Original Article
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Obesity

High-Normal TSH Values in Obesity: Is it Insulin Resistance or Adipose Tissue's Guilt?

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Objective: Clinical evidences reported subclinical alterations of thyroid function in obesity, although the relationship between thyroid status and obesity remains unclear. We cross-sectionally investigated the influence of metabolic features on hypothalamic–pituitary–thyroid axis in obesity.

Design and Methods: We enrolled 60 euthyroid subjects with no history of type 2 diabetes mellitus and assessed the relationship of thyroid function with insulin resistance, measured using euglycemic clamp, and abdominal fat volume, quantified by computed tomography scan (CT scan). Thyroid stimulating hormone (TSH) correlated with BMI ($r = 0.46$; $P = 0.02$), both visceral ($r = 0.58$; $P = 0.02$) and subcutaneous adipose tissue volumes ($r = 0.43$; $P = 0.03$) and insulin resistance (inverse relationship with insulin sensitivity–glucose uptake: $r = -0.40$; $P = 0.04$).

Results: After performing multivariate regression, visceral adipose tissue volume was found to be the most powerful predictor of TSH ($\beta = 3.05$; $P = 0.01$), whereas glucose uptake, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, subcutaneous adipose tissue volume, and triglycerides were not. To further confirm the hypothesis that high-normal TSH values could be dependent on adipose tissue, and not on insulin resistance, we restricted our analyses to moderately obese subjects' BMI ranging 30-35 kg/m^2. This subgroup was then divided as insulin resistant and insulin sensitive according to the glucose uptake ($\leq$ or >5 mg·kg^{-1}·min^{-1}, respectively). We did not find any statistical difference in TSH (insulin resistant: 1.62 $\pm$ 0.65 μU/ml vs. insulin sensitive: 1.46 $\pm$ 0.48; P = not significant) and BMI (insulin resistant: 32.2 $\pm$ 1.6 kg/m^2 vs. insulin sensitive: 32.4 $\pm$ 1.4; P = not significant), thus confirming absence of correlation between thyroid function and insulin sensitivity *per se*.

Conclusion: Our study suggests that the increase in visceral adipose tissue is the best predictor of TSH concentration in obesity, independently from the eventual concurrent presence of insulin resistance.

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Introduction

Several hormonal abnormalities, such as hypogonadism and polycystic ovary syndrome (1), are often accompanied by obesity; among them, thyroid dysfunction is certainly the most frequent hormonal impairment causing weight changes. However, while the effects of frank hyper or hypothyroidism on weight loss or gain are clear, the relationship between subclinical thyroid alterations and obesity is still controversial. Knudsen *et al.* (2) showed a correlation between serum thyroid stimulating hormone (TSH) and BMI, a negative association between BMI and FT4 levels, and no relationship between BMI and FT3 levels in a large population of 4,082 euthyroid subjects. Michalaki *et al.* (3) confirmed that severely obese subjects have higher TSH levels when compared with nonobese subjects; conversely, Manji *et al.* (4) failed to find any association between BMI and both TSH and FT4 levels in 401 euthyroid subjects.

While the relationship between obesity and subclinical thyroid dysfunctions remains unclear, it is overall debated what could eventually be the mechanism(s) linking subclinical thyroid dysfunction to obesity; in particular, whether variations of thyroid function in obesity are related either to the fat accumulation or to insulin resistance. In support to the first hypothesis, Nannipieri *et al.* (5) found reduced gene expression of TSH and FT3 receptors in both subcutaneous and visceral fat in obese subjects. This finding led the authors to speculate

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