Clinical THYROIDOLOGY



Subclinical Hyperthyroidism Is Associated with Increased Coronary Heart Disease Mortality and Atrial Fibrillation

Collet TH, Gussekloo J, Bauer DC, den Elzen WP, Cappola AR, Balmer P, Iervasi G, Åsvold BO, Sgarbi JA, Völzke H, Gencer B, Maciel RM, Molinaro S, Bremner A, Luben RN, Maisonneuve P, Cornuz J, Newman AB, Khaw KT, Westendorp RG, Franklyn JA, Vittinghoff E, Walsh JP, Rodondi N; Thyroid Studies Collaboration. Subclinical hyperthyroidism and the risk of coronary heart disease and mortality. Arch Intern Med 2012;172:799-809.

Background

Subclinical hyperthyroidism has been associated with atrial fibrillation (AF), but studies of its associations with adverse cardiovascular outcomes have been conflicting. The current study is a large, carefully performed analysis of prospective cohort studies of subclinical hyperthyroidism (SHyper) to determine its association with coronary heart disease (CHD), CHD mortality, and atrial fibrillation.

Methods

A systematic literature search was conducted of prospective original studies of endogenous SHyper published up to June 2011. SHyper was defined as TSH <0.45 in a sensitive assay with normal FT₄ and no elevation of T₃ or FT₃. Studies had to include data on incident CHD, related demographic factors, and mortality. Primary analyses were adjusted for age and sex and then further adjusted for traditional cardiovascular risk factors: systolic blood pressure, current or former smoking, total cholesterol, and diabetes.

Results

The study included 10 prospective cohorts totaling

52,674 participants with a median age of 59 years, 58.5% of whom were women. There was a median follow-up of 8.8 years. There were 2188 (4.2%) with suppressed TSH; 1884 (3.6%) had TSH of 0.10 to 0.44 mU/L and 304 (0.6%) had TSH <0.10 mU/L. During follow-up, based on age- and sex-adjusted analyses, the overall hazard ratio (HR) for mortality for subclinical hyperthyroidism as compared with euthyroid participants was 1.24 (95% CI, 1.06 to 1.46). The HR was 1.29 (95% CI, 1.02 to 1.62) for CHD mortality; 1.21 (95% CI, 0.99 to 1.46) for CHD events, and 1.68 (95% CI, 1.16 to 2.43) for incident AF. The HR for CHD mortality was 1.84 (95% CI, 1.12 to 3.00) and for incident AF 2.54 (95% CI, 1.08 to 5.99), which were significantly higher for TSH levels <0.10 mIU/L than those for TSH 0.10 to 0.44 mU/L, but other outcomes did not differ.

Conclusions

Pooled data from prospective cohorts indicates that endogenous subclinical hyperthyroidism is associated with an increased risk of total mortality, CHD mortality, and incident AF, with higher risks of CHD mortality and AF with TSH levels below 0.10 mIU/L.

ANALYSIS AND COMMENTARY • • • • •

This is the strongest study to date showing that subclinical hyperthyroidism increases mortality, including CHD mortality, in addition to atrial fibrillation. The data confirm the retrospective results of Sawin et al. with regard to atrial fibrillation (1) and the results of Vadiveloo et al. with regard to cardiovascular disease (2), with a TSH level of <0.10 mU/L being more hazardous. The data are at variance with the Cardiovascular Health Study, which reported that SHyper is not associated with other cardiovascular disorders or mortality (3). The reason for this *continued on next page*

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is that the current study of over 50,000 participants had more power to show small effects than the study of 2569 subjects in the Cardiovascular Health Study (which was included in the current analysis).

The authors are careful to point out the limitations of the study. One report that was included from Germany had a 24% incidence of SHyper that was attributed to iodine supplementation introduced 4 years earlier, but the results were qualitatively similar when the German report was excluded from the analysis. Another limitation is that the subjects were predominantly white. Although subjects taking thyroid preparations were excluded, not all the studies had data on other medications, such as amiodarone, that could

alter thyroid function. Another limitation is that there were only 304 individuals in the group with TSH <0.10 mIU/L, with only 15 deaths in this group.

Although there is still a lack of a randomized controlled study of treatment of SHyper to show that mortality, CHD, and AF can be prevented or reduced, the current study is further ammunition to treat patients with SHyper, especially when the TSH is <0. 10 mU/L. In an accompanying invited commentary, Ken Burman reviewed the approach to treatment of these patients (4).

– Jerome M. Hershman, MD

References

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