Med Princ Pract 2015;24:99–100
DOI: 10.1159/000365743

Subclinical Hypothyroidism: To Treat or Not to Treat?

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Dear Editor

Subclinical hypothyroidism refers to subjects who have elevated serum thyroid-stimulating hormone levels and whose serum thyroid hormone levels are within the normal reference range. The prevalence of subclinical hypothyroidism in the US population was about 4.3% in NHANES III, and the overall prevalence has been reported to range from 4 to 20% in the general adult population [1, 2]. It is reportedly higher in women aged more than 60 years [3, 4]. Screening and treatment of subclinical hypothyroidism should thus clearly be a public health priority.

Over the past several decades, based on a strong body of evidence, it has been postulated that subclinical hypothyroidism is associated with cardiovascular risk factors (such as cholesterol levels, systolic blood pressure, and atherosclerosis) [5–7]. Since the late 1980s, subclinical hypothyroidism has been the major focus of numerous clinical and autopsy studies on cardiovascular disease, particularly coronary heart disease (CHD) [8, 9]. Although data on the relationship between subclinical hypothyroidism and CHD events or mortality were supported in systematic reviews and quantified in meta-analyses of prospective studies [10–13], not all studies have shown that subclinical hypothyroidism affects risk factors for CHD and cardiovascular and all-cause mortality.

In 2006, Rodondi et al. [10] reported that subclinical hypothyroidism was associated with an increased risk of CHD. This finding was consistent with another previous meta-analysis of Singh et al. [12]. In addition, Singh et al. [12] suggested that mortality from cardiovascular causes, rather than all-cause mortality, was significantly higher at follow-up. However, a meta-analysis including 10 cohort studies from Ochs et al. [13] found that subclinical hypothyroidism may be associated with a modest increased risk for CHD and mortality. Additionally, Völzke et al. [11] suggested that the currently available evidence for a causal relation of hypothyroidism with mortality was weak and should particularly not be used to decide whether patients with subclinical hypothyroidism should be treated.

Recently, in the 16th European Congress of Endocrinology, Andersen et al. [14] reported that levothyroxine is not associated with lower all-cause mortality in patients with subclinical hypothyroidism. Controversy persists about whether screening for and treatment of subclinical hypothyroidism are warranted because the current evidence regarding incidence and mortality is inconsistent, and it is imperative to explore the subsequent concerns. First of all, it is necessary to further summarize higher-quality prospective evidence about the relationship between subclinical hypothyroidism and CHD and cardiovascular or all-cause mortality; it plays a key role in the prevention of CHD incidence and mortality. Secondly, treatment of adults with subclinical hypothyroidism with regard to CHD or mortality should be studied in randomized, placebo-controlled trials to assess the benefits of antithyroid medications. Thirdly, taking into account the untreated individuals, there is a trend toward an increased incidence and mortality; preferably randomized controlled studies on the treatment of subclinical hypothyroidism should have a longer follow-up time.

In summary, regarding whether or not patients with subclinical hypothyroidism require intervention, the following recommendations should be considered: (a) large prospective studies or more comprehensive estimates are necessary to clarify the risk of CHD or mortality in patients with subclinical hypothyroidism, (b) long-term randomized controlled studies are needed to assess the importance of treating patients with subclinical hypothyroidism, and (c) prospective studies could explore whether or not the treatment of subclinical hypothyroidism could improve its adverse health outcomes.

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