to uncoordinated excitability of atrial tissue. This abnormal excitability allows the atrial myocytes to become easily triggered, forming the electrophysiologic basis of AF. Second, abnormalities in ion channels are also involved in the development of AF. In particular, abnormal functioning of sodium, calcium, and potassium channels may lead to abnormal electrical activity in the atrial myocytes, making AF easy to develop and sustain. In addition, structural changes in

the heart are an important factor in AF. Patients with AF are often accompanied by the presence of heart disease, including myocardial infarction, myocardial fibrosis, and atrial dilatation [7]. These structural changes make the atrial tissue more prone to forming foldback loops, which contributes to the development of AF. Finally, metabolic factors such as abnormal thyroid function may also be associated with AF. Thyroid hormones have an effect on both the electrophysiology and structure of the heart, so hyper- or hyperthyroidism may contribute to the development of AF.

2. Mechanisms of the Effect of Thyroid Hormones on Atrial Fibrillation

2.1. Relationship between Thyroid Hormones and Cardiac Electrophysiology

2.1.1. Changes in Electrophysiological Parameters

Thyroid hormones affect cardiac electrophysiologic parameters in a number of ways, most notably cardiac autoregulation and excitability. Under normal conditions, an increase in thyroid hormones increases cardiac autoregulation, making the heart more prone to excitation during the cardiac cycle. This is primarily through its effect on the atrial myocytes, which prompts the depolarization and repolarization processes to occur more frequently. In addition, thyroid hormones can affect the rate of excitation conduction in the heart. In the presence of hyperthyroidism, the heart's conduction system is more rapid, causing impulses to travel through the heart tissue more quickly. This can increase the overall rate of excitation conduction in the heart, but it can also lead to the development of arrhythmias such as atrial fibrillation.

2.1.2. Regulation of Ion Channels

The regulation of cardiac ion channels by thyroid hormones is one of the important mechanisms by which they affect cardiac electrophysiology. Thyroid hormones can directly or indirectly regulate the function of a variety of ion channels, including sodium, potassium, and calcium channels [8]. In the case of sodium channels, the action of thyroid hormones results in increased sodium channel activity in atrial myocytes, promoting the entry of more sodium ions into the cell. This increases the excitability of the atrial myocytes and helps to generate stronger electrical activity in the heart. Modulation of potassium channels is also a key factor in the way thyroid hormones affect cardiac electrophysiology. The action of thyroid hormone inhibits potassium channel activity in atrial myocytes, prolonging the duration of the action potential. This may lead to prolonged propagation of excitation, increasing the risk of arrhythmias such as atrial fibrillation. In addition, thyroid hormone may contribute to more rapid and efficient excitation-contraction coupling in the heart by modulating calcium channels in cardiac cells and enhancing the sensitivity of cardiac muscle cells to calcium ions.

Under normal physiologic conditions, thyroid hormone regulation helps maintain normal cardiac function. However, when thyroid function is abnormal, i.e., hyperthyroidism or hypothyroidism, there may be an imbalance in this regulation, leading to disturbances in cardiac electrophysiology. In a hyperthyroid state, excess thyroid hormone may overexcite the heart and increase the occurrence of arrhythmias such as atrial fibrillation. Conversely, in hypothyroidism, an insufficient amount of thyroid hormone may lead to a weakening of the heart's electrical activity, making the heart

more susceptible to arrhythmias caused by other factors.

2.2. Interaction of Thyroid Hormones with Myocardial Structure

2.2.1. Morphological Changes in Cardiomyocytes

Thyroid hormones are directly involved in shaping the structure of the myocardium by influencing morphological changes in cardiomyocytes. Under normal conditions, moderate levels of thyroid hormones help to maintain cardiomyocytes in a healthy state. [9] This is mainly seen in the regulation of cardiomyocyte volume and the maintenance of intracellular structures. An increase in thyroid hormone promotes the growth and proliferation of cardiomyocytes, leading to an increase in the volume of cardiomyocytes [10]. This process is associated with myocardial hypertrophy, but within moderate limits contributes to the maintenance of normal myocardial structure and function. However, when thyroid hormone levels are abnormally elevated, it may lead to excessive cardiomyocyte growth, which in turn may lead to myocardial hypertrophy, increased cardiac burden, and even heart disease. In addition, thyroid hormone can also affect the structure of organelles within cardiac muscle cells, such as mitochondria and endoplasmic reticulum [11]. These organelles are essential for the normal function of cardiomyocytes, and thyroid hormone regulation plays an important role in maintaining the structure and function of these organelles.

2.2.2. Synthesis and Degradation of Myocardial Proteins

Thyroid hormones have a direct effect on the synthesis and degradation processes of cardiac muscle proteins. Cardiac muscle proteins include actin, troponin, and myosin, which are important components of cardiac muscle cells. Thyroid hormone affects the synthesis level of cardiac muscle proteins by regulating the expression of related genes [12]. Under normal conditions, moderate levels of thyroid hormones help promote the synthesis of cardiac muscle proteins and maintain the normal structure and function of the myocardium. This facilitates the contractile and diastolic processes in cardiomyocytes and maintains normal pumping function of the heart. However, in the case of abnormal thyroid function, this may lead to excessive synthesis or degradation of cardiac muscle proteins, which in turn may trigger changes in myocardial structure and abnormal function.

In addition, thyroid hormones can affect cardiac protein homeostasis by modulating cardiac protein degradation pathways, such as the ubiquitin-proteasome system. This process is critical for the long-term health of cardiomyocytes, in which thyroid hormones play a regulatory role.

2.2.3. Intercellular Junctions and Collagen Deposition

Thyroid hormones are also closely associated with the connections between cardiomyocytes and with collagen deposition. Cardiomyocytes form tight junctions between each other through intercellular junctions that constitute myocardial tissue. Regulation of thyroid hormones can influence the formation and stability of these connections. Under normal conditions, moderate thyroid hormone levels help to maintain the connections between cardiomyocytes and maintain the overall structure of myocardial tissue. However, when thyroid hormone levels are abnormally elevated or lowered, this may lead to loosening or over firming of intercellular connections, affecting the stability of myocardial tissue. In addition, thyroid hormone regulation involves collagen synthesis and degradation. Moderate thyroid

hormone levels help to inhibit excessive collagen synthesis and maintain the elasticity of myocardial tissue. However, in the presence of abnormal thyroid function, this may lead to excessive accumulation of collagen and formation of fibrosis, which affects the elasticity and function of the myocardium.

3. Role and clinical significance of thyroid hormones in atrial fibrillation

3.1. Association of Abnormal Thyroid Function with Atrial Fibrillation

Thyroid hormones play an important role in the regulation of cardiac electrophysiology, one of the most prominent manifestations of which is their effect on the electrical activity of atrial myocytes. Excessive or insufficient thyroid hormone can lead to abnormalities in the electrical activity of the atrial myocytes, thereby increasing the risk of atrial fibrillation. In the case of hyperthyroidism, elevated levels of thyroid hormone may lead to overexcitation of the atrial muscle cells, increasing the probability of atrial fibrillation. This is related to the effects of thyroid hormone on sodium-potassium pumps and calcium channels, leading to depolarization and an unstable electrophysiological state of atrial myocytes [13]. Conversely, in hypothyroidism, the electrical activity of atrial myocytes may be diminished due to decreased thyroid hormone levels, causing the atrial myocardium to respond abnormally to normal electrical signals, thereby increasing susceptibility to AF.

Abnormal thyroid function may also cause changes in the structure of the heart muscle, which can affect the development of AF. Thyroid hormones play an indirect role in the development of AF by regulating cardiomyocyte growth, collagen synthesis, and heart valve function [14]. In the presence of hyperthyroidism, overgrowth of cardiomyocytes and myocardial hypertrophy may lead to structural irregularities in the atria, providing the basis for a greater susceptibility to AF. In addition, the effects of thyroid hormones may cause abnormal accumulation of collagen, increasing the chances of AF. Conversely, in the presence of hypothyroidism, the reduction of cardiomyocytes and relaxation of the heart's structure may lead to dilatation of the atria, also increasing the risk of AF.

Another important aspect of the association between abnormal thyroid function and atrial fibrillation is its ability to influence blood clot formation. Changes in thyroid hormones may affect the clotting properties of the blood, increasing the risk of thrombosis [15]. In the case of hyperthyroidism, the levels of clotting factors in the blood may be elevated due to the increase in thyroid hormones, increasing the tendency for thrombosis. This is particularly important in patients with atrial fibrillation, which is itself a high-risk factor for thrombosis, a risk that is further exacerbated by abnormal thyroid function. Conversely, in the presence of hypothyroidism, coagulation may be suppressed, but the risk of thrombosis still exists, especially in the setting of atrial fibrillation.

3.2. Thyroid Hormones in the Treatment of Atrial Fibrillation

In patients with hyperthyroidism, antithyroid medication, radioactive iodine therapy, or surgical removal of the thyroid gland are common means of regulating thyroid hormone

levels [16]. During this process, monitoring the patient's heart rhythm and cardiac function becomes critical. Hyperthyroidism treatment may lead to a gradual normalization of the heart rate, thus reducing the symptoms of atrial fibrillation [17]. However, adjustment of thyroid hormone levels needs to be done carefully to avoid overcorrection, leading to bradycardia or tachycardia. In patients with hypothyroidism, thyroid hormone replacement therapy is the mainstay of management. Appropriate thyroid hormone replacement therapy helps to maintain normal heart rate and rhythm and reduces the risk of atrial fibrillation. However, the patient's thyroid hormone levels need to be closely monitored to ensure that they are maintained in the appropriate range during the course of treatment.

Patients with atrial fibrillation are often at risk for thrombosis, so anticoagulation is also an important part of treatment [6]. The combination of thyroid hormones and anticoagulants requires comprehensive consideration of the patient's overall condition. In hyperthyroid patients, there may be an increased risk of bleeding, and the type and dose of anticoagulants need to be carefully selected. In contrast, in patients with hypothyroidism, rational anticoagulation can reduce the risk of thrombosis and improve the prognosis of patients with atrial fibrillation. Individual differences in patients need to be considered when developing a thyroid hormone treatment program. The response to thyroid hormone may vary from patient to patient, so individualized treatment strategies are needed. Regular monitoring of the patient's thyroid function, heart rhythm, and cardiac function to make timely adjustments to the treatment regimen is essential to ensure the effectiveness of treatment. In addition, factors such as the patient's age, gender, and comorbidities may influence the choice of treatment. In older patients, the dose of thyroid hormone may need to be adjusted more carefully to avoid overtreatment leading to other adverse effects. Gender differences may also affect a patient's metabolism and response to thyroid hormones [18], and therefore these factors need to be fully considered during treatment.

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