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Changes in body composition and resting energy expenditure after rapid weight loss: is there an energy-metabolism adaptation in obese patients?

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The aim of this study was to assess changes in resting energy expenditure (REE) related to changes in fat free mass (FFM) in nine morbid obese (BMI 43 ± 5.1 kg/m²) hospitalised females on VLCD. REE was measured by 30 min indirect calorimetry before and after 28 days of hospitalisation. Changes in FFM were assessed by bioelectrical impedance analysis (BIA), hydrostatic weighing (HW) and nitrogen balance (N). REE decreased 11.5% from 7.8 ± 1.0 to 6.9 ± 0.8 MJ/d. Total weight loss was 8.4 ± 1.9 kg or 7.4% with an estimated FFM loss of 3.4 ± 1.8 (BIA), 2.9 ± 1.9 (HW) and 1.8 ± 1.0 (N). As the fall in REE was larger than the loss of FFM, it is concluded that morbid obese patients develop an energy saving adaptation during rapid weight loss.

Keywords: obesity, resting energy expenditure, body composition, VLCD

Introduction

Obese individuals who achieve significant weight loss by dieting have several problems in maintaining the reduction. This may be due to decreases in energy expended by the subject for various energy-requiring processes. Since resting energy expenditure (REE) is mainly determined by fat free mass (FFM),[1,2,3] difficulties exist in evaluating whether the REE drop is due to the rapid changes in body composition or to the energy efficiency improvement of metabolically active tissue.

Over the last 10 years, many investigators have attempted to quantify the reduction in REE that can be explained by the reduction of FFM following a very low calorie diet (VLCD) in obese patients (Table 1). In seven of these studies, a decrease in REE/kg of FFM was observed, suggesting an energy metabolism adaptation process. Although a decrease in absolute REE was found in the other six studies, there were no significant changes in REE/kg FFM.

In all the above-mentioned studies, REE was measured by indirect calorimetry. Hence, these inconsistant results could be explained, mainly, on the basis of errors associated with the methods used for measuring the changes in FFM, as suggested recently by Ficker *et al.*[13] Since it is not possible to make direct comparisons between these studies with any degree of accuracy because of the heterogeneity of obese patients investigated (age, gender, body-mass-index), type and duration of diets as well as the amount/type of exercise prescribed, the present study was designed.

(1) to determine the magnitude of REE change related to FFM loss associated with rapid weight loss on a VLCD and

(2) to evaluate three different methods currently employed to assess FFM loss.

Subjects and methods

Subjects

We studied nine women with morbid obesity (BMI > 35 kg/m²) without diabetes mellitus, impaired glucose tolerance (GTT assessment under WHO recommendations[15]), bulimia nervosa[16] or any primary or secondary metabolic disease. The subjects were hospitalised for 28 days. During the previous 3 months all of them had been dieting but body weight had remained stable, suggesting an equilibrium in energy balance.

The study protocol was approved by the ethics committee of the Hospital St. Joan and each subject gave voluntary, fully-informed, written consent to participation in the study.

Study design

On hospitalisation, all the subjects were prescribed a VLCD for weight loss. On day 1 and before VLCD administration and day 28 after dieting, body composition by bioelectrical impedance and hydrostatic weighing together with REE measurements were performed. Nitrogen balance was also assessed to determine changes in FFM.

VLCD

All subjects received a commercial VLCD liquid preparation (Modifast^{R}, Wander SA, Bern, Switzerland) containing

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Table 1 Summary of published studies to-date of energy metabolism adaptation in obese patients on VLCD

Citation	*Subjects*	*Initial % of IBW or BMI*	*FFM assessment method*	*% of weight loss*	*% of decrease in REE*	*% of decrease in REE/kg of FFM*
Bessard *et al.*[4]	F (*n*=5)	156%	Anthropometry	13.8	14.3	9.6*
Welle *et al.*[5]	F (*n*=6)	168%	Total body potassium	11.9	9.3	NS
Ravussin *et al.*[6]	M&F (*n*=7)	146-219%	Anthropometry	13.2	9.2	5.1
Barows & Snook.[7]	F (*n*=15)	159%	Densitometry	21.7	21.0	6.6*
Hill *et al.*[8]	F (*n*=8)	163%	Densitometry	8.3	18.4	13.0*
Hendler & Bonde.[9]	F (*n*=17)	137%	Nitrogen balance	6.7	14.2	11.1*
Elliot *et al.*[10]	F (*n*=7)	37.6 kg/m^2	Densitometry	7.3	22.0	7.2*
Davies *et al.*[11]	F (*n*=8)	39.1 kg/m^2	Total body potassium	13.5	17.0†	NS
Wadden *et al.*[12]	F (*n*=9)	39.7 kg/m^2	Densitometry	21.0	24.4	14.2*
Fricker *et al.*[13]	F (*n*=6)	33.3 kg/m^2	Nitrogen balance	10.5	20.0	17.5*
Stallings *et al.*[14]	M&F (*n*=7)	166%	Total body potassium Total body water Anthropometry	17.6	13.4	10.3 6.4 4.9

F = females; M = males; IBW = ideal body weight; BMI = body mass index; FFM = fat free mass; REE = resting energy expenditure.
† *% of increase in VO_2*
* *Significant decrease of REE-FFM ratio. NS = non significant.*

approximately 52 g protein, 46 g carbohydrate, 6.5 g fat (46%: 41%: 13% percentage energy, respectively). Energy administered by this formula was 1915 KJ/d (458 Kcal/d). The formula also contained electrolytes, trace elements and vitamins in accordance with the recommended dietary allowances.[17] Ketogenesis process was assessed by measuring ketone bodies in urine three times a day during the whole period. In case of ketogenesis, extra energy in the form of 5 g of sacharose supplements was added. None of the patients required more than 20 g/d of sacharose to preempt ketogenesis.

The diet was provided in three isocaloric aliquots (breakfast, lunch and dinner) on each of the 28 days of the study. Daily non-caloric fluid intake was < 2 L.

Resting energy expenditure measurements

REE was assessed using open-circuit indirect calorimetry (Deltatrac^R Datex, Helsinki, Finland), which includes a fast differential paramagnetic O_2 sensor and an infrared CO_2 analyzer. Exhaled air was collected using a canopy.

At 8 am after a 12 h overnight fast, VO_2 and VCO_2 were calculated from 30 min of continuous measurements on basal conditions and after a 30-min equilibration period to avoid unstable energy expenditure.

REE was calculated using Weir's equation:[18]

REE (kJ) = 14.98 VO_2 (L) + 6.06 VCO_2 (L) – 7.42 urinary nitrogen.

Before each test, O_2 and CO_2 sensors were calibrated using gas mixtures of precisely known O_2 and CO_2 concentrations. The precision of the RQ and flow measurements were confirmed periodically by the ethanol cumbustion test.[19] The mean error of RQ and flow determinations were 1% and 1.72% respectively. The within-individual mean standard deviation for day to day replicate measurements of REE, in our laboratory, is 164 kJ which corresponds to a coefficient of variation of analysis of 2.3%.

Body-composition measurements

All measurements were performed under the same conditions at days 1 and 28 of the study. Height was measured to the nearest 1mm using a wall-mounted stadiometer (Hotain, Crosswell, Walles, UK). Weight was measured with an accuracy of ± 100 g. BMI was calculated as wt/ht.^{2}

Whole body density was measured using an hydrostatic weighing system.[20] This method consists of estimating body density from the body weight when the subject is totally immersed in water. The measurements were conducted under fasting conditions and after voiding. The interior dimensions of the weighing tank were 1.80m × 1m × 1.20 m (length × width × depth). Within the tank was a weighted couch suspended from a torsion balance installed in the center of the room's ceiling. The balance was connected to a precision balance display and subsequently to a computer with a software program that provides instantaneous weight measurements, bar graphics of weights and the arithmetic means of selected weight intervals. Before the measurements, patients were seated on the couch with water up to breastlevel and were then requested to recline slowly until the body was totally immersed while exhaling to residual lung volume in the process. This procedure was repeated 7 to 10 times and the final weight was the mean of the three highest weight measurements.

Body density was calculated as follows:[21]

$$D = wt/(wt - UWW - RV - GIV)$$

where wt is weight in air, UWW is weight underwater, RV is residual lung volume calculated with the helium-dilution technique,[22] and GIV is gastrointestinal volume (assumed to be 100 mL). All values used were corrected for the density of water at ambient temperature and barometric pressure.

Body fat was calculated from the equation of Siri,[23] assuming the density of fat to be 0.9 kg/L and the density of lean tissue to be 1.1 kg/L.

$$\% \text{ Fat} = [(4.95/d) - 450] \times 100$$

A value for FFM was obtained by subtracting fat mass from total body weight in air.

Tetrapolar bioelectrical impedance analysis (TBIA)

Whole-body resistance was measured under fasting conditions using a tetrapolar-bioelectrical impedance (Human-Im Scan,® Dietosystem, Spain). Patients lay supine on a bed without shoes or socks or any metallic object, the limbs and arms slightly abduced, fingers extended and palms facing the bed. Self-adhesive electrodes were then positioned on the dorsal surfaces of the hand and foot of the left side. One of the pair of hand electrodes was placed at the wrist in line with the proximal edge of the ulnar tubercle and the other 5 cm away and proximal to the third metacarpal-phalangeal point. Of the pair of electrodes on the foot, one was positioned at the ankle in line with the medial malleolus and the other 6 cm away just proximal to the third metatarsal-phalangeal point. The distal electrodes of the hand and the foot were connected to an excitation current of 800 μA at 50 kHz and the voltage drop due to the passage of current through the patient's body was detected by the proximal electrodes.

The mean coefficient of variation for within-patient impedance (Z) measurements was 0.71%. On all occasions, the observed resistance deviated from the expected value by < 3.5 Ohms.

Fat-Free Mass (FFM_I) was calculated using the following equation validated for obese females:[24]

$$FFM_I = 0.00091186\ ht^2 - 0.01466\ R + 29990\ wt - 0.07012\ A + 9.37938$$

where ht is height in cm; R, Resistance; wt, body weight in kg and A, age in years. Z is assumed to be equal to R at 50kHz.

The FFM_I loss is the result of subtracting FFM_I on day 28 from FFM_I on day 1.

Nitrogen balance (N) measurements

The change in LBM during the VLCD period was estimated from changes in nitrogen balance.

For all patients, 24-h urine samples were collected and analyzed daily for nitrogen content using the Kjeldahl technique.[25] Nitrogen losses via the skin were taken as 5 mg N/kg/d[26] which, for obese patients at rest and in basal conditions, would probably be an over- rather than to an underestimation. Menstrual nitrogen losses were assumed, at the upper range (90–100mL) of menses volume, as 0.1 g N loss/d.[27] Nitrogen losses due to nitrates formation and faecal nitrogen were taken as 0.1 g N/d and 0.003 g N/kg/d respectively, as previously reported.[16]

Changes in LBM were estimated from cumulative nitrogen balance, assuming 1g of nitrogen to be 6.25 g of body protein or 31.25 g of LBM.

On each day of REE measurements, FFM was estimated by two different methods:

(1) TBIA (FFM_I) and (2) densitometry (FFM_D). LBM_N was the difference between FFM_D on day 1 and cumulative N.

Statistical analyses

Statistical analyses were performed using the SPSS/PC package. Results were expressed as mean ± s.d. Data were analyzed by the non parametric Wilcoxon-test for two related samples. Regression analyses were performed for quantitative variables and *r* coefficients were derived. Statistical significance was set at the 0.05 level.

Results

Subjects' physical characteristics on admission are shown in Table 2.

Table 2 Physical characteristics of subjects on admission to hospital

Subject	*Age (years)*	*Body weight (kg)*	*BMI (kg/m²)*	*FFM* (kg)*
1	37	122.2	44.3	62.1
2	40	120.0	42.5	64.6
3	35	135.8	51.7	64.2
4	38	114.3	48.2	53.2
5	43	116.9	45.1	59.2
6	53	115.2	46.1	59.8
7	47	89.9	35.1	47.8
8	48	94.1	37.7	47.6
9	19	114.7	41.3	60.9
× ± s.d.	40.0 ± 9.8	113.7 ± 13.9	43.6 ± 5.1	57.7± 6.6

* *Assessed by densitometry analysis.*

Table 3 Cumulative nitrogen losses, changes in body weight and lean body mass after 28 days on VLCD

Subject	*Urine nitrogen losses (g/4 wk)*	*Fecal nitrogen losses† (g/4 wk)*	*Other nitrogen losses† (g/4 wk)*	*LBM* loss (kg)*	*Body-weight loss (kg)*
1	280.6	7.2	22.7	2.43	7.8
2	291.4	9.9	22.4	2.84	9.9
3	311.1	6.5	24.6	3.42	10.6
4	233.5	5.2	21.6	0.86	6.0
5	254.1	6.8	21.9	1.56	8.2
6	254.3	6.4	21.7	1.55	7.6
7	261.8	6.9	18.2	1.69	7.3
8	213.9	6.8	18.8	0.21	6.5
9	248.3	6.8	21.7	1.37	11.7
× ± s.d.	261.0 ± 29.6	6.9 ± 1.2	21.5 ± 2.0	1.77 ± 0.99	8.4 ± 1.9

* *Assessed by the nitrogen balance method.*
† *Predicted values.*

Table 4 Decreases in FFM and LBM pre- and post-VLCD assessed by three different methods

Subject	FFM_I (kg)			FFM_D (kg)			LBM_N (kg)		
	Pre	Post	Difference	Pre	Post	Difference	Pre	Post	Difference
1	63.2	62.8	0.4	62.1	61.9	0.2	62.1	59.6	2.4
2	66.7	62.1	4.6	64.6	61.4	3.2	64.6	61.8	2.8
3	68.8	63.8	4.2	64.2	57.5	6.7	64.2	60.8	3.4
4	54.8	52.6	2.2	53.2	51.2	2.1	53.2	52.4	0.9
5	59.5	57.6	1.9	59.2	56.6	2.6	59.2	57.7	1.6
6	61.9	57.3	4.6	59.8	57.5.	2.3	59.8	58.2	1.6
7	47.3	44.6	2.7	47.8	45.1	2.7	47.8	46.1	1.7
8	48.6	45.6	3.0	47.6	46.0	1.6	47.6	47.4	0.2
9	61.7	55.2	6.5	60.8	56.1	4.8	60.8	59.5	1.4
× ± s.d.	59.1 ± 7.4	55.7 ± 7.1	3.4 ± 1.8	57.7 ± 7.1	54.8 ± 6.1*	2.9 ± 1.9	57.7 ± 6.6	55.9 ± 5.8**	1.8 ± 1.0

* $P = 0.03$; ** $P < 0.001$ Pre- vs post dietary values.
FFM_I = Fat free mass assessed by tetrapolar bioelectrical impedence analysis.
FFM_D = Fat free mass assessed by densitometry.
LBM_N = Lean body mass assessed by densitometry at the beginning of the study and by subtracting LBM losses estimated by the nitrogen balance method at the end of the dieting period.

Cumulative nitrogen losses and changes in LBM and body weight during VLCD period are presented in Table 3. Mean weight loss during the 28 days of dieting was 8.4 ± 1.9 kg or 7.39% of the initial body weight. Table 4 contains the weight reduction due to FFM, in absolute values and percentages depending on the method used for its measurement. Of the weight loss, 3.4 ± 1.8 kg corresponded to FFM when FFM losses were assessed by TBIA (NS), 2.9 ± 1.9 kg when densitometry was used ($P = 0.03$) and 1.8 ± 1.0 kg when cumulative N was subtracted from FFM_D on day 1 ($P = 0.001$). There was a statistically significant relationship between FFM losses assessed by TBIA and that assessed by densitometry ($r = 0.69$; $P < 0.05$). LBM losses determined by N did not show a significant relationship with other methods of estimating FFM loss.

REE, in absolute values (Table 5), decreased significantly ($P < 0.001$) from day 1 (7827 ± 1034 kcal/d) to day 28 (6867 ± 786 kcal/d). REE values in relation to FFM_I, FFM_D and LBM_N on days 1 and 28 are shown in Table 6. REE/kg of FFM_I, REE/kg of FFM_D and REE/kg of LBM_N decreased significantly after weight loss ($P = 0.006$, $P = 0.006$ and $P < 0.001$, respectively).

From REE and FFM values on day 1, equations to predict REE from FFM measured by TBIA, densitometry and N on day 28 were obtained. Neither age nor any other body composition parameters entered the REE prediction equations. Predicted REE on day 28 were significantly higher than that observed ($P < 0.05$ for REE predicted from FFM_I and FFM_D and $P = 0.001$ for REE predicted from LBM_N).

Table 5 Resting energy expenditure pre- and post-VLCD

Subject	REE (kJ/d)		
	Pre	Post	Difference
1	7716	6837	879
2	8491	7130	1361
3	8196	7349	847
4	7237	6639	598
5	7773	6669	1104
6	9731	7918	1813
7	6548	5848	700
8	6387	5616	771
9	8361	7798	563
× ± s.d.	7827 ± 1034	6867 ± 788*	960 ± 406

* Significantly different from pre-dietary values ($P < 0.001$).

Table 6 REE expressed on the basis of FFM or LBM pre- and post-VLCD

Subject	REE/FFM_I		REE/FFM_D		REE/LBM_N	
	Pre	Post	Pre	Post	Pre	Post
1	122.0	108.8	124.3	110.5	124.3	106.0
2	127.2	114.8	131.4	116.2	131.4	105.7
3	120.5	115.2	127.7	127.8	127.7	108.7
4	132.1	126.3	135.9	129.7	135.9	122.7
5	130.7	115.8	131.2	117.9	131.2	109.7
6	157.2	138.1	162.8	137.8	162.8	129.1
7	138.4	131.2	136.9	129.6	136.9	118.1
8	131.4	123.2	134.2	122.0	134.2	117.5
9	135.5	141.2	137.4	139.1	137.4	125.3
× ± s.d.	132.8 ± 10.8	123.9 ± 11.2*	135.8 ± 11.0	125.6 ± 9.7*	135.8 ± 11.0	115.9 ± 8.7**

*,** Significantly different from pre-dietary values (*$P = 0.006$, ** $P = 0.0001$).

Discussion

Some obese individuals do not have a great deal of difficulty in reducing their body weight when they do decide to follow a dieting program. Others are incapable of achieving appreciable weight reduction. But what is common to nearly all of them is the difficulty they have in maintaining any weight loss achieved. The reasons for this could be psychological. However, possible physiological mechanisms need to be explored to explain the observations that the energy balance in post-obese individuals is very positive after rapid weight loss even when energy intake is similar to that of non-obese subjects of comparable height and weight.[28] Hence, it is essential to study the changes in REE related to FFM during a severe restriction of energy intake; FFM being the main contributor to REE.

In the present study, we observed a significant decrease of the REE-FFM ratio in morbid obese patients after 28 days on VLCD, independent of the method used to assess changes in FFM. Further, the changes in REE did not correlate significantly with changes in FFM. Hence, this drop in REE suggests the presence of a metabolic adaptation associated with underfeeding since REE is the major component of total energy expenditure.

There is general agreement among the previous published studies (see Table 1) in that a relationship exists between energy restriction and a short term drop in absolute REE which is related to the severity of the diet and the amount of weight lost. However, when REE was related to FFM (the major, but not the sole determinant of BMR), the studies were not in consensus on the presence, or absence, of a metabolic adaptation to very low calorie diets.[29] Since they had used similar and very precise methods to assess REE, the reason for this disagreement could be the result of the method used to assess body composition. For this reason, we measured losses of FFM using three different methods.

The TBIA method estimates the greatest absolute FFM loss and the N method, the lowest ($P = 0.05$). No significant relationship was observed between changes in FFM assessed by N *vs* TBIA and densitometry. TBIA values correlated significantly with densitometry values ($r = 0.69$; $P < 0.05$). These differences could be explained on the basis of the potential sources of errors associated with each method when applied in very obese patients on VLCD such as:

(1) The TBIA method is based on the conduction of an applied, constant, low-level, alternating electrical current to the body which results in a frequency-dependent opposition (or impedance) to the flow of current.[30] The body's FFM (containing a preponderance of water and electrolytes) has a high conductivity and a low impedance. In contrast, the body's fat mass, mainly composed of fat or triglyceride, has a low conductivity and a high impedance. Far from measuring FFM itself, the TBIA method provides an estimation of FFM as a reflection of the water and electrolyte content of the body. Any changes in the hydration of fat-free tissues would be a source of error in FFM estimation from TBIA values. This is probably the case for obese patients on a VLCD, since, in the initial phase of the dietary regimen, FFM undergoes a marked dehydration as a result of water losses associated with glycogen utilization and so, consequently, involves an underestimation of FFM at the end of the dieting period. Hence, in the present study, FFM losses by TBIA are greater in absolute terms than when measured by N or HW.

(2) The densitometry method consists of a measurement of body density by weighing individuals while submerged. Assuming that fat mass and FFM densities are constant (0.9 g/cm^3 and 1.1g/cm^3 respectively), it is possible to calculate fat mass and FFM in terms of kg and percentages. Even though densitometry is a reference method to assess body composition, its precision could decrease when FFM density changes. Since the calculated FFM losses reflect mainly losses in the form of water whose density (1 g/cm^3) is lower than that of FFM (1.1 g/cm^3[31]), densitometry would overestimate FFM losses. In our study, FFM changes measured by densitometry, in absolute terms, are greater than those observed by N and lower than by TBIA. These differences, however, were not statistically significant ($P = 0.072$ and $P = 0.39$, respectively).

(3) With respect to the N method, a more precise measurement of rapid changes in FFM wuold be expected since it provides direct measurement of nitrogen intakes and losses. It is generally accepted that the factor of 6.25 used for the conversion of measured nitrogen losses to protein loss has a higher reliability in the estimation of active-cell mass losses (the main energy-consuming compartment of LBM). Faecal, menstrual and skin nitrogen losses are merely estimated and not directly measured in this procedure, but as reported by Munro *et al.*,[31] only represent a 5% of the total nitrogen lost. However, a possibility exists that urine collections were incomplete and this could in part explain the lower FFM losses estimated by N compared to the other two methods.

Several studies failed to observe any drop in the REE corrected for FFM. This could be linked to the use of total body potassium,[32] total body water and anthropometry as methods of FFM assessment. Since all of these methods are largely influenced by tissue hydration, an overestimation of FFM would inevitably result. Anthropometry may not be a suitable method to assess body composition in very obese people and several investigators have expressed reservations regarding interpretable measurements because of instrumental and technical limitations inherent in the method. Moreover, the measurement of peripheral skinfold thickness is not appropriate in evaluating rapid changes in total fat mass since morbid obese patients on a VLCD lose fat mainly from visceral and abdominal subcutaneous tissue.

In principle, the metabolic adaptation after rapid weight loss observed in our patients could explain, at least in part, the weight gained by most obese individuals when they cease the diet program. However, under the present study

design conditions, whether the reduced REE related to FFM observed at the end of the VLCD period is entirely caused by energy restriction or whether obese patients after weight reduction have a permanent decrease in REE, cannot be evaluated.

In conclusion, the present study provides supportive evidence that an increased efficiency in energy utilisation results from rapid, severe weight loss in morbid obese patients. This is apparent irrespective of the method used to assess changes of FFM, provided that the potential sources of error of each method are recognised and controlled for. It seems unlikely that changes in the composition of FFM alone could explain the decrease in REE observed since it does not occur in other patient groups undergoing weight reduction.[33,34] However, data regarding the metabolically active cell mass in obese subjects are not available.

This metabolic adaptation could be linked to changes in the energy required for some metabolic processes involved in the modulation of REE such as protein turnover, ion gradient maintenance, substrate transport and cycling as well as involuntary contraction of striated muscle tissue.[28] Further studies would be necessary to confirm this hypothesis and to determine the possible mechanisms underlying the decrease of REE observed during energy restriction.

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