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Original Article

Development and application of a new equation for estimating energy requirement in metabolic syndrome in a Chinese population

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Abstract: Purpose: A negative energy balance (i.e., daily energy intake less than energy expenditure) is important for dietary interventions in metabolic syndrome (MetS). This study aimed to develop a new energy requirement equation on the basis of negative energy balance to guide dietary intervention with MetS. Methods: This study included two phases. First we developed a new equation for the energy requirement in MetS based on the daily total energy expenditure and daily energy reduction corresponding to a 5~10% annual weight loss in 1292 MetS patients. Second, we randomly assigned 493 MetS patients from the first phase who had greater energy intake than energy expenditure to three groups, including one experimental group and two control groups. For the experimental group (group A, n=164), we estimated the energy requirement using the new estimating equation derived from the first phase, whereas for the control groups, we used either a previously developed energy estimation model for MetS (group B, n=163) or the traditional food exchange method (group C, n=166). Results: After a 6-month intervention, we observed a significant reduction in weight (73.69±7.25 vs.70.19±6.86 kg), waist circumference (92.42±7.13 vs. 88.58±6.75 cm), 2-h postprandial blood glucose (10.63±5.41 vs. 7.53±4.26 mmol/L), and triglyceride level (2.92±1.45 vs. 1.44±1.12 mmol/L) in patients of group A, in parallel with a reduction in energy intake (9.30±2.79 vs. 6.70±1.85 MJ/d). All these changes were significantly different from the measurements in groups B and C over the same period ($P<0.05$). Conclusion: A new energy requirement equation based on a negative energy balance improves the effect of dietary intervention on weight, waist circumference, glucose, and triglycerides in MetS patients.

Keywords: Metabolic syndrome, energy intake, energy expenditure, negative energy balance, equation, dietary intervention

Introduction

Metabolic syndrome (MetS) is a cluster of interrelated cardiometabolic risk factors that are closely related to increased cardiovascular morbidity and mortality [1-3]. Abdominal obesity, dyslipidemia, high blood pressure, and dysglycemia are generally regarded as the main components of MetS [4]. With the progress of urbanization, excessive energy intake, changes in lifestyle, and the increasing obesity prevalence, MetS has emerged as a global epidemic, becoming a public health threat worldwide. In China, the current prevalence of MetS is greater than 15%, representing more than 200 million patients with MetS [5]. Current treatments for MetS are actually aimed at controlling the main components of MetS, such as dyslipidemia, high blood pressure, and hyperglycemia [6].

It is widely accepted that dietary factors play a vital role in the development and treatment of MetS [7, 8]. Therapeutic lifestyle intervention, targeting improved insulin resistance and weight reduction, should be implemented at the initial stage and throughout the whole course of MetS treatment [9, 10]. Controlling energy intake is particularly important for therapeutic lifestyle intervention [11]. Therefore, an accurate estimation of the energy requirement is required to avoid energy excess or shortage

[12, 13]. The most commonly used energy calculation formula for MetS patients is the food exchange method for diabetics [14]. This method, however, does not take into account gender and age, and thus, gives the same energy requirement for a 30-year-old man and an 80-year-old woman as long as they have the same standard weight, body shape, and physical activity levels. The lack of an individualized calculation method results in poor clinical control of lipid metabolism and glucose metabolism.

In a previous study, we explored a new energy calculation model for MetS [15], which improves the management of waist circumference, blood glucose, and insulin resistance index among MetS patients in clinical practice. However, we observed several limitations of the model in further clinical research. First, body mass index (BMI), calculated as body weight (kg) divided by squared height (m), was included in the model as a predictor of energy requirement. This reduced the influence of height, and thus, compromised the sensitivity of the model to height. Second, ambient temperature was taken into account in the model. However, with the wide use of air conditioners, the impact of the ambient temperature on MetS patients' energy requirement is reduced and may even be negligible.

The current study was carried out to improve the estimation of the energy requirement in patients with MetS, incorporating the concept of negative energy balance. Healthy body weight is maintained by a balance between daily energy intake and energy expenditure. Among MetS patients, energy intake is usually greater than energy expenditure, so the body is in positive energy balance. In this condition, excessive energy accumulates in the abdomen in the form of fat. Therefore, the International Diabetes Federation (IDF) recommends that a healthy lifestyle with moderate energy restriction to achieve 5-10% weight loss in the first year should be the primary intervention for MetS patients [16].

In this study, we aimed to develop a new equation for estimating the energy requirement with MetS based on the principle of negative energy balance and to evaluate its utility in comparison with our previous model and the widely used food exchange method for diabetics in a clinical study.

Methods

Part I. Development of a new energy requirement equation in MetS patients

Study population: A total of 1292 MetS patients were recruited between January 2007 and June 2014 from the Health Examination Center, the Department of Endocrinology, and the Department of Nutrition of Xi'an Central Hospital affiliated with Xi'an Jiaotong University. All the MetS cases were diagnosed according to the diagnostic criteria described in a clinical guideline from the Chinese Diabetes Society [17]. A clinical diagnosis of MetS was made if three or more of the following five criteria were met: (1) abdominal obesity: waist circumference ≥90 cm in men or ≥85 cm in women; (2) hyperglycemia: fasting plasma glucose (FPG) ≥6.1 mmol/L or blood glucose level 2 h after glucose load ≥7.8 mmol/L, or previous diagnosis and treatment of diabetes; (3) high blood pressure: blood pressure ≥130/85 mmHg (1 mmHg=0.133 kPa), or previous diagnosis and treatment of hypertension; (4) elevated level of triglycerides (TG): fasting TG ≥1.70 mmol/L; and (5) reduced level of high-density lipoprotein cholesterol (HDL-C): fasting HDL-C <1.04 mmol/L. The Xi'an Central Hospital affiliated with Xi'an Jiaotong University's Ethics Committee approved the study protocol, and all participants provided written informed consent.

Demographic and clinical data, including age, gender, education, occupation, duration of disease, height, weight, waist circumference, physical labor, and medication history were collected. The types and amounts of individual foods consumed during two week days and one weekend day were also assessed using the food frequency questionnaire (FFQ) and the 24-h dietary recall method, and total energy intake was calculated.

Estimation of daily total energy expenditure and energy requirement: We first estimated the participants' daily total energy expenditure. Basal energy expenditure (i.e., the amount of energy expended while at complete rest) was estimated using a pulmonary function test instrument (COSMED, Italy). Daily energy expenditure during physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) [18]. The thermic effect of food (i.e., the energy required to digest and absorb food) was assumed to be 10% of the total energy expenditure in all adults consuming a mixed diet [19]. The daily total energy expenditure was calculated as: daily total energy expenditure=basic energy expenditure ×1.1+ energy expenditure during physical activity.

Next, we estimated daily energy reduction. The IDF recommends a 5~10% weight loss in the first year for MetS patients [16]. Accordingly, we set the goal of weight loss as 10% of the initial body weight within 1 year for MetS patients who were obese (BMI >28.0 kg/m^2), 7.5% for MetS patients who were moderately overweight (BMI: 26.0~27.9 kg/m^2), and 5% for MetS patients who were mildly overweight (BMI: 24.0~25.9 kg/m^2).

Given that a 1-kg body weight reduction equates to an energy expenditure of 29.29 MJ [20], we calculated the amount of daily energy reduction according to the weight loss goal for each participant.

As a result, the daily energy requirement of MetS patients for negative energy balance was estimated as: the daily energy requirement for negative energy balance=daily total energy expenditure-daily energy reduction.

Data analysis: We analyzed the determinants of the daily energy requirement in MetS patients for negative energy balance using a multivariable linear regression analysis. We included the daily energy requirement of MetS patients for negative energy balance as the dependent variable, and the potential factors, such as age (year), gender (female=0, male=1), height (cm), weight (kg), waist circumference (cm), and types of physical labor (low physical labor=0, moderate physical labor=1) as independent variables. Data analysis was performed using SPSS software version 15.0 (Chicago, IL, USA).

Part II. Application of the new energy requirement equation in MetS patients

Study population: To evaluate the clinical utility of the new energy requirement equation taking negative energy balance into account, we conducted an intervention study between July 2014 and August 2015 among 493 MetS patients from participants in the first phase. Patients who had chronic complications of diabetes (e.g., diabetic nephropathy, diabetic retinopathy, and diabetic peripheral neuropathy) and other chronic diseases (e.g., chronic liver disease, kidney diseases, and endocrine diseases) were excluded.

This study was approved by the Ethics Committee of the Xi'an Central Hospital affiliated with Xi'an Jiaotong University. Before participating in the study, the subjects and their families were informed of the importance of diet in the prevention of MetS treatment and which examinations and tests would be conducted during the study. All the patients signed a written informed consent form. Throughout the study, the patients' privacy and treatment information were protected.

Randomization and intervention: Using computer-generated random numbers, the patients were randomly assigned to three dietary intervention groups. The whole process of randomization was blinded to the investigator. The differences in the groups were the ways their energy requirements were estimated: group A (n=164), the new equation based on negative energy balance; group B (n=163), our previous model [15]; and group C (n=166), the traditional food exchange method [14]. After the energy requirement was calculated, patients in all three groups received dietary intervention following the same procedures but corresponding to their personalized energy requirements. First, they were instructed to learn specific recipes for daily meals in a Chinese book entitled "Healthful Lifestyle and Standardized Nutrition Therapy for Metabolic Syndrome" [21]. Second, in order to increase the diversity of food choices, specific food items for equivalent exchange were provided in the "Food Exchange Table" [21]. Third, the weight of different food items in common food containers was provided in the "Food Meter Table" [21], so the amount of different food items can be estimated without weighing. Fourth, a specific "Food Allowance and Taboos Table" [21] was provided to disseminate information regarding which food combinations should be prohibited, limited, allowed, or encouraged from nutrition and food safety perspectives. After the participants were admitted to the hospital, a dietitian or a specialty nurse explained all of the above in detail to the patients and their families and provided specific guidance as illustrated by a food model, until the participants fully understood.

Table 1. Characteristics of participants in Part I (development of new energy requirement equation)

Variables		Men	Women
Number of participants		921	371
Age (years)		52±22	53±21
Education	College or higher	396	93
	Middle school	340	178
	Primary school or lower	185	100
Occupation	White-collar worker	414	208
	Blue-collar worker	507	163
Duration of disease (years)		7±5	6±3
Height (cm)		170.14±5.31	157.24±6.36
Weight (kg)		80.68±7.25	64.27±6.86
Waist circumference (cm)		99.25±7.42	86.24±6.24
Physical labor	Low physical labor	672	341
	Moderate physical labor	249	30
Energy intake (MJ/d)		10.45±1.68	6.94±1.38
Energy expenditure (MJ/d)		8.89±0.84	6.07±0.76

All three groups were given the same instructions regarding physical activity and pharmaceutical treatments.

Follow-up and data collection: Telephone follow-up was done in the first week after patients were discharged from the hospital, and then telephone follow-up was done every 2 weeks for the first 6 months. If patients had any questions, they could contact the dietitian or the specialty nurse as needed. At the 6th month, patients returned to the hospital for a face-to-face interview and health examination.

The participants provided information on their age, gender, education level, and medical history in a questionnaire. Anthropometric measures, including height, weight, and waist circumference, were conducted using standardized methods. Body mass index (BMI) was calculated as body weight (kg) divided by the square of height (m). Blood pressure was measured using a desktop mercury sphygmomanometer, according to an international standardized method. Basal energy expenditure was measured in the morning using a Cardiopulmonary Exercise Testing System (COSMED, Italy), when the participant was awake, fasting, quiet, supine, and without mental stress, and the room temperature was between 20-25°C. The food frequency questionnaire (FFQ) and the 24-h dietary recall method were used to collect information on the types and amounts of foods consumed in 3 consecutive days (2 weekdays and one weekend day), and total energy intake was calculated using nutrient estimation software by Shanghai Zhending Health Science Co., Ltd. The International Physical Activity Questionnaire (IPAQ) was used to assess daily physical activities. Quality control and calculation of physical activity energy expenditure was performed according to standard methods.

Fasting blood samples were collected to analyze glucose and lipid parameters. Fasting plasma glucose (FPG) was measured using the glucose oxidase method, triglycerides (TG) using the glycerol phosphate oxidase (GPO)-peroxidase (POD) method, and high-density lipoprotein cholesterol (HDL-C) using the dextran sulfate-magnesium precipitation method, all on an Olympus AU 600 biochemistry analyzer (Hitachi, Japan). Glycated hemoglobin (HbA1C) was measured by high pressure liquid chromatography with the Bio-Rad D-10 automatic glycated hemoglobin analyzer (Bio-Rad, USA), with the accompanying reagents (Bio-Rad, USA).

Data analysis: After double entry, all the data were checked and analyzed using SPSS software version 15.0 (Chicago, IL, USA). Variables were analyzed for inter-group differences. Fisher χ^2 test was used to compare categorical data between two or among three groups. When comparing data with normal distribution between different periods of the same group, the paired t-test was used, and analysis of variance was used when comparing data with normal distribution between the same periods of three groups. $P<0.05$ was considered statistically significant.

Results

Development of the new energy requirement equation for MetS patients

We included 1292 patients with MetS (921 men, average age 52±22 years; 371 women, average age 53±21 years) in the phase of

Table 2. Variables and respective beta coefficients in the derived new energy requirement equation

Variables	Beta coefficient	Standard Error	95% CI	*P* value
Constant	-5.172	0.135	/	<0.001
Age	-0.030	0.000	-0.031, -0.029	<0.001
Gender	0.287	0.010	0.232, 0.342	<0.001
Height	0.131	0.001	0.123, 0.139	<0.001
Weight	-0.104	0.001	-0.139, -0.069	<0.001
Waist circumference	-0.031	0.001	-0.035, -0.028	<0.001
Physical labor	0.263	0.007	0.210, 0.315	<0.001

Dependent variable: the daily energy requirement.

Table 3. Baseline characteristics of participants in Part II (application of the new energy requirement equation)

Variables	Group A (n=164)	Group B (n=163)	Group C (n=166)
Age (years)	56±8	58±5	57±7
Gender (Male/Female)	105/59	111/52	104/62
Education (C/M/P)*	27/96/41	24/100/39	28/103/35
Duration of disease (years)	4.2±3.1	4.8±3.7	4.4±3.2
Occupation (W/B)#	116/48	113/50	122/44

There were no significant differences among groups in age, gender, education, and occupation (P>0.05). *For educational level: C, College or higher; M, Middle school; P, Primary school or lower. #For occupation: W, white-collar worker; B, blue-collar worker.

developing the new energy requirement equation. The average height, weight, and waist circumference were 170.14±5.31 cm, 80.68±7.25 kg, and 99.25±7.42 cm, respectively, among men and 157.24±6.36 cm, 64.27±6.86 kg, and 86.24±6.24 cm, respectively, among women. The energy intake and energy expenditure (MJ/d) were 10.45±1.68 MJ and 8.89±0.84 MJ, respectively, among men and 6.94±1.38 MJ and 6.07±0.76 MJ, respectively, among women (**Table 1**).

In the linear regression model, we found significant associations between the daily energy requirement and several variables: age (B=-0.030, 95% confidence interval [CI]: -0.031~-0.029), gender (B=0.287, 95% CI: 0.232~0.342), height (B=0.131, 95% CI: 0.123~0.139), weight (B=-0.104, 95% CI: -0.139~-0.069), waist circumference (B=-0.031, 95% CI: -0.035~-0.028), and physical labor (B=0.263, 95% CI: 0.210~0.315; **Table 2**). Accordingly, we derived the daily energy requirement equation for MetS patients for negative energy balance as follows: the daily energy requirement =-0.030× age +0.287× gender +0.131× height -0.104× weight -0.031× waist circumference +0.263× physical labor -5.172. The range of the daily energy requirement was set between 4.18 and 8.79 MJ [15].

Application of the new energy requirement equation for diet intervention among MetS patients

Table 3 shows baseline parameters of general information in the three groups of MetS patients. There was no significant difference in gender, age, educational level, occupation, and disease duration among the three groups at baseline (all P>0.05; **Table 3**).

In this interventional study, we observed significant reductions in BMI, waist circumference, FPG, 2-h postprandial blood glucose, hemoglobin A1c (HbA1c), and TG among MetS patients whose energy requirements were estimated using the new equation, in comparison with our previous equation [15] and the traditional estimation method [14]. There were no significant differences across the groups for other variables, such as blood pressure or HDL-C level (**Table 4**).

(1) Change in weight: Before the study, the average weights of groups A, B, and C were 73.69±7.25, 73.26±5.57, and 73.23±5.86 kg/m^2, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the weight of group C had not changed significantly (72.98±5.67 kg, P>0.05), whereas the weights of groups A and B were decreased significantly (group A: 70.19±6.86 kg, P<0.05; group B: 71.27±6.31 kg, P<0.05). The weight of group A was significantly lower than those of groups B and C. (2) Change in BMI: Before the study, the average BMIs of groups A, B, and C were 27.40±2.34, 27.26±2.42, and 27.75±2.63 kg/m^2, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the BMI of group C had not changed significantly (27.66±2.53 kg/m^2, P>0.05), whereas the BMIs of groups A and B were decreased signifi-

Table 4. Cardiometabolic markers and energy balance in MetS patients before and 6 months after the intervention

Variables	Group A		Group B		Group C	
	Before	After	Before	After	Before	After
Weight (kg)	73.69±7.25	70.19±6.86$^{\#,*,\Delta}$	73.26±5.57	71.27±6.31$^{\#,\Delta}$	73.23±5.86	72.98±5.67
BMI (kg/m^2)	27.40±2.34	25.31±2.12$^{\#,*,\Delta}$	27.26±2.42	26.63±3.21$^{\#,\Delta}$	27.75±2.63	27.66±2.53
Waist circumference (cm)	92.42±7.13	88.58±6.75$^{\#,*,\Delta}$	93.21±6.45	91.46±5.22$^{\#,\Delta}$	92.68±6.21	91.78±5.90
Neck circumference (cm)	37.34±3.57	37.32±2.75	38.33±3.89	37.12±3.67	37.09±2.35	37.56±1.78
FPG (mmol/L)	7.36±4.89	5.82±3.26$^{\#,\Delta}$	7.11±2.87	5.57±3.73$^{\#,\Delta}$	7.83±3.26	7.21±2.36
2-h postprandial glucose (mmol/L)	10.63±5.41	7.53±4.26$^{\#,*,\Delta}$	10.46±5.24	8.76±4.32$^{\#}$	10.51±4.73	9.12±4.63$^{\#}$
HbA1c (%)	6.78±1.63	5.12±1.54$^{\#,\Delta}$	6.67±1.76	5.49±1.87$^{\#,\Delta}$	6.72±1.92	6.42±2.84
Systolic blood pressure (mmHg)	132±14	130±17	133±14	131±11	134±21	133±18
Diastolic blood pressure (mmHg)	83±14	78±13	81±17	80±14	81±18	82±10
CHO (mmol/L)	5.21±1.80	5.78±1.25	5.24±1.85	5.89±1.13	5.33±1.25	5.63±1.85
TG (mmol/L)	2.92±1.45	1.44±1.12$^{\#,*,\Delta}$	2.89±1.53	2.42±1.12	2.86±1.36	2.67±1.25
HDL-C (mmol/L)	1.21±0.64	1.24±0.46	1.24±0.38	1.44±0.83	1.19±0.63	1.26±0.46
LDL-C (mmol/L)	3.58±1.53	3.13±0.89	3.72±1.24	3.41±1.46	3.70±1.31	3.46±1.73

$^{\#}$indicates P<0.05 comparing the variable before and at 6 months after the intervention within each group; *indicates P<0.05 comparing the variable between groups A and B at the same time; $^{\Delta}$indicates P<0.05 comparing the variable in group A or B with that in group C at the same time.

cantly (group A: 25.31±2.12 kg/m^2, P<0.05; group B: 26.63±3.21 kg/m^2, P<0.05). The BMI of group A was significantly lower than those of groups B and C. (3) Change in waist circumference: Before the study, the waist circumference values for groups A, B, and C were 92.42±7.13, 93.21±6.45, and 92.68±6.21 cm, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the waist circumference of group C had not changed significantly (91.78±5.90 cm, P>0.05), whereas the waist circumference measurements of groups A and B had decreased significantly (group A: 88.58±6.75 cm, P<0.05; group B: 91.46±5.22 cm, P<0.05). The waist circumference values for groups A and B were significantly lower than that for group C (P<0.05), whereas the waist circumference of group A was significantly lower than that of group B (P<0.05). (4) Change in FPG: Before the study, the FPG values of groups A, B, and C were 7.36±4.89, 7.11±2.87, and 7.83±3.26 mmol/L, respectively, and there was no significant difference among them (P>0.05). At 6 months after the intervention, the FPG value of group C had not changed significantly (7.21±2.36 mmol/L, P>0.05), whereas the FPG levels of groups A and B had decreased significantly (group A: 5.82±3.26 mmol/L, P<0.05; group B: 5.57±3.73 mmol/L, P<0.05). The FPG values for groups A and B were significantly lower than that of group C (P<0.05). (5) Change in 2-h postprandial blood glucose: Before the study, the 2-h postprandial blood glucose levels of groups A, B, and C were 10.63±5.41, 10.46±5.24, and 10.51±4.73 mmol/L, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, 2-h postprandial blood glucose levels for the three groups all had decreased significantly (group A: 7.53±4.26 mmol/L, P<0.05; group B: 8.76±4.32 mmol/L, P<0.05; group C: 9.12±4.63 mmol/L, P<0.05). The 2-h postprandial blood glucose level of group A was significantly lower than those of groups B and C (P<0.05). (6) Change in HbA1c: Before the study, the HbA1c levels of groups A, B, and C were 6.78±1.63%, 6.67±1.76%, and 6.72±1.92%, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the HbA1c level of group C had not changed significantly (6.42±2.84%, P>0.05), whereas the HbA1c levels of groups A and B had decreased significantly (group A: 5.12±1.54%, P< 0.05; group B: 5.49±1.87%, P<0.05). The HbA1c levels of groups A and B were significantly lower than that of group C (P<0.05). (7) Change in TG: Before the study, the TG levels of groups A, B, and C were 2.92±1.45, 2.89±1.53, and 2.86±1 .36 mmol/L, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the TG of groups B and C had not changed significantly (group B: 2.42±1.12 mmol/L, P>0.05; group C: 2.67±

Table 5. Energy and nutrient intake and energy expenditure in patients with metabolic syndrome

Variables	Group A		Group B		Group C	
	Before	After	Before	After	Before	After
Energy intake (MJ/d)	9.30±2.79	6.70±1.85$^{\#,*,\Delta}$	9.54±2.24	7.05±1.64$^{\#,\Delta}$	9.36±2.53	8.81±2.21
Protein (%)	13.04±2.68	13.55±2.59	12.36±2.38	13.59±2.52	12.37±2.39	12.15±2.59
Protein (g)	63.40±13.42	67.56±11.86	62.78±14.29	66.79±10.64	65.79±15.63	65.58±12.85
Fat (%)	31.59±8.64	27.76±7.64	31.68±10.69	31.76±7.97	30.98±10.53	30.61±11.35
Fat (g)	78.52±22.72	50.68±17.67$^{\#,\Delta}$	79.52±23.79	60.21±14.42$^{\#,\Delta}$	76.78±20.75	63.51±16.86$^{\#}$
Carbohydrate (%)	57.60±8.64	53.78±7.57$^{\#,\Delta}$	57.85±10.37	53.97±6.69$^{\#,\Delta}$	57.75±10.26	54.98±9.36$^{\#}$
Carbohydrate (g)	317.46±68.97	229.57±47.97$^{\#,\Delta}$	325.90±66.46	232.56±41.86$^{\#,\Delta}$	328.75±66.35	255.68±64.64$^{\#}$
Total energy expenditure (MJ/d)	7.90±1.85	7.67±2.53	7.86±2.54	7.78±1.95	7.94±2.57	7.85±2.24
Physical activity expenditure (MJ/d)	1.61±0.85	1.65±0.85	1.62±0.85	1.67±0.85	1.59±0.85	1.64±0.85

$^{\#}$indicates P<0.05 comparing the variable before and at 6 months after the intervention within each group; *indicates P<0.05 comparing the variable between groups A and B at the same time; $^{\Delta}$indicates P<0.05 comparing the variable in group A or B with that in group C at the same time.

1.25 mmol/L, P>0.05), whereas the TG of group A was decreased significantly (1.44±1.12 mmol/L, P<0.05). The TG levels of group A were significantly lower than those of groups B and C (P<0.05).

In terms of dietary changes, we observed significant reductions in energy intake, fat intake, and carbohydrate intake among MetS patients whose energy requirements were estimated using the new equation, in comparison with our previous equation [15] and the traditional estimation method [14]. There were no significant differences across the groups for other variables, such as protein or energy expenditure (**Table 5**).

(1) Change in energy intake: Before the study, energy intakes for groups A, B, and C were 9.30±2.79, 9.54±2.24, and 9.36±2.53 MJ, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the energy intake of group C had not changed significantly (8.81±2.21 MJ, P>0.05), whereas the energy intake of groups A and B had decreased significantly (group A: 6.70±1.85 MJ, P<0.05; group B: 7.05±1.64 MJ, P<0.05). The energy intake values for groups A and B were significantly lower than that of group C (P<0.05), and the energy intake of group A was significantly lower than that of group B (P<0.05). (2) Change in fat: Before the study, the fat intake values for groups A, B, and C were 78.52±22.72, 79.52±23.79, and 76.78±20.75 g, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the fat intake values of groups A, B, and C had decreased significantly (group A: 50.68±17.67 g, P<0.05; group B: 60.21±14.42 g, P<0.05; group C: 63.51±16.86 g, P<0.05). The fat intake value for group A was significantly lower than those of groups B and C (P<0.05). (3) Change in energy proportion of carbohydrates: Before the study, the energy proportions of carbohydrates for groups A. B, and C were 57.60±8.64%, 57.85±10.37%, and 57.75±10.26%, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the energy proportions of carbohydrates for groups A, B, and C had decreased significantly (group A: 53.78±7.57%, P<0.05; group B: 53.97±6.69%, P<0.05; group C: 54.98±9.36%, P<0.05). The energy proportions of carbohydrates for groups A and B were significantly lower than that for group C (P<0.05). (4) Change in carbohydrate intake: Before the study, the carbohydrate intake values for groups A, B, and C were 317.46±68.97, 325.90±66.46, and 328.75±66.35 g, respectively, and there was no significant difference among them (P>0.05). At 6 months after the study, the carbohydrate intake values of groups A, B, and C had decreased significantly (group A: 229.57±47.97 g, P<0.05; group B: 232.56±41.86 g, P<0.05; group C: 255.68±64.64 g, P<0.05). The carbohydrate intake values for groups A and B were significantly lower than that for group C (P<0.05).

Discussion

In this study, we developed a new method, on the basis of negative energy balance, to estimate energy requirement for MetS patients. We found that dietary intervention guided by the new energy requirement equation improved weight, BMI, waist circumference, FPG, 2-h postprandial blood glucose, HbA1c, and TG in MetS patients, compared to conventional approaches.

Negative energy balance achieved through decreasing energy intake and/or increasing energy expenditure is critical in achieving and maintaining healthy weight [22, 23]. An accurate determination of energy requirement requires comprehensive consideration about variations in gender, age, height, weight, and physical activity among the population. For normal-weight healthy adults, their energy intake should be equal to their energy expenditure, which means that they should be in a balanced energy state. Therefore, their energy requirements can be estimated as equivalent to their total energy expenditure [24]. In the Dietary Reference Intakes (DRIs) for the United States and Canada, the recommended energy requirement was determined on the basis of total energy expenditure measured by a double-labeled water method in normal-weight healthy adults [25]. In the DRIs from Japan [26] and Europe [27], the energy requirement was estimated using the factorial approach method, which multiplies basal metabolic rate (BMR) by physical activity level (PAL). However, there is no specific guidance for MetS patients, for whom energy control is critical. The most commonly used energy calculation method for MetS is the diabetic food exchange method [14]. However, this method does not take into account gender or age, and thus, lacks individuality. We previously developed an individualized method to estimate the energy requirement in MetS patients [15]. However, there were also some problems in clinical practice. For example, BMI was included in the model as an independent factor, which reduced the sensitivity of the model to height. In this study, several improvements were made in the estimation equation: First, BMI was replaced by height and weight, increasing the sensitivity to height in the formula. Second, we removed the ambient temperature from the previous equation, because the ambient temperature in most contemporary working and living environments is well-controlled by air conditioners, resulting in a minimal impact on energy expenditure by MetS patients.

To establish a new energy requirement equation, this study considered the following points in the study design. First, waist circumference is negatively associated with energy requirement, and obesity and insulin resistance are considered core features of Me tS [28]. Waist circumference can reflect the extent of abdominal fat deposition, and accumulation of trunk fat is an important risk factor for MetS [29]. Among a variety of diagnostic criteria for MetS, abdominal obesity is considered one of the main diagnostic criteria, because it is more relevant to the risk of metabolic disorders than general obesity. Abdominal obesity is more prominent in Asians, including the Chinese and Japanese populations, and abdominal obesity often exists even in people with normal weight. Therefore, MetS may develop among normal weight people with increased waist circumference [30]. For this reason, waist circumference was included in the new calculation method, and we found that abdominal fat was negatively associated with energy intake in our study population. Second, age is negatively associated with energy requirement. Age is an independent factor in resting energy expenditure (REE), and REE is less in middle-aged and elderly people than in young people [31]. Also, a person's appetite, amount of food intake, and digestive capacity decline with advancing age. Third, the energy requirement is greater in men than in women. Women usually have a lower REE than men [32, 33]. Fourth, when categorizing the types of physical labor in MetS patients, we included "light physical labor" and "moderate physical labor" but omitted "heavy physical labor". This is because heavy physical labor, which was performed by some workers in the past, is hardly performed in the contemporary population, as modern tools and machines are increasingly used in industrial and agricultural production. The vast majority of MetS patients in our study population does not engage in heavy physical labor.

Our study found that dietary intervention on the basis of negative energy balance significantly reduced BMI, waist circumference, FPG, 2-h postprandial blood glucose, and HbA1c levels in MetS patients. Dyslipidemia is closely related to insulin resistance, and it is a risk factor for MetS, type 2 diabetes, and obesity [34, 35]. This study also observed that dietary intervention on the basis of negative energy balance significantly lowered TG levels. These findings are in line with a previous cross-over trial showing benefits of negative energy balance achieved during a hypo-energetic diet in patients with MetS [36]. Shenoy et al found that a healthy DASH-style diet could improve various metabolic disorders, such as hyperglycemia, dyslipidemia, and hypertension, in individuals with MetS [37]. Meta-analyses of randomized controlled trials have demonstrated that lifestyle modification is effective for improving metabolic parameters for MetS [38, 39]. Based on compelling evidence from randomized controlled trials showing that lifestyle intervention prevents or delays the incidence of diabetes among high-risk individuals with impaired glucose tolerance [40-44], it is possible that lifestyle intervention is effective for reducing the risk of developing diabetes among patients with MetS.

A major strength of the current study lies in the fact that we have focused the intervention strategy on negative energy balance. It is clear that MetS develops at least partly because the energy intake is greater than the energy expenditure. Only when negative energy balance is established can the various cardiometabolic disorders of MetS be ameliorated. Our results from the dietary intervention support this. In addition, we chose the control group (group C) as the intervention based on the traditional food exchange method. We are aware that many previous studies of dietary intervention in MetS had a non-dietary intervention as the control group. Such a comparative effectiveness assessment in our study will help facilitate direct translation of our results into clinical practice. Furthermore, we also included a group (group B) based on our previous model for energy requirement estimation, and we found that the new model developed in this study had even better performance compared with our previous model. This study has limitations because of the limited duration of follow-up and sample size, which may reduce the statistical power for identifying significant findings. For instance, we observed suggestive evidence for an increase in HDL-C and a decrease in low-density lipoprotein-cholesterol (LDL-C) in the intervention groups, but the changes were not statistically significant. It is possible that a longer duration of follow-up with a larger sample size are needed to observe significant changes in these indicators.

In conclusion, a new energy requirement equation on the basis of negative energy balance improves the effectiveness of a dietary intervention for reducing body weight, glucose levels, and triglyceride levels for MetS patients. Whether these effects translate into a long-term reduction in clinical outcomes among MetS patients warrants further investigation.

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Disclosure of conflict of interest

None.

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