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PAPER

The prediction of basal metabolic rate in female patients with anorexia nervosa

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OBJECTIVE: To evaluate in female patients with anorexia nervosa the accuracy of a specific predictive formula for basal metabolic rate (BMR) already proposed in the literature and to derive a new disease-specific equation with the same purpose.
DESIGN: Cross-sectional study.
SUBJECTS: One-hundred and twenty adolescent girls (< 18 y) and young-adult women (18 – 30 y) with anorexia nervosa.
MEASUREMENTS: BMR was determined by indirect calorimetry or predicted according to the Schebendach formula, which was specifically derived for anorexia nervosa.
RESULTS: On average the Schebendach formula performed well in the adolescent group but not in the young-adult group. The range including 95% of the predicted – measured differences was in both cases wider than 2000 kJ/day. In the young-adult patients the accuracy of the prediction was also related to age and body mass index. Weight and age (but not height or body mass index) emerged as predictors of BMR in the sample as a whole, and only weight when the two age groups were considered separately, thus leading to three different equations. The intercepts of these regression lines were very close and not significantly different from zero while their standard error of estimate was 500 – 550 kJ/day.
CONCLUSION: The Schebendach formula is not very accurate in estimating the BMR of female anorectic patients. Moreover, in this group the relationship between BMR and weight was altered. The predictive formulas proposed by the present study have a reasonable prediction power.
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Keywords: BMR; energy expenditure; anorexia nervosa; eating disorders; predictive equations

Introduction

Individual energy requirement is strictly dependent upon basal metabolic rate (BMR). This can be measured by indirect calorimetry, but is more often estimated in the clinical setting using sex-specific equations based on individual characteristics such as age, weight and height.[1] The predictive formulas most frequently cited and used are those proposed by Harris and Benedict[2] or those derived by Schofield *et al*[3] by considering data from different countries. These equations, which were originally developed for healthy people, have also been extensively applied in ill subjects after being corrected according to specific factors accounting for hyper- or hypometabolism.[4] As an alternative, disease-specific equations can be derived from data collected in patients all suffering from the same disease.[5]

Individuals (mostly females) with anorexia nervosa have low or very low BMRs,[6–21] while their physical activity varies to a large extent.[12,16,19] The estimation of their BMR is important to better determine energy requirements, and therefore to optimize nutritional treatments and to avoid the medical complications due to the refeeding syndrome (in the first phase of nutritional treatment). But, surprisingly, only scanty and incomplete data are so far available on the prediction of BMR in anorexia nervosa. In particular, although in these patients the Harris – Benedict equation yields estimates of BMR which are significantly higher than actual values,[6–11,14,16–20] only recently a correction of this equation was specifically derived for anorexia nervosa by Schebendach *et al.*[17] Indeed, it was developed in a study

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sample of only 21 patients and has not so far been definitely validated.

The aim of this study was therefore to evaluate in a large sample of adolescent girls and young women with anorexia nervosa the accuracy of the Schebendach predictive equation, and also to derive a new specific formula to estimate BMR in these chronically underfed patients.

Materials and methods

One-hundred and twenty female patients, referred to the Eating Disorders Clinic of the Federico II University Medical School, took part in the study. They met the established criteria for the diagnosis of anorexia nervosa (DSM IV criteria[22]) and had been amenorrheic for at least 6 months before the test. None of them was a heavy smoker, nor was taking oral contraceptives or other drugs affecting energy expenditure. Moreover, none had received any psychiatric or dietary treatment for at least 2 months before the test. The study group was subdivided into 34 adolescent girls aged 13–17 y (ADOL group: 15.6 ± 1.3 y, height 159 ± 6 cm, weight 38.8 ± 5.7 kg, body mass index (BMI = weight/height^2) 15.4 ± 1.9 kg/m^2), and 86 young adult women aged between 18 and 30 y (Y-AD group: 22.2 ± 3.9 y, 160 ± 6 cm, 38.2 ± 5.6 kg, BMI 15.0 ± 1.9 kg/m^2). The patients gave their informed consent to the study, the protocol of which had been approved by the ethical committee of the Federico II University Medical School.

All the tests were performed early in the morning. Weight was measured to the nearest 0.1 kg with a platform beam scale and height to the nearest cm with a stadiometer. The measurements were made with the subjects wearing only light clothing and standing without shoes, with the heels together and the head in the horizontal Frankfurt plane.

BMR was measured (mBMR) by indirect calorimetry (canopy system: MMC Horizon, Sensor Medics, Anaheim, USA) in standardized conditions, ie after a 12–14 h fast, in a quiet environment and at a room temperature of about 24°C. The apparatus was routinely checked by burning ethanol. After an adaptation period of 15–20 min, oxygen consumption and carbon dioxide production were determined for 45 min. Energy expenditure was then calculated with the abbreviated Weir's formula, neglecting protein oxidation.[23] The inter-day coefficient of variation of such measurements (as determined in six patients on subsequent days) was always less than 3%, without any sequence effect.

BMR was also predicted according to the Schebendach formula,[17] which is a correction of the Harris–Benedict equation specifically derived for anorexia nervosa. The adjusting formula is: predicted BMR (kJ/day) = $(-1435 \times 4.186) + 1.84 \times$ Harris–Benedict predicted value.

Calculations and statistics

Data were expressed, when appropriate, as mean and standard deviation (s.d.).

The accuracy of the Schebendach formula was assessed according to Bland and Altman.[24] The predicted–measured (PM) differences and the percentage ratio between predicted value and measured value (%PM ratio = 100 × pBMR/mBMR) were calculated. The 95% limits of agreement (which include 95% of either PM differences or %PM ratios) and the corresponding range were also obtained from mean, standard deviation and the appropriate *t*-value for the number of subjects considered. Two-way ANOVA (repeated measures), simple correlation and multiple regression analysis were used for statistical analyses. Multiple regression analysis was also employed to identify the predictors of BMR (taking into consideration age, height, weight and BMI). The consistency of the set of predictive equations proposed in this article was finally assessed by evaluating PM differences for each of them in 10 random samples, each consisting of 20 anorectics, selected from the entire group of 120 patients.

Results

Measured BMR and predicted BMR

BMR ranged between 1537 and 5208 kJ/day in the sample as a whole and was very similar in the ADOL group (3598 ± 799 kJ/day) and in the Y-AD groups (3681 ± 721 kJ/day).

In the 34 adolescent patients Schebendach-predicted BMR was 3589 ± 448 kJ/day and coincided on the average with measured BMR (Table 1). As a matter of fact, mean PM difference was only –9 kJ/day (% PM ratio = 103%). No significant association of PM differences with age, height, weight or BMI was identified.

Table 1 Predicted–measured differences and predicted basal metabolic rate as a percentage of measured value (%PM ratio) in female adolescents and young-adult women with anorexia nervosa

	PM differences (kJ/day)				*%PM ratio (%)*			
	Mean	*s.d.*	*95% limits of agreement*		*Mean*	*s.d.*	*95% limits of agreement*	
Adolescent group ($n = 34$)	−9	582	−1178	+1170	103	17	68	138
Young-adult group ($n = 86$)	−362*	570	−1497	+773	92*	14	64	120

BMR predicted according to the Schebendach formula.[17]
*$P < 0.01$ *vs* adolescent group.

On the contrary, in the Y-AD group the Schebendach equation significantly underestimated measured BMR by 362 kJ/day (% PM ratio = 92%) with a wide range between the 95% limits of agreement (2270 kJ/day). In addition, according to multiple regression analysis, PM differences were dependent ($P < 0.01$) on both age (regression coefficient −59.3) and BMI (regression coefficient −74.1) (for the entire model $R^2 = 0.16$, $P = 0.001$).

Development of predictive equations

The simple linear correlation showed (Table 2) that BMR was related quite strictly to weight and BMI in the sample as a whole and in the two age groups separately, and to age only in the ADOL group. Age, height, weight and BMI were also considered as possible determinants of BMR to derive specific predictive equations. More detailed information on this procedure is given in Table 3.

To summarize, a multiple regression analysis on 120 patients indicated first that weight is the by far the most important predictor of BMR (Figure 1) according to the equation:

$$\text{BMR (kJ/day)} = 148.3 + 91.5 \times \text{weight (step 1 in Table 3)} \quad (1a)$$

Table 2 Linear correlations between basal metabolic rate (BMR) and main individual characteristics in female adolescents and young-adult women with anorexia nervosa

	Correlation coefficient for BMR vs:			
	Age	*Height*	*Weight*	*BMI*
All patients	0.037	0.282*	0.696**	0.628**
Adolescent patients	0.467*	0.386	0.721**	0.638**
Young-adult patients	−0.062	0.240	0.692**	0.638**

*$P < 0.01$. **$P < 0.001$.

with $r = 0.696$ and a standard error of estimate (s.e.e.) of 538 kJ/day.

The addition of age to the model increased the R to 0.718 with a s.e.e. of 528 kJ/day. Height and BMI did not contribute further to the predictive power of the equation.

$$\text{BMR (kJ/d)} = 93.9 \times \text{weight} + 22.2 \times \text{age} - 394.7 \text{ (step 2 in Table 3)} \quad (1b)$$

On the other hand, when the two age groups were considered separately, weight emerged as the only significant determinant of BMR according to the equations:

for the ADOL group

$$\text{BMR (kJ/day)} = -313.4 + 100.8 \times \text{weight} \quad (2a)$$

for the Y-AD group

$$\text{BMR (kJ/d)} = 297.7 + 88.7 \times \text{weight} \quad (2b)$$

with similar r and s.e.e. to those reported for eqns (1a) and (1b). In eqns (1b), (2a) and (2b) the intercepts were not significantly different from zero (Table 3). Thus, the regressions were forced through the origin, leading to the formulas:

for the entire sample

$$\text{BMR (kJ/day)} = 87.1 \times \text{weight} + 15.9 \times \text{age (step 2 in Table 3)} \quad (3)$$

for the ADOL group

$$\text{BMR (kJ/day)} = 92.8 \times \text{weight} \quad (4a)$$

for the Y-AD group

$$\text{BMR (kJ/day)} = 96.3 \times \text{weight} \quad (4b)$$

No substantial changes in the s.e.e. around the regression line were observed for these formulas in comparison with those with intercept (Table 3). Finally, the reliability of four

Table 3 Calculated equations to predict BMR in female adolescents and young-adult women with anorexia nervosa

	Predictors									
	Intercept			*Weight*			*Age*			
	B_0	*(s.e.)*	P	B_1	*(s.e.)*	P	B_2	*(s.e.)*	P	*s.e.e.*
Equations with intercept										
(1) All patients										
1st step (1a)	148.3	(337.2)	0.661	91.5	(8.7)	0.001		not considered		538
2nd step (1b)	−394.7	(426.7)	0.357	93.9	(8.7)	0.001	22.2	(10.7)	0.044	528
(2a) Adolescent patients	−313.4	(671.8)	0.644	100.8	(17.1)	0.001	NS		0.341	562
(2b) Young-adult patients	297.7	(389.2)	0.446	88.7	(10.1)	0.001	NS		0.206	524
Equations with zero intercept										
(3) All patients										
1st step	0			95.3	(1.3)	0.001		not considered		536
2nd step	0			87.1	(4.6)	0.001	15.9	(7.8)	0.046	528
(4a) Adolescent patients	0			92.8	(2.4)	0.001	NS		0.886	556
(4b) Young-adult patients	0			96.3	(1.5)	0.001	NS		0.156	522

General formula: predicted BMR (kJ/day) = $B_0 + B_1 \times$ weight $+ B_2 \times$ age.
P < 0.001 in each case for the entire model.
NS = regression coefficient not significantly different from zero.

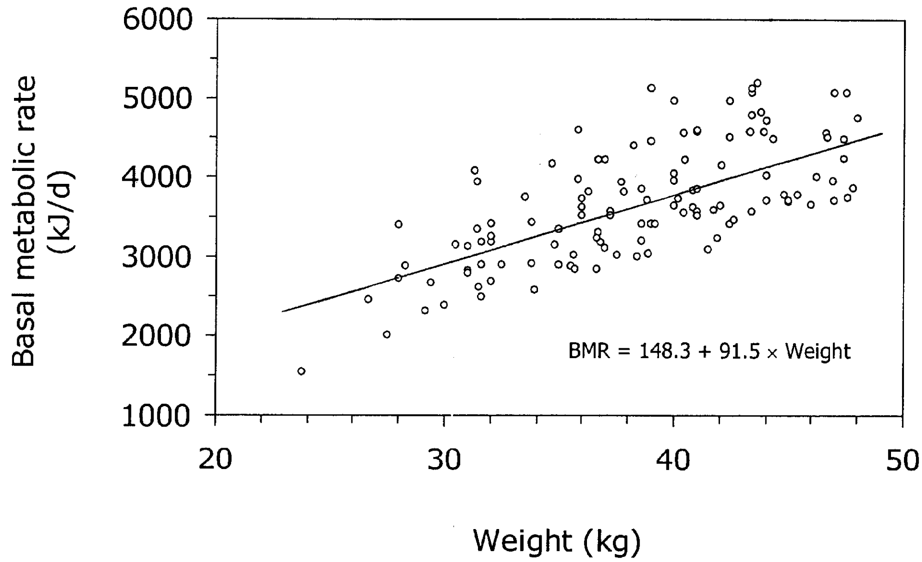

Figure 1 The relationship between basal metabolic rate and weight in 120 female adolescents and young women with anorexia nervosa.

different types of predictive formulas ((1b), (2a)–(2b), (3) and (4a)–(4b), as indicated in Table 3) was assessed in 10 samples randomly selected from the 120 subjects. Mean PM differences (kJ/day) were not significantly different from zero ($P > 0.50$), ranging in the different samples from −88 to +71 kJ/day (general equation with intercept), from −92 to +71 kJ/day (general equation with no intercept), from −117 to +75 kJ/day (age-specific equation with no intercept) and from –109 to +79 kJ/day (age specific equation with no intercept). The s.d. of the PM differences was similar for the four equations considered, being 435–675 kJ/day in the different samples.

Discussion

The present study investigates the possibility of predicting BMR in female adolescents and young women with anorexia nervosa. From a practical point of view, the evaluation of BMR in these chronically underfed subjects is of great interest to obtain more direct, realistic information on their energy needs. But, surprisingly, the equations to predict BMR have only incompletely been evaluated in anorexia nervosa[6–11,14,16–18,20] and used mainly to give an approximate estimate of the extent of hypometabolism.

A sample of 120 anorectic female patients, who widely differed for age, weight and BMI, was considered for our experimental protocol. As observed by several other authors,[6–21] BMR widely varied and was very low in some cases: < 3000 kJ/day in six anorectics (5% of whole sample) and between 3000 and 3500 kJ/day in another 22 (13%). As expected, the Harris–Benedict equation largely overestimated measured BMR (+45 ± 29% in the sample as a whole), in agreement with other reports indicating that in the anorectic patients measured values were, on average, 60–80% of predicted values.[4–9,12,14–16,18]

The Schebendach formula[17] is of greater, specific interest as it has been recently proposed as a correction of the Harris–Benedict formula to be applied in anorectic patients. It performed quite differently in the two age groups, being accurate on average in the ADOL group (mean PM difference: −8.6 kJ/day with 95% CI −211 and 194), but not in the Y-AD one (−367 kJ/day with 95% CI −489 and −244). Furthermore, in the latter case PM differences were related to age and BMI. Thus, the Schebendach correction does not appear to be completely adequate, especially when the patient's age is over 18 y. Moreover, the Harris–Benedict formula is not expected to be used in adolescent individuals and the procedure of adjusting it rather than formulating a specific equation, appears atypical and questionable.

Development of specific predictive equations

The formulas for estimating BMR In anorexia nervosa were developed in the 120 female anorectic patients, who represented a much larger sample than those previously studied for the same purpose.[17] The major individual characteristics (age, height, weight and BMI) were considered as possible determinants of basal energy expenditure. As occurred in healthy people, weight emerged as the variable more strictly associated with BMR either in the sample as a whole, or in the two age groups separately (Figure 1 and Table 3—eqns (1a), (2a) and (2b)). Multiple regression analysis demonstrated that age was the sole other significant predictor of BMR in the entire sample (Table 3—eqn (1b)). Indeed, the inclusion of this variable in the model only slightly improved the prediction power, with a decrease in s.e.e. (which describes the scattering of actual values around the regression line) from 538 to 528 kJ/day. On the other hand, an interesting phenomenon emerged: for the same weight, BMR was lower in the younger patients than in the adult ones with a difference of 22.2 kJ/day (95% CI 0.6–43.8). This finding cannot be explained on the basis of the information here available; it could be attributed to age differences in the response of anorectic patients to chronic underfeeding, but, to our knowledge, this point has so far not been adequately investigated.

Another pertinent finding of this study is that the relationship between BMR and weight is visibly altered in anorexia nervosa. As a matter of fact, the intercepts in eqns (1), eqns (2a) and (2b) were very close to zero and the regression coefficients for weight were greater than 85 kJ/kg, whereas the formulas derived in healthy individuals have intercepts well above zero and flatter slopes. Moreover, when BMR was expressed as a function of body mass power ($weight^b$), the mass exponent '*b*' was much greater in the present study (1.01) in comparison with values obtained in healthy people (0.38–0.65).[25,26] On the basis of current knowledge on the association between energy expenditure and body composition,[27,28] it could be argued that the changed relationship between BMR and weight is due to a different degree of decrease in metabolic rate from one lean tissue to another one or to a gradual change in the ratio between visceral mass and muscle mass. Indeed, the latter hypothesis is unlikely to be true, since BMI was not an independent predictor of BMR, thus suggesting that chronic underfeeding affects energy expenditure independently of the extent of body size modifications. Since the intercepts were so close to zero, it also appeared reasonable to derive a set of simpler equations with the regression forced through the origin (Table 3 — eqn (3) for the entire sample and eqns (4a) and (4b) for the two age groups, separately). No change in s.e.e. was observed in comparison to the corresponding formulas with intercept, suggesting a similar prediction power.

Finally, all the equations proposed from this study showed quite satisfactory stability and reliability when evaluated in samples of patients randomly selected from the original one, with a mean group difference between predicted values and actual values in most cases <50 kJ/day. However, they also share some problems which are common when predictive formulas are used. They do not ensure a very accurate estimate in the single individual, as indicated by the extent of SEE around the regression lines. Furthermore, their validity has to be cross-validated in groups of patients other than the original sample on which they were derived. However, the data of this study yield some consistent information to better estimate BMR and energy needs in anorexia nervosa. The predictive equations here reported were obtained in a representative sample of anorectic patients who varied widely in age and anthropometric characteristics. The measurements were carried out in standardized conditions with advanced equipment, and the formulas obtained have r^2 and s.e.e. comparable with those of the predictive formulas for BMR commonly used for healthy and ill subjects. Still it remains clear that the measurement of BMR by indirect calorimetry may be preferable for patients in more critical conditions and with a very low body mass.

In conclusion, the correction formula proposed by Schebendach *et al*[15] is not very accurate in estimating the BMR of female anorectic patients. In these subjects the relationship between BMR and weight appears to be very changed. The equations proposed by the present study are specific for adolescents and young women with anorexia nervosa. They were derived in a sample of acceptable size and have a reasonable prediction power, but their final validation requires further studies in other groups of anorectic patients.

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