Erciyes Med J 2023; 45(2): 190–6 • DOI: 10.14744/etd.2023.83809
ORIGINAL ARTICLE – OPEN ACCESS

Determining the Body Composition of Patients with Acromegaly as a Cardiovascular Risk

Yasemin Aydoğan Ünsal[1], Özen Öz Gül[2], Şeyma Esenbuğa[3], Coşkun Ateş[2], Ensar Aydemir[2], Soner Cander[2], Canan Ersoy[2], Erdinç Ertürk[2]

Cite this article as:
Aydoğan Ünsal Y, Öz Gül Ö, Esenbuğa Ş, Ateş C, Aydemir E, Cander S, et al. Determining the Body Composition of Patients with Acromegaly as a Cardiovascular Risk. Erciyes Med J 2023; 45(2): 190-6.

[1]Department of Endocrinology and Diseases of Metabolism, Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital, Ankara, Türkiye
[2]Department of Endocrinology and Diseases of Metabolism, Bursa Uludağ University Faculty of Medicine, Bursa, Türkiye
[3]Department Internal Medicine, Bursa Uludağ University Faculty of Medicine, Bursa, Türkiye

Submitted
03.11.2022

Revised
07.12.2022

Accepted
14.01.2023

Available Online
01.03.2023

Correspondence
Yasemin Aydoğan Ünsal, Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital, Department of Endocrinology and Diseases of Metabolism, Ankara, Türkiye
Phone: +90 537 577 52 09
e-mail: yaseminunsalay@gmail.com

ABSTRACT

Objective: This report aimed to examine changes in constituents of body composition that correlate to cardiovascular morbidity and mortality in patients with acromegaly using bioelectrical impedance analysis (BIA).

Materials and Methods: This prospective study included 62 patients who were followed up after their acromegaly diagnosis and 40 healthy volunteers. All patients' body compositions were evaluated using a body composition analyzer (TANITA MC-780-Black) with the BIA method. The laboratory and anthropometric measurements and body composition parameters were compared between the patients with acromegaly and the controls. Moreover, these parameters were examined according to the disease activity.

Results: This study showed that patients with acromegaly have higher plasma glucose levels than the control group (p=0.001). The homeostasis model assessment-insulin resistance index of patients with acromegaly was significantly higher than that of the controls (p=0.02). The compartments of intracellular water (ICW) and extracellular water (ECW) in the patients with acromegaly were larger than that in the controls (respectively; p=0.02 and p=0.001). The lean mass of the patients with acromegaly in the trunk and extremities was significantly higher than the controls (respectively; p=0.002 and p=0.001). The compartment of muscle was significantly larger than that in the controls (p=0.001). The basal metabolism in patients with acromegaly was significantly higher than that in the controls (p=0.002).

Conclusion: Determining the body composition using the BIA method can provide important information about the cardiovascular risks in patients with acromegaly. With the BIA method, cardiovascular risk can be estimated and reduced with effective strategies.

Keywords: Acromegaly, body composition, extracellular water, insulin resistance, intracellular water

INTRODUCTION

Acromegaly is a disease mostly associated with a growth hormone (GH)-secreting pituitary adenoma (1). The GH and insulin-like growth factor-1 (IGF-1) produced after excess GH stimulation cause many complications, such as acral growth, orofacial changes, respiratory comorbidities, musculoskeletal problems, and metabolic and cardiovascular complications (2). GH and IGF-1 have important effects on the body composition (3). GH is an anabolic hormone that is antagonistic to insulin. It leads to protein synthesis, gluconeogenesis, and insulin resistance (IR) in the periphery and liver. Diabetes mellitus and impaired glucose tolerance, frequent comorbidities in patients with acromegaly, are related to the effects of GH and IGF-1 on glucose metabolism (4). GH also has a lipolytic action and increases levels of plasma-free fatty acids (5). Furthermore, excess insulin concentrations in patients with acromegaly are paradoxically associated with reduced total body fat and fat accumulation in metabolic organs (6). The term "acromegaly-specific lipodystrophy" is characterized by low adipose tissue and IR (7). Studies have shown that especially visceral adipose tissue and intrahepatic fat tissue are reduced in correlation with levels of GH (6, 8). GH also affects the body's water composition. GH activates the renin–angiotensin–aldosterone system and produces atrial natriuretic factor, prostaglandins, and nitric oxide. This mechanism results in body water retention (9).

Excess GH and IGF-1 levels in acromegaly lead to hypertension, type 2 diabetes, dyslipidemia, and endothelial dysfunction (10). GH and IGF-I enhance heart contractility, stimulate cardiomyocyte growth, and decrease systemic vascular resistance (11). Increased plasma volume, IR, and diabetes mellitus may increase the risk of hypertension (12). Moreover, the incidence of hypertriglyceridemia is almost 3 times higher in this patient population than in the general population, which may increase cardiovascular risks (13).

The literature contains many studies of body composition and metabolic results in patients with acromegaly. While Moller et al. (13) showed increased basal metabolism in patients with acromegaly than in healthy populations, Freda et al. (3) demonstrated reduced visceral and subcutaneous adipose tissue in patients with acromegaly than in controls. Furthermore, Reid et al. (14) positively correlated IGF-1 levels with skeletal muscle. These cardiovascular complications related to changes in the body composition are the important causes of mortality and morbidity in patients with acromegaly (15).

Many methods evaluate the body composition, such as computed tomography, dual-energy X-ray absorptiometry, and magnetic resonance imaging (MRI) (16). Due to the disadvantages of these methods as releasing radiation and high cost, research into newer methods is necessary. Bioelectrical impedance analysis (BIA) is one of these methods. Different body compositions, such as adipose tissue, body water, muscle, protein, and basal metabolism, can be measured by this method (7). In some studies, compared with other standard methods, it was shown that the correlation indices were at least 98%, which makes the BIA method reliable (16). Moreover, the BIA method is useful in epidemiological studies (17).

In this study, we examined the changes in the body composition of patients with acromegaly, which were associated with cardiovascular risks, using BIA and compared the findings with controls.

MATERIALS and METHODS

Study Design and Patients

This prospective study followed 62 patients diagnosed with acromegaly in the endocrinological clinic of Uludag University Faculty of Medicine between 2019 and 2022. During the same period, 40 healthy volunteers matched for gender, age, menopause status, and body mass index (BMI) were included in the study's control group.

All study participants signed an informed consent. The Uludag University clinical research ethics committee approved this study (No. 2021-18/17 dated 08.12.2021).

Definitions and Criteria

The diagnosis of acromegaly was determined by clinical suspicion and biochemical tests. Elevated levels of IGF-1 and the lowest GH levels above 1 ng/mL after an oral glucose tolerance test with 75-gr glucose supported the diagnosis. The contrast-enhanced MRI of the hypothalamic–pituitary region was made to show the pituitary adenoma. Transsphenoidal surgery, medical treatment, or in some cases, radiotherapy were the treatment choices. The patients were evaluated for having pituitary hormone deficiency after treatment strategies. Patients with low serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and serum levels of total testosterone and/or estrogen were diagnosed with hypogonadism. We used GHrandom <2.5 µg/L and IGF-I <1.2 × upper limit of normal (ULN) to describe "controlled" in our patients. Patients with GHrandom ≥2.5 µg/L and IGF-I ≥1.2 × ULN were described as "active."

This study enrolled patients diagnosed with acromegaly and healthy volunteers matched for gender, age, menopause status, and BMI. Inclusion criteria were being ≥18 years of age and having adequate radiological, laboratory, and clinical examination in the hospital database Exclusion criteria of the study were a medical history of cardiovascular pathologies and insufficient data.

Laboratory and Clinical Investigations

The laboratory parameters of all patients were documented when they came to their routine controls. Fasting plasma glucose (70–100 mg/dL) and the lipid parameters—total cholesterol (0–200 mg/dL), triglycerides (40–150 mg/dL), high-density lipoprotein (>50 mg/dL), low-density lipoprotein (60–130 mg/dL)—were measured using spectrophotometry, an Abbott Architect c16000 clinical chemistry analyzer and Abbott kit. Insulin levels (2–25 mU/L) were measured using the chemiluminescence method, an Abbott Architect Plus i2000 immunoassay analyzer, and an Abbott kit. Insulin resistance was calculated using the homeostasis model assessment system. Serum GH (0.06–5 µg/L) and IGF-1 (57–241 µg/L) were measured via chemiluminescence using a Siemens IMMULİTE 2000 XPI immunoassay analyzer. Moreover, serum creatinine levels (0.7–1.1 mg/dL) were recorded spectrophotometrically using original Roche reagents on Cobas c 501 devices (Roche Diagnostic, Germany), and serum calcium levels (8.5–10.5 mg/dL) were measured using a standard colorimetric method (Roche Diagnostics, Alameda, Calif).

The patients with acromegaly and the controls were admitted to the endocrinology outpatient clinic. The same clinician measured body weight with a digital scale and height, waist, and hip circumference with a tapeline under the same conditions.

The body composition of all patients was evaluated using a body composition analyzer (TANITA MC-780-Black) with the BIA method. The body composition analysis examined parameters, such as intracellular water (ICW), extracellular water (ECW), total body fat, fat mass, lean mass, skeletal muscle, protein, mineral, basal metabolism, and body density.

Statistical Analysis

SPSS software version 23.0 was used for the statistical analysis. Categorical measurements are presented as numbers (n) and percentages (%). The Kolmogorov–Smirnov test was used to determine the normality of the distribution of variables. In keeping with the nonparametric tests, median values were stated. While the Man–Whitney U-test was performed for non-normally distributed variables, categorical variables were analyzed using the Chi-square test. While examining the associations between non-normally distributed variables, the Spearman test was used. A value of $p < 0.05$ was statistically significant.

RESULTS

We examined 62 patients with acromegaly and 40 healthy volunteers as the control group in this study. These two groups were the same according to age, gender, and BMI. Table 1 shows the baseline characteristics of the patients with acromegaly and the controls.

The median age of the patients with acromegaly was 48 years (23–76), with female predominance (59.7%). The median duration of follow-up between diagnosis and final status at the last follow-up was 132 months (12–372). The median BMI of the patients with acromegaly was 29.4 kg/m^2 (20.1–45.6). At the time of the acromegaly diagnosis, the median serum level of GH was 10.7 ng/mL (0.96–40), and the median serum level of IGF-1 was 728 ng/mL (149–1802). Fifty-eight patients with acromegaly (93.5%) had received pituitary surgery, and 13 (20.9%) had irradiated. The median diameter of the tumor was 17 mm (6–45). Postoperative hypogonadism was diagnosed in nine patients with acromegaly (15.5%); 66% were female.

The median age of the controls was 46 years (24–64), and 77.5% of the controls were female. The median BMI of the patients with acromegaly was 27.3 kg/m^2 (20.3–37.5). The con-

Table 1. Baseline characteristics of the patients

Parameters	Patients with acromegaly (n=62)	Controls (n=40)	p
Age (years)	48 (23–76)	46 (24–64)	0.42
Female gender (n/%)	37 (59.7)	31 (77.5)	0.08
BMI (kg/m^2)	29.4 (20.1–45.6)	27.3 (20.3–37.5)	0.41
Glucose (mg/dL)	95 (76–178)	86 (69–99)	**0.001**
Insulin (mU/L)	**8 (1.8–25.6)**	**4.2 (1.9–19)**	**0.04**
HOMA-IR	**2.05 (0.7–10.6)**	**1.25 (0.29–7.5)**	**0.02**
HbA1c (%)	**5.7 (4.7–10.1)**	**5.3 (4.3–5.6)**	**0.001**
Creatinine (mg/dL)	0.73 (0.53–1.02)	0.75 (0.59–1.1)	0.34
Calcium (mg/dL)	9 (8.2–10.3)	8.95 (8.1–10.5)	0.81
Total cholesterol (mg/dL)	195 (133–293)	201 (120–334)	0.60
LDL (mg/dL)	118 (70–243)	122 (38–216)	0.88
HDL (mg/dL)	57 (35–108)	53 (28–94)	0.25
Triglycerides (mg/dL)	101.5 (37–297)	119.5 (42–435)	0.13

BMI: Body mass index; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; HOMA-IR: Homeostatic model assessment-insulin resistance

trols were not diagnosed with any disease after detailed examination, but two of them (5%) were diagnosed and followed up with the diagnosis of hypertension.

This study demonstrated that patients with acromegaly have higher plasma glucose levels than the control group (p=0.001) (Table 1). The detailed analysis showed that 18 patients with acromegaly (29%) were diagnosed with diabetes mellitus, and 3 were using insulin. There was no patient with known or newly diagnosed diabetes mellitus after examination in the group of controls. When 18 patients with a diagnosis of diabetes mellitus were excluded, insulin levels and HOMA-IR index of patients with acromegaly were higher than the controls (respectively; p=0.04 and p=0.02) (Table 1). While 14 patients with acromegaly (22.6%) were diagnosed with hypertension during the follow-up period, 2 controls (5%) were diagnosed with hypertension during the 1-year follow-up period, which was statistically significant (p=0.02). There were no statistically significant differences in total cholesterol, low-density lipoprotein, triglyceride, and high-density lipoprotein levels between acromegalic patients and controls (p=0.6, 0.88, 0.13, 0.25, respectively).

The waist and hip circumferences of the patients with acromegaly were wider than the controls, which were not significant (respectively; p-value; 0.05, 0.05) (Table 2). When we evaluated the body composition of the patients and the controls via the BIA method, we found that the ECW and ICW compartments in patients with acromegaly were larger than the controls (respectively; p-values; 0.001, 0.02) (Table 2). Moreover, patients with acromegaly had a lower percentage of fat mass in the total body, trunk, and extremities than healthy volunteers, which was not significant (respectively; p-values 0.8, 0.54, 0.39, 0.22, 0.29, 0.23). Furthermore, the lean mass of the patients with acromegaly in the trunk and extremities was significantly higher than the controls (respectively; p-values 0.002 and 0.001). The muscle compartment of the patients with acromegaly was significantly larger than others (p=0.001). The percentage of the mineral in the patients with acromegaly was lower than the controls, which was not significant (p=0.92). The basal metabolism in patients with acromegaly was significantly higher in patients with acromegaly than others (p=0.002) (Table 2).

When we evaluated the patients with acromegaly according to the disease activity, 54 patients were controlled (87.1%) and 8 patients (12.9%) had active disease. The serum levels of IGF-1 and GH of the patients with active disease were significantly higher than those with controlled disease, but there were no differences in other laboratory parameters (Table 3). Moreover, there were no significant differences in the means of body composition parameters between the patients with different disease activities (Table 4). Furthermore, there were no significant differences between the activity of the disease and being diagnosed with hypertension (p=0.67).

Finally, the correlations between serum levels of IGF-1, GH, and HOMA-IR and body composition parameters were investigated. Although there were no statistically significant correlations of GH between body composition parameters, there were statistically significant positive correlations of IGF-1 between HOMA-IR (r=0.325, p=0.018). Moreover, there were statistically positive correlations of IGF-1 between ICW and lean mass of the total body (respectively, r=0.237, p=0.035 and r=0.280, p=0.012).

DISCUSSION

Acromegaly is a chronic disease caused by the overproduction of GH and IGF-1 (18). As the effect of excess GH and IGF-1, cardiovascular, metabolic, respiratory, and neoplastic comorbidities are common in these patient populations, especially in patients with active disease (18). Acromegaly is associated with IR, increased glucogenesis, and lipolysis (2). Consistent with these findings, our study showed that patients with acromegaly have higher plasma glucose levels than the control group. Moreover, after the patients with a diagnosis of diabetes mellitus were excluded, the insulin levels and HOMA-IR index of patients with acromegaly were higher than the controls.

Table 2. Comparison of body composition and some clinical parameters between the patients with acromegaly and the controls

Parameters	Patients with acromegaly (n=62)	Controls (n=40)	p
Waist circumference (cm)	101 (65–134)	92 (66–129)	0.05
Hip circumference (cm)	112 (85–140)	103 (85–136)	0.05
ECW (kg)	18.15 (12.8–27.6)	15.2 (12–23.6)	**0.001**
ICW (kg)	18.95 (14.7–37.2)	17.35 (15.3–32.3)	**0.02**
Total body fat (kg)	24.85 (3–48.7)	19.5 (9.7–41.4)	0.25
Fat mass (%)			
Total body	27.21 (4.75–47.83)	28.43 (16.74–43.06)	0.80
Right arm	25.5 (0–55.20)	28.9 (14.9– 45.6)	0.39
Left arm	26 (0–37.4)	29.75 (13.6–45.9)	0.22
Trunk	27.05 (0–43)	23.6 (12–40.1)	0.54
Right leg	28.15 (0–52.1)	33.7 (13.2–49.4)	0.29
Left leg	28 (0–52.1)	34.25 (14.2–49.1)	0.23
Lean mass (kg)			
Right arm	3.25 (0–23.1)	2.5 (1.9–5.1)	**0.001**
Left arm	3.1 (0–7.1)	2.45 (1.9–5)	**0.001**
Trunk	32.6 (0–47.2)	29.5 (23.2–40)	**0.002**
Right leg	9.1 (0–17.8)	7.65 (6.1–13.4)	**0.002**
Left leg	9.1 (0–18.4)	7.7 (6.3–13.5)	**0.001**
Muscles (kg)			
Right arm	3 (0–39)	2.4 (1.7–4.8)	**0.001**
Left arm	2.9 (0–30.8)	2.35 (1.63–4.7)	**0.001**
Trunk	31.2 (0–45.3)	28 (18.79–38.2)	**0.001**
Right leg	8.6 (0–16.8)	7.25 (4.82–12.7)	**0.001**
Left leg	8.6 (0–17.4)	7.3 (4.96–12.8)	**0.001**
Proteins (%)	18.23 (10.82–30.25)	18.14 (10.32–26.38)	0.49
Mineral (%)	4.95 (3.45–6.95)	4.99 (3.46–5.98)	0.92
Basal metabolism (kcal)	1690 (1258–2987)	1523 (1196–6385)	**0.002**
Body density	1.035 (0.989–1.540)	1.034 (0.999–1.060)	0.74

ECW: Extracellular water; ICW: Intracellular water. Normal values of the body composition parameters: Total body fat (kg): 11.51–18.91, fat mass: <14%: low, 4%–23%: normal, >23%: high, lean mass (kg): 63.29–70.69, protein: 14.9%–16.7%, mineral: 5.19%–5.8%, basal metabolism (kcal): 1375–1900, body density: 1.045–1.067

The cardiovascular complications related to acromegaly have a wide spectrum, ranging from hypertension to cardiomyopathy (19). The studies in the literature revealed that oxidative stress, IR, and endothelial dysfunction are the main underlying mechanisms in the development of cardiovascular disease in acromegaly (18). IR is the leading hallmark of acromegaly, related to cardiovascular comorbidities in the acromegaly population (20).

Valvular pathologies and rhythm disorders occur frequently in this patient population. In these studies, the prevalence of hypertension in acromegalic patients is ~35%, and the incidence is higher than in healthy populations (12). A total of 14 patients with acromegaly (22.6%) were diagnosed with hypertension, while 2 controls (5%) were diagnosed with hypertension during the 1-year follow-up period, which was statistically significant in our report. Increased plasma glucose levels, insulin levels, HOMA-IR index, and hypertension prevalence can be associated with an increased risk of cardiovascular diseases.

GH has a lipolytic and anabolic role, leading to adipose tissue breakdown and protein synthesis (7). Because of excessive GH, acromegaly disease is associated with decreased fat mass and increased intermuscular adipose tissue mass, lean body mass, and basal metabolism (3, 21). The studies showed increased fat mass after treatment with decreased basal metabolism and lean mass (6). GH can induce protein synthesis and increase skeletal muscle by inhibiting myostatin in the muscle (22). Our study showed that patients with acromegaly had a lower fat mass percentage in the body, trunk, and extremities than the controls, which was not significant. Furthermore, the lean mass of the patients with acromegaly in the trunk and extremities was significantly higher than the controls. This finding can be supported by positive correlations of IGF-1 between the lean mass of the total body, as found in our study. Paradoxically, insulin concentration is associated with reduced total body fat and even reduced fat accumulation in metabolic organs. A low percentage of fat mass in the

Table 3. Comparison of some clinical and laboratory parameters between the patients with controlled and active disease

Parameters	Patients with controlled disease (n=54)	Patients with an active disease (n=8)	p
Age (years)	48 (23–76)	47.5 (32–53)	0.30
Female gender (n/%)	31 (57.4)	6 (75)	0.45
BMI (kg/m^2)	28.8 (20.1–45.6)	30.95 (21.6–38.6)	0.58
Glucose (mg/dL)	95 (76–178)	98.5 (78–150)	0.58
IGF-1 (µg/L)	143 (51–253)	363 (216–665)	**0.001**
GH (µg/L)	0.69 (0–5.85)	3.52 (0.43–29.3)	**0.001**
Insulin (mU/L)	8.05 (1.8–25.6)	7.7 (5.5–17.3)	0.94
HOMA-IR	1.89 (0.7–5.91)	2.62 (1.57–10.6)	0.14
HbA1c (%)	**5.7 (4.7–8)**	**5.8 (5–10.1)**	**0.67**
Creatinine (mg/dL)	0.76 (0.59–1.27)	0.74 (0.64–0.81)	0.54
Calcium (mg/dL)	8.9 (8.1–10.5)	9.25 (8.6–9.6)	0.19
Total cholesterol (mg/dL)	201 (120–334)	201 (131–277)	0.73
LDL (mg/dL)	121 (38–216)	129 (73–168)	0.99
HDL (mg/dL)	53 (28–94)	57 (40–72)	0.60
Triglycerides (mg/dL)	119 (42–435)	159 (54–272)	0.62

BMI: Body mass index; HDL: High-density lipoprotein; IGF-1: Insulin growth factor-1; GH: Growth hormone; LDL: Low-density lipoprotein; HOMA-IR: Homeostatic model assessment-insulin resistance

body, trunk, and extremities and high levels of lean mass in the trunk and extremities in patients with acromegaly may be considered a hallmark of IR (6). Moreover, we found that the muscle compartment of the patients with acromegaly was significantly larger than the controls, as shown in the studies (3, 22).

Another important effect of GH is on the water metabolism of the body. GH increases the renal sodium reabsorption and total plasma volume via activating the renin–angiotensin–aldosterone system and causes changes in ECW and ICW (9). Consistent with this pathogenesis, the ECW and ICW compartments in patients with acromegaly were larger than the controls. Moreover, our study showed statistically significant positive correlations of IGF-1 between ICW. As a result, this pathogenesis may result in fluid retention in the body and an increased risk of hypertension, which is associated with cardiovascular mortality and morbidity (9).

The studies demonstrated that bone mineral density increased in patients with acromegaly than in the general population (23, 24), but no study has discussed the body's mineral content. In our study, the total body mineral percentage in the patients with acromegaly was lower than the controls, which was not significant, but prospective studies may examine this hypothesis.

The literature demonstrated increased basal metabolism in patients with acromegaly (25). Excess GH levels lead to oxygen consumption and enhanced glucose metabolism. In our study, the basal metabolism of the patients with acromegaly was significantly higher than others.

Stratifying the patients with acromegaly according to disease activity indicated that the serum levels of IGF-1 and GH of patients with active disease were significantly higher than in patients with controlled disease. However, there were no differences in other laboratory parameters and body composition parameters in our study. Furthermore, there were no significant differences between the activity of the disease and being diagnosed with hypertension. Since patients with acromegaly often have ~10 years of active disease before diagnosis, as in our findings, clinically significant changes can occur at the time of diagnosis and even in controlled disease.

BIA is increasingly used to evaluate body composition because it is simple and noninvasive. BMI is an important determinant for obesity in epidemiological studies and does not differentiate between lean and fat mass, which is associated closely with morbidity and mortality. In contrast, the BIA method is a reliable marker for fat and lean mass, unlike BMI (26). In higher degrees of obesity, BMI often underestimates obesity by measuring BMI as changes in body composition with aging. BMI may underestimate the body fat percentage in younger subjects and vice versa in older subjects (25). In our study, we selected matched controls for BMI. Still, the detailed analysis showed that waist and hip circumferences of patients with acromegaly, which are associated with cardiovascular mortality, were wider than the controls, which were not significant.

When we evaluated the patients with acromegaly according to disease activity, there were significant differences between disease activity and levels of IGF-1, GH, the compartment of ICW, and lean mass. However, there was no significant difference in means of having hypertension in patients according to the activation status of the disease. As extracellular water is responsible for plasma volume, despite having a larger compartment of ICW in these patients, there was no significant difference in means of having hypertension.

Table 4. Comparison of body composition and some clinical parameters between the patients with controlled and active disease

Parameters	Patients with controlled disease (n=54)	Patients with an active disease (n=8)	p
Waist circumference (cm)	102 (65–134)	99 (86–110)	0.28
Hip circumference (cm)	113 (85–140)	105.5 (92–118)	0.12
ECW (kg)	18.15 (12.8–27.6)	15.2 (12–23.6)	0.81
ICW (kg)	18.95 (14.7–37.2)	17.5 (15.3–32.3)	0.81
Total body fat (kg)	24.85 (3–48.7)	19.5 (9.7–41.4)	0.91
Fat mass (%)			
Total body	24.76 (17.7–32.69)	23.07 (21.63–31)	0.19
Right arm	24.65 (0–55.20)	34.75 (8.6–39.2)	0.42
Left arm	25.2 (0–55)	34.6 (6.6–37.4)	0.30
Trunk	27.5 (0–43)	26.65 (8.5–36.5)	0.40
Right leg	26.35 (0–52.1)	40.15 (7.8–44.1)	0.25
Left leg	26 (0–52.1)	40.55 (8.4–44)	0.27
Lean mass (kg)			
Right arm	3.3 (0–23.1)	3.1 (2.7–3.9)	0.71
Left arm	3.15 (0–7.1)	3 (2.7–3.9)	0.87
Trunk	32.3 (0–47.2)	33.9 (29.8–40.9)	0.55
Right leg	9.2 (0–17.8)	9 (7.7–11.1)	0.86
Left leg	9.1 (0–18.4)	8.85 (8–11.2)	0.81
Muscles (kg)			
Right arm	3.05 (0–39)	2.9 (2.6–3.7)	0.85
Left arm	2.95 (0–30.8)	2.85 (2.6–3.7)	0.84
Trunk	31 (0–45.3)	32.35 (28.3–38.9)	0.55
Right leg	8.6 (0–16.8)	8.5 (7.3–10.5)	0.96
Left leg	8.6 (0–17.4)	8.35 (7.5–10.6)	0.81
Proteins (%)	18.1 (10.82–30.25)	20.07 (14.01–26.67)	0.34
Mineral (%)	4.95 (3.45–6.95)	4.9 (4.19–6.69)	0.66
Basal metabolism (kcal)	1690 (1258–2987)	1700 (1517–2154)	0.96
Body density	1.036 (0.989–1.540)	1.023 (1.014–1.081)	0.44

ECW: Extracellular water; ICW: Intracellular water. Normal values of the body composition parameters: Total body fat (kg): 11.51–18.91, fat mass: <14%: low, 4%–23%: normal, >23%: high, lean mass (kg): 63.29–70.69, protein: 14.9%–16.7%, mineral: 5.19%–5.8%, basal metabolism (kcal): 1375–1900, body density: 1.045–1.067

Lean mass in the extremities and muscle compartment was significantly higher in patients controlled without medication than in others. These findings could be due to younger age and more male predominance of the patients with acromegaly controlled without any medication. Moreover, we do not know these patients' exercise capacity, which can affect lean mass and muscle compartments. Moreover, studies show that endothelial damage, systemic inflammation, and micro and macrovascular dysfunction are present in uncontrolled and controlled acromegaly. Lean mass, which is associated with cardiovascular mortality, continues to be higher in patients with controlled without any medication (18).

Finally, the study had some limitations. First, we examined patients with acromegaly receiving multiple treatment modalities, which might affect the results. Second, our study has a small sample size, and studies with a larger population are needed to lighten the cardiovascular risks.

CONCLUSION

Acromegaly is associated with a high prevalence of heart disease, hypertension, glucose metabolism disorders, and increased cardiovascular mortality and morbidity. This study's main conclusion is that the changes in body composition in patients with acromegaly, such as increased intracellular and extracellular volume and decreased fat mass, may contribute to an increased risk of cardiovascular diseases. Eventually, as parameters of body composition are simple to obtain in the care setting, frequently evaluating body composition with the BIA method can provide important information about cardiovascular risks and thereby provide appropriate interventions.

Ethics Committee Approval: The Uludağ University Clinical Research Ethics Committee granted approval for this study (date: 08.12.2021, number: 2021-18/17).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – YAÜ, ÖÖG, ŞE, CA, EA, SC, CE, EE; Design – YAÜ, ÖÖG, ŞE, CA, EA, SC, CE, EE; Supervision – YAÜ, ÖÖG, ŞE, CA, EA, SC, CE, EE; Resource – YAÜ; Materials – YAÜ; Data Collection and/or Processing – EA, CA; Analysis and/or Interpretation – YAÜ; Literature Search – YAÜ; Writing – YAÜ; Critical Reviews – ÖÖG, SC.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Vilar L, Vilar CF, Lyra R, Lyra R, Naves LA. Acromegaly: clinical features at diagnosis. Pituitary 2017; 20(1): 22–32. [CrossRef]
2. Rolla M, Jawiarczyk-Przybyłowska A, Halupczok-Żyła J, Kałużny M, Konopka BM, Błoniecka I, et al. Complications and Comorbidities of Acromegaly-Retrospective Study in Polish Center. Front Endocrinol (Lausanne). 2021 Mar 16;12: 642131. doi: 10.3389/fendo.2021.642131. [CrossRef]
3. Freda PU, Shen W, Heymsfield SB, Reyes-Vidal CM, Geer EB, Bruce JN, et al. Lower visceral and subcutaneous but higher intermuscular adipose tissue depots in patients with growth hormone and insulin-like growth factor I excess due to acromegaly. J Clin Endocrinol Metab 2008; 93(6): 2334–43. [CrossRef]
4. Dreval AV, Trigolosova IV, Misnikova IV, Kovalyova YA, Tishenina RS, Barsukov IA, et al. Prevalence of diabetes mellitus in patients with acromegaly. Endocr Connect 2014; 3(2): 93–8. [CrossRef]
5. Gadelha MR, Kasuki L, Lim DST, Fleseriu M. Systemic complications of acromegaly and the impact of the current treatment landscape: An Update. Endocr Rev 2019; 40(1): 268–332. [CrossRef]
6. Reyes-Vidal CM, Mojahed H, Shen W, Jin Z, Arias-Mendoza F, Fernandez JC, et al. Adipose tissue redistribution and ectopic lipid deposition in active acromegaly and effects of surgical treatment. J Clin Endocrinol Metab 2015; 100(8): 2946–55. [CrossRef]
7. Guo X, Gao L, Shi X, Li H, Wang Q, Wang Z, et al. Pre- and postoperative body composition and metabolic characteristics in patients with acromegaly: A prospective study. Int J Endocrinol 2018; 2018: 4125013. [CrossRef]
8. Bredella MA, Schorr M, Dichtel LE, Gerweck AV, Young BJ, Woodmansee WW, et al. Body composition and ectopic lipid changes with biochemical control of acromegaly. J Clin Endocrinol Metab 2017; 102(11): 4218–25. [CrossRef]
9. Katznelson L. Alterations in body composition in acromegaly. Pituitary 2009; 12(2): 136–42. [CrossRef]
10. Lin YC, Yu WC, Kuo CS, Chen HS. Growth hormone control and cardiovascular function in patients with acromegaly. J Chin Med Assoc 2021; 84(2): 165–70. [CrossRef]
11. Mizera Ł, Elbaum M, Daroszewski J, Bolanowski M. Cardiovascular complicatıons of acromegaly. Acta Endocrinol (Buchar) 2018; 14(3): 365–74. [CrossRef]
12. Puglisi S, Terzolo M. Hypertension and acromegaly. Endocrinol Metab Clin North Am 2019; 48(4): 779–93. [CrossRef]
13. Møller N, Schmitz O, Jørgensen JO, Astrup J, Bak JF, Christensen SE, et al. Basal- and insulin-stimulated substrate metabolism in patients with active acromegaly before and after adenomectomy. J Clin Endocrinol Metab 1992; 74(5): 1012–9. [CrossRef]
14. Reid TJ, Jin Z, Shen W, Reyes-Vidal CM, Fernandez JC, Bruce JN, et al. IGF-1 levels across the spectrum of normal to elevated in acromegaly: relationship to insulin sensitivity, markers of cardiovascular risk and body composition. Pituitary 2015; 18(6): 808–19. [CrossRef]
15. Brummer RJ, Lönn L, Kvist H, Grangård U, Bengtsson BA, Sjöström L. Adipose tissue and muscle volume determination by computed tomography in acromegaly, before and 1 year after adenomectomy. Eur J Clin Invest 1993; 23(4): 199–205. [CrossRef]
16. Bosy-Westphal A, Schautz B, Later W, Kehayias JJ, Gallagher D, Müller MJ. What makes a BIA equation unique? Validity of eight-electrode multifrequency BIA to estimate body composition in a healthy adult population. Eur J Clin Nutr 2013; 67 Suppl 1: S14–21. [CrossRef]
17. Sun SS, Chumlea WC, Heymsfield SB, Lukaski HC, Schoeller D, Friedl K, et al. Development of bioelectrical impedance analysis prediction equations for body composition with the use of a multicomponent model for use in epidemiologic surveys. Am J Clin Nutr 2003; 77(2): 331–40. [CrossRef]
18. Wolters TLC, Netea MG, Riksen NP, Hermus ARMM, Netea-Maier RT. Acromegaly, inflammation and cardiovascular disease: a review. Rev Endocr Metab Disord 2020; 21(4): 547–68. [CrossRef]
19. Kamenický P, Maione L, Chanson P. Cardiovascular complications of acromegaly. Ann Endocrinol (Paris) 2021; 82(3-4): 206–9. [CrossRef]
20. Katznelson L, Laws ER Jr, Melmed S, Molitch ME, Murad MH, Utz A, et al; Endocrine Society. Acromegaly: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2014; 99(11): 3933–51.
21. Olarescu NC, Bollerslev J. The impact of adipose tissue on insulin resistance in acromegaly. Trends Endocrinol Metab 2016; 27(4): 226–37.
22. Mazziotti G, Lania AG, Canalis E. Skeletal disorders associated with the growth hormone-insulin-like growth factor 1 axis. Nat Rev Endocrinol 2022; 18(6): 353–65. [CrossRef]
23. Mazziotti G, Biagioli E, Maffezzoni F, Spinello M, Serra V, Maroldi R, et al. Bone turnover, bone mineral density, and fracture risk in acromegaly: a meta-analysis. J Clin Endocrinol Metab 2015; 100(2): 384–94. [CrossRef]
24. Kaji H, Sugimoto T, Nakaoka D, Okimura Y, Kaji H, Abe H, et al. Bone metabolism and body composition in Japanese patients with active acromegaly. Clin Endocrinol (Oxf) 2001; 55(2): 175–81. [CrossRef]
25. Leães CGS, Fernandes MV, Alves L, Araújo B, Rech CGSL, Ferreira NP, et al. Assessment of anthropometric and physical health ındicators before and after pituitary surgery in patients with nonfunctioning pituitary adenomas, acromegaly, and cushing disease. Indian J Endocrinol Metab 2019; 23(4): 473–9. [CrossRef]
26. Deurenberg P, Andreoli A, Borg P, Kukkonen-Harjula K, de Lorenzo A, van Marken et al. The validity of predicted body fat percentage from body mass index and from impedance in samples of five European populations. Eur J Clin Nutr 2001; 55(11): 973–9. [CrossRef]