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Glycemic instability in type 1 diabetic patients: Possible role of ketosis or ketoacidosis at onset of diabetes

Mariko Sassa [a], *Yuichiro Yamada* [b], *Masaya Hosokawa* [a], *Kazuhito Fukuda* [a], *Shimpei Fujimoto* [a], *Kentaro Toyoda* [a], *Katsushi Tsukiyama* [a], *Yutaka Seino* [c], *Nobuya Inagaki* [a,*]

[a] *Department of Diabetes and Clinical Nutrition, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan*

[b] *Department of Endocrinology and Diabetes and Geriatric Medicine, Akita University School of Medicine, Akita, Japan*

[c] *Kansai-Denryoku Hospital, Osaka, Japan*

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ABSTRACT

Aims: In type 1 diabetic patients, some have glycemic instability while others glycemic stability. We have developed criteria for evaluating glycemic instability and investigated the factors responsible.

Methods: Glycemic instability in 52 type 1 diabetic patients was assessed by the mean amplitude of glycemic excursions (MAGE) and M-value, and clinical characteristics of good, fair and poor control groups were compared.

Results: The median MAGE and M-value was 6.6 mmol/L and 18.7, respectively. Then MAGE ≥6.6 mmol/L and M-value ≥18.7 was defined as poor control. In the 32 patients without detectable C-peptide levels, 18 patients (56%) showed poor control. The frequency of ketosis or ketoacidosis at onset of diabetes was dramatically higher in the poor control group not only in the patients as a whole but also in those without detectable C-peptide levels.

Conclusions: A decreased level of C-peptide is a significant factor in glycemic instability. However, some patients have glycemic stability though β-cell function is completely depleted. The presence of ketosis or ketoacidosis at onset of diabetes may be a factor in later glycemic instability, suggesting the importance of examining patients in detail at onset of diabetes for careful follow-up to prevent progression of acute and chronic complications of diabetes.

1. Introduction

Type 1 diabetes mellitus is characterized by various forms of β-cell destruction, exhibiting various modes of onset [1]: acute-onset ('classical'), slow-onset [2] and fulminant [3]. While the incidence rate and mode of onset may differ among various populations, being 20-fold greater in Finland than in Japan, for example [4], β-cell destruction usually results in their complete loss and insulin-dependent diabetes mellitus (insulin-dependency) [5]. In patients with insulin-dependency, not only does the HbA_{1c} level increase, which represents the mean blood glucose level [6], but, as we previously reported [7], the blood glucose level remains unstable despite all efforts to optimize the use of exogenous insulin. Patients with glycemic

* *Corresponding author.* Tel.: +81 75 751 3562; fax: +81 75 771 6601.
E-mail address: inagaki@metab.kuhp.kyoto-u.ac.jp (N. Inagaki).

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instability are at increased risk of chronic macroangiopathic complications [8,9] as well as acute complications such as recurrent ketoacidosis [10], life-threatening hypoglycemia unawareness, and even "dead-in-bed syndrome" [11].

To quantify glycemic instability, the mean amplitude of glycemic excursions (MAGE) [12] and M-value [13] are commonly used [14,15]. However, glycemic instability has not been assessed by these indexes in a large population recently though the development of various new drugs has considerably facilitated glycemic control, and there are no established criteria for glycemic instability suitable for clinical use.

The blood glucose levels of some type 1 diabetic patients are as stable as those of type 2 diabetic patients [7]. To examine the distribution of glycemic instability and clarify the factors responsible for glycemic instability is of clinical importance for careful follow-up to prevent onset and progression of both acute and chronic secondary complications of diabetes.

In the present study, we assessed glycemic instability just before discharge after hospital treatment of at least a week period to exclude the influence of poor adherence to diet and exercise therapy, inappropriate use of exogenous insulin, and stressful circumstances of home or work place. We then compared the clinical characteristics and laboratory data of the patients with poor control and those with good or fair control to clarify the factors responsible.

2. Subjects and methods

2.1. Subjects

We examined all of the type 1 and type 2 diabetic patients admitted to Kyoto University Hospital from January, 2003 to July, 2007, except those meeting the exclusion criteria. A total of 52 type 1 diabetic patients (27 women and 25 men) (median age, 49 years; range, 16–80: median duration of diabetes, 6 years; range, 0–37) and 160 type 2 diabetic patients (64 women and 96 men) (median age, 65 years; range, 16–83: median duration of diabetes, 11 years; range, 0–53) were involved. American Diabetes Association Criteria was used as the criteria of type 1 diabetes [5]. Patients with renal insufficiency (Cre $\geq$ 1.5 mg/dl) were excluded, as were those with liver failure, acute illness such as infection, psychological comorbidities such as eating disorders, depression, needle phobia, those taking steroid medication, or inadequately monitoring blood glucose, and those on short-term admission (<7 days). No patients have learning disorders and apparent manipulative behaviour.

2.2. Assessment of glycemic instability

Seven capillary glucose measurements (before meals, 120 min after meals, and at bedtime) for two successive days just before discharge were analyzed to calculate the mean amplitude of glycemic excursions (MAGE) [12] and M-value, the indexes of glycemic instability. For calculating M-value, the modification [16] of the method of Schlichtkrull et al. [13,17] is commonly used: the average of M_{BS}^{BS} values; $M_{BS}^{BS} = |10 \times \log \frac{BS}{120}|^3$, which is the logarithmic transformation of the deviation of glycemia from the arbitrarily selected standard (120 mg/dl). Recently, 90 mg/dl is often used as the selected standard [18], and we used 100 mg/dl to give greater emphasis to hypoglycemia. Thus, in the present study, M-value is defined as the mean of M_{BS}^{BS} of each successive day: $M_{BS}^{BS} = |10 \times \log \frac{BS}{100}|^3$. The MAGE and M-value of the type 1 diabetic patients suggested a criterion for glycemic instability: MAGE $\geq$ the median and M-value $\geq$ the median representing poor control, MAGE < the first quartile and M-value < the first quartile indicating good control, and fair control comprising the middle ranges.

2.3. Factors responsible for glycemic instability

To clarify the factors responsible for glycemic instability, we compared the clinical characteristics and laboratory data of the good or fair groups and the poor control group of the 51 type 1 diabetic patients receiving intensive insulin therapy based on the guidelines by Japan Diabetes Society [19]. Ketosis was established by ketonuria, elevated serum ketones, or both. Serum and urinary C-peptide levels were measured using a commercially available EIA kit (ST AIA-PACK C-peptide, TOSOH corporation, Tokyo, Japan) with a detection limit of 0.1 ng/ml (intra-assay coefficient of variation [CV] 1.3–2.2%, interassay CV 1.7–2.0%) for serum C-peptide and 0.1 ng/dl (intra-assay CV 3.1–3.8%, inter-assay CV 1.9–2.1%) for urinary C-peptide. This kit has good reproductivity even when the level of C-peptide is lower than 1.0 ng/ml [20]. Diabetic sensorimotor distal symmetric polyneuropathy was assessed by pinprick, vibration perception threshold, and ankle reflexes. Autonomic function was evaluated by the coefficient of variation of the R-R interval (CVR-R) during deep breathing monitored on an electrocardiogram, and values below the reference values of healthy subjects [21] were counted abnormal. The presence of diabetic neuropathy was established by at least one abnormal result in the tests described above.

2.4. Statistical analysis

Qualitative variables were compared using Fisher's exact test. The Mann–Whitney *U* test was used to compare quantitative variables, which were expressed as medians and ranges. Two-sided *P* values <0.05 were considered statistically significant. Data were analyzed using StatView 5.0 (SAS Institute, Cary, NC).

3. Results

3.1. Criteria for glycemic instability

The median MAGE of type 1 diabetic patients was 6.6 mmol/L, significantly higher than that of type 2 diabetic patients ($P < 0.001$) (Fig. 1A). The first quartile MAGE of type 1 diabetic patients was 4.3 mmol/L and the third quartile was 7.5 mmol/L. The median M-value of type 1 diabetic patients was 18.7, significantly higher than that of type 2 diabetic patients ($P < 0.05$) (Fig. 1B). The first quartile M-value of type 1 diabetic patients was 9.2 and the third quartile was 30.2. MAGE was

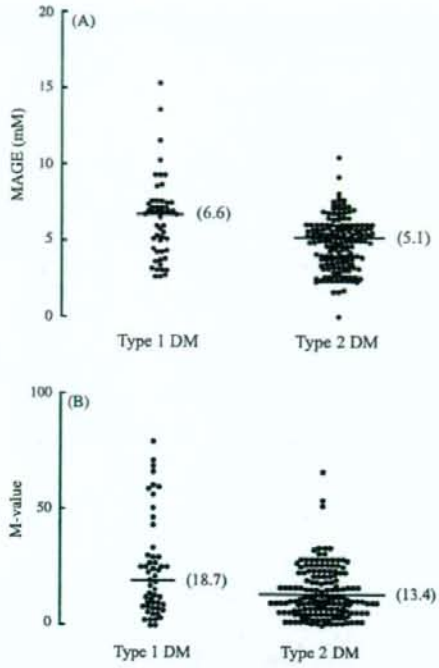

Fig. 1 – (A) MAGE of 52 type 1 diabetic patients and 160 type 2 diabetic patients at discharge who were admitted to Kyoto University Hospital. Horizontal lines represent medians. (B) M-value of 52 type 1 diabetic patients and 160 type 2 diabetic patients at discharge who were admitted to Kyoto University Hospital. Horizontal lines represent medians.

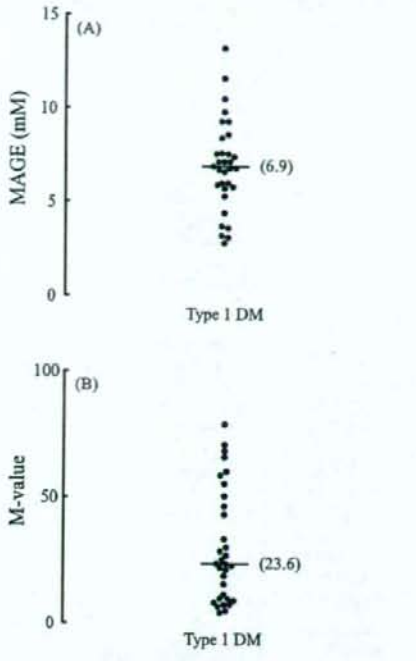

Fig. 2 – (A) MAGE of 32 type 1 diabetic patients without detectable C-peptide levels at discharge who were admitted to Kyoto University Hospital. Horizontal lines represent medians. (B) M-value of 32 type 1 diabetic patients without detectable C-peptide levels at discharge who were admitted to Kyoto University Hospital. Horizontal lines represent medians.

significantly correlated with M-value ($r = 0.71$, $P < 0.0001$). Then MAGE≥6.6 mmol/L and M-value ≥18.7 was defined as poor control, MAGE <4.3 mmol/L and M-value <9.2 good control, and the middle ranges fair control. By these criteria, 57.7% of the type 1 diabetic patients exhibited good or fair control (good: 15.4%, fair: 42.3%, respectively), while 90.0% of the type 2 diabetic patients exhibited good or fair control (good: 20.6%, fair: 69.4%, respectively). Thus, type 1 diabetic patients exhibited significantly greater glycemic instability than type 2 diabetic patients ($P < 0.001$).

3.2. *Clinical characteristics and laboratory data in 51 type 1 diabetic patients*

Clinical characteristics and laboratory data of the good or fair groups vs. the poor control group in 51 type 1 diabetic patients are shown in Table 1. There were no significant differences between the good or fair groups and the poor control group regarding age, sex, BMI, duration of diabetes, IA-2 antibodies, insulin antibodies, HbA_{1c} level, the state of diabetic complications and thyroid function at present admission, age at onset, and GAD antibodies at onset. Serum C-peptide at prestimulation, post glucagon stimulation and urinary C-peptide at present admission were significantly lower in the poor control group than in the good or fair groups ($P < 0.05$). The frequency of ketosis or ketoacidosis at onset of diabetes was significantly higher in the poor control group compared to the good or fair groups ($P < 0.01$; risk ratio [RR] 3.5 [95% CI 1.4–9.0]). In other words, in those with ketosis or ketoacidosis at onset of diabetes, glycemic instability was markedly higher than in those without ketosis or ketoacidosis at onset of diabetes (14 of 23 vs. 4 of 23; $P < 0.01$; [RR] 3.5 [95% CI 1.4–9.0]). There were no significant differences regarding the frequency of ketosis or ketoacidosis at onset of diabetes between those with detectable C-peptide levels and those without (11 of 18 vs. 12 of 28; $P = 0.37$). The frequency of positive GAD antibodies (≥1.5 U/ml) at present admission was significantly lower in the poor control group than in the good or fair groups ($P < 0.05$; [RR] 2.3 [95% CI 1.1–4.8]).

3.3. *Glycemic instability in type 1 diabetic patients without detectable C-peptide levels*

Thirty-two type 1 diabetic patients without detectable serum C-peptide levels at post glucagon stimulation and without detectable urinary C-peptide levels in 24-h urine collections

Table 1 – Clinical characteristics of type 1 diabetic patients

Glycemic instability	Good or fair control	Poor control	P-value or RR (95% CI) good or fair vs. poor
	MAGE <6.6 or M-value <18.7	MAGE ≥6.6 and M-value ≥18.7	
Clinical characteristics at present admission			
Age (years)	49 (16–80)	43 (18–79)	0.76
Sex (female/male)	16/13	11/11	0.78
BMI (kg/m^2)	21.0 (17.8–26.9)	20.8 (16.1–25.3)	0.95
Duration of diabetes (years)	6 (0–37)	7.5 (0–31)	0.95
GAD antibodies (<1.5/≥1.5 U/ml)	11/17	16/6	0.024
			2.3 (1.1–4.8)
IA-2 antibodies (<0.4/≥0.4 U/ml)	7/3	6/2	0.99
Insulin antibodies (%)	10.2 (3.7–77.6)	9.8 (6.6–89.6)	0.67
HbA_{1c} (%)	8.1 (5.6–16.3)	8.3 (5.0–11.6)	0.73
Serum C-peptide at prestimulation (ng/ml)	0 (0–0.90)	0 (0–0.43)	0.023
Serum C-peptide at post glucagon stimulation (ng/ml)	0.15 (0–2.0)	0 (0–0.92)	0.010
Serum ΔC-peptide (ng/ml)	0.05 (0–1.63)	0 (0–0.49)	0.010
Urinary C-peptide (μg/day)	0 (0–57.7)	0 (0–21.0)	0.019
Diabetic retinopathy (NDR/NPDR/PDR)	22/3/4	14/8/0	0.78
Diabetic nephropathy (normoalbuminuria/ microalbuminuria/proteinuria)	25/3/1	17/5/0	0.59
Diabetic neuropathy (negative/positive)	14/15	8/14	0.27
CVR-R (%) (normal/abnormal)	11/10	8/6	0.99
Ankle brachial pressure index (ABI)	1.10 (0.88–1.24)	1.11 (0.72–1.23)	0.86
Carotid intima-media thickness (mm)	0.9 (0.6–1.5)	0.8 (0.7–1.6)	0.69
TSH (μU/ml)	1.80 (0.59–8.02)	1.31 (0–54.8)	0.62
Free T_4 (ng/dl)	1.22 (0.89–1.90)	1.14 (0.57–2.69)	0.42
Clinical characteristics at onset			
Age at onset (years)	40 (7–78)	34 (10–74)	0.52
Ketosis or ketoacidosis (negative/positive)	19/9	4/14	0.0058
			3.5 (1.4–9.0)
GAD antibodies (<1.5/≥1.5 U/ml)	3/18	6/8	0.11
			2.2 (1.0–4.5)

Data are median (range) or number of patients. Serum C-peptide, urinary C-peptide, GAD antibodies and IA-2 antibodies below detection limits are expressed as 0.

were then selected. Of these patients, 18 patients (56%) showed poor control, and the other 14 patients (44%) showed good or fair control (MAGE <6.6 mmol/L in 12 patients, M-value <18.7 in 12 patients) (Fig. 2A and B). In contrast, of the 19 patients with detectable C-peptide levels, 15 (79%) showed good or fair control, and the other 4 (21%) showed poor control.

The good or fair and poor control groups in type 1 diabetic patients without detectable C-peptide levels were then compared. The frequency of ketosis or ketoacidosis at onset was dramatically higher in the poor control group than in the good or fair groups (11 [73%] of 15 vs. 1 [8%] of 13; $P < 0.001$; [RR] 3.7 [95% CI 1.5–8.7]). In other words, of the 13 patients without detectable C-peptide levels but with glycemic stability, 12 patients did not have ketosis or ketoacidosis at onset. The frequency of positive GAD antibodies at present admission was significantly lower in the poor control group than in the good or fair groups (3 [17%] of 18 vs. 8 [62%] of 13; $P < 0.05$; [RR] 2.8 [95% CI 1.0–7.5]).

3.4. *Glycemic instability in acute-onset type 1 diabetic patients*

In the 51 type 1 diabetic patients, 38 patients had acute-onset ('classical') type 1 diabetes, 6 patients fulminant type 1 diabetes [3], and 2 patients latent autoimmune diabetes of adults [2], and 5 patients unknown. Thirty-eight acute-onset type 1 diabetic patients were then examined to exclude the influence of fulminant type 1 diabetes, because the presence of ketosis or ketoacidosis at onset of diabetes, which has been found to be involved in glycemic instability in the present study, is a characteristic of fulminant type 1 diabetes [3], and glycemic instability in fulminant type 1 diabetes was markedly greater than in acute-onset type 1 diabetes (good: 0 of 6, fair: 1 of 6, poor: 5 of 6 vs. good: 6 of 38, fair: 18 of 38, poor: 14 of 38, $P < 0.05$). In acute-onset type 1 diabetic patients, the frequency of ketosis or ketoacidosis at onset was significantly higher in the poor control group than in the good or fair groups (8 [73%] of 11 vs. 7 [29%] of 24; $P < 0.05$; [RR] 3.6 [95% CI 1.1–11.2]).

4. Discussion

It has been reported that factors that influence glycemic instability are deficiency of endogenous insulin secretion [22,23], abnormal response of insulin-counteracting hormones [22,24,25], poor compliance with diet and exercise therapy, stressful life circumstances [26], and inappropriate use of exogenous insulin [27,28].

In the present study, we assessed glycemic instability by MAGE and M-value in 52 type 1 and 160 type 2 diabetic

patients, and proposed criteria for glycemic instability suitable for clinical use. MAGE and M-value of most of the type 2 diabetic patients showed good or fair glycemic stability.

Analysis of the 51 type 1 diabetic patients showed that serum C-peptide at post glucagon stimulation and urinary C-peptide at present admission were significantly lower in the poor control group than in the good or fair groups. In addition, of the 32 patients without detectable C-peptide levels, 18 (56%) showed poor control. These results indicate that decreased endogenous insulin secretion is a significant factor in glycemic instability. However, of the 32 patients without detectable C-peptide levels, 14 (44%) exhibited good or fair control. In addition, of these patients, MAGE of 6 (19%) and the M-value of 10 (31%) were lower than the median values of the type 2 diabetic patients. These results demonstrate that some patients with type 1 diabetic patients have glycemic stability though β-cell function is completely depleted.

The present study suggests that the presence of ketosis or ketoacidosis at onset of diabetes is a factor in later glycemic instability. This is not simply due to the including of fulminant type 1 diabetic patients, because analysis of acute-onset type 1 diabetic patients also showed that the frequency of ketosis or ketoacidosis at onset was significantly higher in the poor control group than in the good or fair groups. Moreover, analysis of the type 1 diabetic patients without detectable C-peptide levels also showed that the frequency of ketosis or ketoacidosis at onset was dramatically higher in the poor control group than in the good or fair groups. The same tendency of the higher frequency of ketosis or ketoacidosis at onset in the poor control group was shown in the patients with detectable C-peptide levels. These results suggest that the presence of ketosis or ketoacidosis at onset is a factor in later glycemic instability, and other factors than C-peptide also exist as the underlying mechanism besides decreased levels of C-peptide.

Then, what is the mechanism whereby ketosis or ketoacidosis at onset of diabetes leads to later glycemic instability? One possibility is decreased β-cell functional reserve as mentioned above. Other factors than C-peptide underlying the mechanism may be the increased levels of counter-regulatory hormones inducing insulin resistance, including glucagon, epinephrine, cortisol and growth hormone [29,30]. Glucagon levels are markedly elevated in certain patients with ketoacidosis including those having preserved endogenous insulin secretion [30]. In addition, not only insulin-dependent diabetic patients but also noninsulin-dependent diabetic patients with hyperglycemia display paradoxical hyperglucagonemia, which contributes to postprandial hyperglycemia and glycemic instability [24,31].

In addition, there have been no studies of type 1 diabetic patients to clarify the association of GAD antibodies with glycemic instability. The present study indicates that negative GAD antibodies at onset may contribute to later glycemic instability. This may be because there is an inverse relation between the level of GAD antibodies and β-cell-destructive T-cell responses [32] or partly because patients with fulminant type 1 diabetes were included.

The present study has limitations in that this is a cross-sectional study and we have little C-peptide data at onset of diabetes. However, the frequency of ketosis or ketoacidosis at onset was clearly higher in the poor control group than in the good or fair groups not only in the patients as a whole but also in those without detectable C-peptide levels at present admission.

In summary, we confirmed that a decreased level of C-peptide is a significant factor in glycemic instability. However, the present study showed that some patients with type 1 diabetic patients have glycemic stability though β-cell function is completely depleted. The present study suggested that ketosis or ketoacidosis at onset of diabetes is a factor in later glycemic instability. In addition, GAD antibodies at onset may also influence later glycemic instability. These results suggest the importance of examining patients in detail at the onset of diabetes. Patients with glycemic instability are at increased risk of both acute and chronic complications of diabetes, so patients exhibiting ketosis or ketoacidosis at onset of type 1 diabetes should be carefully monitored.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Study on Factors of Body Image in Japanese and Vietnamese Adolescents

Ayami SANO[1,2], Duc-Son Nguyen Trung LE[3,4], Minh-Hanh Thi TRAN[4], Ha Thi Ngan PHAM[4], Masayo KANEDA[5], Eiko MURAI[6], Hisao KAMIYAMA[7], Yumiko OOTA[8] and Shigeru YAMAMOTO[2,9,*]

[1]*Department of Food Management, School of Food and Nutritional Sciences, University of Shizuoka, Shizuoka 422–8526, Japan*
[2]*Department of International Public Health Nutrition, Institute of Health Biosciences, The University of Tokushima Graduate School, Tokushima 770–8503, Japan*
[3]*National Institute of Diabetes & Digestive & Kidney Diseases, National Institute of Health, Phoenix, AZ 85016, USA*
[4]*Nutrition Center of Ho Chi Minh City, Ho Chi Minh City, Vietnam*
[5]*Junior College of Kagawa Nutrition University, Tokyo 170–8481, Japan*
[6]*Kokubunji Nanbu Elementary School, Kagawa 769–0103, Japan*
[7]*The Education Board of Tochigi Prefecture, Tochigi 320–8501, Japan*
[8]*The Education Board of Toyama Prefecture, Toyama 930–8501, Japan*
[9]*International Nutrition, Ochanomizu University Graduate School of Humanities and Sciences, 2–1–1 Ohtsuka, Bunkyo-ku, Tokyo 112–8610, Japan*

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Summary Over-concern about thinness, especially among young girls including adolescents, is common in Japan. Behind the problem, there is a complicated social phenomenon and an effective strategy is not known yet. In this study, we tried to find a clue by comparing body image between two countries which have different social backgrounds. Subjects were Japanese and Vietnamese junior high school students from 12 to 15 y old. Three schools each and 1–2 classes from each grade were randomly selected to involve 374 (boys 196, girls 178) and 714 (boys 352, girls 362), respectively, in Japan and Vietnam. Height and weight of subjects were measured and their satisfaction about their body shape and experience with dieting were asked by a questionnaire. Questions about their body image concerning their desire, liking of the opposite sex, own liking and health were answered by marking silhouettes. About 60% of Japanese thought that obese (silhouette 9) is unhealthy, while about 85% of Vietnamese thought that thinness (silhouette 1) is unhealthy. Most of the Japanese girls overestimated their body weight and were dissatisfied with their body shape and 78.3% wanted to lose weight. About 30% of them experienced weight loss including 2.8% of the low BMI students. Vietnamese girls also had similar tendencies in their desire about their body image as the Japanese but they were less serious. The girls in both countries preferred the thinner body image to the healthy body image and thought that boys liked the thinner body image. Japanese boys were mostly satisfied with their body shape; however, about half (46%) of the Vietnamese boys wanted a bigger and more muscular body image. In conclusion, the biggest problem with body image was the over-concern about thinness of the Japanese girls, which was based on their own misconception. Therefore, as the strategy to correct their body image, education about good health and also information about the boys' favorite body image are recommended.

Key Words body image, thinness, adolescents, Japan, Vietnam

The Japanese annual nation-wide nutrition survey in 2004 (*1*) showed that the prevalence of obesity defined as Body Mass Index (BMI) kg/m^2 over 25 was 27.9% and 18.7%, in adult males and females, respectively. While the prevalence of male obesity has been increasing gradually (21.6% in 1994), that of females, especially of young girls, is decreasing (*2*). The prevalence of underweight (BMI less than 18.5) was 14.8% in 1984, 19.0% in 1994 and 21.4% in 2004 (*1–3*). Very strong feelings of dislike against obesity may be the contributory factor. The facts that health professionals have emphasized the unhealthy outcomes of obesity and that society equates thinness with beauty and attractiveness in women facilitated the desire for underweight (*4*).

This trend was not only observed in young adults, but also in adolescents. According to the Statistical Report of School Health (*5, 6*), the prevalence of adolescent underweight increased as well as that of adolescent overweight in recent decades. Comparing the data of

*To whom correspondence should be addressed.
E-mail: yamamoto.shigeru@ocha.ac.jp

12 y-old school children in 1980 and 2000, the prevalence of overweight was 7.48% vs. 11.28% in boys and 7.30% vs. 10.05% in girls, respectively, while the prevalence of underweight was 1.35% vs. 3.53% in boys and 2.38% vs. 4.15% in girls, respectively (5, 6). The recent Annual National Health and Nutrition Survey also reported similar results (7). There are quite a number of studies on body image in young adults; however, there are only a few on adolescents. The adverse effects of the severe dietary restrictions on their present and future health will certainly be more serious in adolescents than in young adults. The methods of education to correct wrong body image in adolescents and university students should be different. Therefore, a strategy to correct over-concern about thinness is very important.

On the other hand in adolescent boys, the percentage of overweight has been increasing little by little. It would be interesting to know whether the boys do not have a desire to lose weight or whether they have it but can not manage it in practice. There is the further question of how strongly the body image of boys affects the girls' desire to lose weight. Therefore, we also studied the body image of adolescent boys.

The main purpose of this study was to find a strategy to correct wrong body image in Japanese adolescents. For this purpose we thought that it would be good to show them that the body image of Japanese adolescents is not the same as for their age group in other countries, which can lead them realize that their body image is only a kind of fashion. We selected Vietnam for the comparison of body image in adolescents, because the social background is quite different and it was easy for us to gain co-operation because of our long collaboration.

METHODS

1. Design and participants. In a cross-sectional survey, male and female junior high school students whose ages ranged from 12 to 15 y in Japan and Vietnam were included. The approval for this study was given by the Ethical Committee of The University of Tokushima in Japan and by the Research and Ethical Review Board of the Nutrition Center of Ho Chi Minh City, in Vietnam.

Japan is geographically divided into 7 regions. One or two public junior high schools were selected randomly from each region. The aim of the study and the fact that the participants' privacy would not be compromised were explained to the principals and teachers of the schools. Finally, only three schools in Kagawa, Tochigi and Toyama prefectures gave their consent to launch the survey. One or 2 classes were selected from each grade and each school. In Vietnam, 3 schools were randomly selected from a list of all public junior high schools in Ho Chi Minh City. A self-reported, anonymous questionnaire was used to measure demographic variables, consciousness and attitude toward current body weight and body image. The questionnaire was translated into Vietnamese with the assistance of native health professionals. By this questionnaire, we confirmed that the students, especially, Japanese girls had a strong desire to lose weight.

2. Physical characteristics. To determine actual body size, height and weight were measured to 0.1 cm and 0.1 kg, respectively. The weight was measured with a digital balance. The height scales placed in each school was used. The measurement was performed with light clothes, without shoes and socks and evaluating them within 1 h after a meal or exercise was avoided. BMI was calculated from height and weight measurements as kg/m^2 and subjects were then classified as low BMI group (0–14 percentile), moderate BMI group (15–84 percentile), and high BMI group (85–100 percentile) based on the actual BMI of each group.

3. Body image. Body image of participants was investigated visually by using the Stunkard silhouette chart (Fig. 1) (8, 9). In the chart, there are 9 silhouette from very thin to obese. The validity of this method has been confirmed by researchers (8). Participants were asked to choose the corresponding figures for the eight questions shown below.

Q1 "Which figure do you think resembles yours?"(CURRENT)

Q2 "Which figure would you like be?" (IDEAL)

Q3 "Which opposite sexual figure do you think the most attractive?" (OPPOSITE ATTRACTIVE)

In case of boy subjects, the meaning is which female figure do you think the most attractive? (Q3b), and vice versa for the girls' question (Q3g).

Q4 "Please choose one figure of the same sex as you, which figure do you think attracts the opposite sex most?" (OPPOSITE FINDS ATTRACTIVE)

In case of boy subjects, the meaning is which male figure do you think attracts females most? (Q4b), and vice versa for the girls' question (Q4g).

Q5 "Which male figure do you think look most healthy?" (HEALTHY MALE)

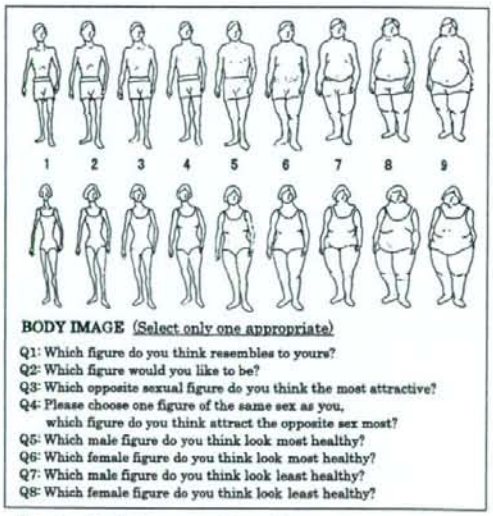

Fig. 1. Body image questionnaire.

Table 1. Physical characteristics.

	Boy			Girl		
	Japanese (n=196)	Vietnamese (n=352)	p value*	Japanese (n=178)	Vietnamese (n=362)	p value*
Height (cm)						
Total	162.5±7.96	156.9±9.34	<0.0001	155.5±5.59	152.4±5.95	<0.0001
Low BMI group	158.0±8.19	151.6±9.46		153.6±5.50	149.5±6.21	
Moderate BMI group	162.3±7.75	157.2±9.16		155.4±5.67	152.6±5.81	
High BMI group	167.5±5.77	160.5±8.07		157.1±4.98	153.8±5.58	
Weight (kg)						
Total	54.8±13.66	48.0±12.32	<0.0001	51.2±10.92	43.4±8.10	<0.0001
Low BMI group	41.8±5.31	34.3±5.13		40.1±3.93	32.7±3.44	
Moderate BMI group	52.7±6.96	46.6±8.22		49.4±5.21	42.8±5.07	
High BMI group	78.1±16.57	67.1±10.43		68.0±13.71	55.9±6.32	
BMI (kg/m^2)						
Total	20.6±3.94	19.3±3.68	<0.0001	21.1±3.99	18.6±2.92	<0.0001
Low BMI group	16.7±0.80	14.8±0.68		17.0±0.80	14.6±0.74	
Moderate BMI group	19.9±1.51	18.7±1.99		20.4±1.66	18.3±1.59	
High BMI group	27.7±5.04	25.9±2.36		27.5±5.06	23.6±1.96	

mean±SD. * t-test (significant national difference: Japanese vs. Vietnamese).

Q6 "Which female figure do you think look most healthy?" (HEALTHY FEMALE)
Q7 "Which male figure do you think look least healthy?" (UNHEALTHY MALE)
Q8 "Which female figure do you think look least healthy?" (UNHEALTHY FEMALE)

4. Data analysis. The t-test was used to determine differences between physical measurement means. The deficit value of the questionnaire was excluded in each question and it was analyzed. The chi-square test was used to determine differences in categorical data. Non-parametric methods, including the Mann-Whitney U-test and Krasukal-Wallis test were used for the comparison of two groups or multigroups' body image scores. The level of significance was set at $p<0.05$. The data were analyzed using SPSS 11.5J for Windows.

RESULTS

1. Subjects

In Japan, of the 387 questionnaires handed out, 378 subjects completed the questionnaires (97.7%), of which 4 subjects were excluded because sexual and physical data missing. The effective answer rate was 98.9%. The number of Japanese boys and girls participating in the study was 196 and 178, respectively. Their mean age was 13.6±0.85 y. In Vietnam, of the 723 questionnaires handed out, 723 subjects completed questionnaires (100%), of which 9 subjects were excluded because of missing sexual and physical data. The effective answer rate was 98.8%. The number of Vietnamese boys and girls was 352 and 362, respectively. Their mean age was 13.0±0.82 y.

Physical characteristics are shown in Table 1. Height, weight and BMI in Japanese were significantly higher than those in Vietnamese in both genders (all $p<0.0001$). In this study, subjects were divided into 3 groups depending upon their BMI distribution. They were low (0–14 percentile), moderate (15–84 percentile) and high (85–100 percentile) BMI groups. However, the cut-off points of BMI in these 3 groups were not same in the Japanese and Vietnamese subjects. Since the purpose of this study was to determine body image in all of the subjects, we thought that the difference in cut-off points of the 3 BMI groups in Japan and Vietnam was acceptable in this study.

2. Body image

Table 2 summarizes the consciousness and attitude toward the current body weight of the students and shows that the Japanese subjects, especially girls, had a strong desire to lose weight.

Japanese boys and girls perceived themselves as overweight more than Vietnamese boys and girls (both $p<0.0001$). Furthermore, Japanese girls described themselves as overweight more than Japanese boys ($p<0.0001$). However, there was no significant gender difference in Vietnamese ($p=0.332$).

About 65% of Japanese boys, Vietnamese boys and girls correctly identified their body weight. 58.6% of Japanese girls overestimated their body weights, which was higher than for the other groups ($p<0.0001$). Both Japanese boys and girls significantly overestimated their body weights compared with Vietnamese boys and girls, (both $p<0.0001$). The gender difference was only significant among Japanese ($p<0.0001$). Besides, 70.8% of Japanese girls overestimated even though their body size was low BMI or moderate BMI (data not shown).

About 45% of Vietnamese boys and girls and Japanese boys were satisfied with their current body weight. Over 80% of Japanese girls had dissatisfaction with their current body weight, which is higher than for the other three groups ($p<0.0001$).

Japanese students intended to lose weight, while Viet-

Table 2. Consciousness and attitude toward own current body weight.

	Boy		Girl		
	Japanese (n=196) % (no.)	Vietnamese (n=352) % (no.)	Japanese (n=178) % (no.)	Vietnamese (n=362) % (no.)	p value*,†,‡
Actual body size					
Low BMI group	14.8 (29)	13.9 (49)	14.0 (25)	13.5 (49)	
Moderate BMI group	70.4 (138)	70.7 (249)	69.1 (123)	71.3 (258)	
High BMI group	14.8 (29)	15.3 (54)	16.9 (30)	15.2 (55)	
Perceived body weight					
Thin	15.4 (30)	33.5 (116)	1.1 (2)	33.6 (117)	
Normal	52.2 (102)	48.3 (167)	33.4 (58)	44.0 (153)	<0.0001[a,b,c]
Overweight	32.3 (63)	18.2 (63)	65.5 (114)	22.4 (78)	
Discrepancy in weight (actual body size vs. perceived body weight)					
Underestimated[1]	8.7 (17)	25.4 (88)	0.6 (1)	22.7 (79)	
Correct[2]	66.7 (130)	65.3 (226)	40.8 (71)	67.0 (233)	<0.0001[a,b,c]
Overestimated[3]	24.6 (48)	9.2 (32)	58.6 (102)	10.3 (36)	
Satisfaction					
Satisfied with actual body weight	48.7 (93)	45.2 (159)	16.7 (29)	42.5 (154)	<0.0001[b,c]
Unsatisfied with actual body weight	51.3 (98)	54.8 (193)	83.3 (145)	57.5 (208)	
Desire for weight change					
Lose	36.1 (69)	25.3 (89)	78.3 (137)	34.3 (124)	
Remain the same	50.8 (97)	29.0 (102)	21.1 (37)	27.1 (98)	<0.0001[a,b,c,d]
Gain	13.1 (25)	45.7 (161)	0.6 (1)	38.7 (140)	
Weight-loss experience					
Yes	3.6 (7)	15.9 (56)	27.0 (48)	15.2 (55)	<0.0001[a,b,c]
No	96.4 (185)	84.1 (296)	73.0 (130)	84.8 (307)	

*Chi-square test (significant 4 groups differences: Japanese boy vs. Vietnamese boy vs. Japanese girl vs. Vietnamese girl). †Chi-square test, p<0.05 (significant national differences; [a]Japanese boy vs. Vietnamese boy, [b]Japanese girl vs. Vietnamese girl). ‡Chi-square test, p<0.05 (significant gender differences; [c]Japanese boy vs. Japanese girl, [d]Vietnamese boy vs. Vietnamese girl). [1]Actual>Perceived (The adolescents were bigger than they thought). [2]Actual=Perceived. [3]Actual<Perceived (The adolescents were thinner than they thought).

Table 3. Number of subjects who answered silhouettes No. 1 or No. 9 was unhealthy.

	Boy		Girl		
	Japanese (n=196) % (no.)	Vietnamese (n=352) % (no.)	Japanese (n=178) % (no.)	Vietnamese (n=362) % (no.)	p value*,†,‡
Male's silhouette					
Silhouette no. 1 (the thinnest)	35.4 (69)	87.6 (254)	40.7 (72)	85.1 (269)	<0.0001[a,b]
Silhouette no. 9 (the biggest)	59.0 (115)	10.3 (30)	58.8 (104)	11.7 (37)	
Female's silhouette					
Silhouette no. 1 (the thinnest)	39.3 (75)	86.5 (249)	42.1 (75)	84.8 (268)	<0.0001[a,b]
Silhouette no. 9 (the biggest)	57.1 (109)	11.1 (32)	57.9 (103)	12.3 (39)	

*Chi-square test (significant 4 groups differences; Japanese boy vs. Vietnamese boy vs. Japanese girl vs. Vietnamese girl). †Chi-square test, p<0.05 (significant national differences; [a]Japanese boy vs. Vietnamese boy, [b]Japanese girl vs. Vietnamese girl). ‡Chi-square test, p<0.05 (significant gender differences; [c]Japanese boy vs. Japanese girl, [d]Vietnamese boy vs. Vietnamese girl).

namese were likely to gain weight. There were national difference between Japan and Vietnam for both boys and girls (p<0.0001). Japanese girls had a significantly stronger desire for weight loss than Japanese boys did (p<0.0001). Vietnamese boys had significantly stronger desire for gaining weight than Vietnamese girls did (p=0.028).

Many Japanese girls (27.0%) had weight-loss experience, which was significantly higher than for the other three groups, despite their actual body size being low BMI or moderate BMI (23.6%). About 15% of Vietnamese boys and girls had weight-loss experience. The gender difference was only observed in Japanese subjects (p<0.0001).

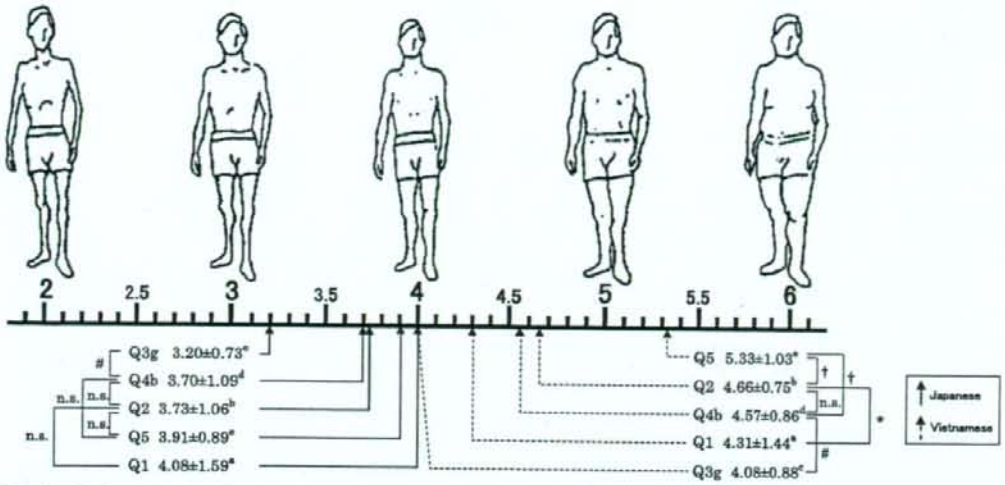

Fig. 2. Body image score (boy). Q1 CURRENT, Q2 IDEAL, Q3g OPPOSITE ATTRACTIVE, Q4b OPPOSITE FINDS ATTRACTIVE, Q5 HEALTHY MALE. ^{a,b,c,d,e}Mann-Whitney *U*-test, $p<0.05$ (significant national differences; Japanese boy vs. Vietnamese boy, respectively body image score). *Mann-Whitney *U*-test, $p<0.05$ (significant between-group difference, Q1 vs. Q2). †Kraskal-Wallis test, $p<0.05$ (significant between-multigroups difference, Q2 vs. Q4b, Q2 vs. Q5, Q4b vs. Q5). #Mann-Whitney *U*-test, $p<0.05$ (significant between-group difference, Q3g vs. Q4b).

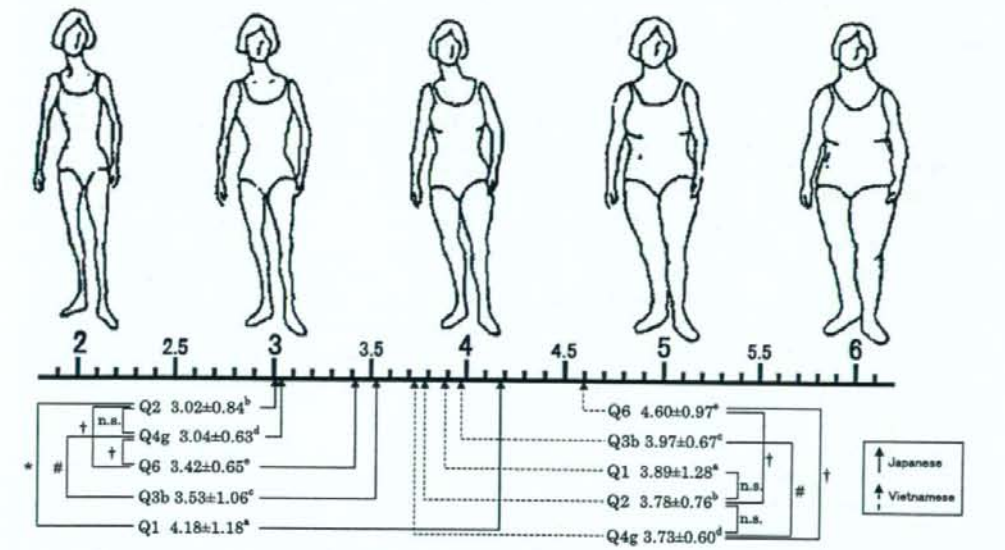

Fig. 3. Body image score (girl). Q1 CURRENT, Q2 IDEAL, Q3b OPPOSITE ATTRACTIVE, Q4g OPPOSITE FINDS ATTRACTIVE, Q6 HEALTHY FEMALE. ^{a,b,c,d,e}Mann-Whitney *U*-test, $p<0.05$ (significant national differences; Japanese girl vs. Vietnamese girl, respectively body image score). *Mann-Whitney *U*-test, $p<0.05$ (significant between-group difference, Q1 vs. Q2). †Kraskal-Wallis test, $p<0.05$ (significant between-multigroups difference, Q2 vs. Q4g, Q2 vs. Q6, Q4g vs. Q6). #Mann-Whitney *U*-test, $p<0.05$ (significant between-group difference, Q3b vs. Q4g).

Silhouettes associated with being unhealthy are shown in Table 3. About 60% of Japanese thought that the obese figure (i.e. No. 9) was unhealthy. On the other hand, about 85% of Vietnamese thought that the thin figure (i.e. No. 1) was unhealthy. There was a national difference in their perceptions of unhealthy body size.

Body image scores of boys are shown in Fig. 2. Body image score from Q1 to Q5 in Japanese boys were significantly lower than those in Vietnamese boys. There was no difference between Q1 (CURRENT) and Q2 (IDEAL) in Japanese boys ($p=0.126$); however, the body image score of Q2 was significantly higher than that of Q1 in

Vietnamese boys ($p<0.0001$). There were significant differences between Q2 vs. Q5 and Q4b vs. Q5 in Vietnamese (both $p<0.0001$); however, there was no difference in Japanese. However, comparing the answer of Q4b from boys with the answer Q3g from girls, the body image score of Q4b was higher than that of Q3g for both Japanese and Vietnamese ($p<0.0001$). That is, girls did not like as big figures as boys thought.

Body image scores of girls are shown in Fig. 3. The body image scores for Q2 to Q6 among Japanese girls were significantly lower than those among Vietnamese girls. The body image score for Q2 (IDEAL) was significantly lower than that for Q1 (CURRENT) in Japanese ($p<0.0001$); while there was no difference between Q1 and Q2 in Vietnamese ($p=0.305$). There were significant differences between Q2 vs. Q6 (Japan $p<0.0001$, Vietnam $p<0.0001$) and Q4g vs. Q6 (both $p<0.0001$). However, comparing the answer of Q4g from girls with the answer of Q3b from boys, the body image score for Q4g was lower than that for Q3b (both $p<0.0001$). That is, boys did not like as thin figures as girls thought.

DISCUSSION

In this study we found some interesting results about the body image among Japanese and Vietnamese adolescents. About 60% of the Japanese subjects thought that the obese silhouette (9) was unhealthy, while about 85% of Vietnamese thought that thinness (silhouette 1) was unhealthy, indicating that depending upon the difference in social background, the concept about health changes. In Japan when the prevalence of obesity was not high and infectious diseases were more common than cardiovascular disease, people thought obese persons were healthier than thin ones. There is no scientific evidence; however, we think that such a concept had been observed until the 1970s. Vietnam is now in a transitional phase and the body image may also undergo a change like Japan has experienced. These means that we can estimate the future direction of body image and it is possible to change the concept about body image.

By reflecting the present concept about health, Japanese young girls have an over-concern with thinness. Most of the Japanese girls overestimated their body weight and were dissatisfied with their body shape (83.3%) and wanted to lose weight (78.3%). About 30% of them experienced weight loss including 2.8% of the low BMI students with BMI<18.0. Although Vietnamese girls also had similar tendencies in their desires about their body image as the Japanese girls, they were less serious. This meant that girls in both countries preferred a thinner body image than the healthy body image and they thought that boys liked a thinner body image than the boys actually did. On the other hand, Japanese boys were satisfied with their body shape although their average BMI was not low. The reason why the girls had so serious a concern about thinness as compared with boys, may be because the evaluation of the society for females is often beauty, while that of males is strength.

On the other hand, about half (46%) of the Vietnamese boys wanted a more muscular body image than the girls' favorite body image for them. The desire of Vietnamese boys was closer to that of Western men (*10*). However, American female college students liked a body image with much less muscular men than the men thought desirable (*11*). Young Western men like unrealistic body shapes and advertising seems to place an increasing value on the male body. This image is now known as the "Adonis complex." Another serious consequence of male body image concerns is the abuse of anabolic-androgenic steroids and other "body image drugs" (*12*).

Some limitations of the present study should be taken into account when interpreting the findings. First, for the high reliability of these data, actual physical characteristics were measured. When the surveys were conducted in Japan, we encountered difficulties on getting consent from schools. Even though we explained that subjects' privacy would not be compromised, most of the public schools refused to participate. Therefore, the participant population was rather small in Japan. However, in this study we could confirm that Japanese students had a strong concern about body weight loss.

Second, the silhouette chart was used to examine body image visually. However, it is difficult to interpret whether the students regarded the body size of this silhouette chart as having excess muscle or fat.

Although there are some limitations, our study provided valuable insights into the body image of adolescents in Japan and Vietnam. The national differences observed in our study were likely to be related to culture and provided evidence for establishing different education programs for Japan and Vietnam.

In conclusion, we confirmed that the biggest problem with body image was the over-concern about thinness of the Japanese girls, which was based on their own misconception. Therefore, as a strategy to correct their body image, the following are recommended: 1) education about good health and 2) information about boys' favorite body image, which is not so thin as girls think.

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Effects of Pre-Germinated Brown Rice on Blood Glucose and Lipid Levels in Free-Living Patients with Impaired Fasting Glucose or Type 2 Diabetes

Tzu-Fang HSU[1], Mitsuo KISE[2], Ming-Fu WANG[3], Yukihiko ITO[2], Mei-Due YANG[3], Hiromichi AOTO[2], Rie YOSHIHARA[4], Jyunichi YOKOYAMA[4], Daisuke KUNII[1] and Shigeru YAMAMOTO[1,5,*]

[1]*Institute of Health Biosciences, The University of Tokushima, Tokushima 770–8503, Japan*
[2]*FANCL Research Institute, FANCL Corporation, Yokohama 224–0806, Japan*
[3]*Department of Food and Nutrition, Providence University, Taichung 43301, Taiwan*
[4]*Jikei University School of Medicine, Tokyo 112–8610, Japan*
[5]*Ochanomizu University Graduate School of Humanities and Sciences, Tokyo, Japan.*

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Summary White rice (WR) is made by polishing brown rice (BR) and has lost various nutrients; however, most people prefer it to BR, maybe because of the hardness of BR. Pre-germinated brown rice (PGBR) improves the problem of BR. It is made by soaking BR kernels in water to germinate and becomes softer than BR. In this study we compared the effects of WR and PGBR on blood glucose and lipid concentrations in the impaired fasting glucose (IFG) or type 2 diabetes patients. Six men and 5 women with impaired fasting glucose (IFG) or type 2 diabetes were randomly allocated to 6 wk on WR or PGBR diet separated by a 2 wk washout interval in a crossover design. Each subject was instructed to consume 3 packs of cooked WR or PGBR (180 g/pack) daily in each intervention phase. Blood samples were collected 4 times (in study weeks 0, 6, 8 and 14) for biochemical examination. Blood concentrations of fasting blood glucose, fructosamine, serum total cholesterol and triacylglycerol levels were favorably improved on the PGBR diet ($p<0.01$), but not on the WR diet. The present results suggest that diets including PGBR may be useful to control blood glucose level.

Key Words white rice, pre-germinated brown rice, impaired fasting glucose (IFG), type 2 diabetes

The incidence of type 2 diabetes continues to rise in the world. Onset of type 2 diabetes closely involves genetics and environmental factors, and diet represents one of the important environmental factors. For example, a high-carbohydrate diet increases postprandial levels of blood glucose and insulin, and long-term consumption leads to insulin resistance (*1*). Furthermore, insulin resistance increases risk for diabetes, obesity and coronary artery disease (*2, 3*). In diabetes, persistent hyperglycemia leads to various complications. Large-scale prospective cohort studies have shown that maintaining blood glucose level is important for the prevention of diabetes and its related complications (*4–6*). Several studies in recent years have documented relationships between ischemic heart diseases and postprandial high blood glucose concentration (*7–9*).

Different carbohydrates are digested differently, and digestibility directly affects blood glucose and insulin levels. Carbohydrates can be classified based on glycemic index (GI) (*10*), and the clinical usefulness of dietary guidance based on glycemic index (GI) appears promising (*11*). Rice is an important staple starchy food consumed by more than half of the global population; however, the glycemic index (GI) of it is high (*12, 13*).

In recent years, a new type of rice has become available in Japan, called pre-germinated brown rice (PGBR). PGBR is made by soaking brown rice kernels in water to slightly germinate. PGBR is considered more healthful than WR, as it is richer in vitamins, minerals and dietary fiber. Regarding the effects of long-term consumption of PGBR, one study using streptozotocine-induced diabetic rats showed that compared to rats fed WR, levels of blood glucose and plasminogen activator inhibitor 1, which may increase the risk of diabetes and myocardial infarction (*14*), were significantly lower for rats fed PGBR, and blood lipid peroxide concentration tended to be lower (*15*). Our previous studies also showed that PGBR was better than WR to prevent the rapid increase of postprandial blood glucose concentration without increasing insulin secretion in humans (*16, 17*). However, clinical evidence does not yet support the usefulness of long-term consumption of PGBR as a staple food.

The present study aimed to ascertain the clinical usefulness of a diet including PGBR on blood glucose management in patients with impaired fasting glucose (IFG) or type 2 diabetes.

*To whom correspondence should be addressed.
E-mail: yamamoto.shigeru@ocha.ac.jp

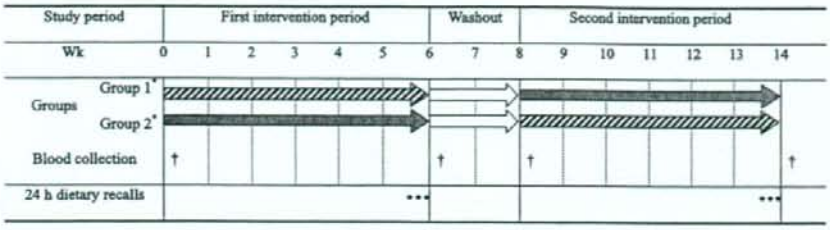

Fig. 1. Study design to observe the effect of WR and PGBR on blood glucose and lipid levels in free-living patients with type 2 diabetes. *Group 1, treatment from WR (n=6) to PGBR (n=5); Group 2, treatment from WR to PGBR. †Blood was collected in the mornings of weeks 0, 6, 8, and 14.

Table 1. Characteristics of test food (/100 g).

	WR	PGBR
Dry matter (%)	64.6	66.9
Protein (g)	2.8	3.2
Fat (g)	0.3	1.1
Carbohydrate (g)	32.2	28.3
Total fiber (g)	0.5	1.4
Insoluble fiber (g)	0.5	1.4
Soluble fiber (g)	N.D.	N.D.
Resistant starch (g)	0.5	0.4
GABA (mg)	N.D.	3.0
γ-Oryzanol (mg)	N.D.	7.9

Data are mean±SE. N.D., not detectable.

SUBJECTS AND METHODS

Eleven free-living subjects with type 2 diabetes (6 men and 5 women; 51.5±16.2 y of age [mean±SE, range 27–72 y]; body mass index (BMI) 25.1±3.4 kg/m^2 [mean±SE, range 18.9–31.2 kg/m^2]) were included in the study. Inclusion criteria were as follows: at the time of entry, fasting blood glucose (FBG)≥110 mg/dL. Throughout the study, the same drugs were administered without altering doses. One subject was administered insulin and 10 subjects were administered oral hypoglycemic agents (sulfonylurea n=8, biguanide n=9, thiazolidiones n=3 and alpha-glucosidase inhibitor n=2). This study was approved by the ethical review boards of both Providence University and Li Shin Hospital in Taiwan and was conducted in accordance with their rules and regulations. The protocol conformed to the Helsinki Declaration. Subjects were recruited through physicians at Li Shin Hospital (Pingjen, Taiwan). Informed consent was obtained from each participant.

The participants were randomly allocated to two experimental periods of 6 wk of WR or PGBR diet in a crossover design (first intervention period: 0 to 6 wk; second intervention period: 8 to 14 wk) (Fig. 1). During the 2 intervention periods, subjects were instructed to consume either WR or PGBR as the staple food. The washout period was set for 2 wk from weeks 6 to 8 of the study. Subjects were allowed to continue performing normal activities of daily living without restriction from entry to the start of the study.

In the present study, cooked rice packages were given to each subject. The rice samples were the same japonica rice variety (Hoshinoyume) and obtained from Hokkaido, Japan. The selected rice was a short grain variety with apparent amylose content of 18% determined on raw rice by the iodine blue colorimetric method. Characteristics of the cooked rice used in the present study are given in Table 1. During the study, each subject was instructed to eat 180 g of the cooked rice 3 times daily. Subjects were instructed to maintain similar activities

Table 2. Energy and nutrient intakes in the first and second intervention periods in Group 1 and 2.†

	First intervention period	Second intervention period
Energy intake (kcal/d)		
Group 1	1892.2±93.0	1891.9±88.2
Group 2	1920.2±68.2	1961.4±73.2
Protein (g/d)		
Group 1	69.2±4.4	70.6±3.5
Group 2	63.8±0.9	62.7±1.3
Fat (g/d)		
Group 1	64.8±3.3	61.0±2.7
Group 2	70.7±3.2	71.7±2.6
Carbohydrate (g/d)		
Group 1	252.6±12.7	253.2±13.0
Group 2	257.2±11.9	266.3±13.1
Dark green vegetable (g/d)		
Group 1	190.6±3.4	185.0±6.9
Group 2	206.7±11.3	203.3±9.7
Yellow vegetable (g/d)		
Group 1	203.9±8.0	198.9±11.1
Group 2	197.7±5.5	192.0±11.7
Fruit (g/d)		
Group 1	301.7±8.1	292.2±10.5
Group 2	310.0±6.7	306.7±15.5
Fiber (g/d)		
Group 1	16.8±1.1	19.8±0.5
Group 2	19.2±0.2	17.1±0.3*

†Group 1 (n=6), treatment from WR to PGBR diet; Group 2 (n=5), treatment from PGBR to WR diet. Data are mean±SE.
*Significant difference from first intervention value by Wilcoxon's signed-rank test at p<0.05.

Table 3. Physical characteristics and biochemical parameters at weeks 0, 6, 8 and 14 in Group 1 and 2.†

	First intervention period		Second intervention period	
	week 0	week 6	week 8	week 14
Weight (kg)				
Group 1	64.4±3.0	64.6±3.0	64.8±3.0	64.7±3.0
Group 2	65.9±5.9	65.9±6.1	65.7±5.9	65.9±6.2
Body fat (%)				
Group 1	27.8±3.1	27.9±3.0	27.8±3.0	27.5±3.0
Group 2	30.6±4.7	30.2±4.5	30.6±4.6	31.1±4.5
BMI (kg/m^2)				
Group 1	24.6±1.6	24.7±1.6	24.7±1.6	24.7±1.6
Group 2	25.6±1.4	25.6±1.4	25.5±1.4	25.5±1.5
W/H ratio				
Group 1	0.9±0	0.9±0	0.9±0	0.9±0
Group 2	0.9±0	0.9±0	0.9±0	0.9±0
SBP (mmHg)				
Group 1	120.3±5.7	118.3±7.0	119.7±7.1	121.7±6.2
Group 2	119.4±5.1	125.6±8.5	125.4±7.7	122.4±6.3
DBP (mmHg)				
Group 1	70.0±4.9	69.0±3.8	67.7±4.2	71.3±4.2
Group 2	71.4±3.4	75.2±3.0	75.2±3.3	70.4±2.3
TP (g/dL)				
Group 1	7.5±0.1	7.3±0.1	7.4±0.1	7.5±0.1
Group 2	7.3±0.3	7.5±0.4	7.2±0.4	7.1±0.3
Alb (g/dL)				
Group 1	4.6±0.1	4.6±0.1	4.6±0.1	4.7±0.1
Group 2	4.3±0.2	4.3±0.2	4.3±0.3	4.4±0.2
Insulin (μU/mL)				
Group 1	7.1±2.5	7.5±1.8	7.9±2.0	7.1±1.0
Group 2	6.4±0.5	8.5±1.9	8.8±2.0	7.8±2.4
TC (mg/dL)				
Group 1	239.5±8.8	241.7±8.0	243.2±7.8	223.3±7.8*
Group 2	241.8±10.1	216.2±7.3*	222.0±8.0	231.4±11.4
TG (mg/dL)				
Group 1	190.7±44.9	192.5±44.2	193.5±45.0	176.5±44.0*
Group 2	121.6±19.6	91.2±15.0*	95.8±15.0	97.4±15.4
HDL-C (mg/dL)				
Group 1	48.0±4.4	46.7±3.8	47.5±3.8	53.3±4.6*
Group 2	52.0±3.5	63.2±4.2*	59.6±3.7	57.4±4.4

†Group 1 (n=6), treatment from WR to PGBR diet; Group 2 (n=5), treatment from PGBR to WR diet. BMI: body mass index, W/H ratio: waist-hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure, TP: total protein, Alb: serum albumin, TC: total cholesterol, TG: triglyceride, HDL-C: HDL-cholesterol.

*Significant difference between the week 0 and weeks 6, 8 and 14 within the same group was analyzed by Wilcoxon's signed-rank test at $p<0.05$. Data are mean±SE.

of daily living, including exercise.

Height was measured only at study week 0. Body weight and blood pressure were measured at study weeks 0, 6, 8, and 14. In each intervention period (WR and PGBR), dietary intakes were ascertained from 24 h dietary recalls conducted by national registered dietitians for 3 consecutive days in the last week of each intervention period (weeks 6 and 14). Using the Taiwan food composition table (*18*), energy consumption, nutrient consumption (proteins, lipids, carbohydrates and cholesterol), were calculated.

Blood samples were taken 4 times, in study weeks 0, 6, 8, and 14. After dividing samples into plasma and serum, serum samples were stored at −70°C until analyzing. Plasma glucose levels were measured using the glucose dehydrogenase method. Levels of serum fructosamine were measured by the colorimetric method. Levels of serum total cholesterol (TC), triacylglycerol (TG) and HDL-cholesterol (HDL-C) were measured using the enzymatic method, the selective inhibition method and the free glycerol diminishing method, respectively. Total protein (TP) and albumin (Alb) concentrations were measured by the timed endpoint method and nephelometry method, respectively (UM Clinical Laboratory, Taichung, Taiwan). Level of insulin was measured using the enzyme immunoassay (SRL, Tokyo, Japan). Laboratory technologists were blinded to the identity of subjects and intervention status, and the

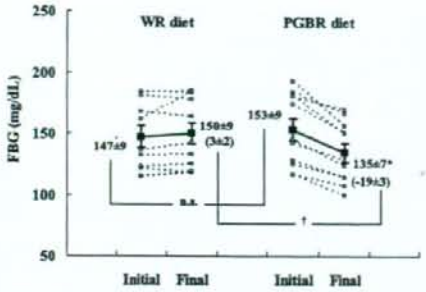

Fig. 2. Change in fasting blood glucose (FBG) concentration during WR diet or PGBR diet groups for 6 wk. Bold line: mean±SE; dotted fine line: individual data. Figure in parenthesis: mean±SE of "initial value−final value". *Significant difference from initial value by Wilcoxon's signed-rank test at $p<0.01$. †Significant difference between WR and PGBR diet groups including the figures in parenthesis ($p<0.01$), n.s.: not statistically significant ($p=0.053$).

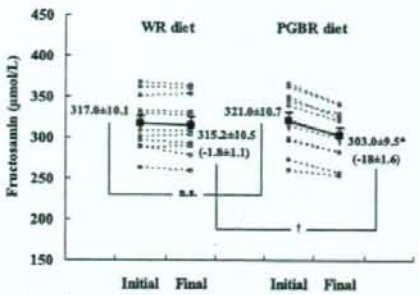

Fig. 3. Change in fructosamin level during WR diet or PGBR diet for 6 wk. Bold line: mean±SE; dotted fine line: individual data. Figure in parenthesis: mean±SE of "initial value−final value". *Significant difference from initial value by Wilcoxon's signed-rank test at $p<0.01$. †Significant difference between WR and PGBR diet groups including the figures in parenthesis ($p<0.01$), n.s.: not statistically significant ($p=0.396$).

person in charge of statistical analyses was blinded to the same information until the time of data analysis.

Numerical data were expressed as mean±SE. Blood glucose management markers, blood lipid-related markers, and dietary consumption were subjected to Wilcoxon's signed-rank tests in each experimental period. Values of $p<0.05$ were considered statistically significant. All statistical analyses were performed with the Stat View 5.0 (SAS Institute, Inc., USA).

RESULTS

Subjects were examined by a physician in study weeks 0, 6, 8, and 14. Table 2 shows energy and nutrient intakes in the first and second intervention periods in Group 1 and 2. Between the WR and PGBR diets, no significant differences in dietary consumption were identified except dietary fiber content of Group 2 were significantly higher ($p<0.05$) after the PGBR diet consumption.

Table 3 shows physical characteristics and biochemical parameters at study weeks 0, 6, 8 and 12 in Group 1 and 2. Throughout the study, no marked shifts were displayed in physical characteristics such as body mass index (BMI) or percent body fat or serum biochemical parameters such as insulin, total protein (TP) or albumin (Alb). Levels of serum total cholesterol (TC), triacylglycerol (TG) and HDL-cholesterol (HDL-C) were significantly improved ($p<0.05$) after the PGBR diet consumption.

With the PGBR diet, fasting blood glucose (FBG) levels decreased significantly from the initial of 153±9 mg/dL to 135±7 mg/dL ($p<0.01$), but no marked changes were observed with the WR diet (147±9 mg/dL vs. 150±9 mg/dL, respectively) (Fig. 2). Means±SE of "Initial FBG value−final FBG value" in each dietary treatment were calculated (Fig. 2). They were 3±2 and −19±3 in the WR and PGBR groups, respectively. The FBG levels decreased more in the PGBR group than in the WR group ($p<0.01$).

In addition, in the PGBR diet, fructosamine levels decreased significantly from the initial of 321.0±10.7 μmol/L to 303.0±9.5 μmol/L ($p<0.01$), but in the WR diet, no marked changes were seen between initial and final intervention (317.0±10.1 μmol/L vs. 315.2±10.5 μmol/L, respectively) (Fig. 3). Means±SE of "Initial fructosamine value−final fructosamine value" in each dietary treatment are shown in Fig. 3. They were −1.8±1.1 and −18±1.6 in WR and PGBR groups, respectively. The decrease of the fructosamine level was greater in the PGBR group than in the WR group ($p<0.01$).

No significant difference in levels of fasting blood glucose (FBG) or fructosamine were noted before consumption of the WR diet or the PGBR diet. Furthermore, levels of fasting blood glucose (FBG) and fructosamine were significantly decreased after consuming the PGBR diet compared to the WR diet ($p<0.01$, each).

DISCUSSION

It has been known the fasting blood glucose (FBG) level represents current blood glucose status; the fructosamine levels represents the history of blood glucose status during the previous 1–2 wk. The present results show that, unlike WR, consuming PGBR as a staple food significantly decreases fasting blood glucose (FBG) and fructosamine in patients with type 2 diabetes ($p<0.01$). Hence, these results suggest that blood glucose levels were maintained favorably during the intervention period. Serum levels of total cholesterol (TC) and triglyceride (TG) significantly improved after consuming the PGBR diet ($p<0.01$). Conversely, no significant changes in blood glucose management or lipid-related markers were noted between initial or final values when taking the WR diet.

Dietary and exercise habits markedly affect levels of blood glucose and lipids (3–5). Subjects in the present study were instructed to avoid changes in dietary and

exercise habits as much as possible to minimize confounding factors. During the 2 study periods, dietary intake was measured by using 24 h dietary recalls in each subject during 3 consecutive days of the two intervention periods. No marked differences in energy or nutrition intakes (Table 2) and no changes in body mass index (BMI) or body fat were observed between the two groups (Table 3). These findings suggest that energy consumption and physical activity were maintained during the study; and dietary and exercise habits did not markedly affect blood glucose or lipid levels. As hypoglycemic agents, 9 subjects were taking sulfonylurea and biguanide drugs, and 1 subject was taking only an insulin preparation. Throughout the study, the same drugs and doses were administered without change. Therefore, the effects from medicine on blood glucose management and lipid-related parameters may be eliminated.

The reason for the improved blood glucose management markers with the PGBR diet is suggested to be that the physical shape of grains delays digestion and absorption of carbohydrates. PGBR comprises endosperm, aleurone layer, bran layer and germ. As the endosperm is covered by the bran layer, starches do not come into contact with digestive enzymes as often as they do with WR. In a study in which humans were instructed to eat either BR or WR, blood glucose and insulin reaction were lower with BR when compared to WR (*19*). An in vitro study showed that the rate of starch hydrolysis was markedly lower for BR than for WR (*20*). Past studies have shown that dietary fibers lower the risk for diabetes (*21*), suggesting that the dietary fibers included in bran suppress the absorption of saccharides broken down by digestive enzymes, ultimately suppressing increases in postprandial blood glucose levels. In the rodent, it has been reported that the blood glucose-lowering effect of PGBR may be derived from the higher dietary fiber of PGBR than WR (*22*).

Consumption of PGBR significantly improved levels of blood lipids. Regarding the mechanisms of improved blood lipid levels, increased fiber intake may be suggested. As the other possible factor, we may be able to suggest the reduced postprandial secretion of insulin, which induces the synthesis of total cholesterol (TC) (*23*) and triacylglycerol (TG) (*24*). Rice bran from PGBR contains γ-oryzanols (ferulate ester of triterpene alcohols) which are effective in improving hyperlipidemia (*25–27*). Furthermore, in vitro studies have shown high adsorption of bile acid by rice bran (*28, 29*). In a recent study, a PGBR diet suppressed hypercholesterolemia, and enhanced fecal bile acid excretion without affecting cholesterol synthesis in the host liver of hepatoma-bearing rats (*30*). With regard to nutritional guidelines for diabetes management, the accuracy of conventional guidance based on high carbohydrate consumption is being questioned. The reason for this is that a high-carbohydrate diet can increase levels of blood glucose, insulin and triacylglycerol (TG) (*31*). The glycemic index (GI) of WR is substantially higher than that of BR, which is less refined. As a result, from the perspective of blood glucose management, consumption of WR should be minimized. At present, insufficient data is available to support the idea that long-term consumption of WR may increase the risk of diabetes or heart disease. In the present study, patients with type 2 diabetes were instructed to consume 180 g of rice 3 times a day for 6 wk, and no changes in blood glucose management or lipid-related markers occurred with the WR diet. Long-term large-scale intervention studies are thus warranted to clarify relationships between WR consumption and diseases such as diabetes and heart disease. The present results show that, in type 2 diabetes patients with favorable blood glucose levels controlled by drug and dietary therapy, consumption of PGBR, which is less refined than WR, significantly improves levels of blood glucose, fructosamine (blood glucose management markers), total cholesterol (TC), triglyceride (TG) and HDL-cholesterol (HDL-C) (lipid-related markers).

While the present study was only a small-scale study lasting 6 wk, the results suggest that consumption of PGBR as a staple food in patients with type 2 diabetes is useful in improving blood glucose and lipid levels.

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