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Loss of Body Cell Mass in Cushing's Syndrome: Effect of Treatment

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Cushing's syndrome (CS) is associated with low fat-free mass, but it is unclear whether hypercortisolism causes a loss of whole body protein. Body composition was studied prospectively in 15 patients with untreated CS (n = 14 pituitary adenoma; n = 1 adrenal adenoma), in 15 nonobese healthy controls, and in 15 weight-matched obese controls by 3 different methods: total body potassium counting (TBP), bioelectrical impedance analysis (BIA), and anthropometry. In 6 patients, body composition was studied before and within 6 months after pituitary surgery.

In CS patients and weight-matched controls, body weight and total body fat were significantly higher than in nonobese controls. In CS patients, TBP was 18.4% lower than predicted, whereas in weight-matched controls TBP was 7.1% higher than predicted. As compared with nonobese and weight-matched controls, in CS patients TBP indicated a significant loss of body cell mass (BCM) of −20.2 and −21.1%, respectively. A significantly reduced arm muscle area of −21.3% compared with weight-matched controls also indicated a loss of whole body protein. In CS, however, BIA overestimated BCM when compared with TBP by +18% and agreement between BIA and TBP in the individual patient was poor (limits of agreement ± 27.6%), indicating the invalidity of standard BIA equations in this population. Measurements performed before and 6 months after successful pituitary surgery demonstrated a significant loss of body weight (−11%) and body fat (−33%), but BCM and muscle mass remained on a constant low level.

In conclusion, this study shows that, in patients with CS, a significantly reduced BCM indicates a true protein loss. The second interesting finding is that in the early recovery after successful treatment of hypercortisolism patients lose body fat without gaining BCM or muscle mass. (*J Clin Endocrinol Metab* 87: 1078–1084, 2002)

CUSHING'S SYNDROME (CS) is associated, among other symptoms, with weight gain, central obesity, and muscle weakness. Body composition studies in these patients have been performed predominantly to evaluate the abnormal body fat distribution and its underlying pathogenic mechanisms (1–5). On the other hand, it has been proposed that endogeneous hypercortisolism causes protein depletion and subsequently a loss of skeletal muscle or fat-free mass (2, 6).

However, it has been shown previously that in CS the mean absolute fat-free mass is not different from nonobese healthy controls but significantly lower than in obese patients with the same anthropometric parameters (2). In healthy subjects, longitudinal changes in fat-free mass are strongly influenced by changes in body weight (7). Therefore, in subjects without hypercortisolism, weight gain is associated with an increase of fat mass as well as with an increase of fat-free mass (8). Obviously, in CS this relationship is disturbed, but to date, it is not clear whether the unproportional low fat-free mass is caused by increased protein degradation or by an inhibition of protein synthesis (6, 9, 10).

Determination of fat-free mass by various methods is a common approach to describe protein depletion in patients with hypercortisolism (1–3, 10, 11). However, in several disease states associated with malnutrition, even a precise measurement of fat-free mass might be inadequate for the detection of protein depletion because of an accompanying increase of the extracellular fluid compartment (12–14). Therefore, the quantitation of body cell mass (BCM) rather than fat-free mass has been regarded more meaningful (15), especially because BCM comprises the metabolically active and protein rich compartment in the body (16). To our knowledge, in patients with CS, determination of BCM has not yet been performed systematically.

Therefore, we prospectively studied the body composition in patients with untreated CS in comparison with age- and gender-matched nonobese healthy controls as well as with weight-matched obese patients with special regard on BCM using total body potassium (TBP) counting, bioelectrical impedance analysis (BIA), and anthropometric measurements. In addition, in a subgroup of 6 patients changes of body composition were studied over a period of time of 6 months after surgical cure of hypercortisolism.

Patients and Methods

Patients and controls

Fifteen consecutive patients with recently diagnosed CS (14 with pituitary adenoma, 1 with benign adrenal tumor) were studied between March 1997 and September 1999 after informed consent was obtained. Malignancies, clinically apparent infection, malabsorption, and hyperthyreoidism were exclusion criteria. All patients had typical signs and symptoms of CS, elevated urinary cortisol excretion, and abnormal plasma cortisol response in the dexamethasone suppression test. The

Abbreviations: α, Phase angle; BIA, bioelectrical impedance analysis; BCM, body cell mass; CS, Cushing's syndrome; R, resistance; reactance; TBP, total body potassium; Xc, reactance.

clinical profile of patients is given in Table 1. The pituitary function was assessed by determination of hormone concentrations in the basal state and after stimulation with releasing hormones. Five patients had an impaired response to LH-releasing hormone, but only in two male patients hormone replacement therapy with testosterone was conducted at the time of study entry. Insufficiency of the somatotropic axis was observed in two female patients who were not treated by GH at the time of study entry. Thyreotropic dysfunction was observed in one patient, treated by thyroxine.

A subgroup of 6 patients with Cushing's disease (3 female, 3 male) was studied repeatedly before, 1, 3, and 6 months after successful transsphenoidal pituitary surgery. In the early postoperative period, the mean reduction in plasma cortisol was 89%, and all 6 patients were on a substitution treatment with hydrocortisone. This treatment could be withdrawn in 5 patients between the first and fifth month after surgery (mean 2.8 ± 1.7 months). Because of persistent signs of adrenal insufficiency, one patient remained on hydrocortisone 15 mg/d during the whole study period. Six months after surgery, mean serum and urinary cortisol values were 76.5% and 92%, respectively (both $P < 0.01$) lower than preoperatively. One month after surgery, gonadotropic insufficiency was observed in 4 patients, which persisted only in 1 female patient (patient no. 2, who showed persistent corticotropic insufficiency), who was not treated by hormone replacement. A transient somatotropic dysfunction was observed in two patients until the third postoperative month. In one of these patients, additional thyreotropic dysfunction was treated with thyroxine during the whole study period. The physical activity was reduced in all patients (working suboptimally, 4 patients; ambulatory, 2 patients) during the first 3 postoperative months. Six months after surgery, only 2 patients reported full recovery, whereas the other 4 patients complained on tiredness and suboptimal working ability.

Fifteen age- and gender-matched nonobese healthy volunteers and 15 age-, gender-, and weight-matched obese patients served as control groups for TBP counting, BIA, and anthropometry. None of these controls had edema or other signs of changes of hydration. The study protocol was approved by the ethics committee of the Universitätsklinikum Charité.

Body composition analysis

TBP counting. Total TBP has been considered to be an accurate reflection of BCM because greater than 97% of all the potassium in the body is intracellular (17). TBP was determined by measuring the amount of the naturally occurring radioisotope ^{40}K using a shielded-room whole-body counter (Nuclear Enterprises Ltd., Edinburgh, UK) working with 4 NaI(TI) detectors (Berthold, Wildbad, Germany) by SE at the Department of Nuclear Medicine, Klinikum Buch as described previously (18). The coeffecient of variation (cv) for repeated measurements was ≤2%. In addition, measured TBP was compared with expected normal values as calculated by the following predictor equations (19): TBP = 35.76× height − 4.51× age − 2483 (male); TBP = 35.76× height − 4.51× age − 3211 (female). BCM was then calculated according to Cohn (20): BCM_{TBP} = TBP × 0.0092.

BIA. BIA was performed by the whole body tetrapolar contact electrode approach using a multifrequency impedance analyzer applying alternating electric currents of 100 μA at 1 kHz, and of 800 μA at 5, 50, and 100 kHz (BIA 2000-M, Data Input GmbH, Hofheim, Germany). Two pairs of current-introducing and voltage-sensing electrodes were attached to the dorsum of hand and foot of the dominant side of the body (21). Resistance (R), reactance (Xc), and the phase angle (α) were measured at each frequency. All impedance measurements were taken after at least 4 h fast and after emptying the bladder with the patient supine for at least 40 min, the arms relaxed at the sides but not touching the body, the thighs separated and at a room temperature of 22–26 C.

For calculation of body compartments from R, Xc, and α, only values obtained at 50 kHz were used. Total body water was calculated as total body water = $0.69\times H^2/R_{50} + 0.8$ (21) and fat-free mass = total body water/0.732. BCM was calculated using R and phase angle α at 50 kHz (22): BCM = fat-free mass × 0.29× ln (α_{50}). The cv for repeated R and Xc measurements at 50 kHz was determined in 4 healthy controls, in 4 obese patients, and in 4 patients with CS. The cv for R and Xc were 0.92 and 2.1% in controls, 1.2 and 2.3% in obese patients, and 1.45 and 2.8% in CS.

Anthropometry. Measurements were performed by the same skilled investigator (M.P.) using a Lange caliper (Holtain, Crymich, UK). The average of three measurements of midarm circumference and triceps skin fold at each site was used for the calculation of arm muscle area and arm fat area according to Gurney and Jelliffe (23). The cv for repeated measurements of midarm circumference and skin folds in healthy controls were 0.93 and <3%, respectively, and in obese patients and in CS <1 and <4.5%, respectively.

Laboratory methods

Serum and urinary cortisol were measured in the clinical chemistry laboratory by an automated analyzer (Immuno, Bayer Corp., Leverkusen, Germany) using ELISA. Serum electrolytes were measured by automated multianalyzers using standard biochemical procedures.

Statistical analysis

All data are given as mean ± SD. Comparison between groups was performed by ANOVA and subsequent least significant difference test, and $P < 0.05$ was considered to be significant. Differences in measurements before and after pituitary surgery were evaluated with multiple

TABLE 1. Baseline characteristics of patients with CS

Patient no.	Age (yr)	Gender (f/m)	Diagnosis	Pituitary dysfunction	Medication	Edema	Physical activity	Smoking (cig./d)	Alcohol
1[a]	33	f	Pituitary	g		+	2	5	+
2[a]	29	m	Pituitary	g	Testosterone, antihypertensive		2		
3[a]	34	m	Pituitary		Antihypertensive	+	2	30	+++
4[a]	31	f	Pituitary			+	3		+
5[a]	33	m	Pituitary			+	2		++
6[a]	41	f	Pituitary	t, g, s	T_4, oral antidiabetic	+	2		
7	39	f	Pituitary		Allopurinol	+	3		+
8	71	f	Pituitary		Antihypertensive, nitrates	+	2		
9	66	f	Pituitary		Diuretic, heparine	++	1		
10	37	f	Pituitary		Oral antidiabetic		3		
11	36	m	Pituitary	g	Testosterone, antihypertensive	+	2	10	+
12	41	f	Pituitary		Antihypertensive, diuretic	+	2		+
13	45	f	Pituitary		Antihypertensive		3		+
14	70	f	Pituitary	s	Antihypertensive, digitoxin	+	1		
15	35	m	Adrenal		Antihypertensive	+	2	15	++

[a] Patients included for follow-up studies; abbreviations: pituitary, pituitary adenoma; adrenal, adrenal adenoma; g, gonadotropic; t, thyreotropic; s, somatotropic axis.

Alcohol intake: +, 1–5 drinks, ++, 6–10 drinks; +++, >10 drinks/wk; leg edema: +, mild; ++, moderate; physical activity: 3, no dysfunction; 2, working suboptimally; 1, ambulatory, 0, bedridden.

t test. Spearman's correlation coefficient was calculated for testing the relationship between different quantities in a bivariate regression model. Agreement between BIA and TBP for BCM estimation was analyzed using the graphic method of Bland and Altman (24).

Results

Age and gender distribution as well as body height were not different between controls and untreated patients with CS (Table 2). Body weight and, thus, body mass index were significantly higher in obese patients and in patients with CS ($P < 0.05$).

Body composition in CS and controls

Body composition assessment by anthropometry showed a significant increase of body fat indicated by increased arm fat area ($P < 0.05$) in obese patients and in CS compared with nonobese controls (Table 3). Arm muscle area was significantly lower in patients with CS ($P < 0.05$, Table 3), indicating a loss of skeletal muscle mass.

In healthy controls, mean BCM estimated by TBP was 4% lower ($P < 0.04$), and in CS patients mean BCM was 18.4% lower ($P < 0.001$) than predicted values (Table 3). In contrast, in weight-matched obese patients, TBP derived BCM was 7% higher than predicted ($P < 0.04$).

In CS patients, the mean absolute measured TBP and the mean TBP derived BCM were also significantly lower when compared with healthy controls (−20.2%; $P < 0.05$) or weight-matched obese patients (−21.1%; $P < 0.05$) (Fig. 1 and Table 3). When expressed as percentage of body weight, BCM_{TBP} was significantly lower in Cushing patients (26.7 ± 4.2% of body weight) than in obese patients (34.4 ± 4.1%) or in healthy controls (39.8 ± 7.5%) (Fig. 2).

Additionally, BIA was performed to study different body compartments. Mean whole body resistance values were not different between patients and controls. In CS, mean whole body reactance was significantly lower than in nonobese controls, and the mean phase angle was significantly lower than in nonobese controls as well as in obese patients (Table 3). Using standard BIA equations, total body water and fat-free mass were not different between Cushing patients and controls or obese patients. In accordance to anthropometry data, mean BIA-derived fat mass was significantly increased in Cushing patients as well as in obese patients compared with nonobese controls. However, in contrast to TBP data, no difference of mean BIA derived BCM was found between patients and controls.

Mean absolute values of BCM_{BIA} were not different from BCM_{TBP} in nonobese controls (Table 3). However, BCM_{BIA} was significantly higher than BCM_{TBP} in obese patients (+ 1.9 ± 2.4 kg; $P < 0.05$) as well as in patients with Cushing's disease (+3.9 ± 3.2 kg; $P < 0.001$), indicating a systematic overestimation of BCM by the BIA approach in both disease states with increased fat mass.

However, there was an excellent and highly significant correlation between BCM_{BIA} and BCM_{TBP} in nonobese controls (r = 0.95; $P < 0.0001$), in weight-matched obese patients (r = 0.96; $P < 0.0001$) as well as in patients with CS (r = 0.85, $P < 0.0001$), data not shown. The limits of agreement (*i.e.* between which 95% of all differences lie) were ±4.0 kg (±14.7%) in controls, ±4.9 kg (±17.4%) in obese patients, and ±6.6 kg (±27.6%) in patients with CS (Fig. 3).

Effect of treatment

In a subgroup of 6 patients with Cushing's disease, TBP, anthropometry, and BIA measurements were performed re-

TABLE 2. Clinical data of the study population

	Controls (n = 15)	Obese (n = 15)	CS (n = 15)
Age (yr)	44.3 ± 6.9	47.0 ± 10	42.7 ± 14.2
Gender (f/m)	10/5	10/5	10/5
Weight (kg)	68.4 ± 9.2	79.3 ± 13.2[a]	81.1 ± 15.4[a]
Height (cm)	172.5 ± 9.3	166.7 ± 8.1	170.3 ± 11
BMI (kg/m^2)	23.0 ± 2.7	28.4 ± 2.9[a]	27.9 ± 3.1[a]

Values are given as mean ± SD.
[a], $P < 0.05$, *vs.* controls.

TABLE 3. Assessment of body composition

	Controls (n = 15)	Obese (n = 15)	CS (n = 15)
Total body potassium			
Body cell mass, measured (kg)	27.2 ± 6.2[e]	27.5 ± 6.6[e]	21.7 ± 5.1[a,c,f]
Body cell mass, predicted (kg)	28.3 ± 6.1	25.7 ± 5.6	26.6 ± 6.7
TBP_m (mol)	2.963 ± 0.672[e]	2.990 ± 0.720[e]	2.360 ± 0.557[a,c,f]
TBP_p (mol)	3.085 ± 0.654	2.797 ± 0.608	2.895 ± 0.734
TBP % predicted	96.0 ± 7.2	107.1 ± 12.2[a]	82.2 ± 12.1[a,d]
Anthropometry			
Arm muscle area (cm^2)	51.5 ± 13.6	60.5 ± 19.0	47.6 ± 8.8[c]
Arm fat area (cm^2)	19.6 ± 8.8	30.3 ± 9.2[a]	31.5 ± 10.1[a]
BIA			
Resistance (Ohm)	552.1 ± 76.4	510.3 ± 107.7	549.6 ± 66.9
Reactance (Ohm)	59.3 ± 7.4	55.1 ± 13.6	49.6 ± 10.2[a]
Phase angle (°)	6.17 ± 0.54	6.18 ± 0.91	5.13 ± 0.88[b,d]
Total body water (l)	37.9 ± 7.7	40.3 ± 10.4	39.6 ± 8.2
Fat free mass (kg)	52.7 ± 9.5	56.0 ± 13.2	54.0 ± 11.2
Fat mass (kg)	15.7 ± 6.4	23.4 ± 3.5[a]	27.0 ± 8.7[b]
Body cell mass (kg)	27.9 ± 5.4	29.4 ± 7.8	25.6 ± 6.2

Values are given as mean ± SD; TBP_m, measured total body potassium; TBP_p, predicted total body potassium; [a] $P < 0.05$; [b] $P < 0.001$ *vs.* controls; [c] $P < 0.05$; [d] $P < 0.001$ *vs.* obese; [e] $P < 0.05$; [f] $P < 0.001$, TBP_m *vs.* TBP_p; body cell mass m *vs.* body cell mass p.

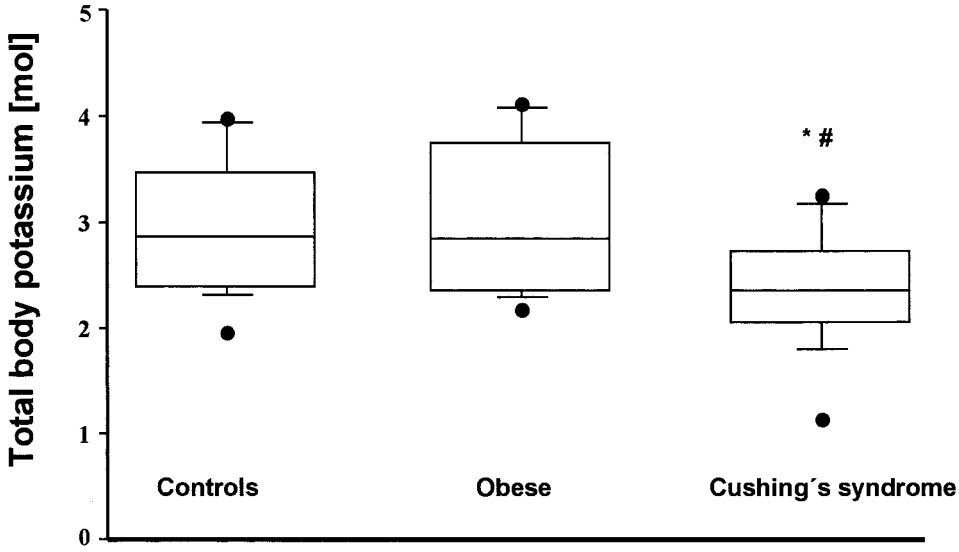

FIG. 1. Box plot displaying the 10th, 25th, 50th, 75th, and 90th percentiles of TBP counting in nonobese controls (n = 15), in weight-matched obese patients (n = 15), and in patients with CS (n = 15). *, $P < 0.05$ controls *vs.* CS; # $P < 0.05$ obese *vs.* CS.

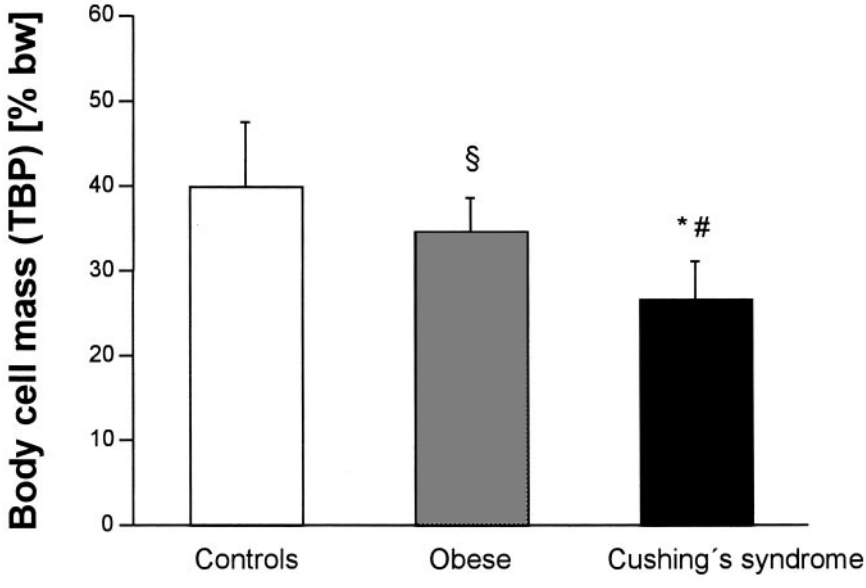

FIG. 2. Comparison of BCM calculated from TBP counting expressed as percentage of body weight in controls (n = 15), in weight-matched obese patients (n = 15), and in patients with CS (n = 15); values are mean ± SD; *, $P < 0.001$, controls *vs.* CS; #, $P < 0.001$ obese *vs.* CS; §, $P < 0.01$ obese *vs.* controls.

peatedly before and 1, 3, and 6 months after successful transsphenoidal pituitary surgery. The results are given in Table 4.

A significant decrease of mean body weight was observed at 3 and 6 months after surgery, respectively (−5.5 kg or −6.1% and −10.7 kg or −11.1%, respectively; both $P < 0.03$) compared with preoperative values. Six months after surgery there was a significant reduction of body fat as determined either by arm fat area (−9.4 cm^2 or −25.9%, $P < 0.05$) or BIA (−11.4 kg or −33.9%, $P < 0.01$. In contrast, mean TBP, arm muscle area, and BIA raw data (resistance, reactance, phase angle) as well as BIA-derived total body water, fat-free mass, and BCM remained unchanged even 6 months after surgery.

Discussion

In this prospective study, the body composition of patients with CS was compared with nonobese healthy controls and with weight-matched obese subjects of similar age, gender, and body height. As expected, body weight as well as total body fat estimated by anthropometry and BIA were significantly higher in obese patients and in patients with CS when compared with nonobese healthy controls. The common assumption of protein catabolism and the clinical impression of muscle wasting and muscle weakness in patients with hypercortisolism (2, 6, 9) was supported by our finding that the anthropometrically obtained arm muscle area was significantly reduced in Cushing patients when compared with weight-matched obese patients (Table 3).

Estimation of BCM by TBP

However, anthropometry provides only a gross estimate of fat-free mass, and we used the TBP approach to calculate BCM to obtain a more meaningful measure of the whole body protein content. Interestingly, in weight-matched obese sub-

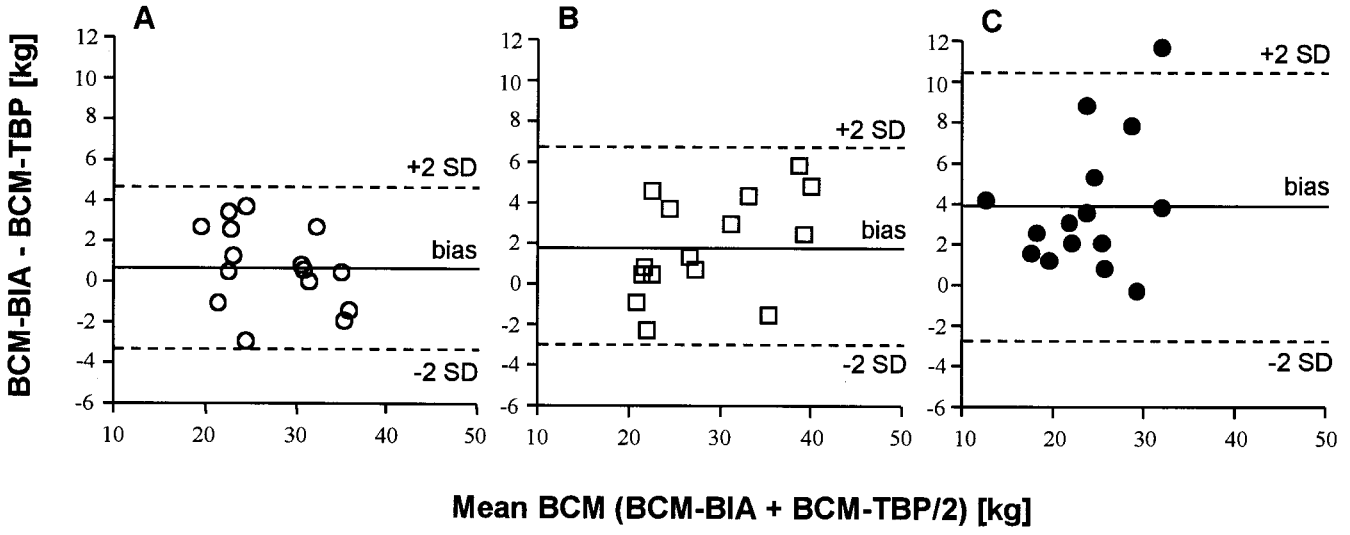

FIG. 3. Agreement between BCM estimated from BIA and BCM estimated from TBP in 15 controls (A), in 15 obese patients (B), and in 15 patients with CS (C). Data are plotted according to Bland and Altman (24). *Solid lines* represent the calculated mean bias between both methods, *dashed lines* represent the limits of agreement (± 2 SD) between which 95% of the differences would be expected. Note the significant overestimation by BIA of BCM in Cushing's patients.

TABLE 4. Changes of body composition in six patients after successful treatment of CS

	Before surgery	After surgery 1 month	3 months	6 months
Serum cortisol (nmol/l)	986.7 ± 350.2	106.6 ± 104.8[a]	162.7 ± 88.3[a]	232.2 ± 156.9[a]
Body weight (kg)	89.9 ± 15.3	89.2 ± 14.3	84.4 ± 13.4[b]	79.2 ± 12.2[b]
Total body potassium				
TBP_m (mol)	2.68 ± 0.54	2.68 ± 0.56	2.6 ± 0.57	2.68 ± 0.57
Body cell mass (kg)	24.6 ± 5	24.6 ± 5.1	23.9 ± 5.2	24.6 ± 5.2
Anthropometry				
Arm muscle area (cm^2)	48.3 ± 7.0	46.8 ± 4.5	48.8 ± 4.2	50.0 ± 3.0
Arm fat area (cm^2)	36.2 ± 10.1	37.5 ± 8.4	34.6 ± 7.0	26.8 ± 3.8[b]
BIA				
Resistance (Ohm)	559.8 ± 56.6	509 ± 14.2	495.6 ± 19.8	511.8 ± 29.8
Reactance (Ohm)	49.8 ± 5	43.6 ± 4.7[b]	42.6 ± 1.1	45.2 ± 2.1
Phase angle (°)	5.1 ± 0.2	4.9 ± 0.5	4.9 ± 0.2	5.1 ± 0.2
Total body water (liters)	41.2 ± 8.1	43 ± 7.3	43.2 ± 7.9	41.7 ± 7.6
Fat mass (kg)	33.6 ± 9.9	30.4 ± 8.9[a]	25.4 ± 8.4[a]	22.2 ± 5.3[a]
Fat free mass (kg)	56.2 ± 11.2	58.8 ± 10	59 ± 10.7	57 ± 10.3
Body cell mass (kg)	26.4 ± 5.3	27.2 ± 6.1	27.3 ± 5.7	26.8 ± 5.3

Values are given as mean ± SD; [a] $P < 0.01$; [b] $P < 0.05$, before *vs.* after surgery.

jects measured BCM was 7% higher than predicted values, whereas in nonobese controls measured BCM was 4% lower than predicted (Table 3), although BCM expressed as percentage of body weight was lower in obese subjects than in lean healthy controls (Fig. 2). This finding is in accordance to previous studies demonstrating that, in simple adiposity, not only the fat mass but also the absolute fat-free mass is higher than in nonobese healthy subjects (2, 8, 25), which can be explained by an enlarged skeletal muscle mass necessary to preserve physical mobility.

In contrast, in CS BCM calculated from TBP was significantly reduced by 18.4% when compared with predicted values, and 20.2% and 21.1% lower than in nonobese controls or in weight-matched obese subjects (Fig. 1 and Table 3). Moreover, in CS BCM expressed as percentage of body weight was markedly reduced when compared with nonobese controls and even when compared with weight-matched obese controls (Fig. 2). These data support the hypothesis that endogenous hypercortisolism causes not only an uncoupling of the parallel increase of fat-free mass and fat mass as observed in simple adiposity, but a true loss of the whole body protein depots (6, 9).

Estimation of BCM by BIA

In contrast, BIA did not indicate a significant loss of fat free or BCM in CS (Table 3). This discrepancy to TBP data or anthropometry is most likely explained by methodological limits of the BIA approach. In general, the validity of standard BIA equations is reduced in adiposity (26), because the trunk of the body contributes as little as 10% to whole body impedance, whereas it represents as much as 50%—and in adiposity even more—of whole body mass (27). In fact, we found an excellent correlation between BCM_{TBP} and BCM_{BIA} in healthy controls and in obese subjects as well as in patients with CS, but we observed a systematic overestimation of

BCM by the BIA approach in obese subjects and in CS (Fig. 3 and Table 3). Moreover, in the individual patient with CS, we found a much lower agreement between both methods compared with controls or obese subjects (Fig. 3). The latter finding suggests that in CS validity of BIA in estimating BCM is not only affected by increased fat mass but might additionally be influenced by fluid retention because lower limb edema were observed in 80% of our patients. Therefore, while the BIA equation used in this study (22) meet a sufficient standard of precision for clinical use in healthy subjects or—as previously demonstrated—in protein-depleted patients with chronic liver disease (12), it might not be appropriate for BCM determination in the individual patient with CS. Therefore, we suggest to develop a population-specific BIA equation for the assessment of BCM in a larger group of patients with CS.

Changes of body composition after surgical treatment

Within 6 months after pituitary surgery, mean body weight decreased significantly by 11% (Table 4) and analysis of body compartments demonstrated that this weight loss was predominantly attributed to a loss of body fat (− 33% of initial values). To our knowledge, there is only one study with a similar longitudinal approach of body composition change in patients with CS: Lonn *et al.* (3) investigated changes of body fat mass by computed tomography in 7 women within 8 ± 2 months after surgical treatment and observed a similar relationship between weight loss and reduced total body fat.

Previous studies on 1(−14) C-leucine turnover suggested that endogeneous hypercortisolism causes inhibition of protein synthesis (10). Therefore, one would expect an increase of protein synthesis and subsequently an increase of the protein depots after normalization of hypercortisolism.

However, in our study mean TBP values as well as anthropometrically obtained arm muscle area remained constant and did not increase to normal values within the 6-month postoperative period (Table 4). Similarly, the reactance and the phase angle as well as BIA-derived total body water, fat-free mass, and BCM also remained on a constant level even 6 months after surgery. These data suggest that in the early recovery from hypercortisolism, only the fat mass changes to normal values, whereas the protein depots remain on a constant low level. A possible explanation for this finding might be that patients in the early recovery from hypercortisolism are of high risk to have a low energy input and low physical exercise due to inappetence and general weakness associated with the corticosteroid withdraw. This might cause a prolonged low protein synthesis. Although we did not study the dietary intake of our patients, evidence for this hypothesis is given by findings on adipose subjects with long-term weight loss during a low energy diet (28, 29). In these patients, a similar constellation is found: the observed weight loss is mainly due to a loss of body fat with a nearly constant fat-free mass. Additional factors causing delayed normalization of protein synthesis might be the transient postoperative gonadotropic and/or somatoropic dysfunction observed in 5 of the 6 patients. Thus, hypogonadism as well as GH deficiency may also contribute to persistent low BCM after surgical treatment of hypercortisolism.

It is tempting to speculate that in our study the observation period of 6 months was too short to show a complete normalization of body composition after surgical cure of hypercortisolism, and it would be of interest to study the TBP in these patients after a longer period of time, for example, 12 months after surgery.

In conclusion, this study shows that in untreated patients with CS the body fat is markedly increased compared with nonobese controls, but a significantly reduced BCM indicates a true protein loss in these patients. In the early recovery from hypercortisolism the observed decrease of body weight is attributed to a loss of body fat, but the low BCM does not normalize within the first 6 months after successful pituitary surgery.

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