# Effects of effective antithyroid therapy on adiposity and skeletal muscle in patients with hyperthyroidism across gender and age groups

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**Abstract. – OBJECTIVE:** The study aimed to evaluate the effects of effective antithyroid therapy on adiposity and skeletal muscle in patients with hyperthyroidism across gender and age groups.

**PATIENTS AND METHODS:** A total of 57 adult hyperthyroid patients (21 males and 36 females) who underwent effective antithyroid medication from January 2018 to January 2021 at Liuzhou People's Hospital and the First Affiliated Hospital of Guangxi Medical University were recruited and followed up for one year to observe the long-term efficacy of the antithyroid therapy. The eligible patients were divided by age and gender groups into male group A (males of <40 years old, n=12), female group A (females of <40 years old, n=19), male group B (males of 40-59 years old, n=8), female group B (female of 40-59 years old, n=13), and group C (patients of ≥60 years old, including one male and four females). A cohort of 57 healthy individuals was also recruited as controls. A Dual Energy X-ray (DXA) was performed to measure changes in fat and lean tissue mass and grip strength of the dominant hand before and after treatment and the body fat percentage (BFP). The whole-body skeletal muscle mass index (ASMI) was calculated to evaluate the long-term effects of antithyroid therapy.

**RESULTS:** The eligible patients of all ages reported significantly increased total fat mass, body fat percentage, and body mass index ($p<0.05$). The total lean tissue mass was markedly increased in male and female group A ($p<0.05$), showed no significant changes in male and female group B ($p>0.05$), and exhibited a marked decline in group C ($p<0.05$). Significantly elevated ASMI after treatment was observed in male and female group A ($p<0.05$), while no significant changes were detected in ASMI after treatment in groups B and C ($p>0.05$). All patients in groups A and B exhibited enhanced grip strength, while the enhancement of grip strength in patients of group C was poor ($p>0.05$).

**CONCLUSIONS:** Effective anti-hyperthyroidism therapy improves fat mass and body fat percentage in patients of all ages. However, gender and age differences exist in the effectiveness of improvements in total muscle mass and ASMI. Suboptimal muscle mass recovery was reported in patients over 40 years after effective anti-hyperthyroid therapy.

*Key Words:*
Hyperthyroidism, Adiposity, Skeletal muscle.

## Introduction

Hyperthyroidism will cause muscle and adipose tissue atrophy in the body, resulting in weight loss. Clinical experience suggests that effective hyperthyroidism therapy could restore patients' body weight by efficaciously enhancing the muscle and adipose tissue weight of the patients[1,2]. However, literature shows significant differences in the recovery of different body parts during hyperthyroidism therapy, with gender and age being important factors in restoring fat and muscle growth. Currently, little knowledge is available about the effects of gender and age on the outcome of fat and skeletal muscle recovery in patients with hyperthyroidism. In this study, we analyzed the changes in adiposity and skeletal muscle in hyperthyroid patients of different genders and ages after access to effective anti-hyperthyroid drug therapy by means of a prospective clinical study to provide more clinical evidence.

## Patients and Methods

### Participants

A total of 57 adult hyperthyroid patients (21 males and 36 females) who underwent effective antithyroid medication from January 2018 to January 2021 in Liuzhou People's Hospital and the First Affiliated Hospital of Guangxi Medical University were recruited and followed up for one year to observe the long-term efficacy of the antithyroid therapy. The eligible patients (aged 37.13±13.88 years for males and 37.28±13.53



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years for females) were divided by age and gender groups into male group A (males of <40 years old, n=12), female group A (females of <40 years old, n=19), male group B (male of 40-59 years old, n=8), female group B (female of 40-59 years old, n=13), and group C (patients of ≥60 years old, including one male and four females).

Patients with elevated Triiodothyronine (T3) and Thyroxine (T4) and decreased Thyroid Stimulating Hormone (TSH) were considered eligible and then recruited. Patients with thyroiditis, who required steroid hormones during treatment, with chronic wasting diseases, such as combined diabetes mellitus and malignancies during pregnancy or short-term planned pregnancy, or who experienced severe adverse drug reactions, altered treatment regimens, or interrupted treatment were excluded. A cohort of 57 gender- and age-matched healthy individuals were recruited as controls.

### Inclusion and Exclusion Criteria

The inclusion criteria for the control group were normal BMI (18-23.9 kg/m$^2$), normal thyroid function, and thyroid ultrasound results, and the exclusion criteria were consistent with those for screening the patients. The mean age was 37.67±12.77 years for males and 38.00±12.57 years for females in the control group. The two cohorts of participants were well-balanced in terms of age ($p$>0.05) and shared the same grouping method, numbering, and sample size of each subgroup.

### Treatment Method and Efficacy of Hyperthyroidism

Patients received 20-30 mg/d of thiamazole as initial therapy and underwent a periodic review of thyroid function, and the dose of medication was adjusted according to the treatment effect. Thiamazole was replaced by propylthiouracil if drug intolerance was reported. The duration of the anti-thyroid medication protocol was one year. The criteria for effective treatment were that T3, T4, and TSH were in the normal range, and the symptoms and signs of hyperthyroidism disappeared.

### Outcome Measures

All patients received body composition analysis and grip strength tests before and after one year of treatment, and the control group received the test at enrollment.

#### Grip strength test

Saehan SH5001 hydraulic grip strength meter (Physiomed Elektromedizin Corp., Bavaria, Germany) was used. The American Hand Therapy Association standardized grip strength measurement method was employed, and the data were recorded after grasping the grip strength device for 5 s. The test was performed three times with an interval of 60 s each time. Both hands were tested, and the highest result was adopted as the grip strength value, and the grip strength value was measured in kg.

#### Body composition analysis

Body composition was measured using a DISCOVERY QDR dual-energy X-ray bone densitometer (Hologic Corp., Bedford, MA, USA) with a CV of 1.69% fat content and 0.53 muscle content. Only close-fitting clothing without metal objects was allowed during the measurement, and calibration and quality testing were performed before measurement. Skeletal muscle mass = total muscle mass of the limbs (kg)/height (m)$^2$.

### Statistical Analysis

All data were statistically analyzed using SPSS 19.0 (IBM Corp., Armonk, NY, USA). Normally distributed variables were expressed as mean ± standard deviation. A paired-sample $t$-test was used for pre- and post-treatment comparisons, and an independent-sample $t$-test was used for intergroup analyses, with differences considered statistically significant at $p$<0.05.

## Results

### Treatment Outcome of Hyperthyroidism

After one year from treatment, male and female patients exhibited decreased T3 and T4 expression and increased TSH expression compared to pretreatment ($p$<0.05). After one year from treatment, no statistical significance was found in the levels of T3, T4, and TSH expression in the patients compared with the controls ($p$>0.05) (Table I).

### Total Fat Mass

Before treatment, total fat mass was lower in all patients than in the controls ($p$<0.05), and after treatment, the patients had significantly increased total fat mass ($p$<0.05). The total fat mass of patients in male group B remained lower than in the control group after treatment ($p$<0.05), and the difference between the control subgroups with other subgroups was not statistically significant ($p$>0.05) (Table II).

**Table I.** Changes in thyroid function in patients of different genders after one year of treatment (x±s).

| Gender | T3 (nmol/ml) | T4 (nmol/ml) | TSH (mIU/l) |
|---|---|---|---|
| Male (n=21) | | | |
| Before treatment | 7.47±1.37 | 241.66±54.16 | 0.001±0.000 |
| 1 year of treatment | 1.45±0.87 | 98.66±55.86 | 2.29±0.43 |
| *t* | 10.194 | 10.056 | -2.322 |
| *p* | 0.000 | 0.000 | 0.036 |
| Male controls (n=21) | 1.12±0.43 | 87.27±24.50 | 2.02±0.59 |
| Before treatment | 7.70±2.09 | 244.49±65.19 | 0.001±0.000 |
| 1 year of treatment | 1.54±2.52 | 101.96±25.43 | 2.31±0.41 |
| *t* | 10.567 | 10.745 | -2.415 |
| *p* | 0.000 | 0.000 | 0.041 |
| Female controls (n=36) | 1.26±0.32 | 98.89±.14.69 | 1.86±0.41 |

**Table II.** Total fat mass, body fat percentage, and body mass index.

| Groups | Total fat mass, (g) | Body fat percentage (%) | Body mass index (kg/m$^2$) |
|---|---|---|---|
| Male group A (n=12) | | | |
| Before treatment | 11,341.68±2,474.69 [b] | 21.80±3.99 | 19.48±3.14 [b] |
| After treatment | 15,474.08±2,844.21 [a] | 25.97±4.42 [a] | 20.99±3.04 [a] |
| Male controls A(n=12) | 15,118.05±1,701.67 | 23.09±1.71 | 22.87±1.73 |
| Female group A (n=19) | | | |
| Before treatment | 12,405.95±1,231.87 [b] | 24.50±2.18 [b] | 16.46±1.93 [b] |
| After treatment | 14,674.96±1,599.92 [a] | 28.94±3.80 [a] | 19.78±2.18 [a] |
| Female controls A (n=19) | 14,853.60±1,656.98 | 29.50±2.18 | 20.58±0.57 |
| Male group B (n=8) | | | |
| Before treatment | 13,324.02±2,186.59 [b] | 25.70±4.65 | 18.65±2.13 [b] |
| After treatment | 16,450.06±3,176.51 [a b] | 27.89±4.99 [a] | 19.17±2.13 [a b] |
| Male controls B (n=8) | 19,030.75±1,477.25 | 27.94±3.11 | 24.29±1.71 |
| Female group B (n=13) | | | |
| Before treatment | 13,335.14±2,186.59 [b] | 30.71±3.62 [b] | 17.64±3.12 [b] |
| After treatment | 16,916.23±2,842.25 [a] | 33.89±3.62 [a] | 20.70±3.41 [a] |
| Female controls B (n=13) | 17,224.23±2,403.30 | 32.71±3.62 | 19.43±1.22 |
| Group C (n=5) | | | |
| Before treatment | 12,625.38±1,231.88 [b] | 27.98±3.68 | 19.74±2.04 |
| After treatment | 15,497.14±1,762.58 [a] | 34.90±3.96 [a b] | 21.07±2.37 [a] |
| Control group C(n=5) | 15,654.31±1,809.30 | 31.34±3.59 | 20.89±0.98 |

[a] indicates $p<0.05$ when compared with before treatment. [b] indicates $p<0.05$ when compared with controls.

### Body Fat Percentage

Before treatment, there was no statistically significant difference ($p> 0.05$) between the body fat percentage of patients in male groups A and B compared with the control group, while the body fat percentage of patients in female groups A, B, and C was lower than that of the control group ($p<0.05$). After treatment, body fat percentage was significantly elevated in all patients ($p<0.05$), with no statistically significant difference between groups A and B and the control group in both sexes ($p>0.05$), while group C showed a higher result than the controls ($p<0.05$) (Table II).

### Body Mass Index

Before treatment, patients in groups A and B had a lower BMI than the controls ($p<0.05$), and there was no statistically significant difference between group C and the control group ($p> 0.05$). After treatment, patients in male group A and female groups A and B exhibited substantially elevated BMI ($p<0.05$), and no significant changes were reported in male group B ($p>0.05$). There was no statistically significant difference in BMI between male A and female A, B, and C groups of patients after treatment compared with the control group ($p>0.05$). In contrast, male group B showed a lower mean BMI than the control group ($p<0.05$). (Table II)

### Total Lean Tissue Mass

The total lean tissue mass was markedly increased in male and female group A ($p<0.05$),

**Table III.** Total lean tissue mass, ASMI, and grip strength.

| Groups | Total lean tissue mass (g) | ASMI (kg/m²) | Grip strength of the dominant hand (kg) |
|---|---|---|---|
| Male group A (n=12) | | | |
| Before treatment | 41,183.75±6,874.62 | 6.13±1.01[b] | 39.83±7.12[b] |
| After treatment | 43,870.45±6,957.62[a] | 6.95±1.22[a] | 42.62±5.35[a] |
| Male controls A(n=12) | 42,492.23±4,043.08 | 7.15±0.95 | 46.45±4.65 |
| Female group A (n=19) | | | |
| Before treatment | 31,150.05±2,663.14[b] | 5.17±0.94[b] | 26.45±6.57 |
| After treatment | 32,255.00±2,786.83[ab] | 5.51±0.99[ab] | 28.00±4.33 |
| Female controls A (n=19) | 36,628.44±2,309.81 | 6.15±0.61 | 27.45±3.14 |
| Male group B (n=8) | | | |
| Before treatment | 38,900.51±8,919.1[b] | 6.22±1.38[b] | 32.83±8.61[b] |
| After treatment | 37,365.08±9,971.78[b] | 6.07±1.55[b] | 38.88±5.44[ab] |
| Male controls B (n=8) | 46,163.87±4,298.24 | 7.27±0.40 | 42.64±5.15 |
| Female group B (n=13) | | | |
| Before treatment | 32,863.58±6,967.25[b] | 4.97±1.21[b] | 21.78±5.66[b] |
| After treatment | 32,480.71±6,705.77[b] | 4.98±1.12[b] | 22.27±4.85 |
| Female controls B (n=13) | 34,141.18±3,405.67 | 5.62±0.51 | 24.25±3.94 |
| Group C (n=5) | | | |
| Before treatment | 31,570.15±9,607.32[b] | 4.13±0.39[b] | 16.56±2.93[b] |
| After treatment | 30,010.78±8,994.67[ab] | 4.04±0.58[b] | 16.99±1.67[b] |
| Control group C (n=5) | 33,471.24±3,711.99 | 5.59±0.60 | 23.65±2.60 |

[a]indicates $p<0.05$ when compared with before treatment. [b]indicates $p<0.05$ when compared with controls.

showed no significant changes in male and female group B ($p>0.05$), and exhibited a marked decline in group C ($p<0.05$) (Table III).

### ASMI

Significantly elevated ASMI after treatment was observed in male and female group A ($p<0.05$), while no significant changes were detected in ASMI after treatment in groups B and C ($p>0.05$) (Table III).

### Grip Strength

All patients in groups A and B exhibited enhanced grip strength, while the enhancement of grip strength in patients of group C was minor ($p>0.05$) (Table III).

## Discussion

The accelerated metabolism caused by hyperthyroidism leads to a decrease in skeletal muscle and fat mass. Clinical experience indicates that effective anti-hyperthyroidism treatment and adequate nutrient supplementation steadily increase body weight throughout treatment[3]. However, the rate of change is inconsistent across body components with variable growth rates. In the early and middle stages of treatment, there is a rapid increase in fat mass[4], which may be associated with various factors, such as increased insulin resistance and downregulation of FGF21 during hyperthyroidism[5-7] and may be related to frugal metabolism following rapid caloric expenditure[8]. It has been reported that an increase in body fat percentage contributes to the increased incidence of metabolic diseases in hyperthyroid patients, whereas muscle mass changes are debated with inconsistent results from different studies. A research[9] based on animal models of hyperthyroidism showed mild to moderate muscle atrophy in 45% of hyperthyroid animals even after the stabilization of thyroxine levels. Clinical studies of hyperthyroidism have demonstrated that fat- and muscle-based lean tissue weight gain occurs after treatment, with rapid growth in fat mass early in treatment and even faster growth in skeletal muscle weight after 3-6 months[10-12]. A study on northern Chinese residents[2] showed that well-controlled male patients with hyperthyroidism still had decreased trunk muscle compared to controls. In contrast, female patients had no significant differences in muscle at all sites compared to controls.

The results of this study showed that patients across all age groups of both sexes had increased body fat percentage after treatment, which was similar to the results of previous studies. Another possibility is that the rate of fat mass growth preceded other body components or that other body components were not effectively restored. The results of this study showed that the total fat mass in each subgroup was not significantly different from the control group, suggesting that the total fat mass remained at an average level. It has been shown that changes in T3 levels may be associated with variations in muscle mass compared with adipose tissue involving various factors, including race, age, gender, and micronutrient availability[13]. Studies[14,15] have revealed a close association between thyroid functional status and skeletal muscle growth and function. In healthy populations, the rate of skeletal muscle growth is lower in middle-aged and elderly people than in adolescents, with an overall trend of decreasing muscle mass and muscle mass and strength in men exceeding that of women. Therefore, the assessment of muscle recovery in patients with hyperthyroidism must involve consideration of the effects of age and gender. The rate of skeletal muscle synthesis tends to decrease with age due to various factors, such as the downregulation of sex and growth hormones[16]. Therefore, skeletal muscle recovery after treatment in hyperthyroid patients is influenced by age.

Skeletal muscle atrophy due to hyperthyroidism is considered a subtype of metabolic sarcopenia. Extensive clinical, patient, and animal model studies[17] have confirmed that hyperthyroidism affects muscle mass, muscle metabolism, and nerve conduction. However, no reliable means of assessing hyperthyroid skeletal muscle other than muscle biopsy is available. Some scholars[18] have studied hyperthyroid skeletal muscle lesions from the perspective of sarcopenia. In this study, we opted for ASMI and grip strength, indicators widely used to assess sarcopenia, and confirmed the value of these indicators in a previous study[19]. We used 40 and 60 years of age as age cut-offs, and the results showed subgroups of patients over 40 years with suboptimal increments in ASMI by gender, which is consistent with our previous hypothesis. The results of this study showed differences in ASMI increments in males and females. Even in patients aged 40-59 years with suboptimal ASMI increments, their grip strength also showed a significant increase, suggesting that anti-hyperthyroidism treatment can improve skeletal muscle strength despite failure to increase muscle mass and that changes in muscle strength levels are associated with interference with skeletal muscle adrenergic receptors by glycogen metabolism, electrolytes and high levels of T3[20,21]. The long-term effects of muscle atrophy in hyperthyroid patients are of concern since sarcopenia increases the risk of falls, decreased exercise capacity, and increased risk of cardiovascular disease development in the elderly.

A study[22] in patients with subclinical hyperthyroidism with toxic nodules suggested that treatment with I131 significantly increased muscle mass in patients >65 years of age and >60 years of age, while muscle mass was not significantly altered in all patients. Another study[23] demonstrated no significant increase in BFP and lean tissue mass three months before I131 treatment, which differed in outcome from our study. Whether the treatment regimen affects the outcome requires further controlled studies for clarification.

## Conclusions

Muscle metabolism is closely related to diet and exercise in addition to unchangeable factors, such as age and sex. A high-protein diet enhances skeletal muscle development, but the effect of a high-protein diet on myasthenia due to hyperthyroidism has not been verified[24]. Research has shown that resistance exercise can improve strength recovery[25] and increase arm circumference. Still, the sample size of this study was small, and the measurement of arm circumference does not accurately reflect skeletal muscle changes. The present study did not restrict the patients' diet nor encourage vigorous exercise during treatment out of safety concerns, which suggests more attention to the changes in body composition of older hyperthyroid patients, considering both BFP and skeletal muscle recovery in the treatment.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### Ethics Approval

The study was started prospectively after the approval of the Ethics Evaluation Committee of our Faculty (188/04.06.2020).

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## Informed Consent

Written informed consent was obtained from all participants.


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