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Coronary Heart Disease May Not Be Increased in Older Patients with Subclinical Hypothyroidism

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Hyland KA, Arnold AM, Lee JS, Cappola AR. Persistent subclinical hypothyroidism and cardiovascular risk in the elderly: the Cardiovascular Health Study. J Clin Endocrinol Metab. November 16, 2012 [Epub ahead of print]. doi:10.1210/jc.2012-2180.

SUMMARY

Background

The effect of subclinical hypothyroidism (SCH) on cardiovascular risk has been controversial. The topic is of interest because many elderly patients have this diagnosis, especially when there is no adjustment for the upper limit of serum TSH based on age; however, if an age adjustment is applied to people over age 70, the number of individuals in this category diminishes substantially (1).

Methods

This is a study of cardiovascular risk in the Cardiovascular Health Study (CHS). TSH was measured on most of the baseline samples from the original cohort of 5888 people who were over age 65 in 1989, and tests were repeated in 1992, 1994, and 1996. Patients were followed for cardiovascular disease, including coronary heart disease (CHD), heart failure and death. Euthyroidism was defined as a TSH concentration of 0.45 to 4.50 mU/L, and subclinical hypothyroidism was defined as a TSH concentration >4.50 mU/L and <20 mU/L with a normal FT_4 concentration based on the first set of tests. Patients with cardiac disease at the initial examination were excluded.

Of the 4863 participants included in the analyses, 926 had only one set of thyroid tests, 980 had two, and 1513 had three; 1444 had measurements at all four time points. Follow-up was censored at 10 years beyond the first baseline measurements.

Results

Based on the first set of thyroid tests, 4184 subjects were euthyroid and 679 had SCH. In the euthyroid group, the mean age was 73.4 years and 45% were men; in the SCH group, the mean age was 74.1 years and 38% were men. Both differences were significant. The mean TSH was 2.1 mU/L in the euthyroid group and 6.7 mU/L in the SCH group. There were no differences between the two groups in the body-mass index, LDL cholesterol, serum creatinine, or the proportion of patients with hypertension or diabetes. The incidence of CHD was about 20% and that of heart failure about 5% in both groups. During the 10-year follow-up period, 225 (33.1%) of the participants in the SCH group and 174 (4.2%) in the euthyroid group initiated thyroid hormone medication.

No association was seen between SCH and incident CHD, heart failure, or cardiovascular mortality in multivariate models with 10 years of follow-up. Additional analyses stratified by degree of TSH elevation (4.5 to 6.9, 7.0 to 9.9, and 10.0 to 19.9 mU/L) showed no increase in risk of any of these cardiovascular events by subgroup of SCH. The number of individuals in each of the three SCH TSH categories was 483, 131, and 65, respectively. When thyroid status was updated based on subsequent TSH measurements, there was again no difference in cardiovascular outcomes between the two groups.

Conclusions

The data do not support an increased risk of CHD, heart failure, or cardiovascular death in older adults with persistent subclinical hypothyroidism.

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ANALYSIS AND COMMENTARY

Although the study is "prospective" in obtaining data on thyroid function, it is observational in that the patients were likely to have been treated by their treating physicians. It is pertinent that one third of those initially classified as having SCH were treated with thyroid hormone. This could have altered cardiovascular outcomes and calls into question the applicability of these data for treatment of older patients with SCH. Did updating the thyroid status place the patients with treated SCH into the euthyroid group? The fact that many of the euthyroid patients were treated with thyroid hormone suggests that a relatively abrupt onset of hypothyroidism was promptly treated by the managing physicians.

In a previous analysis of 3044 patients in this study, the participants with TSH >10 mU/L had a greater incidence of heart failure as compared with euthyroid participants (41.7 vs. 22.9 per 1000 person years; P = 0.01; adjusted hazard ratio, 1.88; 95% CI, 1.05 to 3.34) based on a 12-year follow-up (2). The current paper reports no increase in heart failure in SCH, including the subcategory with TSH >10 mU/L, and reconciles this difference as being due to having a larger number of CHS participants; this resulted in the difference in heart failure no longer being statistically significant. However, their Figure 2B shows an impressive increase in heart failure in those with TSH>10 mU/L after 6 years of follow-up. Their Figure 3A shows an increase in the incidence of cardiovascular deaths in the entire SCH group as compared with the euthyroid group after 6 years of follow-up.

These studies are very difficult to perform and easy to criticize. That said, the current study does not negate the necessity of performing a randomized, controlled study of treatment of SCH in elderly individuals, with the diagnosis based on age-adjusted TSH levels, in order to determine whether therapy with thyroid hormone improves cardiovascular status and many other indicators of health and well-being.

References

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