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Review Article

Atrial fibrillation and hyperthyroidism: A literature review

Vivek Reddy[a,*], Wael Taha[b], Shanker Kundumadam[a], Mazhar Khan[c]

[a] Department of Internal Medicine, Wayne State University, Detroit Medical Center, 4201 St. Antoine Street, Detroit, MI, 48201, United States
[b] Department of Endocrinology, Wayne State University, Detroit Medical Center, 4201 St. Antoine Street, Detroit, MI, 48201, United States
[c] Department of Cardiology, Wayne State University, Detroit Medical Center, 4201 St. Antoine Street, Detroit, MI, 48201, United States

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ABSTRACT

Atrial fibrillation is the most common arrhythmia worldwide with increasing frequency noted with age. Hyperthyroidism is a well-known cause of atrial fibrillation with a 16%–60% prevalence of atrial fibrillation in patients with known hyperthyroidism Ross et al. (2016). While hyperthyroidism as a causative factor of atrial fibrillation is well established, this literature review aims to answer several questions on this topic including:

1. The relationship of atrial fibrillation to hyperthyroidism
2. Atrial fibrillation as a predictor of hyperthyroidism
3. The pathophysiology of thyrotoxic atrial fibrillation
4. Subclinical hyperthyroidism and the relationship with atrial fibrillation
5. Cardioversion and Catheter ablation of hyperthyroid patients with atrial fibrillation
6. Thrombotic risk of hyperthyroid patients with atrial fibrillation
7. Management of Thyrotoxic Atrial fibrillation
8. Pharmacological rhythm control in patients with hyperthyroidism and atrial fibrillation
9. Treatment of Hyperthyroidism to prevent atrial fibrillation
10. Clinical Implications of Hyperthyroidism and Atrial Fibrillation

Contents

1. Introduction

Hyperthyroidism, or thyrotoxicosis occurs due to excess release of thyroid hormone due to an overactive thyroid gland or passive

* Corresponding author.
E-mail address: vreddy@med.wayne.edu (V. Reddy).

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release of the stored hormone. Additionally, hyperthyroidism occurs from over treatment with thyroid hormone. Hyperthyroidism is generally considered overt or subclinical, depending on the biochemical severity of the hyperthyroidism. Overt hyperthyroidism is defined as suppressed (usually undetectable) thyrotropin (TSH) and elevated levels of triiodothyronine (T3) and/or estimated free thyroxine (free T4). Subclinical hyperthyroidism is defined as a low or undetectable serum TSH with values within the normal reference range for both T3 and free T4.[1] Hyperthyroidism should be considered the potential illness whenever TSH level is subnormal.

The prevalence of hyperthyroidism in the United States is approximately 1.2% (0.5% overt and 0.7% subclinical).[2] In an older community in Baltimore, the prevalence of low TSH was 9.6% for participants on thyroid hormone and 0.8% for untreated individuals.[3] In a study performed by Krahn et al., the authors found that <1% of cases of atrial fibrillation are secondary to an acute hyperthyroid state.[4] Despite hyperthyroidism being a relatively rare cause of atrial fibrillation, this review underscores the importance of identifying thyrotoxic atrial fibrillation, understanding differences in pathophysiology and management as well as illustrating the importance of screening for hyperthyroidism in those presenting with atrial fibrillation. We have compiled literature from PubMed, Scopus and Ovid to ensure a thorough and accurate literature review.

2. New onset hyperthyroidism and the relationship with atrial fibrillation

Hyperthyroidism is a well-known cause of atrial fibrillation. In a large population based study by frost and colleagues, all patients with new onset hyperthyroidism in the inpatient setting were followed ±30 days from the diagnosis of hyperthyroidism to observe for a new onset diagnosis of atrial fibrillation or atrial flutter. It was found that 8.3% of such patients had a new onset diagnosis of atrial fibrillation or atrial flutter.[2] In patients with hyperthyroidism it was found that those who were male, advancing age, coronary artery disease, congestive heart failure and valvular heart disease were found to have a higher incidence of atrial fibrillation.[5]

2.1. Atrial fibrillation as a predictor of developing hyperthyroidism

In a large nationwide cohort study performed in Denmark by Selmer and colleagues, patients who were diagnosed with new onset atrial fibrillation were followed in the outpatient setting for 13 years to identify if they would develop hyperthyroidism.[6] In the 13 year follow up there was a significantly higher incidence of hyperthyroidism being diagnosed particularly in the male population between the ages of 51–60 when compared to the general population of that age without a diagnosis of atrial fibrillation. Another Canadian study was performed testing this association on a smaller scale and failed to show an association.[7] However, as the study performed by Selmer and colleagues was the most comprehensive study, its clinical application includes routine screening for hyperthyroidism in patients with new onset atrial fibrillation. While there are no studies on the incidence of subclinical hyperthyroidism after presenting with atrial fibrillation, routine monitoring of thyroid studies would identify this subgroup. The authors believed that these findings may have been secondary to:

1 Autoantibody formation against β1-adrenergic and M2-muscarinic receptors has been known to occur in hyperthyroidism and may trigger Atrial fibrillation prior to thyroid dysfunction.[8]
2 A genetic susceptibility to atrial fibrillation may be linked to hyperthyroidism[9]
3 Patients may have relative rises or falls in thyroid function testing, yet still remain within normal limits compared to reference values. Such variation may increase the risk of developing atrial fibrillation and will subsequently increase the risk of clinical hyperthyroidism in the future[10, 11]

Current guidelines are not available regarding frequency of screening and are per clinician discretion.

3. Pathophysiology

Atrial fibrillation irrespective of thyroid function is believed to be due to chaotic electrical activity resulting in a micro-reentrant tachycardia.[12] The wavelength theory described by Allessie and coworkers describes a wavelength, which is a product of atrial refractoriness and conduction velocity. If the patient has a long wavelength as per this theory then re-entry will not be maintained and thus self terminate.[13] In order for atrial fibrillation to be sustained the wavelength has to be short enough such that wavefronts can circulate the atrium without termination. As per this theory, atrial refractoriness, conduction velocity or both has to be sufficiently reduced to allow re-entry of wavefronts and sustainment of atrial fibrillatory waves. Other theories exist regarding the mechanism of atrial fibrillation including the presence of anatomical substrate and abnormal ectopic atrial firing. Because anyone of these abnormal findings can result in atrial fibrillation, it is important to note differences in pathophysiology between those who have atrial fibrillation with hyperthyroid and euthyroid functions. In those patients who were hyperthyroid it was found that elevated thyroid hormone altered the β1-adrenergic and M2-muscarinic receptors of the heart resulting in increased sympathetic function, tachycardia and decreased atrial refractory period. It is also known that thyroid hormone plays a role in altering ionic channels. In a study performed by Watanbe et al. the effects of thyroid hormone on mRNA expression and currents of major ionic channels were studied in murine atria. The authors found that thyroid hormone resulted in such major changes[14]:

1.) Decreased L-type Calcium channel mRNA expression
2.) Increased expression of Kv 1.5 mRNA
3.) The above changes resulted in increased outward current and decreased inward current resulting in shorter action potential duration

In another study performed in rats, the authors compared action potential duration and whole cell currents in the right and left atria in both euthyroid and hyperthyroid mice. The authors found more significant shortening of APD and greater delayed rectifier potassium current increases in the right atrium than the left atrium in hyperthyroid rats which can further increase the risk for atrial arrhythmias.[15] A separate study performed by Chen et al. studied the effects of thyroid hormone on the arrhythmogenic activity of pulmonary vein cardiomyocytes in rabbits. The authors found that thyroid hormone had the following effects on arrhythmogenesis[16]:

1.) Decreased APD
2.) Increased spontaneous activity in pulmonary vein cardiomyocytes
3.) Increased occurrence of delayed after-depolarizations in pulmonary vein beating and non-beating cardiomyocytes
4.) Increased after-depolarizations in beating cardiomyocytes

With the following changes noted, the authors concluded that thyroid hormone plays a role on arrhythmogenesis with an

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