Association Between Body Mass Index and Thyroid Function in Euthyroid Chinese Adults

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Background: Obesity can influence thyroid function through multiple routes, even in people who are euthyroid. The correlation between weight and thyroid function is a matter of debate. The present study investigated the relationship between body weight and thyroid function in euthyroid Chinese adults.

Material/Methods: A total of 1564 participants with serum thyrotropin (TSH) and thyroid hormone levels within the reference range were included. All of them were tested for thyroid function parameters and categorized, based on body mass index (BMI), into 3 groups: normal weight, overweight, and obese. The effects of BMI on thyroid function were examined using linear (continuous values) and logistic (dichotomous levels according to medians or means) regression and controlling for age and sex.

Results: There were significant differences in free triiodothyronine (FT3) levels and FT3/free thyroxine (FT4) ratios among participants who were normal weight, overweight, and obese (both \( P < 0.001 \)). Multivariable regression analysis (\( P < 0.001 \)) showed that BMI was positively associated with FT3 levels and FT3/FT4 ratios. Compared with the normal weight group, the patients who were overweight or obese had significantly higher FT3 levels and FT3/FT4 ratios that were higher than average, according to logistic regression analyses.

Conclusions: We found that Chinese adults who are obese may have higher FT3 levels and FT3/FT4 ratios than those who are of normal weight, even if their thyroid function values are within the normal range.

Keywords: Body Mass Index • Obesity • Thyroid Function Tests

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Background

Obesity is becoming a worldwide epidemic disease and it is highly prevalent in developed countries. An estimated 30% of the adult population in the United States is obese; in the UK, the proportion is 25% [1-3]. In developing countries, with growth in their economies, the incidence of obesity has been shown to rise rapidly. Between 2002 and 2012, the prevalence of obesity in Chinese adults increased from 7.1% to 11.9% and the overall prevalence of obesity and overweight increased from 29.9% to 42% [4].

Previous studies have revealed that the effects of obesity on the endocrine system are multifaceted, although that is seldom noted. Obesity can affect thyroid function and the release of gonadotropin releasing hormone (GnRH), alter the luteinizing hormone pulse amplitude [5], decrease growth hormone levels, and increase cortisol levels. Thyroid function is closely related to obesity and obesity-related metabolic disease. Therefore, increasing attention is being focused on the effects of obesity on thyroid function.

Several studies have explored alterations in thyroid function associated with differences in body mass index (BMI) in individuals who are euthyroid [6-10]. The results, however, have been rather inconsistent. Most of these studies have had small sample sizes and concentrated on the effects of thyroid function on BMI. We aimed to investigate the effects of BMI on thyroid function in the present cross-sectional study with a relatively large sample size in China.

Material and Methods

Subjects and Methods

For the present study, 1564 adults aged 18 to 70 years were recruited between November 2018 and November 2019 at Beijing Chaoyang Hospital, Capital Medical University. All of them were asked about their medical histories and they received physical examinations and underwent laboratory tests. The exclusion criteria included known history of cardiovascular disease or diabetes; thyroid dysfunction, use of hormone replacement therapy such as thyroid or sex hormones; use of hormone pulse amplitude [5], decrease growth hormone levels, and increase cortisol levels. Thyroid function is closely related to obesity and obesity-related metabolic disease. Therefore, increasing attention is being focused on the effects of obesity on thyroid function.

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A total of 1564 participants were included in the final analysis, of whom 468 were women. Demographics and baseline characteristics of the participants are shown in Table 1. BMI was 22.77±1.65, 27.01±1.34 and 32.07±1.98 kg/m$^2$ ($P<0.001$), in the normal weight, overweight, and obese groups, respectively. The mean ages of the 3 groups were 47.18±12.68, 46.97±9.03, and 46.40±10.87 years, respectively. There were no statistically significant differences in age or sex among the 3 groups. As BMI increased, there were obvious changes in serum lipid profile. The levels of TC, TG, and LDL-C also tended to rise in the 3 groups in keeping with BMI ($P<0.001$). The levels of HDL-C decreased significantly as BMI increased ($P<0.001$). There were significant differences among the 3 groups in glucose metabolism indexes. The FBG levels in the groups who were of normal weight, overweight, and obesity were 5.42±0.52, 5.60±0.54, and 5.67±0.56 mmol/L ($P<0.001$).
and obese were 5.42±0.52, 5.60±0.54, and 5.67±0.56 mmol/L, respectively (P<0.001). Fasting insulin, HOMA-β, and HOMA-IR levels also increased along with increasing BMI. A similar trend also was apparent regarding the numbers of WBCs, neutrophils, lymphocytes, and platelets; however, there were no statistically significant differences in NLR among the 3 groups. Tukey post hoc tests revealed statistically significant differences among the 3 groups in all pairwise comparisons of BMI, HDL-C, TG, FINS, HOMA-IR, HOMA-β, WBCs, neutrophils, and lymphocytes.

Table 1 shows that thyroid function differed among the 3 groups. FT3 levels were 5.28±0.54, 5.36±0.56 and 5.46±0.52 pmol/L in the groups who were of normal weight, overweight, and obese, respectively (P<0.001). Their FT3/FT4 ratios were 0.32±0.04, 0.33±0.04, and 0.34±0.04, respectively (P<0.001). Post hoc tests revealed that all pairwise comparisons of FT3 and FT3/FT4 levels were statistically significant. TPOAb levels were lower in the group with normal weight than in the other 2 groups. With the increase in BMI, TSH levels tended to increase, although the differences were not statistically significant. There were no statistically significant differences in FT4 or TgAb levels among the 3 groups (Figures 1, 2).

Table 2 shows the relationships between thyroid parameters and laboratory indices. We found that TSH, FT3, and FT3/FT4 were significantly correlated with FINS, HOMA-IR, and HOMA-β, respectively. FT3/FT4 was negatively correlated with TC, HDL-C, and NLR. FT4 was positively associated with WBC and neutrophil counts. After adjustment for age and sex, multivariable regression analysis showed no significant correlations between BMI and FT4 or between BMI and TSH, but BMI was positively correlated with FT3 and FT3/FT4 (both P<0.01).

After adjustment for age and sex, logistic regression analyses showed that, compared with normal weight, both overweight and obesity were significantly associated with an increased risk of higher FT3 (ORs 1.350 and 1.875, respectively) as were FT3/FT4 ratio (ORs 1.415 and 2.118, respectively). Also compared with normal weight, obesity was associated with an increased risk of a higher TSH level (OR 1.609, 95% CI 1.113-2.285) (Table 3).
Table 2. Associations between thyroid function and laboratory indices.

|          | TSH       | FT3       | FT3/FT4  |
|----------|-----------|-----------|----------|
|          | r         | P value   | \( \beta \) | P value | r         | P value   | \( \beta \) | P value |
| BMI      | 0.052**   | <0.001    | 0.120**  | <0.001  |
| TC       | 0.020     | 0.041     | 0.040    | 0.115   | -0.060*   | 0.021     | -0.035    | 0.140   |
| LDL-C    | 0.005     | 0.838     | -0.001   | 0.998   | 0.027     | 0.302     | 0.030     | 0.212   |
| HDL-C    | -0.015    | 0.551     | -0.021   | 0.459   | -0.187**  | <0.001    | -0.029    | 0.274   |
| TG       | 0.076**   | 0.003     | 0.015    | 0.564   | 0.015     | 0.561     | -0.055*   | 0.023   |
| FBG      | -0.018    | 0.476     | -0.021   | 0.424   | 0.039     | 0.133     | 0.018     | 0.464   |
| FINS     | 0.078**   | 0.002     | 0.080**  | 0.006   | 0.148**   | <0.001    | 0.097**   | <0.001  |
| HOMA-IR  | 0.063*    | 0.014     | 0.059*   | 0.045   | 0.140**   | <0.001    | 0.084**   | 0.002   |
| HOMA-\( \beta \) | 0.075**   | 0.004     | 0.091**  | 0.001   | 0.107**   | <0.001    | 0.060*    | 0.021   |
| WBC      | -0.012    | 0.628     | -0.015   | 0.576   | 0.088**   | 0.001     | 0.013     | 0.581   |
| Neutrophils | -0.010    | 0.707     | -0.023   | 0.370   | 0.042     | 0.105     | -0.007    | 0.775   |
| Lymphocyte | -0.012    | 0.637     | 0.006    | 0.816   | 0.108**   | 0.000     | 0.039     | 0.105   |
| Platelet | 0.009     | 0.721     | -0.027   | 0.310   | -0.021    | 0.412     | 0.023     | 0.352   |
| NLR      | -0.009    | 0.717     | -0.024   | 0.351   | -0.044    | 0.085     | -0.030    | 0.200   |

Values of \( r \) represent correlation coefficient. Values of \( \beta \) are standardized regression coefficients. BMI – body mass index; TSH – thyroid stimulating hormone; FT3 – free triiodothyronine; FT4 – free thyroxine; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; FBG – fasting blood glucose; FINS – fasting serum insulin; HOMA-IR – homeostasis model assessment of insulin resistance; HOMA-\( \beta \) – homeostasis model assessment of \( \beta \) cell function; WBC – white blood cell; NLR – neutrophil to lymphocyte ratio. BMI was estimated after adjustment for gender and age; other variables were estimated after adjustment for gender, age and BMI. * \( P < 0.05 \); ** \( P < 0.01 \).
Table 3. Logistic regression analyses of the risk of higher levels of indices for thyroid function.

|                | TSH          | FT3         | FT4          | FT3/FT4      |
|----------------|--------------|-------------|--------------|--------------|
|                | OR 95% CI    | P value     | OR 95% CI    | P value      |
| Model 1        |              |             |              |              |
| Normal weight  | Ref          | Ref         | Ref          | Ref          |
| Overweight     | 1.151 0.932-1.421 0.192 1.279 1.035-1.581 0.022 |
| Obesity        | 1.624** 1.145-2.302 0.007 1.778** 1.254-2.521 0.001 |
| Model 2        |              |             |              |              |
| Normal weight  | Ref          | Ref         | Ref          | Ref          |
| Overweight     | 1.138 0.921-1.407 0.232 1.350** 1.082-1.684 0.008 |
| Obesity        | 1.609** 1.133-2.285 0.008 1.871** 1.294-2.707 0.001 |

Discussion

Prior studies have noted the importance of the relationship between obesity and thyroid dysfunction. However, reports on the exact relationship between obesity and thyroid function are limited and inconsistent. Fontenelle et al summarized multiple studies published between 2005 and 2015 on the status of thyroid hormones in euthyroid obese adults [11]. Half of the studies (9/19) reported a significant positive correlation between BMI and TSH, whereas the other half did not. Similarly, half of the studies (6/11) found a positive correlation between BMI and FT3 or total triiodothyronine. Of the 16 studies, only 3 reported a negative correlation between BMI and FT4.

The present study was designed to assess the association between BMI and thyroid function in euthyroid Chinese adults. Our results showed positive associations between BMI and FT3 levels and between BMI and FT3/FT4 ratios. However, no statistically significant differences in FT4 levels were found among the different BMI groups.

The mechanism and clinical implications of the changes in thyroid function associated with obesity have not yet been fully elucidated. At present, obesity is believed to affect thyroid function via several mechanisms, including dysfunction of adipose tissue, effects of hyperinsulinemia, and changes in thyroid gland structure and function. Several studies have suggested that dysfunction of adipose tissue is the major factor responsible for variations in the homeostasis of thyroid hormones [12-15].

Adipose tissue, which is endocrine in nature, can produce and secrete leptin. Patients who are obese have higher leptin levels than those who are not obese. Leptin plays an important role in thermoregulation and energy balance and interacts with thyroid hormones. A defect in leptin secretion could affect the rhythm of TSH secretion. In addition, leptin could promote the expression of thyrotropin-releasing hormone messenger RNA. Leptin could trigger an increase in the number of thyroid cells by binding to the leptin receptor on the cells [16]. In addition, leptin also can modulate deiodinase activity.
in different organs, thereby affecting the level of thyroid hormone [17-22]. These mechanisms, in part, may underly the elevated FT3/FT4 ratios and FT3 levels in the group in the present study that was obese.

On the other hand, thyroid hormones within the euthyroid range are also found to be involved in metabolic diseases. Xu et al conducted a study with 16 975 subjects and found that thyroid function could influence body weight and contribute to the development of obesity [23]. Thyroid hormone influences body weight through regulation of resting energy expenditure but the precise mechanism has not been fully clarified [24]. Although not all resting energy expenditure is thyroid hormone-dependent, minor changes in thyroid hormone levels have a significant effect on resting energy expenditure. For instance, resting energy expenditure decreases by 75 to 150 kcal/d, while serum TSH concentration increases by 0.5 to 1 mIU/L, which is still within the normal range. If this change persists over the long term, it can result in significant weight gain [25].

Clearly, the interactions between thyroid function and insulin sensitivity are complex and multifaceted. Our data suggest that FINS levels, HOMA-IR, and HOMA-β are associated with thyroid function. Our results are consistent with other research, which shows that thyroid function can be influenced by insulin resistance in obese, euthyroid individuals. The putative mechanism is the potential contribution of obesity-associated insulin resistance to reduction in deiodinase enzyme D2 activity in thyrotrophic cells, which leads to changes in the levels of thyroid hormones [26-28].

Obesity is recognized as a chronic, low-grade, inflammatory condition. Several inflammatory markers, such as WBC, neutrophil, and lymphocyte counts, are found to increase in people who are obese [29,30]. Although the mechanism by which WBCs and neutrophils affect thyroid function is not well known, a recent study found that these inflammatory markers play some role in the development of nodular thyroid disease [31]. The number of participants in the present study was small, particularly in the group that was obese. A possible reason is that individuals who are obese often pay less attention to their health and are less inclined to have check-ups than their counterparts who are not obese. Therefore, with a relatively small sample size, we did not find a linear association between BMI and TSH levels. Nevertheless, using logistic regression analyses, we still found that obese individuals were more likely to have higher TSH levels than those who were normal weight, indicating that BMI may have an effect on TSH levels only in patients who are obese.

**Conclusions**

In conclusion, we observed that Chinese adults who were obese had higher FT3 levels and FT3/FT4 ratios compared with those who were of normal weight, even though their thyroid function was within the normal range. These findings will help us to better understand changes in thyroid function that accompany an increase in body fat. Because the present study was cross-sectional, no direct causal associations can be inferred. Therefore, longitudinal studies are needed to thoroughly elucidate the complex interplay between body weight and thyroid function that is within the normal range.

**Department and Institution Where Work Was Done**

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**Conflicts of Interest**

None.
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