J Cardiol 1999; 33: 327−338

Responsiveness to a Self-Administered Diet History Questionnaire in a Work-Site Dietary Intervention Trial for Mildly Hypercholesterolemic Japanese Subjects: Correlation Between Change in Dietary Habits and Serum Cholesterol Levels

Satoshi SASAKI, MD*[1,2]
Toyomi ISHIKAWA, MD*[1,3]
Ryoko YANAGIBORI, MD*[4]
Keiko AMANO, MD, FJCC*[5]

Abstract

Modification of lifestyle, especially of diet, is considered important for prevention of cardiovascular disease. Dietary assessment is generally too troublesome to use in a large number of subjects for prevention. We have therefore developed a self-administered diet history questionnaire (DHQ), an easier dietary assessment method than conventional methods, with reasonable validity for use in dietary intervention studies. Responsiveness, *i.e.*, sensitivity to a change in a target variable, is one type of validity required for a dietary assessment method which is used for the evaluation of the effect of dietary interventions.

We examined the responsiveness of the DHQ using the data from a 12-week work-site dietary intervention trial including 63 (54 men and 9 women) mildly hypercholesterolemic Japanese (age range: 22−59 years, serum cholesterol ≥ 200 mg/d*l*). Dietary habits were assessed by the DHQ before and after the trial. Pearson's correlation coefficients between the change in serum cholesterol and Keys score calculated from the dietary data were 0.33 and 0.32 ($p < 0.01$) with and without adjustment for possible confounding factors, respectively. Forty-two percent of the total variation of serum cholesterol change was explained by the initial serum cholesterol level, the change in body mass index, and the Keys score.

The results suggest that the DHQ showed adequate responsiveness to the serum cholesterol change resulting from dietary intervention.

J Cardiol 1999; 33 (6): 327−338

Key Words
■ **Diet** ■ **Epidemiologic methods (dietary assessment method)** ■ **Cholesterol**
■ **Prevention** ■ **Interventional cardiology**

INTRODUCTION

Several epidemiologic studies in both Western countries[1,2] and Japan[3] have reported that hypercholesterolemia is one of the risk factors for coronary heart disease. They showed a positive relationship within the ranges of serum cholesterol of the populations, even in populations with low levels

[1]名古屋市立大学医学部 公衆衛生学：〒467−8601 名古屋市瑞穂区瑞穂町字川澄1；[2](現)国立がんセンター研究所支所臨床疫学研究部：〒277−8577 千葉県柏市柏の葉6−5−1；*[3]東邦ガス株式会社，名古屋；*[4]愛知県立看護大学，名古屋；*[5]東京水産大学保健管理センター，東京
*[1]Department of Public Health, Nagoya City University School of Medicine, Nagoya; *[2](present) Epidemiology and Biostatistics Division, National Cancer Center Research Institute, East, Chiba; *[3]Toho Gas Co., Nagoya; *[4]Aichi Prefectural College of Nursing and Health, Nagoya; *[5]Tokyo University of Fisheries, Tokyo
Address for reprints: SASAKI S, MD, Epidemiology and Biostatistics Division, National Cancer Center Research Institute, East, Kashiwanoha 6−5−1, Kashiwa, Chiba 277−8577
Manuscript received November 13, 1998; revised February 15, 1999; accepted March 12, 1999

(147−182 mg/dl) in the Chinese study[4], and no evidence of threshold. From the viewpoint of prevention, lifestyle modification for mildly hypercholesterolemic persons is as important as pharmacological treatment for severely hypercholesterolemic patients because the risk reduction at a population level, *i.e.*, benefit as a population, is as great in the former strategy as in the latter[5]. Dietary modification is recommended by the expert panel as a first-step treatment for mild hypercholesterolemia (serum cholesterol: 200−239 mg/dl) without definite coronary heart disease[6]. Several dietary intervention trials have therefore been conducted to establish effective educational methods to reduce serum cholesterol levels among subjects with various serum cholesterol ranges. For example, mean serum cholesterol levels of studies included in a meta-analysis on serum cholesterol change by dietary intervention in free-living subjects varied from 186 to 294 mg/dl[7].

Among several dietary factors related to serum cholesterol, saturated fatty acid (SFA), polyunsaturated fatty acid (PUFA), and cholesterol have long been of interest[7−13]. Although several dietary indicators have been postulated to predict change in serum cholesterol from intakes of the above 3 nutrients[8−13]. The Keys score is one of the most frequently used indices[9], and is defined as:

$$\Phi\ (\text{unit}) = 2.7\,(\Delta \text{SFA} - \text{PUFA}/2) + 1.5\,\Delta\sqrt{(\text{Chol})}$$

where Φ is the Keys score which predicts a 1 mg/dl decrease in serum cholesterol level by 1 unit decrease in the score, ΔSFA is change in SFA intake expressed as a percentage of total energy, ΔPUFA is change in PUFA intake expressed as a percentage of total energy, and $\Delta\sqrt{(\text{Chol})}$ is change in the square root of cholesterol intake (mg/1,000 kcal).

Mean serum cholesterol levels and prevalence of hypercholesterolemia have recently been increasing in Japan[14]. The establishment of an effective system of dietary education against hypercholesterolemia is also necessary in Japan. Although some dietary intervention trials have been conducted in Japan[15,16], the results were inconclusive. Moreover, no study has reported a quantitative association between change in dietary habits and change in serum cholesterol level at an individual level in Japanese subjects.

Several nutrients including SFA, PUFA, and cholesterol need quite long periods to obtain reliable intakes at an individual level because of the wide day-to-day variation[17,18]. For example, SFA and cholesterol need 71 and 139 days in men, respectively, to obtain values within the range of true intakes of individuals ±5% with 5% error[17]. In Japan, a dietary record or recall over a few days has usually been used for the dietary assessment of an evaluation of dietary change by intervention. These are not appropriate methods for the reasons above. Moreover, these methods need relatively large manpower of dietitians and cooperation of subjects. Their feasibility for use in trials in a field-setting is therefore questionable. In order to overcome these problems, several semiquantitative dietary assessment methods have been developed in Western countries[19,20]. However, they cannot be directly used for Japanese subjects because of the different dietary habits and foods available.

We have therefore developed a self-administered diet history questionnaire (DHQ) which can be used for dietary interventions in Japanese[21,22]. One validation study compared nutrient intakes estimated from the DHQ and those from 3-day dietary record using mildly hypercholesterolemic women before education[22]. The other examined the validity using 24-hour urinary excretion of sodium and potassium as biomarkers[21]. The purpose of these studies was a cross-sectional validation. Guyatt *et al.*[23] first proposed "responsiveness" to describe the sensitivity to change of an evaluation instrument. Responsiveness is another type of validity of dietary assessment method. We recently reported the effectiveness of a brief individual dietary counseling approach based on the DHQ to modify intakes of target nutrients for mildly hypercholesterolemic persons at a group level[24]. This did not report the change in serum cholesterol level by the counseling because of the small number of subjects ($n=32$ in the case-group). Therefore, the responsiveness of DHQ at an individual level to serum cholesterol change remains unresolved. This study examined responsiveness of the DHQ using the data of a 12-week work-site dietary intervention trial for mildly hypercholesterolemic subjects using the established education method.

METHODS

Subjects and study design

Subjects with a non-fasting serum cholesterol level of 220 mg/dl or more were screened at an annual health checkup at Toho Gas Company, Nagoya, Japan, in October, 1995. Subjects with 200−219 mg/d*l* serum cholesterol accompanied by hypertriglyceridemia (serum triglyceride ≥ 300 mg/d*l*), hyperglycemia (whole blood glucose ≥ 120 mg/d*l*) and/or overweight [body mass index (BMI) ≥ 25.0 kg/m^2] were also screened. Total subjects screened were 269 (235 men and 34 women). An invitation letter for the dietary intervention trial with a full explanation of the purpose of the study was mailed to them in March, 1996. Seventy subjects agreed to participate in the study. One person who agreed to the participation canceled before the trial started. The program of the trial and the DHQ was mailed to the 69 subjects. The DHQs were returned by mail. One dietitian and 5 staff (4 nurses and one fitness-trainer) with special training for the questionnaire-handling checked the answers. Any illogical answers were resolved and the blanks were filled by telephone interviews within 2 weeks. Individual education schemes were prepared based on the results of the dietary survey. Individual result sheets used in the education consisted of 7 pages, and included a summary of the characteristics of personal dietary habits and how to modify the diet, a comprehensive table on nutrient intakes by food group, and other information necessary for education. The brief, approximately 15 min, individual counseling was performed by trained nurses in June or July. During the subsequent 12 weeks, a newsletter was sent to participants every week. The newsletter consisted of an easy-to-understand story on "how to normalize your serum cholesterol level modifying your diet?" or the related topics on one page of A4-size paper. A brief questionnaire on diets during the previous week was attached to the newsletter. The completed questionnaire was sent back to the staff. Newsletters were used to maintain the motivation through the trial. A brief comment from the nurses according to the answers of the previous brief questionnaire was sent back at the next mailing of the newsletter and the questionnaire. Six subjects dropped out (drop-out rate: 9%) and 63 (54 men and 9 women, mean ± standard deviation: 45.1 ± 8.3 years, age range: 22−59 years) completed the trial. After the trial was completed (in September or October), the DHQs to evaluate the change in dietary habits were mailed to the subjects and the filled DHQs were mailed back to the staff (dietary survey after intervention). The same staff checked the answers. Illogical answers were resolved and the blanks were filled by telephone interviews within 2 weeks. The subjects received the annual health checkup in October, 1996. The period was similar to those of the second dietary survey. The results were returned to the subjects in December, 1996. (All hardcopy materials used in the study are available from the authors on request.) The number of subjects at each step of the trial from the screening to the completion of the trial is shown in **Fig. 1**.

Self-administered diet history questionnaire

The DHQ used in this study was a slight modification of the test-version[21,22]. The questions were designed to assess dietary habits in the previous 1 month, and consisted of 7 sections: 1) Eleven questions on dietary behaviors such as 'how often and how much "shoyu (soy-sauce)" do you usually use at table?', 2) semi-quantitative frequency questions on 127 selected food items including 6 diet foods and 10 supplements, 3) questions on frequency and quantity of rice, noodles, breads, and miso-soup, 4) major cooking methods for fish, meats, eggs, and vegetables, 5) frequency and quantity of 6 types of alcoholic beverages, 6) types, frequency, and quantity of supplements, and 7) open-ended questions to describe names and the quantities of foods eaten regularly (at least once per week) which were not listed in the questions. For questions about rice and miso-soup, sizes of bowls usually used were asked. For foods listed in the semi-quantitative frequency question section, standard portion sizes were given in words such as 'a half' for apples and 'one big leaf' for cabbage. The food items and the portion sizes listed in the semi-quantitative frequency question section were chosen as foods commonly consumed in Japan. They were selected mainly from a food list used in the National Nutrition Survey of Japan[25]. Local foods and menus were not considered for food selection. Frequency was asked using 8 categories: 1) More than or equal to twice per day, 2) once per day, 3) 4−6 times per week, 4) 2−3 times per week, 5) once per week, 6) 2−3 times per month, 7) once per month, and 8) less than once per month. Relative portion size was asked by 5 categories compared to a standard portion size indicated in the questionnaire: 1) Very small (50% or less), 2) small (about 70−80%), 3) medium (about same as a standard portion size), 4) large (20−30% larger), and 5) very large (50% larger or more). The questionnaire took about 30−60 min to answer.

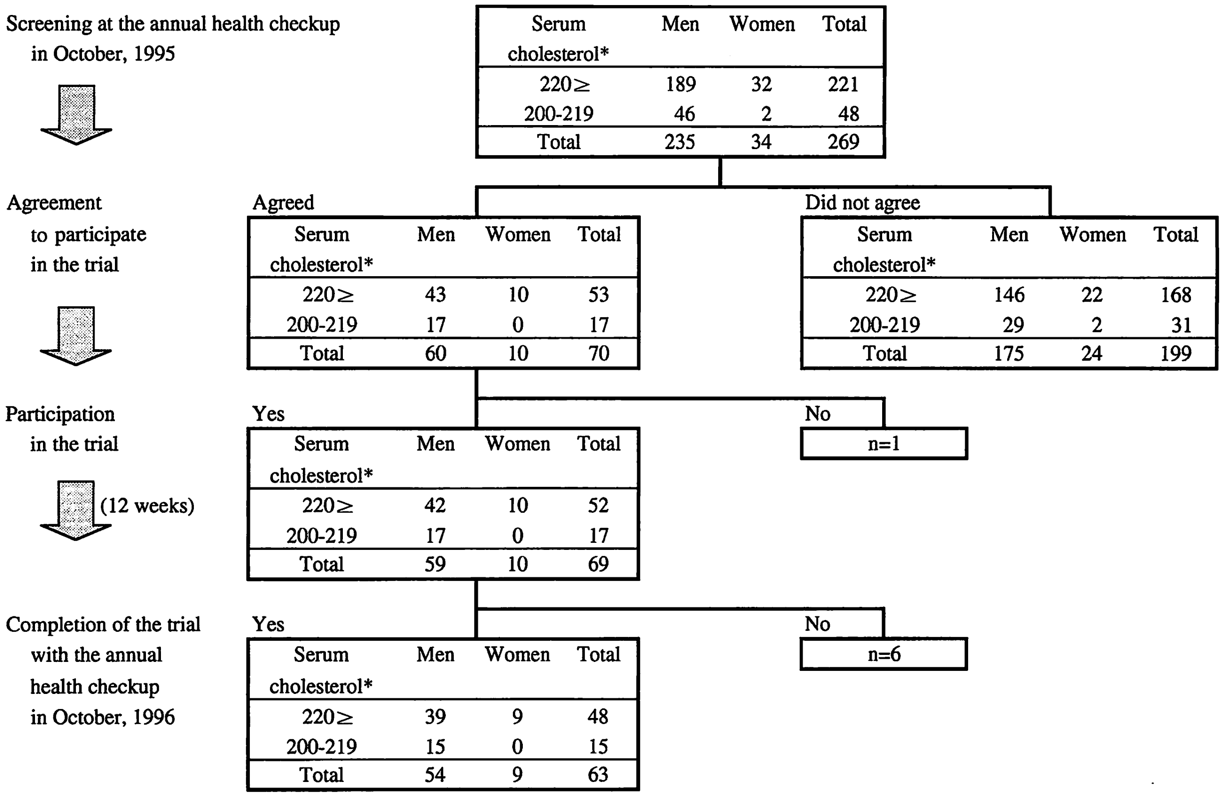

Fig. 1 Number of subjects in the trial
* Serum cholesterol (mg/d*l*) at the checkup in 1995.

Nutrient intake was calculated using an *ad hoc* computer program developed to analyze the questionnaire. The Japanese food composition tables, 4th edition[26,27], and the others[28] were used as the data-base for food composition tables.

We were particularly interested in all fats ingested rather than only visible fat and intake of types of fat, *i.e.*, fatty acids, rather than total fat. Such an assessment has been very difficult or almost impossible for dietary assessment questionnaires previously developed in Japan because of the absence of enough theory and methods to estimate invisible fat intake such as cooking oil, and a lack of reliable fatty acid composition table of Japanese foods for nutrient calculation[29,30]. To overcome the former problem, we used the theory of dietary history method first proposed by Burke[31] which assesses food intakes (including seasonings) from the combination of questions on food consumption and dietary behaviors such as cooking methods and seasoning use. This method originally needed the full experience and technique of dietitians. Some groups have developed computer algorithms and questionnaires based on this theory and made the assessment more systematic and rapid and reduced the burden of subjects and dietitians[32-34]. We developed a similar type of computer algorithm and a questionnaire considering Japanese dietary characteristics after extensive search of the information on oil- and seasoning-use during cooking processes and at table. This method was also used for sodium and sugar intakes. The conceptual structure of the algorithm is as follows. Sodium, sugar, and cooking oil added during cooking were estimated from the combination of questions on dietary behaviors, *i.e.*, the major cooking methods of vegetables, fish and meats, and food intakes obtained from the semi-quantitative food frequency question section. Salt from salted seasonings such as soy-sauce and from table salt were also considered for salt intake. Fat preference asked in the dietary behavior question section was considered to choose types of meats consumed. For the solution of the latter problem, missing values of fatty acid and/or cholesterol compositions were substituted with those of foods with similar compositions. In this case, the composition of substituted fatty acids was adjusted for total fat. Additional information was used for fatty acid

Table 1 Age, body size, and serum lipid concentrations at screening and after intervention ($n=63$)

	At screening (October, 1995)	After intervention (October, 1996)	Crude change	Percentage change†
Age (yr)	45.1±8.3 (Range=22-59)			
Body height (cm)	165.8±8.0	165.8±7.9	0.0±0.7	0
Body weight (kg)	67.8±9.3	67.0±9.2	−0.8±2.5*	−1
Body mass index (kg/m²)	24.6±2.5	24.3±2.5	−0.3±1.0*	−1
Serum cholesterol (mg/d*l*)‡	243±24	228±30	−15±26***	−6
HDL cholesterol (mg/d*l*)‡	50±16	53±15	3±6***	7
Triglyceride (mg/d*l*)‡	344±201	205±133	−138±144***	−40

†Percentage change= (mean after intervention − mean at screening) / mean at screening.
‡The blood was sampled at non-fasting condition.
Significance for the change between at screening and after intervention: *$p<0.05$, **$p<0.01$, ***$p<0.001$.
Values are mean±SD.
HDL=high-density lipoprotein.

compositions of some foods[28]. Most foods are beverages, fruits and vegetables, with total fat less than 1.0 g per 100 g portion and without fatty acid composition, so the values remain unknown. For cooked foods and processed foods which were not listed in the food composition tables of Japanese foods[26,27], the nutrient compositions were calculated using the recipes prepared by a dietitian. In this case, to ensure as much accuracy as possible, other major nutrients in addition to fat and energy were considered.

Statistical analysis

Serum lipid concentrations, total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride, were also measured just before the trial with more strict quality control than usual annual health checkups. However, as the comparison of these 2 values was difficult because of the different level of quality control, the values measured in 2 health checkups in 1995 and 1996 were used for the follow-up evaluation in this study. Intake levels were calculated for total energy and 18 nutrients. Foods in the open-ended question section and supplements were not included for nutrient calculation because the foods reported in the open-ended question section were negligible for the purpose of nutrient calculation and no reliable food composition table was available for most supplements. From the viewpoint of nutrient-disease association, nutrient intakes considering body size and energy requirement of each person are more interesting than the absolute intakes. Among several methods for energy-adjustment[35,36], the density model was used in this study[36].

Pearson's correlations between the change in serum cholesterol and change in dietary factors were calculated with and without adjustment for possible confounding factors. Multiple regression analysis was performed to examine the correlation between the change in serum cholesterol levels, and Keys score[9] and other possible risk factors. Serum cholesterol at screening, and change in BMI were included in the analysis as possible non-dietary risk factors. Age was also included in the model. Because of a possible different response to the intervention between men and women and the small sample size for women ($n=9$), we performed the same analyses for men only ($n=54$). The results were similar to those in both sexes combined, although the most of the results were slightly less marked because of the smaller number of subjects. Therefore, only the analyses for both sexes combined are presented here. To exclude sex-related differences as much as possible, sex (as a dummy variable) was included in the model. We also examined the model with body weight in place of BMI because some previous studies reported a serum cholesterol lowering effect of reduction in body weight[37]. We additionally examined the model with the change in intakes of SFA, PUFA, and cholesterol at one time in place of Keys score. The result is also presented here because the determination coefficient was comparable with those observed in the model with Keys score.

RESULTS

Table 1 shows age, body size, and the changes in

Table 2 Nutrient intakes before and after intervention ($n=63$)

	Before intervention (May, 1996)	After intervention (October, 1996)	Crude change	Percentage change†
Energy (kcal/day)	2,129±470	1,984±508	−145±518*	−7
Protein (%E)	13.0±2.1	14.6±2.5	1.6±2.1***	12
Carbohydrate (%E)	55.3±8.0	56.2±7.3	0.9±6.4	2
Total fat (%E)	23.9±5.3	21.0±4.6	−2.8±5.4***	−12
SFA (%E)	7.6±1.9	5.9±1.5	−1.7±1.9***	−22
MUFA (%E)	8.2±2.1	7.0±1.8	−1.2±2.2***	−15
PUFA (%E)	5.4±1.5	5.6±1.4	0.2±1.5	3
n-3 PUFA (%E)	1.1±0.4	1.2±0.4	0.1±0.4*	12
n-6 PUFA (%E)	4.4±1.3	4.4±1.2	0.0±1.3	0
Vitamin C (mg/1,000 kcal)	65.9±108.6	67.3±81.2	1.4±52.7	2
Vitamin A (IU/1,000 kcal)	1,002±693	1,212±630	210±720*	21
Retinol (μg/1,000 kcal)	148±174	192±141	44±194	30
Carotene (μg/1,000 kcal)	896±549	1,084±639	188±494**	21
Cholesterol (mg/1,000 kcal)	128±52	121±40	−7±53	−5
Keys score (unit)‡	−	−	−5.1±5.9	−
Ethanol (%E)	10.6±9.6	11.0±10.4	0.3±6.8	3
Dietary fiber (g/1,000 kcal)	8.7±3.1	8.9±2.4	0.2±2.9	2
Water soluble fiber (g/1,000 kcal)	1.3±0.5	1.4±0.4	0.1±0.4	5
Non-water soluble fiber (g/1,000 kcal)	7.4±2.7	7.5±2.1	0.1±2.5	1

†Percentage change = (mean after intervention − mean before intervention)/mean before intervention.
‡Keys score (unit) $= 2.7(\Delta SFA - \Delta PUFA/2) + 1.5\Delta\sqrt{(Chol)}$, where ΔSFA = change in SFA intake (%E), ΔPUFA = change in PUFA intake (%E), and $\Delta\sqrt{(Chol)}$ = change in the square root of cholesterol intake (mg/1,000 kcal).
Significance for the change: *$p<0.05$, **$p<0.01$, ***$p<0.001$.
Values are mean±SD.
%E = percentage of total energy; SFA = saturated fatty acid; MUFA = monounsaturated fatty acid; PUFA = polyunsaturated fatty acid.

serum lipid concentrations. Age range was 22−59 years. A significant decrease was observed in serum cholesterol, triglyceride ($p<0.001$), body weight, and BMI ($p<0.05$). An increase was observed in HDL cholesterol ($p<0.001$).

Table 2 shows the change in nutrient intake levels. Mean total fat, SFA, and monounsaturated fatty acid intakes decreased and protein intake increased significantly ($p<0.001$). Keys score calculated from the change in SFA, PUFA, and cholesterol intakes was −5.1 units.

Pearson's correlation coefficients between the change in nutrient intakes and the change in serum cholesterol levels are shown in **Table 3**. The change in SFA intake showed the highest degree of positive correlation with the change in serum cholesterol levels in univariate analysis. The correlation between Keys score and the change in serum cholesterol levels is shown in **Fig. 2**. After adjustment for possible confounding factors, Keys score showed the highest degree of positive correlation, followed by the change in SFA and cholesterol (**Table 3**). No other significant correlation was observed except for total fat and total energy.

The results of multiple regression analysis on the correlation between change in serum cholesterol, Keys score, the change in BMI, and serum cholesterol at screening are shown in **Table 4**. The change in BMI ($p<0.001$) and Keys score ($p<0.01$) were positively, and serum cholesterol at screening ($p<0.001$) negatively correlated with the change in serum cholesterol. Forty-two percent of the total variation of the change in serum cholesterol levels in the subjects was explained by this model. Similar results were observed in the model with the change in intakes of SFA, PUFA, and cholesterol in place of Keys score. However, the correlations for these nutrients were not significant. The results for the model with body weight was similar to those with BMI, but the determination coefficient was

Table 3 Correlations between the change in serum cholesterol levels and change in indicated nutrient intakes ($n=63$)

	Pearson's univariate correlation coefficient	Partial†
Energy (kcal/day)	0.32*	0.21
Protein (%E)	−0.05	0.05
Carbohydrate (%E)	−0.14	−0.12
Total fat (%E)	0.26*	0.16
SFA (%E)	0.33**	0.25
MUFA (%E)	0.23	0.10
PUFA (%E)	0.15	0.06
n-3 PUFA (%E)	0.08	0.10
n-6 PUFA (%E)	0.15	0.04
Vitamin C (mg/1,000 kcal)	0.00	0.03
Vitamin A (IU/1,000 kcal)	−0.11	−0.12
Retinol (μg/1,000 kcal)	−0.09	−0.12
Carotene (μg/1,000 kcal)	−0.08	−0.01
Cholesterol (mg/1,000 kcal)	0.14	0.22
Keys score (unit)	0.32*	0.33**
Ethanol (%E)	−0.09	−0.05
Dietary fiber (g/1,000 kcal)	−0.12	−0.12
Water soluble dietary fiber (g/1,000 kcal)	−0.10	−0.11
Non-water soluble dietary fiber (g/1,000 kcal)	−0.12	−0.11

†Adjusted for sex, age, serum cholesterol at screening, and change in body mass index.
Significance level from null correlation: $^{*}p<0.05$, $^{**}p<0.01$.
Formula of the Key score and abbreviations as in Table 2.

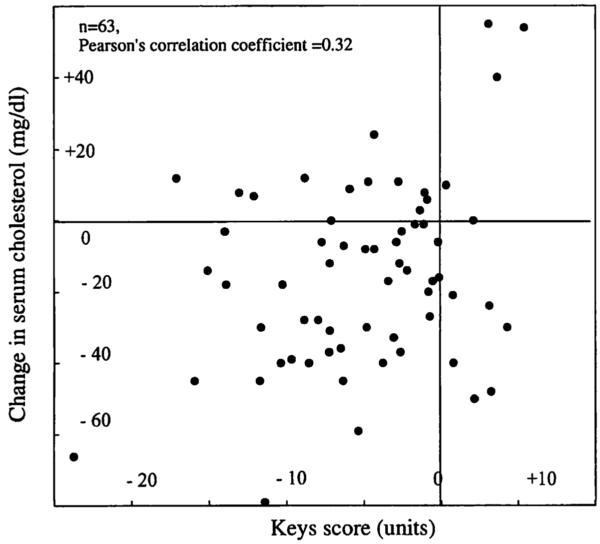

Fig. 2 Correlation between Keys score and the change in serum cholesterol level between screening and after intervention
Formula of the Keys score as in Table 2.

slightly lower.

DISCUSSION

We evaluated the responsiveness of the DHQ by examining diet-serum cholesterol association using the data of a 12-week dietary intervention trial for mildly hypercholesterolemic subjects. To our knowledge, this is the first study quantitatively reporting the individual relationship between dietary change and the change in serum cholesterol levels among mildly hypercholesterolemic subjects in Japan. The study was particularly important from the viewpoint of development of dietary assessment methods used in dietary interventions and dietary educations for cardiovascular prevention.

In order to examine the responsiveness of the DHQ at an individual level, we performed correlation analysis and multiple regression analysis using Keys score and other confounding factors. After adjustment for possible confounding factors, Keys score showed the highest degree of positive correlation ($p < 0.01$), followed by SFA and cholesterol

Table 4 Multiple regression analysis of the change in serum cholesterol levels with serum cholesterol at screening, the change in BMI (Models 1 and 2) or body weight (Models 3 and 4), and Keys score (Models 1 and 3), or the changes in SFA, PUFA, and cholesterol intakes (Models 2 and 4), as independent variables adjusted for sex and age (n=63)

Independent variable in the Models	Partial regression coefficient (β)	95% confidence interval of β	Pearson's partial correlation coefficient
Model 1 (R^2=0.42)			
Serum cholesterol at screening (mg/d*l*)	−0.44	(−0.68 to −0.21)	−0.44
Change in body mass index (kg/m²)	13.2	(7.5 to 18.9)	0.51
Keys score (unit)	1.22	(0.32 to 2.11)	0.33
Intercept	118	–	–
Model 2 (R^2=0.41)			
Serum cholesterol at screening (mg/d*l*)	−0.45	(−0.70 to −0.20)	−0.44
Change in body mass index (kg/m²)	13.3	(7.3 to 19.3)	0.50
Change in SFA intake (%E)	3.27	(−0.17 to 6.70)	0.24
Change in PUFA intake (%E)	−2.18	(−6.58 to 2.22)	−0.13
Change in cholesterol intake (mg/1,000 kcal)	0.08	(−0.03 to 0.19)	0.19
Intercept	119	–	–
Model 3 (R^2=0.39)			
Serum cholesterol at screening (mg/d*l*)	−0.43	(−0.67 to −0.19)	−0.42
Change in body weight (kg)	4.7	(2.4 to 6.9)	0.48
Keys score (unit)	1.28	(0.36 to 2.19)	0.34
Intercept	119	–	–
Model 4 (R^2=0.38)			
Serum cholesterol at screening (mg/d*l*)	−0.43	(−0.68 to −0.18)	−0.41
Change in body weight (kg)	4.6	(2.3 to 7.0)	0.46
Change in SFA intake (%E)	3.47	(−0.05 to 6.99)	0.25
Change in PUFA intake (%E)	−1.68	(−6.19 to 2.83)	−0.10
Change in cholesterol intake (mg/1,000 kcal)	0.08	(−0.03 to 0.19)	0.18
Intercept	118	–	–

R^2=determination coefficient. Formula of the Keys score and other abbreviations as in Table 2.

(**Table 3**). The partial regression coefficient indicated that 1 unit decrease in Keys score indicated a decrease of 1.2 mg/d*l* in serum cholesterol (**Table 4**). This was slightly larger than, and presumably comparable to, the original predictive value of this score, *i.e.*, 1 mg/d*l* by 1 unit change[9]. We also included other dietary variables into the model. As expected from the partial correlation analysis (**Table 3**), no other dietary variables shown in **Table 3** showed stronger correlation with serum cholesterol change than Keys score.

The level of correlation was high for serum cholesterol at screening ($p < 0.001$). Response to a cholesterol-lowering diet is greater in hypercholesterolemic subjects compared to subjects with lower cholesterol levels after adjustment for regression to the mean[38]. Therefore, the observed highly significant negative correlation between serum cholesterol at screening and the change in serum cholesterol is presumably attributable to both, *i.e.*, "greater response to the dietary education among subjects with higher level of serum cholesterol" and "regression to the mean".

Some previous studies reported that dietary fiber, especially the water soluble type, decreased serum cholesterol levels[39]. In this study, a non-significant negative relationship was observed between the change in dietary fiber intake and the change in serum cholesterol. More subjects are necessary to examine the possible effect of serum cholesterol reduction by dietary fiber.

We examined the effect of weight reduction in multiple regression analysis including body weight instead of BMI. The predictive decrease in serum cholesterol by 1.0kg weight reduction was 4.7 mg/d*l* (**Table 4**). This was greater than the previously reported value, 1.9 mg/d*l*, estimated by a meta-analysis[37]. Although inconclusive, the serum cholesterol levels of the Japanese subjects might be more sensitive to weight change than those of Westerners. Smoking also influence serum cholesterol levels[40]. However, the effect is negligible in this study because smoking habits did not change between the 2 health checkups. In a previous study, physical activity, but only those with intensity greater than 9 kcal/min, correlated negatively with serum cholesterol after controlling confounding factors[41]. We also recommended to engage in physical activity. But we could not include a change in any indicator of physical activity into the analysis because of insufficient data-collection. The results might be obscured by this lack of information.

Level of low-density lipoprotein (LDL) cholesterol is also responsive to a change in dietary habits[10-13]. However, we did not estimate LDL cholesterol levels from total and HDL cholesterol, and triglyceride by the Friedewald formula[42] because 43% of the subjects showed high levels of triglyceride ($\geq$ 400 mg/d*l*) at the checkup in 1995, probably because of non-fasting condition at the blood sampling.

Quantitative evaluation of dietary change in interventions has usually used the dietary record or recall method with a few days in Japan. However, a few days for dietary record or recall is not enough for nutrients with wide day-to-day variation within individuals[17,18]. This is the case for SFA, PUFA, and cholesterol for assessment at an individual level[17,18]. A semi-quantitative dietary assessment questionnaire which assesses diets for a longer period is recommended for these nutrients[17,43]. Considering the results of these previous methodological studies, the duration of this trial, and feasibility for the subjects, the DHQ was designed to assess dietary habits in the previous 1 month.

A study examined means of sodium reduction by 24-hour dietary record and by urinary excretion of sodium in a hypertension prevention trial, and reported more marked decrease in sodium intake by dietary record, 44%, than the actual decrease estimated from urinary excretion, 16%[44]. This tendency, so-called over-adherence, has been observed in several dietary intervention studies[45]. This may appear more severely in the results assessed by a self-administered dietary assessment questionnaire. However, in one previous study which compared nutrient intakes between the 4-day dietary record and a self-administered semi-quantitative food frequency questionnaire, no marked difference was observed in the evaluated changes by the 2 assessment methods[46]. In this study, the 95% confidence interval of the partial regression coefficient of Keys score in multiple regression analysis was 0.32–2.11 (**Table 4**). Because of this wide, although significant, confidence interval, the possible existence of over-adherence in this study was difficult to examine. Further studies are necessary to examine this topic.

We used serum cholesterol levels of single measurement at each checkup. A previous study revealed that single serum cholesterol measurement was not enough to evaluate the intervention effect because of the within-individual variation[47]. Moreover, the blood sampling was done in the no-fasting condition, which might bias the results. Although diet was assessed just before the trial, serum lipid levels measured at the screening in the health checkup in 1995, *i.e.*, about 7 months prior to the dietary assessment, were used for the analysis. This also introduced a bias to the results. Although these shortcomings of the study design might have obscured the results, the responsiveness observed in this study was presumably underestimated rather than overestimated because the possible biases were likely to affect the results randomly, rather than systematically.

The observed correlation between the Keys score and the change in serum cholesterol ($p < 0.01$) was much weaker than some previously reported values, for example $p < 0.001$ in the special care group of the Multiple Risk Factor Intervention Trial[48]. This difference could be attributed to the several shortcomings of the study design mentioned above, such as lack of information on physical activity, inaccurany of serum cholesterol level at the start of the intervention, and single measurement of serum cholesterol. Because most previous studies were conducted in Western countries, a possible difference of serum cholesterol response to dietary change between races cannot be excluded. Furthermore, a recent review article which summarized the results of dietary intervention studies to lower blood cholesterol in free-living subjects pointed out the lower effect of intervention in free-living subjects than the reductions predicted from the Keys score[9]. This indicates more unexpected and uncontrolled factors in studies for free-living subjects than in clinical settings. This work-site study may also have been biased by unknown factors related to serum cholesterol.

Another shortcoming of this study was the lack of a control group. For example, the observed change in serum lipids and dietary habits before and after intervention might be attributed to seasonal variation rather than to intervention effect because seasonal variations have been reported both for serum lipids and dietary habits[49,50]. This is a serious problem when the intervention effect is evaluated at a group level. However, we examined the relationship between the change in serum cholesterol level and the change in dietary habits only at an individual level. If the possible seasonal variations occur in the same direction for all, or for the majority, of the subjects, it is theoretically not a major bias when the relationship at an individual level is concerned. However, as unknown factors beside the possible seasonal variations of serum lipids and dietary habits cannot be fully excluded by this study design, the results obtained in this study should be examined in a further study with an adequate control group.

Compared to conventional dietary assessments such as dietary record and dietary recall, the burden on both subjects and staff was reduced in the DHQ. However, 30−60 min was needed to answer the DHQ, and might have been troublesome for some subjects at a work-site. Some groups in Western countries have developed a short-version questionnaire to assess intake levels of limited, but target, nutrients[51,52]. From the view-point of feasibility, a short-version of the DHQ should be developed for an assessment of target nutrients and dietary behaviors needed for dietary interventions with a special purpose such as serum cholesterol reduction.

In conclusion, the Keys score assessed by the DHQ predicted the change in serum cholesterol levels at an individual level. The results suggested that the DHQ was responsive enough at least to indicate serum cholesterol change in a dietary intervention.

Acknowledgement

We are grateful to Akiko Kuno, Takaaki Seko, Kazue Ando, Kazuko Kino, Noriko Ogawa, and Yoshihiro Senda for the data collection and processing, and dietary education, and Shoichiro Tsugane and Akane Katagiri for their technical comments.

要　約

軽度高コレステロール血症を有する企業従業員を対象とした食事介入研究における自記式食事歴法質問票の感度: 個人レベルでの血清コレステロール値の変化と栄養素摂取量の変化との関連

佐々木　敏　　石川　豊美　　柳堀　朗子　　天野　恵子

生活習慣の改善，とくに食事改善による循環器疾患予防の重要性は近年広く認識されつつある．しかし，食事指導(食事介入研究)を行う場合に必要な食事調査は一般に煩雑であり，予防のために多人数を対象として実施することは困難である．そこで我々は食事指導に用いることを目的に，調査が比較的容易で同時に高い信頼性を有する調査法として，自記式食事歴法質問票(DHQ)の開発を行っている．一方，食事指導で用いる食事調査法に必要とされる信頼性の一つに感度(ここでは目的変数の変化の評価能力を意味する)がある．また，食習慣を変化させた場合には飽和脂肪酸，多価不飽和脂肪酸およびコレステロールの摂取量の変化から計算されるKeysの値と血清総コレステロール値の変化との間に高い相関があることが知られている．

そこで，軽度高コレステロール血症(血清総コレステロール値≥200 mg/d*l*)を有する一企業従業

員63例(男性54例，女性9例，年齢22−59歳)を対象とした12週間の食事介入研究において，介入前後にDHQを用いて実施した食事調査より得られたKeysの値と血清コレステロール値の変化量を用いてDHQの感度を検討した．関連する他の因子の補正を施した場合の両者間の積率相関係数は0.33，施さない場合は0.32と，いずれも有意な正の相関($p < 0.01$)を示した．また，個人レベルにおける血清コレステロール値の変化量のばらつきの42%が，介入前の血清コレステロール値，body mass indexおよびKeysの値によって説明された．

血清コレステロール値の変化量を指標とした場合，食事指導(食事介入研究)においてDHQによる食事調査が十分な感度を有することが示唆された．

J Cardiol 1999; 33(6): 327−338

References

1) Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D: Serum cholesterol, blood pressure, and mortality: Implications from a cohort of 361, 662 men. Lancet 1986; **II**: 933−936
2) Law MR, Wald NJ, Thompson SG: By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? BMJ 1994; **308**: 367−372
3) Kitamura A, Iso H, Naito Y, Iida M, Konishi M, Folsom AR, Sato S, Kiyama M, Nakamura M, Sankai T, Shimamoto T, Komachi Y: High-density lipoprotein cholesterol and premature coronary heart disease in urban Japanese men. Circulation 1994; **89**: 2533−2539
4) Chen Z, Peto R, Collins R, MacMahon S, Lu J, Li W: Serum cholesterol concentration and coronary heart disease in population with low cholesterol concentrations. BMJ 1991; **303**: 276−282
5) Rose G: High-risk and population strategies of prevention: Ethical considerations. Ann Med 1989; **21**: 409−413
6) The expert panel: Report of the national cholesterol education program expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Arch Intern Med 1988; **148**: 36−69
7) Tang JL, Armitage JM, Lancaster T, Silagy CA, Fowler GH, Neil HAW: Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects. BMJ 1998; **316**: 1213−1220
8) Hegsted DM, McGandy RB, Myers ML, Stare FJ: Quantitative effects of dietary fat on serum cholesterol in man. Am J Clin Nutr 1965; **17**: 281−295
9) Keys A, Parlin RW: Serum cholesterol response to changes in dietary lipids. Am J Clin Nutr 1966; **19**: 175−181
10) Mensink RP, Katan MB: Effect of dietary fatty acids on serum lipids and lipoproteins: A meta-analysis of 27 trials. Arterioscler Thromb 1992; **12**: 911−919
11) Hegsted DM, Ausman LM, Johnson JA, Dallal GE: Dietary fat and serum lipids: An evaluation of the experimental data. Am J Clin Nutr 1993; **57**: 875−883
12) Katan MB, Zock PL, Mensink RP: Effects of fats and fatty acids on blood lipids in humans: An overview. Am J Clin Nutr 1994; **60** (6 Suppl): 1017S−1022S
13) Howell WH, McNamara DJ, Tosca MA, Smith BT, Gaines JA: Plasma lipid lipoprotein responses to dietary fat and cholesterol: A meta-analysis. Am J Clin Nutr 1997; **65**: 1747−1764
14) Ueshima H: Changes in dietary habits, cardiovascular risk factors and mortality in Japan. Acta Cardiol 1990; **44**: 311−327
15) Iso H, Konishi M, Terao A, Kiyama M, Tanigaki M, Baba M, Takemori T, Taketsuna K, Nakamura M, Sato S, Iida M, Shimamoto T, Komachi Y: A community-based education program for serum cholesterol reduction in urban hypercholesterolemic persons: Comparison of intensive and usual education groups. Jpn J Public Health 1992; **38**: 751−761 (in Jpn with Eng abstr)
16) Nakazawa A, Nishimura S, Higashi A, Ozasa K, Hayashi K, Watanabe Y, Aoike A, Kawai K, Ikeda J: Effect of dietary guidance for hypercholesterolemia after health checkup. Jpn J Nutr 1996; **54**: 173−182 (in Jpn with Eng abstr)
17) Basiotis PP, Welsh SO, Cronin FJ, Kelsay JL, Mertz W: Number of days of food intake records required to estimate individual and group nutrient intakes with defined confidence. J Nutr 1987; **117**: 1638−1641
18) Nelson M, Black AE, Morris JA, Cole TJ: Between- and within-subject variation in nutrient intake from infancy to old age: Estimating the number of days required to rank dietary intakes with desired precision. Am J Clin Nutr 1989; **50**: 155−167
19) O'Donnell MG, Nelson M, Wise PH, Walker DM: A computerized diet questionnaire for use in diet health education: 1. Development and validation. Br J Nutr 1991; **66**: 3−15
20) Kristal AR, Feng Z, Coates RJ, Oberman A, George V: Associations of race/ethnicity, education, and dietary intervention with the validity and reliability of a food frequency questionnaire: The Women's Health Trial Feasibility Study in Minority Populations. Am J Epidemiol 1997; **146**: 856−869
21) Sasaki S, Yanagibori R, Amano K: Validity of a self-administered diet history questionnaire for assessment of sodium and potassium: Comparison with single 24-hour urinary excretion. Jpn Circ J 1998; **62**: 431−435
22) Sasaki S, Yanagibori R, Amano K: 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 1998; **8**: 203−215
23) Guyatt G, Walter S, Norman G: Measuring change over time: Assessing the usefulness of evaluation instruments. J

Chron Dis 1987; **40**: 171−178
24) Sasaki S, Yanagibori R: Brief individual dietary counselling approach based on a self-administered diet history questionnaire in a community-based health education program for borderline hypercholesterolemic persons: The effect on change in nutrient intake levels. Jpn J Nutr 1998; **56**: 327−337 (in Jpn with Eng abstr)
25) Ministry of Health and Welfare: Kokumin Eiyou no Genjou (Results of National Nutrition Survey, 1992). Daiichi Shuppan Publishers, Tokyo, 1994 (in Japanese)
26) Science and Technology Agency: Standard Tables of Food Composition in Japan. 4th Ed. Printing Bureau, Ministry of Finance, Tokyo, 1982 (in Japanese)
27) Science and Technology Agency: Fatty acids, cholesterol, vitamin E composition table of Japanese foods. Ishiyaku Shuppan Publishers, Tokyo, 1990 (in Japanese)
28) Sakai K, Nakajima M, Watanabe S, Kobayashi T: Available data on assessments of dietary fatty acid intake (1). J Lipid Nutr 1995; **4**: 97−103 (in Japanese)
29) Takatsuka N, Kurisu Y, Nagata C, Owaki A, Kawakami N, Shimizu H: Validation of simplified diet history questionnaire. J Epidemiol 1997; **7**: 33−41
30) Katagiri A, Hashimoto S, Ohashi Y, Shirogane K, Sakamoto N, Makimoto S: Reproducibility and validity of a semi-quantitative food frequency questionnaire. Jpn J Public Health 1998; **45**; 1127−1136 (in Jpn with Eng abstr)
31) Burke BS: The dietary history as a tool in research. J Am Diet Assoc 1947; **23**: 1041−1046
32) Hankin JH, Nomura AM, Lee J, Hirohata T, Kolonel LN: Reproducibility of a diet history questionnaire in a case-control study of breast cancer. Am J Clin Nutr 1983; **37**: 981−985
33) Block G, Woods M, Potosky A, Clifford C: Validation of a self-administered diet history questionnaire using multiple diet records. J Clin Epidemiol 1990; **43**: 1327−1335
34) McDonald A, Van Horn L, Slattery M, Hilner J, Bragg C, Caan B, Jacobs O Jr, Liu K, Hubert H, Gernhofer N, Betz E, Havlik D: The CARDIA dietary history: Development, implimentation, and evaluation. J Am Diet Assoc 1991; **91**: 1104−1112
35) Willett W, Stampfer MJ: Total energy intake: Implications for epidemiologic analysis. Am J Epidemiol 1986; **124**: 17−27
36) Kipnis V, Freedman LS, Brown CC, Hartman A, Schatzkin A, Wacholder S: Interpretation of energy adjustment models for nutritional epidemiology. Am J Epidemiol 1993; **137**: 1376−1380
37) Dattilo AM, Kris-Etherton PM: Effects of weight reduction on blood lipids and lipoproteins: A meta-analysis. Am J Clin Nutr 1992; **56**: 320−328
38) Denke MA, Frantz ID Jr: Response to a cholesterol-lowering diet: Efficacy is greater in hypercholesterolemic subjects even after adjustment for regression to the mean. Am J Med 1993; **94**: 626−631
39) Ripsin CM, Keenan JM, Jacobs DR Jr, Elmer PJ, Welch RR, Van Horn L, Liu K, Turnbull WH, Thye FW, Kestin M, Hegsted M, Davidson DM, Davidson MH, Dugan LD, Demark-Wahnefried W, Beling S: Oat products and lipid lowering: A meta-analysis. JAMA 1992; **267**: 3317−3325
40) Craig WY, Palomaki GE, Haddow JE: Cigarette smoking and serum lipid and lipoprotein concentrations: An analysis of published data. BMJ 1989; **298**: 784−788
41) Marrugat J, Elosua R, Covas MI, Milina L, Rubis-Prat J, the MARATHOM Investigators: Amount and intensity of physical activity, physical fitness, and serum lipids in men. Am J Epidemiol 1996; **143**: 562−569
42) Friedewald WT, Levy RI, Fredrickson DS: Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; **18**: 499−502
43) Willett WC: Future directions in the development of food-frequency questionnaires. Am J Clin Nutr 1994; **59** (1 Suppl): 171S−174S
44) Forster JL, Jeffery RW, VanNatta M, Pirie P: Hypertension prevention trial: Do 24-h food records capture usual eating behavior in a dietary change study? Am J Clin Nutr 1990; **51**: 253−257
45) Gordon DJ, Salz KM, Roggenkamp KJ, Franklin FA Jr: Dietary determinants of plasma cholesterol change in the recruitment phase of the Lipid Research Clinics Coronary Primary Prevention Trial. Arteriosclerosis 1982; **2**: 537−548
46) Kristal AR, Beresford SA, Lazovich D: Assessing change in diet-intervention research. Am J Clin Nutr 1994; **59** (1 Suppl): 185S−189S
47) Irwig L, Glasziou P, Wilson A, Macaskill P: Estimating an individuals true cholesterol level and response to intervention. JAMA 1991; **266**: 1678−1685
48) Stamler J, Briefel RR, Milas C, Grandits GA, Caggiula AW: Relation of changes in dietary lipids and weight, trial years 1−6, to changes in blood lipids in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. Am J Clin Nutr 1997; **65** (1 Suppl): 272S−288S
49) Gordon DJ, Trost DC, Hyde J, Whaley FS, Hannan PJ, Jacobs DR Jr, Ekelund LG: Seasonal cholesterol cycles: The Lipid Research Clinics Coronary Primary Prevention Trial placebo group. Circulation 1987; **76**: 1224−1231
50) Owaki A, Takatsuka N, Kawakami N, Shimizu H: Seasonal variations of nutrient intake assessed by 24 hour recall method. Jpn J Nutr 1996; **54**: 11−18 (in Jpn with Eng abstr)
51) Hopkins PN, Williams RR, Kuida H, Stults BM, Hunt SC, Barlow GK, Ash KO: Predictive value of a short dietary questionnaire for changes in serum lipids in high-risk Utah families. Am J Clin Nutr 1989; **50**: 292−300
52) Wilson P, Horwath C: Validation of a short food frequency questionnaire for assessment of dietary calcium intake in women. Eur J Clin Nutr 1996; **50**: 220−228