



THYROID FUNCTION

Cause of increased mortality differs for Graves disease and toxic nodular goiter

Graves disease and toxic nodular goiter are both associated with increased mortality, report Danish researchers. However, the cause of death differs; mortality owing to cardiovascular disease is increased in Graves disease, whereas cancer-related mortality is increased in toxic nodular goiter.

“Both causes of hyperthyroidism were associated with increased all-cause mortality”

Hyperthyroidism has been found to be associated with increased mortality in a number of studies. However, few studies have been conducted to analyse the association between hyperthyroidism and disease-specific mortality. Some studies have reported increased mortality from cardiovascular disease in patients with hyperthyroidism, even in individuals with subclinical hyperthyroidism. Nevertheless, the influence of the underlying cause of hyperthyroidism—either Graves disease or toxic nodular goiter—on overall mortality or disease-specific mortality is not known. The few studies conducted on

this topic have had conflicting findings, as mortality was either found not to be increased in Graves disease or toxic nodular goiter, or to be increased in toxic nodular goiter but not Graves disease.

The study included hospital-treated, adult patients with Graves disease ($n = 1,291$) or toxic nodular goiter ($n = 861$) identified from record-linkage data from nationwide health registers. Participants were followed up until death or 31 December 2008; mean length of follow up was 11 years. Each patient was matched for age and sex with four control individuals without hyperthyroidism. In the cohort, patients with Graves disease were younger and had been diagnosed at a younger age than those with toxic nodular goiter.

Both causes of hyperthyroidism were associated with increased all-cause mortality. The hazard ratios for mortality for Graves disease and toxic nodular goiter were 1.42 (95% CI 1.25–1.60) and 1.22 (95% CI 1.07–1.40), respectively, after adjustment for age, sex, and comorbidities before the diagnosis of hyperthyroidism. However, causes of increased mortality for Graves disease and toxic nodular goiter differed. Mortality from cardiovascular disease (HR 1.49,

95% CI 1.25–1.77) and lung disease (HR 1.91, 95% CI 1.37–2.65) was increased in Graves disease, after adjustment for comorbidities before the diagnosis of hyperthyroidism. By contrast, mortality from cardiovascular disease was not increased in patients with toxic nodular goiter, but mortality from cancer (HR 1.36, 95% CI 1.06–1.75) was increased in patients with this disease.

Brandt *et al.* suggest that previous reports of mortality in patients with Graves disease or toxic nodular goiter could have been limited by including only radioiodine-treated patients. However, the researchers concede that the pathophysiological mechanisms underlying the different causes of increased mortality in Graves diseases and toxic nodular goiter require further investigation.

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Original article Brandt, F. *et al.* Graves disease and toxic nodular goiter are both associated with increased mortality but differ with respect to the cause of death. A Danish population-based register study. *Thyroid* doi:10.1089/thy.2012.0500