The Biochemical Prognostic Factors of Subclinical Hypothyroidism (*Endocrinol Metab* 2014;29:154-62, Myung Won Lee et al.)

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We sincerely thank the editors and reviewers for giving us the opportunity to publish this article. Our response to Professors Ahn and Chung's letter are included below.

Previous studies of subclinical hypothyroidism (SHT) mainly focused on the aggravation of SHT to overt hypothyroidism [1,2]. However, the clinical significance of long-term, persistent SHT and clinically reliable prognostic factors for predicting the disease course of SHT, including aggravation, maintenance, and improvement, have not been established. Given our present clinical environment, in which increasing numbers of patients with SHT are consistently increasing, as well as our corresponding need to manage them as clinicians, we aimed to identify factors that influence the natural course of SHT. In line with this purpose, our study primarily focused on initial clues and evidence that enable us to predict whether newly-diagnosed SHT will improve spontaneously to a euthyroid state.

In this retrospective study, we compared two groups according to thyroid function at follow-up: an SHT maintenance group and a spontaneous improvement group. The mean follow-up period was 10.1 months for the SHT maintenance group and 9.6 months for the spontaneous improvement group. By comparing initial parameters in patients with newly-diagnosed SHT between the two groups using *t* tests, this study presents evidence that only initial thyroid stimulating

hormone (TSH) level was a definite prognostic factor for SHT, and that thyroid peroxidase antibody (TPO-Ab) titer was also a helpful prognostic factor for SHT in cases with mildly elevated TSH levels. As mentioned in the letter from the reviewers, multivariate Cox regression analysis would be a more concrete method to prove the prognostic value of a specific factor because it can correct for the influence of other confounding variables on prognosis. However, our data were determined to be inappropriate for a Cox regression model by the test of goodness of fit during the analysis. There are several possible reasons for this relating to the characteristics of our patients. The range of TSH levels was too narrow: subjects with TSH levels of 5 to 7 μ IU/mL accounted for 59.5% of all subjects. When we also consider the short follow-up period in this study (less than 12.0 months), it was difficult to detect a significant odds ratio for SHT prognosis according to TSH range. Also, with regard to TPO-Ab, a large majority of subjects (79.3%) had TPO-Ab titers of <60 U/mL, i.e., within the normal range. With data for TSH and TPO-Ab with wider ranges and a longer follow-up period, we think that TSH level and TPO-Ab titer might have been shown to be strong prognostic factors for SHT in more powerful and sophisticated analyses, such as multivariate Cox regression analysis and survival analysis.

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In spite of these limitations, this study is useful for daily practice in clinics. Faced with patients with newly-diagnosed SHT, TSH level and TPO-Ab titer at initial presentation could be considered as evidence to predict spontaneous improvement. Also, another notable finding of this study is that TSH level was a very strong prognostic factor in SHT. As Professors Ahn and Chung mention, a large-scale, prospective study is needed to definitively identify prognostic factors for SHT.

Thank you again for your insightful and comprehensive review of our paper.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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