



Comparison of Indirect Calorimetry and Predictive Equations in Estimating Resting Metabolic Rate in Underweight Females

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Abstract

Background: Underweight as a public health problem in young women is associated with nutritional deficiencies, menstrual irregularity, eating disorders, reduced fertility, etc. Since resting metabolic rate (RMR) is a necessary component in the development of nutrition support therapy, therefore we determined the accuracy of commonly used predictive equations against RMR measured by indirect calorimetry among healthy young underweight females.

Methods: This cross-sectional study was conducted on 104 underweight females aged 18-30 years old with body mass index (BMI) $<18.5 \text{ kg/m}^2$ in 2013. After collecting anthropometric data, body composition was measured by bioelectric impedance analysis (BIA). RMR was measured by using indirect calorimetry (FitMate™) and was estimated by 10 commonly used predictive equations. Comparisons were conducted using paired *t*-test. The accuracy of the RMR equations was evaluated on the basis of the percentage of subjects' predicted RMR within 10% of measured RMR.

Results: The mean BMI of subjects was $17.3 \pm 1.3 \text{ kg/m}^2$. The measured RMR ranged 736-1490 kcal/day (mean $1084.7 \pm 175 \text{ kcal/day}$). Findings indicated that except Muller and Abbreviation, other equations significantly overestimated RMR, compared to measured value ($P < 0.05$). As an individual prediction accuracy, these predictive equations showed poor performance with the highest accuracy rate of 54.8% for Muller equation (22.1% under and 23.1% over-prediction) and 43.3% for Abbreviation equation (31.7% under and 25% over-prediction), the percentage bias was 1.8% and 0.63% and RMSE was 162 and 173 kcal/d, respectively.

Conclusion: Although Muller equation gave fairly acceptable prediction, more suitable new equations are needed to be developed to help better management of nutritional plans in young underweight people.

Keywords: Resting metabolic rate, Predictive equation, Indirect calorimetry, Underweight

Introduction

In spite of increasing the prevalence of overweight worldwide, underweight remains a major public health problem in the developing countries (1). Underweight might actually be more frequent than obesity (2). Underweight is associated with nutritional deficiencies, negative body image, fatigue, menstrual irregularity, eating disorders and

may also predict an increased risk of osteoporosis and reduced fertility as an adult (3-5). In addition, 81% of non-western societies prefer plump or moderately fat women (6). Therefore, in these societies underweight has been linked to body image dissatisfaction which induces a tendency to

achieve desirable body weight and shape by self-diet management or consulting the dietitian.

Measurement of resting metabolic rate (RMR), as a major component of energy expenditure, plays a critical role in the development of nutrition support therapy to estimate total energy requirements (7-9). Indirect calorimetry is the reference standard for measurement of RMR in research studies (10, 11). However due to complexity, high cost of application, lack of skilled staff, hard feasibility and time consuming, is not always possible to be used in clinical settings (12, 13). Various studies have been undertaken to develop some predictive equations for estimating RMR such as Harris-Benedict, Mifflin, WHO/FAO/UNU, Muller, Owen, Schofield and Liu formulas (14-20). These equations are based upon regressive analysis of body weight, height, sex, age, fat free mass, fat mass, body surface area as independent variables. Besides, it has been reported that ethnicity is an effective factor in RMR prediction (20). Therefore determination of the most appropriate equations that can accurately predict RMR for different ethnic groups has been suggested (20, 21). Frankenfield and colleagues identified that there are disparities in knowledge regarding the applicability of current metabolic rate prediction equation in different populations and suggested validation studies in different racial/ethnic populations (10). More recently, several authors have validated RMR predictive equations in healthy subjects with different weights and races/ethnicities. They have indicated that several commonly used equations such as Harris-Benedict, FAO/WHO/UNU, Mifflin and Owen et al formulas may not be appropriate for metabolic rate prediction in certain different weights and racial/ethnic groups (17, 21- 23). In addition, most of the commonly used predictive equations were developed from studies in normal, overweight and obese subjects and such equations were less accurate for underweight subjects (16). Therefore, they developed different formulas for different ranges of body mass index, including one for BMI <18.5 kg/m².

In order to determine the most appropriate predictive equation for the Iranian underweight fe-

males, this study aimed to compare the accuracy of the commonly used RMR predictive equations with RMR measured by indirect calorimetry.

Materials and Methods

Subjects

In this cross-sectional study conducted in 2013, 104 volunteer female students were recruited from Tabriz universities via flyers and announcements. Inclusion criteria were included: being apparently healthy had no chronic disease (e.g. cancer, type 2 diabetes, etc.), age range of 18-30 years old and had BMI <18.5 kg/m². Exclusion criteria were included: pregnancy, lactation, being athlete and current using of medications known to affect RMR (e.g. diuretics, corticosteroids, anti-psychotic and thyroid drugs). The protocol of this study was approved by the Ethics Committee of Tabriz University of Medical Sciences and. Before study written informed consent document was obtained from all participants.

Anthropometric measurements

Weight was measured to the nearest 0.1 kg using the in-built BIA as a weight scale; participants were weighed in light clothing without shoes. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer while subjects were standing without shoes with shoulders in a standard position. Body mass index (BMI) was calculated as the weight in kilograms divided by the height in square meters (kg/m²). Waist circumference was measured between the inferior margin of the last rib and the iliac crest. The greatest circumference of hip was considered as the hip circumference and the waist to hip ratio (WHR) was calculated.

Body composition

Body composition was measured by bioelectrical impedance analysis (BIA). This method is widely used because it is relatively cheap, quick, and non-invasive and requires limited operator training (24). TANITA BC-418 MA eight electrode, hand to foot system (Tanita Co., Tokyo, Japan) was used

for measurements of impedance ($\pm 1 \Omega$), estimation of body fat ($\pm 0.1\%$), FM (± 0.1 kg) and FFM (± 0.1 kg), at a frequency of 50 kHz. The subjects' age, gender, and height of each subject were entered in to the machine, and a standard 2 kg was entered as an adjustment for clothing weight in all participants. Subjects were then asked to stand barefoot on the metal foot-plates of the machine while holding the handles for ~ 30 sec.

Resting metabolic rate

RMR was determined by using of the Fitmate instrument. The Fitmate was developed by Cosmed (Roma, Italy) is a new portable metabolic analyzer designed to measure oxygen consumption and resting metabolic rate. This instrument uses a turbine flow meter that is located at the end of a disposable face mask for measuring minute volume and galvanic full cell oxygen sensor for analyzing the FeO₂. Using a fixed RQ (Respiratory Quotient) of 0.85, calculation of RMR is allowed. In a previous study, FitMate™ gave reproducible and

accurate oxygen consumption and RMR measurements when compared to the Douglas bag method and no significant differences were reported between two techniques for oxygen consumption and RMR in a wide range of BMI (25).

In this study, participants underwent to evaluation between 8:00 to 10 am in the morning after 10-12 h fasting and were advised to avoid strenuous exercise from 24h before RMR measurement and refrain from caffeinated beverages and medications. Subjects sat quietly for 20 minutes prior to RMR measurement, then they were asked to put Fitmate mask on their nose and mouth at sitting and supine position in a quiet room with temperature around 25 °C. Using the Fit Mate™ metabolic system for 15 minutes, the resting energy expenditure was measured. Calibration was done automatically for every measurement (25)

For each subject, RMR was estimated using the selected equations, as listed in Table 1 and compared to measure RMR.

Table 1: Equations used to predict resting metabolic rate (kcal/day)

| | |
|-----------------|---|
| Mifflin | $9.99 \times \text{weight} + 6.25 \times \text{height} - 4.92 \times \text{age} - 161$ |
| Muller | $(0.08961 \times \text{FFM} + 0.05662 \times \text{FM} + 0.667) \times 238.84$ |
| Owen | $795 + 7.18 \times \text{weight}$ |
| Schofield* | $14.8 \times \text{weight} + 487$ |
| Schofield** | $13.6 \times \text{weight} + 283 \times \text{height}^2 + 98$ |
| Harris-Benedict | $665 + 9.56 \times \text{weight} + 1.84 \times \text{height} - 4.67 \times \text{age}$ |
| Abbreviation | $0.95 \times 24 \times \text{weight}$ |
| WHO* | $8.7 \times \text{weight} + 829$ |
| WHO** | $8.7 \times \text{weight} + (25 \times \text{height}^2) + 865$ |
| Liu | $(13.88 \times \text{weight}) + (4.16 \times \text{height}) - (3.43 \times \text{age}) + 54.34$ |

* Weight based formula.

**Weight and height based formula

Statistical analysis

All data were reported as means \pm standard deviation. Paired t-test was used to evaluate the difference between the measured RMR values and those estimated by predictive equations. Accuracy of predictive formulas at the individual level was defined as percentage of the subjects who's predicted RMR was within $\pm 10\%$ of measured RMR

(12, 26). A prediction $< 90\%$ of measured RMR was considered as under-prediction, and a prediction $> 110\%$ of measured RMR was considered as over-prediction. Group level accuracy was considered as the mean percentage difference (bias) between measured and predicted RMR. The root mean squared prediction error (RMSE) was used to indicate how well the model predicted in our

data set (12). Bland-Altman analysis was used to determine the extent of error for predictive equations compared to measure RMR (27, 28). Data were analyzed using SPSS statistical package, version 16 (SPSS Inc., Chicago, IL). P -value <0.05 was considered as statistically significant.

Results

Physical characteristics of 104 underweight female students have been shown in Table 2. All subjects were between 18 and 30 years old. The mean body mass index (BMI) was 17.3 ± 1.3 kg/m² (13.4-19.2). Comparison of measured RMR with predicted RMR are presented in Table 3, the mean measured RMR derived from the FitMate™ was 1084.7 ± 175 kcal/day (736-1490). There were no significant differences between measured RMR and RMR calculated by Muller and Abbreviation equations.

Table 2: Baseline Characteristics of underweight female subjects (n=104)

| Variable | Mean \pm SD |
|-----------------------------|------------------|
| Age(yr) | 21.9 \pm 2.2 |
| Weight(kg) | 46.3 \pm 4.6 |
| Height(cm) | 163.6 \pm 4.8 |
| BMI(kg/m ²)* | 17.3 \pm 1.3 |
| Wrist circumference (cm) | 14.6 \pm 0.6 |
| Waist circumference (cm) | 66.3 \pm 7.5 |
| Hip circumference (cm) | 89.7 \pm 5.2 |
| WHR [†] | 0.7 \pm 0.1 |
| FFM [§] (kg) | 38.1 \pm 3.8 |
| FM [£] (kg) | 8.0 \pm 2.9 |
| FM (%) | 16.8 \pm 4.9 |
| RMR [†] (kcal/day) | 1084.7 \pm 175 |

* BMI, body mass index

[†] WHR, Waist to hip ratio

[§] FFM, fat free mass

[£] FM, fat mass

[†] RMR, Resting metabolic rate

Table 3: Comparison of measured RMR with predicted RMR in underweight females

| Variable | Meas \pm SD (kcal/day) | Mean difference \pm SD (kcal/day) | 95% Confidence Interval | P value [¶] |
|-----------------|-----------------------------|--|-------------------------|----------------------|
| Measured RMR | 1084.7 \pm 175.0 | - | - | - |
| Predicted RMR | | | | |
| Mifflin | 1216.5 \pm 70.9 | 131.8 \pm 165.9 | 99.6 to 164.1 | <0.001 |
| Muller | 1082.0 \pm 97.3 | -2.8 \pm 163.1 | -34.5 to 29.0 | .863 |
| Owen | 1126.9 \pm 33.2 | 42.2 \pm 166.7 | 9.8 to 74.6 | .011 |
| Schofield* | 1172.3 \pm 68.5 | 87.5 \pm 164.9 | 55.5 to 119.6 | <0.001 |
| Schofield** | 1190.7 \pm 73.0 | 105.9 \pm 165.3 | 73.8 to 138.1 | <0.001 |
| Abbreviation | 1055.7 \pm 105.6 | -29.0 \pm 171.0 | -62.3 to 4.2 | .087 |
| Harris-Benedict | 1306.6 \pm 51.3 | 221.9 \pm 164.9 | 189.8 to 254.0 | <0.001 |
| WHO* | 1231.9 \pm 40.3 | 147.1 \pm 165.8 | 114.9 to 179.4 | <0.001 |
| WHO** | 1308.7 \pm 41.1 | 224.0 \pm 165.7 | 191.7 to 256.2 | <0.001 |
| liu | 1302.6 \pm 79.4 | 217.9 \pm 166.0 | 185.6 to 250.2 | <0.001 |

* Weight based formula/ ** Weight and height based formula

[¶] P values are obtained by paired t-test analysis.

Bland-Altman plots displaying bias and agreement of 3 selected predicted equations are presented in Fig. 1. The lowest mean difference between measured RMR and estimated RMR was found in the Muller prediction equation with mean difference

of -2.8 kcal/day and the 95% limits of agreement from 316.9 to -322.5 kcal/day.

Compared to measured RMR values, the Abbreviation and Muller equations slightly under-predicted RMR, while other equations significantly

over-predicted it. Maximum over-prediction was provided by Harris-Benedict equation (76.9%). Table 4 shows the accuracy rates, percentage bias and the RMSE values (in kcal/d) of different predicted equations in studied subjects. As indicated in Table 4, the range of accuracy varied between equations from 23.1% to 54.8%. The percentage bias for equations varied from -0.63% to 24.6%, and the RMSE varied from 162 to 278 kcal/d. Among ten equations, the highest accuracy rate was produced by the Muller equation, with 54.8%

accurate prediction (22.1% under-prediction and 23.1% over prediction) and a small percentage bias of 1.8% and RMSE of 162 kcal/d. The lowest percentage bias was found in the abbreviation equation (-0.63); however the accuracy rate was 43.3% and RMSE was 173 kcal/d. The Owen equation provided 47.1% accurate prediction (with 16.3% under-prediction and 36.5% over-prediction), with a bias of 6.8% and RMSE of 171 kcal/d.

Table 4: The accuracy rates of RMR predicted by different equations in underweight female subjects (n=104)

| RMR predictive equations | Accurate predictions [¶] (%) | Under-predictions [§] (%) | Over-predictions [£] (%) | Bias [†] (%) | Maximum negative error [‡] (%) | Maximum positive error [§] (%) | RMSE (kcal/d) |
|--------------------------|---------------------------------------|------------------------------------|-----------------------------------|-----------------------|---|---|---------------|
| Mifflin | 40.1 | 7.7 | 51.9 | 15.4 | -13.6 | 60.01 | 211 |
| Muller | 54.8 | 22.1 | 23.1 | 1.8 | -36 | 38 | 162 |
| Owen | 47.1 | 16.3 | 36.5 | 6.8 | -22 | 47 | 171 |
| Schofield* | 39.4 | 12.5 | 48.1 | 11 | -16 | 53 | 186 |
| Schofield** | 37.5 | 11.6 | 50.9 | 12.8 | -14 | 56 | 195 |
| Harris-Benedict | 23.1 | 0 | 76.9 | 24.3 | -8 | 68 | 276 |
| Abbreviation | 43.3 | 31.7 | 25 | -0.63 | -27 | 45 | 173 |
| WHO* | 35.6 | 6.7 | 57.7 | 17.02 | -14 | 60 | 221 |
| WHO** | 25 | 0 | 75 | 24.6 | -9 | 70 | 278 |
| Liu | 26.9 | 0 | 73.1 | 23.8 | -6 | 72 | 273 |

*Weight based formula

**Weight and height based formula

[¶] The percentage of subjects predicted by this predictive equation within $\pm 10\%$ of the measured value.

[§] The percentage of subjects predicted by this predictive equation within $<10\%$ of the measured value.

[£] The percentage of subjects predicted by this predictive equation within $>10\%$ of the measured value.

[†] Mean percentage error between predictive equation and measured value.

[‡] The largest under-prediction that was found with this predictive equation as a percentage of the measured value.

[§] The largest over-prediction that was found with this predictive equation as a percentage of the measured value.

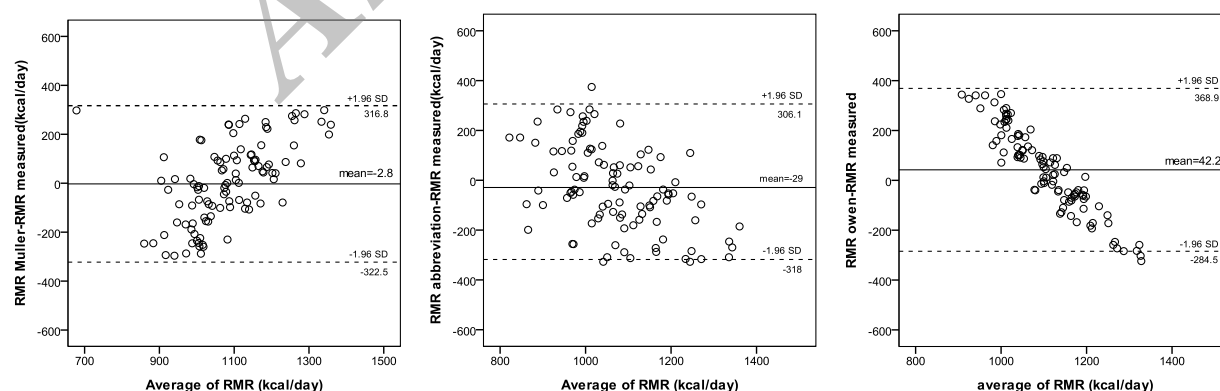


Fig. 1: Bland-Altman plots for 3 selected BMR predictive equations. Solid lines indicate the mean difference between predicted and measured RMR values. Dashed lines indicate the limit of agreement

Discussion

The commonly used predictive equations were not appropriate for underweight subjects and created a new predictive equation for this specific population (17). In this study, we evaluated accuracy of Muller and different previously developed RMR predictive equations against measured RMR in 104 Iranian healthy underweight female students. We found that among 10 RMR predictive equations that were used in this study, Muller et al. equation gave a fairly acceptable RMR prediction, while most of the commonly used RMR predictive equations did not accurately predict RMR at both group and individual levels. Our data also showed that all of the equations except Muller and Abbreviation equations significantly overestimated RMR in underweight young females, with mean differences ranging from 42.2 to 224kcal/day. Overestimations may be due to: first, it has been reported that energy requirements of people from developing countries are low and using standard equations might lead to greater bias and overestimation of energy requirements (29). Second, in underweight people adaptation to under-eating and underweight may result in hypometabolic status (30). Third, underweight subjects such as anorexia nervosa patients who are considered to be physically healthy, seem to be characterized by elevated RQ larger than 0.8. Since FitMate calculates RMR from oxygen consumption using a fixed RQ of 0.85, if RQ is between 0.85 and 1, underestimation is possible (31-33).

Since WHO equations have been derived from researches in subjects with a wide range of BMI, they are often applied for estimating RMR in underweight subjects (10). However in our study there were significant differences in RMR predicted by WHO equations and measured RMR with accuracy rates of 35.6% for weight-base and 25% for weight-based and height-base equations. Since WHO equations have been developed from research in Europeans and considering the impact of ethnicity on RMR, the WHO equations may not be appropriate for Asians, especially for Iranian underweight females. In addition, WHO

weight-base predictive equation overestimates RMR at low body mass index (10).

It was reputed that Owen equation can be used for all weight group classifications (18). In this study, in spite of 47.1% accuracy rate, Owen equation had statistically significant difference with those measured by indirect calorimetry in group means. Although, Owen equation was developed from a sample of 44 women aged 18 to 65 years old, only one of them was underweight. Therefore, it appears that the Owen equation is not suitable for prediction of RMR in underweight individuals. These discrepancies could be due in part to the differences in the body composition and physical activity level between subjects in the previous and current studies (34). It has been reported that the fat free mass play an important role in RMR value (7, 9) and the physical activity training also can influence RMR by increasing lean tissue mass and influencing residual metabolism rate (35). Furthermore, most of the equations have been developed from researches in western Caucasian people; it is likely that a greater proportion of body weight in western women is made up of muscle and viscera with higher energy expenditure, as compared to their Asian counterparts (34, 36). Harris-Benedict and WHO equations overestimated the RMR in Asian women (22). They indicated that measured RMR was significantly lower than predictive RMR using Harris-Benedict and WHO equations by 8.5% ($P<.001$) and 5.4% ($P<.01$), respectively (22). The differences between measured and predicted RMR values may be partially explained by methodological problems. Since there are no reference databases for methodological approaches, the accuracy of studies can be affected by the different criteria of measurements such as measurement condition, time and etc. (8).

Limitations of this study include: first, the research was restricted to women with narrow age range (18-30 years old). Secondly, the absence of control group which would have helped to clarify potential BMI differences. Thirdly, we measured each subject only once thereby we could not estimate the intra-individual variation in RMR.

Conclusion

Muller equation gave fairly acceptable prediction in underweight female population. However, for better management of nutritional plans in this specific range of BMI, further studies are needed to develop and validate more suitable new equations.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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