OBSERVATIONS

Subclinical Hypothyroidism Is Associated With Reduced All-Cause Mortality in Patients With Type 2 Diabetes

Subclinical hypothyroidism has been associated with a greater prevalence of cardiovascular disease (1) and is relatively common in patients with type 2 diabetes (2). If subclinical hypothyroidism contributed to an increase in cardiovascular risk, then, intuitively, its effect would be exaggerated in patients with type 2 diabetes.

Patients were identified from a diabetes database at Hull Royal Infirmary from 1993–2005 for retrospective analysis. From the database, 6,540 consecutive patients enrolled through the end of 2000 were selected, and 472 patients with type 2 diabetes who had a raised thyrotropin-stimulating hormone (TSH) (on two occasions 6 months apart) and normal free T4 (fT4) were identified (subsequent case-note review reduced this number to 394 patients). They were compared with 472 consecutive age-matched type 2 diabetic patients with TSH 0.5–3.0 mU/l. Sample size was powered to detect a difference between case subjects and control subjects of 90% (1). TSH assays were performed on AxSYM ultrasensitive hTSHII Assay (normal 0.49–4.67 mIU/l), and fT4 assays were performed on AxSYM FT4 Assay (normal 9–24 pmol/l; Abbott Diagnostics Division, U.K.). There was no change in assay during the study period.

The relationship between subclinical hypothyroidism and cardiovascular mortality was assessed by logistic regression. The case and control subjects were matched by age (1:1 pair-wise matching). Matching was broken and analyzed as independent sets by unconditional logistic regression because this method is preferable when the groups are very different to except for the matching variable (3). Data are presented as means ± SEM.

Mean age of patients with subclinical hypothyroidism was 73.1 ± 0.6 versus 71.1 ± 0.8 years in patients without subclinical hypothyroidism. There were more female subjects in patients with subclinical hypothyroidism (83.7%) than in the other group (18%). BMI, blood pressure, lipid profile, A1C (8.2 ± 0.1 vs. 8.1 ± 0.1%), and background cardiovascular disease were comparable. The mean TSH level in patients with subclinical hypothyroidism was 8.1 ± 0.01 versus 1.1 ± 0.02 mmol/l, whereas mean fT4 in patients with subclinical hypothyroidism was 12.2 ± 0.2 versus 14.3 ± 0.3 pmol/l in patients without subclinical hypothyroidism. The mean duration from the diagnosis of subclinical hypothyroidism was 7.9 years.

There were 222 new cardiovascular events in patients with subclinical hypothyroidism versus 246 events in patients without subclinical hypothyroidism. There were 96 (24.4%) all-cause mortalities in patients with subclinical hypothyroidism versus 155 (32.8%) in patients without subclinical hypothyroidism. There were 47 (11.9%) noncardiovascular mortalities in patients with subclinical hypothyroidism (respiratory, 30; neoplasm, 12; other, 5) versus 103 (21.8%) in the other group (respiratory, 79; neoplasm, 18; other, 6).

There was no relationship between baseline TSH and cardiovascular mortality. The unadjusted odds ratio (OR) for cardiovascular mortality was 1.17 (95% CI [0.89–1.53]; $P = 0.25$). Adjusting for age, sex, or the other covariates did not alter the nature of this relationship. The unadjusted OR for all-cause mortality was 0.40 (0.30–0.56; $P < 0.01$) and, after adjusting for covariates, 0.41 (0.12–0.98; $P < 0.01$).

Patients with subclinical hypothyroidism and type 2 diabetes did not have an increased cardiovascular mortality than patients with type 2 diabetes without subclinical hypothyroidism. Unexpectedly, there was a significant reduction in all-cause mortality in patients with subclinical hypothyroidism and diabetes. These data are in accord with studies showing that elderly individuals with higher levels of TSH were found to have a prolonged life (4,5). In conclusion, subclinical hypothyroidism may have a protective effect on noncardiovascular mortality in type 2 diabetes; however, it is not additive to relative higher cardiovascular risk in type 2 diabetic patients ≥5 years after its diagnosis.

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DOI: 10.2337/dc09-1555

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

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