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Subclinical Hyperthyroidism and Subclinical Hypothyroidism Increase the Incidence of Heart Failure in Older Persons

Nanchen D, Gussekloo J, Westendorp RG, Stott DJ, Jukema JW, Trompet S, Ford I, Welsh P, Sattar N, Macfarlane PW, Mooijaart SP, Rodondi N, de Craen AJ; on behalf of the PROSPER Group. Subclinical thyroid dysfunction and the risk of heart failure in older persons at high cardiovascular risk. J Clin Endocrinol Metab. January 11, 2012 [Epub ahead of print].

SUMMARY

Background

In many studies, subclinical thyroid dysfunction has been associated with cardiovascular disease (CVD), but there is still controversy about these associations. The purpose of this study was to examine the association between subclinical thyroid dysfunction and adjudicated cardiovascular events in a large prospective study of older people with cardiovascular risk factors or preexisting CVD.

Methods

The patient population consisted of 5316 patients who were part of the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial. Patients had measurements of serum TSH and FT_4 and were categorized into one of three groups: euthyroid, subclinical hyperthyroidism based on TSH levels <0.45 mU/L with normal FT_4, or subclinical hypothyroidism based on TSH levels >4.5 mU/L with normal FT_4. Cardiovascular outcomes were defined and judged by an expert committee.

Results

The mean (±SD) age of the population was 75±3.3 years and did not differ between the three groups. Subclinical hypothyroidism was present in 199 participants (3.7%) at baseline, and 34 of them were taking thyroid hormone. Subclinical hyperthyroidism was present in 71 participants (1.3%) and 5 of them were taking thyroid hormone. The incidence rate of hospitalization for heart failure was higher during a 3.2-year follow-up period in those with subclinical hyperthyroidism, as compared with the euthyroid group (P<0.01), with a sex- and age-adjusted hazard ratio (HR) of 2.93 (95% CI, 1.37 to 6.24), and worse in those with TSH levels <0.1 mU/L (age- and sex-adjusted HR, 4.61; 95% CI, 1.71 to 12.47). In the 38 patients with subclinical hypothyroidism with TSH levels above 10 mU/L, the incidence rate of heart failure was significantly higher in the age- and sex-adjusted model as compared with euthyroid participants (HR, 3.01; 95% CI, 1.12 to 8.11).

During the 3.2-year follow-up, 9.4% had atrial fibrillation, 11.0% had myocardial infarction, and 10.3% died. There were no differences in these conditions between the euthyroid and hypothyroid groups. In the group of patients with subclinical hyperthyroidism with TSH <0.1 mU/L who were not taking pravastatin, there was significantly higher cardiovascular mortality (HR, 4.61; 95% CI, 1.71 to 12.47).

Persistent subclinical hypothyroidism with TSH above 10 mIU/L remained associated with heart failure hospitalization as compared with euthyroidism with an age- and sex-adjusted HR of 4.99 (95% CI, 1.59 to 15.67).

Conclusions

In older patients with CVD who also have subclinical hyperthyroidism, especially those with TSH <0.1 mU/L, there is an increased incidence of heart failure. In those with subclinical hypothyroidism and TSH >10 mU/L, there is an increased incidence of heart failure and hospitalization for heart failure.

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ANALYSIS AND COMMENTARY

This carefully performed retrospective European study shows that subclinical hyperthyroidism increases the incidence of heart failure in older patients with a history of CVD. The data are most impressive for those with TSH <0.1 mU/L. The mechanisms by which subclinical hyperthyroidism might contribute to heart failure include increased heart rate, larger left ventricle size, impaired diastolic function, and atrial fibrillation.

The data concerning atrial fibrillation do not confirm the study of Sawin et al. in the Framingham population in 1994 that reported a nearly 3-fold increased risk of atrial fibrillation in those with TSH <0.1 mU/L (1), but there were only 71 patients in the European group with subclinical hyperthyroidism, of whom only 28 had TSH <0.1 mU/L. The increased incidence of atrial fibrillation in subclinical hyperthyroidism was also found in another study of a large geriatric population (2). It is noteworthy that serum T_3 was not measured in the current study, so the diagnosis of T_3 thyrotoxicosis could not be assessed.

The increased incidence of heart failure in the patients with subclinical hypothyroidism is significant only for those with TSH >10 mU/L, as shown previously in the study by Rodondi et al (3). Because TSH is a modifiable risk factor, the authors recommend that elderly patients with subclinical hyperthyroidism who have TSH <0.1 mU/L and those with subclinical hypothyroidism who have TSH >10 mU/L be treated appropriately to avoid the cardiovascular consequences of these disorders.

— Jerome M. Hershman, MD

References

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