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Research paper

Body composition and resting energy expenditure in a group of children with achondroplasia: Effectiveness of predictive models in the treatment of obesity

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ABSTRACT

Background: Persons with achondroplasia develop early obesity, which is a comorbidity associated with other complications. Currently, there are no validated specific predictive equations to estimate resting energy expenditure in achondroplasia.
Methods: We analyzed the influence of body composition on this parameter and determined whether predictive models used for children with standard height are adjusted to achondroplasia. In this cross-sectional study, we measured anthropometric parameters in children with achondroplasia. Fat mass was obtained using the Slaughter skinfold-thickness equation and resting energy expenditure was determined with a Fitmate-Cosmed calorimeter and with predictive models validated for children with average height (Schofield, Institute of Medicine, and Tverskaya).
Results: All of the equations yielded a lower mean value than resting energy expenditure with indirect calorimetry (1256±200 kcal/day [mean±SD]) but the closest was the Tverskaya equation (1017 ± 64 kcal/day), although the difference remained statistically significant. We conclude that weight and height have the greatest influence on resting energy expenditure.
Conclusion: We recommend studying the relationship between body composition and energy expenditure in achondroplasia in more depth. In the absence of valid predictive models suitable for clinical use to estimate body composition and resting energy expenditure in achondroplasia, it is recommended to use the gold standard methods by taking into account certain anthropometric parameters.

Introduction

Studies in the literature agree that obesity is a common clinical sign in people with achondroplasia (ACH) [1,2], and it is linked to their condition [3−5]. It begins in early childhood, a critical period in the development of obesity that is associated with morbidity and mortality in adulthood [6,7]. There is a methodological and data gap in the estimation of energy requirements in the pediatric population with ACH. However, all of this information is key for designing a reasonable and effective dietary intervention [3,4]. The gold standard method for estimating resting energy expenditure (REE) by indirect calorimetry (IC) is not accessible in daily clinical practice, leading to the development of predictive models. In principle these equations are more advantageous in terms of cost and simplicity of application, but they are not as precise as measurements due to the great variability in estimates when they are used in individuals with different characteristics than those populations for whom they have been validated [8]. Currently, there is no specific and validated predictive model for people with ACH in any age group. Thus, it is not possible to establish an energy recommendation as part of a dietary treatment for individuals with ACH based on the REE, nor to monitor its evolution over time.

Therefore, there is a need to study the REE in the ACH population group and to analyze the relationship between body composition

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and REE. The first objective of the current study was to determine whether there is a relationship between the estimated REE and the various anthropometric measures characterizing the body composition of children with ACH. The second objective was to establish whether predictive models for the estimation of REE designed for children with standard stature are adjusted to children with ACH.

Material and methods

Study design

A descriptive cross-sectional study was carried out in a pediatric population with ACH (age range: 6–13 years) at the La Paz Hospital in Madrid, at the NUNTIA Nutritional Guidance Office in Pamplona, and at the ALPE Foundation in Gijón, for 6 months.

The inclusion criteria were as follows: a radiological or genetic diagnosis of ACH [2]; being the required age; not having undergone previous bone elongation surgery; not having suffered paralysis due to spinal cord compression; committing to compliance with the protocol prior to the estimation of REE, prepared according to the recommendations based on levels of evidence [8]; and signing a informed consent form. The following exclusion criteria were established: oscillations greater than 2 kg in the last 2 months; fever; recent trauma; drug consumption that affects REE; and non-compliance with the indications included in the previous protocol.

Participating families were informed and recruited by the researcher and collaborating entities: the ALPE Foundation and/or the Achondroplasia Unit of the Virgen de la Victoria Hospital in Malaga. The Ethics Committee of the Public University of Navarre (PI-0001/17) authorized the study, designed in accordance with the ethical requirements of the Helsinki Declaration.

Data collection

All the measurements were carried out in a fasting state (minimum 5 h), after a mandatory 10–20-min rest and without having carried out any type of physical exercise in the previous 14 h [8].

REE was determined by IC with an open-circuit portable indirect calorimeter with face mask (Fitmate-COSMED), which enables determination of O_2 consumption, but not CO_2 production, and therefore, does not enable calculation of the respiratory quotient (RQ) nor estimation of the oxidation of substrates. The equipment performs a self-calibration for 20 s before each measurement. An 18-mm diameter bi-directional digital turbine flowmeter, located at the mask outlet, measures the volume of ventilation per minute, with a ventilation range of 0–50 L/min, a flow resistance less than 0.7 cm H_2O/L at 3 L/s, and an accuracy of ± 2 %. A galvanic cell-type oxygen analyzer measures the fraction of oxygen in expired gases, with a measurement range of 0–25 % and an accuracy of ± 0.02 %. The equipment has sensors that measure temperature and gas pressure.

To carry out the comparative study between the REE-IC and the predictive models, we selected five validated equations for pediatric populations of standard height (Table 1): the Schofield equations (Schofield-A and Schofield-B) [9] based on children with healthy weight and children with obesity aged 6–10 years and 10–13 years; the Institute of Medicine equations [10] (IOM-A and IOM-B), validated in children with healthy weight and children with obesity, respectively, from 3 to 18 years of age; and the Tverskaya equation [11] for children with obesity from 6 to 18 years of age. The variables of body composition, fat mass (FM), and fat-free mass (FFM) of the Tverskaya equation were estimated using the Slaughter equation [12], validated for children aged 8–13 years of standard height.

This predictive model uses the two-component system to calculate FFM in children (thus, FFM = total body mass − FM) [13]. In the absence of gold standard techniques for estimating FM, we chose this equation because it predicts the percentage of FM using skinfold thicknesses (triceps and half leg).

Table 1
Equations used to predict resting energy expenditure (REE) and fat mass percentage in the study.

Name	Sex	Age	Formula
Schofield-A*	Boys	3–10 years	REE= (22.695*WT) +504.1
		10–13 years	REE= (17.678*WT) +657.9
	Girls	3–10 years	REE= (20.306*WT) +485.7
		10–13 years	REE= (13.378*WT) +692.3
Schofield-B*	Boys	3–10 years	REE= (19.589*WT) + (1.302*HT) +414.7
		10–13 years	REE= (16.245*WT) + (1.371*HT) +515.3
	Girls	3–10 years	REE = (16.961*WT) + (1.617*HT) +371
		10–13 years	REE= (8.361*WT) + (4.654*HT) +200
IOM A*	Boys	3–18 years	REE= 68-(43.3*AGE) +(7.12*HT) +(19.2*WT)
	Girls	3–18 years	REE= 189-(17.6*AGE) +(6.25*HT) +(7.9*WT)
IOM B*	Boys	3–18 years	REE= 419.9-(33.5*AGE) +(4.189*HT) +(16.7*WT)
	Girls	3–18 years	REE= 515. 8-(26.8*AGE) +(3.47*HT) +(12.4*WT)
Tverskaya*	Boys	6–18 years	REE= 775+ (28.4*FFM)–37*AGE) +(3.3*FM) +(82×1)
	Girls	6–18 years	REE= 775+ (28.4*FFM)–37*AGE) +(3.3*FM) +(82×0)
Slaughter*	Boys	8–13 years	%Fat Mass=0.735*(ΣT-HL) +1
	Girls	8–13 years	%Fat Mass=0.610*(ΣT-HL) +5.1

Abbreviations: REE: resting energy expenditure; WT: weight in kg; HT: height in cm; AGE: age in years; FFM: fat-free mass in kg; FM: fat mass in kg; T: triceps fold in mm; HL: half leg fold in mm.

* Schofield-A equation based on children with healthy weight; Schofield-B equation based on children with obesity; IOM-A equation based on children with healthy weight; IOM-B equation based on children with obesity; Tverskaya equation based on children with obesity; Slaughter equation based on children with healthy weight and estimated with the triceps and half leg skinfolds.

Statistical analysis

All quantitative variables were studied for their direct influence on REE. The normality of the distribution of the variables was evaluated with the Shapiro–Wilk test and the homogeneity of variances with the *F* test for equality of variances. Quantitative variables that followed a normal distribution are described with the mean and standard deviation, and the variables that did not, with the median and interquartile range. Qualitative variables are described with the absolute and relative frequency.

The hypothesis tests between quantitative variables of two independent samples, according to gender, were performed with the Student *t*-test, for normal variables and the Mann–Whitney test, for non-normal variables. The hypothesis tests between the quantitative variables of paired samples were studied using the paired Student *t*-test for repeated measures or the Wilcoxon test, depending on the normality of the variables. The relationships between body composition variables and age, and between body composition variables and the estimated REE with IC (REE-IC), were analyzed by linear regression.

The comparison between REE-IC versus REE obtained by predictive equations was made (a) quantitatively using the paired Student *t*-test for repeated measures or the Wilcoxon test, based on the normality of the variables, and (b) qualitatively through Bland–Altman analysis. Multiple linear regression was employed to identify the most influential variables in the estimated REE and to try to build a new equation.

The level of statistical significance was established at $p<0.05$ for all the analyses performed.

The statistical package R, version 3.4.4, was used for all the analyses, using a specialized bibliography for the management of R as reference.

Results

Study population

The study group was made up of 18 children with ACH, eight boys and 10 girls, aged between 6 and 13 years (44 % and 56 %, respectively), as shown in Table 2. The calorimeter used showed that their respiratory rate was fast and shallow, typical of a stressful situation. We had to exclude eight children aged 3−6 years who were part of the initial study group because a high respiratory rate was recorded, as if the children were in a stressful situation. Consequently, the comparative study was not conducted, and the analysis of anthropometric variables within this age group (6–8 years) did not take place.

Table 2
Body composition variables.

	Study group *n* = 18 Mean ± SD	Boys *n* = 8 (44 %) Mean ± SD	Girls *n* = 10 (56 %) Mean ± SD
Age (years)	8.4 ± 2.3	8.9 ± 2.4	8 ± 2.2
Height (m)	1.03 ± 0.11	1.04 ± 0.15	1.02 ± 0.08
Weight (kg)	22.2 ± 6.7	22.4 ± 8.3	22 ± 5.6
BMI (kg/m^2)	20.1 ± 2.4	20.1 ± 2.4	21. 0 ± 2.5
Triceps fold (mm)	11.9 ± 4	11.1 ± 3.7	12.6 ± 4.4
Half leg fold (mm)	9.8 ± 3.8	9.4 ± 3.3	10.1 ± 4.2
Slaughter gat mass (kg)	4.1 ± 2	3.8 ± 2.2	4.4 ± 2.1
Slaughter fat mass (%)	18 ± 5	16 ± 5	19.5 ± 4.7
Slaughter fat-free mass (kg)	18.1 ± 5.1	18.7 ± 6.6	17.5 ± 3.8
Slaughter fat-free mass (%)	82.1 ± 4.2	83.9 ± 4.9	80.7 ± 4.7
Fat mass index (kg/m^2)	3.8 ± 1.41	3.3 ± 1.2	4.2 ± 1.49
Fat-free mass index (kg/m^2)	16.8 ± 1.6	16.8 ± 1.99	16.8 ± 1.33

BMI: body mass index; SD: standard deviation.

Resting energy expenditure study

Body composition and REE-IC

The mean value of REE-IC was 1256 kcal/day±200 (boys: 1332 kcal/day±228, girls: 1196 kcal/day±161). Boys exhibited slightly higher mean FFM values (Table 2) and REE-IC values (Table 3), although these discrepancies did not reach statistical significance. Weight (r = 0.78, $p<0.05$; girls, r = 0.87, $p<0.05$; boys, r = 0.76, $p<0.05$) had the highest correlation with the REE-IC (Table 4). In our sample, the correlation between REE-IC and weight was comparable between girls and boys (r = 0.73, $p<0.05$; girls, r = 0.89, $p<0.05$; boys, r = 0.67, $p>0.05$).

By contrast, REE-IC showed a moderate correlation with body mass index (BMI) and fat-free mass index (FFMI; r = 0.50, $p<0.05$; r = 0.47, $p>0.05$, respectively) and low correlation with fat mass index (FMI; r = 0.33, $p<0.05$). The correlations between REE-IC and weight and REE-IC and height were significant and stronger in girls.

As evidenced in Table 5, there was a positive correlation between FFMI and FMI and REE values in boys. Similarly, in the case of girls, a positive relationship was observed between the increase in REE values and the growth in height, weight, and FFMI. On the other hand, a negative correlation was observed between the decrease in REE and lower values of BMI, FFMI, and FMI both in boys and girls.

The REE-IC expressed per unit of body weight was 59 ± 13 kcal/kg (girls: 56 ± 7 kcal/kg, boys: 60 ± 18 kcal/kg). Age, weight, height, and body composition variables had an inverse relationship with REE per unit of body weight.

Predicted REE and REE-IC

Table 3 shows the results obtained in the estimation of the REE-IC and the equations studied. A difference of 400 kcal/day was found between the average value of the REE-IC and the IOM-A equation, which yielded the lowest average (858 kcal/day±109). The

Table 3
Measured REE via indirect calorimetry vs. REE via the Schofield-A, Schofield-B, IOM-A, IOM-B, and Tverskaya equations.

	Study group *n* = 18 Mean ± SD (kcal/day)	Boys *n* = 8 (44 %) Mean ± SD (kcal/day)	Girls *n* = 10 (56 %) Mean ± SD (kcal/day)
Indirect calorimetry REE measured	1256 ± 200	1332 ± 228	1196 ± 161
Schofield-A	966 ± 147*,†	1012 ± 183*,†	930 ± 108*,†
Schofield-B	939 ± 139*,†	990 ± 179*,†	899 ± 87*,†
IOM-A	858 ± 109*,†	860 ± 155*,†	860 ± 60*,†
IOM-B	931 ± 84*,†	937 ± 117*,††	927 ± 52*,†
Tverskaya	1017 ± 64*,†	1050 ± 62*,†	992 ± 57*,†

SD: standard deviation; REE: resting energy expenditure; Schofield-A equation based on children with healthy weight; Schofield-B equation based on children with obesity; IOM-A equation based on children with healthy weight; IOM-B equation based on children with obesity.

* Significant difference from measured REE ($p<0.05$).

† Paired Student *t*-test.

†† Wilcoxon test.

Table 4
Correlations between BMI, FFMI, FMI, height, weight, age, and REE-IC on the study group.

	BMI kg/m^2	FMI kg/m^2	FFMI kg/m^2	Height m	Weight kg	Age years	REE-IC kcal/day
BMI	x	0.78* (0.89*, 0.58)	0.83* (0.86*, 0.87*)	0.44 (0.45, 0.53)	0.75 * (0.80*, 0.78*)	0.38 (0.57, 0.31)	0.50 * (0.55, 0.67)
FMI	0.78* (0.89*, 0.58)	x	0.29 (0.54*, 0.10)	0.40 (0.47, 0.52)	0.59* (0.75*, 0.58)	0.21 (0.36, 0.24)	0.33 (0.49, 0.50)
FFMI	0.83* (0.86*, 0.87*)	0.29 (0.54*, 0.10)	x	0.31 (0.30, 0.32)	0.62* (0.65*, 0.60)	0.39 (0.48, 0.29*)	0.47 (0.47, 0.51)
Height	0.44 (0.45, 0.53)	0.40 (0.47, 0.52)	0.31 (0.30, 0.32)	x	0.92* (0.89*, 0.94*)	0.91* (0.96, 0.88)	0.73* (0.89*, 0.67)
Weight	0.75* (0.80*, 0.78*)	0.59* (0.75*, 0.58)	0.62* (0.65*, 0.60)	0.92* (0.89*, 0.94*)	x	0.84* (0.94, 0.75*)	0.78* (0.87*, 0.76*)
Age	0.38 (0.57, 0.31)	0.21 (0.36, 0.24)	0.39 (0.48, 0.29*)	0.91* (0.96, 0.88)	0.84* (0.94, 0.75*)	x	0.72* (0.63*, 0.80)
REE-IC	0.50 * (0.55, 0.67)	0.33 (0.49, 0.50)	0.47 (0.47, 0.51)	0.73* (0.89*, 0.67)	0.78* (0.87*, 0.76*)	0.72* (0.63*, 0.80)	x

Correlation for the entire group *n* = 18 (correlation for girls, *n* = 10; correlation for boys, *n* = 8).
REE-IC: resting energy expenditure – indirect calorimetry; BMI: body mass index; FFMI: fat-free mass index; FMI: fat mass index.

* Correlation is significant at the 0.05 level (two-tailed).

Table 5
BMI, FMI, FFMI, height (H), weight (W), and REE-IC according to BMI-for-age for children with ACH in the study group.

BMI-for-age Percentile	Girls, *n* = 10						Boys, *n* = 8					
	BMI kg/m^2	FMI kg/m^2	FFMI kg/m^2	H m	W kg	REE-IC kcal/day	BMI kg/m^2	FMI kg/m^2	FFMI kg/m^2	H m	W kg	REE-IC kcal/day
<P3	17.1	2.3	14.9	1.039	18.5	1203	17	1.5	15.4	0.953	15.4	1266
P10–24	18.5	3.3	15.3	0.946	16.6	1016	18.3	2.9	15.4	0.036	19.6	1289
	20	4	16	1.028	21.1	1346	19.3	3.7	15.6	1.194	27.5	1404
	22	5.1	16.8	1.067	25	1232						
P25–49	19.9	4.2	15.7	0.998	19.8	1047	19.2	2.8	16.4	0.926	16.5	887
	23.6	4.8	18.8	1.183	33	1521	19.4	3	16.4	0.975	18.4	1266
P50–74	21	3.9	17	1.008	21.3	1268	22.3	5.8	16.5	1.183	31.2	1567
	20.9	3.4	17.6	0.877	16.1	1002	24.6	3.2	21.4	1.220	36.6	1633
	21	3	17.9	0.952	19	1118						
P75–94							20.8	3.3	17.5	0.827	14.2	1363
>P95	26	7.7	18.3	1.065	29.5	1343						

ACH: achondroplasia; REE-IC: resting energy expenditure – indirect calorimetry; BMI: body mass index; FFMI: fat-free mass index; FMI: fat mass index.

differences between the mean values of the Schofield-A and Schofield-B equations (using as variables weight and weight and height, respectively) were not statistically significant (966 kcal/day±147; 939 kcal/day±139), and neither were the differences between the IOM-A and IOM-B equations adjusted by adding age (IOM-*A* = 858 kcal/day±109; IOM-*B* = 931 kcal/day±84). The highest average value and the one closest to the REE-IC was the Tverskaya equation, which uses age, gender, FM, and FFM (1017 kcal/day±64) as variables.

The average values obtained from measurement of the REE-IC, both for the whole group and separately for boys and girls, were significantly higher than the average values obtained in the determinations of the predictive equations. The Bland–Altman test results, presented in Fig. 1, showed a lack of concordance between the REE-IC and the estimates obtained with each of the predictive equations used: Schofield-A, Schofield-B, IOM-A, IOM-B, and Tverskaya. The differences in the pairs of observed values are analyzed against their average value, in each of the comparisons. There was a lack of concordance in all the analyses carried out. Despite the lack of data, the trend in the point cloud is linear and is determined by the amplitude of the differences between the results of each comparison, in pairs. The dispersion between the points is also significant since more variability means less agreement. There are also values that exceed the limits considered acceptable for concordance among the estimation methods.

Discussion

Obesity has a real impact in the health and quality of life of people with ACH starting from childhood. It is essential to study the origin, development, and variables that characterize obesity with respect to body composition [4], as well as their relationship to REE.

Resting energy expenditure status

Influence of body composition on REE-IC

In children of standard height, FFMI is strongly associated with height and REE with FFMI. Body composition is highly variable in children with ACH, and these differences influence the REE. The present results show that REE-IC has a slightly higher correlation with weight compared to height, which is attributed to the short rhizomelic stature. Additionally, it demonstrates a higher reliance on FFMI rather than on FMI. As shown in the results, the pathologically low stature characteristic of ACH influences body composition, REE-IC per unit of body weight and overall REE-IC. This would seem to explain that children with ACH exhibit a greater proportion of tissue with high metabolic rate (splanchnic mass) with respect to total body weight than children of standard height. There is a need for studies that analyze the contribution to REE of metabolically active tissue belonging to FFM (organ mass and muscular tissue) in children with ACH, and the part corresponding to FM (white and brown fat).

The REE per unit of body weight obtained in our group is higher than expected with respect to the variables of weight and height. This finding can be explained through various hypotheses, although we have not found studies carried out with children who have ACH and, therefore, the studies that are cited report results from adult patients.

Owen et al. [14] reported that people with ACH have a higher proportion of high metabolic rate tissue (splanchnic mass) than medium and low metabolic rate tissue (muscle mass and FM, respectively) with respect to total body mass, compared to average-sized adults. In adults of standard height, the splanchnic mass constitutes 6 % of the total body mass and contributes 60–70 % of the REE, compared to skeletal muscle, which, despite representing 40–50 % of the total weight, only contributes to 20–30 % of the REE [15]. During childhood, the proportion of splanchnic mass to total body mass is higher. For instance, in newborns, the brain constitutes 50 % of total body mass. Consequently, its relative contribution to REE will be more significant in the early years of life and will gradually decrease with age, aligning with our findings.

Mackler et al. [16] described mitochondrial abnormalities related to cytochrome oxidase A3 and oxidative phosphorylation in ACH. This hypothesis would justify a higher metabolic rate due to an increase in thermogenesis in the FFM of people with ACH.

Sims et al. [17] compared the oxygen consumption (VO$_2$) and metabolic cost of a group of 10 adults with ACH, during walking and running, with those of a standard-height control group of the same age. The value of VO$_2$ and the metabolic cost in relation to the total body mass and the FFM were higher in the group with ACH. According to the authors, the difference in leg length (38 % lower in the group with ACH) requires a greater stride frequency and would produce a higher VO$_2$. Compared to controls, the study group's higher metabolic cost could be due to anthropometric differences (less kilograms of skeletal muscle mass in the lower extremities).

Takken et al. [18] in their study (seven boys and 11 girls with ACH; mean age, 11±3.3 years) observed a higher breathing frequency and a higher heart rate to capture 1 L of oxygen, compared to the control group. A lower ventilator efficiency, resulting from their smaller thoracic volume, justifies the higher energy requirement per unit body weight. These findings are consistent with our observations. We had to exclude eight children aged 3–6 years who were part of the initial study group because a high respiratory rate was recorded, as if the children were in a stressful situation. An explanation for this higher respiratory rate is that it was caused by the smaller lung capacity in children with ACH, who have a narrower chest and, in many cases, by a partial obstruction in the upper respiratory tract. This superficial and rapid ventilation, characteristic of children with ACH, was not adequately

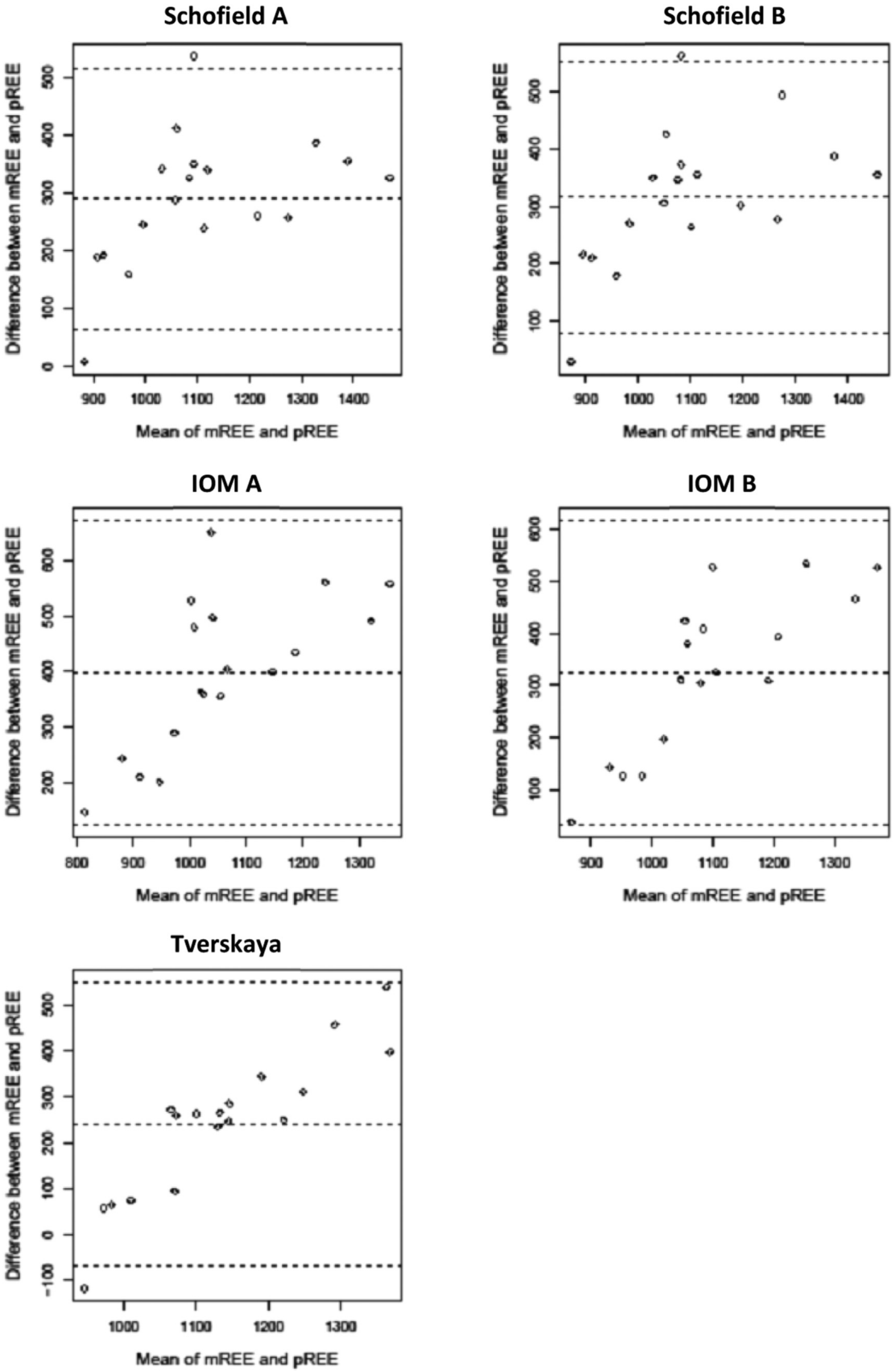

Fig. 1. Bland−Altman graphs for concordance between measured resting energy expenditure (mREE) via indirect calorimetry and via Schofield-A, Schofield-B, IOM-A, IOM-B, and Tverskaya equations in the study group (boys and girls). pREE: predicted resting energy expenditure.

Schofield-A equation based on children with healthy weight; Schofield-B equation based on children with obesity; IOM-A equation based on children with healthy weight; IOM-B equation based on children with obesity.

interpreted by the calorimeter. No precedents were found in the literature review at the time that our study was designed.

Predicted and measured REE: comparative study

None of the predictive equations was adequate for determining the REE in a pediatric population with ACH, according to the results of the comparative study and the Bland−Altman analysis (Table 3 and Fig. 1). This is an expected result, if we compare the anthropometric characteristics of the groups (weight, height, BMI) for which the different equations have been validated with those of the study group (Table 6).

Because weight and height in ACH do not increase with age in the same proportion as expected for children with standard height, height is a determining factor of distortion for estimating REE in all formulas that include it. By including pathological short height as an independent variable in the predictive formulas (Schofield-B), the value of the REE was smaller than the REE obtained via the equation that only used the weight (Schofield-A). Moreover, the REE calculated with IOM-A (including age, weight, and height) was the lowest of the results obtained.

Body composition influences REE (Table 6). People with obesity have a lower metabolic rate per unit of body weight than people with healthy weight. Overweight is due to excess FM, which is characterized by a low metabolic rate compared to the metabolic rates of skeletal muscle and splanchnic mass. Validated equations for populations with obesity underestimate the REE of people with a healthy weight. Children with ACH have a higher BMI than average-sized children, due not only to FM but also to the body proportions of people with short rhizomelic stature. In our group, although IOM-B underestimated REE, it fit better than IOM-A because the equation is validated in children with a higher BMI and is similar to Schofield-B, based on children with healthy weight and with obesity. The Tverskaya equation estimated the highest mean REE and was closest to the REE-IC. The equation is validated for children with obesity, excludes weight and height, and uses the variables of age, gender, FM and FFM, both expressed in kilograms. Tverskaya's study population had a very high BMI and percentage of FM compared to our group; therefore, it can be interpreted that the BMI was higher, specifically due to the difference in kilograms of FM. In this equation, age is adjusted for weight gain in the form of kg FM and kg FFM, but not for the expected height as in the other equations, which is a major distortion factor. The REE calculated by the Tverskaya equation depends more on the kg FFM than on the kg FM. The study population showed a proportion between kg FM and kg FFM that corresponds to people with obesity. This was the most important anthropometric difference observed between both groups and may be the reason that the Tverskaya equation underestimated the REE in our group. On the other hand, the Slaughter formula with which we obtained FM and FFM in our group is not specific to children with ACH. The equation is adjusted to estimate the FM with fat skinfolds and is based on body density estimates of children of standard height. We used the Slaughter equation, assuming the estimation error of the FM, in the absence of a specific predictive model for children with ACH and because of a lack of standard methods for the estimation of body composition.

A validated portable calorimeter with face mask (Fitmate-Cosmed) was used to obtain reliable REE measurements. Vandarakis et al. [19] demonstrated in different studies that this calorimeter model makes reliable estimates compared to the gold standard calorimeter, the Deltatrac-II, in healthy adults [20]. According to Compher et al. [21], the maximum average coefficient of variation tolerated in the estimation of the VO_2 consumed in the IC measurements is 10 %. Above this value, the variability in the REE measure is not reliable. Some of the children between 6 and 8 years of age exceeded this variability of 10 %, and thus their results in estimating the REE would not be reliable. The error due to the coefficient of variation for the consumed VO_2 causes the calorimeter to estimate a higher REE value because the higher the oxygen consumption, the higher the REE. However, as already discussed, Takken et al. [18] observed a higher respiratory rate and a higher heart rate to capture 1 L of oxygen in their group of children with ACH compared to the controls of standard size. Hence, this variation may pose an issue linked to the calorimeter type utilized, leading to inaccuracies in the estimation of REE based on the measured oxygen consumption in these children, rather

Table 6
Characteristics of the study group and of the predictive equations.

	Boys		Girls	
Study sample	Mean ± SD *n* = 8		Mean ± SD *n* = 10	
Age (years)	8.9 ± 2.4		8 ± 2.2	
Height (m)	1.04 ± 0.15		1.02 ± 0.08	
Weight (kg)	22.4 ± 8.3		22 ± 5.6	
BMI (kg/m^2)	20.1 ± 2.4		21 ± 2.5	
% Fat mass	16 ± 5		19.5 ± 5	
IOM-A Sample	*n* = 154		*n* = 397	
Age (years)	7.8 ± 3		9.3 ± 3.1	
Height (m)	1.30 ± 5.2		1.36 ± 5.7	
Weight (kg)	27.3 ± 11		31.4 ± 11.6	
BMI (kg/m^2)	16.1 ± 1.6		16.8 ± 2.1	
IOM-B Sample	*n* = 157		*n* = 249	
Age (years)	7.5 ± 2.5		8.9 ± 3.2	
Height (m)	1.33 ± 6.2		1.40 ± 6.9	
Weight (kg)	39.3 ± 16.1		45.0 ± 19.6	
BMI (kg/m^2)	22.1 ± 4.6		22.9 ± 4.9	
Schofield Sample	*n* = 1072		*n* = 988	
Age (years)	7.5 ± 1.8	13.7 ± 2.4	7.6 ± 1.7	12.8 ± 2.3
Height (m)	1.18 ± 4.1		1.18 ± 4.3	
Weight (kg)	21.5 ± 4.4	41.8 ± 14.6	21.4 ± 4.7	38.5 ± 11.2
BMI (kg/m^2)	15.3 ± 1.3	18.1 ± 2.7	15.3 ± 1.5	17.6 ± 2.6
Tverskaya Sample	*n* = 22	*n* = 28	*n* = 16	*n* = 44
Age (years)	8.2 ± 1.5	13.4 ± 1.7	9 ± 0.9	13.0 ± 1.9
Height (m)	136 ± 6	163 ± 10	139 ± 8	158 ± 9
Weight (kg)	52 ± 10	87 ± 35	55 ± 13	83 ± 21
BMI (kg/m^2)	28.1 ± 1.3	32.7 ± 2.7	28.5 ± 1.5	33.2 ± 2.6
% Fat mass	34 ± 7	38 ± 4	36 ± 4	40 ± 5

BMI: body mass index; SD: standard deviation; IOM-A equation based on children with healthy weight; IOM-B equation based on children with obesity.

than stemming from stress experienced by the children during the calorimetry test. The validity of the calorimeter model used has been demonstrated. However, there have been no previous studies conducted with ACH populations using this calorimeter model. Furthermore, there is no calorimeter model specifically validated for the pediatric population with ACH.

Limitations

The main limitation of the study is the absence of validated gold standard techniques for the ACH population (methods for estimating body composition and REE) to validate the established predictive models used for the standard-height population and to compare with new predictive models tailored specifically for the ACH population. Furthermore, the variability in results due to our small sample size has, unfortunately, prevented us from obtaining the necessary scientific evidence within our sample to create an algorithm adjusted for this population.

Conclusions

Our work showed that none of the existing predictive models are adapted for characterizing obesity in ACH patients. Anthropometric techniques (weight, height, BMI, FFMI, FMI) are valid tools for long-term monitoring of this population, and body weight and height were found to have the greatest influence on the values of the measured REE-IC. With these procedures, professionals assisting ACH patients could offer a personalized dietetic and nutritional therapy based on objective diagnostic criteria such as REE, total FM, and visceral and subcutaneous fat. In the absence of valid predictive models suitable for clinical use to estimate energy requirements in ACH, it is recommended to use the gold standard method of IC.

Declaration of Competing Interest

None.

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