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Low validity of predictive equations for calculating resting energy expenditure in overweight and obese women with polycystic ovary syndrome

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Keywords
indirect calorimetry, obesity, overweight, polycystic ovary syndrome, predictive equations, resting energy expenditure.

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The present study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (protocol No. 0244.0.0203.000). ClinicalTrials.gov Identifier: NCT02435888.

The study was performed in the Borges da Costa Ambulatory, Avenue Alfredo Balena no 190, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Abstract

Background: Predictive equations are the main clinical tools for determining resting energy expenditure (REE). However, their adequate use in overweight and obese individuals is unclear. Thus, we investigated the best predictive equations for estimating REE in overweight and obese women with polycystic ovary syndrome (PCOS).
Methods: Eleven analyses were performed with prediction equations (pREE) based on anthropometric parameters in 30 overweight or obese women with PCOS without other chronic diseases. The measured REE (mREE) was calculated by indirect calorimetry. The validity of the equations was investigated by comparison, accuracy and agreement tests between pREE and mREE at both the individual and group level.
Results: Four analyses were similar to those of mREE, and smallest mean differences were observed for the World Health Organization/Food and Agriculture Organization of the United Nations/United Nations University (WHO/FAO/UNU) considering weight (W) [0.07 (1.13) MJ (16 [270] kcal)]. Individual accuracy was greater than 50% for Harris and Benedict, Müller and Lazzer equations. The percentage of REE underestimation ranged between 16.7% and 73.3%, whereas higher rates of overestimation were observed in the De Luis (66.7%) and Ireton-Jones (43.3%) equations. Mean bias at the group level was lowest in the WHO/FAO/UNU W and WHO/FAO/UNU considering weight and height (WH), Müller and Lazzer equations (–2.8 to 0.5). The WHO/FAO/UNU W and WHO/FAO/UNU WH formulas were optimal in individual agreement (33.3%).
Conclusions: FAO/WHO/UNU W equations may estimate the REE in overweight and obese women with PCOS. However, the low individual accuracy and agreement in relation to mREE suggest caution regarding when to use the formula to perform an individual nutritional plan.

Introduction

Polycystic ovary syndrome (PCOS) is characterised by the presence of at least two of the following factors: chronic anovulation, clinical or biochemical signs of hyperandrogenism, and the presence of polycystic ovaries [(1)]. It affects up to 15% of women who are of reproductive age [(2)] and is associated with being overweight in 38–88% of cases [(3)]. Obesity influences the phenotypic expression of the syndrome and plays an important role in the pathophysiology of hyperandrogenism and chronic anovulation [2–4]. Obese patients with PCOS have more cardiovascular and metabolic risk factors compared to normal-weight patients with PCOS [5]. Therefore, decreased weight and improved body composition may improve general symptoms and quality of life for these women [3,4].

The development of an appropriate nutritional care plan to achieve healthy weight and improve health requires individualised determination of total energy expenditure (TEE) [6–8]. However, there are some controversies regarding the calculation of resting energy expenditure (REE), which is the main component of TEE among obese patients, because body composition does not change linearly with increasing weight [8]. Furthermore, there is a controversy about the presence of abnormalities in the TEE in women with PCOS [9,10]. A reduction of postprandial thermogenesis was found [10], despite lower REE only occurring in a subgroup of women with PCOS [9].

Indirect calorimetry (IC) is considered the most accurate method to determine REE among healthy individuals and those with underlying diseases, regardless of sex and age. Over recent years, portable IC devices have been developed, although their use in clinical practice is limited because of their high cost, the time required for examination, and the need for trained staff to conduct the examination [6,7,11,12]. Because of these limitations, predictive equations from data using IC remain the main tool for obtaining REE [6,7,11]. Several equations are available and their accuracy and agreement with respect to overweight and obese individuals must be investigated because most equations were developed for individuals with normal weight and/or with different body compositions, ages and ethnicities [6,8,11,13].

Despite several predictive formulas being available, up to now, there is a lack of studies demonstrating their use in overweight and obese women with PCOS. Therefore, the present study investigated the validity of predictive equations that determine REE in this population to guide the nutritional practice associated with weight reduction.

Materials and methods

This cross-sectional study evaluated patients with PCOS, which was defined according to the Rotterdam criteria [1]. These patients were treated in an endocrinology centre that specialised in hyperandrogenism, in a university hospital in Belo Horizonte, state of Minas Gerais, Brazil, between October 2012 and June 2013. The patients were of reproductive age (range 18–45 years), nonsmokers, and were overweight or obese [body mass index (BMI) $\geq$ 25.0 kg m^{-2}] [14]. All participants were free of cardiovascular, respiratory, kidney, liver, inflammatory and metabolic diseases (e.g. hypertension, asthma, coronary heart disease or type 2 diabetes). Women who were pregnant, lactating, diagnosed with hypo- or hyperthyroidism, or had high physical activity levels [15] were excluded from the study. None of the participants used medications that could interfere in REE.

The estimation of the sample size (29 participants) was based on the number of patients with PCOS who initiated nutritional treatment each month (six patients) [16] in the Endocrinology Center of our Institution, considering a minimum prevalence of being overweight of 38% [2,3], a confidence interval of 90% and an acceptable error of 10% [17].

The procedures were conducted in accordance with the ethical standards of the Institutional Research Ethics Committee approving the study (Protocol No. 0244.0.0203.000) and all participants provided their written informed consent statement (ClinicalTrials.gov Identifier: NCT02435888).

Anthropometry

Anthropometric measurements were performed in triplicate by the same investigator and included body weight, height, waist circumference and hip circumference, with criteria established by the World Health Organization (WHO) [14,18]. Anthropometry was assessed when volunteers were standing straight, barefoot and wearing light clothes. Body weight (kg) and height (cm) were measured to the nearest 0.5 cm and nearest 0.1 kg, respectively, using a floor model physician's scale/stadiometer (Filizola®, São Paulo City, Brazil). BMI was calculated and allowed for overweight status (BMI of 25.0–29.9 kg m^{-2}) or obese (BMI > 30.0 kg m^{-2}) [14]. Waist and hip circumference was measured with an inelastic tape with an accuracy of 0.1 cm. Waist circumference was measured in a standing position at the narrowest area between the lateral lower rib and the iliac [18]. Physical activity level was assessed using criteria established by the Institute of Medicine [15].

Resting energy expenditure

The measured REE (mREE) was calculated by indirect calorimetry using an open-circuit calorimeter (MetaCheck™ metabolic rate analysis system, model 7100; Korr Medical Technologies, Salt Lake City, UT, USA). Its accuracy was tested with the nitrogen injection method, as described in the medical and physiological literature [19]. The mean percentage difference across all measurements against actual values was 0.84% [0.05 MJ day^{-1} (13.2 kcal day^{-1})], and the SE was 1.3% [0.11 MJ day^{-1}

(25.8 kcal day^{-1})], with a strong correlation between methods (r^2 = 0.9992) [19]. The machine was autocalibrated prior to each measurement in accordance with the manufacturer's instructions.

The patients attended the clinic in the morning after 12 h of fasting overnight, with minimum physical effort, and remained at rest for 30 min before the evaluation. Patients were seated in a comfortable position and breathed through a disposable mouthpiece connected to the MetaCheck device. A nose clip was used to ensure that all air passed through the mouthpiece. Subjects were reminded to relax, breathe normally, avoid coughing, hold the unit at a horizontal position, and minimise movement until the test was completed (approximately 10 min). Oxygen consumption was measured and energy expenditure was calculated using the equation proposed by Weir [20] with an assumed respiratory quotient of 0.83 [21]. The examination took place in a quiet environment and at an approximate temperature of 20 °C [12]. All portable indirect calorimeter tests were conducted by two trained staff members.

Resting energy expenditure prediction equations

The 10 predictive equations for REE (pREE) used in the present study were obtained by screening previous publications for frequency of use and clinical relevance of the equations [6–13,21,22]. All equations evaluated were based on anthropometric parameters and are summarised in Table 1. For each patient, REE was predicted in all equations in MJ day^{-1} (kcal day^{-1}) and compared with the mREE. The actual body weight at the time of IC measurement was calculated for all equations. Additional analyses were performed using the adjusted weight [adjusted weight = (actual weight − ideal weight) + 0.25 × ideal weight (considering that the ideal weight corresponded to a BMI of 21.5 kg m^{-2})] in obese women using the Harris and Benedict equation. Eleven analyses were performed in the present study.

Statistical analysis

Categorical variables were described as absolute and relative frequencies. All quantitative data are presented as the mean (SD). The Kolmogorov–Smirnov test was used to assess whether the variables followed a normal distribution. A paired Student's *t*-test (parametric variables) and Wilcoxon's test (nonparametric variables) were used to compare the mREE and pREE. In addition, the 95% confidence interval (95% CI) of the difference between pREE and mREE was calculated. Predictions between 90% and 110% of mREE were considered to be accurate measurements at the individual level. Predictive values less than 90% or more than 110% of mREE were classified as underestimates and overestimates, respectively [6,12,13,21]. The mean percentage difference between pREE and mREE (bias) was the measurement of accuracy at the group level [7,13,21]. The level of agreement in the individual classification according to the mREE and pREE was examined using frequencies and similarities among quartiles and the Bland and Altman method [31]. Data were analysed using SPSS, version 19.0 (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

Table 1 Prediction equations used to estimate the resting energy expenditure (pREE) in overweight and obese women with polycystic ovary syndrome

Reference	Prediction equations
Harris and Benedict [23]	655.1 + 9.56 × W (kg) + 1.84 × H (cm) − 4.67 × A (years)
WHO/FAO/UNU W [24]	18–30 years: 14.7 × W (kg) + 496 31–60 years: 8.7 × W (kg) + 829
WHO/FAO/UNU WH [24]	18–30 years: 13.3 × W (kg) + 334 × H (m) + 35 31–60 years: 8.7 × W (kg) − 25 × H (m) + 865
Owen [25]	795 + 7.18 × W (kg)
Mifflin-St Jeor [26]	9.99 × W (kg) + 6.25 × H (cm) − 4.92 × A (years) − 161
Institute of Medicine [15]	247 − 2.67 × A (years) + 401.5 × H (cm) + 8.60 × W (kg)
Ireton-Jones [27]	629 − 11 × A (years) + 25 × W (kg) − 609
Müller [28]	For BMI of 25–30 kg/m²: 10.76 × W (kg) − 3.71 × A (years) + 813.75 For BMI > 30 kg/m²: 11.94 × W (kg) − 3.79 × A (years) + 698.38
De Luis [29]	1272.5 + 9.8 × W (kg) + 1.8496 × H (cm) − 4.6756 × A (years)
Lazzer [30]	10.03 × W (kg) + 864.38 × H (m) − 639.63

A, age; BMI, body mass index; H, height; W, weight; WHO/FAO/UNU W, World Health Organization/Food and Agriculture Organization/United Nations University considering weight; WHO/FAO/UNU WH, World Health Organization/Food and Agriculture Organization/United Nations University considering weight and height.

Results

We recruited 38 women in total. Of these, 30 met the inclusion criteria and enrolled in the study. Table 2 shows the characteristics of participants with a mean (SD) age of 30.8 (5.4) years and BMI of 32.6 (3.7) kg m^{-2}. The analysis of patient physical activity level indicated that 66.7% of participants were sedentary and 33.3% had low activity level, although this level was not significantly different between overweight and obese women.

The mean mREE according to IC was [7.02 (0.88) MJ 1677 [210] kcal) and only 36% of the analyses showed results similar to those of mREE. The statistical difference of means of mREE was found for the formulas Harris and Benedict ($P = 0.047$), WHO/Food and Agriculture Organization of the United Nations/United Nations University (WHO/FAO/UNU) considering weight and height (WH) ($P = 0.004$), Owen ($P = 0.009$), Mifflin-St Jeor ($P < 0.001$), Müller ($P < 0.001$), De Luis ($P = 0.005$) and Lazzer ($P = 0.043$). The WHO/FAO/UNU considering weight (W) equation presented the mean smallest difference. Individual accuracy (precision) was greater or equal than 50% for Harris and Benedict, WHO/FAO/UNU W, Müller and Lazzer equations. The highest percentage of REE underestimation used the Owen. Overestimation was identified in the De Luis and Ireton-Jones formulas. Adjusted weight reduced the individual accuracy of the Harris and Benedict equation, and the mean smallest bias (accuracy of the group) lowered the two WHO/FAO/UNU equations, plus the Müller and Lazzer equations (Table 3).

The adequacy of the quartile classification for REE is shown in Figure 1. The total proportion of women classified in the same quartile of the mREE was low for all equations. The best results were found in the WHO/FAO/UNU W (33.3%) and WHO/FAO/UNU WH (33.3%) formulas.

Table 2 Characteristics of the study group

Characteristics	All (n = 30)	Overweight (n = 8)	Obese (n = 22)
Age (years)*	30.8 (5.4)	30.0 (6.9)	31.0 (5.0)
Weight (kg)*	85.3 (13.1)	72.4 (8.4)‡	90.0 (11.2)
Body mass index (kg m^{-2})*	32.6 (3.7)	27.6 (1.4)‡	34.5 (2.4)
Waist circumference (cm)*	94.1 (9.1)	83.1 (5.0)‡	98.1 (6.5)
Waist/hip ratio*	0.9 (0.1)	0.8 (0.1)‡	0.9 (0.1)
Activity level†	% (n)	% (n)	% (n)
Sedentary	66.7 (10)	50.0 (4)	72.7 (16)
Low activity level	33.3 (20)	50.0 (4)	27.3 (6)

All values are the mean (SD).
**t*-test for independent samples.
†Chi-squared test.
‡Statistical difference among overweight and obese subjects ($P < 0.001$).

Figure 2 shows the agreement between the methods evaluated, as proposed by Bland and Altman (1986). None of the formulas tested for estimating REE in the present study showed high agreement with mREE values. The best results were found using Harris and Benedict, WHO/FAO/UNU W, WHO/FAO/UNU WH, Mifflin-St Jeor, Müller, and Lazzer formulas.

Discussion

The present study showed that, among the equations tested, the WHO/FAO/UNU W (considering weight) was the best predictor of REE in the group studied, demonstrating: (i) similar results to those of mREE; (ii) mean smallest difference compared to mREE; (iii) mean smallest bias (accuracy) at the group level; and (iv) one of the best-tested formulas for individual accuracy and agreement. However, large individual errors may have clinical importance when the equations are used for developing interventions designed for weight management in overweight and obese populations [6,12]. Therefore, frequent revaluation of TEE during the individualised nutritional care is recommended [6–8].

The low individual accuracy and agreement of pREE observed in the present study have also been observed among the general obese population [6–8]. Frankenfield *et al.* [6] showed that the prediction rate was lower and individual variation errors were higher in pREE of overweight and obese adults than in individuals with normal weight. Less than 70% of overweight and obese individuals presented pREE within 10% of mREE values when individual accuracy was evaluated [6,8,11,32]. Some studies have postulated that the low predictive value of equations for estimating REE is a result of differences in body composition among overweight and obese individuals, which are partly the result of a nonlinear increase of fat-free mass (FFM) during weight gain [13,33].

The equations tested in the present study used only anthropometric variables to determine REE, comprising data regarding routine nutritional care for this patient group. Wilms *et al.* [11] investigated whether the predictive value of equations increased by using variables related to body composition, FFM and fat mass among obese women, although no improvement in formula accuracy was found when body composition variables were included. Similarly, Weijs [21] did not identify any increase in the predictive power of equations with variables in the overweight and obese class of I and II adults, aged 18–65 years. In 2010, Weijs and Vansant [13] tested 27 formulas, nine including body composition data for predicting REE among women across BMI groups. Five

Table 3 Comparison between the predicted REE and measured REE for patients with polycystic ovary syndrome

			Difference		Prediction			
	MJ day^{-1} (kcal day^{-1})	*P*	kcal day^{-1}	95% CI	Accuracy* % (*n*)	Underestimation % (*n*)	Overestimation % (*n*)	Bias† (%)
Indirect calorimetry	70.16 (0.88) [1677 (21)]		–	–	–	–	–	–
Harris and Benedict [23]‡	73.76 (0.56) [1763 (13.4)]	0.047	−86 (22.6)	−170; −1.0	56.7 (17)	13.3 (4)	30.0 (9)	−13.5
Harris and Benedict [23], AW‡	65.012 (0.48) [1554 (0.12)]	0.744	123 (22)	40; 205	46.7 (14)	43.3 (13)	9.7 (10)	−24.4
WHO/FAO/UNU W [24]‡	69.49 (0.82) [1661 (0.19)]	0.458	16 (27)	−84; 117	50.0 (15)	26.7 (8)	23.3 (7)	0.5
WHO/FAO/UNU WH [24]‡	68.66 (0.76) [1641 (0.18)]	0.004	36 (26.1)	−62; 113	46.7 (14)	33.3 (10)	20.0 (6)	−0.7
Owen [25]§	58.86 (0.39) [1407 (9.4)]	0.009	270 (21.1)	191; 349	20.0 (6)	73.3 (22)	6.7 (2)	−30.9
Mifflin-St. Jeor [26]‡	64.82 (0.67) [1549 (0.16)]	<0.001	128 (25.2)	34; 222	43.3 (13)	46.7 (14)	10.0 (3)	−27.6
Institute of Medicine [15]‡	0000 (000) [1546 (13.4)]	0.163	131 (22.8)	46; 216	43.3 (13)	43.3 (13)	10.0 (3)	−24.6
Ireton-Jones [27]‡	75.89 (1.39) [1814 (33.3)]	0.118	−137 (35.3)	−268; −5	40.0 (12)	16.7 (5)	43.3 (13)	−31.7
Müller [28]§	75.89 (0.62) [1814 (14.8)]	<0.001	68 (23.2)	−18; 155	56.7 (17)	33.3 (10)	10.0 (3)	−2.5
De Luis [29]‡	82.30 (0.55) [1967 (13.1)]	0.005	−290 (22.2)	−373; −207	3.3 (1)	30.0 (9)	66.7 (20)	−4.1
Lazzer [30]§	67.40 (0.74) [1611 (17.8)	0.043	66 (25.3)	−28; 161	56.7 (17)	33.3 (10)	10.0 (3)	−2.8

*Predictions between 90% and 110% of mREE (individual level).

†The mean percentage difference between pREE and mREE (group level).

‡Student's *t* test.

§Wilcoxon's test.

AW, adjusted weight; CI, confidence interval; WHO/FAO/UNU W, World Health Organization/Food and Agriculture Organization/United Nations University considering weight; WHO/FAO/UNU WH, World Health Organization/Food and Agriculture Organization/United Nations University considering weight and height.

equations showed better accuracy, of which only one contained body composition data [13]. This suggests that the present study may not be biased for low results of pREE in women with PCOS because the effect of fat mass and free fat mass in REE is well established [15,25,26]. Androgen excess may predispose to abdominal fat deposition and modify body composition of PCOS women; they have a higher percentage of body fat, especially abdominal fat, than the control group [2,3], which may explain changes in REE, along with low accuracy and agreement of equations in the present sample.

REE in women with PCOS has not been studied extensively. In two groups of women with the syndrome, there was no evidence of altered resting metabolic rate [9,34]. However, when REE was adjusted for FFM, fat mass, sex and age, differences were identified between women with PCOS and biochemical hyperandrogenism that were associated with insulin resistance problems [10]. The results suggest that intrinsic factors in PCOS (e.g. chronic anovulation) may interfere in REE [9]. Abnormal glucose metabolism in PCOS has been suggested to affect REE independent of body weight [10], as well as other conditions, such as type II diabetes [35]. These factors may contribute to the low accuracy and agreement of the equations in different contexts of metabolic abnormalities associated with PCOS.

None of the formulas used in the present study have an excellent accuracy or agreement with mREE in overweight and obese women with PCOS. However, it is important to note that the WHO/FAO/UNU W equations exhibited better estimates of REE in this sample, thus contradicting previous research. Various studies recommend use of the Mifflin-St Jeor equation for overweight and obese individuals, whereas a recent systematic review concluded that no single prediction equation provides accurate and precise REE estimates in all obese adults [36]. The result may change according to BMI subgroups and the method of analysis (by participants or study subgroups). Their recommendation was to use the Mifflin-St Jeor equation for this population, although errors exceeded 10% in 25% of those assessed [36]. In a previous systematic review, the Mifflin-St Jeor equation was the most reliable, and better predicted REE within 10% of the mREE in non-obese and obese individuals than any

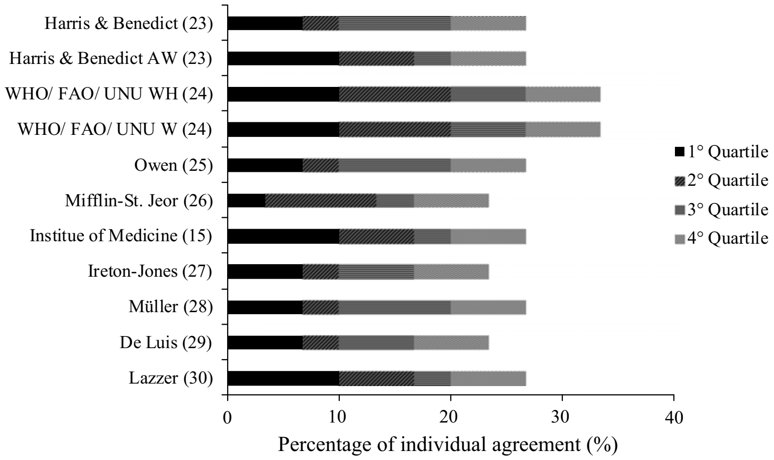

Figure 1 Percentage of individual agreement between the resting energy expenditure (REE) obtained by indirect calorimetry (IC) and the different predictive equations, by quartile. AW, adjusted weight; CI, confidence interval; WHO/FAO/UNU W, World Health Organization/Food and Agriculture Organization/United Nations University considering weight; WHO/FAO/UNU WH, World Health Organization/Food and Agriculture Organization/United Nations University considering weight and height.

other equation, having the narrowest error range [6]. Other studies supported the use of the Mifflin-St Jeor equation to estimate REE in American overweight and obese adults [21,22]. In Belgian women, Mifflin-St Jeor and original Harris and Benedict equations were reliable for predicting REE across a wide range of BMI values (18.5–50.0 kg m^{-2}) [13]. The WHO/FAO/UNU was found to be the best equation only for overweight Dutch [21], whereas, in the study by Hasson [12], the WHO/FAO/UNU equation was useful for female participant cohorts [BMI 24.8 (4.9) kg m^{-2}]. Thus, caution is warranted when generalising the results of the present study to other populations.

A growing body of evidence suggests that the low predictive power of REE equations is a result of the distinct characteristics of the reference population used to establish these equations [6,,11,13]. In the present study, the predictive value of four formulas developed for obese individuals was investigated (Ireton-Jones, Müller, de Luis e Lazzer). However, the REE obtained did not improve accuracy and agreement to the value measured by IC. Indeed, previous studies have shown that the use of predictive formulas developed specifically for obese individuals in different populations and context of diseases did not increase the predictive value of REE [11,13,32]. By contrast, in a subgroup analysed using the variables sex, age and BMI, such formulations showed better results [7,8,21]. For most equations, overweight and obese individuals were included, although their relative contribution to the final equation often remained unclear [21]. In this sense, the level of being overweight and obesity may be an important factor that interferes with the accuracy of the predictive equation.

The effect of ethnicity on the REE must also be considered [6,15,22,37]. The pREE calculation does not include ethnicity as a variable, which may contribute to its low accuracy [6]. In the present study, ethnicity was not evaluated because of difficulty in determining different races of the Brazilian population. African American adults exhibited significantly lower REE (approximately 10%) than adult Caucasians [15]. A reduction of REE was identified in Asian-Indian men compared to Chinese men living in Singapore, after adjustment for body weight, FFM, fat mass and brain volume [37]. The prediction formulas arose for mathematical equations, as developed from measurements obtained by indirect calorimetry in a specific population. Therefore, the use of the equation in a different ethnic group versus that of development was associated with increased error [6,15,20,21]. In Brazil, miscegenation ethnicity could interfere with the accuracy and concordance of predictive formulas.

The original equation of Harris and Benedict was developed for healthy individuals with normal weight and those who are overweight [24]. There is some doubt about which weight measurement (actual or adjusted) should be used for estimating REE. In the present study, adjusted weight did not contribute to increased accuracy. Indeed, there was an increased rate of underestimation and bias, thereby confirming previous studies [6,14,32] that did not adjust weight for estimate REE [6,13,32].

The study includes only women with PCOS and BMI > 25 kg m^{-2}, which may limit the interpretation of the results. However, the study was performed with patients undergoing treatment in a specialised centre for hyperandrogenism. During the data collection, only four women with a BMI < 25 kg m^{-2} initiated the nutritional

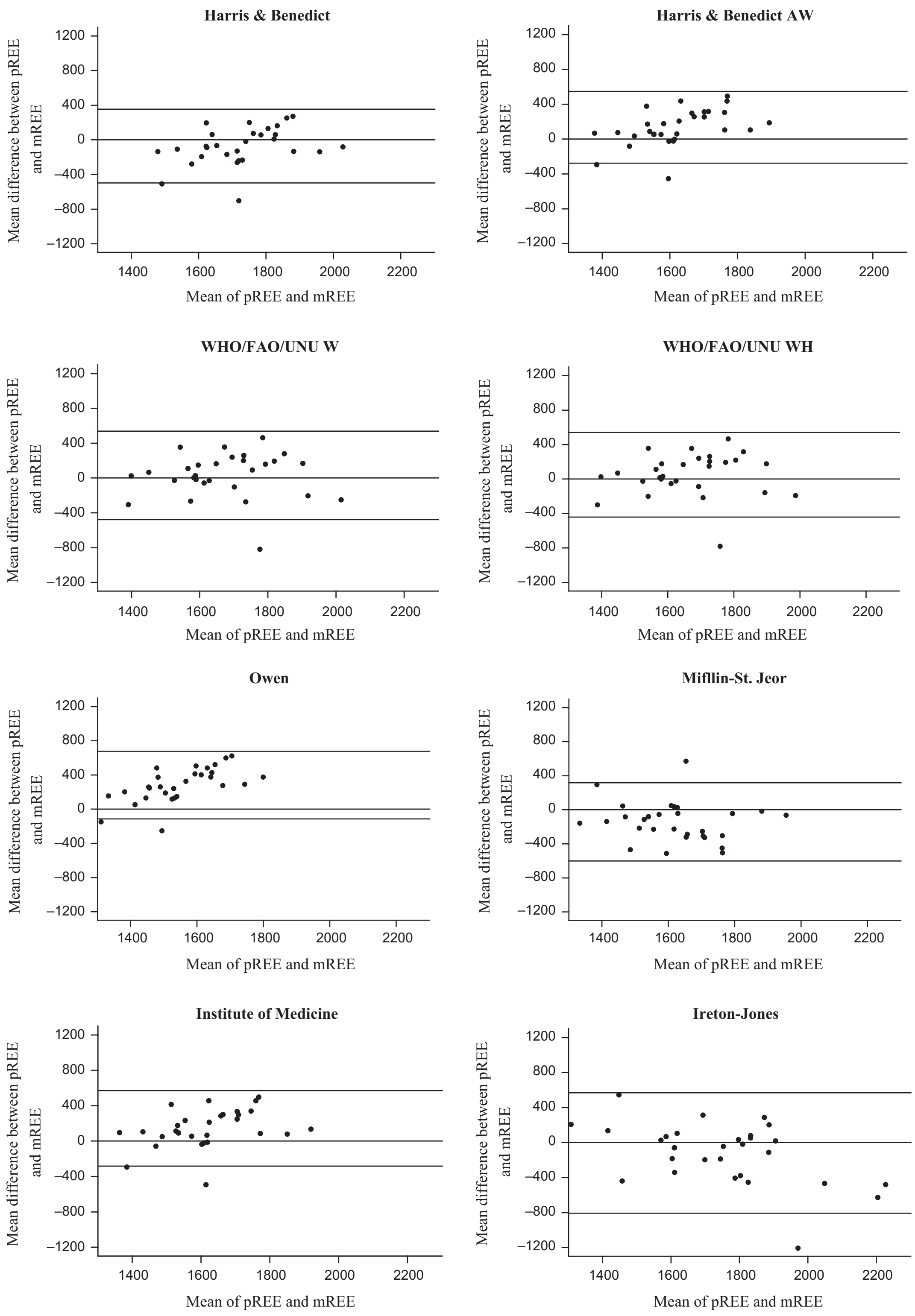

Figure 2 Agreement using the Bland and Altman method between the resting energy expenditure (REE) measured by indirect calorimetry (IC) and the values estimated by predictive equations on the basis of anthropometric parameters in the study group. AW, adjusted weight; mREE, measured resting energy expenditure; pREE, predicted resting energy expenditure; WHO/FAO/UNU W, World Health Organization/Food and Agriculture Organization/United Nations University considering weight; WHO/FAO/UNU WH, World Health Organization/Food and Agriculture Organization/United Nations University considering weight and height.

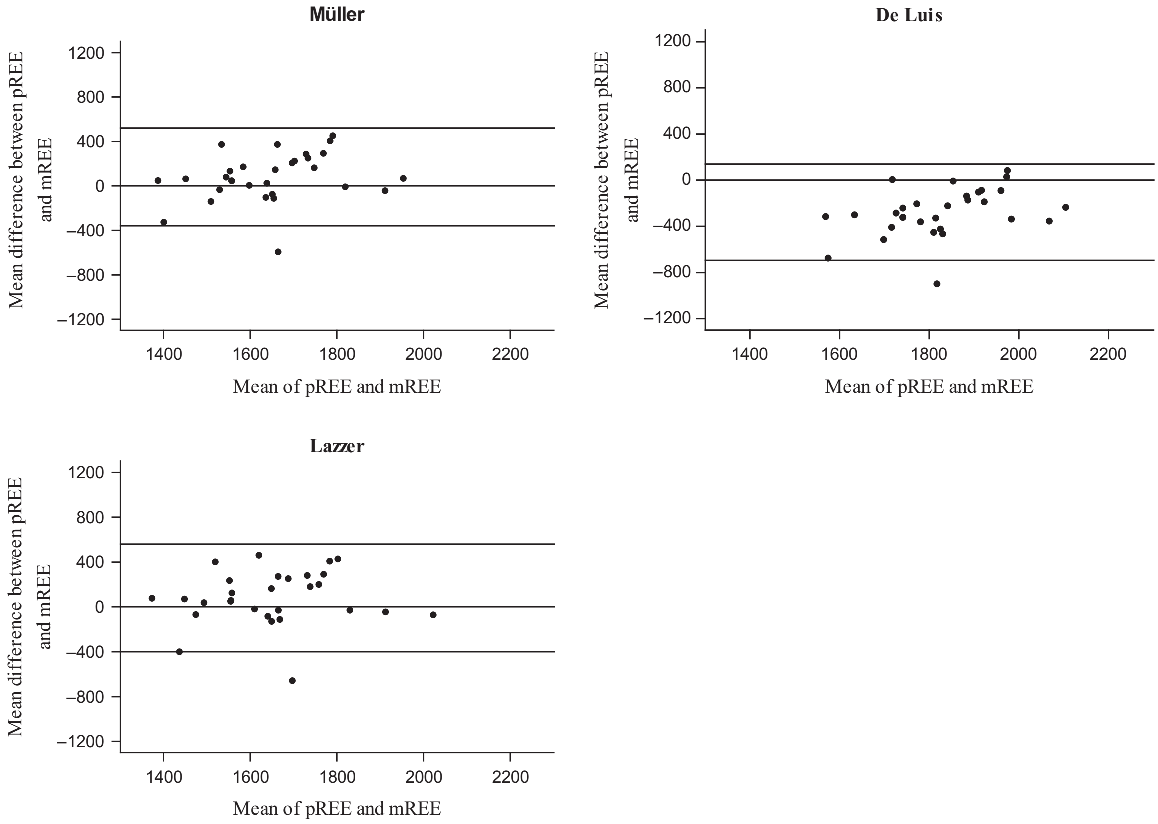

Figure 2 Continued

treatment for controlling weight and symptoms of the syndrome. Thus, as already shown in the literature, in clinical practice, there is difficulty with respect to recruiting patients with such characteristics [38,39]. To calculate the mREE, we used the equation proposed by Weir [20]. This comprises the most frequent equation used for metabolic rate measure in IC [15,20–31]. However, this method may underestimate the heat production associated with protein oxidation [40]. The calorimeter in the present study has an oxygen analyser to estimate REE, assuming a fixed ratio to carbon dioxide production and oxygen consumption (VCO_2/VO_2). Such equipment can reduce accuracy because the respiratory quotient may vary from 0.7 to 1.0. Yet validation tests demonstrate that it is possible to accurately assess the REE only by oxygen consumption (VO_2) [12,41]. Another limitation of the present study may be related to the patient's position during indirect calorimetry (sitting and holding the mouthpiece). Certain positions are associated with increased muscle tone and consequent increase in energy expenditure [42]. However, we followed guidelines outlined by the manufacturer, similar to those used in other portable indirect calorimeters [19,29,41]. To minimise potential precision errors, specific measurements related to patients (fasting, exercise, prior rest, comfortable position and minimum movements) and equipment (fixed position calibration and test time) [6] were performed.

REE overestimation found in the present study for most tested formulas may represent a serious problem in relation to nutritional care for overweight and obese women with PCOS. Because REE is the main determinant of TEE, values greater than those established by IC will impair body weight reduction [6,8,11,12]. However, the high rate of underestimation obtained in some equations is concerning because it can promote more rigorous energy restrictions, with consequent abandonment of nutritional treatment [8] essential for management of PCOS.

The present study has high clinical relevance. It is the first to investigate the use of predictive equations to determine REE among overweight and obese women with PCOS. Nutritional interventions that provide guidance for implementing mild to moderate weight reduction via a negative energy balance can yield significant health benefits for these women directly [4] or indirectly by improving diet quality [16]. Therefore, determining REE becomes crucial for individualised eating plan calculations and promotion of adequate weight loss [9,11]. The results obtained in the present study suggest that the WHO/FAO/UNU W equation can estimate the REE in this population, even with poor accuracy and agreement. In clinical practice, the nutritionist should evaluate weight loss and make changes in nutritional intervention to correct possible individual errors of REE underestimation or overestimation. We suggest further studies are conducted aiming to investigate the development of an equation for women with PCOS and obesity because the acquisition of a calorimeter may be not available to everyone.

Transparency Declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study. No important aspects of the study was omitted and any discrepancies from the study as planned was explained. The reporting of this work is compliant with STROBE guideline.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
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AMSR participated in the design of the study; acquisition, analysis and interpretation of data; and manuscript preparation. ABPC, DLC and MPSS collaborated regarding the acquisition analysis and the interpretation of data. ALC, LCS and AVMF contributed to the conception and design of the study; interpretation and critical revision of data; and approval of the final version. All authors critically reviewed the manuscript and approved the final version submitted for publication.

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