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Resting energy expenditure in patients with cirrhosis of the liver measured by indirect calorimetry, anthropometry and bioelectrical impedance analysis

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Abstract. Energy expenditure was investigated in 15 patients with liver cirrhosis and 20 healthy controls by three methods: indirect calorimetry, anthropometry using the Harris–Benedict equation and bioelectrical impedance analysis. The energy expenditure was expressed in kcal/day, kcal/kg BW/day (BW – body weight), kcal/kg LBM/day (LBM – lean body mass, derived by bioelectrical impedance analysis) or in kcal/m^2/day. We did not find statistical differences between values of resting energy expenditure obtained in patients with cirrhosis of the liver and healthy controls whichever method we used. We also did not find statistical differences between values obtained by indirect calorimetry, anthropometry and bioelectrical impedance analysis. There was a significant correlation between indirect calorimetry and anthropometry in both groups. We found significant correlations between indirect calorimetry and anthropometry, and between indirect calorimetry and bioelectrical impedance analysis, in the control group only. We can conclude that (1) resting energy expenditure of patients with cirrhosis of the liver is not changed when compared with healthy controls, and (2) bioelectrical impedance is a useful method to calculate body composition from which energy expenditure is derived; however, it gives an appropriate result only in healthy people, and only approximate values in patients with cirrhosis.
Key words. Energy expenditure; liver cirrhosis; indirect calorimetry; bioelectrical impedance analysis; anthropometry; Harris–Benedict equation.

Patients with liver cirrhosis were shown to have an increased[1–4], normal[3,5,6] or decreased[3,7] resting metabolic rate. Hypermetabolism is more frequently observed in advanced stages of cirrhosis and in malnourished patients[3,8]. The patients differed with respect to the cause of cirrhosis, clinical staging, nutritional state and degree of parenchymal cell destruction[3]. Indirect calorimetry determines the resting energy expenditure, but the method disregards both the conditions under which the measurement is taken and body composition[9]. When the calculation of resting energy expenditure is performed using the predictive formula of Harris–Benedict, the results are overestimated because the equation misrepresents the extracellular fluids accumulated in the peritoneal cavity, lower limbs and the sacroiliac area[9,10]. Another method to define body composition, and to calculate resting energy expenditure indirectly, is bioelectrical impedance analysis (BIA).

The purpose of this study was to investigate whether resting energy expenditure in cirrhotic patients is different from that in healthy controls. Another issue we have decided to investigate is whether bioelectrical impedance and anthropometry (based on the Harris–Benedict equation) are useful methods to define resting energy expenditure in patients with cirrhosis of the liver.

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Materials and methods

Fifteen patients with liver cirrhosis were compared with 20 healthy subjects. Patients were on a weight-maintaining diet for 1 week before the start of the study. The diet contained protein at 1 g/kg of body weight/day, fat also at 1 g/kg of body weight/day and carbohydrates at about 300 g/day. The fuel value of the diet was about 20–25% higher than the resting energy expenditure of each person. Physical effort was forbidden. Ten patients were men and five were women. Liver cirrhosis was diagnosed by means of clinical, ultrasonographic and biochemical methods, by measuring the pressure in hepatic veins (in eight cases), and by liver biopsy. Liver cirrhosis had a viral aetiology in all cases except two patients, in whom the aetiology was unknown. None had sepsis, fever, hepatic encephalopathy or digestive bleeding. Administration of corticosteroids or any other drugs that might affect basal energy expenditure was ruled out. On examination, all patients were in a stable clinical state – 7 in stage A and 8 in stage B according to Child's classification (they had bilirubin levels below 3 mg%, albumin level above 3 g%, had no or only mild ascites, had no neurological disturbances and had good alimentary status). None of the patients had a history of thyroid dysfunction or other endocrine or metabolic disease. Patients with elevated body temperature and

subjects with a history of cardiac and pulmonary diseases were excluded from the study protocol.

Experimental protocol. All patients stayed in our hospital for at least 7 days before the test. Measurements were performed after an overnight fast. Patients were asked to stay in bed in the morning (until 8.30 a.m.) and afterwards they were transferred to the metabolic ward. They rested in a quiet room at a constant temperature of 21–23 °C. The measurements were started at 9 a.m. using indirect calorimetry (computer system MedGraphics 2001, St. Paul, Minnesota, USA). A clear plastic ventilated hood was placed over the patient's head, and gas samples were collected automatically by respiratory diagnostic system. The estimation of metabolic rate took at least 30 min. A steady state was reached between 10 and 20 min. Calibrations were performed just before the measurements. Energy expenditure was calculated from the respiratory exchange data automatically by the computer system. Predicted resting energy expenditure according to Harris–Benedict equation[11] was calculated using the formula:

$$HB_{REE} = 66.5 + 13.75 \times W + 5.0 \times H - 6.75 \times A$$

– for men, and

$$HB_{REE} = 665.1 + 9.56 \times W + 1.85 \times H - 4.676 \times A$$

– for women,

where W = body mass (kg), H = height (cm), A = age (years).

The body surface area BSA (m^2) was calculated using the formula[12]:

$$BSA = 0.0235 \times H^{0.42246} \times W^{0.51456},$$

and the body mass index (BMI):

$BMI = W/H^2$ (where W is expressed in kilograms, H in meters).

The third method we used to calculate energy expenditure was bioelectrical impedance analysis (BIA) using a Body Fat Analyzer BT-905 MALTRON (Reyleigh, Essex, UK). We placed the electrodes at exactly the same site positions on each patient according to the manufacturer's instruction. All placements of skin electrodes were performed by the same skilled observer (M. Janusz). After introducing the data concerning age, height, sex and weight, the analyzer displayed the amount of body fat, lean body mass and water (all in kilograms and percent), and automatically calculated energy expenditure (BIA_{REE}). Measurements were performed with the patient lying quietly in bed.

Statistical analysis. All data are presented as means ±SD. Differences between groups were calculated by the Mann–Whitney two-sample (non-matched) test. Differences between results obtained by the three methods were calculated by analysis of covariance. $p < 0.05$ was considered significant. Afterwards we performed regression analysis between methods. Calculations were performed using a personal computer and program SOLO 4.0 BMDP statistical software.

Results

The main characteristics of both groups of persons are presented in table 1. The group of patients with liver cirrhosis and the control group were no different with respect to age, body weight, height, body mass index and body surface. Fat and water content, as well as lean body mass, were also comparable. Some important biochemical parameters of both groups are presented in table 1.

Mean resting energy expenditure (REE) measured by indirect calorimetry was 1693 ± 400 kcal/day in patients

Table 1. Main clinical and biochemical data of the patients with cirrhosis and control subjects.

Parameters	Units	Cirrhotic patients	Control subjects
Age	yr	37.7 ± 9.9	31.9 ± 8.6
Sex	M/F	10/5	13/7
Height	m	1.70 ± 0.09	1.75 ± 0.10
Weight	kg	72.5 ± 17.0	70.4 ± 13.3
Body mass index	kg/m^2	24.7 ± 4.2	23.1 ± 3.2
Body surface area	m^2	1.86 ± 0.26	1.84 ± 0.20
Fat	kg	12.9 ± 4.8	14.5 ± 7.1
Lean	kg	59.6 ± 13.6	55.9 ± 10.4
Water	kg	41.0 ± 9.9	42.3 ± 8.8
Total bilirubin	µmol/l	34.6 ± 11.8	14.95 ± 2.4
Asparagine transaminase	IU/l	82.1 ± 46.1*	22.7 ± 7.6
Alanine transaminase	IU/l	105.1 ± 54.2*	19.8 ± 6.79
γ-Glutamyl-transpeptidase	IU/l	110.5 ± 36.10*	35.5 ± 17.9
Alkaline phosphatase	IU/l	169.3 ± 54.7*	35.5 ± 17.9
Cholesterol	mg/dl	152.5 ± 44.8*	205.6 ± 41.9
Albumin	g/dl	36.3 ± 2.8*	40.6 ± 1.5
Prothrombin index	%	65.4 ± 14.7*	95 ± 5.38

*significantly different ($p < 0.05$ or less) from control subjects.

Table 2. Energy expenditure (mean and standard deviation) measured by indirect calorimetry (REE) and calculated by the Harris–Benedict method (HB_{REE}) or bioelectrical impedance analysis (BIA_{REE}). p = statistical difference between groups.

	Cirrhosis		Control		p
	mean	SD	mean	SD	
REE (kcal/d)	1693	400	1756	344	NS
REE (kcal/kg BW/day)	23.6	4.19	24.9	3.7	NS
REE (kcal/kg LBM/day)	28.4	4.87	31.4	4.0	NS
REE (kcal/m^2/day)	910	133	954	129	NS
HB_{REE} (kcal/d)	1571	291	1695	260	NS
HB_{REE} (kcal/kg BW/day)	21.7	3.0	24.1	1.7	NS
HB_{REE} (kcal/kg LBM/day)	26.3	3.9	30.3	2.3	NS
HB_{REE} (kcal/m^2/day)	848	64	921	59	NS
BIA_{REE} (kcal/d)	1587	292	1694	228	NS
BIA_{REE} (kcal/kg BW/day)	21.9	4.4	24.1	2.84	NS
BIA_{REE} (kcal/kg LBM/day)	26.6	6.0	30.3	1.7	NS
BIA_{REE} (kcal/m^{2}day)	853	98	921	61	NS

Table 3. Correlations of energy expenditure measured by indirect calorimetry (REE), or derived from anthropometry using the Harris–Benedict equation (HB_{REE}) and bioelectrical impedance analysis (BIA_{REE}).

	Methods	r	p
Cirrhosis	REE–HB_{REE}	0.61	0.0165
	REE–BIA_{REE}	0.34	0.2182
	HB_{REE}–BIA_{REE}	0.46	0.0851
Control	REE–HB_{REE}	0.60	0.0049
	REE–BIA_{REE}	0.28	0.2349
	HB_{REE}–BIA_{REE}	0.62	0.0035

with liver cirrhosis and 1756 ± 344 in healthy controls. Corresponding values calculated by the Harris–Benedict method were 1571 ± 291 and 1695 ± 260, respectively. When resting energy expenditure was calculated using bioelectrical impedance analysis, the corresponding values were 1587 ± 292 and 1694 ± 228 (fig. 1). The results obtained by each method did not vary between groups. There were also no statistical differences between groups when we expressed resting metabolic rate as kcal/kg BW/day (fig. 2), kcal/kg LBM/day (fig. 3), kcal/m^2/day (fig. 4) (table 2). When we compared the three methods used to define resting energy expenditure we did not find statistical differences between them, although the covariates (kg BW and kg LBM, but not body surface) were very significant in the study group and the control. We found significant correlation between indirect calorimetry and anthropometry in both groups. Significant correlation between anthropometry and bioelectrical impedance was observed in the control group only (table 3).

Discussion

This study was carried out to determine whether REE was altered in patients with liver cirrhosis. We found that REE measured by indirect calorimetry had almost the same value in the cirrhotic group and in the control group. There was no statistical difference between these two groups when the results were expressed as kcal/day, kcal/kg BW/day, kcal/kg LBM/day or kcal/m^2/day. Some clinical studies demonstrated that cirrhotic patients were hypermetabolic[1–4] or hypometabolic[3,7]. Muller et al.[3] found that only 18% of 123 patients were hypermetabolic, and 31% were hypometabolic. Another paper[8] reported that an increase in REE was more pronounced in patients with ethanol-induced cirrhosis, at advanced stages of the disease, and in association with decreased body cell mass. Energy expenditure in our cirrhotic patients was the same as in the control group. However, in all but two of our patients cirrhosis followed viral hepatitis and the disease was not advanced (Child's classification A and B). These facts could be the reason of our results being opposite to those reported in some papers[1–4,7].

John et al.[13] found that energy expenditure was not elevated in patients with alcoholic hepatitis. However, energy expenditure calculated per gram of creatinine excreted in urine was increased[13]. Pierruges et al.[14] reported that mean REE was significantly lower in malnourished cirrhotic patients (Child's classification A to C) than in well-nourished patients. However, the difference was insignificant and disappeared when the measurement of energy expenditure was corrected for 24-h urinary creatinine excretion. In another study[15] basal energy expenditure and REE measured three times a day were similar in cirrhotics and in controls. Energy expenditure predicted by the Harris–Benedict equation differed from measured basal energy expenditure (BEE) by 21% in individual controls and by 26% in cirrhotics[15].

Dolz et al.[9] found that ascites might be associated, at least in some patients, with increased REE measured by anthropometry. This seems obvious because the higher weight observed in the presence of ascites is a critical factor in the Harris–Benedict equation. We suppose that severe ascites can also be the reason for increased REE measured by indirect calorimetry due to increased

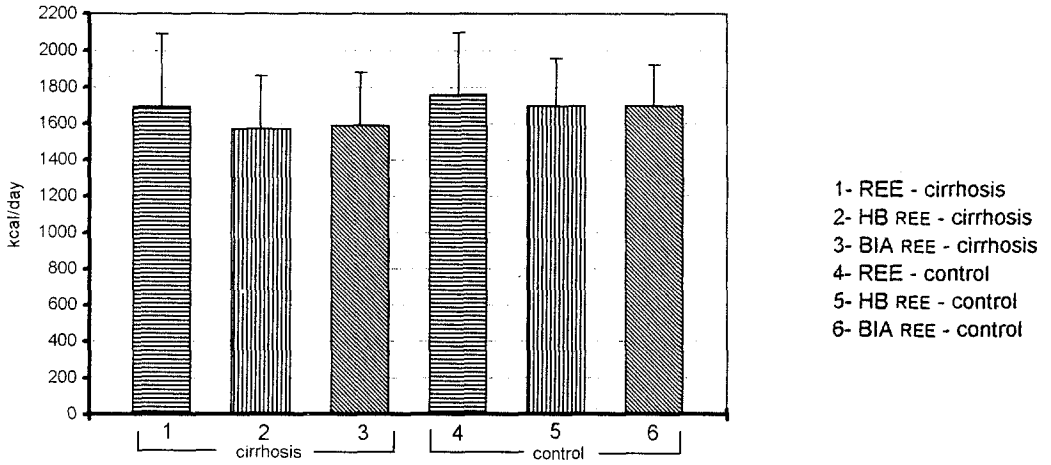

Figure 1. Resting energy expenditure of the whole body (mean + standard deviation) measured by three methods (kcal/day).

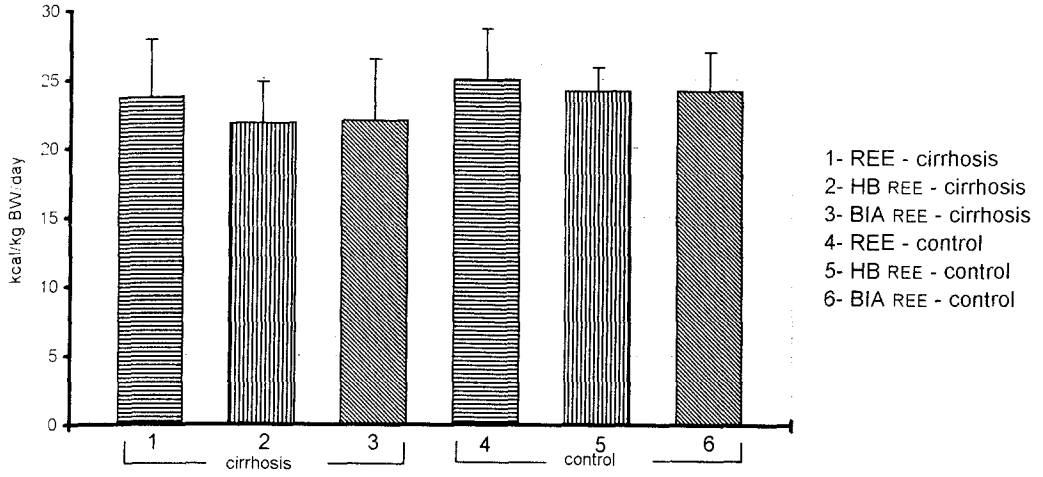

Figure 2. Resting energy expenditure expressed per kilogram of body mass (mean + standard deviation) measured by three methods (kcal/kgBW/day).

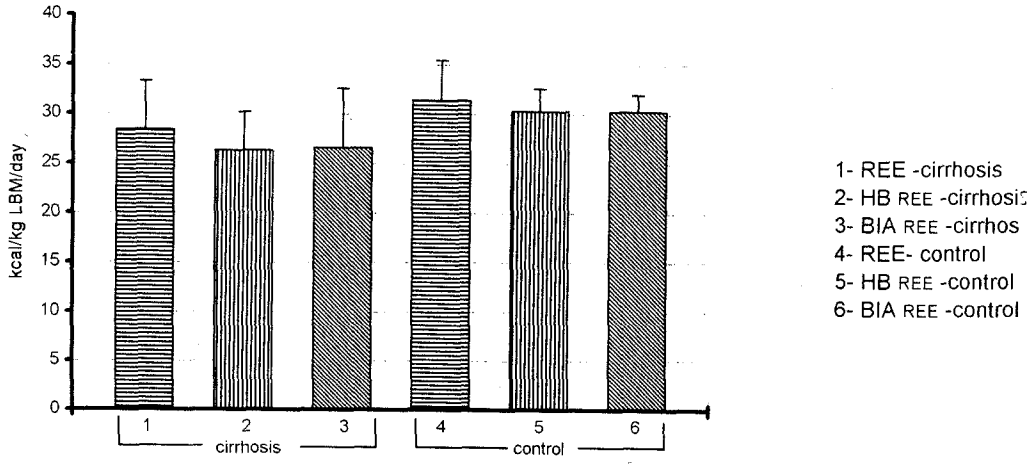

Figure 3. Resting energy expenditure expressed per kilogram of lean body mass (mean + standard deviation) measured by three methods (kcal/kg LBM/day).

respiratory work. It is possible that higher pressure in the hepatic vascular bed can be the cause of increased cardiac work. These two factors can increase energy expenditure; however, when ascites is mild, they might not be of much importance. Energy expenditure expressed as kcal/kg BW/day or kcal/kg LBM/day can be

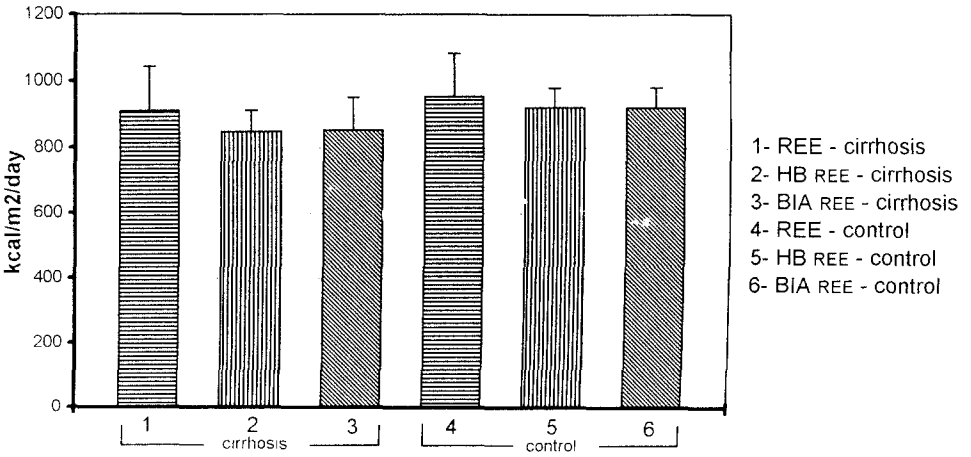

Figure 4. Resting energy expenditure expressed per square meter of the body surface (mean + standard deviation) measured by three methods (kcal/m^2/day).

even lower, because ascites is not metabolically active. The best possible method for measuring body composition should be chosen before calculation of resting energy expenditure is performed.

We define energy expenditure by three methods: indirect calorimetry, anthropometry (using the Harris–Benedict equation) and bioelectrical impedance analysis. Some authors used the bioelectrical impedance method for analysis of body composition and assessing lipid storage[16–22], and concluded that this safe, convenient and noninvasive method is useful for routine monitoring of body composition[2]. This method is also useful in patients affected by anorexia nervosa[23], in overweight adults[24] and during weight loss[25]. Other authors compared bioelectrical impedance with skinfold anthropometry[26], densitometry[27], near-infrared interactance[28], hydrostatic weighing, infrared spectrophotometry, and anthropometry[29]. In general, bioelectrical impedance was no better than the other methods. Some other studies[20,22,30,31,32] used bioelectrical impedance analysis to assess body composition in patients with chronic liver diseases. There are some important restrictions on the application of bioelectrical impedance analysis for estimating body composition in patients with advanced cirrhosis. Patients with advanced chronic liver disease retain fluid[21,33]. The mean percentage of body fat, assessed using bioelectrical impedance analysis, was significantly higher than the value obtained by skinfold anthropometry[30]. Some findings suggest that bioelectrical impedance analysis is a more accurate method in healthy volunteers[34,35]. For these reasons we decided to include in our study only patients with Child's grade A and B cirrhosis. We suspected that the use of bioelectrical impedance in more advanced stages of cirrhosis could yield inaccurate results. We were able to apply this method to define resting metabolic expenditure by using an apparatus which automatically calculated this data. Results obtained by this method were compared with those obtained by indirect calorimetry and anthropometry. We found that there were no significant differences in means measured by these three methods in the cirrhotic group and in the control group, no matter whether results were expressed in kcal/day, kcal/m^2/day, kcal/kg BW/day or kcal/kg LBM/day. However, we found a high correlation only between indirect calorimetry and anthropometry in both groups. There was a high correlation between anthropometry and bioelectrical impedance method in the control group, but not in the cirrhotic group. These results confirm the previous suggestions (cited above) that bioelectrical impedance is not useful in patients with cirrhosis.

In conclusion, our data indicate that energy expenditure did not differ between patients with liver cirrhosis and healthy subjects. The results obtained by indirect calorimetry, anthropometry and bioelectrical impedance analysis were very similar. However, the slight correlation between indirect calorimetry and bioelectrical impedance analysis in patients with cirrhosis indicates that the latter method is not precise and gives only approximate values.

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