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## History of Thyroid Disorders in Relation to Clinical Outcomes in Atrial Fibrillation



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#### ABSTRACT

**BACKGROUND:** Atrial fibrillation is the most common cardiac complication of hyperthyroidism. The association between history of hyperthyroidism and stroke remains unclear. We sought to determine whether history of thyroid dysfunction is a thromboembolic risk factor in patients with atrial fibrillation.

**METHODS:** Patients with atrial fibrillation seen in an academic institution between 2000 and 2010 were identified and followed-up. Clinical events (stroke/systemic embolism, bleeding, all-cause death) were recorded and related to thyroid status and disorders. Associations were examined in time-dependent models with adjustment for relevant confounders.

**RESULTS:** Among 8962 patients, 141 patients had a history of hyperthyroidism, 540 had a history of hypothyroidism, and 8271 had no thyroid dysfunction. Mean follow-up was  $929 \pm 1082$  days. A total of 715 strokes/systemic embolism were recorded, with no significant difference in the rates of these events in patients with a history of thyroid dysfunction vs those without thyroid problems in either univariate or multivariable analysis (hazard ratio [HR] 0.85; 95% confidence interval [CI], 0.41-1.76 for hyperthyroid-ism; HR 0.98; 95% CI, 0.73-1.34 for hypothyroidism). There were 791 bleeding events; history of hypothyroidism was independently related to a higher rate of bleeding events (HR 1.35; 95% CI, 1.02-1.79). No significant difference among the 3 groups was observed for the incidence of death.

**CONCLUSIONS:** History of hyperthyroidism was not an independent risk factor for stroke/systemic embolism in atrial fibrillation, whereas hypothyroidism was associated with a higher risk of bleeding events. These data suggest no additional benefit from the inclusion of thyroid dysfunction in thromboembolic prediction models in atrial fibrillation.

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KEYWORDS: Atrial fibrillation; Hyperthyroidism; Hypothyroidism; Stroke

Hyperthyroidism is a common endocrine disorder, affecting between 0.5% and 2% of the general population.<sup>1</sup> Atrial fibrillation is the most common cardiac

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complication of hyperthyroidism, occurring in an estimated 10% to 25% of overtly hyperthyroid patients. In comparison, 1.5% to 2% of the general population has atrial fibrillation.<sup>2-5</sup> Although hyperthyroidism may have cardiovascular consequences, the association between the natural history of hyperthyroidism and ischemic stroke remains unclear in patients with atrial fibrillation. The Congestive heart failure, Hypertension, Age  $\geq$ 75 years, Diabetes, previous Stroke, Vascular disease, Age 65-74 years, Sex category (female) stroke risk-prediction (CHA<sub>2</sub>DS<sub>2</sub>-VASc) score can be used to determine the optimal treatment strategy for stroke prevention. Hyperthyroidism is not among the thromboembolic risk factors included in the CHA2DS2-VASc score, and the use of anticoagulation to prevent thromboembolic complications of thyrotoxic atrial fibrillation is controversial.

Conflict of Interest: None.

Authorship: LF, HB, and ABB made the primary contribution to data collection. LF contributed to the study conception and design. LF and HB performed the analyses and produced the initial manuscript. All authors contributed to interpretation of results, revising the manuscript critically for important intellectual content, and all approved the final manuscript. All authors had access to the data. Sophie Rushton-Smith, PhD, provided editorial support on the final version of the manuscript and was funded by the authors.

Furthermore, national guideline recommendations for use of anticoagulation in this population are inconsistent.<sup>3-5</sup> Guidelines from the American College of Chest Physicians<sup>3</sup> conclude that thyrotoxicosis does not appear to be a valid risk factor in stroke, and recommend antithrombotic therapy regardless of whether hyperthyroidism is

**CLINICAL SIGNIFICANCE** 

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present. Conversely, the American College of Cardiology/ American Heart Association guidelines<sup>5</sup> state that anticoagulation is recommended in atrial fibrillation patients with hyperthyroidism, in the absence of a specific contraindication, at least until a euthyroid state has been restored. The aim of our study was to determine whether history of thyroid dysfunction, particularly hyperthyroidism, is a thromboembolic risk factor in patients with atrial fibrillation.

### MATERIALS AND METHODS

### **Study Population**

We included all patients with a diagnosis of atrial fibrillation or atrial flutter seen in our institution between January 2000 and December 2010. The patients' characteristics were obtained from computerized medical records held in our institution. Extensive information was collected, including dates of admission and discharge, clinical presentation, diagnosis, presence of comorbid conditions, medication use, and subsequent hospitalization. The patients' CHA<sub>2</sub>DS<sub>2</sub>-VASc score and Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65 years), Drugs/ alcohol concomitantly (HAS-BLED) score were calculated retrospectively.<sup>4</sup>

Patients with a thyroid disorder at the time of entry into the registry (ie, at baseline for a given patient when atrial fibrillation was diagnosed) were identified using the computerized codification system completed for each patient using the International Classification of Diseases, 10<sup>th</sup> Revision of the World Health Organization, with codes E00 to E07, and by screening clinical reports. On the basis of this information, the following were determined: history of hyperthyroidism or hypothyroidism, thyroid status at baseline (when atrial fibrillation was diagnosed), and amiodarone-induced thyroid dysfunction. Patients were divided into 3 groups: patients with no thyroid dysfunction, patients with a history of hyperthyroidism, and patients with a history of hypothyroidism. Hospitalization reports were screened to collect data on medication use at discharge from hospital.

Patients were followed-up to collect data on stroke/ systemic embolism, bleeding events, and all-cause death. Information was also obtained from the computerized database in our institution, which provides specialist services across 4 sites, and covers a catchment area of around 4000 km<sup>2</sup> with a population of approximately 400,000.<sup>6</sup> In addition, deaths were identified using an online search tool dedicated to local news, covering an area of 35,000 km<sup>2</sup>.<sup>7</sup>

The study was approved by the institutional review board of the Pole Coeur Thorax Vaisseaux from the Trousseau University Hospital on December 7, 2010 and registered as a clinical audit. Ethical review was therefore not required. Patient consent was not sought. The study was conducted retrospectively, patients were not involved in its conduct, and there was no impact on their care.

#### **Statistical Analysis**

The characteristics of the patients are given as counts and percentages or means  $\pm$  SDs. The chi-

squared test was used to compare categorical variables, and Student's t test or the nonparametric Kruskal-Wallis test, where appropriate, to compare continuous variables. Multivariable analysis with a proportional hazards model was used to investigate the association between thyroid dysfunction and outcomes. We also compared the rates of thromboembolic events in the 3 groups according to the Congestive heart failure, Hypertension, Age  $\geq$ 75, Diabetes, Stroke [Doubled] (CHADS<sub>2</sub>) score, with additional adjustment on anticoagulant use based on the assumption that vitamin K antagonist (VKA) medication reduces the risk of thromboembolic events by 64% in patients who received this therapy within each stratum of risk.<sup>3</sup> A P value < .05was considered to be statistically significant. Statistical analysis was carried out with Statview 5.0 software (Abacus Concepts, Berkeley, CA, USA).

#### RESULTS

A total of 8962 patients with atrial fibrillation were included in this study between 2000 and 2010: 8281 (92%) patients had normal thyroid function, 141 (2%) had a history of hyperthyroidism, and 540 (6%) had a history of hypothyroidism. Patient characteristics are presented in **Table 1**. Amiodarone-induced thyroid dysfunction was present in 42 (30%) patients with a history of hyperthyroidism and in 76 (14%) patients with a history of hypothyroidism. Thyroid-stimulating hormone values measured in the previous 6 months were available for 109 patients with a thyroid disorder; mean concentrations were significantly lower in patients with a history of hyperthyroidism than in those with hypothyroidism (1.0  $\pm$  3.1 vs 12.3  $\pm$  20.1 mIU/L, P = .0002). Download English Version:

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