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ORIGINAL ARTICLE

Standard medical nutrition therapy of 25 kcal/kg ideal bodyweight/day often does not reach even resting energy expenditure for patients with type 2 diabetes

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ABSTRACT

Aims/Introduction: In Japan, an ideal bodyweight (IBW) calculated by 22 × height $(m)^2$ has commonly been used in the planning of medical nutrition therapy (MNT). However, there have been concerns regarding calorie deficits in fulfilling resting energy expenditure (REE) for patients with type 2 diabetes undergoing MNT as defined by 25 kcal/kg IBW/day. The objective of the present study was to measure REE in patients with type 2 diabetes and verify the validity of MNT with 25 kcal/kg IBW/day.

Materials and Methods: A retrospective cross-sectional study was carried out in 52 patients with type 2 diabetes (mean age was 65.9 ± 7.3 years, bodyweight 65.0 ± 11.3 kg, body mass index 24.9 ± 3.8 kg/m^2). REE was measured by indirect calorimetry.

Results: The mean REE was 1,601.0 ± 253.1 kcal/day. Assuming that all patients strictly observed daily energy intake as 25 kcal/kg IBW/day, 41 of 52 patients (78.9%) did not reach their REE. The greater the bodyweight, the greater the difference between assumed energy intake as 25 kcal/kg IBW and REE.

Conclusions: We call attention to the potential risk of total dietary energy intake set to 25 kcal/kg IBW/day. Clinicians should carefully plan MNT to not fall below a patient's REE to prevent sarcopenia and ensure MNT continuity.

INTRODUCTION

Diabetes mellitus is a syndrome showing chronic hyperglycemia, originating from insufficiency of insulin activity and insulin resistance[1]. As overweight and obesity conditions are generally associated with insulin resistance, appropriate dietary therapy is essential in the treatment of diabetes. The American Diabetes Association has declared that medical nutrition therapy (MNT) is integral to overall management of diabetes, and all diabetes patients should be referred to individualized MNT[2]. Additionally, the American Diabetes Association recommends weight loss with lifestyle programs that achieve a 500–750 kcal/day energy deficit, suggesting a caloric intake of 1,500–1,800 kcal/day for men and 1,200–1,500 kcal/day for women, adjusted for the individual's baseline bodyweight[2,3].

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Recommended calorie intake for MNT is often calculated by an equation that includes the ideal bodyweight (IBW); several equations have been proposed to determine IBW[4,5]. In Japan, Matsuzawa *et al.*[6] in 1990 proposed IBW calculated as 22 × height $(m)^2$. They investigated the average body mass index (BMI) with the lowest morbidity using 4,565 Japanese men and women aged 30–59 years, and reported that the BMI associated with the lowest morbidity was calculated to be 22.2 kg/m^2 for men and 21.9 kg/m^2 for women. Building on this concept of IBW, the practical guidelines provided by the Japan Diabetes Society[7] recommended the total daily energy intake to be 25–30 kcal/kg IBW for diabetes patients with light physical activity (e.g., jobs mainly involving desk work), 30–35 kcal/kg IBW for patients with moderate physical activity (e.g., jobs mainly involving standing work) and >35 kcal/kg IBW for patients with heavy physical activity (e.g., jobs mainly involving heavy physical labor).

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In weight management, it is essential to pay attention to both caloric intake and energy expenditure, as it is critical to maintain the metabolic equilibrium. Resting energy expenditure (REE) is defined as the energy expenditure to maintain minimal metabolic activities during a non-active period, representing 60–70% of the daily total energy expenditure (TEE)[8]. In clinical practice, indirect calorimetry is used to determine REE by measuring oxygen uptake and carbon dioxide output. Indirect calorimetry is a non-invasive method with reasonable accuracy and high reproducibility[8,9]. Measuring REE provides the appropriate data necessary to determine calorie intake for safe and effective weight loss, and maintenance of a healthy weight after successful weight loss[10].

When overweight or obese diabetes patients are admitted to hospital for treatment for their diabetes, hospital therapeutic diets are often served as calculated by 25 kcal/kg IBW/day. Although adequate MNT is effective for diabetes patients, there is concern about a lack of calories in some cases. Therefore, we assessed REE in patients with type 2 diabetes, and verified the validity of MNT with 25 kcal/kg IBW/day for diabetes patients in Japan.

METHODS

Enrolled patients and anthropometry

This was a retrospective analysis of measurements using indirect calorimetry carried out in patients with type 2 diabetes from a previous clinical study registered as clinical trial ID UMIN000012059. We screened outpatients with type 2 diabetes at the Kyoto Prefectural University of Medicine, Kyoto, Japan, if they were aged 35–75 years, and treated with diet and exercise, oral antidiabetic agents or glucagon like peptide-1 receptor agonists. In the present study, we excluded patients treated with insulin therapy. Additionally, the following patients were excluded: those with severe renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m^2), liver damage (aspartate aminotransferase >100 U/L or alanine aminotransferase >100 U/L) and pregnant women.

We recorded patient demographics, medical history, smoking status and medication usage of all the patients. BMI was calculated by weight in kilograms divided by height in meters squared. IBW was calculated by height (m) × height (m) × 22 (kg/m^2)[6]. Body surface area (BSA) was calculated by the following equation, which was proposed by Fujimoto *et al.*[11] to fit the Japanese standard physique: bodyweight $(kg)^{0.444}$ × height $(m)^{0.663}$ × 88.63.

The present study was examined and approved by the institutional review board of Kyoto Prefectural University of Medicine (ERB-C-56-1), and was administered in accordance with Good Clinical Practices. The researcher or subresearcher explained the study design to each candidate patient using a leaflet and informed consent form authorized by the institutional review board before we enrolled the patient in the study. Written informed consent was given by each patient before participation in the study.

Indirect calorimetry and other measurements

After an overnight fast, measurements were carried out in the morning in a room at constant temperature (approximately 23°C). On the day of measurement, smoking was not allowed for current smokers. The participants rested in the supine position for at least 30 min, and wore a face mask to collect respiratory gases. Respiratory gas exchange was measured continuously for 30 min with an Aeromonitor (AE-310S; Minato Medical Science, Osaka, Japan), to collect indirect calorimetry. Continuous gas exchange measurements were obtained for a minimum of 30 min, and the values for the last 15 min were used for analysis. REE was calculated from oxygen consumption (VO_2) and carbon dioxide production (VCO_2) according to the modified Weir formula as follows: REE (kcal) = (3.9 × VO_2 [L/min] + 1.1 × VCO_2 [l/min]) × 1,440 min[12].

Fasting blood samples were obtained in the morning. A central laboratory institute carried out the laboratory blood tests. Hemoglobin A_{1c} was measured with high-performance liquid chromatography, and was expressed as a National Glycohemoglobin Standardization Program unit. We calculated the estimated glomerular filtration rate using the Japanese Society of Nephrology equation: estimated glomerular filtration rate (mL/min/1.73 m^2) = 194 × $Cr^{-1.094}$ × $age^{-0.287}$ (×0.739 for women)[13].

Statistical analysis

JMP version 10.0 software (SAS Institute Inc., Cary, NC, USA) was used to carry out all statistical analyses. The mean values are expressed as the mean ± standard deviation. All statistical tests were two-tailed, and we considered a P-value < 0.05 as statistically significant. Differences in categorical variables between the two groups were evaluated with Fisher's exact test. If appropriate for non-normally distributed data, continuous variables were compared using Student's t-test and the Mann–Whitney U-test. Pearson's correlation was used to verify the relationship between REE and clinical parameters. Multivariate linear regression analyses were used to evaluate independent determinants of REE.

RESULTS

Between December 2013 and July 2014, we enrolled 52 patients (24 men and 28 women). All measurements were carried out according to the protocol. The clinical and laboratory characteristics of patients are summarized in Table 1. The mean measured REE was 1,601.0 ± 253.1 kcal/day. Table 2 shows the correlation between REE and clinical parameters. In the univariate analyses, REE was positively correlated with height, bodyweight, IBW, BMI and BSA. In contrast, REE was negatively correlated with age. There was no significant correlation between REE and fasting plasma glucose or insulin. Multiple regression analyses showed that BSA had the highest standardized regression coefficient after adjusting for other variables (β = 0.679; P < 0.001).

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Table 1 | Clinical and laboratory characteristics of patients

Characteristic	
Age (years)	65.9 ± 7.3
Sex (male/female)	24/28
Height (m)	1.62 ± 0.10
Bodyweight (kg)	65.0 ± 11.3
BMI (kg/m^2)	24.9 ± 3.8
BSA (m^2)	1.65 ± 0.17
Duration of diabetes (years)	11.9 ± 6.1
Smoking (none/past/current)	34/9/9
Sulfonylurea (–/+)	26/26
Dipeptidyl peptidase-4 inhibitor (–/+)	21/31
Glucagon like peptide-1 receptor agonist (–/+)	49/3
Pioglitazone (–/+)	49/3
Metformin (–/+)	22/30
Systolic blood pressure (mmHg)	136.3 ± 19.1
Diastolic blood pressure (mmHg)	76.1 ± 10.5
Hemoglobin A_{1c} (%)	7.07 ± 0.84
Hemoglobin A_{1c} (mmol/mol)	53.7 ± 9.1
Fasting plasma glucose (mg/dL)	148.0 ± 26.5
Insulin (μIU/mL)	7.08 ± 3.24
Serum creatinine (mg/dL)	0.74 ± 0.23
eGFR (mL/min/1.73 m^2)	75.2 ± 19.4
Oxygen consumption (mL/min)	228.8 ± 36.5
Carbon dioxide output (mL/min)	189.4 ± 31.9
REE (kcal/day)	1,601.0 ± 253.1

Sample size: *n* = 52. Data are the mean ± standard deviation or number of patients. BMI, body mass index; BSA, body surface area; eGFR, estimated glomerular filtration rate; NDR, no diabetic retinopathy; PDR, proliferative diabetic retinopathy; REE, resting energy expenditure; SDR, simple diabetic retinopathy.

Then, we compared measured REE with assumed recommended calories calculated by 25 kcal/kg IBW/day. In Table 3, patients were divided into two groups according to a comparison between REE versus recommended calculated calories (RCC). We defined patients whose REE was over RCC as the "REE>RCC group," and patients whose REE was less than or equal to RCC as the "REE ≤ RCC group." Assuming that all the patients strictly observed daily energy intake as 25 kcal/kg IBW/day, the caloric intake of 41 of 52 patients (78.9%) did not reach their REE. The patients in the REE > RCC group showed higher bodyweight, BMI, BSA and REE than the patients in the REE ≤ RCC group, whereas there was no significances between the two groups in age, sex and height. RCC–REE differences of patients in the REE > RCC group and patients in the REE ≤ RCC group were –230.4 (95% confidence interval –272.3 to –188.6) kcal/day and 99.3 (95% confidence interval 54.0–144.6) kcal/day, respectively. The patient with the highest RCC–REE difference had a caloric deficit of 645 kcal/day.

Figure 1a shows a strong correlation between actual bodyweight and RCC–REE differences. In contrast, there was no significant correlation between IBW and RCC–REE differences (Figure 1b). Assuming that all the patients strictly observed their daily energy intake as 30 kcal/kg IBW/day, 40 of 52 patients (76.9%) surpassed their REE (Figure 2a). Figure 2a also shows a strong correlation between actual bodyweight and RCC–REE differences, whereas there was no significant correlation between IBW and RCC–REE differences (Figure 2b).

DISCUSSION

When MNT is prescribed for diabetes patients with light physical activity, the total dietary energy intake is often set at 25 kcal/kg IBW/day in Japan. In the present study, we compared the measured REE with the assumed daily calorie intake, as calculated by 25 kcal/kg IBW. We show that nearly 80% of patients did not reach their REE, and Figure 1a demonstrates a greater difference in the RCC–REE with a greater rise in bodyweight. Conversely, Figure 1b shows that IBW could not estimate the RCC–REE difference. Despite previous studies reporting that MNT as calculated by 25 kcal/kg IBW/day for patients with diabetes was practically useful for bodyweight reduction and for improving metabolic parameters[14], the present results suggest a concern of caloric deficit to fulfill REE.

As the Japanese population rapidly ages, the number of elderly diabetes patietns is increasing markedly[15]. Aging is

Table 2 | Univariate correlations and multiple regression analyses on resting energy expenditure

Characteristic	*r*	*P*	β	*P*	β	*P*	β	*P*	β	*P*
Age (years)	–0.434	<0.01	–0.215	<0.01	–0.206	<0.05	–0.304	<0.001	–0.171	<0.05
Sex (male = 1, female = 0)	0.643	<0.001	0.324	<0.001	0.243	0.13	0.612	<0.001	0.144	0.15
Height (m)	0.689	<0.001	–	–	–	–	–	–	–	–
Bodyweight (kg)	0.792	<0.001	0.548	<0.001	–	–	–	–	–	–
IBW (kg)	0.695	<0.001	–	–	0.460	<0.001	–	–	–	–
BMI (kg/m^2)	0.389	<0.01	–	–	–	–	0.378	<0.001	–	–
BSA (m^2)	0.848	<0.001	–	–	–	–	–	–	0.679	<0.001
Fasting plasma glucose (mg/dL)	0.175	0.21	0.127	0.19	0.142	0.14	0.044	0.59	0.131	0.07
Insulin (μIU/mL)	0.210	0.14	0.095	0.28	0.250	<0.01	0.124	0.16	0.097	0.19

Sample size: *n* = 52. *r* indicates correlation coefficient and β indicates multiple linear regression coefficients. Ideal bodyweight (IBW) is defined as 22 × height (m)^2. BMI, body mass index; BSA, body surface area.

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Table 3 | Clinical and laboratory characteristics of patients divided by comparison between resting energy expenditure and recommended calculated calorie

Characteristic	REE > RCC	REE ≤ RCC	*P*
n (%)	41 (78.9)	11 (21.1)	–
Age (years)	65.4 ± 7.8	67.6 ± 4.9	0.37
Sex (male/ female)	21/ 20	3/ 8	0.19
Height (m)	1.62 ± 0.10	1.60 ± 0.07	0.32
Bodyweight (kg)	68.0 ± 10.0	54.0 ± 9.2	<0.001
BMI (kg/m^2)	26.0 ± 3.5	20.9 ± 2.1	<0.001
BSA (m^2)	1.68 ± 0.16	1.51 ± 0.15	<0.01
Duration of diabetes (years)	11.9 ± 6.2	11.8 ± 6.2	0.98
Smoking (none/past/current)	27/7/7	7/2/2	0.99
Systolic blood pressure (mmHg)	140.5 ± 18.0	121.7 ± 15.6	<0.01
Diastolic blood pressure (mmHg)	77.9 ± 9.9	69.6 ± 10.4	<0.01
Hemoglobin A_{1c} (%)	7.17 ± 0.82	6.70 ± 0.82	0.05
Hemoglobin A_{1c} (mmol/mol)	54.8 ± 9.0	49.7 ± 9.0	0.05
Fasting plasma glucose (mg/dL)	152.2 ± 26.3	132.4 ± 21.9	<0.05
Insulin (μIU/mL)	7.73 ± 3.23	4.65 ± 1.93	<0.01
Serum creatinine (mg/dL)	0.77 ± 0.24	0.63 ± 0.16	<0.05
eGFR (mL/min/1.73 m^2)	73.6 ± 20.1	81.3 ± 16.1	0.88
Oxygen consumption (mL/min)	239.9 ± 30.6	190.6 ± 30.8	<0.001
Carbon dioxide output (mL/min)	197.9 ± 29.1	160.7 ± 25.4	<0.001
REE (kcal/day)	1,677.4 ± 213.6	1,316.0 ± 175.7	<0.001
RCC–REE differences (kcal/day)	–230.4 (–272.3 to –188.6)	99.3 (54.0 to 144.6)	<0.001

Data are the mean ± standard deviation, mean ± 95% confidence interval or number of patients. Recommended calculated calorie (RCC) is defined as 25 kcal/kg ideal bodyweight/day. BMI, body mass index; BSA, body surface area; eGFR, estimated glomerular filtration rate; REE, resting energy expenditure.

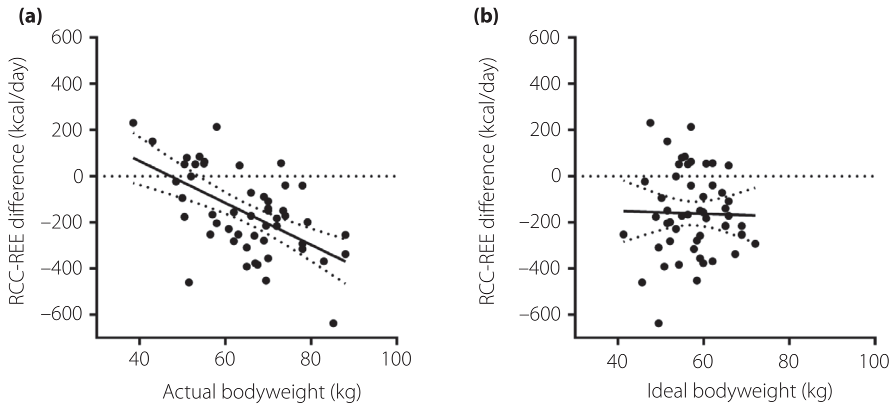

Figure 1 | Correlation between recommended calculated calorie (RCC) and resting energy expenditure (REE) differences (25 kcal/kg) and bodyweight or ideal bodyweight. (a) The correlation coefficient is –0.564 ($P < 0.001$). (b) The correlation coefficient is –0.022 ($P = 0.87$). The dotted lines indicate 95% confidence intervals for the regression line. RCC is defined as 25 kcal/kg ideal bodyweight/day.

associated with an increased risk of sarcopenia, or a loss of skeletal muscle[16]. It is well known that older diabetes patients are at increased risk for sarcopenia[17,18]. Skeletal muscle accounts for a little more than 20% of REE[19]. Yoshimura *et al.*[20] reported that caloric restriction to 25 kcal/kg IBW/day without aerobic exercise led to a loss in skeletal muscle in elderly people, although diet-induced weight loss with aerobic exercise attenuated this loss in skeletal muscle mass. This suggests that people treated with 25 kcal/kg IBW/day caloric restriction were at risk of reducing activities of daily living secondary to skeletal muscle loss.

Masuda *et al.*[21] compared the effect of MNT between the 25 kcal/kg IBW/day group (25 kcal group) and 30 kcal/kg IBW/day group (30 kcal group) on obese or overweight

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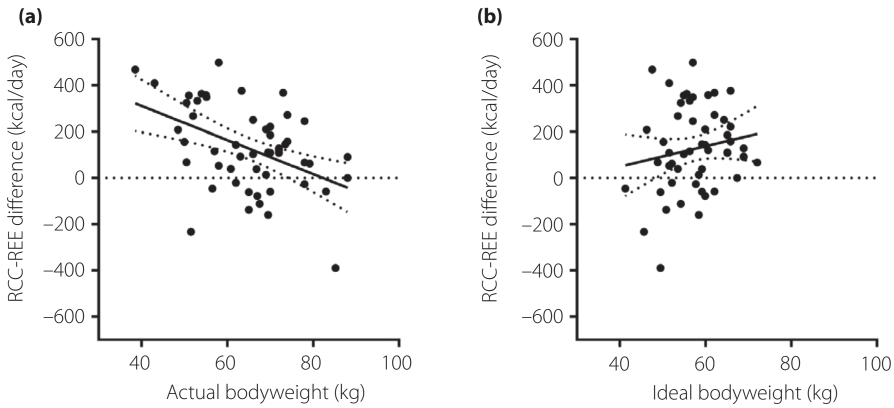

Figure 2 | Correlation between recommended calculated calories (RCC) and resting energy expenditure (REE) differences (30 kcal/kg) and bodyweight or ideal bodyweight. (a) The correlation coefficient is –0.450 ($P < 0.001$). (b) The correlation coefficient is 0.164 ($P = 0.25$). The dotted lines indicate 95% confidence intervals for the regression line. RCC is defined as 30 kcal/kg ideal bodyweight/day.

inpatients with type 2 diabetes. At discharge, the BMI of the 25 kcal group was significantly lower than values before hospitalization, whereas there were no significant changes in BMI of the 30 kcal group. However, the BMI of the 30 kcal group was prone to decrease from the time of hospitalization to 12 months after hospital discharge, whereas the BMI of the 25 kcal group was eventually regained because of patient difficulty in maintaining the lower set daily calories. In the present study, assuming that all patients strictly observed their prescribed daily energy intake as 30 kcal/kg IBW/day, 40 of 52 patients (76.9%) were able to reach their REE (Figure 2a). Therefore, to improve continuity of MNT and prevent sarcopenia, the present data suggest that 30 kcal/kg IBW/day is preferable over 25 kcal/kg IBW/day for MNT in patients with type 2 diabetes.

In our analyses, REE was more strongly correlated with BSA than with bodyweight or IBW. Although BSA is easily calculated with height and bodyweight[11], and plays a key role in several medical fields, including cancer chemotherapy[22,23] or transplantology[24], little notice is taken of BSA in MNT for diabetes patients. This is partly explained by the individual variation in BSA[25]. Gibson *et al.*[26] showed that the respiratory and gastrointestinal tracts ignored in BSA calculations are one of the causes of the limitation of BSA, because those are metabolically active and comprise a substantial surface area.

When planning IBW-based MNT for diabetes patients, clinicians should ideally take care of not only their REE, but also their physical activity-related energy expenditure, depending on the patients. Although some useful uniaxial or triaxial accelerometers to assess physical activity-related energy expenditure are commercially available[27,28], access to indirect calorimetry has been limited due to the equipment cost and the methodological efforts to date. Yamada *et al.*[27] reported that TEE estimated using triaxial accelerometers in the elderly approximated the value of TEE measured by the doubly labeled water method, which was the gold standard for the evaluation of TEE. Because REE and physical activity-related energy expenditure are two major components of TEE, assessment of TEE using such a device might be useful at the point of care in clinical settings.

Finally, the present study had some limitations that warrant discussion. First, this study had a small sample size. However, the average age, BMI and hemoglobin A_{1c} of patients in the present study were nearly the same as other diabetes patients registered with the Japan Diabetes Clinical Data Management Study Group[29]. Therefore, patients in the present study represent the most recent clinical profile of Japanese diabetes patients. Second, this study did not include healthy people; therefore, we were not able to compare the REE of patients with type 2 diabetes with that of healthy people. Third, body composition data was not collected; therefore, we were unable to analyze the relationship between fat-free mass and REE, or other relevant clinical parameters, although it was well-known that REE is more strongly correlated with fat-free mass than with bodyweight[30,31]. Last, the present study consisted of Japanese patients only, and, thus, these findings might not be generalizable to other biogeographic ethnic groups.

In conclusion, although the diet therapy recommended by the Japan Diabetes Society can be a useful and simple program for controlling bodyweight, we draw attention to the potential risk of a total dietary energy intake set at 25 kcal/kg IBW/day. When we plan MNT for diabetes patients, we must take care that their caloric intake does not fall below REE to prevent sarcopenia and improve continuity of MNT.

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