Subclinical thyroid disorders – Consequences and implications for treatment

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Abstract

Subclinical hyperthyroidism is characterized by low circulating TSH concentrations, together with normal concentrations of free T4 and free T3. The clinical significance of low but detectable TSH values is likely to be different from undetectable TSH values. The question remains as to whether endogenous and exogenous (iatrogenic) causes of low serum TSH have the same clinical significance. Subclinical hypothyroidism is characterized by high serum TSH concentrations, together with normal free T4 values.

Keywords: Subclinical hyperthyroidism; Subclinical hypothyroidism; Atrial fibrillation; Osteoporosis

1. Subclinical hyperthyroidism

Subclinical hyperthyroidism is a common condition which may reflect Graves’ disease or toxic nodular hyperthyroidism, and is found in up to 5% of individuals over 60 years of age in the general population. In addition, about 20% of patients who are taking T4 therapy have low serum TSH concentrations, providing biochemical evidence for over-treatment. In those not prescribed T4 it is important to exclude other causes of low serum TSH, especially non-thyroidal illness and drug therapies.

The potential risks of subclinical hyperthyroidism are the development of cardiovascular diseases and osteoporosis.

Cardiovascular diseases: effects on cardiac function are well documented, including an increased risk of atrial fibrillation (evidence from two US populations), as well as increased vascular mortality (evidence from Birmingham, UK population).

Osteoporosis: bone mineral density may be reduced, especially in post menopausal women, and there is emerging evidence of an effect on fracture risk. There are no studies of intervention determining effects on clinical endpoints, apart from evidence of improvement in bone mineral density.

2. Subclinical hypothyroidism

Subclinical hypothyroidism is also a common condition, which affects more than 10% of individuals over 60 years of age. The prevalence rises with age. It is also found in about 25% of patients taking T4 therapy, providing evidence for under-treatment.

Possible risks include hyperlipidaemia (resulting in vascular risk), alterations of cognitive function, and decreased well being.

Subclinical hypothyroidism does progress to overt hypothyroidism (with a variable rate of progression). A weak association has been described with increased total and LDL cholesterol values. There is conflicting evidence concerning a possible association with increased vascular morbidity/mortality, but there is increasing evidence that subclinical hypothyroidism is associated with ischemic heart disease risk. Little if any association has been found with changes in cognitive function or neuropsychiatric symptoms.

Studies of intervention only show minor effect on lipids. There is insufficient evidence for an effect of treatment on symptoms and on clinical endpoints. Treatment is therefore initiated principally to prevent progression to overt symptoms and signs.
3. Conclusions: whether to treat subclinical thyroid dysfunction?

The main indication for treatment of *subclinical hyperthyroidism* is the cardiovascular risk (although there is no proven evidence for benefit from intervention trials). A recent consensus panel has suggested consideration of treatment in the elderly, and in those with subclinical hyperthyroidism secondary to Graves’ disease or toxic nodular goitre, especially in those with atrial fibrillation or other vascular disease.

The main indication for treatment of *subclinical hypothyroidism* is the risk of progression to overt disease. There is little evidence to support treatment on basis of symptoms or other long-term risks. A recent consensus panel has suggested consideration of treatment in those with more severe disease, i.e. serum TSH > 10 mU/L, but not in those with more equivocal biochemistry. Subclinical hypothyroidism may, however, be of relevance in pregnancy and probably warrants treatment in that situation.

**Further reading**


Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Evidence-based consensus guidelines for the diagnosis and management of subclinical thyroid disease. JAMA 2004;291:228–38.
