

資 料

- 1) Murakami K, Sasaki S, Okubo H, Takahashi Y, Hosoi Y, Itabashi M, the Freshmen in Dietetic Courses Study II Group. Food intake and functional constipation: a cross-sectional study of 3,835 Japanese women aged 18-20 years. *J Nutr Sci Vitaminol (Tokyo)* 2007; 53: 30-6.
- 2) Okubo H, Sasaki S, Rafamantanantsoa HH, Ishikawa-Takata K, Okazaki K, Tabata I. Validation of self-reported energy intake by a self-administered diet history questionnaire using the doubly labeled water method in 140 Japanese adults *Eur J Clin Nutr* 2008; 62: 1343-50.
- 3) Murakami K, Sasaki S, Takahashi Y, Uenishi K, the Japan Dietetic Students' Study for Nutrition and Biomarkers Group. Association between dietary acid-base load and cardiometabolic risk factors in young Japanese women. *Br J Nutr* 2008; 100: 642-51.
- 4) Murakami K, Sasaki S, Takahashi Y, Uenishi K, Watanabe T, Kohri T, Yamasaki M, Watanabe R, Baba K, Shibata K, Takahashi T, Hayabuchi H, Ohki K, Suzuki J. Dietary glycemic index is associated with decreased premenstrual symptoms in young Japanese women. *Nutrition* 2008; 24: 554-61.
- 5) Murakami K, Sasaki S, Takahashi Y, Uenishi K, Yamasaki M, Hayabuchi H, Goda T, Oka J, Baba K, Ohki K, Muramatsu K, Sugiyama Y. Total n-3 polyunsaturated fatty acid intake is inversely associated with serum C-reactive protein in young Japanese women. *Nutr Res* 2008; 28: 309-14.
- 6) Murakami K, Sasaki S, Takahashi Y, Okubo H, Hirota N, Notsu A, Fukui M, Date C. Comparability of weighed dietary records and a self-administered diet history questionnaire for estimating monetary cost of dietary energy. *Environmental Health Insights* 2008; 1: 35-43.
- 7) Murakami K, Sasaki S, Takahashi Y, Uenishi K, Watanabe T, Kohri T, Yamasaki M, Watanabe R, Baba K, Shibata K, Takahashi T, Hayabuchi H, Ohki K, Suzuki J. Lower estimates of δ -5 desaturase and elongase activity are related to adverse profiles for several metabolic risk factors in young Japanese women. *Nutr Res* 2008; 28: 816-24.

- 8) Satoshi S. Dietary Reference Intakes (DRIs) in Japan. *Asia Pac J Clin Nutr* 2008; 17(S2): 420-44.
- 9) 佐々木敏. 特集糖尿病食事療法のエビデンス 食事摂取基準のエビデンス 内分泌・糖尿病科 2009; 28 (2) : 97-102.

Food Intake and Functional Constipation: A Cross-Sectional Study of 3,835 Japanese Women Aged 18–20 Years

Kentaro MURAKAMI¹, Satoshi SASAKI^{1,*}, Hitomi OKUBO², Yoshiko TAKAHASHI¹, Yoko HOSOI¹, Mami ITABASHI¹ and the Freshmen in Dietetic Courses Study II Group

¹Nutritional Epidemiology Program, National Institute of Health and Nutrition, Tokyo 162–8636, Japan

²Department of Nutrition Sciences, Kagawa Nutrition University, Saitama 350–0288, Japan

(Received July 14, 2006)

Summary Although we previously observed significant associations between intakes of several foods and constipation, definition of constipation was completely based on subjective perception assessed by a quite simple and single question: do you often have constipation? In this study, we examined the associations between food intake and functional constipation as defined according to symptom-based criteria (Rome I criteria: straining, hard stools, incomplete evacuation, and infrequency of bowel movement). Subjects were 3,835 female Japanese dietetic students aged 18–20 y from 53 institutions in Japan. Dietary intake was estimated with a validated, self-administered diet history questionnaire. The prevalence of functional constipation was 26.2%. Dietary intakes of several foods were significantly associated with functional constipation. A multivariate adjusted odds ratio (95% confidence interval; *p* for trend) for women in the highest quintile of dietary intake compared with those in the lowest was 0.59 (0.46–0.75; <0.0001) for rice, 0.77 (0.61–0.97; 0.003) for pulses, 1.64 (1.30–2.08; <0.0001) for confectioneries, and 1.41 (1.11–1.78; 0.01) for bread. In conclusion, intake of rice and pulse was negatively and that of confectioneries and bread was positively associated with functional constipation among a population of young Japanese women, which was generally consistent with our previous study where constipation was assessed by a quite simple question.

Key Words dietary fiber, food, rice, functional constipation, epidemiology

Constipation is a common health problem (1–4), and food intake is considered to be a major modifiable lifestyle factors associated with this condition (5, 6). Foods related to constipation in previous observational studies include dairy products (7), beans (7), meats (7), fruits (7), vegetables (7), rice (3, 8, 9), eggs (9), confectioneries (8), and several nonalcoholic beverages (3, 7, 8, 10, 11). However, while most previous studies have defined constipation according to the infrequency of bowel movement only (10–13) or the subjective perception of patients (7, 8), a consensus definition of constipation consists of straining, hard stools, and incomplete evacuation in addition to infrequency (Rome criteria) (14). Further, although Wong et al. (3) and Nakaji et al. (9) defined constipation using the Rome criteria and original subjective criteria, respectively, they assessed diet with a non-validated, relatively simple food frequency questionnaire. Moreover, although we previously observed associations between intakes of several foods and constipation (11), using a previously validated, self-administered, diet history questionnaire (DHQ) (15–17), the definition of constipation was completely based on subjective perception assessed by a quite simple and single question: do you often have constipation?

Thus, to our knowledge, no study has so far investigated the relationship of food intake, as assessed with a validated assessment method, to functional constipation, as defined using symptom-based criteria. Here, we examined the associations between food intake, estimated using DHQ, and functional constipation as defined according to the Rome criteria (14).

SUBJECTS AND METHODS

Subjects and survey procedure. The present study was based on a self-administered questionnaire survey among dietetic students ($n=4,679$) from 54 institutions in Japan. Staff at each institution distributed a dietary assessment questionnaire (i.e., DHQ) and another questionnaire on other lifestyle items during the preceding month to students during an orientation session or a first lecture designed for freshman students entering dietetic courses in April 2005; in most institutions, this was carried out within 2 wk after the course began to minimize the influence of new school year life on the answers. Students filled out the questionnaires during the session, lecture, or at home and then submitted the completed forms to staff at each institution. Questionnaires used in the present study included the explanation on how to answer questions. To standardize the survey procedure, when students asked how to answer questionnaires, staff at each institution did not

*To whom correspondence should be addressed.
E-mail: stssasak@nih.go.jp

provide any advice and only asked students to read the explanation on questionnaires carefully. In addition to the two questionnaires for the preceding month, a third questionnaire on lifestyle during the previous 6 y (i.e., junior high school and high school) was also distributed and answered in a similar fashion; in most institutions, this was carried out within 4 wk after the course began because it was considered burdensome for subjects to answer all three questionnaires at the same time and it was considered unlikely that new school year life would influence the answers for lifestyle during the previous 6 y.

The staff at each institution checked the responses according to the survey protocol. When missing answers or logical errors were identified, the student was asked to complete the questionnaire again. The staff at each institution mailed the questionnaires to the survey center. Staff at the survey center checked the answers again, and when necessary returned problematic questionnaires to staff at the respective institution, and the student was asked to complete the questionnaires again. All questionnaires were thus checked at least once by staff at each institution and by staff at the survey center. Most surveys were completed by May 2005. The protocol of the present study was approved by the Ethics Committee of the National Institute of Health and Nutrition.

In total, 4,286 students (4,066 women and 220 men) answered all three questionnaires (91.6%). For the current analysis, we selected female subjects aged 18–20 y ($n=3,967$) because of the small number of male subjects and women aged >20 y. We then excluded women who were in an institution where the survey had been conducted at the end of May ($n=97$) because the answers were likely influenced by the new school year life. We further excluded those with extremely low or high energy intake (<500 kcal/d or $>4,000$ kcal/d) ($n=23$) because their estimated dietary intake was likely unreliable. We finally excluded those with missing information on the variables used ($n=24$) for the purpose of multivariate analyses. As some subjects were in more than one exclusion category, the final analysis sample comprised 3,825 women. Although intentional dietary change or use of oral laxatives might have influence on dietary intake or constipation, further exclusion of subjects with intentional dietary change within the preceding year ($n=649$), those habitually using oral laxatives ($n=231$), or both did not materially alter the findings, and these subjects were therefore included in the analyses.

Dietary intake. Dietary habits during the previous month were assessed using a previously validated, self-administered DHQ (15–17). This is a 16-page structured questionnaire that consists of the following seven sections: general dietary behavior; major cooking methods; consumption frequency and amount of six alcoholic beverages; consumption frequency and semi-quantitative portion size of 121 selected food and non-alcoholic beverage items; dietary supplements; consumption frequency and semi-quantitative portion size

of 19 staple foods (rice, bread, and noodles) and miso (fermented soybean paste) soup; and open-ended items for foods consumed regularly (\geq once/wk) but not appearing in the DHQ. The food and beverage items and portion sizes in the DHQ were derived primarily from data in the National Nutrition Survey of Japan (18) and several recipe books for Japanese dishes (15).

Estimates of dietary intake for 147 food and beverage items and energy were calculated using an ad hoc computer algorithm for the DHQ, which was based on the Standard Tables of Food Composition in Japan (19). Information on dietary supplements and data from the open-ended questionnaire items were not used in the calculation of dietary intake. The food and nonalcoholic beverage items were grouped into the 18 food groups (as shown in Table 2). Detailed descriptions of the methods used for calculating dietary intake and the validity of the DHQ have been published elsewhere (15–17). The Pearson correlation coefficient (20) between DHQ and 3-d estimated dietary records was 0.48 for energy among 47 women (15). In addition, the mean value of the Spearman correlation coefficients (20) for energy-adjusted intakes (g/1,000 kcal) of 16 food groups was 0.35 (range: 0.05–0.59) among 92 women (Sasaki S, unpublished observations, 2004).

Constipation. A constipation questionnaire was developed based on a previous study (2) and incorporated into the 20-page questionnaire for lifestyle during the previous 6 y. We used the definition of functional constipation recommended by an international workshop on the management of constipation (Rome I criteria) (14). Although the Rome I criteria were modified in 1999 (Rome II criteria) (21), epidemiologic studies have consistently shown that the latter may be too restrictive for the diagnosis of constipation (2, 4); we therefore used the former. The Rome I criteria are a consensus definition of constipation consisting of various symptoms including bowel movement frequency (as shown below) (14), and have become the research standard for the definition of constipation (1). The following four questions were used to assess Rome I-defined functional constipation: 1) Do you strain during a bowel movement?; 2) Do you feel an incomplete emptying sensation after a bowel movement?; 3) How often are your stools hard?; and 4) How many bowel movements do you usually have each week? These questions referred to the last 12 mo. For questions 1–3, four answers were offered: never, sometimes ($<25\%$ of the time), often ($\geq 25\%$ of the time), and always. Functional constipation was defined as meeting two or more of the four criteria [an answer of *often* or *always* to questions 1–3 and <3 bowel movements per week (question 4)].

Confounding factors. In epidemiologic research, it is usual to divide the main dependent variables (food intake in the present study) and confounding factors (other lifestyle factors described below in the present study) based on previous studies (1–13). Thus, we assessed not only dietary intake but also several lifestyle factors described below in the present survey. In the questionnaires, subjects reported body weight and

Table 1. Characteristics of subjects.^a

Variable	All (n=3,825)	Subjects with functional constipation ^b (n=1,002)	Subjects without functional constipation (n=2,823)	<i>p</i> ^c
Body mass index (kg/m ²)	21.0±2.8	20.8±2.5	21.0±2.9	0.08
<18.5	557 (14.6)	139 (13.9)	418 (14.8)	0.19
18.5–24.9	2,976 (77.8)	798 (79.6)	2,178 (77.2)	
≥25	292 (7.6)	65 (6.5)	227 (8.0)	
Residential block				0.20
Hokkaido and Tohoku	375 (9.8)	93 (9.3)	282 (10.0)	
Kanto	1,310 (34.3)	351 (35.0)	959 (34.0)	
Hokuriku and Tokai	537 (14.0)	159 (15.9)	378 (13.4)	
Kinki	765 (20.0)	203 (20.3)	562 (19.9)	
Chugoku and Shikoku	421 (11.0)	99 (9.9)	322 (11.4)	
Kyushu	417 (10.9)	97 (9.7)	320 (11.3)	
Size of residential area				0.98
City with a population ≥1 million	745 (19.5)	195 (19.5)	550 (19.5)	
City with a population <1 million	2,495 (65.2)	652 (65.1)	1,843 (65.3)	
Town and village	585 (15.3)	155 (15.5)	430 (15.2)	
Current smoking				0.02
No	3,769 (98.5)	980 (97.8)	2,789 (98.8)	
Yes	56 (1.5)	22 (2.2)	34 (1.2)	
Current alcohol drinking				0.0001
No	3,097 (81.0)	770 (76.9)	2,327 (82.4)	
Yes	728 (19.0)	232 (23.2)	496 (17.6)	
Oral medication usage				<0.0001
No	3,447 (90.1)	840 (83.8)	2,607 (92.4)	
Yes	378 (9.9)	62 (6.2)	216 (7.7)	
Physical activity level	1.45±0.15	1.45±0.16	1.45±0.15	0.56
Quintile 1 (<1.36)	758 (19.8)	200 (20.0)	558 (19.8)	0.96
Quintile 2 (1.36–1.38)	772 (20.2)	205 (20.5)	567 (20.1)	
Quintile 3 (1.39–1.42)	765 (20.0)	206 (20.6)	559 (19.8)	
Quintile 4 (1.43–1.49)	765 (20.0)	196 (19.6)	569 (20.2)	
Quintile 5 (>1.49)	765 (20.0)	195 (19.5)	570 (20.2)	
Energy intake (kcal/d)	1,819±502	1,835±531	1,814±491	0.26
Quintile 1 (<1,407)	765 (20.0)	206 (20.6)	559 (19.8)	0.19
Quintile 2 (1,407–1,636)	765 (20.0)	195 (19.5)	570 (20.2)	
Quintile 3 (1,637–1,869)	765 (20.0)	191 (19.1)	574 (20.3)	
Quintile 4 (1,870–2,181)	765 (20.0)	186 (18.6)	579 (20.5)	
Quintile 5 (>2,182)	765 (20.0)	224 (22.4)	541 (19.2)	

^a Values are mean ± standard deviation or n (%).

^b Defined according to the Rome I criteria (14).

^c For continuous variables, independent *t*-test was used; for categorical variables, chi-square test was used.

height, residential area, current smoking (yes or no), and oral medication usage (yes or no). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). We classified BMI into three categories (<18.5, 18.5–24.9, and ≥25 kg/m²) according to the Japan Society for the Study of Obesity (22). The reported residential areas were grouped into six categories (Hokkaido and Tohoku; Kanto; Hokuriku and Tokai; Kinki; Chugoku and Shikoku; and Kyushu) based on the regional blocks used in the National Nutrition Survey in Japan (23) (hereafter referred to as 'residential block'). The residential areas were also grouped into three categories according to population size (city with population ≥1 million; city with population <1 million; and town and village) (hereafter referred to as 'size of residential area').

Additionally, subjects reported the time when they usually went to bed and arose in the morning, which was used to calculate sleeping hours, and the frequency and duration of high- and moderate-intensity activities, walking, and sedentary activities. Each activity was assigned a metabolic equivalent (MET) value (24, 25). The number of hours spent per day on each activity was multiplied by the MET value of that activity, and all MET-hour products were summed to give a total MET-hour score for the day. Physical activity level was then calculated by dividing total MET-hour score (kcal/kg of body weight/d) by the standard value of basal metabolic rate for Japanese women aged 18–29 y (23.6 kcal/kg of body weight/d) (26).

Statistical analysis. Associations between functional constipation (the dependent variable) and energy-

Table 2. Multivariate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for functional constipation^a by quintiles of food intake^b (n = 3,825).

	Quintile category of food intake					p for trend
	1	2	3	4	5	
Rice (g/1,000 kcal) ^c	78 [0-101]	119 [101-135]	152 [135-169]	188 [169-214]	251 [214-448]	
n with/without functional constipation	247/518	206/559	191/574	197/568	161/604	
Multivariate adjusted OR (95% CI) ^d	1.00	0.81 (0.65-1.02)	0.73 (0.58-0.92)	0.76 (0.60-0.96)	0.59 (0.46-0.75)	<0.0001
Bread (g/1,000 kcal) ^c	4 [0-9]	14 [9-18]	23 [18-28]	34 [28-41]	53 [41-171]	
n with/without functional constipation	178/587	199/566	206/559	195/570	224/541	
Multivariate adjusted OR (95% CI) ^d	1.00	1.16 (0.92-1.47)	1.27 (1.00-1.61)	1.17 (0.92-1.49)	1.41 (1.11-1.78)	0.01
Noodles (g/1,000 kcal) ^c	0 [0-11]	16 [11-24]	31 [24-38]	47 [38-59]	79 [59-355]	
n with/without functional constipation	204/561	211/554	207/558	185/580	195/570	
Multivariate adjusted OR (95% CI) ^d	1.00	1.06 (0.84-1.33)	1.02 (0.81-1.29)	0.90 (0.71-1.14)	0.94 (0.75-1.19)	0.30
Potatoes (g/1,000 kcal) ^c	6 [0-8]	10 [8-11]	13 [11-15]	18 [15-22]	29 [22-165]	
n with/without functional constipation	199/566	169/596	206/559	218/547	210/555	
Multivariate adjusted OR (95% CI) ^d	1.00	0.80 (0.63-1.02)	1.03 (0.82-1.30)	1.10 (0.87-1.38)	1.04 (0.83-1.31)	0.15
Confectioneries ^e (g/1,000 kcal) ^c	18 [1-24]	29 [24-33]	37 [33-42]	47 [42-54]	63 [54-142]	
n with/without functional constipation	162/603	185/580	191/574	224/541	240/525	
Multivariate adjusted OR (95% CI) ^d	1.00	1.17 (0.92-1.50)	1.20 (0.94-1.53)	1.51 (1.19-1.92)	1.64 (1.30-2.08)	<0.0001
Fat and oil (g/1,000 kcal) ^c	7 [1-8]	10 [8-11]	12 [11-14]	15 [14-18]	21 [18-67]	
n with/without functional constipation	196/569	210/555	205/560	194/571	197/568	
Multivariate adjusted OR (95% CI) ^d	1.00	1.14 (0.91-1.44)	1.11 (0.88-1.40)	1.04 (0.82-1.32)	1.03 (0.81-1.31)	0.90
Pulses ^f (g/1,000 kcal) ^c	7 [0-10]	13 [10-17]	20 [17-25]	30 [25-37]	48 [37-174]	
n with/without functional constipation	234/531	216/549	174/591	181/584	197/568	
Multivariate adjusted OR (95% CI) ^d	1.00	0.90 (0.72-1.12)	0.64 (0.50-0.80)	0.68 (0.54-0.86)	0.77 (0.61-0.97)	0.003
Fish and shellfish (g/1,000 kcal) ^c	11 [0-16]	20 [16-24]	27 [24-31]	35 [31-41]	50 [41-164]	
n with/without functional constipation	209/556	208/557	194/571	184/581	207/558	
Multivariate adjusted OR (95% CI) ^d	1.00	1.00 (0.80-1.26)	0.92 (0.73-1.16)	0.88 (0.70-1.11)	0.98 (0.78-1.23)	0.54
Meats (g/1,000 kcal) ^c	15 [0-20]	23 [20-27]	31 [27-35]	39 [35-46]	55 [46-134]	
n with/without functional constipation	199/566	192/573	194/571	219/546	198/567	
Multivariate adjusted OR (95% CI) ^d	1.00	0.98 (0.78-1.24)	1.03 (0.81-1.29)	1.17 (0.93-1.47)	1.03 (0.81-1.30)	0.39
Eggs (g/1,000 kcal) ^c	3 [0-5]	8 [5-13]	15 [13-20]	25 [20-29]	36 [29-127]	
n with/without functional constipation	192/573	211/554	197/568	200/565	202/563	
Multivariate adjusted OR (95% CI) ^d	1.00	1.12 (0.89-1.42)	1.02 (0.80-1.29)	1.04 (0.82-1.31)	1.12 (0.89-1.42)	0.58
Dairy products (g/1,000 kcal) ^c	16 [0-26]	38 [26-52]	66 [52-82]	100 [82-123]	172 [123-596]	
n with/without functional constipation	212/553	200/565	198/567	193/572	199/566	
Multivariate adjusted OR (95% CI) ^d	1.00	0.90 (0.72-1.14)	0.88 (0.70-1.11)	0.87 (0.69-1.10)	0.91 (0.72-1.15)	0.39
Vegetables ^g (g/1,000 kcal) ^c	49 [2-67]	80 [67-95]	110 [95-126]	146 [126-173]	221 [173-1142]	
n with/without functional constipation	218/547	201/564	187/578	197/568	199/566	
Multivariate adjusted OR (95% CI) ^d	1.00	0.89 (0.71-1.12)	0.81 (0.64-1.02)	0.84 (0.67-1.06)	0.86 (0.68-1.09)	0.18
Fruits (g/1,000 kcal) ^c	8 [0-14]	20 [14-27]	36 [27-45]	57 [45-74]	104 [74-614]	
n with/without functional constipation	224/541	189/576	201/564	176/589	212/553	
Multivariate adjusted OR (95% CI) ^d	1.00	0.80 (0.64-1.01)	0.84 (0.67-1.06)	0.70 (0.55-0.89)	0.87 (0.69-1.09)	0.11
Water (g/1,000 kcal) ^c	0 [0]	11 [2-14]	34 [14-62]	96 [62-185]	319 [185-1649]	
n with/without functional constipation	319/950	62/199	205/560	203/562	213/552	
Multivariate adjusted OR (95% CI) ^d	1.00	0.93 (0.68-1.28)	1.05 (0.85-1.29)	1.04 (0.84-1.28)	1.10 (0.89-1.35)	0.36
Japanese and Chinese tea ^h (g/1,000 kcal) ^c	44 [0-80]	124 [80-189]	237 [189-288]	366 [288-459]	635 [459-1806]	
n with/without functional constipation	212/553	190/575	188/577	210/555	202/563	
Multivariate adjusted OR (95% CI) ^d	1.00	0.87 (0.69-1.09)	0.86 (0.68-1.09)	1.00 (0.79-1.26)	0.93 (0.74-1.17)	0.97
Black tea ⁱ (g/1,000 kcal) ^c	0 [0]	11 [2-14]	25 [14-40]	72 [40-1069]		
n with/without functional constipation	482/1,351	108/354	206/559	206/559		
Multivariate adjusted OR (95% CI) ^d	1.00	1.02 (0.83-1.24)	0.83 (0.63-1.09)	1.02 (0.81-1.28)		0.99
Coffee (g/1,000 kcal) ^c	0 [0]	13 [4-29]	65 [29-1282]			
n with/without functional constipation	638/1,800	171/451	193/572			
Multivariate adjusted OR (95% CI) ^d	1.00	1.10 (0.91-1.34)	1.11 (0.87-1.42)			0.41
Other nonalcoholic beverages (g/1,000 kcal) ^c	0 [0-0.002]	4 [0.002-10]	18 [10-29]	42 [29-61]	96 [61-860]	
n with/without functional constipation	197/568	212/553	178/587	198/567	217/548	
Multivariate adjusted OR (95% CI) ^d	1.00	1.11 (0.88-1.40)	0.87 (0.69-1.11)	1.02 (0.81-1.29)	1.11 (0.88-1.40)	0.60

^a Defined according to the Rome I criteria (14).^b Except for water (5 categories), black tea (4 categories), and coffee (3 categories) because of more than one fifth nonconsumers.^c Values are median [range].^d Adjusted for body mass index (<18.5, 18.5-24.9, and ≥25 kg/m²), residential block (Hokkaido and Tohoku; Kanto; Hokuriku and Tokai; Kinki; Chugoku and Shikoku; and Kyushu), size of residential area (city with a population ≥1 million; city with a population <1 million; and town and village), current smoking (yes or no), current alcohol drinking (yes or no), oral medication usage (yes or no), physical activity level (quintiles), and energy intake (quintiles).^e Including sugar and sweeteners.^f Including nuts.^g Including mushrooms and sea vegetables.^h Non- and semifermented tea.ⁱ Fermented tea.

adjusted intakes (g/1,000 kcal) of the 18 food groups (as shown in Table 2) were examined. We calculated both crude and multivariate adjusted odds ratios (ORs) and 95% confidence intervals for functional constipation for each quintile category of dietary variables (except for several drinks because more than one-fifth of subjects were nonconsumers) using logistic regression analysis (20). Multivariate adjusted ORs were calculated by adjusting for BMI, residential block, size of residential area, current smoking, current alcohol drinking (yes or no, because of extremely low alcohol intake: mean=0.8 g/d), oral medication usage, physical activity level (quintiles), and energy intake (quintiles). As results for the crude and multivariate analyses were similar for all variables analyzed, we presented only those derived from the multivariate models. Trend of association was assessed by a logistic regression model assigning scores to the levels of the independent variable. All statistical analyses were performed using SAS statistical software, version 8.2 (SAS Institute Inc., Cary, NC, USA). All reported *p* values are 2-tailed, and a *p* value of <0.05 was considered statistically significant.

RESULTS

Basic characteristics of the subjects are shown in Table 1. Mean (\pm standard deviation) age, body height, and body weight was 18.1 \pm 0.3 y, 157.9 \pm 5.3 cm, and 52.3 \pm 7.7 kg, respectively. A total of 1,002 women (26.2%) were classified as having constipation. There were more current smokers, alcohol drinkers, and oral medication users among subjects with constipation. Table 2 shows the association between food intake and constipation. There was a clear dose-response relationship between an increased intake of rice and a decreased prevalence of constipation. In comparison with women in the 1st (lowest) quintile of rice consumption, the multivariate adjusted OR for women in the 2nd, 3rd, 4th, and 5th quintiles were 0.81, 0.73, 0.76, and 0.59, respectively (*p* for trend <0.0001). Pulse intake was also inversely associated with constipation. Multivariate OR in the 2nd, 3rd, 4th, and 5th quintiles compared with the 1st quintile were 0.90, 0.64, 0.68, and 0.77, respectively (*p* for trend=0.003). In contrast, the prevalence of constipation clearly increased with increasing intake of confectioneries. In comparison with women in the 1st quintile, the multivariate adjusted OR for women in the 2nd, 3rd, 4th, and 5th quintiles were 1.17, 1.20, 1.51, and 1.64, respectively (*p* for trend <0.0001). A positive relationship was also seen between bread intake and constipation. Multivariate OR in the highest quintile was 1.41 compared with those in the lowest quintile (*p* for trend=0.01). No clear associations were observed between constipation and the intake of other foods examined.

DISCUSSION

To our knowledge, this study is the first to examine food intake as assessed by a validated assessment method (DHQ in the present study) in relation to func-

tional constipation, as defined according to the Rome I criteria. We found that after controlling for a series of potential confounding factors, the consumption of rice and pulses and of confectioneries and bread were negatively and positively associated with functional constipation, respectively, among this group of young women.

The prevalence of Rome I-defined functional constipation in the present group was 26.2%. A similar prevalence by these criteria has been observed in Canadian (21.0%) (4) and Spanish (28.6%) (2) women, whereas a somewhat smaller ratio was seen in elderly Singaporean women (10.5%) (3).

We found clear dose-response relationships between increased intake of rice with a decreased prevalence of constipation (Table 2). The favorable effect of rice on constipation has been consistently reported in previous studies conducted in Asian countries, where rice is the main staple food (3, 8, 9). The reason for the association is unknown. Nakaji et al. (9) hypothesized that the effect of rice is due to its dietary fiber, given that rice is the largest source of dietary fiber for Japanese people (27). In contrast, Wong et al. (3) hypothesized that the effect is explained by the increased energy intake because rice is the largest source of energy. These hypotheses could not be investigated further, however, because the authors used a simple diet questionnaire which did not allow the estimation of dietary intake (3, 9). Our previous results (8) do not support these hypotheses because the association between rice and constipation was not dependent on either energy or dietary fiber intake. Additionally, in the present study, the association between rice and constipation was independent of energy intake; mean dietary fiber intake (11.8 g/d) was much lower than the Dietary Goal of dietary fiber of the Dietary Reference Intakes for Japanese, 2005 for this age range (17 g/d) (26), and the contribution of rice to dietary fiber was only 10% (the top contributor was vegetables (37%)). These findings suggest that the effect of rice on constipation is unlikely due to its energy or dietary fiber. Relation of dietary fiber to functional constipation in this population is published elsewhere (28). Rice is a staple food in Japan and a major contributor of many nutrients; some constituents of rice may, either alone or combination, exert a preventive effect on constipation. Alternatively, rice intake might merely reflect an overall healthier lifestyle that may not have been accurately captured and controlled in our analysis.

An inverse association between pulse intake and constipation was observed (Table 2). A similar finding has been reported in a study of the US (7). We also found an adverse effect of confectionery intake (Table 2), which is in agreement with our previous study of young Japanese women (8). Additionally, a positive association of bread intake to constipation was found (Table 2), although we are not aware of any previous report of this association. It is unclear why these foods had such effects on constipation. Given the large number of statistical analyses conducted in the present study, our findings regarding these foods may have been due to

chance alone. Alternatively, their intake may be a marker of other unknown lifestyle factors that were not addressed in the present study.

In contrast to previous studies (3, 7-11), we found no association between constipation and the intake of dairy products, meats, fruits, vegetables, eggs, Japanese and Chinese tea, black tea, coffee, and other nonalcoholic beverages (Table 2). These discrepancies may be at least partly explained by the different populations investigated, different dietary assessment methods used, different definitions of constipation, and differences in the number and type of variables used as confounding factors.

Because it is possible that subjects suffering from constipation might change their diet, our findings, particularly those regarding foods significantly associated with the presence or absence of constipation (rice, pulses, confectioneries, and bread), should be interpreted with caution. We cannot deny the possibility that the associations merely reflect dietary behaviors changed after, not before, the development of constipation, although these foods are not generally considered to influence constipation. As mentioned above, however, previous studies have shown similar findings for rice (3, 8, 9), pulses (7), and confectioneries (8), but not bread.

All self-reported dietary assessment methods are subject to measurement error and selective under- and overestimation of dietary intake (29). To minimize these possibilities, we used a previously validated DHQ (15-17). Additionally, the same tendency of associations between food intakes and constipation was observed in a repeated analysis of 2,717 subjects with a 'physiologically plausible' energy intake, namely those possessing a ratio of reported energy intake to estimated basal metabolic rate [standard value of basal metabolic rate for Japanese women aged 18-29 y (23.6 kcal/kg of body weight/d) multiplied by body weight of each subjects (kg) (26)] of 1.2 to 2.5 (30) (data not shown). Thus, although the possibility of measurement error and selective under- or overestimation of dietary intake can never be excluded, data inaccuracy is unlikely to have had a major impact on the findings in the present study.

Given that our subjects were selected female dietetic students who may be highly health conscious, our results are likely not extrapolatable to general populations. Additionally, although we attempted to adjust for a wide range of potential confounding variables, we cannot rule out residual confounding due to these or poorly measured variables such as physical activity level, which was assessed by a limited number of non-validated questions, or other unknown variables.

In conclusion, after adjustment for a variety of potential confounders, the intake of rice and pulses and that of confectioneries and bread were negatively and positively associated with functional constipation, respectively, among young women. However, owing to the cross-sectional nature of the present study, which precludes any causal inferences, and the lack of biological explanation for these relationships, further observational and experimental studies are required to clarify

these relationships.

Member list of the Freshmen in Dietetic Courses Study II Group

The members of the Freshmen in Dietetic Courses Study II Group (in addition to the authors) are as follows (shown in alphabetical order of the affiliation): Shiro Awata (Beppu University); Tomoko Watanabe and Ayuho Suzuki (Chiba College of Health Science); Tomoko Abe (Doshisha Women's College); Hitomi Hayabuchi (Fukuoka Women's University); Reiko Ueda (Futaba Nutrition College); Noriko Takeda and Tomoko Matsubara (Hiroshima Bunkyo Women's University); Hiroko Ohwada and Kumi Hirayama (Ibaraki Christian University); Chizuko Maruyama (Japan Women's University); Miyuki Makino (Jin-ai Women's College); Shigeru Tanaka and Nobue Nagasawa (Jumonji University); Fumiko Tonzuka and Sanae Osada (Junior College of Kagawa Nutrition University); Kazuhiro Uenishi (Kagawa Nutrition University); Takiko Sagara (Kanazawa Gakuin College); Yusuke Enomoto, Kazuyo Okayama, and Hideo Ooe (Kitasato Junior College of Health and Hygienic Sciences); Kazuko Nakayama and Michi Furuya (Kochi Gakuen College); Noriko Yagi and Kumiko Soeda (Koshien University); Junko Ikeda (Kyoto Bunkyo Junior College); Ikumi Kitagawa (Kyoto Koka Women's University); Keiko Yokoyama and Reiko Nakayama (Kyoto Women's University); Ayako Miura (Kwassui Women's College); Keiko Baba (Mie Chukyo University Junior College); Yoshiko Sugiyama and Mika Furuki (Minami Kyushu University); Tamami Oyama (Miyagi Gakuin Women's University); Yoshihiko Naito and Makoto Kato (Mukogawa Women's University); Naoko Hirota (Nagano Prefectural College); Tomiko Tsuji and Kaei Washino (Nagoya Bunri University); Takiko Yawata and Chiho Shimamura (Nara Saho College); Nobuko Murayama (Niigata University of Health and Welfare); Reiko Watanabe (Niigata Women's College); Mitsuyo Yamasaki (Nishikyusyu University); Mari Kitamura (Osaka Aoyama College); Tamami Iwamoto (Prefectural University of Hiroshima); Isao Suzuki and Yuki Sugishima (Prefectural University of Kumamoto); Mieko Aoki (Sanyo Gakuen College); Shoko Nishi (Seibo Jogakuin Junior College); Kenji Toyama and Rie Amamoto (Seinan Jo Gakuin University); Nobuko Takahashi and Ruriko Sasaki (Sendai Shirayuri Women's College); Naoko Kakibuchi (Setouchi Junior College); Miyoko Goto (Shokei Gakuin College); Mariko Watanabe and Masako Yokotsuka (Showa Women's University); Michiyo Kimura (Takasaki University of Health and Welfare); Michiko Hara and Nobuko Klya (Tenshi College); Junko Hirose, Tomiho Fukui, and Katsumi Shibata (The University of Shiga Prefecture); Ryoko Nishiyama (Toita Women's College); Noriyo Tomita (Tokuiwa Junior College); Jun Oka and Tomoko Ide (Tokyo Kasei University); Takamoto Uemura and Tadasu Furusho (Tokyo University of Agriculture); Akiko Notsu and Yae Yokoyama (Tottori College); Toyomi Kuwamori (Toyama College); Setsuko Shirono (Ube Frontier College); Toshinao Goda (University of Shizuoka); Kumiko

Suizu (Yamaguchi Prefectural University); Hiroko Okamoto (Yamanashi Gakuin Junior College).

REFERENCES

- Higgins PD, Johanson JF. 2004. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol* **99**: 750-759.
- Garrigues V, Galvez C, Ortiz V, Ponce M, Nos P, Ponce J. 2004. Prevalence of constipation: agreement among several criteria and evaluation of the diagnostic accuracy of qualifying symptoms and self-reported definition in a population-based survey in Spain. *Am J Epidemiol* **159**: 520-526.
- Wong ML, Wee S, Pin CH, Gan GL, Ye HC. 1999. Socio-demographic and lifestyle factors associated with constipation in an elderly Asian community. *Am J Gastroenterol* **94**: 1283-1291.
- Pare P, Ferrazzi S, Thompson WG, Irvine EJ, Rance L. 2001. An epidemiological survey of constipation in Canada: definitions, rates, demographics, and predictors of health care seeking. *Am J Gastroenterol* **96**: 3130-3137.
- Talley NJ. 2004. Definitions, epidemiology, and impact of chronic constipation. *Rev Gastroenterol Disord* **4**: S3-S10.
- Locke GR 3rd, Pemberton JH, Phillips SF. 2000. AGA technical review on constipation. American Gastroenterological Association. *Gastroenterology* **119**: 1766-1778.
- Sandler RS, Jordan MC, Shelton BJ. 1990. Demographic and dietary determinants of constipation in the US population. *Am J Public Health* **80**: 185-189.
- Murakami K, Okubo H, Sasaki S. 2006. Dietary intake in relation to self-reported constipation among Japanese women aged 18-20 years. *Eur J Clin Nutr* **60**: 650-657.
- Nakaji S, Tokunaga S, Sakamoto J, Todate M, Shimoyama T, Umeda T, Sugawara K. 2002. Relationship between lifestyle factors and defecation in a Japanese population. *Eur J Nutr* **41**: 244-248.
- Dukas L, Willett WC, Giovannucci EL. 2003. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. *Am J Gastroenterol* **98**: 1790-1796.
- Sanjoaquin MA, Appleby PN, Spencer EA, Key TJ. 2004. Nutrition and lifestyle in relation to bowel movement frequency: a cross-sectional study of 20630 men and women in EPIC-Oxford. *Public Health Nutr* **7**: 77-83.
- Towers AL, Burgio KL, Locher JL, Merkel IS, Safaiean M, Wald A. 1994. Constipation in the elderly: influence of dietary, psychological, and physiological factors. *J Am Geriatr Soc* **42**: 701-706.
- Campbell AJ, Busby WJ, Horwath CC. 1993. Factors associated with constipation in a community based sample of people aged 70 years and over. *J Epidemiol Commun Health* **47**: 23-26.
- Whitehead WE, Chaussade S, Corazzari E, Kumar D. 1991. Report of an international workshop on management of constipation. *Gastroenterol Int* **4**: 99-113.
- Sasaki S, Yanagibori R, Amano K. 1998. Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *J Epidemiol* **8**: 203-215.
- Sasaki S, Yanagibori R, Amano K. 1998. Validity of a self-administered diet history questionnaire for assessment of sodium and potassium: comparison with single 24-hour urinary excretion. *Jpn Circ J* **62**: 431-435.
- Sasaki S, Ushio F, Amano K, Morihara M, Todoriki T, Uehara Y, Toyooka T. 2000. Serum biomarker-based validation of a self-administered diet history questionnaire for Japanese subjects. *J Nutr Sci Vitamino* **46**: 285-296.
- Ministry of Health and Welfare. 1994. The National Nutrition Survey in Japan, 1992. Ministry of Health and Welfare, Tokyo (in Japanese).
- Science and Technology Agency. 2000. Standard Tables of Food Composition in Japan, 5th revised ed. Printing Bureau of the Ministry of Finance, Tokyo (in Japanese).
- Altman DG. 1991. Practical Statistics for Medical Research. Chapman and Hall, New York.
- Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. 1999. Functional bowel disorders and functional abdominal pain. *Gut* **45**: II43-II47.
- Matsuzawa Y, Inoue S, Ikeda Y, Sakata T, Saito Y, Sato Y, Shirai K, Ono M, Miyazaki S, Tokunaga K, Fukagawa K, Yamanouchi K, Nakamura T. 2000. The judgment criteria for new overweight, and the diagnostic standard for obesity. *Himan Kenkyu* **6**: 18-28 (in Japanese).
- Ministry of Health, Labour, and Welfare. 2004. The National Nutrition Survey in Japan, 2002. Ministry of Health, Labour, and Welfare, Tokyo (in Japanese).
- Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. 1993. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* **25**: 71-80.
- Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. 2000. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* **32**: S498-S504.
- Ministry of Health, Labour, and Welfare, Japan. 2005. Dietary Reference Intakes for Japanese, 2005. Daiichi Shuppan Publishing Co., Ltd., Tokyo (in Japanese).
- Sasaki S, Matsumura Y, Ishihara J, Tsugane S. 2003. Validity of a self-administered food frequency questionnaire used in the 5-year follow-up survey of the JPHC Study Cohort I to assess dietary fiber intake: comparison with dietary records. *J Epidemiol* **13**: S106-S114.
- Murakami K, Sasaki S, Okubo H, Takahashi Y, Hosoi Y, Itabashi M, the Freshmen in Dietetic Courses Study II Group. 2006. Association between dietary fiber, water and magnesium intake and functional constipation among young Japanese women. *Eur J Clin Nutr* (advance online publication, December 6, 2006; doi:10.1038/sj.ejcn.1602573).
- Livingstone MBE, Black AE. 2003. Markers of the validity of reported energy intake. *J Nutr* **133**: 895S-920S.
- Black AE, Coward WA, Cole TJ, Prentice AM. 1996. Human energy expenditure in affluent societies: an analysis of 574 doubly-labelled water measurements. *Eur J Clin Nutr* **50**: 72-92.



ORIGINAL ARTICLE

Validation of self-reported energy intake by a self-administered diet history questionnaire using the doubly labeled water method in 140 Japanese adults

H Okubo^{1,2}, S Sasaki², HH Rafamantanantsoa³, K Ishikawa-Takata⁴, H Okazaki⁴ and I Tabata⁴

¹Department of Nutrition Science, Kagawa Nutrition University, Saitama, Japan; ²Nutritional Epidemiology Program, National Institute of Health and Nutrition, Tokyo, Japan; ³Department of Exercise and Sport Sciences, Shanghai Institute of Physical Education, Shanghai, PR China and ⁴Health Promotion and Exercise Program, National Institute of Health and Nutrition, Tokyo, Japan

Objective: To validate reported energy intake (rEI) with a self-administered diet history questionnaire (DHQ) against total energy expenditure (TEE) by the doubly labeled water (DLW) method.

Subjects: A total of 140 healthy Japanese adults (67 men and 73 women) aged 20–59 years living in four areas in Japan.

Methods: Energy intake was assessed twice with DHQ over a 1-month period before and after TEE measurement (rEI_{DHQ1} and rEI_{DHQ2}, respectively). TEE was measured by DLW during 2 weeks (TEE_{DLW}).

Results: Mean rEI_{DHQ1} was lower than those of TEE_{DLW} by 1.9 ± 2.4 MJ/day (16.4%, $P < 0.001$) for men and 0.6 ± 1.9 MJ/day (6.0%, $P < 0.01$) for women. In men and women together, 62 subjects (44%) were defined as underreporters (rEI_{DHQ1}/TEE_{DLW} < 0.84), 58 (41%) as acceptable reporters (0.84–1.16) and 20 (14%) as over-reporters (> 1.16). Pearson correlation coefficient was 0.34 for men and 0.22 for women. After adjustment for the dietary and non-dietary factors related to rEI_{DHQ1}/TEE_{DLW}, the correlation coefficient improved to 0.42 and 0.37, respectively.

Conclusion: The energy intake assessed with DHQ correlated low to modestly with TEE measured by DLW. In addition, DHQ underestimated energy intake at a group level. Caution is needed when energy intake was evaluated by DHQ at both individual and group levels.

European Journal of Clinical Nutrition (2008) 62, 1343–1350; doi:10.1038/sj.ejcn.1602858; published online 1 August 2007

Keywords: doubly labeled water; energy intake; self-administered diet history questionnaire; validation; Japanese adults

Introduction

Dietary intake estimates from self-administered dietary assessment methods such as questionnaires are commonly used in large-scale nutritional epidemiologic studies. Dietary assessment questionnaires have been developed for assessing habitual dietary intake and for ranking subjects according to

their dietary intake. However, they cannot entirely avoid reporting errors (Barrett-Connor, 1991), including not only random but also systematic errors (Black and Cole, 2001; Livingstone and Black, 2003), due to the fact that they are self-reported.

In validation studies, data from dietary assessment questionnaires have often been compared with data from reference methods such as weighed diet records or 24 h recall (Willett and Lenart, 1998). However, all these dietary assessment methods were based on self-reporting. Therefore, the errors of both the new and reference methods might be correlated each other. The doubly labeled water (DLW) method, which measures the total energy expenditure (TEE) of subjects in free-living situations, has made it possible to validate reported energy intake (rEI) with an external biomarker (Hill and Davies, 2001; Trabulsi and Schoeller, 2001). The error of the DLW method is independent of self-rEI error (Livingstone and Black, 2003). However,

Correspondence: Dr S Sasaki, Nutritional Epidemiology Program, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8636, Japan.

E-mail: stssasaki@nih.go.jp

Guarantor: S Sasaki.

Contributors: HO conducted the field management, data collection, statistical analysis and wrote the paper. SS conducted the study design and edited the paper. HHR, KIT and HO conducted data collection and IRMS analyses. IT conducted the overall management. All authors participated in the discussion and interpretation of the results, and in drafting and editing the paper.

Received 29 June 2006; revised 14 June 2007; accepted 18 June 2007; published online 1 August 2007

relatively few validation studies of food frequency questionnaires against the DLW method have appeared (Sawaya *et al.*, 1996; Andersen *et al.*, 2003; Subar *et al.*, 2003). Furthermore, no such studies have been reported in non-Western countries.

The purpose of the present study was to examine the validity of energy intake assessed with a self-administered diet history questionnaire (DHQ) (Sasaki *et al.*, 1998) in comparison with TEE, as measured by the DLW method in a Japanese population.

Subjects and methods

Study population

This study was conducted in four districts of Japan from May to August 2003. We invited 40 healthy subjects (20 men and 20 women) aged 20–59 years from each of the four areas to participate, and distributed five subjects equally in each sex and age class of 20–29, 30–39, 40–49 and 50–59 years. Details of study recruitment and enrollment were described previously (Ishikawa-Takata *et al.*, 2007). All subjects providing written informed consent were finally considered eligible for the study. The total number of participants was 157 (78 men and 79 women).

Procedures

The study protocol was approved by the Ethics Committee of the National Institute of Health and Nutrition in Japan. The participants completed three visits over the study period and all participants completed the study. After recruitment, the participants were mailed an introductory letter and two dietary questionnaires including a DHQ, four physical activity questionnaires, and a supplemental questionnaire on lifestyle variables, and asked to fill them out and mail them back before the first visit (visit 1).

At visit 1, the participants had their questionnaires reviewed, their body weight and height measured and provided a baseline urine sample. At visit 2, on the morning following visit 1, they received a dose of DLW after an overnight fast. At visit 3, 14 days after visit 2, the participants brought urine samples and had their body weight and height measured.

After visit 3, the participants were mailed two dietary questionnaires including the DHQ, four physical activity questionnaires, supplemental questionnaire on lifestyle variables and diary about lifestyle during the period of TEE measurement.

All the collected questionnaires were checked by trained dietitians in each local center and again then in the study center. When missing answers, errors or both were found, the subjects were requested to answer the questions again.

Dietary assessment methods

Self-administered DHQ. The DHQ is a validated 16-page structured questionnaire, which assesses dietary habits in the preceding 1-month period (Sasaki *et al.*, 1998, 2000). Details of the questionnaire, methods of calculating nutrients and validity are given elsewhere (Sasaki *et al.*, 1998, 2000). Briefly, the DHQ consists of seven sections; (1) general dietary behavior, (2) major cooking methods, (3) consumption frequency and amount of six alcoholic beverages, (4) consumption frequency and semiquantitative portion size of 121 selected food and nonalcoholic beverage items, (5) dietary supplements, (6) consumption frequency and amount of 19 staple foods (rice, bread, noodles and other wheat foods) and miso soup (fermented soybean paste soup), and (7) open-ended items for foods consumed regularly (=once/week), which are not listed in the question. The food and beverage items and portion sizes in the DHQ were derived primarily from the data in the National Nutrition Survey of Japan (Sasaki *et al.*, 1998) and several recipe books for Japanese dishes. Measures of energy and dietary intakes for food and beverage items and dietary supplements with energy (148 food items in total) were calculated using an ad hoc computer algorithm for the DHQ, which was based on the Standard Tables of Food Composition in Japan (Science and Technology Agency, 2000). Information on dietary supplements, such as tablet, powder and liquid, which contained few energy and on data from the open-ended questionnaire items were not used in the calculation of dietary intake.

Anthropometric measures

Anthropometric measures were obtained at visits 1 and 3 by a single-trained study member. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, in subjects wearing light clothing and no shoes. Body mass index (BMI) was calculated as body weight (kg) divided by the square of body height (m²).

Measurement of TEE with the DLW method

At visit 2, after a baseline urine sample was obtained, a single dose of approximately 0.06 g/kg body weight of ²H₂O (99.8 atom%, Cambridge Isotope Laboratories, MA, USA) and 0.14 g/kg body weight of H₂¹⁸O (10.0 atom%, Cambridge Isotope Laboratories, MA, USA) was orally given to each subject via a drinking straw. After the dose administration, the subjects refrained from eating and drinking over a 4-h equilibration period (4 h sampling) for measurement of total body water. The second voided urine in the morning of day 1 (the day after the DLW dose) and day 14 (at the same time as the voiding on day 1) were collected for measurement of the isotopic (²H and ¹⁸O) elimination rate.

The procedure for specimen analysis and for subsequent data analyses was described previously (Ishikawa-Takata *et al.*, 2007). Briefly, the isotopic analyses were conducted

using the Isotope Ratio Mass Spectrometry (IRMS) DELTA Plus equipment (Thermo Electron Corporation, Bremen, Germany) and calibrated using Vienna Standard Mean Ocean Water (V-SMOW), 302B, and the Greenland Ice Sheet Precipitation (GISP) standard provided by the International Atomic Energy Agency. Each measurement of samples and the corresponding references was performed in duplicate. The average s.d. through the analyses were 0.5‰ for ^2H and 0.03‰ for ^{18}O .

TEE (kcal/day) calculation was performed using a modified Weir's formula Weir, 1949 based on rCO_2 (mol/day) and food quotient (FQ):

$$\text{TEE} = 3.9 \times (\text{rCO}_2/\text{FQ}) + 1.1 \times (\text{rCO}_2)$$

FQ was derived from the dietary assessment data (g/day) of DHQ using an equation of Black *et al.* (1986). The average value of all subjects (0.867) was used for all subjects to estimate TEE.

Assessment of other variables possibly related to the rEI

Lifestyle, behavioral and psychological variables possibly related to the rEI were obtained from the four-page questionnaire as follows: educational attainment, alcohol drinking, history of diet experiences, desire for body weight change, and difference between ideal and measured body weight.

A physical activity level was calculated as TEE divided by basal metabolic rate (BMR). BMR was estimated according to the 6th Recommended Dietary Allowances for Japanese Ministry of Health Welfare (1999).

Statistical analysis

We excluded 17 subjects who were non-Japanese ($n=1$), who was obese ($n=1$), who did not complete at least first or second DHQ ($n=2$), who had left more than 40 items blank in the questions regarding frequency for 121 selected food and beverage items in DHQ ($n=4$), who rEI outside the range of 3.0–16.0 MJ/day ($n=2$), or who did not provide sufficient urine sample volume ($n=7$). Thus, 140 subjects (67 men and 73 women) were included in the present analysis.

As we monitored the body weight change during the assessment period of rEI by second DHQ (rEI_{DHQ2}), we estimated EI (eEI) from TEE_{DLW} with a correction for change in body energy store during the survey period (Bathalon *et al.*, 2000):

$$\text{eEI} = \text{TEE} + (\Delta\text{wt} \times 0.03)$$

where TEE is measured as MJ/day, Δwt is measured as g/day between visits 1 and 3, and 0.03 MJ/day (7 kcal/day) is the energy cost of weight change (Saltzman and Roberts, 1995). The eEI was used for the validation of rEI_{DHQ2} . In contrast, this correction of change in body energy store was not considered for the validation of rEI_{DHQ1} because of the lack of the monitoring.

The results were expressed as the mean and s.d. Mean differences between sexes and among methods were tested by the non-paired *t*-test and paired *t*-test, respectively. The Pearson and Spearman correlation coefficient was used to examine correlations between the test and the reference methods. Furthermore, the study participants were classified into tertiles of energy intake according to the distribution of

Table 1 Characteristics of 140 Japanese men and women aged 20–59 years included in the analyses^a

	Men ($n=67$)	Women ($n=73$)
Age (years)	39.4 ± 11.1	38.5 ± 10.4
Body height (cm)	169.3 ± 6.3	157.9 ± 6.1 ^e
Body weight (kg)	67.3 ± 9.7	53.9 ± 7.3 ^e
BMI (kg/m ²) ^b	23.3 ± 2.9	21.6 ± 2.7 ^e
< 18.5	5 (7)	10 (14) ^f
18.5–24.9	39 (58)	55 (75)
≥ 25.0	23 (34)	8 (11)
<i>Educational attainment</i>		
High school or less	28 (42)	23 (32) ^h
Technical or professional school	5 (7)	28 (38)
University or more	34 (51)	22 (30)
<i>History of diet experience^c</i>		
No	58 (87)	57 (78)
Yes	9 (13)	16 (22)
<i>Desire for weight change</i>		
Reduction	37 (55)	50 (68)
No change	20 (30)	20 (27)
Increase	10 (15)	3 (4)
Difference between ideal and measured body weight (kg) ^d	−4.2 ± 6.7	−4.5 ± 4.3
Frequency of alcohol intake (times/week)	2.6 ± 2.7	1.0 ± 1.9 ^e
Physical activity level	1.70 ± 0.21	1.69 ± 0.27
Body weight change during survey (g/day)	−23 ± 55 ⁱ	−2 ± 45 ^g
TEE_{DLW} (MJ/day)	10.7 ± 1.7	8.3 ± 1.2 ^e
eEI _{DLW} (MJ/day)	10.0 ± 2.1	8.2 ± 2.0 ^e
rEI_{DHQ1} (MJ/day)	8.8 ± 2.4	7.7 ± 1.7 ^f
rEI_{DHQ2} (MJ/day)	8.9 ± 2.5	7.4 ± 1.5 ^e

Abbreviations: BMI, body mass index; DHQ, diet history questionnaire; DHQ1, first measurement of DHQ before dose of DLW; DHQ2, second measurement of DHQ 2 weeks after dose of DLW; DLW, doubly labeled water method; eEI, estimated energy intake = TEE_{DLW} + (body weight change during survey × 0.03); rEI_{DHQ} , reported energy intake assessed with self-administered DHQ; TEE_{DLW} , total energy expenditure measured by DLW.

^aMean ± s.d. or n (%).

^bThe categorization was based on the Japan Society for the Study of Obesity (Matsuzawa *et al.*, 2000).

^cDiETING was defined as at least 2 kg intentional reduction of body weight within 1 month.

^dIdeal body weight was evaluated by the following question: how many kilograms is your ideal body weight? Difference between ideal and measured body weight was calculated, as ideal body weight (kg) – measured body weight (kg), to evaluate the degree of desire for body weight change.

^e^gDifference between sexes by non-paired *t*-test: ^e $P < 0.001$, ^g $P < 0.01$, ^f $P < 0.05$.

^hSignificant difference between sexes in all categories by χ^2 test: ^h $P < 0.001$, ⁱ $P < 0.01$.

^jDifference within sexes from 0 by paired *t*-test: $P < 0.01$.

the test and the reference methods, and the proportions of subjects classified into the same, adjacent or opposite tertiles were determined.

To evaluate the prevalence of under- or over-reporters, we calculated 95% confidence limits of rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} as a cutoff value proposed by Livingstone and Black (2003). Then, subjects with rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} smaller than 0.84 or larger than 1.16 were considered as under- or over-reporters, respectively.

A stepwise multiple regression analysis was performed to evaluate the influence of sociodemographic, lifestyle, behavioral and psychological factors on rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} , simultaneously. The following potential factors were entered into the model as the independent variables: age, BMI, body height, residential area, educational attainment, physical activity level, frequency of alcohol drinking, desire for body weight change, difference between ideal and measured body weight, and history of diet experience.

To examine the reproducibility, we compared mean $rEIs$ between first and second DHQs (DHQ1 and DHQ2, respectively). Furthermore, the Pearson correlation coefficients were used to compare the $rEIs$ assessed with DHQ1 and DHQ2.

All statistical analyses were performed using version 8.2 of the SAS software package (SAS Institute Inc., Cary, NC, USA). The test was considered significant at a P -value of <0.05 .

Results

Basic characteristics of the study subjects, the mean TEE_{DLW} , eEI , first and second measurements of rEI by the DHQ (rEI_{DHQ1} and rEI_{DHQ2}) are shown in Table 1. Men had the higher BMI than women (23.3 versus 21.6 kg/m², $P<0.001$).

Twenty-three of 67 men and eight of 73 women were overweight (BMI ≥ 25 kg/m²). This table also shows body weight change during the TEE measurement, between visits 1 and 3. Mean body weight in men, although not in women, significantly changed by -23 ± 55 g/day ($P<0.01$ by paired t -test). Mean rEI_{DHQ1} was significantly lower than mean TEE_{DLW} by 1.9 ± 2.4 MJ/day (16.4%, $P<0.001$) for men and 0.6 ± 1.9 MJ/day (6.0%, $P<0.01$) for women. Mean rEI_{DHQ2} was also significantly lower than mean eEI_{DLW} by 1.1 ± 2.7 MJ/day (9.1%, $P<0.001$) for men and 0.8 ± 2.4 MJ/day (4.6%, $P<0.01$) for women.

Table 2 shows reporting accuracy of energy intake assessed with DHQ expressed as rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} . The rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} was 0.84 and 0.91 for men and 0.94 and 0.95 for women, respectively, resulting in a significantly lower rEI_{DHQ1}/TEE_{DLW} ratio for men than for women ($P<0.05$). There was a wide range in reporting accuracy of DHQ1; 31 and 51% were identified as acceptable, and 58 and 32% as under-, and 10 and 18% as over-reporters for men and women, respectively.

The rEI_{DHQ1} and TEE_{DLW} were significantly correlated only for men (Pearson correlation coefficient = 0.34, Spearman correlation coefficient = 0.33), but not for women (0.22 and 0.16, respectively). Forty-one, 45 and 14% of the subjects were cross-classified into the same, the adjacent and the opposite tertiles of the respective distributions of rEI_{DHQ1} and TEE_{DLW} , respectively (Figure 1a). The results of the correlation between rEI_{DHQ2} and eEI_{DLW} were similar (Figure 1b).

Table 3 shows the results of multiple regression analysis with rEI_{DHQ1}/TEE_{DLW} and rEI_{DHQ2}/eEI_{DLW} , as the dependent variables to examine the prediction of accuracy of reporting energy intake. For men, frequency of drinking alcohol, the difference between ideal and measured body weight, and history of diet experience correlated significantly and

Table 2 Reporting accuracy of energy intake determined by the self-administered diet history questionnaire^a

	DHQ1			DHQ2		
	All (n = 140)	Men (n = 67)	Women (n = 73)	All (n = 140)	Men (n = 67)	Women (n = 73)
Reporting accuracy ^b	0.89 ± 0.22	0.84 ± 0.21	0.94 ± 0.22 ^c	0.93 ± 0.30	0.91 ± 0.26	0.95 ± 0.33
Underreporters (n (%))	62 (44)	39 (58)	23 (32) ^d	64 (46)	30 (45)	34 (47)
Acceptable reporters (n (%))	58 (41)	21 (31)	37(51)	48 (34)	27 (40)	21 (29)
Overreporters (n (%))	20 (14)	7 (10)	13 (18)	28 (20)	10 (15)	18 (25)
Pearson's correlation coefficient	0.40 ^e	0.34 ^f	0.22	0.36 ^e	0.35 ^f	0.11
Spearman correlation coefficient	0.35 ^e	0.33 ^f	0.16	0.36 ^e	0.41 ^e	0.07

Abbreviations: DHQ1, first measurement of DHQ before dose of DLW; DHQ2, second measurement of DHQ 2 weeks after dose of DLW; DLW, doubly labeled water; eEI, estimated EI.

^aMean ± s.d. or n (%).

^bReporting accuracy was assessed as the ratio of energy intake to total energy expenditure (rEI_{DHQ1}/TEE_{DLW}) and the ratio of energy intake to estimated energy intake (rEI_{DHQ2}/eEI_{DLW}), respectively. eEI was determined by using a correction for change in body energy during the measurement period, as $TEE \pm$ (body weight change during survey $\times 0.03$). Under-, acceptable, and over-reporters were defined as the ratio rEI_{DHQ1}/TEE_{DLW} and $rEI_{DHQ2}/eEI_{DLW} < 0.84$, 0.84–1.16 and > 1.16 , respectively.

^cDifference between sex by non-paired t -test: $P<0.01$.

^dSignificant difference between sexes in all categories by χ^2 test: $P<0.01$.

^eCorrelation coefficients between two methods: ^e $P<0.001$, ^f $P<0.01$.

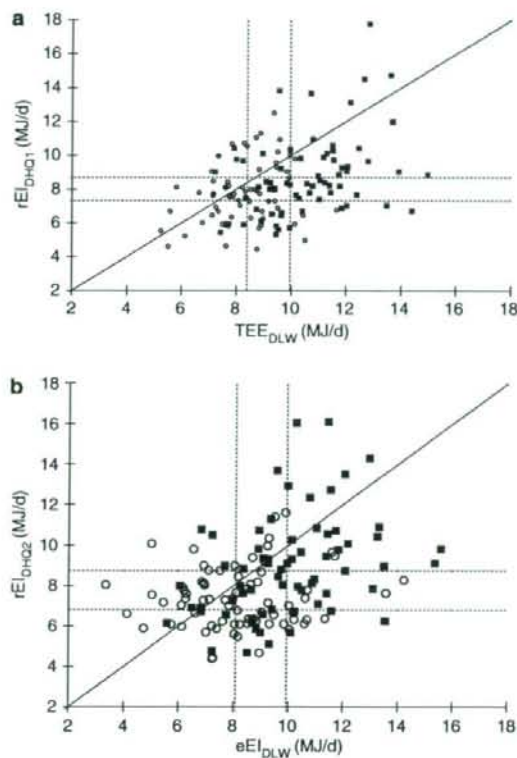


Figure 1 (a) Comparison of the first measurement of energy intake determined by the self-administered diet history questionnaire (rEI_{DHQ1}) with total energy expenditure measured by the doubly labeled water method (TEE_{DLW}) (\blacksquare = 67 men, \circ = 73 women). The dotted lines divide intake according to the tertiles of distribution. A straight line is $y = x$. Pearson and Spearman correlation coefficient was 0.40 and 0.35, respectively (both $P < 0.001$). (b) Comparison of the second measurement of energy intake determined by the self-administered diet history questionnaire (rEI_{DHQ2}) with estimated energy intake (eEI_{DLW}) determined by a correction of body weight change during survey period, as $TEE + (\Delta wt \times 0.03)$, (\blacksquare = 67 men, \circ = 73 women). The dotted lines divide intake according to the tertiles of distribution. A straight line is $y = x$. Pearson and Spearman correlation coefficient was both 0.36 ($P < 0.001$).

positively, and physical activity level negatively with rEI_{DHQ1}/TEE_{DLW} . For women, age and educational attainment correlated significantly and positively, and BMI negatively with rEI_{DHQ1}/TEE_{DLW} . We also conducted the same analysis with rEI_{DHQ2}/eEI_{DLW} . Body height, BMI and physical activity level significantly and negatively correlated with rEI_{DHQ2}/eEI_{DLW} for women. On the other hand, no factors attained the significance level for men.

The Pearson correlation coefficients between rEI_{DHQ1} and TEE_{DLW} slightly improved in both sexes after adjustment for

the above-mentioned related factors (0.42 for men and 0.37 for women).

We also examined reproducibility of energy intake between $DHQ1$ and $DHQ2$. The rEI_{DHQ2} was significantly lower than rEI_{DHQ1} for women (the difference was -0.3 ± 1.1 MJ/day, $P = 0.03$), but not for men. The Pearson correlation coefficient between rEI_{DHQ1} and rEI_{DHQ2} was 0.79 for men and 0.76 for women.

Discussion

To our knowledge, this is the first report in a non-Western country to validate energy intake estimated with a dietary assessment questionnaire against TEE measured by DLW method. Moreover, the sample size was relatively large compared to the previous studies with the same purpose and method (Sawaya *et al.*, 1996; Kroke *et al.*, 1999; Andersen *et al.*, 2003).

The mean rEI_{DHQ1} was 11.0% less (16.4% for men and 6.0% for women) than the mean TEE_{DLW} . Several validation studies have shown that dietary assessment instruments underestimated daily energy intake (Livingstone *et al.*, 1990; Hill and Davis, 2001). The degree of such error, under- or overestimation, has also been examined using TEE measured by the DLW method (Sawaya *et al.*, 1996; Kroke *et al.*, 1999; Andersen *et al.*, 2003; Livingstone and Black, 2003). Average underreporting in the previous studies between EI from dietary assessment questionnaires and TEE measured by DLW ranged from 10 to 38% (Sawaya *et al.*, 1996; Subar *et al.*, 2003), which depends on sample size and subjects (Trabulsi and Schoeller, 2001).

For the individual ranking, the rEI_{DHQ1} significantly and positively correlated with TEE_{DLW} ($r = 0.40$, $P < 0.001$), showing a correlation similar to or relatively higher than those observed in the previous studies ($r = 0.06$ – 0.48) (Kroke *et al.*, 1999; Bathalon *et al.*, 2000). Acceptable reporting was observed in 41% of the subjects, whereas 44% underreported and 14% over-reported. Underreporting of energy intake therefore seems to be a more serious problem than over-reporting.

In this study, the mean rEI_{DHQ1}/TEE_{DLW} ratio was significantly lower in men than in women. Further, the rate of underreporting was higher in men than in women. In a previous analysis of individual data from 21 studies, in contrast, the proportion of underreporters did not statistically differ between sexes (Black, 2000). In our previous study using semi-weighted diet records in 4 days \times 4 seasons, the mean value of the ratio of rEI to BMR estimated from sex, age and body weight was not statistically different between sexes (Okubo *et al.*, 2006). In the DHQ , the portion sizes of food items are standardized regardless of sex, for example as 'one small cup'. The subjects then select the relative portion size from the five categories given except for rice, bread, noodles, other wheat foods and miso soup. This structure

Table 3 Result of multiple regression analysis by stepwise procedure with the ratio of energy intake to total energy expenditure ($E_{D_{1-2}}/TEE_{D_{1-2}}$ and $E_{D_{1-2}}/TEE_{D_{1-2}}$) as dependent variables^a

Independent variable ^b	Men (n = 67)				Women (n = 73)			
	DHQ1		DHQ2		DHQ1		DHQ2	
	Partial regression coefficient ^c	s.e. ^d	Partial regression coefficient ^c	s.e. ^d	Partial regression coefficient ^c	s.e. ^d	Partial regression coefficient ^c	s.e. ^d
Age (years)	—	—	—	—	0.005	0.002	—	—
BMI (kg/m ²)	—	—	—	—	-0.036	0.009	-0.049	0.015
Body height (cm)	—	—	—	—	—	—	-0.016	0.006
Residential area	—	—	—	—	—	—	—	—
Educational attainment, (more than University versus high school or less as reference)	—	—	—	—	0.145	0.053	—	—
Physical activity level	-0.356	0.120	—	—	—	—	-0.480	0.154
Frequency of drinking alcohol (times/week)	0.026	0.009	—	—	—	—	—	—
Desire for body weight change	—	—	—	—	—	—	—	—
Difference between ideal and measured body weight (kg) (yes versus no as reference)	0.013	0.003	—	—	—	—	—	—
History of diet experience (yes versus no as reference)	0.170	0.071	—	—	—	—	—	—

^a $TEE_{D_{1-2}}$, total energy expenditure measured by doubly labeled water method (DLW); $E_{D_{1-2}}$, reported energy intake assessed with self-administered diet history questionnaire (DHQ); DHQ1, first measurement of DHQ before dose of DLW; DHQ2, second measurement of DHQ 2 weeks after dose of DLW. Reporting accuracy were assessed as the ratio of energy intake to total energy expenditure ($E_{D_{1-2}}/TEE_{D_{1-2}}$) and the ratio of energy intake to estimated energy intake ($E_{D_{1-2}}/E_{D_{1-2}}$), respectively. Estimated EI (eEI) was determined by using a correction for change in body energy during the measurement period, as $TEE + (\text{body weight change during survey} \times 0.03)$.

^bSee table 1 for the definition of each independent variable. Age (as a continuous variable), BMI (as a continuous variable), body height (as a continuous variable), residential area (Hokuriku, Shikoku, North Kyushu, and South Kyushu), educational attainment (high school or less, technical or professional school, or university or more), physical activity level (as a continuous variable), frequency of alcohol drinking (as a continuous variable), desire for body weight change (reduction, no change or increase), difference between ideal and measured body weight (as a continuous variable), history of diet experience (yes or no).

^cPartial regression coefficient; change in dependent variable related to a 1-U change in independent variable.

^dStandard error (s.e.) of the regression coefficient.

might have led to relative over- and underreporting of energy in women and men, respectively.

The $r_{EI_{DHQ1}/TEE_{DLW}}$ was significantly and independently correlated with several anthropometric and behavioral factors (Table 3). Several previous studies have already examined non-dietary factors, such as physiological (Zhang et al., 2000; Livingstone and Black, 2003) and psychological (Johansson et al., 1998; Bathalon et al., 2000; Tooze et al., 2004) factors associated with reporting accuracy of energy intake. After adjusting for these variables, the validity slightly improved (Pearson correlation coefficient was 0.42 for men and 0.37 for women). Therefore, these non-dietary factors are needed to consider when evaluating rEI.

This study has several limitations. First, FQ was derived from dietary assessment data by DHQ. Therefore, TEE was not theoretically independent of EI. Second, the surveyed period for the first measurement of EI by DHQ (DHQ1) was ahead of, and not overlapping with, TEE measurement by the DLW method. Third, we used the TEE as gold standard for the validation of DHQ1 without any consideration for a possible body weight change during the assessment period because of lack of the data. Fourth, we used the TEE with a correction for change in body weight during the survey period as gold standard for the validation of DHQ2, because the body weight has significantly changed in men. Fifth, the change in body composition, such as change in fat mass and fat-free mass, is probably the better indicator than the change in body weight for the correction of energy content for the study purpose. Sixth, the $r_{EI_{DHQ1}}$ was significantly lower than the $r_{EI_{DHQ2}}$ for women. Intentional or non-intentional intervention effect might have influenced dietary behaviors between the first and the second measurement. As shown in Table 3, the factors affecting reporting accuracy of energy intake were different between the two measurements. This may be one of the reasons. Seventh, we applied a two-point rather than multipoint method for the measurement of TEE_{DLW} . Eighth, the subjects were not randomly sampled from the general Japanese population. Moreover, the survey areas were not equally distributed over the country but were rather selected mostly from the Western parts of Japan.

In summary, the energy intake assessed with DHQ correlated low to modestly with TEE measured by DLW. In addition, DHQ underestimated energy intake at a group level. Caution is needed when energy intake was evaluated by DHQ at both individual and group levels.

References

- Andersen LF, Tomten H, Haggarty P, Lovo A, Hustvedt BE (2003). Validation of energy intake estimated from a food frequency questionnaire: a doubly labelled water study. *Eur J Clin Nutr* 57, 279–284.
- Barrett-Connor E (1991). Nutrition epidemiology: how do we know what they ate? *Am J Clin Nutr* 54 (Suppl 1), 182S–187S.
- Bathalon GP, Tucker KL, Hays NP, Vinken AG, Greenberg AS, McCrory MA et al (2000). Psychological measures of eating behavior and the accuracy of 3 common dietary assessment methods in healthy postmenopausal women. *Am J Clin Nutr* 71, 739–745.
- Black AE (2000). The sensitivity and specificity of the Goldberg cut-off for EI-BMR for identifying diet reports of poor validity. *Eur J Clin Nutr* 54, 395–404.
- Black AE, Cole TJ (2001). Biased over- or under-reporting is characteristic of individuals whether over time or by different assessment methods. *J Am Diet Assoc* 101, 70–80.
- Black AE, Prentice AM, Coward WA (1986). Use of food quotients to predict respiratory quotients for the doubly labelled water method of measuring energy expenditure. *Hum Nutr Clin Nutr* 40C, 381–391.
- Hill RJ, Davies PS (2001). The validity of self-reported energy intake as determined using the doubly labelled water technique. *Br J Nutr* 85, 415–430.
- Ishikawa-Takata K, Tabata I, Sasaki S, Rafamantanantsoa HH, Okazaki H, Okubo H et al (2007). Physical activity level in healthy free-living Japanese estimated by doubly labelled water method and International Physical Activity Questionnaire. *Eur J Clin Nutr* advance online publication, 23 May 2007; doi:10.1038/sj.ejcn.1602805.
- Johansson L, Solvoll K, Bjørneboe G-EA (1998). Under- and over-reporting of energy intake related to weight status and lifestyle in a nationwide sample. *Am J Clin Nutr* 68, 266–274.
- Kroke A, Klipstein-Grobusch K, Voss S, Moseneder J, Thielecke E, Noack R et al (1999). Validation of a self-administered food-frequency questionnaire administered in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study: comparison of energy, protein, and macronutrient intakes estimated with the doubly labeled water, urinary nitrogen, and repeated 24-h dietary recall methods. *Am J Clin Nutr* 70, 439–447.
- Livingstone MB, Black AE (2003). Markers of the validity of reported energy intake. *J Nutr* 133 (Suppl 3), S895–S920.
- Livingstone MB, Prentice AM, Strain JJ, Coward WA, Black AE, Barker ME et al (1990). Accuracy of weighed dietary records in studies of diet and health. *BMJ* 300, 708–712.
- Matsuzawa Y, Inoue S, Ikeda Y, Sakata T, Saito Y, Sato Y et al (2000). The judgment criteria for new overweight, and the diagnostic standard for obesity. *Obes Res* 6, 18–28. (in Japanese).
- Ministry of Health Welfare (1999). *Recommended dietary allowance for Japanese: dietary reference intakes*. 6th revised edn Ministry of Health and Welfare: Tokyo. (in Japanese).
- Okubo H, Sasaki S, Hirota H, Notsu A, Todoriki H, Miura A et al (2006). The influence of age and body mass index to relative accuracy of energy intake among Japanese adults. *Public Health Nutr* 9, 651–657.
- Saltzman E, Roberts SB (1995). The role of energy expenditure in energy regulation findings from a decade of research. *Nutr Rev* 53, 209–220. Review.
- Sasaki S, Ushio F, Amano K, Morihara M, Todoriki O, Uehara Y et al (2000). Serum biomarker-based validation of a self-administered diet history questionnaire for Japanese subjects. *J Nutr Sci Vitaminol (Tokyo)* 46, 285–296.
- Sasaki S, Yanagibori R, Amano K (1998). Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *J Epidemiol* 8, 203–215.
- Sawaya AL, Tucker K, Tsay R, Willett W, Saltzman E, Dallal GE et al (1996). Evaluation of four methods for determining energy intake in young and older women: comparison with doubly labeled water measurements of total energy expenditure. *Am J Clin Nutr* 63, 491–499.
- Science and Technology Agency (2000). *Standard Tables of Food Composition in Japan* 5th revised edn Printing Bureau, Ministry of Finance: Tokyo. (in Japanese).
- Subar AF, Kipnis V, Troiano RP, Midthune D, Schoeller DA, Bingham S et al (2003). Using intake biomarkers to evaluate the extent of

- dietary misreporting in a large sample of adults: the OPEN study. *Am J Epidemiol* 158, 1–13.
- Toozé JA, Subar AF, Thompson FE, Troiano R, Schatzkin A, Kipnis V (2004). Psychosocial predictors of energy underreporting in a large doubly labeled water study. *Am J Clin Nutr* 79, 795–804.
- Trabulsi J, Schoeller DA (2001). Evaluation of dietary assessment instruments against doubly labeled water, a biomarker of habitual energy intake. *Am J Physiol Endocrinol Metab* 281, E891–899.
- Weir JBdV (1949). New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol* 109, 1–9.
- Willett WC, Lenart E (1998). Reproducibility and validity of food-frequency questionnaires. In: Willett WC (ed). *Nutritional epidemiology*, 2nd edn. Oxford University Press: New York. pp 101–147.
- Zhang J, Temme EH, Sasaki S, Kesteloot H (2000). Under- and overreporting of energy intake using urinary cations as biomarkers: relation to body mass index. *Am J Epidemiol* 152, 453–462.

Association between dietary acid–base load and cardiometabolic risk factors in young Japanese women

Kentaro Murakami^{1,2}, Satoshi Sasaki^{1,3*}, Yoshiko Takahashi^{1,4}, Kazuhiro Uenishi⁵ and the Japan Dietetic Students' Study for Nutrition and Biomarkers Group†

¹Nutritional Epidemiology Program, National Institute of Health and Nutrition, Tokyo, Japan

²Department of Epidemiology and International Health, Research Institute, International Medical Center of Japan, Tokyo, Japan

³Department of Social and Preventive Epidemiology, School of Public Health, University of Tokyo, Tokyo, Japan

⁴Department of Health and Nutrition, School of Home Economics, Wayo Women's University, Chiba, Japan

⁵Laboratory of Physiological Nutrition, Kagawa Nutrition University, Saitama, Japan

(Received 11 June 2007 – Revised 22 November 2007 – Accepted 23 November 2007 – First published online 18 February 2008)

Mild metabolic acidosis, which can be caused by diet, may adversely affect cardiometabolic risk factors, possibly by increasing cortisol production. Methodologies for estimating diet-induced acid–base load using dietary-intake information have been established. To our knowledge, however, the possible association between dietary acid–base load and cardiometabolic risk factors has not been investigated. We cross-sectionally examined associations between dietary acid–base load and cardiometabolic risk factors in a free-living population. The subjects were 1136 female Japanese dietetic students aged 18–22 years. Dietary acid–base load was characterized as the potential renal acid load (PRAL), which was determined using an algorithm including dietary protein, P, K, Ca and Mg, as well as the ratio of dietary protein to K (Pro:K). Estimates of each nutrient were obtained from a validated comprehensive self-administered diet history questionnaire. Body height and weight, waist circumference and blood pressure were measured. Fasting blood samples were collected. After adjustment for potential confounding factors, higher PRAL and Pro:K (more acidic dietary acid–base loads) were associated with higher systolic and diastolic blood pressure (P for trend=0.028 and 0.035 for PRAL and 0.012 and 0.009 for Pro:K, respectively). PRAL was also independently positively associated with total and LDL-cholesterol (n 1121; P for trend=0.042 and 0.021, respectively). Additionally, Pro:K showed an independent positive association with BMI and waist circumference (P for trend=0.024 and 0.012, respectively). In conclusion, more acidic dietary acid–base load was independently associated with adverse profile of several cardiometabolic risk factors in free-living young Japanese women.

Acid–base balance: Potential renal acid load: Ratio of dietary protein to potassium: Blood pressure

The potential importance of acid–base homeostasis to cardiometabolic risk factors has been recently suggested in the literature^(1,2). Mild metabolic acidosis, which can be caused by diet^(3–5), may adversely affect blood pressure^(6–8), possibly by increasing cortisol production⁽³⁾, increasing Ca excretion^(9,10) or decreasing citrate excretion⁽¹¹⁾. Increased cortisol production caused by mild metabolic acidosis^(3–5) may also have a detrimental influence on other cardiometabolic risk factors, including obesity and cholesterol^(12–14).

Since acid–base status is markedly influenced by diet^(15,16), diet-dependent acid–base load can be calculated based on dietary intake information. Remer and colleagues developed an equation for estimating potential renal acid load (PRAL), an indicator of dietary acid–base load, using the dietary intake of five nutrients (protein, P, K, Ca and Mg)^(15,17). In addition, Frassetto and colleagues proposed the ratio of dietary protein to K (Pro:K) as an indicator of dietary acid–base load⁽¹⁶⁾. Both PRAL and Pro:K estimated from dietary

Abbreviations: DHQ, diet history questionnaire; MET, metabolic equivalents; NAE, net acid excretion; OA, organic acids; PRAL, potential renal acid load; Pro:K, ratio of dietary protein to K.

* **Corresponding author:** Dr Satoshi Sasaki, fax +81 3 5841 7873, email stssasak@m.u-tokyo.ac.jp

† The members of the Japan Dietetic Students' Study for Nutrition and Biomarkers Group (in addition to the authors) are as follows: Mitsuyo Yamasaki, Yuko Hisatomi, Junko Soezima, and Kazumi Takedomi (Nishikyushu University); Toshiyuki Kohri and Naoko Kaba (Kinki University); Etsuko Uneoka (Otemae College of Nutrition); Hitomi Hayabuchi and Yoko Umeki (Fukuoka Women's University); Keiko Baba and Maiko Suzuki (Mie Chukyo University Junior College); Reiko Watanabe and Kanako Muramatsu (Niigata Women's College); Kazuko Ohki, Seigo Shiga, Hidemichi Ebisawa, and Masako Fuwa (Shoya Women's University); Tomoko Watanabe, Ayuh Suzuki, and Fumiyo Kudo (Chiba College of Health Science); Katsumi Shibata, Tsutomu Fukuwatari, and Junko Hirose (The University of Shiga Prefecture); Toru Takahashi and Masako Kato (Mimasaka University); Toshihiro Goda and Yoko Ichikawa (University of Shizuoka); Junko Suzuki, Yoko Niida, Satomi Morohashi, Chiaki Shimizu, and Naomi Takeuchi (Hokkaido Bunkyo University); Jun Oka and Tomoko Ide (Tokyo Kasei University); and Yoshiko Sugiyama and Mika Furuki (Minamikyushu University).

intake information have been validated against objective measures of acid-base load determined from 24 h urine (i.e. PRAL and net acid excretion (NAE), respectively)⁽¹⁷⁾. Using these measures, an expected negative relationship of dietary acid-base load with bone health was demonstrated in several epidemiologic studies that relied on a dietary questionnaire for nutrient intake estimation⁽¹⁸⁻²²⁾.

Despite the potential influence of dietary acid-base load on cardiometabolic risk factors and the availability of dietary acid-base load measurements using dietary intake data, no study has examined the possible association between measures of dietary acid-base load and cardiometabolic risk factors. Here, we investigated the associations of measures of dietary acid-base load (i.e. PRAL and Pro:K), calculated using nutrient intake estimates obtained from a validated self-administered comprehensive diet history questionnaire (DHQ)⁽²³⁻²⁵⁾ with several cardiometabolic risk factors including BMI, waist circumference, systolic and diastolic blood pressure, total, HDL, and LDL cholesterol, fasting TAG, fasting glucose and glycated Hb, using data gathered from a cross-sectional observational study of free-living young Japanese women.

Subjects and methods

Subjects

The present study was based on a cross-sectional multi-centre survey conducted from February to March 2006 and from January to March 2007 among female dietetic students from fifteen institutions in Japan. All measurements at each institution were conducted according to the survey protocol. Briefly, staff at each institution explained an outline of the survey to potential subjects. Those who responded positively were then provided detailed written and oral explanations of the survey's general purpose and procedure. The protocol of the study was approved by the Ethics Committee of the National Institute of Health and Nutrition, and written informed consent was obtained from each subject, and also from a parent for subjects aged < 20 years.

A total of 1176 Japanese women took part. For the present analysis, women aged 18-22 years were selected (*n* 1154), not only because dietetic students outside this age range are rare in Japan but also because their dietary and cardiometabolic characteristics may differ from those of dietetic students aged 18-22 years. We then excluded from the 1154 women aged 18-22 years those not completing survey questionnaires (*n* 1), those with extremely low or high reported energy intakes (< 2092 or > 16 736 kJ/d; *n* 2), those currently receiving dietary counselling from a doctor or dietitian (*n* 13), those with previously diagnosed diabetes, hypertension or CVD (*n* 1), and those without measurement of body height and weight (*n* 2). Additionally, women with missing information regarding cardiometabolic risk factors were excluded from the respective analyses (*n* 2 for BMI, *n* 2 for waist circumference, *n* 0 for systolic and diastolic blood pressure, *n* 16 for cholesterol (total, HDL and LDL), *n* 16 for TAG, *n* 15 for glucose, and *n* 16 for glycated Hb). Further, those providing non-fasting blood samples (*n* 34) were excluded from the fasting TAG and glucose analyses. Some women fell into more than one exclusion category. The final sample size was 1136 for BMI, waist circumference, and systolic and diastolic blood pressure,

1121 for cholesterol (total, HDL, and LDL) and glycated Hb, 1089 for fasting glucose, and 1088 for fasting TAG.

Dietary assessment

Dietary habits during the preceding month were assessed using a self-administered comprehensive DHQ⁽²³⁻²⁵⁾. Responses to the DHQ, as well as to a lifestyle questionnaire, were checked at least twice for completeness. When necessary, forms were reviewed with the subject to ensure the clarity of answers. The DHQ is a sixteen-page structured questionnaire that consists of the following seven sections: general dietary behaviour; major cooking methods; consumption frequency and amount of six alcoholic beverages; consumption frequency and semi-quantitative portion size of 118 selected food and nonalcoholic beverage items; dietary supplements; consumption frequency and semi-quantitative portion size of nineteen cereals (rice, bread, and noodles), soup consumed with noodles, and *miso* (fermented soyabean paste) soup; and open-ended items for foods consumed regularly (\geq once/week), but not appearing in the DHQ⁽²³⁾. The food and beverage items were selected as foods commonly consumed in Japan, mainly from a food list used in the National Nutrition Survey of Japan, and standard portion sizes were derived mainly from several recipe books for Japanese dishes⁽²³⁾.

Estimates of dietary intake for a total of 150 food and beverage items (including five seasonings), energy, and nutrients were calculated using an *ad hoc* computer algorithm for the DHQ based on the Standard Tables of Food Composition in Japan⁽²⁶⁾. Information on dietary supplements and data from the open-ended questionnaire items were not used in the calculation of dietary intake⁽²³⁾. Nutrient and food intake was energy-adjusted using the residual method⁽²⁷⁾. Detailed descriptions of the methods used to calculate dietary intake and the validity of the DHQ regarding nutrients have been published elsewhere⁽²³⁻²⁵⁾. The Pearson correlation coefficients between the DHQ and the 3 d estimated dietary records for forty-seven women were 0.48 for protein, 0.59 for P, 0.68 for K, and 0.49 for Ca (data not available for Mg)⁽²³⁾. The Pearson correlation coefficients between the DHQ and the 16 d weighed dietary records for ninety-two women were 0.52 for protein, 0.55 for P, 0.55 for K, 0.56 for Ca, and 0.56 for Mg (S. Sasaki, unpublished results). In addition, the Spearman correlation coefficients were 0.66 for meats, 0.55 for fish and shellfish, 0.38 for eggs, 0.61 for dairy products, and 0.40 for fruits, 0.57 for vegetables, and 0.46 for cereals in ninety-two women (S. Sasaki, unpublished results). Furthermore, the Pearson correlation coefficient between the DHQ and the 24 h urinary excretion for K was 0.40 in sixty-nine women⁽²⁴⁾.

Calculation and validation of dietary acid-base load measures

Urinary NAE is an established index of net endogenous acid production^(16,17), which is difficult to measure directly^(28,29). Because the sum of cations excreted in the urine equals the sum of anions, urinary NAE is also equal to the difference between the sum of the major urinary non-bicarbonate anions minus the sum of the non-titratable acid and non-ammonium cations⁽³⁰⁾. The amounts of these non-bicarbonate

anions and mineral cations in urine (excluding organic acids (OA)) are primarily influenced by dietary nutrient intake^(15,16). OA are largely independent of dietary acid load or macronutrient composition^(15,17,31,32), and can be reasonably estimated from body surface area⁽³²⁾:

$$\text{OA (mEq/d)} = \text{body surface area (m}^2\text{)} \times 41/1.73,$$

$$\text{where body surface area (m}^2\text{)} = 0.0007484$$

$$\times \text{body height (cm)}^{0.725}$$

$$\times \text{body weight (kg)}^{0.425}.$$

Thus, the estimate of the urinary difference in non-bicarbonate anions (without OA) and mineral cations can be considered an index of diet-induced acid load⁽¹⁷⁾. Remer and colleagues referred to this estimate as PRAL (i.e. $\text{NAE} = \text{PRAL} + \text{OA}$)⁽¹⁷⁾, and developed the equation for estimating PRAL from dietary information^(15,17,30):

$$\text{PRAL (mEq/d)} = 0.4888 \times \text{protein (g/d)} + 0.0366$$

$$\times \text{P (mg/d)} - 0.0205 \times \text{K (mg/d)} - 0.0125$$

$$\times \text{Ca (mg/d)} - 0.0263 \times \text{Mg (mg/d)}.$$

The validity of PRAL estimated from this equation has been established against PRAL measured from 24 h urine^(15,17).

The rate of H_2SO_4 production from protein metabolism and the rate of bicarbonate generation from the metabolism of intestinally absorbed K salts are major and highly variable components of net endogenous acid production⁽²⁹⁾. Based on this, Frassetto and colleagues proposed the ratio of dietary protein (g/d) to K (mEq/d) (i.e. Pro:K) as an index of diet-induced acid load⁽¹⁶⁾. The validity of Pro:K has been established against NAE measured in 24 h urine⁽¹⁷⁾.

In the present study PRAL and Pro:K were used as measures of dietary acid-base load. PRAL and Pro:K were calculated according to the equations described above using crude nutrient intake data estimated from the DHQ. Higher values of PRAL and Pro:K mean more acidic dietary acid-base load. Calculated PRAL and Pro:K were then energy-adjusted using the residual method⁽²⁷⁾. Prior to the present analysis, the relative validity of PRAL and Pro:K estimated from the DHQ was examined against that from the 16 d weighed dietary records in ninety-two women aged 31–69 years. The Pearson correlation coefficient between the two methods was 0.35 for PRAL and 0.37 for Pro:K (S. Sasaki, unpublished results).

Cardiometabolic risk factors

Cardiometabolic risk factors were measured 1–3 d after completion of the questionnaires. Body height was measured to the nearest 0.1 cm with the subject standing without shoes. Body weight in light indoor clothes was measured to the nearest 0.1 kg. BMI was calculated as body weight (kg) divided by the square of body height (m). Waist circumference was measured at the level of the umbilicus to the nearest 0.1 cm. The measurement was taken at the end of a normal expiration

while the subject was standing erect with her arms at her side and feet together. Systolic and diastolic blood pressure was measured on the left arm with an automatic device (Omron model HEM-770A; Omron Health Care, Kyoto, Japan) after the subject had been sitting quietly for ≥ 3 min. A second measurement was carried out about 1 min after the first, and the mean value of the two was used. Peripheral blood samples were obtained from subjects after an overnight fast. Blood was collected in evacuated tubes containing no additives, allowed to clot, and centrifuged at 3000 g for 10 min at room temperature to separate the serum. Blood samples for glycated Hb measurements were also collected in evacuated tubes containing no additives. In accordance with the survey protocol, blood samples were transported at -20°C by car or airplane to ensure delivery to a laboratory in Tokyo, Japan (SRL, Inc. in the 2006 survey and Mitsubishi Kagaku Bio-Clinical Laboratories (MBCL), Inc. in the 2007 survey). Biochemical variables were assayed at SRL in the 2006 survey and MBCL in the 2007 survey within 1–2 d of collection to avoid significant degradation, as follows. Serum total cholesterol concentration was measured enzymically using a kit from Wako Junyaku Co. Ltd (Tokyo, Japan) at SRL and using a kit from Daiya Shiyaku Co. Ltd (Tokyo, Japan) at MBCL. Serum LDL- and HDL-cholesterol concentrations were measured enzymically using a kit from Daiichi Kagaku Co. Ltd at SRL and using a kit from Daiichi Kagaku Co. Ltd at MBCL. Serum TAG concentration was measured enzymically using a kit from Daiichi Kagaku Co. Ltd at SRL and using a kit from Kyowa Medex Co. Ltd (Tokyo, Japan) at MBCL. Serum glucose concentration was measured enzymically using a kit from Shino Tesuto Co. Ltd (Tokyo, Japan) at SRL and using a kit from Kanto Kagaku Co. Ltd (Tokyo, Japan) at MBCL. Glycated Hb was measured using whole blood by latex agglutination-turbidimetric immunoassay (Fuji Revio Co. Ltd (Tokyo, Japan) at SRL and Kyowa Medex Co. Ltd (Tokyo, Japan) at MBCL). In-house quality-control procedures for all assays were conducted at SRL in the 2006 survey and MBCL in the 2007 survey.

Other variables

In the lifestyle questionnaire, the subject reported her residential area, which was grouped into one of three regions (residential block: north (Kanto, Hokkaido, and Tohoku); central (Tokai, Hokuriku, and Kinki) or south (Kyushu and Chugoku)). The residential areas were also grouped into three categories according to population size (size of residential area: city with population ≥ 1 million; city with population < 1 million or town and village). Current smoking (yes or no) was self-reported in the lifestyle questionnaire. Physical activity was computed as the average metabolic equivalents (MET)-hours per day⁽³³⁾ on the basis of the frequency and duration of five different activities (sleeping, high- and moderate-intensity activities, walking, and sedentary activities) over the preceding month, as reported in the lifestyle questionnaire.

Statistical analysis

Measures of dietary acid-base load, i.e. PRAL and Pro:K, were examined in relation to ten cardiometabolic risk factors, namely BMI, waist circumference, systolic and diastolic blood