



Development of new predictive equations for basal metabolic rate in Iranian healthy adults: negligible effect of sex

Bahareh Nikooyeh, Nastaran Shariatzadeh, Ali Kalayi, Maliheh Zahedirad, and Tirang R. Neyestani 

National Nutrition and Food Technology Research Institute and Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract: Some studies have reported inaccuracy of predicting basal metabolic rate (BMR) by using common equations for Asian people. Thus, this study was undertaken to develop new predictive equations for the Iranian community and also to compare their accuracy with the commonly used formulas. Anthropometric measures and thyroid function were evaluated for 267 healthy subjects (18–60 y). Indirect calorimetry (InCal) was performed only for those participants with normal thyroid function tests ($n = 252$). Comparison of predicted RMR (both kcal/d and kcal.kg.wt⁻¹.d⁻¹) using current predictive formulas and measured RMR revealed that Harris-Benedict and FAO/WHO/UNU significantly over-estimated and Mifflin-St. Jeor significantly under-estimated RMR as compared to InCal measurements. In stepwise regression analysis for developing new equations, the highest r^2 ($=0.89$) was from a model comprising sex, height and weight. However, further analyses revealed that unlike the subjects under 30 y, the association between age and the measured RMR in subjects 30 y and plus was negative ($r = -0.241$, $p = 0.001$). As a result, two separate equations were developed for these two age groups. Over 80 percent of variations were covered by the new equations. In conclusion, there were statistical significant under- and over-estimation of RMR using common predictive equations in our subjects. Using the new equations, the accuracy of the calculated RMR increased remarkably.

Keywords: basal metabolic rate, RMR predictive equations, indirect calorimetry

Abbreviations

Anti-TPO-Ab: anti thyroid peroxidase antibody; BIA: bio-electrical impedance analysis; BMR: basal metabolic rate; EIA: enzyme immunoassay; EE: Energy expenditure; FAO/WHO/UNU: Food and Agriculture Organization/World Health Organization/ United Nations University; FM: fat mass; fT4: free thyroxine; HC: hip circumference; InCal: indirect calorimetry; LBM: lean body mass; RMR: resting metabolic rate; SD: standard deviation; SPSS: Statistical Package for Social Science; TEF: thermic effect of food; TSH: thyroid stimulating hormone; WC: waist circumference.

Introduction

Accurate estimation of energy expenditure (EE) has a crucial importance for providing nutrition care in clinical settings and in nutrition policy-making at the community

level [1–5]. EE comprised of different components including basal metabolic rate (BMR), thermic effect of food (TEF) and exercise and non-exercise activity thermogenesis (NEAT) [6]. It is believed that BMR, contributing over 60% of EE, is influenced by body composition, age, sex and race [7]. In most, if not all, studies, the conditions used to measure metabolic rate are less restrictive than what are needed for measuring BMR. Therefore, resting metabolic rate (RMR) is measured. However, the terms “RMR” and “BMR” are usually used interchangeably.

There are several methodologies to determine EE and metabolic rate in humans including direct and indirect methods [8]. High cost, sophisticated instruments and expertise have actually confined direct methods just for research purposes. Indirect methods, on the other hand, are far less expensive and more applicable. Notwithstanding, not all hospitals and clinics have access to the appropriate instruments including body composition analyzers that are capable to estimate metabolic rate. As a result, most clinical nutritionists and clinicians require estimating

BMR and EE by using predictive equations. Some of the most commonly used equations are Harris-Benedict [9], Schofield [10], FAO/WHO/UNU [11] and Mifflin-St. Jeor [12] which are mostly based on age, sex, weight and height. Mifflin-St. Jeor and Harris-Benedict equations have been proven accurate in a sample of the American adults [13] and Iranian hospitalized patients [14] but over-estimated BMR in Asian samples [15–18]. This may be due to difference in body composition and higher percent of body fat mass (FM) and lower lean body mass (LBM) in Asians as compared with European and American people [19]. Consequently, RMR of Asian people may be 15–20% less than that of Europeans and Americans [20, 21]. This difference could be misleading in decision making for clinical as well as community interventions. We, therefore, hypothesized that there is a significant difference between RMR measured by indirect calorimetry and estimated RMR using common predictive equations in Iranian subjects. Thus, the aims of our study were: (i) to evaluate the accuracy of the RMR calculated by commonly used formulas of Harris-Benedict, FAO/WHO/UNU, Mifflin-St. Jeor and RMR estimated by bioelectrical impedance analysis with the RMR measured by indirect calorimetry in a sample of Iranian healthy adults; (ii) to develop new predictive equations for the Iranian community; and (iii) to compare the accuracy of new equations with the commonly used aforementioned formulas.

Subjects and methods

The study protocol

The comprehensive protocol of this study has already been reported [22]. Briefly, the study was conducted from October 2017 to April 2018. Using a general announcement, healthy adult subjects aged 18–60 y were recruited to the Laboratory of Nutrition Research, National Nutrition and Food Technology Research Institute (NNFTRI). Sample size was calculated for multiple regression models and the general definition of the effect size index f^2 used in this procedure was: $f^2 = VS/VE$, where VS is the proportion of variance explained by a set of predictors and VE is the residual or error variance ($VE + VS = 1$). The effect size of 0.35 is considered large [23]. We calculated that with assuming an effect size of 0.3, a sample size of 50 participants in each subgroup would have the power of 90%. Those who met the initial inclusion criteria that determined through an interview were enrolled. The study protocol and objectives were fully explained for the participants before they signed an informed written consent. First, 2 mL blood sample was taken to assess thyroid markers status. The subjects with

normal thyroid function test results invited to participate in the study. The demographic data were gathered using a questionnaire and face to face interview. Then anthropometric measures and a fasting venous blood sample for thyroid function tests were taken. Finally, indirect calorimetry was performed only for those participants with normal thyroid tests results. This study was approved ethically and scientifically by the Ethics Committee and the Research Committee of NNFTRI, respectively (Ethical code: ir.sbmunnftri.rec.1395.87).

Subjects

The inclusion criteria were: age 18–60 y; normal thyroid function test results; not pregnant, lactating or menses at the time of assessments; not having clinical disease including endocrine, cardiac, renal, hepatic and malignant diseases; not using medications affecting RMR including drugs used for cardiac and endocrine disorders and chemotherapeutic agents. Professional athletes were also excluded.

Assessments

Anthropometric measures

Weight was measured with light clothing and without shoes using a digital scale (Seca 808; Seca, Hamburg, Germany) to the nearest of 0.1 kg. Height was measured using a stadiometer (Seca 216, Seca, Hamburg, Germany) to the nearest of 0.1 cm. Body mass index (BMI) was calculated using the equation $\text{body weight (kg)}/\text{height}^2 \text{ (m)}$. Categorization of BMI was: underweight: $< 18.4 \text{ kg/m}^2$; normal weight: $18.5\text{--}24.9 \text{ kg/m}^2$; overweight: $25.0\text{--}29.9 \text{ kg/m}^2$; and obese $> 30.0 \text{ kg/m}^2$ [24]. Waist circumference (WC) and hip circumference (HC) were both measured using a measuring tape to the nearest of 0.1 cm.

Evaluation of total and visceral fat mass

Percent of total body fat mass (FM) was estimated using bioelectrical impedance analysis (BIA) system (Quadscan 4000, Bodystat, Isle of Man, UK). This system also estimates RMR using Brozek and Grande formula which is based on lean body weight instead of total body weight. Percent of truncal and visceral fat was evaluated by applying ViScan (AB140, Tanita, Tokyo, Japan).

Laboratory investigations

Blood sampling and handling

At the same day, after performing indirect calorimetry, 10 mL antecubital venous blood was taken from each participant after an overnight fasting. Sera were separated and

kept frozen until the analysis day as described elsewhere [22].

Thyroid function tests

The concentrations of serum thyroid stimulating hormone (TSH), free thyroxine (fT4; both from Pishtaz Teb, Tehran, Iran) and anti-thyroid peroxidase antibody (anti-TPO-Ab; Aeskulisa, Wendelsheim, Germany) were determined using enzyme immunoassay (EIA) commercial kits. The normal range of serum TSH and fT4 were 0.32–5.2 mIU/L and 0.7–1.8 ng/dL, respectively. In this study, subjects with higher than normal levels of anti-TPO (>500 IU/mL) but normal TSH and fT4 were considered as euthyroid [25, 26].

Indirect calorimetry

Indirect calorimetry (InCal) was performed using a calibrated respiratory gas analyzer (Fitmate pro, Cosmed, Rome, Italy) at room temperature ($25 \pm 2^\circ\text{C}$) while the subject was in supine position with a face mask and light clothing. The preconditions of InCal were: (a) being 12 h fasting; (b) after 30 min resting at room temperature (RT); and (c) at least 48 h after light to vigorous exercise. None of the participants were tobacco users or on a weight-loss diet. For females InCal was not measured during luteal phase [27]. To minimize any possible variations, all measurements were performed by a single device and operator under the same conditions. Total duration of the test was 15 minutes (5 minutes for test phase to discard and 10 minutes for data acquisition phase). Measurements with over 3 “non valid” data (more or less than 3 SD of mean for more than three minutes) were repeated on another day. The validity of this system has been shown elsewhere [28–32]. In this paper, the same terminology as originally applied in citations is used. However, when discussing our data we refer to RMR.

Statistical analyses

Normality of data distribution was evaluated using Shapiro-Wilk test. Mean and standard deviation (SD) were used to describe quantitative data while absolute and relative frequencies were applied for qualitative variables. In order to check homogeneity of inter-group variances, Leven’s test was applied. The mean of calculated values with each equations were compared with measured values using repeated measures analysis of variance.

Correlation between two sets of data (calculated values with different equations and predicted RMR) was evaluated by using Pearson (r ; for data with normal distribution) or Spearman (r_s ; for data with non-normal distribution) equations. Inter-method agreement was checked by

Bland-Altman. Accuracy was considered as the proportion of the subjects whose predicted RMR was 90–110% of their measured RMR [33]. Multivariable regression analysis was applied to develop new predictive equations for RMR based on independent variables (age, sex, weight and height). In this study $p < 0.05$ was considered as statistically significant. All statistical analyses were performed by using Statistical Package for Social Science (SPSS version 21; SPSS Inc, Chicago, IL).

Results

Initially 267 subjects were enrolled but later 15 were excluded due to abnormal results of thyroid function tests. Finally, 252 subjects including 121 males and 131 females aged 39.4 ± 10.7 y were studied (Table 1).

There was a strong correlation between measured RMR and predicted RMR (Table 2) using Harris-Benedict ($r = 0.890$, $p < 0.001$), FAO/WHO/UNU ($r = 0.872$, $p < 0.001$), Mifflin St. Jeor ($r = 0.902$, $p < 0.001$) and BIA ($r = 0.835$, $p < 0.001$) equations. However, comparison of predicted RMR (both kcal/d and kcal.kg.wt⁻¹.d⁻¹) using these predictive formulas and measured RMR revealed that that Harris-Benedict and FAO/WHO/UNU significantly over-estimated and Mifflin-St. Jeor significantly under-estimated RMR as compared with measured RMR in both males and females (Table 3). Mifflin-St. Jeor equation had the most accuracy in both sex while it had the most under-estimation, as well. Harris-Benedict showed 19% accuracy in men and 58% in women. Percent of error of the studied equations ranged from –2.8% to 17.7% with the highest from Harris-Benedict in men (Table 4). Bland-Altman analysis revealed that the least agreement was between FAO/WHO/UNU equation and measured RMR ((–262.7) – (369.7) in males and (–262.1) – (–357.5) in females; Figure 1).

In order to determine the best predictive model for RMR, multiple regression analysis was employed. Initially, there was a statistical significant association between measured RMR and weight ($r = 0.843$, $p < 0.001$), height ($r = 0.768$, $p < 0.001$), WC ($r = 0.531$, $p < 0.001$) and total FM ($r = -0.339$, $p < 0.001$). Also, there was a significant association between age and total body fat ($r = 0.313$, $p < 0.001$). However, further analyses revealed that in the subjects under 30 y, the association between age and the measured RMR was positive ($r = 0.711$, $p < 0.001$) whereas in subjects 30 y and over, this association was negative ($r = -0.241$, $p = 0.001$). As a result, two separate equations were developed for these two age subgroups. The stepwise regression analysis in subjects older than 30 y showed that the highest r^2 was for a model comprising sex, height and weight

Table 1. Comparison of the studied variables between male and female subjects

Variable	Male (n = 121)	Female (n = 131)	p value*	Total (n = 252)
	mean \pm sd (95 %CI)	mean \pm sd (95 %CI)		mean \pm sd (95 %CI)
Age (y)	39.7 \pm 9.9 (38.0, 42.1)	39.0 \pm 11.4 (37.0, 41.0)	0.606	39.4 \pm 10.7 (38.0, 40.9)
Height (cm)	175 \pm 7.07 (172.4, 175.4)	160.4 \pm 5.5 (159.4, 161.4)	<0.001	167 \pm 9.4 (164.8, 168.2)
Weight (kg)	85.0 \pm 14.3 (81.2, 87.1)	68.4 \pm 11.5 (66.4, 70.4)	<0.001	76.4 \pm 1.4 (72.9, 76.9)
BMI (kg/m ²)	27.9 \pm 4.2 (26.9, 28.7)	26.6 \pm 4.5 (25.8, 27.4)	0.023	27.2 \pm 4.4 (26.5, 27.7)
WC (cm)	100 \pm 11.4 (97.8, 102.5)	93.8 \pm 11.7 (91.8, 95.9)	<0.001	96.5 \pm 12.0 (94.9, 98.1)
HC (cm)	108 \pm 8.1 (106.2, 109.6)	106 \pm 9.0 (104.8, 108.0)	0.206	107 \pm 8.7 (105.9, 108.2)
TBFM (%)	23.4 \pm 6.4 (22.2, 25.2)	34.8 \pm 6.9 (33.9, 36.4)	<0.001	30.1 \pm 8.8 (29.2, 31.7)
Truncal fat (%)	33.1 \pm 9.3 (31.7, 36.0)	39.9 \pm 7.2 (38.6, 41.4)	<0.001	37.1 \pm 8.8 (36.3, 38.7)
Visceral fat (%)	13.7 \pm 5.7 (12.9, 15.4)	10.3 \pm 4.4 (9.5, 11.1)	<0.001	11.7 \pm 5.3 (11.1, 12.6)
TSH (mIU/L)	2.1 \pm 1.0 (1.9, 2.5)	2.4 \pm 1.1 (2.3, 3.0)	0.059	2.3 \pm 1.1 (2.28, 2.74)
fT4 (ng/dL)	0.9 \pm 0.2 (0.8, 1.0)	0.8 \pm 0.1 (0.78, 0.89)	0.001	0.9 \pm 0.1 (0.87, 0.92)
Anti-TPO-Ab (IU/mL)	18.1 \pm 48.4 (8.7, 35.2)	46.5 \pm 96.8 (35.4, 74.7)	0.100	34.5 \pm 81.1 (28.6, 54.5)

* Independent sample *t* test.

Abbreviations: Anti-TPO-Ab: anti-thyroid peroxidase antibody; BMI: body mass index; fT4: free thyroxine; HC: hip circumference; TBFM: total body fat mass; TSH: thyroid stimulating hormone; WC: waist circumference.

Table 2. Predictive equations for basal metabolism rate used in present study

Predictive equations	
Harris-Benedict (Kcal/day)	Men, BMR = 66.5 + (13.75 \times weight in kg) + (5.003 \times height in cm) – (6.755 \times age in years) Women, BMR = 655.1 + (9.563 \times weight in kg) + (1.850 \times height in cm) – (4.676 \times age in years)
FAO/WHO/UNU (Kcal/day)	Men: 18–30 y, 15.3 \times weight in kg + 679 Men: 30–60 y, 11.6 \times weight in kg + 879 Women: 18–30 y, 14.7 \times weight in kg + 496 Women: 30–60 y, 8.7 \times weight in kg + 829
Mifflin St Jeor Equation (Kcal/day)	Men: (9.99 \times weight in kg) + (6.25 \times height in cm) – (4.92 \times age in years) + 5 Female: (9.99 \times weight in kg) + (6.25 \times height in cm) – (4.92 \times age in years) – 161

Table 3. Comparison of measured (by indirect calorimetry) and predicted (by different equations) resting metabolic rate (RMR) in male and female subjects

	RMR (kcal.d ⁻¹)		RMR (kcal.kg. wt ⁻¹ .d ⁻¹)	
	Mean \pm sd (95 %CI)	p value*	Mean \pm sd (95 %CI)	p value*
Males (n₁ = 121)				
Indirect calorimetry	1831 \pm 234 (1797.5, 1879.0)	–	21.8 \pm 2.4 (21.4, 22.2)	–
Harris-Benedict	2148 \pm 266 (2099.8, 2195.4)	<0.001	25.5 \pm 1.8 (25.1, 25.7)	<0.001
FAO/WHO/UNU	1884 \pm 175 (1852.7, 1915.7)	<0.001	22.4 \pm 1.9 (22.0, 22.7)	<0.001
Mifflin St. Jeor	1751 \pm 170 (1720.7, 1782.0)	<0.001	20.9 \pm 2.0 (20.4, 21.2)	<0.001
BIA	1920 \pm 241 (1863.1, 1977.0)	<0.001	22.7 \pm 2.6 (22.1, 23.3)	<0.001
Females (n₂ = 131)				
Indirect calorimetry	1389 \pm 207 (1374.4, 1440.7)	–	20.5 \pm 2.6 (20.3, 21.1)	–
Harris-Benedict	1434 \pm 111 (1414.4, 1452.7)	0.001	21.3 \pm 2.4 (20.8, 21.7)	<0.001
FAO/WHO/UNU	1437 \pm 111 (1417.5, 1455.7)	0.001	21.3 \pm 2.1 (20.9, 21.6)	<0.001
Mifflin St. Jeor	1334 \pm 127 (1311.8, 1355.7)	<0.001	19.8 \pm 2.2 (19.3, 20.1)	<0.001
BIA	1464 \pm 166 (1409.6, 1491.3)	<0.001	21.7 \pm 3.7 (20.7, 22.3)	<0.001

*Comparison between measured and calculated RMR.

Table 4. Accuracy and precision of the predicted RMR compared with the measured RMR

	Mean difference \pm SD (95 %CI) (kcal/d)	Bias ¹ (%)	Accuracy ² (%)	Underestimation ³ (%)	Overestimation ⁴ (%)
<i>Males ($n_1 = 121$)</i>					
Harris-Benedict	317 \pm 153 (289.3, 344.5)	17.7 \pm 9.0 (16.0, 19.3)	19.0	0	81.0
FAO/WHO/UNU	53.5 \pm 158 (25.1, 82.0)	3.7 \pm 9.2 (2.0, 5.3)	73.6	4.1	22.3
Mifflin St. Jeor	-79.2 \pm 137 (-103.9, -54.5)	-3.7 \pm 7.1 (-4.9, -2.4)	74.3	20.7	5.0
BIA	99.0 \pm 162.4 (63.9, 127.8)	5.8 \pm 9.1 (4.1, 7.4)	66.2	4.2	29.6
<i>Females ($n_2 = 131$)</i>					
Harris-Benedict	44.6 \pm 148 (18.9, 70.3)	4.7 \pm 11.6 (2.7, 6.6)	58.0	11.5	30.5
FAO/WHO/UNU	47.7 \pm 155 (20.9, 74.4)	4.9 \pm 11.8 (2.8, 6.9)	50.8	10.7	31.3
Mifflin St. Jeor	-55.1 \pm 142 (-79.6, -30.4)	-2.8 \pm 10.3 (-4.5, -1.0)	66.4	21.4	12.2
BIA	90.1 \pm 179 (12.3, 95.1)	7.7 \pm 14.2 (5.2, 10.1)	64	4.9	31.1

Mean differences: mean of difference between predicted and measured basal metabolic rate.

1) [(predicted REE – measured REE)/measured REE] \times 100.

2) Percentage of subjects predicted by equation within 90% to 110% of measured REE.

3) Percentage of subjects predicted by equation < 90% of measured REE.

4) Percentage of subjects predicted by equation > 110% of measured REE.

($r^2 = 0.89$). However, in participants aged < 30 y, the model comprised of height, age, weight and total FM had highest r^2 , i.e. 0.85. When the total fat was excluded and sex of subjects was introduced instead, r^2 slightly declined to 0.84. In this way, over 80 percent of variations were covered by the new equations (Table 5). The mean difference between measured RMR and predicted RMR using new equations was not statistically significant (Table 6). The percent of error for the new equations was $0.8 \pm 7.0\%$ for < 30 y and $-0.1 \pm 5.9\%$ for > 30 y. The accuracy of the new predictive equations for RMR was 88% for both age subgroups. Evaluation of the agreement between measured RMR and predicted RMR using new equations demonstrated that the limit of agreement was 400 kcal indicating the higher agreement with the predicted RMR using new equations, as compared with the other studied equations (Figure 2).

In order to cross-validate the new equations, an independent population (<30 yr, $n = 25$ and > 30, $n = 89$) were selected from the participants of our other previous projects. The needed data, including sex, age, anthropometric measures and InCal RMR were obtained from our databank. The associations between measured RMR with InCal and predicted RMR using new equations were $r = 0.955$, $p < 0.001$ and $r = 0.903$, $p < 0.001$ in younger and older than 30 years old subjects, respectively. In addition, there were no statistical significant differences between InCal RMR and predicted RMR in both age groups (<30 yr: -36.6 ± 14.9 , $p = 0.701$, > 30 yr: 35.2 ± 12.5 , $p = 0.665$).

Discussion

Our findings indicate that calculation of RMR using the three current equations as well as the estimated RMR by

the BIA system are accompanied by either over-estimation (Harris-Benedict, FAO/WHO/UNU and BIA) or under-estimation (Mifflin St. Jeor) in our sample of Iranian adults. The issue of over-estimation by Harris-Benedict has already been reported [34]. In contrast, in a study on American subjects (mostly Caucasians) aged 18–65 y from both sexes, estimation of RMR using Harris-Benedict and FAO/WHO/UNU equations showed the least bias from the measured RMR while estimations derived from other formulas significantly differed from the numbers obtained from InCal. In that study, prediction bias was inversely associated with both range of RMR and fat free mass [35]. Regardless of the small sample size for a rather wide range of age and BMI ($n = 30$), the findings of that study well endorsed the influence of body composition (percent of FM and LBM) on basal metabolism and the degree of agreement between predicted and measured numbers. Along the same line of evidence, a recent study conducted on 406 Jordanian healthy subjects (206 men and 200 women) aged 18–25 y including normal weight, overweight and obese persons, Harris-Benedict equation demonstrated the most agreement with measured RMR in all BMI categories just in women and numbers calculated by other formulas including FAO/WHO/UNU, Mifflin-St. Jeor and Owen were all significantly different from measured RMR [36]. On the other hand, another study on 337 healthy subjects in a broad range of BMI (from less than 20 to over 50 kg/m²) reported the most agreement between Mifflin-St. Jeor equation and measured RMR [13]. Notwithstanding, in a study on 96 Chinese-Singaporean healthy adults aged 21–40 y with BMI range of 18.5–30 kg/m², the calculated numbers for RMR by FAO/WHO/UNU, Harris-Benedict and Mifflin St. Jeor, as compared with measured RMR, had 7.5%, 6.0% and 2.4% over-estimation, respectively and Bland-Altman analysis did not show a good agreement

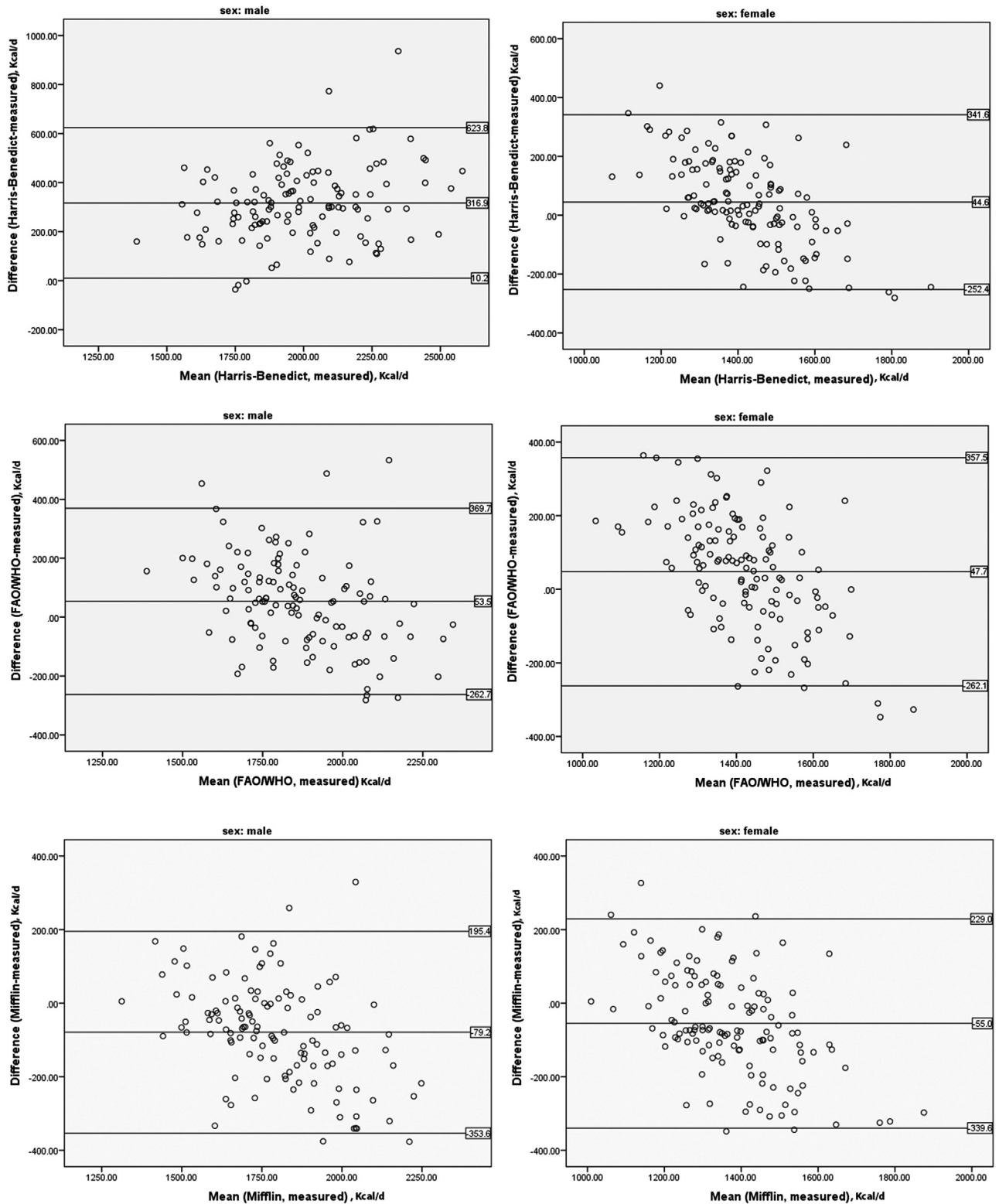


Figure 1. Bland-Altman plot for RMR calculated using Harris-Benedict, FAO/WHO/UNU and Mifflin St. Jeor equations vs. indirect calorimetry in male and females. Mean in the X axis represents the averaged RMR calculated by a predictive equation and RMR measured by indirect calorimetry.

Table 5. Proposed predictive RMR equations for Iranian populations

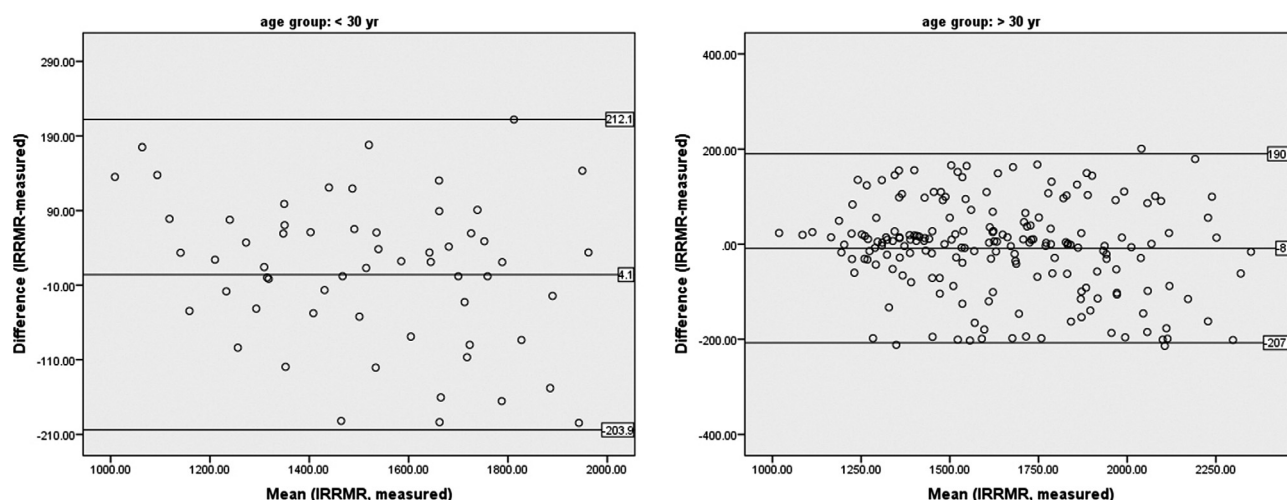
18–30 y	Adjusted r^2
<i>Males</i>	0.84
$(8.4 \times H \text{ in cm}) + (5 \times W \text{ in kg}) + (27.5 \times A \text{ in year}) - 869.7$	
<i>Females</i>	
$(8.4 \times H \text{ in cm}) + (5 \times W \text{ in kg}) + (27.5 \times A \text{ in year}) - 979.7$	
31–60 y	
<i>Males</i>	0.89
$(7.8 \times H \text{ in cm}) + (12.5 \times W \text{ in kg}) - (5.64 \times A \text{ in year}) - 349.9$	
<i>Females</i>	
$(7.8 \times H \text{ in cm}) + (12.5 \times W \text{ in kg}) - (5.64 \times A \text{ in year}) - 455.4$	

H: Height, W: weight, A: Age.

Table 6. Accuracy and precision of the calculated RMR using the new equation compared with the measured RMR

	Mean difference \pm SD (kcal/d)	Bias ¹ (%)	Accuracy ² (%)	Underestimation ³ (%)	Overestimation ⁴ (%)
18–30 y ($n_1 = 60$)					
New equation	4.1 ± 104 (–22.2, 30.4)	0.8 ± 7.0 (–0.9, 2.5)	88.3	5.0	6.7
31–60 y ($n_2 = 192$)					
New equation	-8.6 ± 99.4 (–22.6, 5.4)	-0.1 ± 5.9 (–0.9, 0.7)	88.0	6.3	5.7

Mean differences: mean of difference between predicted and measured basal metabolic rate.

¹ [(predicted RMR – measured RMR)/measured RMR] \times 100.² Percentage of subjects predicted by equation within 90% to 110% of measured RMR.³ Percentage of subjects predicted by equation < 90% of measured RMR.⁴ Percentage of subjects predicted by equation > 110% of measured RMR.**Figure 2.** Bland-Altman plot for RMR calculated using the new equation vs. indirect calorimetry in the subjects < 30 (left) and ≥ 30 years old. Mean in the X axis represents the averaged RMR (kcal/d) calculated by the new predictive equation (IRMR) and RMR measured by indirect calorimetry (kcal/d).

among these equations [37]. These findings are in oppose the reported acceptable agreement between Mifflin St. Jeor and InCal in Chinese normal weight adults [21].

The reasons of disagreement between predictive equations and measured RMR could be many including populations with different body compositions as well as the methods of data analysis [38] and dynamic nature of

metabolic rate [39]. Also, racial and ethnic differences in percent of FM and LBM across similar BMIs might, to some extent, explain these discrepancies [40]. In accord with this notion, we found an inverse association between FM and RMR. However, estimation of FM necessitates additional instrumentation which may not be accessible in a community research setting or even in many clinics. We, therefore,

propose the new equations comprising age and anthropometric measures to maximize their feasibility.

One of our noticeable findings is decrement of RMR after the age 30 y which might be due to increasing of FM with age. This is in accord with findings of a study that reviewed 351 studies in nine subgroups based on sex and age and reported a decline in RMR based on $\text{kcal.kg}^{-1}.\text{h}^{-1}$ after the age 30 y [41]. Though this may be due to decrement of LBM with age [42], it has been suggested that the decline in RMR with aging may not be explained just by changes of thyroid function or decrease of LBM [43]. Alterations in cell membrane functions due to aging may also contribute to this phenomenon [44].

We found that sex has a negligible influence on predicting of RMR. It has been suggested that sex difference in metabolic rate exists even before puberty and would continue thereafter [45]. However, a large study on 8780 obese subjects (1412 children and adolescents and 7368 adults) found that sex is a determinant of RMR just in children and adolescents but not in adults [42].

Strengths and limitations

To the best of our knowledge, this is the first report of development of predictive equations to estimate metabolic rate in Iranians. We used a rather large sample size and exclude all subjects with thyroid problems which could affect metabolic rate. Nevertheless, some limitations of this study must be acknowledged. Calorimetry by a respiration chamber or a ventilated canopy would be more preferable than a respiratory gas analyzer with a face mask. Nonetheless, the results of estimation of RMR using ventilated canopy and a face mask are comparable [46]. Though ViScan may have some limitations in estimating visceral fat in obese subjects [47], its accuracy has been reported acceptable for clinical use [48]. Finally, Iran population comprises various ethnicities which may cause some differences in metabolic rate. However, separation of different ethnic subpopulations actually was barely possible, if not impossible, due to inter-ethnic marriages.

Conclusions

We found significant under- and over-estimation of RMR using the three predictive equations in our subjects supporting the findings of other studies [7, 21, 37, 49, 50]. To overcome this problem, calculation of bias factor for predictive equations as well as development of new population-specific equations have been suggested [51]. In this study, we developed new predictive equations for two age groups, i.e. 18–29 y and 30–60 y. Using these equations, the percent

of error decreased and accuracy of the predicted RMR increased remarkably. Further studies are needed for evaluation of the efficacy of the proposed equations in both clinical and community nutritional assessments and interventions.

References

1. Carpenter A, Pencharz P, Mouzaki M. Accurate estimation of energy requirements of young patients. *J Pediatr Gastroenterol Nutr.* 2015;60(1):4–10.
2. Ndahimana D, Kim EK. Energy requirements in critically ill patients. *Clin Nutr Res.* 2018;7(2):81–90.
3. Quiroz-Olguin G, Medina-Vera I, Serralde-Zuniga AE, Gulas-Herrero A, Sanchez-Rosales AI, Guevara-Cruz M. Accurate determination of energy requirements in hospitalised patients with parenteral nutrition. *J Hum Nutr Diet.* 2018;31(6):810–7.
4. Shetty P. Energy requirements of adults. *Public Health Nutr.* 2005;8(7a7A):994–1009.
5. Slavin JL. The challenges of nutrition policymaking. *Nutr J.* 2015;14(1):15.
6. Levine JA. Measurement of energy expenditure. *Public Health Nutr.* 2005;8(7A):1123–32.
7. Pavlidou E, Petridis D, Tolia M, Tsoukalas N, Poultsidi A, Fasoulas A, et al. Estimating the agreement between the metabolic rate calculated from prediction equations and from a portable indirect calorimetry device: An effort to develop a new equation for predicting resting metabolic rate. *Nutr Metab (Lond).* 2018;15:41.
8. Leonard WR. Laboratory and field methods for measuring human energy expenditure. *Am J Hum Biol.* 2012;24(3):372–84.
9. Roza AM, Shizgal HM. The Harris Benedict equation reevaluated: Resting energy requirements and the body cell mass. *Am J Clin Nutr.* 1984;40(1):168–82.
10. Schofield W. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr.* 1985;39: 5–41.
11. World Health Organization. Energy and protein requirements. Report of a Joint FAO/WHO/UNU Expert Consultation; 1981 Oct 5–17; Rome, Italy. Geneva: WHO; 1985.
12. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr.* 1990;51(2):241–7.
13. Frankenfield DC. Bias and accuracy of resting metabolic rate equations in non-obese and obese adults. *Clin Nutr.* 2013; 32(6):976–82.
14. Amirkalali B, Hosseini S, Heshmat R, Larijani B. Comparison of Harris Benedict and Mifflin-ST Jeor equations with indirect calorimetry in evaluating resting energy expenditure. *Indian J Med Sci.* 2008;62(7):283–90.
15. Case KO, Braehler CJ, Heiss C. Resting energy expenditures in Asian women measured by indirect calorimetry are lower than expenditures calculated from prediction equations. *J Am Diet Asso.* 1997;97(11):1288–92.
16. Leung R, Woo J, Chan D, Tang N. Validation of prediction equations for basal metabolic rate in Chinese subjects. *Eur J Clin Nutr.* 2000;54(7):551–4.
17. Azcue M, Pencharz P, Zello G. Are the FAO/WHO/UNU predictive equations for resting metabolic rate accurate? *Am J Clin Nutr.* 1991;54(3):613–4.
18. Nhung B, Khan N, Hop L, Lien D, Le D, Hien V, et al. FAO/WHO/UNU equations overestimate resting metabolic rate in Vietnamese adults. *Eur J Clin Nutr.* 2005;59(10):1099–104.

19. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* (London, England). 2004;363(9403):157–63.
20. Tseng C-K, Hsu H-S, Ho C-T, Huang H-Y, Liu C-S, Lin C-C, et al. Predictive equation of resting energy expenditure in obese adult Taiwanese. *Obesity Res Clin Pract*. 2011;5(4):e313–e9.
21. Rao Z-y, Wu X-t, Liang B-m, Wang M-y, Hu W. Comparison of five equations for estimating resting energy expenditure in Chinese young, normal weight healthy adults. *Eur J Med Res*. 2012;17(1);26.
22. Nikooyeh B, Neyestani TR. Development of new predictive equations to estimate basal metabolic rates in Iranian adults: A study protocol. *Nutr Food Sci Res*. 2019;6(2):1–4.
23. Cohen J. Statistical power analysis. *Curr Directions Psychol Sci*. 1992;1(3):98–101.
24. World Health Organization. WHO Technical Report Series. 894, Obesity: Preventing and managing the global epidemic. Geneva: WHO; 2000.
25. Hutfless S, Matos P, Talor MV, Caturegli P, Rose NR. Significance of prediagnostic thyroid antibodies in women with autoimmune thyroid disease. *J Clin Endocrinol Metab*. 2011;96(9):E1466–E71.
26. Tipu HN, Ahmed D, Bashir MM, Asif N. Significance of testing anti-thyroid autoantibodies in patients with deranged thyroid profile. *J Thyroid Res*. 2018;2018:9610497.
27. Henry CJK, Lightowler HJ, Marchini J. Intra-individual variation in resting metabolic rate during the menstrual cycle. *Brit J Nutr*. 2003;89(6):811–7.
28. Nieman DC, Austin MD, Benezra L, Pearce S, McInnis T, Unick J, et al. Validation of Cosmed's FitMate in measuring oxygen consumption and estimating resting metabolic rate. *Res Sports Med*. 2006;14(2):89–96.
29. Nieman DC, Lasasso H, Austin MD, Pearce S, McInnis T, Unick J. Validation of Cosmed's FitMate in measuring exercise metabolism. *Res Sports Med*. 2007;15(1):67–75.
30. Lee JM, Bassett DR Jr, Thompson DL, Fitzhugh EC. Validation of the Cosmed Fitmate for prediction of maximal oxygen consumption. *J Strength Cond Res*. 2011;25(9):2573–9.
31. Vandarakis D, Salacinski AJ, Broeder CE. A comparison of COSMED metabolic systems for the determination of resting metabolic rate. *Res Sports Med*. 2013;21(2):187–94.
32. Brisswalter J, Tartaruga MP. Comparison of COSMED'S FitMate and K4b2 metabolic systems reliability during graded cycling exercise. *Scand J Clin Lab Invest*. 2014;74(8):722–4.
33. Xue J, Li S, Zhang Y, Hong P. Accuracy of predictive resting-metabolic-rate equations in Chinese Mainland adults. *Int J Environ Res Public Health*. 2019;16(15):2747.
34. Willis EA, Herrmann SD, Ptomey LT, Honas JJ, Bessmer CT, Donnelly JE, et al. Predicting resting energy expenditure in young adults. *Obes Res Clin Pract*. 2016;10(3):304–14.
35. Flack KD, Siders WA, Johnson L, Roemmich JN. Cross-Validation validation of resting metabolic rate prediction equations. *J Acad Nutr Diet*. 2016;116(9):1413–22.
36. Al-Domi H, Al-Shorman A. Validation of resting metabolic rate equations in obese and non-obese young healthy adults. *Clin Nutr ESPEN*. 2018;26:91–6.
37. Song T, Venkataraman K, Gluckman P, Seng CY, Meng KC, Khoo EY, et al. Validation of prediction equations for resting energy expenditure in Singaporean Chinese men. *Obes Res Clin Pract*. 2014;8(3):e201–98.
38. Sanchez-Delgado G, Alcantara JMA, Ortiz-Alvarez L, Xu H, Martinez-Tellez B, Labayen I, et al. Reliability of resting metabolic rate measurements in young adults: Impact of methods for data analysis. *Clin Nutr*. 2018;37(5):1618–24.
39. Steiner AA. The dynamic nature of resting metabolic rate. *Temperature* (Austin). 2017;4(3):206–7.
40. Heymsfield S, Peterson C, Thomas D, Heo M, Schuna J Jr. Why are there race/ethnic differences in adult body mass index–adiposity relationships? A quantitative critical review. *Obes Rev*. 2016;17(3):262–75.
41. McMurray RG, Soares J, Caspersen CJ, McCurdy T. Examining variations of resting metabolic rate of adults: A public health perspective. *Med Sci Sports Exerc*. 2014;46(7):1352.
42. Lazzer S, Bedogni G, Lafortuna CL, Marazzi N, Busti C, Galli R, et al. Relationship between basal metabolic rate, gender, age, and body composition in 8,780 white obese subjects. *Obesity* (Silver Spring). 2010;18(1):71–8.
43. Meunier N, Beattie JH, Ciarapica D, O'Connor JM, Andriollo-Sanchez M, Taras A, et al. Basal metabolic rate and thyroid hormones of late-middle-aged and older human subjects: the The ZENITH study. *Eur J Clin Nutr*. 2005;59(Suppl 2):S53–7.
44. Hulbert AJ, Else PL. Membranes and the setting of energy demand. *J Exp Biol*. 2005;208(Pt 9):1593–9.
45. Henry CJ. Mechanisms of changes in basal metabolism during ageing. *Eur J Clin Nutr*. 2000;54(Suppl 3):S77–91.
46. Isbell TR, Klesges RC, Meyers AW, Klesges LM. Measurement reliability and reactivity using repeated measurements of resting energy expenditure with a face mask, mouthpiece, and ventilated canopy. *J Parenter Enteral Nutr*. 1991;15(2):165–8.
47. Thomas EL, Collins AL, McCarthy J, Fitzpatrick J, Durighel G, Goldstone AP, et al. Estimation of abdominal fat compartments by bioelectrical impedance: The validity of the ViScan measurement system in comparison with MRI. *Eur J Clin Nutr*. 2010;64(5):525–33.
48. Gomez-Ambrosi J, Gonzalez-Crespo I, Catalan V, Rodriguez A, Moncada R, Valenti V, et al. Clinical usefulness of abdominal bioimpedance (ViScan) in the determination of visceral fat and its application in the diagnosis and management of obesity and its comorbidities. *Clin Nutr*. 2018;37(2):580–9.
49. Miller S, Milliron BJ, Woolf K. Common prediction equations overestimate measured resting metabolic rate in young Hispanic women. *Top Clin Nutr*. 2013;28(2):120–35.
50. Nhung BT, Khan NC, Hop LT, Lien DT, Le DS, Hien VT, et al. FAO/WHO/UNU equations overestimate resting metabolic rate in Vietnamese adults. *Eur J Clin Nutr*. 2005;59(10):1099–104.
51. Yao E, Buchholz AC, Edwards AM, Simpson JA. Predicted and measured resting metabolic rate in young, non-obese women. *Can J Diet Pract Res*. 2013;74(3):124–30.

History

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Conflict of interest

The authors declare that there are no conflicts of interest.

ORCID

Tirang R. Neyestani

 <https://orcid.org/0000-0002-0953-2594>

Professor Tirang R. Neyestani

Laboratory of Nutrition Research

National Nutrition and Food Technology Research Institute

Shahid Beheshti University of Medical Sciences

Tehran

Iran

t.neyestani@sbmu.ac.ir; neytr@yahoo.com