Letter to the Editor

Cancer Epidemiology, Biomarkers & Prevention

TSH, Thyroid Hormone, and PTC—Letter

Silvia Franceschi and Sabina Rinaldi

Huang and colleagues (1) reported on the relationship between papillary thyroid cancer risk and prediagnostic levels of thyroid-stimulating hormone (TSH) and lent support to our previous findings (2) on the existence of an inverse association. The two studies were case–control studies nested in very different populations, that is, U.S. military staff mainly below age 50 years (400 male and 341 female cases; ref. 1) and healthy volunteers from the European Prospective Investigation in Cancer and Nutrition cohort (300 and 57, respectively, median age 51; ref. 2). The strength of the inverse association among the vast majority of women and men who had TSH levels within the reference limits was similar, that is, ORs of approximately 0.60 in the highest versus the lowest tertile in Huang and colleagues (1) or gender-specific quartile in our study (2). However, gender-specific analyses of individuals with TSH levels outside the reference limits led Huang and colleagues (1) to a different conclusion, that is, that increased thyroid cancer risk was associated with TSH below the reference limits among women but above the reference limits among men (1). We caution against overinterpreting differences by gender in these subgroups that are small (1) and potentially attributable to different thyroid problems (3, 4). Of note, the reference limits of TSH are controversial (3), and calls have been made to define them on the basis of age, sex, race, and amount of iodine intake (3, 4) and, notably, to lower or increase the current upper limit of approximately 4.0 mU/l (3). Small numbers in gender-specific analyses may also blur, in our view, the overall appreciation of the influence of TSH level on thyroid cancer risk depending on tumor size ($\leq$/>10 mm) or papillary subtype (classical or the rare follicular subtype; ref. 1). Although the attempt to show data on TSH in an unprecedented granular form must be commended, we think that subgroup findings should be considered hypothesis generating and do not eclipse the substantial agreement between the U.S. (1) and European (2) study. The counterintuitive inverse association between TSH level and differentiated thyroid cancer risk has needed large cohort studies to emerge and deserves to be studied again in different populations. However, as stated by Huang and colleagues (1), a better understanding of the implications of TSH levels in the onset and management of an increasingly common cancer (5) may have important consequences, including the avoidance of unnecessary and even harmful treatments in people with and without differentiated thyroid cancer.

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