

Chronic Renal Disease is a Clinical indication for Thyroid Replacement Therapy in Subclinical Hypothyroidism

Shin DH, Lee MJ, Kim SJ, Oh HJ, Kim HR, Han JH, Koo HM, Doh FM, Park JT, Han SH, Yoo T-H, Kang S-W. Preservation of renal function by thyroid hormone replacement therapy in chronic kidney disease patients with subclinical hypothyroidism. *J Clin Endocrinol Metab.* June 20, 2012 [Epub ahead of print].

SUMMARY ●●●●●●●●●●●●●●●●

Background

Subclinical hypothyroidism is not a rare condition, but the use of thyroid hormones to treat subclinical hypothyroidism is an issue of debate. This study was undertaken to investigate the impact of thyroid hormone therapy on the changes in estimated glomerular filtration rate (eGFR) in patients with subclinical hypothyroidism who also have stage 2 to 4 chronic kidney disease.

Methods

A total of 309 patients were included in the final analysis. The changes in eGFR over time were compared between patients with and without thyroid hormone-replacement therapy using a linear mixed model. Kaplan–Meier curves were constructed to determine the effect of thyroid hormone on renal outcome, a reduction of eGFR by 50%, or end-stage renal disease. The independent prognostic value of subclinical hypothyroidism treatment for renal outcome was ascertained by multivariate Cox regression analysis.

Results

Among the 309 patients, 180 (58.3%) took thyroid

hormone (treatment group), whereas 129 (41.7%) did not (nontreatment group). During the mean follow-up of 34.8 ± 24.3 months, the overall rate of decline in eGFR was significantly greater in the nontreatment group as compared with the treatment group (−5.93±1.65 vs. −2.11±1.12 ml/min/yr/1.73 m²; P = 0.04). Moreover, a linear mixed model revealed that there was a significant difference in the rates of eGFR decline over time between the two groups (P < 0.01). Kaplan–Meier analysis also showed that renal event-free survival was significantly lower in the nontreatment group (P < 0.01). In multivariate Cox regression analysis, thyroid hormone-replacement therapy was found to be an independent predictor of renal outcome (hazard ratio, 0.28; 95% CI, 0.12 to 0.68; P = 0.01).

Conclusions

Thyroid hormone-replacement therapy not only preserved renal function better, but it was also an independent predictor of renal outcome in patients with chronic kidney disease who had subclinical hypothyroidism, suggesting that thyroid hormone replacement should be considered in these patients.

ANALYSIS AND COMMENTARY ●●●●●

With the exception of women planning a pregnancy or who are pregnant, the use of thyroid hormone-replacement therapy in subclinical hypothyroidism is controversial, unless the serum TSH value is over 10 mIU/L (1,2). Thyroid hypofunction in patients with

renal disease is not uncommon; in the third National Health and Nutrition Examination Survey (NHANES III) (3), the prevalence of hypothyroidism was reported as 10.9 to 23.1% in patients with stage 2 to 5 chronic kidney disease (CKD), 56% of these cases were considered subclinical. In another report, the prevalence of subclinical hypothyroidism was 17.9%

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in patients with stage 3 to 5 CKD, independent of age, sex, and fasting plasma glucose, total cholesterol, and triglyceride concentrations (4). It has been postulated that the beneficial effect of thyroid hormone replacement on cardiac dysfunction, dyslipidemia, and blood pressure could be explained by preservation of renal function in treated hypothyroidism (5,6). For this study, Shin et al. excluded patients <18 or >75 years of age; those with nephrotic syndrome, terminal malignancy, or pregnancy; those undergoing thyroid replacement therapy, and those followed for less than 12 months. To exclude the possibility of transient elevation of serum TSH concentration, measurement of serum TSH level was repeated within 3 months before starting thyroid hormone-replacement therapy in order to confirm the diagnosis. The initial dose was usually 25 µg/day, adjusted as needed. Because it was a retrospective medical record-based

study, the authors recognize that the possibility of selection bias could not be completely ruled out, such as selecting those patients with higher cardiovascular risk factors or positive TPOAb for thyroid therapy.

This preliminary study needs to be confirmed, but in the meantime it appears very reasonable to normalize thyroid-function tests in patients with subclinical hypothyroidism who have any degree of renal insufficiency, starting with a low levothyroxine dose and adjusting it at regular intervals to avoid levothyroxine toxicity. If further studies support the conclusions of Shin et al., renal insufficiency should be added to the selective group of women who have subclinical hypothyroidism in their reproductive years that could benefit from thyroid replacement therapy (7).

— Jorge H. Mestman, MD

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