Body Composition Assessed by Bioelectrical Impedance Analysis (BIA) in Patients with Graves' Disease Before and After Treatment[#]

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Abstract. Body composition was assessed by bioelectrical impedance analysis (BIA) in 11 female patients with Graves' disease and in 49 age-matched healthy Japanese women. Patients with Graves' disease were examined in the hyperthyroid state before treatment and in the stable euthyroid state after treatment with antithyroid drugs for 6 to 18 months. Body weight (BW), percent body fat (BF/BW), percent lean body mass (LBM/BW) and percent total body water (TBW/BW) were not statistically different between hyperthyroid Graves' patients and healthy subjects. Percent body cell mass (BCM/BW) was much lower in hyperthyroid Graves' patients than in healthy subjects (mean $\pm$ SEM; $33.9 \pm 2.4\%$ vs. $41.5 \pm 0.5\%$, $P < 0.001$). Percent ratio of extracellular water to total body water (ECW/TBW) was much greater in hyperthyroid Graves' patients than in healthy subjects ($53.9 \pm 3.0\%$ vs. $41.8 \pm 0.5\%$, $P < 0.001$). These abnormal ratios, BCM/BW and ECW/TBW, were normalized after treatment. Serum free T_4 levels showed a positive correlation with ECW/TBW ($r = 0.779$) and a reverse correlation with BCM/BW ($r = -0.760$) in all of the patients with Graves' disease examined. These findings indicate that body composition is affected by thyroid hormones and that body composition in hyperthyroid Graves' disease is characterized by decreased BCM associated with increased ECW.

Key words: Body composition, Bioelectrical impedance analysis, Body cell mass, Extracellular water, Free T_4 , Graves' disease

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ASSESSMENT of body composition by bioelectrical impedance analysis (BIA) has been validated by a strong correlation with hydro-densitometry and the isotope dilution method [1–7]. Recent studies also indicated a strong correlation between BIA and dual energy X-ray absorptiometry (DEXA) [8, 9]. By measuring resistance and reactance simultaneously, BIA delineates human body weight (BW) as composed of three compartments: body fat mass

(BF), body cell mass (BCM) and extracellular mass (ECM). BCM and ECM are called lean body mass (LBM). BCM is defined as the total mass of the protein-rich portion of the body and is associated with supporting intracellular water (ICW). ECM reflects the constituents of the body involved in transport and support, including extracellular water (ECW) and the skeleton [10]. The relative distribution of total body water (TBW) in intracellular and extracellular compartments can serve as an indicator of the compositional change [11].

It is well known that the body composition changes strikingly with the increase in gonadal hormone levels and secondary sexual maturation. Men have 1.5 times LBM and almost 1.5 times the skeletal mass of women, whereas women have twice as much BF as men [12, 13]. Recently, body

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composition assessed by BIA as well as the isotope dilution method showed an increase in BCM as well as the ECW/ICW ratio, and a decrease in BF in patients with acromegaly [14, 15]. Whereas body composition of patients with GH deficiency was characterized by increased BF and decreased TBW [15, 16]. Other investigators have indicated that body composition in cases of malnutrition is characterized by a depletion of BCM associated with an expansion of ECM [17, 18]. Every patient with hyperthyroidism is generally associated with a varying degree of muscular atrophy [19], which is difficult to assess in the average patient. The body composition of patients with hyperthyroidism remains to be assessed by BIA.

In the present study, we applied BIA to the investigation of body composition in 11 patients with Graves' disease before and after treatment.

Subjects and Methods

Subjects

Eleven female patients with Graves' disease aged 15 to 71 (mean $\pm$ SEM: 36.3 ± 6.0 yr), and 49 healthy Japanese women aged 17 to 65 yr (38.3 ± 1.8 yr), were examined in the present study. The patients were examined in the hyperthyroid state before treatment and also in the stable euthyroid state after treatment with antithyroid drugs. Age and sex matched healthy subjects were selected from healthy medical staff and the general population.

All the patients were followed by our outpatient clinic for the evaluation of thyroid functions every one to three months. Either thimazole (TMA) or propylthiouracil (PTU) was prescribed to treat hyperthyroidism for 6 to 18 months. The antithyroid agents were ceased when serum free thyroxine (FT₄), thyrotropin (TSH) and thyrotropin binding inhibiting immunoglobulin (TBII) entered their normal ranges, and normal responses of serum TSH and triiodothyronine (T₃) to thyrotropin releasing hormone (TRH) were restored as described previously [20]. The euthyroid state remained for more than 3 months without any medication as confirmed by examination after treatment.

Thyroid functions

Basal serum T₃, T₄, FT₄ and TSH were measured

by conventional RIA kits [20]. Normal ranges for serum T₃, T₄, FT₄ and TSH are 90–195 ng/dl, 5.4–13.5 μ g/dl, 0.7–1.9 ng/dl and 0.32–3.70 μ U/ml, respectively. ⁹⁹Tc scintigraphy of the thyroid and serum TBII were also monitored [20].

Bioelectrical impedance analysis

The BIA was performed by means of Spectrum II 286 equipment (RJL System Inc., Detroit, Michigan, USA) as described previously [15]. The body composition was calculated by a computerized program, Weight Manager Professional, which was provided by the manufacturer. According to the three-compartment model, BW is considered to consist of BF, BCM and ECM [14]. Total body water (TBW) is the sum of ECW and ICW.

Statistics

The results are given as the mean $\pm$ SEM. Statistical significance was evaluated by analysis of the variance in combination with Student's *t*-test. The correlation among variables was analyzed by standard linear regression. *P* value less than 0.05 was considered significant.

Results

The thyroid functions were considerably elevated in our Graves' patients before treatment (hyperthyroid Graves' patients) with the mean ($\pm$ SEM) serum T₃, T₄, FT₄, TSH and TBII levels being 571.0 ± 94.6 ng/dl, 22.1 ± 1.7 μ g/dl, 6.8 ± 0.7 ng/dl, 0.04 ± 0.02 μ g/ml and $47.6 \pm 8.6\%$, respectively, and they were normalized after treatment (euthyroid Graves' patients: T₃, 118.8 ± 6.3 ng/dl; T₄, 7.7 ± 0.7 μ g/dl; FT₄, 1.2 ± 0.1 ng/dl; TSH, 1.43 ± 0.43 μ U/ml; TBII, $8.0 \pm 2.5\%$).

There was no statistical difference in BW, BMI, percent body fat (BF/BW), percent lean body mass (LBM/BW) and percent total body water (TBW/BW) between the hyperthyroid Graves' patients and the healthy subjects (Fig. 1 and Table 1). The percent body cell mass (BCM/BW) was much lower in the hyperthyroid Graves' patients than in the healthy subjects ($33.9 \pm 2.4\%$ vs. $41.5 \pm 0.5\%$, $P < 0.001$). The percent ratio of extracellular water to total body water (ECW/TBW) was much greater in the hyperthyroid Graves' patients than in the

healthy subjects ($53.9 \pm 3.0\%$ vs. $41.8 \pm 0.5\%$, $P < 0.001$), and these altered BCM/BW and ECW/TBW were corrected in the euthyroid Graves' patients ($39.9 \pm 0.9\%$ and $43.3 \pm 0.6\%$, respectively).

In all the patients with Graves' disease, before and after treatment, there was a reverse correlation between BCM/BW and serum FT₄ levels ($r = -0.760$, $P < 0.0001$, Fig. 2) and a positive correlation between ECW/TBW and serum FT₄ levels

($r = 0.779$, $P < 0.0001$, Fig. 3). Serum T₃ and T₄ levels also showed a reverse correlation with BCM/BW ($r = -0.686$, $P < 0.0005$ and $r = -0.640$, $P < 0.002$, respectively) and a positive correlation with ECW/TBW ($r = 0.741$, $P < 0.0001$ and $r = 0.738$, $P < 0.0001$, respectively).

In the healthy subjects, there was a positive cor-

Fig. 1. Percent body fat (BF/BW), percent body cell mass (BCM/BW) and percent extracellular water (ECW/TBW) in 11 patients with Graves' disease in the hyperthyroid state and in the euthyroid state, and in 49 healthy Japanese women. Mean ($\pm$ SEM) values are shown. a, $P < 0.001$ vs. healthy subjects; b, $P < 0.025$ vs. hyperthyroid patients; c, $P < 0.05$ vs. hyperthyroid patients.

Fig. 2. Correlation between percent body cell mass (BCM/BW) and serum free T₄ levels in 11 patients with hyperthyroid Graves' disease in the hyperthyroid state (○) and in the euthyroid state (●). A linear regression line was obtained ($y = -1.532x + 43.425$, $r = -0.760$, $P < 0.0001$).

Table 1. Body composition in 11 female patients with Graves' disease and 49 healthy women

	Graves' disease		Healthy
	Hyperthyroid	Euthyroid	
n	11	11	49
Age (yr)	36.3 $\pm$ 6.0	40.1 $\pm$ 3.4	38.3 $\pm$ 1.8
BW (kg)	49.5 $\pm$ 2.2	52.8 $\pm$ 1.3	51.6 $\pm$ 0.5
BMI (kg/m ²)	20.5 $\pm$ 0.6 ^a	22.6 $\pm$ 0.6 ^d	21.7 $\pm$ 0.2
Resistance (Ω)	586.5 $\pm$ 10.6	546.1 $\pm$ 14.3 ^c	564.0 $\pm$ 7.0
Reactance (Ω)	47.3 $\pm$ 4.5 ^b	54.9 $\pm$ 1.7 ^a	60.6 $\pm$ 1.2
BF/BW (%)	22.0 $\pm$ 1.4	21.2 $\pm$ 1.3	20.8 $\pm$ 0.6
LBM/BW (%)	78.0 $\pm$ 1.4	78.8 $\pm$ 1.3	79.2 $\pm$ 0.6
BCM/BW (%)	33.9 $\pm$ 2.4 ^c	39.9 $\pm$ 0.9 ^d	41.5 $\pm$ 0.5
TBW/BW (%)	57.1 $\pm$ 1.0	58.3 $\pm$ 0.8	58.0 $\pm$ 0.4
ECW/TBW (%)	53.9 $\pm$ 3.0 ^c	43.3 $\pm$ 0.6 ^e	41.8 $\pm$ 0.5

Values are shown as the mean $\pm$ SEM. ^a, $P < 0.05$, ^b, $P < 0.025$, ^c, $P < 0.001$ vs. healthy subjects; ^d, $P < 0.05$, ^e, $P < 0.025$ vs. hyperthyroid. LBM/BW, percent lean body mass in body weight; BCM/BW, percent body cell mass in body weight; TBW/BW, percent total body water in body weight; ECW/TBW, percent ratio of extracellular water to total body water.

Fig. 3. Correlation between percent extracellular water (ECW/TBW) and serum free T_4 levels in 11 patients with Graves' disease in the hyperthyroid state ($\circ$) and in the euthyroid state ($\bullet$). A linear regression line was obtained ($y=2.142x + 39.472$, $r=0.779$, $P<0.0001$).

relation between ECW/TBW and age ($r=0.313$, $P<0.05$, Fig. 4, upper panel). In contrast, no such correlation was obtained in the patients with hyperthyroid Graves' disease (Figs. 4, lower panel).

Discussion

In the present study, we found that the body composition of hyperthyroid Graves' patients is characterized by a lowered BCM/BW and an elevated ECW/BW. These findings are consistent with those of patients with malnutrition derived from different diseases [10, 11, 15, 16]. In contrast to a malnutritional state, however, BF/BW, LBM/BW and TBW/BW in the hyperthyroid patients were not different from those of healthy subjects.

Thyroid hormones play an important role in a variety of metabolic processes in the body, influencing the growth and maturation of tissues, total energy expenditure, etc. [21]. No tissue or organ system escapes the adverse effects of thyroid hormone excess. In the hypermetabolic state induced by hyperthyroidism, calorogenesis is enhanced by transmembrane Na^+ - K^+ -ATPase activity due to an increased number of pumps [22–24]. Glucose utilization, especially in the skeletal muscle, is

Fig. 4. Correlation between percent extracellular water (ECW/TBW) and age in 49 healthy women (upper panel), and in 11 female patients with hyperthyroid Graves' disease (lower panel). A linear regression line was obtained in healthy women ($y=0.089x + 38.423$, $r=0.313$, $P<0.05$).

stimulated [25, 26] and protein synthesis is inhibited with increased nitrogen excretion. The increased transmembrane exchange of extracellular K^+ for intracellular Na^+ in hyperthyroidism may result in an abnormal electrochemical gradient, which is characterized by a loss of ICW in the BCM and an expansion of ECW in the ECM.

It has been reported that BCM changes correlate with energy and protein intakes [10]. In hyperthyroidism, despite an increased food intake, a state of chronic caloric and nutritional inadequacy en-

sues resulting in a negative nitrogen balance, muscle wasting, weakness and loss of weight. BCM depletion and ECW expansion in the hyperthyroid Graves' patients may have been the result of increased energy expenditure or protein catabolism induced by thyroid hormones excess, and it is deducible that BCM and ECW are relatively more sensitive to the metabolic action of thyroid hormones than BF and TBW.

We previously reported that BF/BW is correlated with age in healthy subjects [15]. In the present study, ECW/TBW showed a correlation with age in healthy subjects whereas there was no correlation in hyperthyroid Graves' patients, although the variations of the values were large in a small number of subjects.

The present study indicates that BIA reflects altered body composition in patients with Graves' disease, suggesting that BCM/BW and ECW/TBW

may serve as a sensitive indicator of metabolic conditions in patients with Graves' disease before and after treatment. Further studies with a large number of patients are however required to address this issue.

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