Original Article

Practical Dietary Calorie Management, Body Weight Control and Energy Expenditure of Diabetic Patients in Short-term Hospitalization

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***Aim*: We investigated how dietary management affected body weight (BW) reduction and energy expenditure in obese and normal-weight type 2 diabetic patients.**
***Methods*: Type 2 diabetic patients who were hospitalized for diabetic control (93 men and 51 women) were checked for resting energy expenditure (REE). Subjects were divided into the two groups according to body mass index (BMI): obese (BMI ≥25), and normal-weight (BMI <25). Following the recommendations by JDS, JAS and JASSO, ideal body weight was calculated as [IBW=height (m)×height (m)×22 (kg/m^2)], and dietary calorie (kcal/day) was determined as 25 kcal/kg IBW.**
***Results*: Dietary calorie intake during hospitalization was similar in both groups. REE was greater in obese than in normal-weight patients. The difference between the calorie intake and energy expenditure (Δcalorie) was −222±26 kcal in obese patients and 69±27 kcal in normal-weight patients. Obese patients therefore had larger BW decreases than normal-weight patients (−171±12 vs. −92±11 g/day, $p<0.005$). In the obese group, a positive correlation was found between the change of BW and Δcalorie. This correlation remained after adjusting for age, BMI, gender, and respiratory quotient. Serum lipid profiles were significantly improved in both groups.**
***Conclusion*: These diet instructions showed the appropriate calorie restriction depending on the BMI and induced reasonable BW reduction in both obese and normal-weight subjects. The dietary program recommended by JDS, JAS and JASSO is practically useful for BW control and for improving lipid metabolism in type 2 diabetic patients.**

J Atheroscler Thromb, 2010; 17:558-567.

Key words; Diabetes, Obese, Nutrition, Energy expenditure, Indirect calorimetry

Introduction

Diet therapy is a basic and important approach for diabetic patients, especially obese patients. Daily calorie restriction is the principal method of diet therapy for type 2 diabetics. It has been reported that daily calorie restriction induced life extension not only in humans[1)] but in other species[2)]. This approach is expected to improve glycemic control or other metabolic factors of diabetic patients and to reduce the risks of complications[3, 4)]. Although it has also been recommended that various macronutrients should be taken, total calorie intake is the most important approach in aiming for a healthy weight. In spite of several studies on calorie restriction, it is still unclear how much calorie intake is required for weight control and diabetic treatment in a patient's daily life.

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Received: August 31, 2009
Accepted for publication: November 17, 2009

The American Diabetes Association (ADA) emphasizes the importance of controlling body weight (BW) to reduce the risks of diabetic complications[5]. In the ADA's recommendations, detailed values concerning energy intake for individuals are not described. Overweight patients (BMI ≥25kg/m^2) or obese patients (BMI ≥30kg/m^2) are expected to eat 500−1,000 lower calories than estimated for necessary weight maintenance. According to the recommendations of the European Association for the Study of Diabetes (EASD), it is unnecessary to give advice concerning total energy intake unless patients are overweight or steadily gaining weight over the years[6]. If patients are obese or have metabolic disturbances associated with obesity, they should be encouraged to reduce their calorie intake (at least −500 kcal/day) and to improve their BMI towards the recommended range (BMI 18.5−25.0 kg/m^2). As indicated above, the importance of diet therapy is established, but specific or unified daily calories have not been established.

A "tailor-made" diet therapy is important in each patient because dietary habits differ among patients, requiring a practical and clinical approach for each patient every day. Therefore, a definitive suggestion concerning total daily calorie intake is useful when starting a patient on diet therapy. Joslin's Diabetes Mellitus describes one method of estimating calorie intake; 1) basal calories are 10 kcal/lb desirable BW/day, and 2) add 10−40% of basal calories according to daily activity[7]. According to the recommendations of the Japan Diabetes Society (JDS), Japan Atherosclerosis Society (JAS) and Japan Society for the Study of Obesity (JASSO), total dietary calorie is calculated as follows: 1) ideal body weight (IBW) is defined as the weight that equals 22 times the square of the height, and 2) total dietary calorie (kcal/day) is estimated from the formula (25−35 kcal/kg IBW/day) depending on daily activity[8-11]. Although diet therapy based on the IBW of each patient is common in Japan, there have been few reports on BW changes after that approach.

In the present study, we adopted the diet therapy recommended by JDS, JAS and JASSO, and investigated how this approach affected the sequential changes of BW related to energy expenditure (EE) in obese and normal-weight subjects.

Subjects and Methods

Subjects

Out of 528 in-patients with type 2 diabetes mellitus, in whom resting energy expenditure (REE) was measured, 144 patients (93 men and 51 women, aged 20−79 years old) were enrolled in the present study following exclusion criteria. All were admitted for diabetic control to Nippon Medical School Hospital from 2005 to 2009. The exclusion criteria were: poor compliance with dietary management, proliferative retinopathy which limited physical activity, macroalbuminuria (urinary albumin excretion ≥300 mg/day), evidence of liver or endocrine diseases, recent myocardial infarction or cerebral vascular diseases, unstable angina pectoris, heart failure, infectious diseases and any carcinoma. Subjects were divided into two groups according to body mass index (BMI): obese group (BMI ≥25) and normal-weight group (BMI <25). IBW was estimated from the following formula, recommended by JDS and JASSO: IBW (kg) = height (m) × height (m) × 22 (BMI, kg/m^2). Following the precepts of JDS and JASSO, BMI = 22 is considered desirable or ideal for Japanese. All diets were based on JDS guidelines[8, 9, 11]. If patients were being treated with sulphonylurea, glinide or thiazolidinedione at the time of admission, these agents were stopped or switched to multiple daily insulin injection on day 2 of hospitalization after collecting the baseline data. We took the daily profile of plasma glucose level at the baseline into consideration and applied necessary and minimal doses of insulin (2−6 units in each injection) to each subject three or four times a day at the start. During hospitalization, we managed the quantity of insulin every other day appropriately. We also stopped αGI and metformin in principle but, for some patients, continued those drugs based on the judgment of the medical attendant. At discharge, in the case of patients who could not continue self-injection, we chose metformin or glinide as a substitute for insulin therapy. Subjects were informed regarding the purpose of this study and informed consent was obtained from each subject.

Methods

The subjects were checked for height, BW, and waist circumstance on the first morning of hospitalization. Systolic and diastolic blood pressures (sBP and dBP, respectively, mmHg) were measured in a sitting position after resting for more than 30 minutes in the morning. Blood samples were collected from the cubital vein after overnight fasting, and serum was prepared by centrifugation for 15 minutes at 4℃. Plasma glucose (mg/dL) and HbA1c (%) were measured by the glucose oxidase method (ADAMS Glucose GA-1170; ARKRAY, Inc., city Japan) and high performance liquid chromatography (ARKRAY Inc.), respectively. The plasma C-peptide level (ng/mL) was measured by chemiluminescent enzyme immunoassay

(Fujirebio Inc., city Japan). Serum total cholesterol (TC, mg/dL) and triglyceride (TG, mg/dL) concentrations were measured enzymatically methods (Sekisui Medical Co. Ltd., city Japan). The serum level of high-density lipoprotein cholesterol (HDL-C, mg/dL) was also measured by direct measurement (Sekisui Medical Co., Ltd.). Low-density lipoprotein cholesterol (LDL-C, mg/dL) level was calculated according to the Friedewald formula as follows: LDL-C (mg/dL) = TC (mg/dL) − HDL-C (mg/dL) − TG (mg/dL)/5, excluding 3 patients with high TG levels ≥ 400 (mg/dL). Non-HDL-C levels were calculated as the difference between TC and HDL-C levels.

Dietary treatment was started for all subjects on the day of admission. Total dietary calories (kcal/day) were calculated as 25 kcal/kg IBW, and rounded up appropriarely. The diet contained 20% calories from fat, 25% from protein and 55% from carbohydrate. Because we intended to evaluate the efficacy of the dietary program, physical activities such as walking were kept to within each patient's usual intensity without specific exercise programs. Under this dietary treatment, diurnal glucose variability was studied by measuring plasma glucose levels at seven time points (30 minutes before, and 2 hours after each meal, and at bedtime, 2100 h). The M-value was calculated according to Schlichtkrull's formula[12].

Respiratory gas exchange was continuously measured in the supine position for 30 minutes at 1500 h with an Aeromonitor (Minato Medical Science city, country), based on indirect calorimetry. After lunch (at 1200 h), the patient rested until respiratory gas measurement. The values for the last 15 minutes of a 30-minute measurement were used for analysis.

REE (kcal/min) and the respiratory quotient (RQ) were calculated according to the following formula: REE (kcal/min) = $3.9 \times VO_2$ (oxygen consumption, l/min) + $1.1 \times VCO_2$ (carbon dioxide production, l/min) (Weir's formula), and RQ = VCO_2/VO_2[13]. In general, REE is lower in the morning and increases in the afternoon, reflecting diet-induced thermogenesis (DIT). We adopted the EE measurement at 1500 h to predict the daily energy expenditure in this study. In order to confirm this condition in our subjects, the EE (kcal/min) and RQ of 21 subjects were assessed in the morning (fasting at 0900 h) and the afternoon (postprandial state at 1500 h).

Statistical Analysis

The data are expressed as the mean ± SE. Analysis was performed using computer software JMP 7.0.1 (SAS institute Inc., city, state USA). Statistical comparisons of sequential changes in BW and differences in laboratory data between obese and normal-weight groups were studied by *t*-test. Pearson's correlations between continuous variables were used for analysis of association. For exploratory purposes, a multivariate regression model was applied to determine the most statistically significant predictors of BW reduction. For all statistical analysis, *p*-values < 0.05 were considered significant.

Results

Clinical and Laboratory Data

In men, mean age (20–79 years old) was significantly lower (52 ± 2 vs. 58 ± 2, $p < 0.01$) and mean waist circumference was significantly greater (95.9 ± 1.1 vs. 83.0 ± 1.0 cm, $p < 0.0001$) in the obese group ($n = 46$) than in the normal-weight group ($n = 47$). In women, the age (24–79 years old) was not different between groups, but the waist circumference was significantly greater (98.1 ± 1.7 vs. 80.4 ± 1.9 cm, $p < 0.0001$) in the obese group ($n = 28$) than in the normal-weight group ($n = 22$).

At the time of admission, 81 of the 144 subjects (56.3%) had been treated with insulin or oral antidiabetic agents. Hypertension was observed in 74 cases (51.4%), and 47 hypertensive subjects were treated with anti-hypertensive agents. The number of subjects who did not have insulin therapy through hospitalization was 10 in the obese group and 10 in the normal-weight group. During hospitalization, there were no differences in the therapeutic approaches to blood glucose control between groups; diet/exercise alone was 9.3% and 7.2%, insulin was 86.7% and 85.5%, and others were 4.0% and 7.2% in the obese and normal-weight groups, respectively. No adverse effect of the therapy, such as severe hypoglycemia, was observed during hospitalization. At discharge, 6 patients in the obese group and 8 in the normal-weight group changed treatment to approaches other than insulin (diet and exercise, metformin or glinide). We used glinide as a change of treatment in one patient in the obese group and 7 in the normal-weight group. There were no differences in the therapeutic approach to hyperlipidemia between groups; statins were 12.0% (9 cases) and 15.9% (11 cases), fibrate was 1.0% (2 cases) and 4.3% (3 cases), eicosapentaenoic acid was 0% (0 case) and 1.4% (1 case), and ezetimibe was 0% (0 case) and 1.4% (1 case) in the obese and normal-weight groups, respectively. Other hypolipidemic compounds were not used.

Fasting plasma C-peptide levels were also significantly higher ($p < 0.005$) in the obese group (2.29 ± 0.10 ng/mL) than in the normal-weight group (1.83

Table 1. Clinical and laboratory characteristics of obese and normal-weight group

Characteristic	obese ($n=75$)		p value (baseline vs. discharge)	normal-weight ($n=69$)		p value (baseline vs. discharge)
	baseline	discharge		baseline	discharge	
No. of males	46			47		
Age (yr)	53 ± 2 [§]			58 ± 1		
Duration of hospitalization	15.1 ± 2.5			15.4 ± 2.8		
BW (kg)	77.9 ± 1.4 [†]	75.4 ± 1.4 [†]	< 0.0001	59.4 ± 1.0	58.1 ± 1.0	< 0.0001
BW change (kg)		− 2.5 ± 0.2 [†]			− 1.3 ± 0.2	
BW change (g/day)		− 171 ± 12 [†]			− 92 ± 11	
BMI (kg/m^2)	28.9 ± 0.4 [†]	28.0 ± 0.4 [†]	< 0.0001	22.2 ± 0.2	21.7 ± 0.2	< 0.0001
BMI change (kg/m^2)		− 0.93 ± 0.06 [†]			− 0.48 ± 0.06	
Systolic BP (mmHg)	133 ± 2	122 ± 1	< 0.0001	130 ± 2	119 ± 1	< 0.0001
Diastolic BP (mmHg)	80 ± 2	71 ± 1	< 0.0001	77 ± 1	70 ± 1	< 0.0001
FPG (mg/dL)	169 ± 7	144 ± 2	< 0.0001	172 ± 6	115 ± 3	< 0.0001
HbA1c (%)	9.4 ± 0.2			9.9 ± 0.2		
Duration of diabetes (yr)	7.5 ± 1.0			6.7 ± 1.0		
M value	42.7 ± 5.9	11.9 ± 1.1	< 0.0001	44.7 ± 5.0	11.2 ± 0.9	< 0.0001
Therapeutic approaches (n)						
Diet and excise only	30	7		33	5	
Insulin	14	59		4	51	
Amount of insulin at discharge (U/day)		25.4 ± 1.4			23.8 ± 1.3	
SU	23	0		20	0	
Glinide	5	1		4	7	
αGI	12	0		8	4	
Metformin	22	14		12	8	
Thiazolidinedione	6	0		2	0	
Total cholesterol (mg/dL)	207 ± 4	182 ± 4	< 0.0001	201 ± 4	185 ± 4	< 0.0001
HDL-C (mg/dL)	45 ± 1 [§]	41 ± 1 [§]	< 0.0001	50 ± 2	45 ± 1	< 0.0001
LDL-C (mg/dL)	129 ± 3	116 ± 4	0.0005	125 ± 4	117 ± 3	0.0005
	(72 subjects)					
Non HDL-C (mg/dL)	163 ± 4	141 ± 4	< 0.0001	151 ± 4	140 ± 4	0.0002
Triglyceride (mg/dL)	182 ± 21 [§]	127 ± 10	< 0.0001	130 ± 7	114 ± 7	0.0069

Differences between obese and normal-weight groups were assessed by unpaired t-test ([†]$p<0.005$, [§]$p<0.05$, respectively). LDL-C levels was calculated according to the Friedewald formula. Three subjects in obese group were excluded from statistical analysisof LDL-C, because they had hypertriglyceridemia (400 mg/dL) at the baseline. Differences between baseline and discharge were assessed by paired t-test. Data are the mean ± S.E.

± 0.10 ng/mL). There were no differences in the duration of diabetes, fasting plasma glucose (FPG), HbA1c levels, and M-values between groups, and these data indicated poor control of diabetes.

The laboratory data at the two points of baseline and discharge are shown in **Table 1**. The duration of hospitalization was 10−21 days and no difference was observed between groups. Blood pressure in the two groups decreased similarly and significantly during hospitalization, even if anti-hypertensive agents were not changed. With short-term intensive therapy, FPG and M-value significantly decreased, and did not differ between groups. There was a significant decrease in serum lipid levels (TC, HDL-C, LDL-C, non-HDL-C and TG) in both groups. These statistical tendencies were observed when subjects treated with hypolipidemic agents were excluded.

Sequential Changes in Body Weight and BMI

BW and BMI changes are shown in **Table 1**. BW and BMI in the obese group were significantly greater than in the normal-weight group. The decrease of BW was − 2.5 ± 0.2 kg (171 ± 12 g/day) in the obese group and −1.3 ± 0.2 kg (92 ± 11 g/day) in the normal-weight group during hospitalization. The decrease of BMI was − 0.93 ± 0.06 kg/m^2 and − 0.48 ± 0.06 kg/m^2, respectively. BW and BMI changes were significantly greater in the obese group than in the normal-

Table 2. Comparison of energy metabolism between obese and normal-weight group

Characteristic	obese ($n=75$)	normal-weight ($n=69$)	p value (over vs. normal)
Dietary calories (kcal)	1,545 ± 19	1,570 ± 20	NS
Dietary calories/IBW (kcal/kg)	26.1 ± 0.2	26.8 ± 0.2	0.0065
REE (kcal/min)	1.23 ± 0.02	1.04 ± 0.02	< 0.0001
Daily energy expenditure (kcal/day)	1,767 ± 31	1,501 ± 33	< 0.0001
Δcalorie (kcal)	− 222 ± 26	69 ± 27	< 0.0001
RQ	0.85 ± 0.01	0.88 ± 0.01	0.0028

Daily energy expenditure was calculated by the formula as follows; Daily energy expenditure = REE (kcal/min) × 60 (min) × 24 (hour). The difference in dietary calories minus daily energy expenditure is expressed as Δcalorie. Data are the mean ± S.E.

weight group (**Table 1**). Waist circumstance was significantly decreased in the obese group (96.9 ± 1.1 to 94.3 ± 1.0 cm, $p<0.0001$) and the normal-weight group (82.4 ± 1.0 to 79.3 ± 0.9 cm, $p<0.0001$), respectively.

Energy Metabolism

Energy metabolism is shown in **Table 2**. Daily calorie intake was almost identical in the obese group (1,545 kcal/day) and the normal-weight group (1,570 kcal/day). REE (kcal/min) was significantly greater in the obese group than in the normal-weight group; therefore, the difference between the real calorie intake (dietary calorie, kcal/day) and daily EE [REE (kcal/min) × 60 (min) × 24 (hour)], which was expressed as Δcalorie, was a negative value in the obese group (**Table 2**). RQ was significantly lower in the obese group than in the normal-weight group. These results suggested that the daily calorie intake indicated by JDS was appropriate for the EE of sedentary normal-weight subjects, whereas it has been calculated for obese subjects.

EE (kcal/min) was studied in 21 subjects at 0900 h and 1500 h, as shown in **Fig. 1**. It was increased in the afternoon compared to in the morning and the increment was thought to result from the meal effect (**Fig. 1A**). In the obese group, EE increase (1.09 ± 0.23 to 1.20 ± 0.25 kcal/min) was significant, whereas the increase in the normal-weight group (0.87 ± 0.16 to 0.94 ± 0.17 kcal/min) was small (**Fig. 1C**). One-way analysis of variance (ANOVA) did not show a significant difference between the EE increments of the two groups.

On the other hand, the RQ significantly rose from 0900 h to 1500 h, reflecting increased carbohydrate oxidation (**Fig. 1B**). When subjects were divided into two groups, the RQ of the normal-weight group rose significantly in the afternoon compared to in the morning, but that of the obese group did not (**Fig. 1D**). ANOVA did not show a significant difference in the rise of RQ between groups.

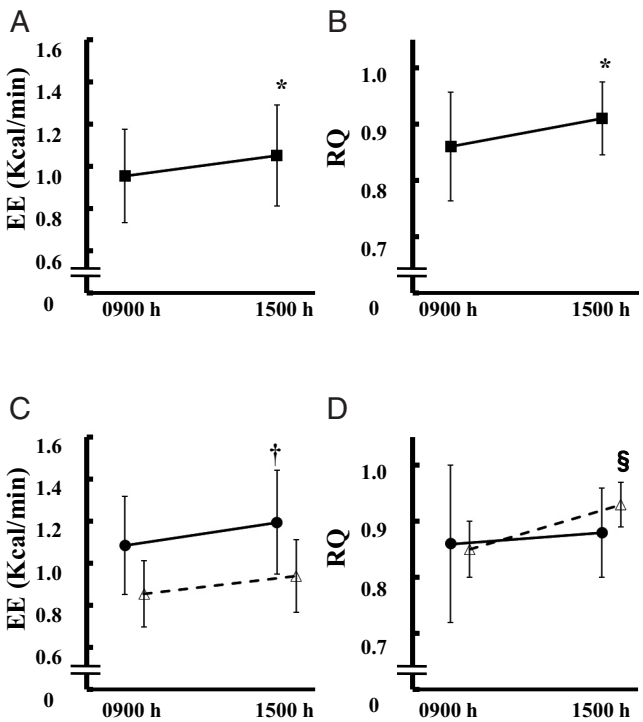

Fig. 1. A, B: Differences of all subjects' EE (A), and RQ (B), from 0900 h to 1500 h were assessed by paired t-test ($n=21$, $^{*}p<0.05$). C, D: Changes of EE (C) and RQ (D) from 0900 h to 1500 h were assessed by paired t-test in the subgroup by BMI. In the obese group (closed circle, $n=9$), EE increased significantly ($^{\dagger}p<0.05$), but RQ change was not significant. In the normal-weight group (open triangle, $n=12$), EE change was not significant, whereas the RQ increased significantly ($^{\S}p<0.05$). Data are expressed as the mean ± SD.

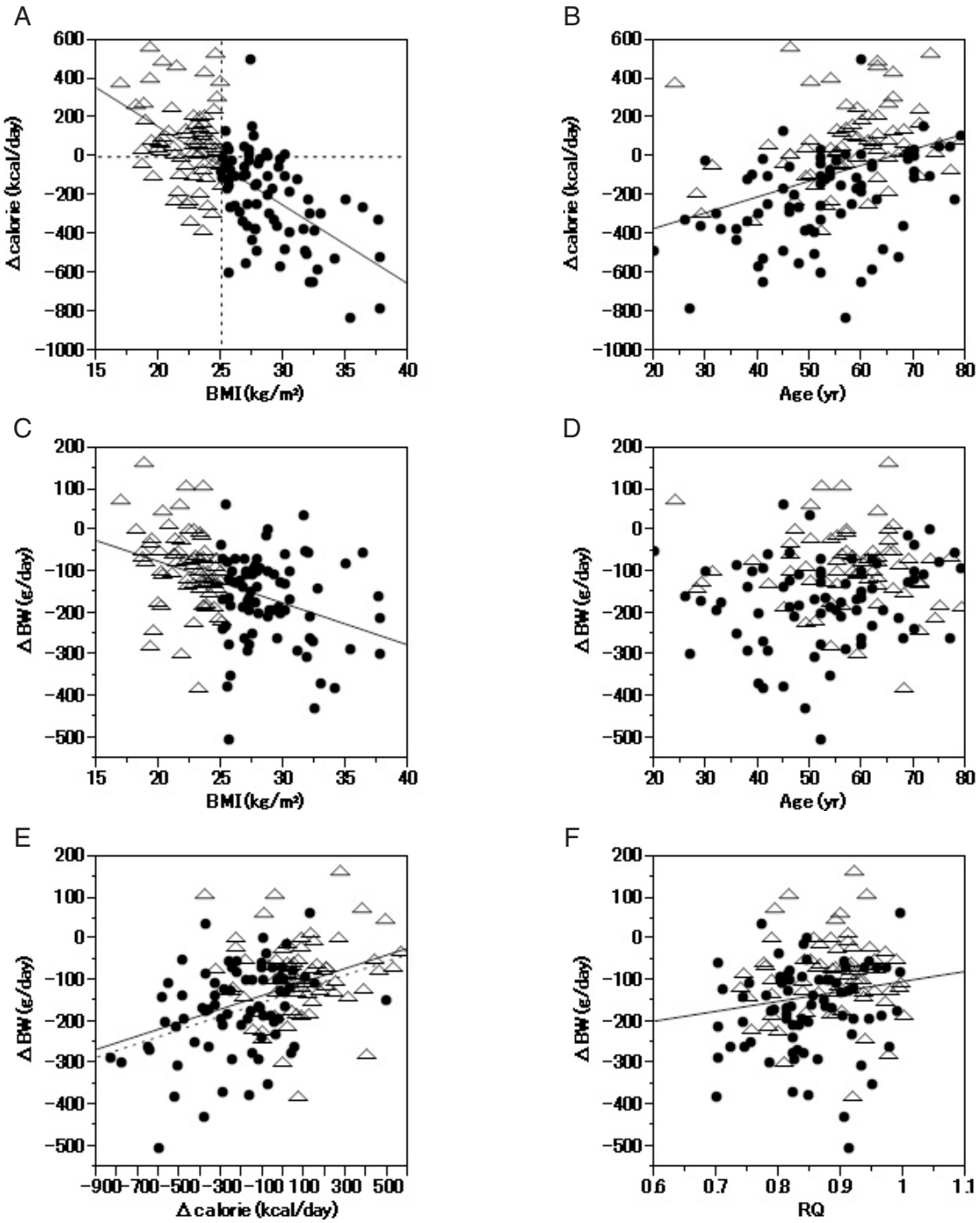

Fig. 2. A, B: Δcalorie (kcal) in relation to BMI (A) and age (B). There was a negative correlation between Δcalorie and BMI ($r=0.656$, $p<0.0001$), and a positive correlation between Δcalorie and age ($r=0.383$, $p<0.0001$). C, D: ΔBW (g/day) in relation to BMI (C) and age (D). There was a positive correlation between ΔBW and BMI ($r=0.397$, $p<0.0001$), whereas there was no relation between ΔBW and age. E: There was a positive correlation between Δcalorie (kcal/day) and ΔBW (g/day) in all subjects (straight line, $r=0.398$, $p<0.0001$). In the obese group, Δcalorie was related to ΔBW (dotted line, $r=0.370$, $p=0.011$). Such a correlation was not observed in the normal-weight group. F: There was a positive correlation between RQ and ΔBW (g/day) in all subjects ($r=0.164$, $p=0.049$). When subjects were divided into two groups, such a correlation was not observed. Closed circle and open triangle indicate obese and normal-weight groups, respectively.

Table 3. Multiple regression models predicting body weight changes

(Obese group)	Model 1			Model 2			Model 3		
Variable	β coefficient	*t* value	*p* value	β coefficient	*t* value	*p* value	β coefficient	*t* value	*p* value
Gender [F]				−0.098	−0.79	0.432	−0.097	−0.77	0.442
Age	0.021	0.18	0.858	0.022	0.19	0.853	0.022	0.18	0.855
BMI	0.090	0.69	0.493	0.1343	0.97	0.335	0.142	0.95	0.346
Δcalorie	0.411	2.93	0.005	0.444	3.02	0.004	0.447	2.94	0.004
RQ							−0.011	−0.09	0.929
r^2			0.14			0.15			0.15
p value			0.012			0.021			0.042

(Normal-weight group)	Model 1			Model 2			Model 3		
Variable	β coefficient	*t* value	*p* value	β coefficient	*t* value	*p* value	β coefficient	*t* value	*p* value
Gender [F]				0.059	0.49	0.624	0.057	0.47	0.643
Age	−0.140	−0.14	0.258	−0.133	−1.08	0.286	−0.133	−1.07	0.289
BMI	0.274	−2.25	0.028	−0.268	−2.18	0.033	−0.269	−2.14	0.036
Δcalorie	0.055	0.44	0.660	0.056	0.44	0.660	0.057	0.44	0.661
RQ							−0.006	−0.05	0.960
r^2			0.11			0.11			0.11
p value			0.060			0.108			0.184

Model 1 was adjusted for age, BMI and Δcalorie. Model 2 was adjusted for gender, age, BMI and Δcalorie. Model 3 was adjusted for gender, age, BMI, Δcalorie and RQ.

Correlation between Energy Balance and Body Weight Change

The relationship between Δcalorie and BMI or age is shown in **Fig. 2A**, **2B**. EE increased following the increase of BMI or BW and, as a result, the value of Δcalorie became negative. There was a positive correlation between Δcalorie and age. The data showed that aging induced the decrease of EE and dietary calorie was relatively high compared to EE.

We defined ΔBW (g/day) as BW change divided the duration of hospitalization. The relationship between ΔBW (g/day) and BMI or age is shown in **Fig. 2C**, **2D**. The absolute value of ΔBW increased following the increase of BMI, whereas there was no relation between ΔBW and age. In the obese group, a positive correlation was found between ΔBW and Δcalorie, as shown in **Fig. 2E**. Such a correlation was not observed in the normal-weight group. The data suggested that negative energy balance would induce BW change, especially in the obese group. A weak positive correlation ($r=0.164$) between RQ and ΔBW of all subjects was found, but there was no relation in each group when subjects were divided into two groups (**Fig. 2F**).

To define the effect of the negative energy balance on BW change, multiple regression analysis was studied (**Table 3**). In the obese group, ΔBW was significantly related with Δcalorie, which was the difference between real energy intake and EE. This relationship was preserved after adjusting for age, BMI, gender, and RQ, as shown in Model 1, 2, and 3. The normal-weight group had a negative correlation between BMI and ΔBW, whereas Δcalorie was not related to ΔBW. The RQ correlated to ΔBW in all subjects (**Fig. 2F**, $r=0.398$, $p<0.0001$), but the relationship disappeared after adjusting for age, BMI or Δcalorie (data not shown). These results suggest that obese subjects were more easily able to decrease BW than the normal-weight subjects, and the diet instructions from JDS had more efficacy for obese subjects. These instructions indicated an appropriate negative energy balance inducing BW reduction in obese subjects.

Discussion

Until now, specific calorie restriction has not been clearly established in diet therapy for diabetes mellitus, especially for obese subjects. JDS, JAS and JASSO have recommended that daily calorie intake should be calculated from IBW, as shown above, but BW changes after diet therapy were not clearly indicated by energy balance, shown as "Δcalorie", which

means the difference between dietary calorie intake and EE. The present study indicated that the specific diet therapy induced a negative energy balance in obese subjects and, as a result, BW reduction was effectively achieved during short-term hospitalization.

Previous reports have shown that BW decreased by dietary calorie restriction[14] and a decrease of 0.5–0.9 kg/week could be achieved by calorie restriction of 500–1,000 kcal/day[5]; however, standard or specific daily total calorie has not been indicated, except in the JDS recommendations. A method for establishing the desirable BW and calorie requirement is indicated in the textbook Joslin's Diabetes Mellitus. It is recommended that frame size be calculated based on height, and basal calories were 10 kcal/pound. Total daily calorie intake should be calculated from the above considerations and additional calories should be supplemented by taking physical activity into consideration. JDS's recommendations for diet therapy are similar to the concepts in Joslin's Diabetes Mellitus; body size is shown as IBW, and the daily total calorie is 25–35 kcal/kg IBW, depending on physical activity. In the present study we determined daily dietary energy according to the recommendations of JDS, and BW reduction (2.5 and 1.3 kg in obese and normal-weight groups, respectively) was achieved during short-term hospitalization. Thus, BW reduction was greater in the obese than in the normal-weight group. These results suggested that a diet therapy program in accordance with JDS's recommendations would be appropriate to maintain a healthy BW.

The difference (Δcalorie) between specific dietary calorie and EE in obese patients was a minus number (−222 kcal/day), and this negative energy balance might have induced BW reduction (−171 g/day) during hospitalization. The total daily calorie calculated according to JDS's recommendation was similar for both the obese and normal-weight groups. The present study suggested that dietary calories based on IBW could be easily calculated and put into practice for all patients. In addition, our data suggested that the instructions calculated the dietary calories as lower than the real energy expenditure, especially in young obese subjects, whose BW was expected to decrease. We did not assess the exact lean body mass or body composition changes related to BW reduction; however, it was thought that their mesenteric fat mass had decreased effectively because the waist circumference had decreased in both groups.

The dietary program and multiple daily insulin injections during short-term hospitalization improved not only hyperglycemia but also dyslipidemia in both groups (**Table 1**). Although HDL-C levels decreased in both groups in this study, this result might have been caused by the reduction of total cholesterol levels. Some studies have shown that dietary intervention reduced HDL-C levels accompanied by an overall reduction of cholesterol levels[4, 15].

The most important component of the energy requirement is basal energy expenditure (BEE), which accounts for about 60–75% of the daily EE in a sedentary person[16-18]. Although the Harris-Benedict formula can be used to calculate BEE[19], calorimetry is more accurate[20]. The increase of EE is induced by food intake, digestion, absorption and energy storage; diet-induced thermogenesis (DIT)[21, 22], and the energy is also consumed by activities [AEE and NEAT; activity energy expenditure and nonexercise active thermogenesis][23, 24], each of which comprises daily EE. The human respiratory chamber is sometimes used for the exact measurement of total daily EE over 24 hours, but this system is not convenient. In the present study we used the Aeromonitor, because total EE could be estimated based on short-term measurement. We adopted the EE measurement at 1500 h to predict daily energy expenditure in this study. This value was able to reflect the each subject's BEE and individual DIT. In this study, EE related to physical activities was similar among subjects, because all subjects were hospitalized and their physical activities were kept to the usual intensity of each patient without a specific exercise program. It is well known that DIT accounts for about 10% of REE[21]. The increment of EE from 0900 h to 1500 h could reflect DIT, and the changes (8.0–10.1%) were similar to a previous report[21] (**Fig. 1A**); therefore, measuring EE at 1500 h was thought to be an appropriate method of estimating total EE for sedentary subjects.

There are many arguments about why patients are obese in spite of a high total EE. Several studies have indicated that obese subjects show a lower DIT[22]; but some investigators have recently shown no difference in DIT between non-obese and obese subjects[25]. Our data did not show any difference between obese and normal-weight subjects in EE increase from pre-prandial (0900 h) to post-prandial (1500 h) measurements (**Fig. 1C**). It is supposed that DIT variation cannot explain the metabolic characteristic of the obese subjects.

The mean RQ tended to be lower in the obese group than in the normal-weight group. The obese group did not show a significant increase of RQ from 0900 h to 1500 h although the normal-weight group did (**Fig. 1D**). Some studies have reported that a high RQ was associated with BW and predicted BW gain[26-28], while others did not show an association

between RQ and subsequent BW changes[29]. Although it is controversial whether RQ is related to the development of obesity, a high RQ obviously indicates that carbohydrates, rather than lipids, are utilized for oxidation and lipogenesis. In our study, the difference in RQ between the two groups would seem to reflect disorders of glucose metabolism or greater insulin resistance in obese subjects. As shown in **Fig. 2F** and **Table 3**, however, the RQ value might only correlate to BW reduction weakly.

REE is often measured to estimate necessary calorie intake, but it varies according to gender, age, BMI and lean body mass. It is reported that race and diabetes status also influence REE[30]. The EE of our subjects, whose HbA1c levels were high at baseline, might be a little higher than the values of normoglycemia populations[30]. A limitation of our study was that REE change after discharge was not measured. It has been reported that REE normalized and decreased after glycemic control or weight reduction[31, 32]. Whether that change would influence the efficacy of calorie restriction after discharge is unknown and should be explored for a long-term period. Even after taking this limitation into consideration, this study should contribute to the initial approach of developing a practical dietary program for patients with diabetes mellitus, dyslipidemia or obesity.

In conclusion, the diet therapy recommended by JDS, JAS and JASSO can be a useful and simple program for the control of BW, hyperglycemia and hyperlipidemia in the daily life. Total daily calories are simply calculated from IBW, as shown here. IBW is not an absolute value, and is based on the appropriate BMI, which is 22 in Japan. The optimum BMI and the setting of IBW will vary among countries and patients. The concept of this diet therapy may be appropriate and practical for concrete calculation of total daily calories, which brings this therapy close to "tailor-made therapy".

Acknowledgments

This study was partially supported by the Committee for the Dietary Management for the Diabetic Patients, Japan Diabetes Society. We are grateful to the staff of the Department of Nutrition, Nippon Medical School Hospital.

Conflicts of Interest

All authors reviewed the manuscript. The authors declare no conflicts of interest.

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