OVERT HYPERTHYROIDISM CAUSES 20% INCREASED RISK OF MORTALITY

Brandt F, Green A, Hegedüs L, Brix T. Is the association between overt hyperthyroidism and mortality causal? Critical review and meta-analysis. Eur J Endocrinol. July 1, 2011 [Epub ahead of print]. doi: 10.1530/EJE-11-0299.

SUMMARY • • • •

BACKGROUND

Overt hyperthyroidism is associated with cardiac arrhythmias, hypercoagulopathy, stroke and pulmonary embolism, which all may increase mortality. Most but not all studies demonstrate an increased mortality in patients with overt hyperthyroidism. This critical review and statistical meta-analysis was conducted to determine whether overt hyperthyroidism is associated with an increased risk of death.

METHODS AND RESULTS

Case–control and cohort studies written in English were selected based on a PubMed search using the terms: hyperthyroidism, thyrotoxicosis, and mortality or survival. Eight studies fulfilled the inclusion criteria (number of subjects >10, inclusion of control group, overall mortality data, thyrotropin and peripheral hormone levels), and six of these studies showed an increased all-cause mortality. One study could not be used in the meta-analysis because it contained only risk estimates and not the number of deaths. Seven studies, with a total of 31,138 patients and 400,000 person-years at risk, were analyzed and subjected to meta-analysis. The relative risk (RR) of overall mortality was 1.21 (95% confidence interval [CI].1.05 to 1.38). After adjusting for setting, treatment, and

control for comorbidities, the increased risk of mortality persisted. An increased, but not statistically significant, mortality was found when pooling all studies treating with radioiodine. Four of six studies examining cardiovascular risk found increased mortality with hyperthyroidism. Pooling the six studies showed that there was a higher mortality in patients with hyperthyroidism than in control subjects (RR, 1.19; 95% CI, 1.00 to 1.29).

CONCLUSIONS

Clinically, it is well known that overt hyperthyroidism is associated with significant complications, including structural changes in the heart, dehydration, tachycardia, atrial arrhythmia, muscle weakness, and osteoporosis. But the data proving that hyperthyroidism increases mortality have not been conclusive. The variation in reported mortality risks has been attributed to differences in study design, characteristics of the patients, differences in treatments, or the influence of confounding factors (1). This meta-analysis demonstrates that overt hyperthyroidism is associated with an approximate 20% increased risk of mortality. Future studies including genetic susceptibility will need to address whether the cause of this increased mortality is from the hyperthyroidism or other factors, such as smoking or comorbidities.

COMMENTARY • • • • •

This meta-analysis shows a 20% increased risk of mortality with overt hyperthyroidism. This is a strong statistical association despite the heterogeneity of the subjects, their treatments, and the different methods of the included studies. Several questions remain unanswered. Is mortality is associated with severity or length of time that hyperthyroidism has

been present? Is mortality higher in the different forms of hyperthyroidism when the level of thyroid excess is taken into account? Does treatment such as radioactive iodine increase risk of mortality, as has been reported by Franklyn et al.(2)? Finally, does the risk regress to the level of the control population after the hyperthyroidism is treated? There are still many questions to be answered before we know how this continued on next page

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study applies to our patients. It makes sense to try to reduce the very high levels of thyroid hormone to the reference range as quickly as possible by one of the usual treatments—antithyroid drugs, radioiodine, or thyroidectomy. The current reason to bring the high thyroid levels to normal may not be to reduce mortality but because our patients feel better and

because important morbidities of hyperthyroidism such as tachycardia, atrial arrhythmias, tremor, and accelerated bone loss are reduced by lowering the thyroid hormone levels.

- Stephanie L. Lee, MD, PhD

References

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