

Does High-Normal Thyroid Function Increase Risk for Atrial Fibrillation?

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Selmer C, Olesen JB, Hansen ML, Lindhardsen J, Olsen AM, Madsen JC, Faber J, Hansen PR, Pedersen OD, Torp-Pedersen C, Gislason GH. The spectrum of thyroid disease and risk of new onset atrial fibrillation: a large population cohort study. BMJ. November 27, 2012 [Epub ahead of print].

Background

Patients with subclinical and overt hyperthyroidism are known to be at increased risk for the development of atrial fibrillation (1–5). However, the risk for incident atrial fibrillation had not previously been assessed in a very large population across the whole spectrum of thyroid function.

Methods

The study population consisted of 586,460 adult Danish primary care patients (mean age, 50.2 years; 61% women) who underwent thyroid-function testing in Copenhagen between 2000 and 2010. Patients were followed until the end of 2010 or until they moved from the study area or died. Individuals with prevalent atrial fibrillation or treated thyroid dysfunction at baseline were excluded, as were patients with a history of amiodarone, digoxin, or vitamin K use. Information about comorbidities and mortality was obtained from national Danish registries. The primary outcome was new-onset atrial fibrillation, ascertained by inpatient International Classification of Diseases, 10th Revision (ICD-10) codes. Time-dependent Poisson regression analyses were adjusted for age, sex, calendar year, an index of comorbidities, and socioeconomic status. The reference range for serum TSH was 0.2 to 5.0 mIU/L. Individuals with serum TSH <0.2 mIU/L and elevated FT₄ were considered to have overt hyperthyroidism and those with TSH <0.2 mIU/L and normal FT_4 were considered to have subclinical hyperthyroidism; conversely, individuals with serum TSH >5.0 mIU/L and low FT₄ were considered to have overt hypothyroidism and those with serum TSH >5.0 mIU/L and normal FT_4 were considered to have subclinical hypothyroidism. Sensitivity analyses were performed to account for changes in both thyroid function and thyroid treatment status over time, with adjustment for atrial fibrillation risk factors including baseline history of hypertension, heart failure, myocardial infarction, valvular hear disease, and diabetes.

Results

At baseline, 96% of patients were euthyroid, 0.3% had overt hyperthyroidism, 2% had subclinical hyperthyroidism, 2% had subclinical hypothyroidism, and 0.7% had overt hypothyroidism. Individuals were followed for a mean of 5.5 years, over which time 17,154 (2.9%) were diagnosed with new atrial fibrillation while hospitalized. As compared with euthyroid individuals, the risk for atrial fibrillation was increased in patients with overt hyperthyroidism (adjusted incidence rate ratio [IRR], 1.41; 95% CI, 1.22 to 1.63) and patients with subclinical hyperthyroidism (IRR, 1.30; 95% CI ,1.18 to 1.43) as well as in individuals with high-normal thyroid function (defined as serum TSH 0.2 to 0.4 mIU/L with normal FT₄; IRR, 1.12; 95% CI, 1.03 to 1.21). Risk for atrial fibrillation was found to be decreased in overt (IRR, 0.67; 95% CI, 0.50 to 0.92) and subclinical (IRR, 0.88; 95% CI, 0.79-0.97) hypothyroidism as compared with the euthyroid subjects. Sensitivity analyses did not substantially alter the results, although treatment of subclinical and overt hyperthyroidism was associated with a slight attenuation of atrial fibrillation risk.

Conclusions

This study demonstrates a linear inverse association between atrial fibrillation incidence and serum TSH. Even among euthyroid patients, lower serum TSH values were associated with a significantly increased risk for atrial fibrillation.

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ANALYSIS AND COMMENTARY • • • • • •

A major strength of this study is its very large sample size. Important limitations include the potential for misclassification of outcomes given the limitations of ICD-10 codes and the fact that only in-hospital atrial fibrillation diagnoses were ascertained. Findings in this largely white and sociodemographically homogeneous population may not be generalizable to other settings. Information was not available regarding potentially important covariates such as body-mass index, smoking status, thyroid antibody status, serum lipid levels, and echocardiographic parameters. Future observational studies with more information about covariates could better characterize risk factors for atrial fibrillation among individuals with low serum TSH, although it is unlikely that larger samples will be studied in the future. Overall, further research is needed to determine the effects of treatment of subclinical hyperthyroidism on the risk for atrial fibrillation.

References

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