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Body Composition Assessed by Bioelectrical Impedance Analysis (BIA) and the Correlation with Plasma Insulin-Like Growth Factor I (IGF-I) in Normal Japanese Subjects and Patients with Acromegaly and GH Deficiency

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Abstract. Body composition was assessed by bioelectrical impedance analysis (BIA) in 100 Japanese normal adults, 9 patients with acromegaly and 11 patients with growth hormone (GH) deficiency. Body weight (BW) was greater in normal males than in normal females. Percent body fat (BF/BW) was greater in females than in males and was increased with age in both sexes. Percent total body water (TBW/BW) was less in females than in males. Although percent extracellular water (ECW/BW) was not different between both sexes, the ECW/TBW ratio was greater in females than in males. Percent body cell mass (BCM/BW) was lower in females than in males. The patients with acromegaly had a lower percent BF but a higher percent TBW, percent ECW and ECW/TBW ratio than normal subjects, while the patients with GH deficiency had a higher percent BF and ECW/TBW ratio, but lower percent TBW. Percent body cell mass (BCM/BW) was higher in acromegaly and lower in GH deficiency than in normals. There was a negative correlation ($r=-0.62$) between plasma IGF-I levels and percent BF, whereas a positive correlation ($r=0.51$) was found between the plasma IGF-I level and percent BCM. It is suggested, therefore, that body composition is affected by sex and age in normals, and by GH secretion in patients with pituitary dysfunction. Plasma IGF-I levels may be one of the factors responsible for alterations in body composition.

Key words: Body composition, BIA, Body fat, IGF-I, Acromegaly, GH deficiency.

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BIOELECTRICAL impedance analysis (BIA) is being increasingly utilized for estimating body composition such as total body water (TBW), lean body mass (LBM) and body fat (BF) [1–3]. The principle of BIA is based on the conduction of applied electrical current. The resistance of LBM is far less than that of BF due to the distribution of body fluids and electrolytes. Cell membranes in the body, which separate extracellular water (ECW) and intracellular water (ICW), act as capacitors and are responsible for the reactance of the body [1–3]. Body composition can therefore be evaluated by BIA, in which both resistance and reactance are measured and computed on the basis of mathematical relationships and physiological assumptions [4]. BIA was proved to be accurate in normal subjects by comparing it with isotope dilution methods and hydrodensitometry [1, 2, 5–7]. BIA has also been validated in the assessment of body composition in patients with acromegaly [9] and obesity [10].

Body composition assessed by isotope dilution methods showed an increase in body cell mass (BCM) as well as the ECW/ICW ratio, and a de-

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crease in BF in patients with acromegaly [11, 12]. On the other hand, the body composition of patients with GH deficiency was characterized by increased BF and decreased TBW [13, 14]. These influences of GH may be due to its anabolic, lipolytic and anti-natriuretic effects. GH secretion is well reflected by plasma insulin-like growth factor I (IGF-I) levels in these subjects [15–18]. However, the relationship between body composition assessed by BIA and plasma IGF-I has not been fully elucidated.

In the present study, we first investigated the body composition in normal Japanese adults, and the relationship between body composition and plasma IGF-I in normal adults and adult patients with acromegaly and GH deficiency.

Materials and Methods

Subjects

One hundred normal Japanese adults, 68 males and 32 females, aged 21 to 70 yr, 9 patients with acromegaly, 8 males and 1 female, aged 39 to 70 yr, and 11 patients with GH deficiency, 8 males and 3 females, aged 20 to 73 yr, were examined in the present study. Normal adults were screened by both physical and biochemical examinations in a mass health checkup. The diagnosis of acromegaly was made by typical clinical findings, supported by their high plasma GH and IGF-I levels. The diagnosis of patients with GH deficiency was supported by low levels of plasma IGF-I and by a lack of plasma GH responses to provocative stimuli. Thyroid and adrenal functions were kept normal by appropriate supplement therapy.

BIA and blood examinations were performed in all the subjects after overnight fasting. Body weight and height were measured in barefoot in the morning.

Bioelectrical impedance analysis

Bioelectrical impedance was obtained by measuring resistance and reactance in the supine position by means of Spectrum II 286 equipment (RJL Systems Inc, Detroit, Michigan, USA) according to the instructions from the manufacturer. The tetrapolar electrodes were placed in the middle of the dorsal surface of the right hand and foot, respectively. The introduction electrodes were positioned proximally to the metacarpal-phalangeal and metatarsal-phalangeal joints. The detecting electrodes were positioned medially between the distal prominences of the radius and the ulna and between the medial and lateral malleoli at the ankle. A 800 μA of at 50 kHz was introduced as the exciting current.

Body composition was calculated by means of two different programs, Weight Manager (version 2.0) and Weight Manager Professional, which were provided by the manufacturer, for analysis of a two-compartment model and a three-compartment model, respectively. According to the two-compartment model, body weight (BW) is the sum of BF and LBM. In the three-compartment model, BW is considered to consist of BF, BCM and extracellular mass (ECM) [19, 20]. TBW and ECW were also obtained by means of the Weight Manager Professional, based on the relationship in which body resistance reflects TBW [2] whereas whole body reactance is closely related to ECW [21]. TBW is the sum of ECW and ICW.

Plasma IGF-I concentrations

Blood samples were collected from the antecubital vein. Plasma was promptly separated and stored at $-20°C$ until assayed. IGF-I concentrations were determined by specific radioimmunoassay after extraction with acid-ethanol as described previously [22]. Recombinant human IGF-I (lot B1516YS) and anti-IGF-I antibody (lot B0166S) were kindly supplied by Fujisawa Pharmaceutical Co. (Osaka, Japan). The IGF-I was iodinated with ^{125}I (Amersham, UK) by the lactoperoxidase method. The minimum detectable quantity was 0.5 ng/m*l* and the mean intra- and interassay coefficients of variation were 3.8% and 5.6%, respectively.

Statistics

Statistical differences were evaluated by analysis of variance in combination with Student's *t* test. The correlation between two variables was analyzed by linear regression. *P* value less than 0.05 was considered significant.

Results

Body weight (BW) was greater in normal males than in normal females. Percent BF (BF/BW) was greater in females than in males (mean ± SEM, 20.4±0.6% *vs.* 15.5±0.4%, $P<0.005$), while percent TBW (TBW/BW) was less in females than in males (58.3±0.4% *vs.* 61.8±0.3%, $P<0.005$) (Table 1). Furthermore, the percent BF was increased with age in both sexes and a positive correlation was obtained between percent BF and age (males r=0.41, $P<0.01$; females r=0.41, $P<0.025$, Fig. 1). The percent ratio of ECW/TBW was greater in females than in males (41.0±0.6% *vs.* 39.3±0.4%, $P<0.025$). In contrast, percent BCM (BCM/BW) was greater in males than in females (48.2±0.4% *vs.* 42.3±0.4%, $P<0.005$).

Acromegalic patients had a lower percent BF and higher percent TBW than normal subjects as a

Table 1. Body composition in normal adults and adult patients with acromegaly and GH deficiency

	Normal			Acromegaly	GH deficiency
	Male	Female	Total		
n	68	32	100	9	11
Age (yr)	42.4±1.2[a]	41.3±1.7	42.0±1.0	45.7±3.3	47.2±7.3
BW (kg)	61.6±0.7	51.1±0.7[c]	58.2±0.7	68.9±3.0[e]	71.3±2.5[e]
BMI (kg/m²)	22.5±0.2	21.6±0.2[c]	22.2±0.1	23.5±0.4[d]	24.3±0.9[d]
BF/BW (%)	15.5±0.4	20.4±0.6[c]	17.1±0.4	11.0±1.3[e]	27.8±2.2[e]
TBW/BW (%)	61.8±0.3	58.3±0.4[c]	60.7±0.3	65.2±1.0[e]	52.9±1.6[e]
BCM/BW (%)	48.1±0.4	42.3±0.7[c]	46.2±0.4	50.0±2.1[d]	36.8±1.3[e]
ECW/BW (%)	24.3±0.3	23.9±0.4	24.2±0.2	27.8±0.8[e]	25.2±1.2
ECW/TBW (%)	39.4±0.4	41.0±0.6[b]	39.9±0.3	42.7±0.8[e]	47.9±2.2[d]

[a], mean±SEM; [b], $P<0.025$ *vs.* males; [c], $P<0.005$ *vs.* males; [d], $P<0.025$ *vs.* normal (total); [e], $P<0.005$ *vs.* normal (total). BF/BW, percent body fat; TBW/BW, percent total body water; BCM/BW, percent body cell mass; ECW/BW, percent extracellular water; ECW/TBW, percent ratio of extracellular water to total body water.

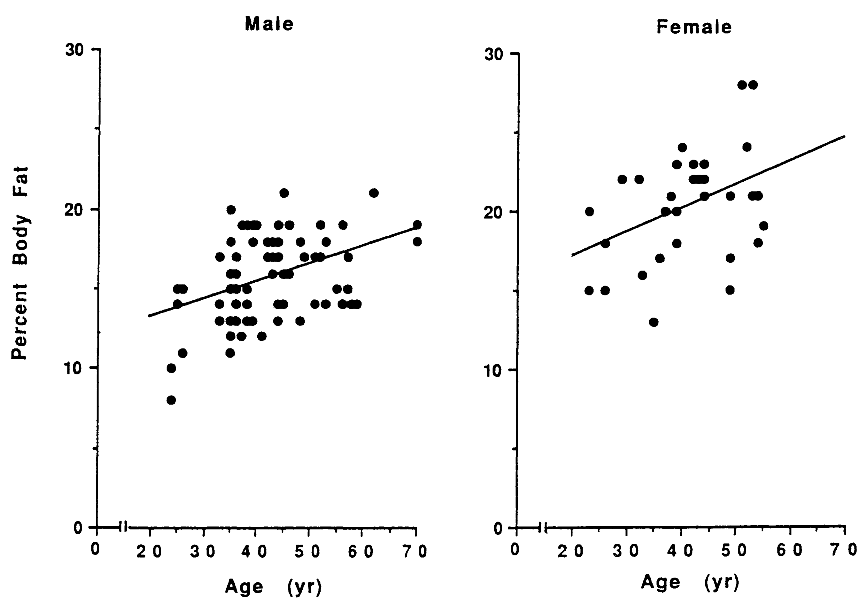

Fig. 1. Correlation between percent body fat and age in normal Japanese male and female adults. A linear regression line was obtained for each sex and the slope was steeper in females (right panel) than in males (left panel) (males y=11.050+0.109x r=0.41, $P<0.01$; females y=14.086+0.152x, r=0.41, $P<0.025$).

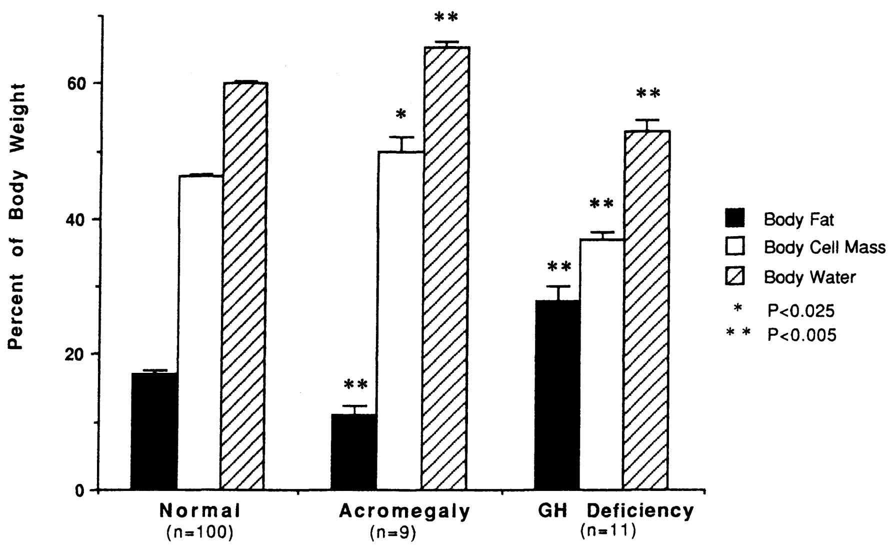

Fig. 2. Percent body fat (BF/BW), percent body cell mass (BCM/BW) and percent total body water (TBW/BW) of body weight (BW) in normal subjects and patients with acromegaly and GH deficiency. Mean (±SEM) values are shown. *, $P<0.05$, **, $P<0.005$ *vs.* normal subjects. Numbers of subjects are shown in parentheses.

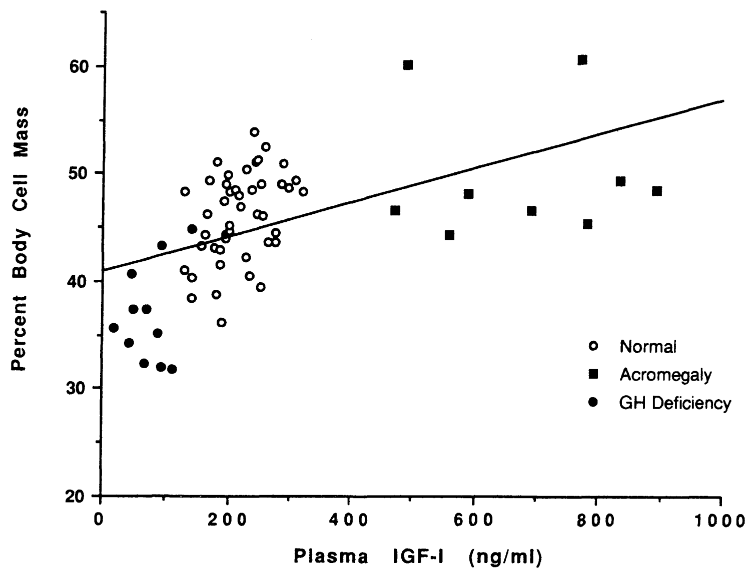

Fig. 3. Correlation between body fat (BF/BW) as a percentage of body weight (BW) and plasma IGF-I levels in normal adults (○) and adult patients with acromegaly (■) and GH deficiency (●). A linear regression line was obtained (y=23.844−0.021x, r=−0.62, $P<0.005$).

total (BF/BW, 11.0±1.3% *vs.* 17.1±0.4%, $P<0.005$; TBW/BW, 65.2±1.0% *vs.* 60.7±0.3%, $P<0.005$) (Fig. 2). The patients with acromegaly were also associated with a higher percent BCM, percent ECW and percent ratio of ECW/TBW (Table 1). In contrast, GH deficiency had a higher percent BF (27.8±2.2%, $P<0.005$) but a lower percent TBW (52.4±1.6%, $P<0.005$) than normal subjects (Fig. 2). They also had a lower percent BCM and higher percent ratio of ECW/TBW than normal subjects

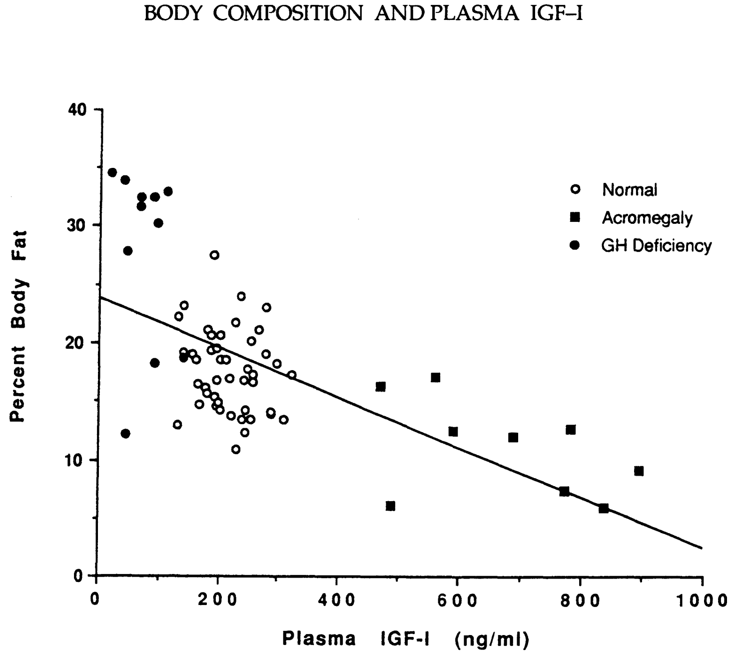

Fig. 4. Correlation between percent body cell mass (BCM/BW) and plasma IGF-I levels in normal adults (○) and adult patients with acromegaly (■) and GH deficiency (●). A linear regression line was obtained (y=40.932+0.016x, r=0.51, $P<0.005$).

(Table 1). There was no significant difference between normal subjects and those with GH deficiency in the percent ECW.

Mean (±SE) plasma IGF-I concentrations were 217±7 ng/m*l* in normal subjects. Plasma IGF-I levels were higher in acromegaly (675±51 ng/m*l*, $P<0.01$) and lower in GH deficiency (74±11 ng/m*l*, $P<0.005$) than in normal subjects. Plasma IGF-I concentrations were negatively correlated with percent BF (r=−0.62, $P<0.005$) (Fig. 3) and positively correlated with percent BCM (r=0.51, $P<0.005$), respectively, in all of the subjects examined (Fig. 4).

Discussion

The bioelectrical impedance technique was validated to assess body composition by a number of studies [1–3, 5–10] and BIA was proved to be a more accurate method to assess human body composition than anthropometry [9] and the body mass index (BMI) [23]. In addition, BIA can measure resistance and reactance simultaneously. The reactance is known to represent the quantity of cell membrane capacitance [3] and is inversely related to both the ECM/BCM ratio [20] and ECW [21]. This makes it possible that body composition is estimated by three compartments in which BCM can represent the metabolically active components of the body [19]. BCM was previously assessed by total body potassium (TBK) since 98 to 99% of potassium is distributed intracellularly [24] and the correlation between BIA and TBK was validated [2, 20]. The two-compartment model is based on the assumption that LBM is constant during body weight changes. Patients suffering from metabolic diseases, however, may have disproportionate body compartments due to the breakdown of cell membrane barriers with a shift of fluid to the extracellular space. Since none of the three compartments of the body is of a fixed size, weight changes may be reflected in changes in BF, BCM or ECW/TBW. The ECW/TBW ratio is known to reflect the distribution of body water composition [25].

In the present study, we first measured body composition by BIA in normal Japanese adults, and in patients with acromegaly and GH deficiency. In normal adults, percent BF was greater and percent BCM as well as percent TBW was less in females than in males. The ECW/TBW ratio was higher in females than in males. Percent BF was increased with age in both sexes, suggesting that age-related metabolic or hormonal changes are, at least partly, involved in body composition. Rudman [26] suggested that the somatotrophic effect of GH declines with advancing age and the ratio of adipose tissue in the body is progressively increased.

Our findings that acromegaly was associated with less BF and greater BCM, ECW and TBW than normal controls and that GH deficiency was associated with greater BF and less BCM and TBW were consistent with other reports [11–14]. Our results indicating that percent ECW was not decreased in GH deficiency are inconsistent with other previous studies [13, 14]. The discrepancy could be explained by the ECW value which was determined directly from reactance in the present study whereas ECW was estimated indirectly from TBW [13] and resistance [14] in the previous studies. Segal *et al.* [27] reported that ECW was best predicted by resistance measured at 5 kHz. Recently, however, Scheltinga *et al.* [21] clearly demonstrated a significant relationship between whole body reactance (X_c) and the volume of ECW (X_c=116–3.73ECW, r=−0.67, P<0.005). The significant difference in percent BCM may reflect the anabolic effect of GH.

Plasma IGF-I is mainly derived from the liver under the control of GH secreted from the pituitary [18, 28], although IGF-I production in the liver is also influenced by the nutritional status [29–31]. We previously reported that plasma IGF-I declines with age more steeply in females than in males [21]. In the present study, we first demonstrated a negative correlation between percent BF and plasma IGF-I and a positive correlation between percent BCM and plasma IGF-I. These findings indicate that plasma IGF-I levels may reflect body composition in patients with pituitary disorders. The extent and possible difference in the physiological roles of GH and IGF-I in regulating body composition remain to be further investigated.

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