

Association between a Serum Thyroid-stimulating Hormone Concentration within the Normal Range and Indices of Obesity in Japanese Men and Women

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Abstract

Objective This cross-sectional study investigated the associations between the serum thyroid-stimulating hormone (TSH) concentration and indices of obesity in middle-aged Japanese men and women.

Methods The participants were 2,037 employees (1,044 men and 993 women; age, 36-55 yr) of a metal products factory in Japan. Clinical examinations were conducted in 2009. We obtained a medical history and anthropometric measurements (body weight, body mass index [BMI] and waist circumference) and measured the serum TSH concentrations. The anthropometric indices were compared across serum TSH quartiles. The associations were evaluated separately according to the smoking status in men.

Results The mean body weight (kg), BMI (kg/m²) and waist circumference (cm) were 69.2, 23.7 and 83.2 in men and 55.3, 22.3 and 74.3 in women, respectively. Men with a higher TSH concentration had higher body weight and BMI values (*p* for trend=0.016 and 0.019, respectively), and these significant associations were observed even after adjusting for age, smoking status and other potential confounders. The TSH level was not associated with waist circumference. We found a significant interaction between the TSH level and the smoking status on body weight (*p* for interaction=0.013) and a significant association between the TSH level and body weight in nonsmokers, but not in current smokers. No significant associations were observed between the TSH level and the anthropometric indices in women.

Conclusion Significant positive associations between the serum TSH concentration, body weight and BMI were detected in men only, and an interaction with the smoking status was observed for this association.

Key words: thyroid-stimulating hormone, body weight, obesity, smoking, epidemiology

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Introduction

Thyroid dysfunction is associated with body weight and adiposity (1, 2). In previous studies, the potential impact of minor changes in the thyroid function on body weight and other anthropometric indices in euthyroid participants was investigated (3-6). A recent review of population-based studies indicated that seven of 12 studies found positive associations (7); however, the two studies conducted in Asian populations did not (8, 9).

Gender is associated with the thyroid-stimulating hormone (TSH) concentration (10) and may also affect the relationship between the TSH level and body mass index (BMI) (11). The smoking status is also associated with the thyroid function (12) and body weight (13). The smoking rates in East Asian men, such as those living in Japan and South Korea, are relatively high compared to those observed in Western countries (14). However, of the four studies that evaluated the association between the TSH level and obesity in Asian populations, two were based solely on clinical samples and included only women (15, 16), while the other two population-based studies evaluated the associations in men and women simultaneously without considering the smoking status as a confounding factor (8, 9). Hence, no studies have evaluated the interaction between the TSH level and the smoking status in Asian men.

We therefore investigated the relationship between the serum TSH concentration and anthropometric indices of obesity (body weight, BMI and waist circumference) in this cross-sectional study of middle-aged Japanese men and women. The objectives were: (i) to investigate whether the serum TSH concentration is associated with indices of obesity; (ii) to determine whether a gender difference is observed in the relationship; and (iii) to investigate how this relationship is influenced by the smoking status.

Materials and Methods

Participants

The participants of this study included 36- to 55-year-old employees of a zipper and aluminum sash-producing factory in Toyama Prefecture, Japan. In the spring of 2009, 2,362 (1,219 men and 1,143 women) employees received health examinations. Of these potential participants, 325 (14%) were excluded, including 122 patients with missing baseline data, such as those for body weight, waist circumference and smoking status, 182 patients with a serum TSH concentration outside the normal range (<0.4 or >4.0 $\mu\text{U/mL}$) and 21 patients with a present/past history of thyroid disease, such as chronic thyroiditis or Graves' disease. Therefore, a total of 2,037 participants (1,044 men and 993 women) were included in this study.

Data collection

The annual health examinations included a medical history, physical examination, anthropometric measurements and measurements of the fasting plasma glucose and serum lipid levels. Height, weight and waist circumference were measured in all subjects, except women who were pregnant, during the routine annual medical checkups. Height was measured to the nearest 0.1 cm without shoes using a stadiometer. Weight was measured in light clothing without shoes using a standard scale and recorded to the nearest 0.1 kg. BMI was calculated as weight/height^2 (kg/m^2). Waist circumference was measured to the nearest 0.1 cm above the iliac crest and below the lowest rib margin at minimal respiration in a standing position. Blood pressure was measured using an automatic manometer (BP 103i, Nippon Colin, Komaki, Japan) after the subjects had rested for five minutes in a seated position. Trained staff obtained the measurements.

The blood samples were obtained in the morning after overnight fasting. The plasma glucose levels were measured enzymatically using an Abbott glucose UV test (Abbott Laboratories, Chicago, USA). The total cholesterol and triglyceride levels were measured using an enzymatic assay. The LDL-cholesterol concentration was calculated using the Friedewald formula (17). Serum was separated immediately after blood collection and stored at -80°C . The stored samples were used to measure the TSH concentrations using a chemiluminescent immunoassay (Chemilumi ACS-TSH, Siemens Healthcare Diagnostics K.K., Tokyo, Japan).

A self-administered questionnaire was used to collect information regarding medical treatment for hypertension, dyslipidemia and diabetes. Metabolic abnormalities were defined according to the Japanese guidelines for metabolic syndrome (18). High blood pressure was defined as a systolic blood pressure of at least 130 mmHg, a diastolic blood pressure of at least 85 mmHg or the current use of antihypertensive medications. Dyslipidemia was defined as a serum triglyceride level of at least 150 mg/dL, an HDL-cholesterol level not exceeding 40 mg/dL or the current use of antihyperlipidemic medications. High fasting plasma glucose was defined as a fasting plasma glucose level of at least 110 mg/dL or the use of antidiabetic medications. Hypercholesterolemia was defined as a serum LDL-cholesterol level of at least 160 mg/dL or the current use of antihyperlipidemic medications.

Statistical analysis

The characteristics of the study participants were compared according to quartiles of the serum TSH concentration. The percentage or prevalence among TSH quartiles was compared using the chi-square test. Linear trends with increasing levels of TSH were tested by assigning each participant a median value for the category and modeling this value as a continuous variable. Multivariate-adjusted *p* values for the trend were calculated using multiple linear re-

Table 1. Characteristics of the Male Participants according to Thyroid-stimulating Hormone Quartiles

TSH (range, μ U/mL)	All	TSH quartile				p^a
		Q1 (lowest) 0.4-1.0	Q2 1.1-1.3	Q3 1.4-1.9	Q4 (highest) 2.0-4.0	
n	1,044	332	202	265	245	
Age (y)	44.1 \pm 6.1	44.7 \pm 6.1	43.2 \pm 5.8	44.6 \pm 6.2	43.5 \pm 6.0	0.077
Current smokers (%)	39.8	46.4	45.5	38.5	27.3	<0.001
Alcohol drinking						0.433
Nondrinker (%)	16.5	16.9	19.3	16.2	13.9	
Occasional drinker (%)	18.1	15.7	18.3	17.4	22.0	
\geq 1 time/week (%)	65.4	67.5	62.4	66.4	64.1	
Habitual exercise_yes (%)	50.1	49.1	51.0	49.8	51.0	0.962
High blood pressure (%) ^b	31.6	29.2	32.2	35.1	30.6	0.473
Dyslipidemia (%) ^b	30.2	30.7	30.7	27.5	31.8	0.738
Hypercholesterolemia (%) ^b	18.5	17.8	20.3	19.6	16.7	0.734
High plasma glucose (%) ^b	11.3	12.0	8.4	11.7	12.2	0.548

The data are presented as n, mean \pm standard deviation or %.

TSH: thyroid-stimulating hormone

^a p for the trend analyses or *chi*-square tests.

^b Metabolic abnormalities were defined as follows: high blood pressure, a systolic blood pressure of \geq 130 mmHg, a diastolic blood pressure of \geq 85 mmHg or the current use of antihypertensive medications; dyslipidemia, a serum triglyceride level of \geq 150 mg/dL, an HDL cholesterol level of \leq 40 mg/dL or the current use of antihyperlipidemic medications; high fasting plasma glucose, a fasting plasma glucose level of \geq 110 mg/dL or the use of antidiabetic medications; hypercholesterolemia, a serum LDL cholesterol level of \geq 160 mg/dL or the current use of antihyperlipidemic medications.

Table 2. Characteristics of the Female Participants according to Thyroid-stimulating Hormone Quartiles

TSH (range, μ U/mL)	All	TSH quartile				p^a
		Q1 (lowest) 0.4-1.2	Q2 1.3-1.7	Q3 1.8-2.3	Q4 (highest) 2.4-4.0	
n	993	285	245	217	246	
Age (y)	45.0 \pm 6.0	44.8 \pm 5.9	44.4 \pm 6.0	45.1 \pm 6.2	45.9 \pm 5.9	0.013
Current smokers (%)	6.0	8.4	6.9	4.6	3.7	0.092
Alcohol drinking						0.936
Nondrinker (%)	9.1	9.8	7.8	8.3	10.2	
Occasional drinker (%)	46.1	47.4	45.3	46.1	45.5	
\geq 1 time/week (%)	44.8	42.8	46.9	45.6	44.3	
Habitual exercise_yes (%)	61.5	61.1	61.2	62.7	61.4	0.984
High blood pressure (%) ^b	17.6	18.2	16.3	16.6	19.1	0.827
Dyslipidemia (%) ^b	7.0	7.4	6.1	7.4	7.3	0.935
Hypercholesterolemia (%) ^b	13.0	13.3	10.6	14.3	13.8	0.631
High plasma glucose (%) ^b	4.1	4.9	2.9	5.1	3.7	0.559

The data are presented as n, mean \pm standard deviation or %.

TSH: thyroid-stimulating hormone

^a p for the trend analyses or *chi*-square tests.

^b Metabolic abnormalities were defined as follows: high blood pressure, a systolic blood pressure of at least 130 mmHg, a diastolic blood pressure of at least 85 mmHg or the current use of antihypertensive medications; dyslipidemia, a serum triglyceride level of at least 150 mg/dL, an HDL-cholesterol level not exceeding 40 mg/dL or the current use of antihyperlipidemic medications; high fasting plasma glucose, a fasting plasma glucose level of at least 110 mg/dL or the use of antidiabetic medications; hypercholesterolemia, a serum LDL-cholesterol level of at least 160 mg/dL or the current use of antihyperlipidemic medications.

gression analyses of the obesity variables. Adjustment for possible confounders was performed sequentially for age (model 2), plus current smoking status (yes, no) (model 3), plus alcohol drinking (nondrinker, occasional, drinking one time or more/week), habitual exercise (no, yes), presence of hypertension (no, yes), presence of dyslipidemia (no, yes) and presence of high fasting plasma glucose (no, yes) (model 4). Because both the TSH level and anthropometric indices are associated with the smoking status in men, the associations between the TSH levels and the obesity indices in men were evaluated according to the smoking status (“nonsmokers/ex-smokers” versus “current smokers”). We were unable to evaluate these associations in women because the number of female smokers was too small. The statistical analyses were conducted using the Statistical Pack-

age for the Social Sciences version 12.0J (SPSS, Tokyo, Japan). A p value of <0.05 was considered to be statistically significant.

The present study was approved by the Institutional Review Committee for Ethical Issues at Kanazawa Medical University.

Results

The participants had a mean serum TSH concentration of 1.5 (standard deviation 0.8) μ U/mL for men and 1.8 (0.8) μ U/mL for women, which was significantly higher in women than in men (p <0.001). The characteristics of the study participants are shown in Tables 1 (men) and 2 (women). Men had a mean age of 44.1 years and women

Table 3. Associations between the Anthropometric Indices for Obesity and Serum Thyroid-stimulating Hormone Concentrations in Men and Women

	TSH quartile				p for trend ^a			
	Q1 (lowest)	Q2	Q3	Q4 (highest)	Model 1	Model 2	Model 3	Model 4
Men								
Body weight (kg)	68.1±0.5	69.8±0.7	69.2±0.6	70.4±0.7	0.016	0.010	0.021	0.035
Body mass index (kg/m ²)	23.4±0.2	23.8±0.2	23.7±0.2	24.1±0.2	0.019	0.007	0.023	0.044
Waist circumference (cm)	82.4±0.5	83.7±0.6	83.6±0.6	83.5±0.6	0.175	0.075	0.128	0.280
Women								
Body weight (kg)	54.5±0.5	55.6±0.6	57.0±0.8	54.8±0.6	0.665	0.684	0.700	0.563
Body mass index (kg/m ²)	21.9±0.2	22.2±0.2	23.1±0.3	22.1±0.2	0.377	0.572	0.568	0.422
Waist circumference (cm)	73.4±0.6	74.1±0.6	76.0±0.8	74.0±0.6	0.358	0.594	0.584	0.422

The data are presented as the mean ± standard error.

TSH: thyroid-stimulating hormone

^aModel 1, univariate model; Model 2, adjusted for age; Model 3, adjusted for age and smoking; Model 4, adjusted for age, smoking, alcohol drinking, habitual exercise and the presence of high blood pressure, dyslipidemia and high fasting plasma glucose.

Table 4. Associations between the Anthropometric Indices for Obesity and Serum Thyroid-stimulating Hormone Concentrations according to the Smoking Status in Men

	TSH quartile				p for trend	p for interaction
	Q1 (lowest)	Q2	Q3	Q4 (highest)		
n (nonsmokers, ex-smokers / current smokers)	178/154	110/92	163/102	178/67		
Body weight (kg)						
Nonsmokers, ex-smokers	68.0±0.7	70.1±0.9	69.7±0.7	71.6±0.7	0.001	0.013
Current smokers	68.3±0.7	69.0±1.0	68.8±0.9	67.0±1.1	0.400	
Body mass index (kg/m²)						
Nonsmokers, ex-smokers	23.5±0.2	23.9±0.3	24.0±0.2	24.4±0.2	0.005	0.068
Current smokers	23.2±0.2	23.7±0.3	23.4±0.3	23.1±0.3	0.639	
Waist circumference (cm)						
Nonsmokers, ex-smokers	82.4±0.6	83.9±0.8	83.7±0.7	84.5±0.6	0.031	0.057
Current smokers	82.3±0.6	83.5±0.8	83.5±0.8	80.8±1.0	0.295	

The data are presented as the mean ± standard error.

TSH: thyroid-stimulating hormone

The means and standard errors of the anthropometric indices were calculated in each TSH quartile adjusted for age, alcohol drinking, habitual exercise and the presence of high blood pressure, dyslipidemia and high fasting plasma glucose.

had a mean age of 45.0 years. Higher TSH concentrations were associated with a lower percentage of current smokers in men and an older age in women. No associations were observed between the serum TSH concentrations and alcohol drinking, habitual exercise or the prevalence of metabolic abnormalities.

The participants had a mean body weight of 69.2 kg in men and 55.3 kg in women, a mean BMI of 23.7 kg/m² in men and 22.3 kg/m² in women and a mean waist circumference of 83.2 cm in men and 74.3 cm in women. Table 3 shows the anthropometric obesity indices according to the TSH concentration quartiles. Men with higher TSH concentrations had higher body weight and BMI values. These significant associations were observed even after adjusting for age (model 2), smoking status (model 3) and other potential confounders (model 4). The TSH concentration was not associated with waist circumference. No significant associations were observed in women between the serum TSH concentrations and the anthropometric indices of obesity.

We evaluated the association between the TSH concentra-

tion and obesity in men according to the smoking status. Compared to the nonsmoker/past smokers, the current smokers had lower serum TSH concentrations (1.4±0.6 μU/mL for current smokers vs. 1.6±0.8 μU/mL for nonsmokers/ex-smokers, p<0.001), body weight values (68.3±9.9 vs. 69.8±10.3 kg, p=0.02) and BMI measurements (23.3±3.0 vs. 24.0±3.4 kg/m², p=0.002). The waist circumference values did not differ between the two groups (83.4±8.5 vs. 84.1±9.1 cm, p=0.169). We found a significant interaction between the serum TSH concentration and the smoking status on the relationship with body weight, and the nonsmoking participants with a higher TSH concentration had a significantly higher body weight (Table 4). Similarly, higher TSH concentrations were significantly associated with higher BMI and waist circumference values in nonsmokers only; however, the p values for the interaction were 0.068 and 0.057, respectively, and we found no significant interactions between the TSH concentration and the smoking status (Table 4).

Discussion

Thyroid dysfunction is associated with body weight and adiposity (1, 2). However, it is controversial whether different levels of the thyroid function within the normal range affect body weight and adiposity. In several previous population-based studies, the TSH level was found to be associated with BMI (3, 5, 6, 11, 19-21); yet, four of the six studies reported a lack of association between the serum TSH level and waist circumference (15, 22-24). These results support our findings in men that the serum TSH level is associated with body weight and BMI, but not waist circumference. Waist circumference is more closely associated with visceral fat than BMI (25), and another study reported that the TSH concentration is associated with the amount of subcutaneous, but not preperitoneal fat (22), indicating that the serum TSH concentration may have a more marked effect on total body fat than on visceral fat.

We found a gender difference in the association between the serum TSH concentration and BMI; a significant association was found in men only. In most previous reports, this association was evaluated in men and women together (4, 12, 19, 21, 23). Among previous studies that evaluated the association between the serum TSH concentration and obesity in men and women separately, three showed no gender differences in the association (3, 6, 26), while one found a significant association exclusively in women (11). The gender differences may have resulted from variations in sex hormones, the TSH concentration, fat distribution or the degree of obesity between men and women. Similarly, the differences between our results and those of previous studies may have resulted from differences in ethnicity. Interestingly, all previous studies from Asian countries showed no significant associations between the serum TSH concentration and BMI in either women only (15, 16) or in both men and women (8, 9). In contrast, the association between the TSH concentration and BMI is stronger in severely obese participants than in mildly obese participants (27). Because the mean BMI values are lower in Asian populations, particularly in Asian women, the degree of obesity, as well as ethnicity, may have affected the differences in the associations found between the genders and between Asian and Western populations.

Although the smoking status is associated with the thyroid function (12) and body weight (13), the interaction between the smoking status and the TSH level on indices of obesity is also controversial. Similar to our results, two studies reported a positive association between BMI and the serum TSH level among nonsmokers only (3, 4). One study indicated that this association was somewhat stronger in female nonsmokers than in female smokers (6). In contrast, another study found the association to be stronger among current smokers than nonsmokers (5). Smokers are reported to have lower serum TSH concentrations (12) and lower BMI measurements (13) than nonsmokers. Since the asso-

ciation between smoking and BMI is strong (3), smoking may mask a potential relationship between the TSH level and BMI.

The mechanisms underlying the association between the TSH level and adiposity have been discussed. A high TSH concentration may be the result of a lower thyroid function, even when the TSH level is within the normal range, which may lead to a lower basal metabolic rate (19) and obesity. Some reports have indicated that the direct action of TSH in stimulating adipogenesis causes body fat accumulation (28, 29). Another hypothesis is that adipose tissue influences the thyroid function, possibly through the effects of leptin (30). Obesity itself may also affect the serum TSH concentration independent of the thyroid function (31). The thyroid function and obesity may affect each other; thus, a prospective study is needed to evaluate whether a lower TSH concentration, even within the normal range, causes obesity and increases cardiovascular risks.

The strengths of this study include the relatively large sample size. Several studies evaluating the association between the serum TSH level and obesity did not fully evaluate the effects of gender, age or smoking status on the association. We evaluated the association both adjusted for these possible confounders and separately according to gender and the smoking status. There are some limitations to this study. First, we evaluated only the serum TSH concentrations. Because we did not evaluate other thyroid hormones, thyroid autoantibodies or thyroid ultrasonography findings, we were unable to exclude patients with latent thyroid disorders and a normal TSH concentration. However, participants with self-reported thyroid disorders and those with an abnormal serum TSH concentration were excluded; thus, almost all participants were considered to be healthy euthyroid participants. Second, the sample included only subjects who were employed. Poor health may exclude some individuals from working; hence, the prevalence of obesity may be lower in our sample than in the general Japanese population. Third, the number of female smokers was so small that we were unable to evaluate the association between the serum TSH level and indices of obesity in women separately according to the smoking status. Similarly, the number of ex-smokers was so small that we were unable to evaluate the effects of smoking cessation on the TSH-obesity association. Fourth, this was a cross-sectional study, and the use of a prospective design may provide additional information regarding the causal relationship between the serum TSH level and obesity.

In conclusion, significant positive associations were observed between the serum TSH concentration and body weight and BMI in men only. In addition, the association between the serum TSH concentration and body weight was influenced by the smoking status. Further prospective studies are needed to evaluate whether a subclinically low thyroid function, even that within the normal serum TSH concentration range, causes obesity and increases cardiovascular risks.

The authors state that they have no Conflict of Interest (COI).

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