Subclinical Hypothyroidism May Spontaneously Revert to Euthyroidism in Elderly Patients Negative for TPO Antibodies

Somwaru LL, Rariy CM, Arnold AM, Cappola AR. The natural history of subclinical hypothyroidism in the elderly: the cardiovascular health study. J Clin Endocrinol Metab 2012;97:1962-9. Epub March 21, 2012.

SUMMARY • • • • • • • • • • • •

Background

Subclinical hypothyroidism (SH) is common in the elderly and there is controversy about the efficacy of therapy for this condition, although a number of studies have shown that SH is associated with cardiovascular risk factors that are improved by therapy with levothyroxine (1). The criteria for subclinical hypothyroidism have varied to some extent based on what the upper limit of normal is for serum TSH in the elderly (2), as reviewed in last month's issue of Clinical Thyroidology (3). Several reports have shown that the serum TSH may return to normal without therapy in a significant proportion of patients with SH. The authors of the current paper have used data from a large study of community-dwelling individuals 65 years of age or over to demonstrate the natural history of SH over a 4-year period, including the rates of persistence, resolution, and progression of subclinical thyroid dysfunction at 2 and 4 years.

Methods

Subjects were community-living people over age 65 in 4 U.S. areas who were in the Cardiovascular Health Study.

Subclinical hypothyroidism was defined as a TSH of 4.5 to 19.9 mU/L, with a normal free T_4 concentration.

Results

At baseline, 3996 individuals had thyroid-function tests; 402 were excluded because they were taking thyroid medication. Of the remaining 3594 subjects, 459 (12.8%) had SH (median TSH, 6.7 mU/L) and 22 (0.6%) had overt hypothyroidism. At baseline, 69% of the SH had a TSH between 4.5 and 6.9 mU/L, 20%

had a TSH between 7.0 and 10 mU/L, and 11% had a TSH >10 mU/L.

Mortality was similar in those who were euthyroid and those who had subclinical hypothyroidism at baseline at either 2 years (5.3 vs. 5.9%) or 4 years (12.9 vs. 12.6%) of follow-up.

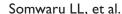
After 2 years, the incidence of SH in those who were euthyroid was 2.7%. In the SH group, 369 of 459 were available for evaluation: 56% (208) continued to have SH, 35% (128) reverted to euthyroidism, 2% (8) became overtly hypothyroid, and 7% (25) were treated with thyroid hormone. Of those with baseline TSH levels of 4.5 to 6.9 mU/L, 46% became euthyroid at 2 years, in contrast with only 7% of those who had TSH levels >10 mU/L. Progression to overt hypothyroidism occurred in 10% of those with TSH levels >10 mU/L. There was no difference in progression based on age (65–75 vs. >75 years) or sex. Thirty-five percent of those with SH had positive TPO antibody, and these subjects were less likely to revert to euthyroidism (15% vs. 48% if TPO-negative).

Of the SH group who had thyroid tests at year 4, 58% (62 of 107) of those who were euthyroid at year 2 remained euthyroid at year 4, 38% (41 of 107) of those who were euthyroid at year 2 returned to SH at year 4, and 76% (122 of 161) of those with persistent SH at year 2 continued to have SH at year 4.

Conclusions

Subclinical hypothyroidism persists for 4 years in just over half of older individuals, with high rates of reversion to euthyroidism in individuals with lower TSH concentrations and negative TPO antibody.

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ANALYSIS AND COMMENTARY • • • •

This is the largest study of an elderly cohort that examined the natural history of subclinical hypothyroidism. The conclusions are likely to be valid even though for about 10% of the SH group sera was not available for testing at 2 years. The results are similar to the Spanish study of 107 patients over 55 years of age who had SH (4) that reported 37% of patients reverted to a euthyroid state during a follow-up of 6 months to 6 years; they also found that progression to overt hypothyroidism was related to the height of the baseline serum TSH.

In regard to therapy for SH, these data provide some reassurance that the current clinical practice of treating those with TSH levels >10 mU/L and positive anti-TPO is reasonable because these

patients are much more likely to progress to overt hypothyroidism.

Would the results be different if the upper limit of serum TSH was age-adjusted? If the upper TSH limit was in the range of 5 to 6 mU/L, then the population of those with SH would be smaller, especially the group with TSH levels of 4.5 to 6.9 mU/L who had the highest reversion to normal. Regardless of the cutoff for classification, those with mild elevations of serum TSH need to be retested before they are consigned to long-term therapy with levothyroxine. Another study by the Spanish group showed that a large majority of the normalization of the serum TSH occurred within the first 2 years of follow-up (5), a finding that is consistent with the current study.

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