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Original Article

The Lack of Validity of Predictive Equations for Calculating Resting Energy Expenditure in Asian Indian Patients with Type 1 and Type 2 Diabetes Mellitus

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Abstract

Introduction: Predictive equations are used routinely to calculate resting energy expenditure and administer appropriate nutrition to patients. Validity of routinely used equations for calculating resting energy expenditure was not verified in Asian Indian population. In this study we aim to compare the predictive equations with indirectly calorimetry to test their validity in Indian population.

Methods: The study included 45 male Indian subjects divided into following groups: 16 patients with Type 1 diabetes mellitus, 13 patients with Type 2 Diabetes mellitus and 16 normoglycemic subjects. All underwent anthropometric measurements, body composition measurement by DEXA scan and indirect calorimetry. REE calculated from routinely used equations and a body composition based equation was compared with REE measured by indirect calorimetry by means of Bland-Altman plot analysis. Total and mean error was also calculated for the predictive equations. Statistical analysis was done in R programming language version 3.2.4.

Results: Total error of different predictive equations when compared with indirect calorimetry ranged from 375 kcal/day to 726 kcal/day across the studied groups. Bland-Altman plot analysis showed negative proportional bias i.e. equations overestimate at lower values and underestimate at higher values of measured REE.

Conclusion: Routinely used predictive equations and recently introduced body composition based equation were all poor in accuracy as reflected from their high total error for estimating resting energy expenditure in Indian population when compared with indirect calorimetry. We conclude that a predictive equation for estimating resting energy expenditure must be established for use in Indian population.

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Introduction

Malnutrition is a major threat to global public health. While 795 million people are undernourished, around two billion people are either overweight or obese (1, 2). Countries with a lower socioeconomic status have people struggling with under-nutrition and developed countries face an obesity epidemic. As a developing country, India faces both forms of malnutrition (3,4). Assessments of the adequacy of energy intake and dietary recommendations that aim to prevent malnutrition rely on accurately predicting the energy expenditure of the subject. Several methods are in practice to determine the different components of energy expenditure and they include indirect calorimetry, bio-impedance and predictive equations (5). Indirect calorimetry, though considered accurate, is not routinely used due to its practical limitations, technology involved and expertise required for operating the device (5, 6). Alternatively, multiple predictive equations are available to estimate the total energy expenditure, basal metabolic rate and resting energy expenditure (REE) (7). More recently, a predictive equation has utilized body composition measured by Dual Energy X-ray Absorptiometry (DEXA)(8).

Ethnicity is known to affect the accuracy of predictive equations, as are the characteristics of the subjects, which include obesity and disease conditions such as diabetes (9–11). Though predictive equations are modelled based on mostly Caucasian populations, we continue to use those equations routinely in Indian subjects. In our previous experiences we have encountered discrepancies between predicted and measured REE in different groups. In a study conducted among weightlifters, we found that existing predictive equations were inaccurate when compared to indirect calorimetry and proposed a predictive equation for weightlifters which was more accurate than other predictive equations (12). In another study on patients with fibrocalculous pancreatic diabetes (FCPD), we reported that predictive equations to calculate REE were inaccurate (13). We have also studied the patterns of REE in relation to birth weight, in low birth weight subjects in the Indian population (14). These experiences have prompted us to verify the validity of the available predictive equations in the Asian Indian population. In this study we aim to verify the accuracy of predictive equations when compared to indirect calorimetry in Asian Indian subjects with and without different types of Diabetes mellitus. Apart from normal subjects, predictive equations are routinely used in clinical practice for devising diet plan for subjects with diabetes mellitus. So it is imperative to assess the accuracy of predictive equations of resting energy expenditure in both normal and diabetic subjects.

Methods

Statement of Human Rights:

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for being included in the study.

The study protocol was approved by the Institutional Review Board of Christian Medical College, Vellore, India (Research Committee Minute No: 7722, 2012). The study included 16 patients diagnosed with Type 1 diabetes mellitus (Type 1 DM) and 13 patients with Type 2 Diabetes mellitus (Type 2 DM), as defined by the American Diabetes Association criteria, and 16 normoglycemic subjects and included male patients exclusively. The study was conducted in the Department of Endocrinology, Diabetes & Metabolism, Christian Medical College, Vellore, India. Informed consent was obtained from all subjects. They underwent anthropometric measurements and body composition analysis using a DEXA scanner with a Hologic Delphi W (S/N 70471).

Indirect calorimetry was performed on all patients using an indirect calorimeter (Jaegar Oxycon pro, Germany). Patients were kept fasting overnight and were awake during the procedure. The indirect calorimeter measured Oxygen intake (VO2) and Carbon dioxide output (VCO2) and calculated resting energy expenditure using the abbreviated Weir equation:

$$REE = 3.9\ (VO2) + 1.1\ (VCO2) \times 1.44 \quad (6)$$

Resting energy expenditure was defined as the energy spent by the body in 24 hours under resting (awake) conditions (5).

Table I depicts the predictive equations that were used to calculate REE in this study. The list includes one of the equations that were published more recently that utilizes body composition results from DEXA. This is a mechanistic model which is based on the principle that different tissues of the body spend energy at different rates (15). The mass of each tissue was calculated utilizing DEXA. The calculated tissue components are bone mass (BM), adipose tissue mass (AT), skeletal muscle mass (SM) and residual mass (RM). Bone mass andadipose tissue mass are calculated from DEXA as described by previous authors (16).

Skeletal muscle mass was calculated using a predictive formula published by Kim et. al. (17). The residual mass was defined as the difference between total body weight and the sum of the four other components. Once the mass of individual components was calculated, whole body REE is calculated by multiplying the mass of each component with its energy expenditure as expressed as kcal/kg/day. Wang et.al. used previously published data to arrive at the energy expenditure of each tissue component and it is used by subsequent researchers (8, 15).

Statistical analysis was done in R programming language version 3.2.4.

Results

Table II shows the age and anthropometric details of subjects in each group. The study included 45 male subjects divided into Normoglycemic, Type 1 DM and Type 2DM. Participants were generally younger and of normal weight except for Type 2DM subjects. Type 2 DM subjects had an average BMI of 25.5 kg/ m^2. Insulin resistance was measured by HOMA-IR (18). Type 2 DM subjects had higher HOMA-IR values than other groups.

Table III shows body composition parameters in each group as measured by DEXA.

Table IV shows the mean and total error of predicted REE by various methods with measured REE. REE value from indirect calorimetry is considered as measured REE.

Mean error and the standard deviation of error have been calculated as the average and the standard deviation of the difference between predicted and measured REE in each group for different methods.

The total error is the root mean squared error (RMSE) calculated as:

Square root of (Σ(predicted REE – measured REE)^2/ N), where N is the number of samples.

The total error or RMSE is an estimate of the accuracy

TABLE I: Equations to predict REE.

Equation	*Formulaafor REE (kcal/day)*
Harris-Benedict (21)	66.437 + (13.752* weight) + (5.03* height) – (6.755* age)
Schofield (22)	18-29 years: 15.057* (weight) + 692.2 30-59 years: 11.472* (weight) + 873.1
WHO/FAO/UNU (23)	18-30 years: 15.4* weight – 27* (height/100) + 717 31-60 years: 11.3* weight + 16* (height/100) + 901
Mifflin-St Jeor (24)	9.99* weight + 6.25* height – 4.92* age + 5
REE from DEXAb (16)	2.3*BM + 4.5*AT + 13*SM + 54*RM

a-Weight in kg, height in cm, age in years
b-BM is bone mass, AT is adipose tissue mass, SM is skeletal muscle mass, RM is residual mass. All are calculated from DEXA according to a previously published method.

TABLE II: Basic characteristics of the study participants.

Group	*Number of subjects*	*Age in years (Mean±SD)*	*Height in cm (Mean±SD)*	*Weight in Kg (Mean±SD)*	*BMI in Kg/m^2 (Mean±SD)*	*Duration of diabetes in years (Mean±SD)*	*HOMA-IR (Mean±SD)*
Normoglycemic	16	34.1±8	169.4±7	63.7±11	22.2±4		1.2±0.8
Type 1 DM	16	28.6±6	166.3±7	56.8±5	20.6±2	9.9±6	3.0±1.9
Type 2 DM	13	36.9±6	168.2±7	71.9±5	25.5±2	2.9±5	3.6±2.5

TABLE III: Body composition of the study participants from DEXA.

Group	*Weight Kg (Mean±SD)*	*Bone mineral content in g (Mean±SD)*	*Total fat in g (Mean±SD)*
Normoglycemic	63.7±11	2414.07±292.54	11580.00±5946.03
Type 1 DM	56.8±5	2803.72±529.29	8925.3±2685.63
Type 2 DM	71.9±5	2663.32±799.55	17896.98±3459.25

TABLE IV: Total and mean error of predictive equations.

Group	*Method*	*REE (Mean±SD) kcal/day*	*Mean error (Mean±SD) kcal/day*	*Total error kcal/day*
Normoglycemic	Indirect calorimetry	1701±398		
	REE from DEXA	1273±247	–428±361	448
	Harris Benedict	1564±174	–137±361	375
	Schofield	1624±139	–77±388	384
	WHO/FAO/UNU	1648±139	–53±397	388
	Mifflin-St Jeor	1532±139	201±335	382
Type 1 DM	Indirect calorimetry	1983±383		
	REE from DEXA	1344±132	–639±357	726
	Harris Benedict	1492±86	–491±377	612
	Schofield	1536±61	–447±375	576
	WHO/FAO/UNU	1555±68	–428±376	562
	Mifflin-St Jeor	1472±74	511±375	627
Type 2 DM	Indirect calorimetry	1919±551		
	REE from DEXA	1539±214	–380±511	621
	Harris Benedict	1652±101	–267±541	584
	Schofield	1705±71	–214±529	551
	WHO/FAO/UNU	1745±66	–174±530	538
	Mifflin-St Jeor	1593±87	326±546	618

of the methods. All the methods to predict REE had poor accuracy as evident from the table. Total error worsens further in subjects with diabetes mellitus. However among the predictive equations, the Harris Benedict equation had the least error in normoglycemic subjects. In case of other groups, the WHO/FAO/UNU equation had the least error.

Table V shows results from Bland Altman analysis. There is no statistically significant fixed bias in any of the methods studied in all groups. The confidence intervals for fixed bias were too wide, indicating the inaccuracy of the methods studied. However there is a statistically significant negative proportional bias in almost all methods in every group studied. A negative proportional bias means predicted equations overestimate REE at lower values and underestimate at higher values of measured REE. Most of the methods had a significant negative proportional bias.

Discussion

Predictive equations for REE have been widely used in Indians in both health and disease without ever

TABLE V: Bland-Altman plot analysis.

Group	*Method*	*Fixed bias CI 95%*		*Proportional bias*	
		Lower limit	*Upper limit*	*r*	*P value*
Normo-glycemic	DEXA	–1010	561	0.69	0.030
	Harris Benedict	–845	571	–0.71	0.002
	Schofield	–838	684	–0.79	<0.001
	WHO/FAO/UNO	–831	726	–0.79	<0.001
	Mifflin-St-Jeor	–863	526	0.71	0.002
Type 1 DM	DEXA	–1338	60	–0.81	<0.001
	Harris Benedict	–1231	249	–0.91	<0.001
	Schofield	–1182	288	–0.95	<0.001
	WHO/FAO/UNO	–1166	310	–0.08	0.774
	Mifflin-St-Jeor	–1246	224	0.93	<0.001
Type 2 DM	DEXA	–1381	621	–0.76	0.003
	Harris Benedict	–1327	793	–0.94	<0.001
	Schofield	–1251	823	–0.97	<0.001
	WHO/FAO/UNO	–1212	863	–0.29	0.324
	Mifflin-St-Jeor	–1397	745	0.95	<0.001

verifying the accuracy of these equations. In this study we analysed the accuracy of various predictive equation of REE in use in 45 male subjects of age 19 to 49 years divided into three groups: Normoglycemic, Type 1 DM and Type 2 DM.

The results of the study revealed that predicted equations are far from accurate, even in normoglycemic subjects; predicted equations including DEXA were inaccurate by around 22% to 26% of measured REE on average. The total error for the normoglycemic subjects were around 400 kcal for all equations. If the predictive equations are inaccurate by 400 kcal on average, they may not serve any practical purpose for their intended use.

Predictive equations performed even more poorly in subjects with diabetes in all studied types as the total error was around 30% of measured REE for all predictive equations. This might be due to increased insulin resistance among subjects with diabetes mellitus since insulin resistance is known to alter resting energy expenditure (19). Moreover predictive equations are known to perform poorly among obese subjects and Type 2 DM subjects had higher BMI than other groups (10).

These equations were not specific to the Indian population. Ethnicity is known to influence REE and the accuracy of predictive equations. Indian subjects are known to have a lower REE when compared to other populations (20). Also, differences in body composition in Indians might affect the accuracy of predictive equations. Along with ethnicity, underlying diseases state, especially different forms of Diabetes mellitus could affect the accuracy of these equations.

The Bland-Altman plot analysis shows that there was no fixed bias for any of the equations in all groups. However, there was significant proportional bias, particularly a negative bias in most equations among all groups. This indicates that these equations overestimate at lower values and underestimate at higher values of measured REE.

Interestingly the total error was highest for DEXA-derived REE in all groups.

REE has been predicted from body composition measurements done by DEXA (16). As each organ expends energy at particular rate, calculating the mass of various tissue compartments such as the brain, muscle, fat, skeletal muscle and bone mass and multiplying each mass with a term corresponding to the energy expenditure by the organ can predict resting energy expenditure (15). The prediction of REE by DEXA was found to be more accurate than other simpler predictive equations (16). However the rate at which each organ expends energy used in the formula of DEXA-predicted REE and the equations to calculate the mass of tissue components from DEXA are not specific for Indian subjects. This might lead to inaccuracy of the DEXA-predicted REE in Indian subjects.

Interestingly, the ‘mechanistic’ model of predicting REE from DEXA is inaccurate in Indian subjects. This might be due to several reasons. Previously published methods for calculating mass of tissue components from DEXA may not be appropriate for Indian subjects. Also we cannot exclude the possibility of energy expenditure of individual tissue components in Indian subjects being different from the one used for calculating the DEXA based equation.

Though our sample size is small and did not include female subjects, our results have shown that

predictive equations including DEXA based measurements were not appropriate for use in the Indian population due to a high degree of inaccuracy. Therefore, we conclude that there is a need to establish a predictive equation appropriate for use in the Indian population. To use DEXA for measuring REE, the methods for calculating mass of tissue components using DEXA must be verified with the whole body MRI measurement of tissue components and energy expenditure of individual tissue components must be established.

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