Original Article

Accuracy of basal metabolic rate estimated by predictive equations in Japanese with type 2 diabetes

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Background and Objectives: Estimation of energy demand using basal metabolic rate (BMR) is a rational approach for optimizing glycemic control and weight management in patients with type 2 diabetes mellitus (T2DM). Here, we assessed the accuracy of predictive equations in estimating BMR in Japanese patients with T2DM. **Methods and Study Design:** BMR was measured indirectly (BMR_m) with a portable gas analyzer in the fasting state in 69 Japanese patients with T2DM. BMR was estimated using the Harris-Benedict equation (BMR_{hb}) and Ganpule equation (BMR_g). An original predictive equation (BMR_{dm}) was formulated by stepwise multiple regression analysis using subject age, lean soft tissue mass, fat mass and bone mineral content. Mean differences and 95% limits of agreement between measured and three estimated BMRs were evaluated by Bland-Altman plots. In addition, subjects were divided into three BMI groups (normal, BMI <25; overweight, BMI ≥25; obese, BMI ≥30), and the influence of BMI on the error size between measured and estimated BMRs was assessed. **Results:** Between BMR_m and the three estimated BMRs (BMR_{hb}, BMR_g, and BMR_{dm}), there were small systematic errors with large random errors (mean difference±2SD ; −32±365 kcal, 26±405 kcal, and −1.6±349 kcal, respectively) and significant proportional errors (r=0.42, 0.44, and 0.30, respectively). BMI subgroup analysis revealed that the obese group showed larger random errors and significant proportional errors compared to the overweight and normal weight groups. **Conclusion:** Predictive equations provide unacceptably inaccurate estimates of BMR in Japanese patients with T2DM, particularly in obese individuals.

Key Words: basal metabolic rate (BMR), predictive equation, diabetes, portable gas analyzer, Japanese

INTRODUCTION

Reducing energy intake is a recommended way to promote weight loss and improve glycemic control in patients with type 2 diabetes mellitus (T2DM).[1] Basal metabolic rate (BMR) accounts for approximately 60–75% of total daily energy expenditure,[2] making it the most important parameter for determining appropriate energy intake. Since it is difficult to directly measure BMR, indirect calorimetry or predictive equations have been used. Indirect calorimetry determines energy expenditure by measuring oxygen uptake (VO_2) and carbon dioxide output (VCO_2).[3] Recently, portable gas analyzers have been used to rapidly measure respiratory gases and calculate energy expenditure at the bedside. The most commonly used predictive equation in clinical practice in Japan is the Harris-Benedict equation, which takes into account age, height and body mass (BM). The Harris-Benedict equation was formulated in the USA approximately 100 years ago, at which time the majority of subjects were young, healthy and of normal weight.[4,5] However, recent studies from various countries, including Asian countries, have reported that the Harris-Benedict equation tends to overestimate BMR compared with indirect calorimetry in healthy, normal-weight and obese subjects.[6-8] In 2007, the National Institute of Health and Nutrition in Tokyo developed a new equation, the Ganpule equation, based on data from healthy Japanese.[9] The Ganpule equation is reported to produce smaller differences between measured and estimated BMR in healthy Japanese subjects compared to other popular equations, such as Dietary Reference Intakes for Japanese (Japan-DRI) 2010, the Harris-Benedict equation, and the Schofield and Food and Agriculture Organization (FAO)/World Health Organization (WHO)/United Nations University (UNU) equations.[10] Although predictive equations have been widely used to estimate BMR in healthy individuals, few studies have applied them to Japanese patients with T2DM.[11,12]

The aims of the present study were to assess the accuracy of BMR predicted by the Harris-Benedict and Ganpule equations by comparing with BMR measured indirectly with a portable gas analyzer in Japanese patients

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with T2DM, and to reveal factors responsible for the error size between these predicted and measured BMRs.

MATERIALS AND METHODS

Subjects

Subjects were 37 males (mean±standard deviation (SD); 57±12 years) and 32 females (64±11 years) with T2DM hospitalized at the Diabetes Center of Kitasato Institute Hospital for glycemic control from April 2008 to March 2010. Both insulin-treated (5 males and 16 females) and non-insulin-treated patients (32 males and 16 females) were included. Patients with health problems such as dementia in whom BMR could not be correctly measured were excluded. All protocols were approved by the Research Ethics Committee of Kitasato Institute Hospital in Tokyo, Japan (#08013). Written informed consent was obtained from all subjects prior to participation. From the first day of admission, subjects were given an energy-restricted diet calculated according to the Treatment Guide for Diabetes of the Japan Diabetes Society (JDS).[13] Ideal body weight (IBW) was calculated as height (m) × height (m) × 22 (kg/m^2), and daily energy intake (kcal/day) was determined as 25 kcal/kg IBW.[13]

Anthropometry

Height was measured with an automatic scale. Fat mass (FM), lean soft tissue mass (LSTM), bone mineral density (BMD), and bone mineral content (BMC) were estimated by dual-energy X-ray absorptiometry (Lunar iDXA; GE Healthcare, Madison, WI, USA). BM was calculated as FM + LSTM + BMC. Percent body fat (FAT%) was calculated as FM/BM × 100. Body mass index (BMI) was calculated as BM/square of height.

Blood samples

On the second day of admission, venous blood samples were collected for measurement of fasting plasma glucose (FPG), HbA1c, and immuno-reactive insulin (IRI). According to the JDS guideline, HbA1c (%) was estimated as the NGSP equivalent value (%), calculated by the formula HbA1c (%) = HbA1c (JDS) (%) + 0.4%.[14] In non-insulin-treated patients, the homeostasis model assessment ratio (HOMA-R) was calculated by the formula HOMA-R = IRI (μU/mL) × FPG (mg/dL) / 405.

Determination of BMR

On the third day of admission, BMR was measured (BMR_m) indirectly in the fasting state with a Fitmate-Pro portable gas analyzer (Cosmed, Italy). Fitmate-Pro uses a dynamic mixing chamber to measure VO_2, minute ventilation volume and respiratory rate while wearing a facemask. The gas analyzer was calibrated using atmospheric air prior to measurement. The day before measurement, subjects were instructed to avoid eating after dinner, which was given at 6 pm. On the day of measurements, they were instructed to maintain a supine position in bed after waking, immediately wear the facemask, and measure BMR for 10–15 min.

Fitmate-Pro calculates BMR according to the Weir equation: BMR (kcal/day) = (3.9 × VO_2 [mL/min] + 1.1 × VCO_2 [mL/min]) × 1.44.[15] Since Fitmate-Pro is unable to measure VCO_2, it calculates BMR by fixing the respiratory quotient (RQ) at 0.85, set as the default by the manufacturer. Therefore, BMR was calculated as: BMR (kcal/day) = 4.84 × VO2 (mL/min) × 1.44.

Estimated BMR was calculated using the Harris-Benedict (BMR_{hb}) and the Ganpule (BMR_g) equations (Table 1).

Statistical analysis

The unpaired t-test was used to analyze differences between males and females. One-way repeated-measures analysis of variance (ANOVA) and Bonferroni post hoc test were used to assess differences between BMR_m and the two estimated BMRs (BMR_{hb} and BMR_g) in each sex. Pearson's correlation analysis and partial correlation analysis were conducted to evaluate the correlation between the two variables.

Three models were evaluated by stepwise multiple regression analysis to formulate an original predictive equation for BMR. Explanatory variables were age, gender, height, and BM (Model 1), BMI (Model 2), or FM, LSTM, and BMC (Model 3). The model showing the best predictive power was adopted as our original predictive equation for BMR (BMR_{dm}).

Bland-Altman plots were used to analyze the agreement between BMR_m and the three estimated BMRs (BMR_{hb}, BMR_g, and BMR_{dm}).[16] Systematic error and random error were evaluated by calculating the mean difference and 95% limits of agreement (LOA) for each comparison (±2SD of the difference). The proportional error was evaluated as the degree of correlation between differences and means when the slope of the regression line was significant.

Subjects were divided into three BMI groups (normal, BMI <25; overweight, BMI ≥25; obese, BMI ≥30) according to the WHO guidelines,[17] and the effect of BMI on the error size between measured and estimated BMRs was analyzed using Bland-Altman plots. Intergroup comparison was analyzed by one-way ANOVA and the Bonferroni post hoc test. We also calculated BMR_m using different fasting RQs according to the level of BMI, i.e.,

Table 1. Predictive equations for basal metabolic rate in males and females

Predictive equation (kcal/day)	Males	Females
Harris-Benedict	66.5 + 13.7 × [BM in kg] + 5.0 × [Height in cm] − 6.8 × [Age in years]	655 + 9.6 × [BM in kg] + 1.9 × [Height in cm] − 4.7 × [Age in years]
Ganpule	(0.0481 × [BM in kg] + 0.0234 × [Height in cm] − 0.0138 × [Age in years] − 0.424) × 1,000 / 4.186	(0.0481 × [BM in kg] + 0.0234 × [Height in cm] − 0.0138 × [Age in years] − 0.971) × 1,000 / 4.19

BM: body mass.

RQ=0.85 for the normal and overweight groups and RQ=0.80 for the obese group,[18] and assessed the variation in error size.

Data were reported as mean±SD. Statistical analyses were performed using IBM SPSS Statistics for Mac OS (Ver.22). A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Table 2 summarizes the characteristics of the subjects in our study. Participants tended to be overweight or obese and showed poor glycemic control. Females were older, had a higher FAT% and a significantly lower BMC than males. BMR_m, BMR_{hb}, and BMR_g were significantly higher for males than females (Table 3). Repeated-measures ANOVA showed that BMR_{hb} was significantly higher than BMR_g for all subjects, and male and female categories.

Bland-Altman plots revealed small systematic errors with large random errors (±350–400 kcal) and significant proportional errors between measured and estimated BMRs (Figures 1A and 1B). Correlation analysis showed that BMR_m in males was significantly correlated with age (r=−0.77, $p<0.001$), height (r=0.33, $p=0.05$), BM (r=0.83, $p<0.001$), BMI (r=0.76, $p<0.001$), FAT% (r=0.41, $p=0.012$), FM (r=0.66, $p<0.001$), and LSTM (r=0.85, $p<0.001$). In females, BMR_m was significantly correlated with age (r=−0.41, $p=0.019$), BM (r=0.63, $p<0.001$), BMI (r=0.52, $p=0.002$), FM (r=0.50, $p=0.003$), LSTM (r=0.68, $p<0.001$), and BMC (r=0.40, $p=0.025$). Partial correlation analysis adjusted for age, height, and BM did not show a significant relationship between BMR_m and FPG or HbA1c. Partial correlation analysis adjusted for age and BMI only showed that BMR_m was significantly correlated with FPG (r=0.28, $p=0.024$) and HbA1c (r=0.27, $p=0.026$) in all subjects.

In stepwise multiple regression analysis (Model 3) calculated according to our original predictive formula as $BMR_{dm}=-262 + 10.1 \times [FM] + 41.1 \times [LSTM] - 165 \times [BMC]$, showed better predictive power than the other two models (Table 4). However, even when Model 3 was used to estimate BMR, the random error of the estimation was still large, and the proportional error was significant (Figure 1C). Gender had no impact on the prediction capacity of Model 3.

Correlation analysis showed that BMI and HOMA-R were significantly correlated with the differences between measured and estimated BMR using the Ganpule equation (r=0.31, $p=0.009$ and r=0.30, $p=0.039$, respectively). Therefore, subjects were divided into three groups according to BMI. One-way ANOVA revealed that the obese group was significantly younger than the normal weight and overweight groups ($p<0.001$ for both groups), and that HbA1c was lower but HOMA-R was higher in the obese group than in the normal weight group ($p=0.003$ and $p=0.012$, respectively). In addition, the obese group showed larger random errors and significant proportional errors compared to the normal weight and overweight groups, regardless of which predictive equation was used (Table 5).

When we used 0.85 as the RQ for the normal weight and overweight groups, and 0.80 for the obese group, the random error between BMR_m and the two estimated BMRs (BMR_{hb} and BMR_g) were slightly reduced (mean

Table 2. Subject characteristics

Variable	All (n=69)	Males (n=37)	Females (n=32)	*p*-value
Age (years)	60±12 (27-82)	57±12 (27-82)	64±11 (39-82)	0.011
Height (cm)	162±9 (140-182)	168±6 (155-182)	155±6 (140-168)	<0.001
Body mass (kg)	67.5±12.9 (42.9-105.5)	71.3±13.9 (51.4-105.5)	63.1±10.2 (42.9-87.6)	0.007
BMI	25.7±4.1 (18.4-37.5)	25.4±4.7 (18.4-37.5)	26.1±3.4 (18.8-34.5)	NS
Body fat (%)	32.2±7.9(15.1-48.8)	28.1±7.6 (15.1-44.2)	37.1±5.1 (21.4-48.8)	<0.001
LSTM (kg)	43.1±7.5 (30.1-63.4)	47.9±6.2 (37.2-63.4)	37.5±4.4 (30.1-50.6)	<0.001
FM (kg)	22.2±8.2 (8.4-46.0)	20.8±9.4 (8.4-46.0)	23.7±6.5 (9.2-42.6)	NS
BMC (kg)	2.3±0.5 (1.3-3.3)	2.6±0.4 (2.0-3.3)	1.9±0.4 (1.3-3.2)	<0.001
FPG (mg/dL)	154±63 (48-400)	165±74 (63-400)	141±44 (48-274)	NS
HbA1c (%)	9.3±2.1(5.6-16.1)	9.4±2.2 (5.6-16.1)	9.1±2.0 (6.5-15.0)	NS
HOMA-R	2.4±1.7 (0.5-7.7) (n=48)	2.3±1.5 (0.6-6.0) (n=32)	2.7±2.1 (0.5-7.7) (n=16)	NS

BMI: body mass index; LSTM: lean soft tissue mass; FM: fat mass; BMC: bone mineral content; FPG: fasting plasma glucose; HOMA-R: homeostasis model assessment ratio; NS: not significant.
Values are given as mean±SD (range). Differences between males and females were analyzed using the unpaired t-test.
p-values: males vs females.
HOMA-R was not measured in insulin users.

Table 3. Basal metabolic rate measured using three equations

BMR (kcal/day)	All (n=69)	Males (n=37)	Females (n=32)	*p*-value
BMRm	1358±334 (761-2606)	1477±363 (930-2606)	1222±237 (761-1880)	0.001
BMRhb	1386±245(1025-2182)***	1497±262(1059-2182)***	1256±140(1025-1632)***	<0.001
BMRg	1322±243 (863-1985)	1469±200 (1150-1985)	1151±164 (863-1586)	<0.001

BMR: basal metabolic rate (m=measured, hb=Harris-Benedict, g=Ganpule).
Values are given as mean±SD (range). Differences between males and females were analyzed using the unpaired t-test.
p-values: males vs females.
Differences between BMRm and the two estimated BMRs (BMRhb and BMRg) were analyzed using one-way repeated-measures ANOVA and the Bonferroni post hoc test. ***$p<0.001$ vs BMRg.

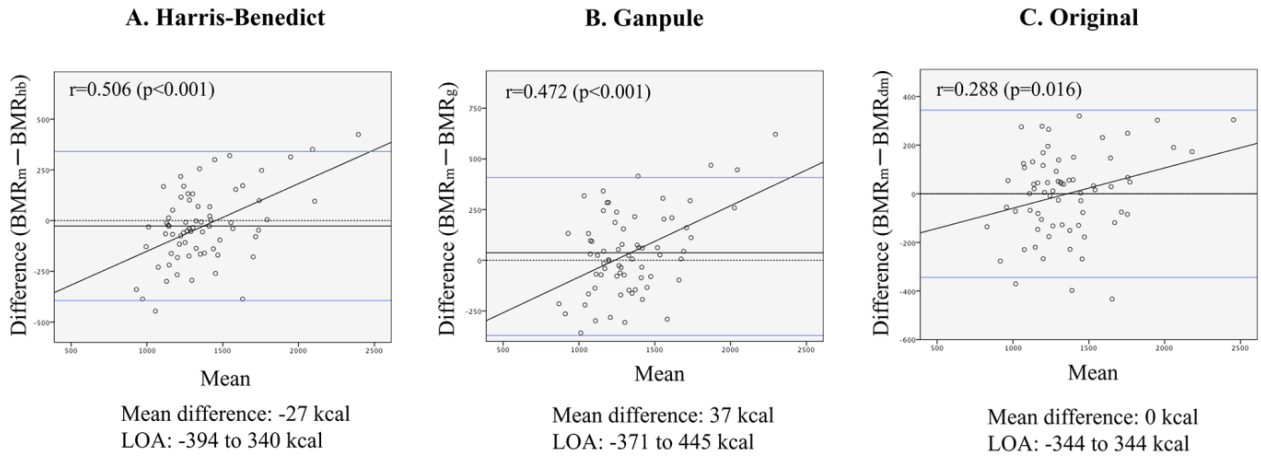

Figure 1. Bland-Altman plots were used to analyze the agreement between BMR_m and 3 estimated BMRs (BMR_{hb}, BMR_g, and BMR_{dm}). The mean difference and LOA were indicated by dotted lines. BMR: basal metabolic rate (m=measured, hb=Harris-Benedict, g=Ganpule, dm=Original); LOA: limits of agreement.

Table 4. Stepwise regression of basal metabolic rate using three models

Model	Predictor	Unstandardized coefficient		Change in $\%R^2$	*p*-value
		B	Standard error		
Model 1	Constant	797	279		
	BM	15.7	2.33	62.7	<0.001
	Age	-8.30	2.50	4.9	0.001
	Total			67.6	
Model 2	Constant	957	262		
	Age	-11.6	2.25	46.1	<0.001
	BMI	38.5	6.27	13.5	<0.001
	Gender	200	50.0	7.5	<0.001
	Total			67.1	
Model 3	Constant	-262	127		
	LSTM	41.1	4.79	63.1	<0.001
	FM	10.1	2.77	7.1	0.001
	BMC	-165	67.8	2	0.018
	Total			72.2	

BM: body mass; BMI: body mass index; LSTM: lean soft tissue mass; FM: fat mass; BMC: bone mineral content. Explanatory variables were age, gender, height, and also BM (model 1), BMI (model 2), or FM, LSTM, and BMC (model 3).
The constant was determined by the method of least squares.

difference±2SD: −30±362 kcal and 34±402 kcal, respectively), but proportional errors remained significant (r=0.483, p<0.001 and r=0.452, p<0.001, respectively).

Correlation analysis showed that BMD was significantly correlated with age (r=−0.41, p<0.001), height (r=0.63, p<0.001), BM (r=0.48, p<0.001), LSTM (r=0.64, p<0.001), and HOMA-R (r=0.32, p=0.025). BMC was significantly correlated with age (r=−0.50, p<0.001), height (r=0.82, p<0.001), BM (r=0.55, p<0.001), LSTM (r=0.77, p<0.001), FAT% (r=−0.31, p=0.009), and FPG (r=0.25, p=0.037).

DISCUSSION

As the principal result of this study, we found that predictive equations of BMR produce small systematic errors but large random errors with significant proportional errors in Japanese patients with T2DM, particularly in obese individuals. Consistent with this, a number of previous studies also reported that the Harris-Benedict equation overestimated BMR.[6-8] Conversely, another study demonstrated that the Harris-Benedict equation provided the most accurate prediction of resting metabolic rate (RMR) when predicted and indirectly measured RMR were compared in patients with cerebral infarction.[19] However, this study excluded subjects with poorly controlled diabetes mellitus, and the subjects were older (mean age; 79.5 years) and leaner (mean BMI; 22.4) than those in the present study. Miyake et al. reported that the difference between indirectly measured BMR and BMR estimated by the Ganpule equation in healthy Japanese adults was smaller than that determined using other predictive equations, including the Harris-Benedict equation.[10] Differences between measured and estimated BMR in non-diabetic, pre-diabetic and diabetic subjects were previously reported as (mean difference±SD) 99±127, 98±159, and −19±-110 kcal for the Harris-Benedict equation, and 25±119, 17±148, and 110±99 kcal for the Ganpule equation, respectively.[11] Random errors calculated as twice the reported SD values were comparable to those found in the present study (254, 318, and 220 kcal for Harris-Benedict, and 238, 296, and 198 kcal for Ganpule in non-diabetic, pre-diabetic and diabetic subjects,

Table 5. Subject characteristics according to BMI group (top); agreement between measured BMR (BMRm) and three estimated BMRs (BMRhb, BMRg, and BMRdm)

Variable		Normal (BMI<25)	Overweight (25<BMI<30)	Obese (BMI>30)
n (males, females)		28 (20, 8)	30 (11, 19)	11 (6, 5)
Age (years)		61.9±9.2 (42-82)	62.8±11.1 (41-82)	46.9±13.2 (27-63)*** †††
Height (cm)		165±7.4 (151-182)	159±9.2 (140-176)	164±6.5 (151-173)
Body mass (kg)		59.8±6.6 (42.9-71.8)	67.0±8.7 (50.1-85.9)	88.7±11.4 (68.7-106)*** †††
BMI		22.1±1.7 (18.4-24.4)	26.6±1.3 (25.0-30.0)	32.9±2.6 (30.1-37.5)***†††
Body fat (%)		26.4±7.0 (15.1-36.8)	34.7±5.4 (19.2-42.3)	40.4±5.0 (29.8-48.8)*** †
LSTM (kg)		41.7±6.2 (30.1-54.7)	41.8±7.3 (30.7-57.1)	50.4±7.3 (38.9-63.4)**†††
FM (kg)		15.8±4.4 (8.4-23.0)	23.1±3.8 (12.7-29.0)	35.9±6.6 (23.9-46.0)***†††
BMC (kg)		2.3±0.5 (1.3-3.3)	2.2±0.5 (1.5-3.3)	2.4±0.5 (1.7-3.2)
FPG (mg/dL)		171±81.7 (48-400)	150±45.9 (88-274)	122±25.1 (87-160)
HbA1c (%)		9.7±2.4 (5.2-15.7)	9.2±1.7 (6.5-14.0)	7.7±1.2 (6.1-9.1)**
HOMA-R (n=48)		1.7±1.2 (0.5-4.6)	2.7±1.7 (1.0-6.8)	3.8±2.3 (1.6-7.7)**
BMRm (kcal/day)		1253±217 (761-1717)	1298±251 (778-1795)	1793±446 (1197-2606)***†††
BMRhb (kcal/day)		1291±143 (1025-1559)	1350±208 (1026-1790)	1725±268 (1305-2182)***†††
BMRg (kcal/day)		1264±167 (875-1513)	1265±229 (863-1708)	1622±236 (1194-1985)***†††
BMRdm (kcal/day)		1230±190 (897-1570)	1328±226 (941-1797)	1770±278 (1329-2302)***†††
Mean difference ±2SD	Harris-Benedict	-38±309	-52±340	68±521
	Ganpule	-11±344	32±365	172±566
	Original	23±290	-30±334	24±488
Proportional bias	Harris-Benedict	r=0.519, p=0.005	NS	r=0.711, p=0.014
	Ganpule	NS	NS	r=0.773, p=0.005
	Original	NS	NS	r=0.71, p=0.014

BMI: body mass index; LSTM: lean soft tissue mass; FM: fat mass; BMC: bone mineral content; FPG: fasting plasma glucose; HOMA-R: homeostasis model assessment ratio; BMR: basal metabolic rate (m=measured, hb=Harris-Benedict, g=Ganpule, dm=Original); NS: not significant; SD: standard deviation.

Values are given as mean±SD (range).

Intergroup comparison was done using ANOVA and the Bonferroni post hoc test.

$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ vs normal (BMI<25), $^{†}p<0.05$, $^{††}p<0.01$, $^{†††}p<0.001$ vs overweight (25<BMI<30). Systematic error and random error were evaluated by calculating the mean difference and 95% limits of agreement for each comparison (±2SD of the difference).

The proportional bias was evaluated as the degree of correlation between differences and means when the slope of the regression line is significant.

HOMA-R was not measured in insulin users.

respectively). The present study revealed large random errors and significant proportional errors even using Model 3, which had the best predictive power to estimate BMR in Japanese patients with T2DM. According to the Japan-DRI 2010, total energy expenditure (TEE) is calculated by BMR × physical activity level (PAL). PAL for Japanese adults aged 18–69 years is divided into three categories: 1.50, 1.75, or 2.00.[20] Given a predictive equation which over- or underestimates BMR by approximately 400 kcal, the calculated TEE would result in a possible difference of 600, 700, or 800 kcal per day. The prediction error of PAL could also contribute to the error size of the TEE calculation. This magnitude of error is not acceptable for individualized dietary treatment in diabetic patients.

The large error size observed due to poor accuracy of the measurement device, Fitmate, might be of concern. However, accuracy of the Fitmate, an earlier model of the Fitmate-Pro, has been reported as (mean difference±SD) 5.8±80.7 kcal/day.[21] The magnitude of this difference is substantially smaller than the error size of estimated BMRs shown in the present and previous studies. Hence, the large error size between measured and estimated BMR among T2DM patients is likely due to other factors.

To our knowledge, this is the first study to show the contribution of BMI to the error size of predicted BMR. Miyake et al previously reported that residual BMR (error size) correlated significantly with FPG and $\log_e$ HbA1c.[11] We assessed the accuracy of predictive equations separately according to BMI and showed that the obese group had large errors regardless of which predictive equation was used. Both the Harris-Benedict and Ganpule equations were originally formulated based on a non-diabetic, healthy population with a lower mean BMI (21.4 and 21.5 (Harris-Benedict), 23.4 and 21.4 (Ganpule) for males and females, respectively) than that used in the present study.[4,5,9] Therefore, the large error size observed in the present study might be due to the presence of obese patients (BMI>30) among the subjects.

Fasting RQ values in obese diabetic patients have been inconsistent among previous studies. Some studies reported that the 24 hour RQ did not significantly differ between non-diabetic lean and obese subjects.[22,23] We therefore considered it reasonable to use a fixed-value RQ for BMR calculation regardless of BMI, as in previous studies using Fitmate.[20] However, RQ value is influenced by BMI[18] and diet,[23] particularly in diabetic patients, as well as by medication used to lower plasma glucose.[24,25] For example, Blaak et al reported that fasting fat oxidation increased and fasting RQ decreased with increasing BMI category and that the mean fasting RQ of obese subjects (BMI ≥30) with insulin resistance was around 0.80–0.81.[18] Moreover, because insulin and sulfonylurea induce metabolic changes,[24] diabetic patients treated with

these drugs were reported to have higher RQ values than normal subjects, non-treated diabetic patients,[25] and non-diabetic obese subjects.[24] Accordingly, RQ values might change according to the degree of obesity. When we used 0.80 to indicate fasting RQ for the obese group, however, a slight improvement in the random error size was observed, but proportional errors between measured and estimated BMRs from formerly established equations remained significant. Thus, the use of a fixed RQ value of 0.85 in the assessment of BMR among our subjects was not likely to be a major cause of the large error size of the BMR estimation.

Another possible factor is the influence of a high glycemic level on the BMR of diabetic patients. Patients with T2DM have a higher BMR than non-diabetic people. Miyake et al reported that obese Japanese people with T2DM have a higher BMR than obese Japanese people without T2DM, and that the fasting glucose level might be a major determinant of this increase.[11]Gougeon et al. reported that in a population of obese subjects with T2DM, estimation of RMR was improved when FPG was included as a variable.[8] Although the physiological mechanisms responsible for the increased BMR in T2DM remain unclear, they are thought to be associated with increased glycogenolysis, gluconeogenesis, hyperglucagonemia, increased protein turnover and increased sympathetic system activity.[26,27] Our present results are consistent with these previous findings in that measured BMR was significantly correlated with FPG and HbA1c after adjustment for age and BMI. However, FPG and HbA1c were not among the factors to influence error size between measured and estimated BMR.

Importantly, we found that not only FM and LSTM but also BMC was a significant predictor of BMR. To our knowledge, no previous equation for the prediction of BMR has included BMC as a variable. Energy expenditure derived from BMC had little impact on RMR (0.3%) in non-diabetic subjects.[28] With regard to diabetic patients, a number of studies have demonstrated an increase in BMD in T2DM patients.[29,30] Increased BM elevates BMD and helps maintain the skeletal framework.[31] This is consistent with our present results, where BMD and BMC were positively correlated with BM. Interestingly, BMC was also positively correlated with FPG. Although the exact mechanisms are unclear, high BMC due to excess BM and hyperglycemia among T2DM patients might be related to the adaptation of BMC to the predictive equation of BMR.

Both BMR and RMR provide an estimate of the 24-hour energy requirements for maintaining basic body functions. Although BMR and RMR are sometimes used interchangeably, they are measured under different conditions and have slightly different interpretations. BMR is measured under more restrictive conditions than RMR, requiring that the subject be completely rested both before and during the measurement, and be fasted for at least 10–12 h to reduce calorigenic influences. In addition, the subject should be free from emotional stress and familiar with the apparatus used.[32] RMR is measured under less restrictive conditions (5 h fasting and 10–30 min rest) and does not require that the subject spends the night before measurement sleeping in the test facility.[33] The subjects were instructed to rest and fast for about 12 h before measurements. Conditions in the present study therefore met the above requirements for the measurement of BMR. A systematic review has also reported that, after discarding the first 5 minutes of data, only 5 to 10 minutes is needed to obtain an accurate measurement of RMR, provided that steady-state conditions can be obtained.[33] Therefore, our measurement period using the Fitmate-pro (10-15 minutes) was sufficient to accurately measure BMR.

A limitation of the present study is its small sample size. In addition, we did not consider the influence of medication used by T2DM subjects. Fagour et al reported that RMR was reduced after starting insulin therapy,[34] and Buscemi et al also recently reported that RMR was reduced after an insulin venous bolus via a suppressive effect on gluconeogenesis in diabetic patients.[35] Further studies with larger sample sizes that consider the effect of diabetic medications in pre-diabetic or mild diabetic patients alongside healthy individuals are necessary. In addition, we need to perform cross-validation tests to determine the accuracy of our original equation for use in clinical practice.

Predictive equations for BMR yielded small systematic errors but large random errors with significant proportional errors in Japanese patients with T2DM. The size of the random error was too large to accurately determine daily energy requirements, particularly for obese individuals. We therefore discourage the use of predictive equations in Japanese patients with T2DM, and instead recommend the use of an indirect measurement of BMR.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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