



Associations between dietary diversity and dyslipidemia among Japanese workers: cross-sectional study and longitudinal study findings

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Abstract

Objective The aim of this study was to determine the associations between dietary diversity and risk of dyslipidemia in Japanese workers.

Methods The cross-sectional study included 1399 participants aged 20–63 years and the longitudinal study included 751 participants aged 20–60 years in 2012–2013 (baseline) who participated at least once from 2013 to 2017 with cumulative participation times of 4.9 times. Dietary intake was assessed using a food frequency questionnaire, and dietary diversity score (DDS) was determined using the Quantitative Index for Dietary Diversity. Dyslipidemia was diagnosed when at least one of the following conditions was met: hypertriglyceridemia, high LDL-cholesterol, low HDL-cholesterol, high non-HDL-cholesterol, and a history of dyslipidemia. Multivariable logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for dyslipidemia with control of confounding factors in cross-sectional analysis. Generalized estimating equations were used for calculating the ORs (95% CI) for dyslipidemia in the follow-up period according to the DDS at baseline with control of confounding factors in longitudinal analysis.

Results Cross-sectional analysis showed that the highest DDS reduced the odds of dyslipidemia in men (OR [95% CI] in Tertile 3: 0.67 [0.48–0.95], p value = 0.023). In longitudinal analysis, a moderate DDS reduced the risk of dyslipidemia (OR [95% CI] in Tertile 2: 0.21 [0.07–0.60], p value = 0.003) in women.

Conclusions The results of cross-sectional analysis in this study suggest that the higher diversity of diet might reduce the presence of dyslipidemia in men and the results of longitudinal analysis suggest that a moderate DDS might reduce the risk of dyslipidemia in women. Further studies are needed since the results of cross-sectional and longitudinal analyses in this study were inconsistent.

Keywords Dietary diversity · Dyslipidemia · Japanese workers · Cross-sectional study · Longitudinal study

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Introduction

An unbalanced diet such a diet with an insufficient intake of healthy food has become a public health problem in Japan. According to the National Health and Nutrition Survey in Japan, the intake of healthy food groups such as vegetables, fruits, and beans has decreased and the intake of healthy food groups was lowest in individuals aged 20–30 years [1]. Dietary guidelines for Japanese have recommended eating a variety of food groups [2]. Studies conducted in other countries have also indicated that adherence to dietary diversity is associated with a low risk for the development of non-communicable diseases [3–5].

Cardiovascular diseases (CVDs) are the leading causes of death worldwide and the prevalence of CVDs is expected to increase in the future due to population aging and the increasing prevalence of metabolic disease [6, 7]. Since dyslipidemia can lead to arteriosclerosis, metabolic syndrome, and other lifestyle-related diseases, prevention of dyslipidemia is an important public health issue [8]. According to the report of the Patient Survey, the number of Japanese individuals with dyslipidemia has continued to increase, with estimated numbers being 1.14 million in 1999 and 2.21 million in 2017 [9]. The results of the National Health and Nutrition Survey conducted in Japan showed that some age groups were not treated despite a suspicion of dyslipidemia and that the treatment rates were lower in younger age groups [1]. Primary prevention of dyslipidemia is essential for preventing more severe health consequences.

Among the various potential risk factors for dyslipidemia, including genetic and lifestyle factors, diet is one of the most modifiable risk factors [10]. Nutritional policies to provide dietary recommendations for preventing chronic diseases have been established in many countries [11]. A study conducted in China showed that good dietary diversity according to guidelines in China was associated with a significantly lower risk of low HDL-C [12]. A study conducted in Thailand showed that higher dietary diversity was associated with a lower risk of cardiovascular diseases among Thai older people [13]. A study on the benefits of a high dietary diversity score on cardiovascular risk factors in patients with metabolic syndrome showed that patients with lower dietary diversity scores had higher serum triglycerides and higher systolic blood pressure [14]. A study in which the associations between dietary diversity score and cardiovascular risk factors in patients with pemphigus vulgaris were assessed showed positive associations of dietary diversity score with levels of high-density lipoprotein cholesterol (HDL-C) and total cholesterol [15]. A study conducted in Japan showed that a middle-high dietary diversity score was negatively associated with the

development of hypertriglyceridemia [16]. The methods used for calculating dietary diversity scores in previous studies differed, and the scores in most previous studies were calculated on the basis of the frequency of consumption of food groups in the diet. Therefore, objective comparisons among different populations or time points in previous studies in which different methods were used for calculation of scores were difficult, and an objective diversity score that is based on the quantitative distribution of consumed food groups has yet to be established. Thus, we analyzed cross-sectional and longitudinal associations between dietary diversity scores calculated by the proportion of foods that contribute to the total amount of food in the diet and risk of dyslipidemia in Japanese workers including young workers.

Methods and materials

Study design and participants

The cross-sectional analysis in the present study was based on data from the fifth wave (June 2012 to February 2013) of an occupation-based dynamic cohort established in Tokushima Prefecture in Japan. Details of the occupation-based annual examinations in Tokushima Prefecture have been reported elsewhere [17]. In brief, participants in the occupation-based annual examinations included voluntary workers in Tokushima Prefecture in Japan. The first wave of the occupation-based annual examinations was carried out from June 2008 to February 2009 and included 821 participants (550 men and 271 women; age range, 20–60 years). The participants were followed up every year. Male and female workers aged 20 years or older were also newly recruited annually. For dietary intake and physical activity assessment, the participants were followed up with an interval of 5 years from the fifth wave.

The study population in the fifth wave included 1399 men and women aged 20–63 years who were living in Tokushima Prefecture, Japan. Subjects who participated in the fifth wave for whom there were incomplete data for lipid markers ($n = 1$), physical activity ($n = 1$), and drinking habits ($n = 3$) were excluded. Data for the remaining 1394 participants (1025 men and 396 women; age range, 20–63 years) were used for the cross-sectional analysis. For the longitudinal analysis in the present study, we selected subjects who participated in the fifth-wave survey (baseline) and at least once in the sixth to tenth-wave surveys (follow-up surveys): fifth study survey (2012–2013, $n = 1394$), sixth study survey (2013–2014, $n = 1432$), seventh study survey (2014–2015, $n = 1414$), eighth study survey (2015–2016, $n = 1430$), ninth study survey (2016–2017, $n = 1455$), and tenth study survey (2017–2018, $n = 1394$). From 1394 participants used for the

cross-sectional analysis, we excluded subjects who only participated in the baseline survey ($n=235$). We also excluded one subject lacking data for all lipid profiles in the follow-up period ($n=1$) and subjects with dyslipidemia at baseline ($n=407$). The remaining 751 subjects (514 men and 237 women) were used for analysis (Fig. 1).

Overview of the participants. For 1399 participants aged 20–63 years, we excluded 5 subjects due to missing information on lipid profile, drinking habits, and physical activity. Data for 1394 participants were used for cross-sectional analysis in the baseline survey. In the longitudinal analysis, we excluded 235 participants who participated in only the baseline survey. We also excluded one subject with missing information for lipid markers in the follow-up period and 407 subjects who were diagnosed with dyslipidemia in the baseline survey. Data for 751 subjects (514 men and 237 women) were analyzed in the longitudinal study.

Dietary assessment

The participants were asked about meals taken in the past month using a food frequency questionnaire (FFQ), “FFQg ver 2.0” (Kenpakusha Inc.), to determine the frequency of food intake. The amount of food intake was calculated as

the product of the frequency and amount consumed at each meal for the following 17 food groups: cereals, potatoes and starches, deep yellow vegetables, other vegetables and mushrooms, algae, pulse, fish, mollusks and crustaceans, meat, eggs, milk and milk products, fruits, confectionaries, beverages, sugars and sweeteners, nuts and seeds, fats and oils, and seasoning and spices [18]. The validity of this FFQg was verified by comparing food intake amounts using the weighting method for 7 consecutive days [19]. The questionnaire included questions on how many times and how much of each food group were consumed per week. The amount of food consumed (per week) was calculated as the frequency of eating and the amount of the product at each meal.

The dietary diversity score was calculated using the Quantitative Index for Dietary Diversity (QUANTIDD) developed by Katanoda et al. [20]. The QUANTIDD score is calculated by the proportion of foods that contribute to total energy or the amount of food and the number of food groups using the following formula:

$$\text{QUANTIDD} = \frac{1 - \sum_j^n \text{prop}(j)^2}{1 - \frac{1}{n}}$$

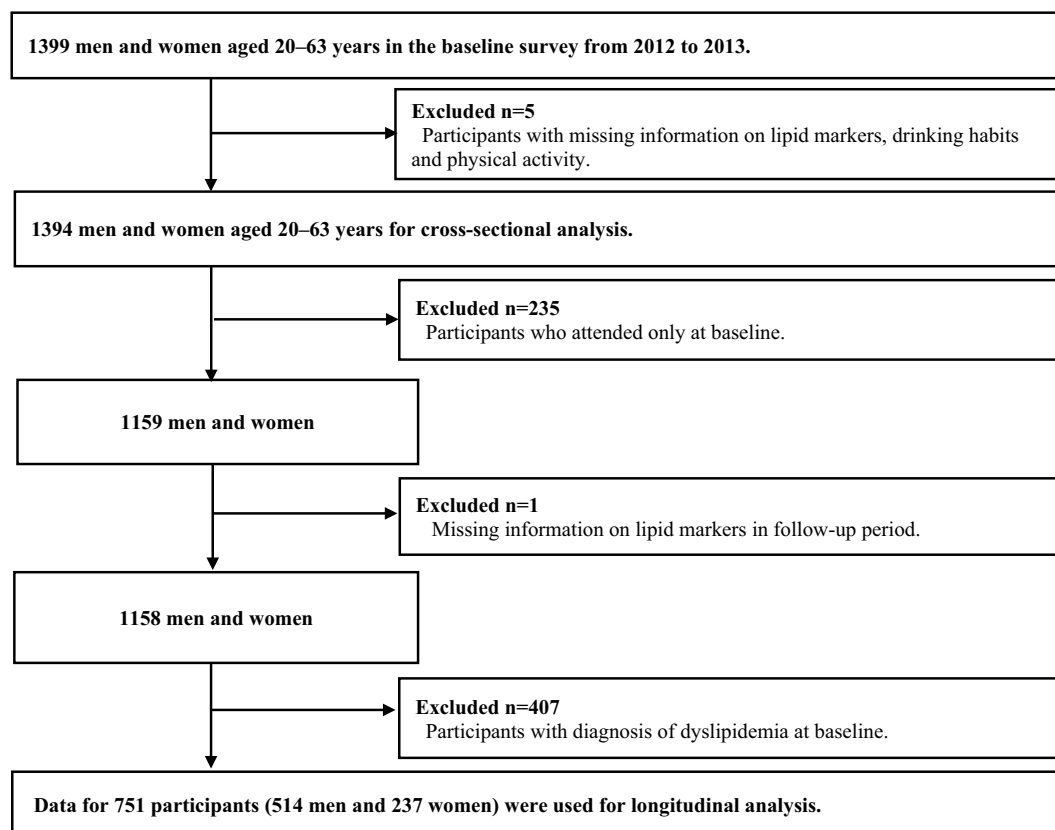


Fig. 1 Flow chart of the study participants

where $\text{prop}[j]$ is the proportion of each food group(s) j contributing to total energy or nutrient intake and n is the number of food groups. The possible score ranges from 0 to 1. In this study, we estimated the score based on the amounts of 16 food groups excluding the beverages group.

Dietary patterns that consist of a correlation matrix for 17 food groups were assessed using principal component factor analysis. The principal components were selected on the basis of eigenvalues >1.3 , with factor loading of each food group of over 0.38 and interpretability (Supplemental Table 1). Principal component scores were saved for each individual and were used as continuous variables. The first principal component was named the healthy pattern because it contained higher factor loading of ten food groups: other vegetables and mushrooms, deep yellow vegetables, pulses, algae, fish, mollusks and crustaceans, potatoes and starches, sugars and sweeteners, fruits, seasonings and spices, and fats and oils. This pattern explained 22.8% of the variance. The second principal component, named the western pattern, consisted of higher factor loading of eight food groups including beverages, meat, cereals, eggs, fats and oils, seasoning and spices, and fruits and it explained 9.7% of the variance. The third component, named the snack pattern, consisted of higher factor loading of confectionary food and it explained 7.7% of the variance. Scores of the three principal components were saved for each participant and used for analysis.

Diagnosis of dyslipidemia

Data for serum levels of total cholesterol (TC), triglycerides (TG), LDL-cholesterol, and HDL-cholesterol were obtained during the medical health check-ups. Venous blood was taken via an antecubital vein in the morning for serum biochemical measurements in both the baseline survey and follow-up surveys. The diagnosis of dyslipidemia was based on the criteria of the Japan Atherosclerosis Society [21]. Subjects were diagnosed with high LDL-cholesterol when LDL-cholesterol was 140 mg/dl or higher, low HDL-cholesterol when HDL-cholesterol was less than 40 mg/dl, and high non-HDL-cholesterol when non-HDL-cholesterol ($\text{non-HDL-C} = \text{TC} - \text{HDL-C}$) was 170 mg/dl or higher in both fasting and non-fasting blood tests. Subjects were diagnosed with hypertriglyceridemia when TG was 150 mg/dl or higher in fasting blood test and TG was 175 mg/dl or higher in non-fasting blood test. History of dyslipidemia was defined as a history diagnosis of dyslipidemia in a medical report or/and used of lipid-lowering medication. Subjects were diagnosed as having dyslipidemia when they fulfilled at least one of the following conditions: hypertriglyceridemia, high LDL-cholesterol, low HDL-cholesterol, high non-HDL-cholesterol and having a history of dyslipidemia. Furthermore, in longitudinal analysis, the participant was defined with

dyslipidemia at a survey, this participant was considered as dyslipidemia at all subsequent follow-ups.

Other measurements

Body height was measured to the nearest 0.1 cm with participants standing without shoes or sandals. Body weight was measured to the nearest 100 g with participants wearing light clothing. Body mass index (BMI) was calculated using the following formula: $\text{BMI} = \text{weight (kg)} / [\text{height (m)}]^2$. Daily values of physical activity (MET-h/week) were calculated using the International Physical Activity Questionnaire [22]. Information on medical history (binary; yes or no), education level (categorical; elementary, junior high and high school, tertiary college, career college and junior college, college, and graduate school or other), drinking habit (categorical; current, former, never), and smoking habit (categorical; current, former, never) was obtained by a self-administered questionnaire. Subjects completed the questionnaire before the physical examination day, and it was checked and collected.

Statistical analysis

The basic characteristics of the participants according to dyslipidemia status are shown for each gender. Continuous variables were presented as means \pm standard deviation (SD) or medians (25 percentile, 75 percentile), and comparisons of mean values were made using Student's t test or the Mann–Whitney test. Categorical variables were expressed as numbers (percentages, %), and comparisons of proportions were made using the chi-square test.

Multivariable logistic regression analysis was used to calculate the odds ratios (ORs) and 95% confidence intervals (95% CIs) for dyslipidemia components according to tertiles of dietary diversity score after controlling for the following variables in Model 1: age, energy intake (continuous, kcal/day), body mass index (continuous, kg/m^2), physical activity (continuous, MET-h/week), smoking habit (categorical; current, former, never), drinking habit (categorical; current, former, never), and education (categorical; elementary, junior high and high school, tertiary college, career college and junior college, college, and graduate school or other). Moreover, to assess the effects of specific dietary patterns, we calculated the association between dietary diversity score and dyslipidemia after adjustment for the following dietary patterns: Model 2 consisting of Model 1 and healthy dietary pattern score, Model 3 consisting of Model 1 and western dietary pattern score, and Model 4 consisting of Model 1 and snack pattern score. Among women, in cross-sectional analysis, there were only 7 cases of low HDL-cholesterol and no case in tertile 3 of dietary

diversity score, and we therefore could not calculate the OR (95% CI) of dietary diversity score and risk of low HDL-C.

In the longitudinal analysis, cumulative data obtained during follow-up surveys were analyzed using generalized estimating equations (GEEs). A GEE takes into account the dependency of repeated observations within participants. An additional advantage of a GEE is that missing values can also be used during analysis. Thus, subjects who were lost to follow-up surveys after early wave examination were also included in the analyses. GEE models were fitted by the GENLIN syntax in SPSS. This procedure corresponds to generalized linear models. In the present analyses, compound symmetry was specified for the correlation structure. GEE analyses were used to estimate the ORs and 95% CIs for dyslipidemia in follow-up surveys according to the tertile of dietary diversity at baseline after controlling for the following variables. The confounding variables that were adjusted in Model 1 were age, energy intake (continuous, kcal/day), body mass index (continuous, kg/m²), physical activity (continuous, MET-h/week), smoking habit (categorical; current, former, never), drinking habit (categorical; current, former, never), education (categorical; elementary, junior high and high school, tertiary college, career college and junior college, college, and graduate school or other), and follow-up time (continuous, years). Model 2 consisted of the adjustments in Model 1 and adjustment for healthy dietary pattern score, Model 3 consisted of the adjustments in Model 1 and adjustment for western dietary pattern score, and Model 4 consisted of the adjustments in Model 1 and adjustment for snack pattern score. There were only 42 cases of low HDL-cholesterol in the 5-year follow-up period and no case in tertile 2 of the dietary diversity score, and we therefore could not calculate the OR (95% CI) of dietary diversity score and risk of low HDL-cholesterol among participants separated by gender. Moreover, in women, the number of cases of hypertriglyceridemia and high non-HDL-cholesterol were very small (only 8 cases of hypertriglyceridemia and 30 cases of high non-HDL-cholesterol); there was no case in tertile 2 of the dietary diversity score and we therefore could not calculate the OR (95% CI) of dietary diversity score and risk of high triglycerides and high non-HDL-cholesterol in longitudinal analysis.

All statistical analyses were performed separately by gender using SPSS (IBM Corporation, Tokyo, Japan) version 28.0 for Windows. All statistical tests were based on two-sided probabilities, and all *p* values <0.05 were considered statistically significant.

Results

Characteristics of participants

The mean QUANTIDD scores were 0.84 ± 0.074 in men and 0.87 ± 0.052 in women. Dyslipidemia was diagnosed in 493 participants (33.0%) including 433 men (42.2%) and 60 women (16.3%). The characteristics of the male and female participants for whom data were used in the cross-sectional analysis are shown in Table 1. The participants diagnosed with dyslipidemia tended to be older than those without dyslipidemia and they had higher BMI than that in the participants without dyslipidemia. There were no significant differences in physical activity, energy intake, and drinking habits between participants with and those without dyslipidemia. There was no significant difference in smoking habit between women with and those without dyslipidemia, but men without dyslipidemia tended to smoke more than did men with dyslipidemia. There were no significant differences in amounts of intake of food groups in participants with and those without dyslipidemia, though intake of nuts and seeds was higher in women with dyslipidemia than in women without dyslipidemia (Supplemental Table 2).

Association between dietary diversity score and dyslipidemia in cross-sectional analysis

Table 2 shows the associations between dietary diversity and dyslipidemia in men and women. The OR for dyslipidemia in men with the highest diversity (Tertile 3) was 0.67 (95% CI: 0.48–0.95; *p* value = 0.023). In the analysis with adjustment for dietary patterns, a similar association between dietary diversity and dyslipidemia in men was found after additional adjustments for the western and snack patterns, but the association disappeared after additional adjustment for the healthy pattern. There was an inverse association between dietary diversity and low HDL-cholesterol in Model 1 (*p* for trend = 0.003). Moreover, the inverse association between dietary diversity and low HDL-cholesterol was robust after additional adjustments for all dietary patterns. In the additional analysis for age groups, similar associations were found in Age ≥ 40 years groups in men (Supplemental Table 4).

The cross-sectional analysis showed no associations between dietary diversity score and dyslipidemia or its components in women.

Table 1 Characteristics of participants with and those without dyslipidemia by gender

	Men (<i>n</i> = 1025)		<i>p</i> value	Women (<i>n</i> = 369)		<i>p</i> value
	Dyslipidemia	Normal		Dyslipidemia	Normal	
Number of subjects	433 (42.2)	592 (57.8)		60 (16.3)	309 (83.7)	
Age (years) ^{†,¶}	42.7 ± 9.7	40.3 ± 10.1	<0.001	46.4 ± 10.2	38.5 ± 9.2	<0.001
Body mass index (kg/m ²) ^{†,¶}	25.1 ± 3.4	23.0 ± 3.1	<0.001	23.3 ± 3.5	20.9 ± 2.9	<0.001
HDL-cholesterol (mg/dL) ^{†,¶}	47.2 ± 10.0	58.4 ± 12.0	<0.001	58.2 ± 15.4	67.5 ± 13.6	<0.001
LDL-cholesterol (mg/dL) ^{†,¶}	136.9 ± 31.3	107.1 ± 20.1	<0.001	149.5 ± 25.0	99.4 ± 20.0	<0.001
Triglycerides (mg/dL) ^{†,¶}	165.6 ± 106.7	78.4 ± 31.3	<0.001	99.0 ± 43.6	56.7 ± 22.1	<0.001
nonHDL-cholesterol (mg/dL) ^{†,¶}	165.8 ± 30.3	124.1 ± 21.4	<0.001	170.7 ± 26.0	115.2 ± 21.1	<0.001
Physical activity (MET-h/week) ^{§,††}	10.1 [1.5–25.4]	13.0 [3.7–34.9]	0.126	6.7 [1.5–16.9]	8.2 [2.6–17.3]	0.623
Energy intake (kcal/day) ^{†,¶}	1846.1 ± 455.6	1845.9 ± 436.1	0.993	1657.3 ± 435.1	1653.5 ± 370.7	0.949
Smoking habit ^{‡,‡‡}			0.007			0.715
Current	166 (38.3)	189 (31.9)		3 (5.0)	21 (6.8)	
Former	156 (36.0)	271 (45.8)		54 (90.0)	266 (86.1)	
Never	111 (25.6)	132 (22.3)		3 (5.0)	22 (7.1)	
Drinking habit ^{‡,‡‡} (<i>p</i> = 0.136)						
Current	252 (58.2)	371 (62.7)		14 (23.3)	106 (34.3)	0.060
Former	168 (38.8)	212 (35.8)		46 (76.7)	192 (62.1)	
Never	13 (3.0)	9 (1.5)		0 (0.0)	11 (3.6)	
Education level ^{‡,‡‡}			0.138			0.012
Elementary, junior high schools and high school	109 (25.2)	147 (24.8)		22 (36.7)	81 (26.2)	
Tertiary college, career college and junior college	82 (18.9)	133 (22.5)		19 (31.7)	69 (22.3)	
College and graduate school	239 (55.2)	300 (50.7)		14 (23.3)	143 (46.3)	
Other	3 (0.7)	12 (2.0)		5 (8.3)	16 (5.2)	

[†] Mean ± standard deviation

[‡] Number (%)

[§] Median [25th, 75th percentile]

[¶] Student's *t* test was used to calculate the *p* value

^{††} Mann–Whitney test was used to calculate the *p* value

^{‡‡} The Chi-square test was used to calculate the *p* value

Longitudinal analysis of the association of dietary diversity score and dyslipidemia

Table 3 shows the cumulative incidences of dyslipidemia, mean cumulative participation times, and mean cumulative follow-up periods (years). The cumulative incidences of dyslipidemia were 17.3% in men (*n* = 443) and 8.1% in women (*n* = 93). The cumulative participation times and follow-up periods were 4.9 times and 2.8 years, respectively, in men and 4.8 times and 2.9 years, respectively, in women.

The ORs and 95% CIs for the risk of dyslipidemia according to the tertiles of dietary diversity score are shown in Table 4. Among women, the OR for dyslipidemia with a moderate dietary diversity score (Tertile 2) was 0.21 (95% CI: 0.07–0.60, *p* value = 0.003) after adjustments in Model 1 including adjustments for age, body mass index, physical activity, energy intake, drinking habit, smoking habit, education level, and follow-up time. Additionally, in the analysis

with adjustment for dietary patterns, similar associations between dietary diversity and dyslipidemia in women were found after additional adjustment for all three patterns (healthy, western, and snack patterns). In longitudinal analysis, there were similar associations between dietary diversity and high LDL-cholesterol among women (Supplemental Table 6). In the additional analysis for age groups, similar associations were found in Age < 40 years groups in women (Supplemental Table 6 and Supplemental Table 7).

The association between dietary diversity score and dyslipidemia in men was no longer statistically significant in longitudinal analysis.

Discussion

The cross-sectional analysis in our study showed that the highest dietary diversity score was associated with a reduced odds of dyslipidemia in men, and the association was

Table 2 Odds ratio (95% confidence intervals) of dyslipidemia according to tertiles of dietary diversity score in men in cross-sectional analysis[‡]

	QUANTIDD score in men [§]			<i>p</i> for trend	QUANTIDD score in women ^{§,¶}			<i>p</i> for trend
	Tertile 1 refer- ence	Tertile 2 (95% CI)	Tertile 3 (95% CI)		Tertile 1 refer- ence	Tertile 2 (95% CI)	Tertile 3 (95% CI)	
<i>Dyslipidemia</i>								
No. of cases/ subjects	151/342	159/341	123/342		15/123	27/123	18/123	
Model 1	1	1.12 (0.81– 1.55)	0.67* (0.48– 0.95)	0.054	1	1.80 (0.82– 3.94)	1.01 (0.41– 2.46)	0.703
Model 2	1	1.11 (0.79– 1.55)	0.66 (0.44– 1.00)	0.132	1	1.78 (0.79– 4.01)	0.98 (0.35– 2.70)	0.683
Model 3	1	1.08 (0.78– 1.51)	0.63* (0.43– 0.90)	0.033	1	1.77 (0.80– 3.89)	0.94 (0.36– 2.47)	0.716
Model 4	1	1.10 (0.79– 1.52)	0.66* (0.46– 0.93)	0.040	1	1.90 (0.86– 4.18)	0.96 (0.39– 2.36)	0.746
<i>High-LDL-cholesterol</i>								
No. of cases/ subjects	71/342	94/341	71/342		14/123	23/123	14/123	
Model 1	1	1.50* (1.04– 2.16)	1.02 (0.68– 1.51)	0.678	1	1.56 (0.69– 3.55)	0.57 (0.29– 1.97)	0.843
Model 2	1	1.47* (1.00– 2.15)	0.97 (0.60– 1.56)	0.727	1	1.62 (0.69– 3.81)	0.81 (0.27– 2.40)	0.937
Model 3	1	1.40 (0.96– 2.02)	0.84 (0.55– 1.29)	0.694	1	1.47 (0.64– 3.35)	0.58 (0.20– 1.65)	0.637
Model 4	1	1.43 (0.99– 2.07)	0.94 (0.63– 1.41)	0.975	1	1.65 (0.72– 3.77)	0.70 (0.27– 1.85)	0.782
<i>Hypertriglyceridemia</i>								
No. of cases/ subjects	65/342	75/341	60/342		1/123	4/123	5/123	
Model 1	1	1.20 (0.81– 1.78)	0.90 (0.59– 1.37)	0.762	1	2.76 (0.25– 31.09)	3.37 (0.28– 41.13)	0.336
Model 2	1	1.17 (0.78– 1.76)	0.84 (0.50– 1.40)	0.694	1	3.13 (0.25– 39.99)	4.16 (0.25– 70.09)	0.320
Model 3	1	1.27 (0.85– 1.88)	1.10 (0.65– 1.61)	0.799	1	2.70 (0.25– 29.77)	3.99 (0.31– 51.77)	0.488
Model 4	1	1.22 (0.82– 1.81)	0.92 (0.60– 1.41)	0.852	1	3.16 (0.26– 38.53)	3.58 (0.28– 45.91)	0.323
<i>High-nonHDL-cholesterol</i>								
No. of cases/ subjects	51/342	70/341	63/342		7/123	18/123	11/123	
Model 1	1	1.46 (0.97– 2.21)	1.22 (0.79– 1.90)	0.287	1	3.02* (1.07– 8.55)	1.37 (0.42– 4.50)	0.353
Model 2	1	1.65* (1.07– 2.55)	1.62 (0.95– 2.73)	0.045	1	3.02* (1.03– 8.89)	1.37 (0.36– 5.30)	0.317
Model 3	1	1.40 (0.92– 2.12)	1.09 (0.68– 1.74)	0.060	1	2.91* (1.02– 8.28)	1.18 (0.32– 4.38)	0.404
Model 4	1	1.37 (0.90– 2.08)	1.10 (0.70– 1.71)	0.583	1	3.10* (1.09– 8.79)	1.34 (0.41– 4.42)	0.365
<i>Low-HDL-cholesterol</i>								
No. of cases/ subjects	57/342	38/341	28/342					
Model 1	1	0.64 (0.40– 1.02)	0.46** (0.27–0.78)	0.003	NA	NA	NA	NA
Model 2	1	0.60* (0.37– 0.98)	0.39** (0.21–0.75)	0.003	NA	NA	NA	NA

Table 2 (continued)

	QUANTIDD score in men [§]			<i>p</i> for trend	QUANTIDD score in women ^{§,¶}			<i>p</i> for trend
	Tertile 1 reference	Tertile 2 (95% CI)	Tertile 3 (95% CI)		Tertile 1 reference	Tertile 2 (95% CI)	Tertile 3 (95% CI)	
Model 3	1	0.63 (0.39–1.01)	0.45** (0.25–0.79)	0.002	NA	NA	NA	NA
Model 4	1	0.65 (0.40–1.03)	0.47** (0.27–0.80)	0.004	NA	NA	NA	NA

[‡]Multiple logistic regression analysis was used to estimate odds ratios and 95% confidence intervals

Model 1: Adjusted for age, energy intake (continuous, kcal/day), body mass index (continuous, kg/m²), physical activity (continuous, MET-h/week), smoking habit (categorical; current, former, never), drinking habit (categorical; current, former, never), education (categorical; elementary, junior high and high school, tertiary college, career college and junior college, college, and graduate school or other)

Model 2: Adjusted for Model 1 and healthy pattern score (continuous)

Model 3: Adjusted for Model 1 and western pattern score (continuous)

Model 4: Adjusted for Model 1 and snack pattern score (continuous)

* *p* value <0.05; ** *p* value <0.01

[§] QUANTIDD score: T1: 0–0.7951, T2: 0.7952–0.8592, T3: 0.8593–1.00 for men, T1: 0–0.8539, T2: 0.8540–0.8991, T3: 0.8992–1.00 for women

[¶] In women, there was only 7 cases of low HDL-cholesterol and no case in T3 of the dietary diversity score, so we could not calculate the odds ratio (95% CIs) of dietary diversity score and the odds of low HDL-cholesterol

Table 3 Incidences of dyslipidemia in follow-up periods

Follow-up year	Men [†]		Women [†]	
	No. of subjects	Case (%)	No. of subjects	Case (%)
2012	514	–	237	–
2013	480	91 (19.0)	215	12 (5.6)
2014	437	88 (20.1)	193	16 (8.3)
2015	401	81 (20.2)	165	20 (12.1)
2016	380	87 (22.9)	172	25 (14.5)
2017	353	96 (27.2)	167	20 (12.0)
Total observation	2565	443 (17.3)	1149	93 (8.1)
Mean cumulative participation (times) [‡]	4.9 ± 1.40		4.8 ± 1.43	
Mean cumulative follow-up years (years) [‡]	2.8 ± 1.41		2.9 ± 1.44	

[†] Number (%)

[‡] Mean ± standard deviation

essentially the same after adjusting for western and snack patterns. Moreover, there was an inverse association between higher dietary diversity scores and the risk of low HDL cholesterol. In contrast to the results for men, no significant association was found in women by the cross-sectional analysis (Table 2). In the occupation-based longitudinal analysis, we found that moderate dietary diversity was associated with a reduced risk of dyslipidemia in women during the 5-year follow-up period. The inverse association between dietary diversity score and dyslipidemia among men was no longer statistically significant (Table 4).

Inverse associations of dietary diversity score with dyslipidemia and low HDL-cholesterol in men were shown in this cross-sectional analysis, and these results are consistent with the results of some previous studies [12, 23, 24]. In a

study conducted in Chinese adults, participants with good dietary diversity had a significantly lower risk of low HDL-cholesterol [12]. In previous studies conducted in Tehran, higher dietary quality was shown to be associated with lower risks for a high level of triglycerides, a high level of LDL cholesterol, and a low level of HDL cholesterol [23, 24]. A study conducted in Japan showed that higher intake of fiber, potassium, and vitamins was associated with a significantly reduced risk of metabolic syndrome and its components [25]. Another study conducted in Japan showed that a healthy dietary pattern with high intake of vegetables and high intake of a juice/milk diet reduced cardiometabolic risks, particularly the risk for dyslipidemia [26]. Our results also suggested that a higher dietary diversity score reduces the risk of dyslipidemia in female Japanese adults.

Table 4 Odds ratios (95% confidence intervals) of dyslipidemia according to tertiles of dietary diversity score in longitudinal analysis[‡]

	QUANTIDD score [§]			
	Tertile 1 reference	Tertile 2 (95% CI)	Tertile 3 (95% CI)	<i>p</i> for trend
<i>Men</i>				
No of subjects at baseline	171	172	171	
No. of cases/subjects	146/868	143/849	154/848	
Age-adjusted model	1	0.99 (0.67–1.46)	1.01 (0.68–1.48)	0.989
Model 1	1	1.05 (0.71–1.55)	1.01 (0.68–1.15)	0.924
Model 2	1	1.08 (0.73–1.62)	1.11 (0.71–1.75)	0.631
Model 3	1	1.00 (0.67–1.51)	0.92 (0.59–1.43)	0.741
Model 4	1	1.04 (0.70–1.55)	1.01 (0.66–1.54)	0.938
<i>Women</i>				
No of subjects at baseline	79	79	79	
No. of cases/subjects	39/382	16/385	38/382	
Age-adjusted model	1	0.29** (0.12–0.73)	0.66 (0.30–1.45)	0.181
Model 1	1	0.21** (0.07–0.61)	0.53 (0.22–1.29)	0.092
Model 2	1	0.19** (0.07–0.57)	0.45 (0.16–1.22)	0.067
Model 3	1	0.20** (0.07–0.54)	0.42 (0.17–1.03)	0.023
Model 4	1	0.21** (0.07–0.61)	0.54 (0.22–1.33)	0.098

[‡]Generalized estimating equations were used to estimate odds ratios and 95% confidence intervals

Age-adjusted model: adjusted for age, follow-up time (continuous, years)

Model 1: Adjusted for age, energy intake (continuous, kcal/day), body mass index (continuous, kg/m²), physical activity (continuous, MET-h/week), smoking habit (categorical; current, former, never), drinking habit (categorical; current, former, never), education (categorical; elementary, junior high and high school, tertiary college, career college and junior college, college, and graduate school or other), follow-up time (continuous, years)

Model 2: Adjusted for Model 1 and healthy pattern score (continuous)

Model 3: Adjusted for Model 1 and western pattern score (continuous)

Model 4: Adjusted for Model 1 and snack pattern score (continuous)

** *p* value <0.01

[§] QUANTIDD score: T1: 0–0.7987, T2: 0.7988–0.8623, T3: 0.8624–1.00 for men; T1: 0–0.8499, T2: 0.8500–0.8991, T3: 0.8992–1.00 for women

A higher dietary diversity seems to reflect healthy nutritional habits. It has been shown that dietary diversity is related to food quality [27]. This is consistent with our results showing that there was an inverse association between dietary diversity and presence of dyslipidemia and that the association was robust after adjustments for western and snack patterns but disappeared after adjustment for the healthy pattern in the analysis for men (Table 2). Furthermore, diets with greater varieties are associated with an increased intake of essential micronutrients including vitamin C, calcium, and dietary fiber while having low carbohydrate intake [24]. In a previous study, it was shown that fiber was the only diet component significantly associated with changes in blood lipids [28]. Another study conducted in Korea showed that higher carbohydrate nutrition is associated with higher prevalence of dyslipidemia and diabetes in the Korean adult population [29]. In our study, participants with higher dietary diversity scores tended to consume more healthy food and have a low intake of cereals (Supplemental Table 3).

In the longitudinal analysis, women with moderate dietary diversity (Tertile 2) had a lower risk for the development of dyslipidemia after adjusting for confounding factors and additional adjustments for dietary patterns (Table 4). The trend was similar for high LDL-C (Supplemental Table 5). In contrast, in men, there was no association between dietary diversity score and risk of dyslipidemia. Some previous cohort studies showed associations between dietary quality and dyslipidemia and between dietary quality and lipid profiles [24, 30–33]. In a previous multiethnic cohort study conducted in five ethnic groups, the associations of dietary quality indices with risk of type 2 diabetes and biomarkers were assessed in 166,550 participants including White, African American, Native Hawaiian, Japanese American, and Latino participants aged 45–75 years over a 10-year follow-up period. The results of that study showed that the Healthy Eating Index-2010 (HEI-2010) and the Dietary Approaches to Stop Hypertension (DASH) were directly related to HDL cholesterol in women and that higher scores of dietary quality indices were related to a low level of triglycerides

[32]. In another study, the associations between diet quality and blood lipids were assessed during a 16-year follow-up period in Sweden and it was shown that high diet quality (based on amounts of intake of saturated fat, polyunsaturated fat, sucrose, fiber, fruits, vegetables, and fish) was associated with lower risks of a high level of triglycerides and a high level of LDL cholesterol [34]. In a study conducted in China, the associations of dietary quality with diabetes and major cardiometabolic risks were examined in 4440 participants who were 18–65 years of age. The results of that study showed that with tailored Alternative Healthy Eating Index 2010 (tAHEI), male and female participants in the top quintile compared with the bottom quintile showed 36% and 33% lower odds of high LDL-C, respectively, while the China Dietary Guideline Index scores showed 35% lower odds of high LDL-C in men only [33]. The results of studies differed due to differences in the indices used to assess dietary quality and dyslipidemia and its components. Still, all of the studies indicated that higher diet quality is associated with reduced risk of dyslipidemia. Our study showed that moderate dietary diversity was related to reduced risks of dyslipidemia and high LDL-cholesterol only in women.

Dyslipidemia is likely to be associated with intake of confectionaries, sugars and sweeteners, and beverages. Previous studies showed that beverage consumption [35, 36], and intake of sugars and sweeteners [37, 38] were positively associated with lipid concentrations in blood and dyslipidemia and that reduction in the intake of those foods could reduce the risk of dyslipidemia. In our study, participants with the top tertiles of diet diversity score had the highest consumption of confectionaries, sugars and sweeteners, and beverages (Supplemental Table 3), which might have been the cause of the development of dyslipidemia in the follow-up periods. Another possible reason for the development of dyslipidemia may be related to the reduced estrogen concentration in women. Estrogen is a key element in the control of metabolic disorders. Estrogen is the reason for the difference in the prevalences of metabolic disease in men and women, and the decrease in estrogen concentration is the cause of the increase in the prevalence of dyslipidemia with aging in women [39–42]. Our results showed that participants with the highest dietary diversity score were older than the other participants (Supplemental Table 5). Estrogen concentration reduction might have caused a change in the association between dietary diversity and risk of dyslipidemia in women in the follow-up period. Further studies with a large number of subjects and longer follow-up period are needed to confirm our results.

We are aware that our study has several limitations. First, the participants in our study lived in a small residential area and included only workers, and the findings in our study might not be generalizable to other populations because the study participants were only Japanese

workers. Second, the number of participants in our study, especially women, was small. Only 8.1% (93) of the women in our study had dyslipidemia in the 5-year follow-up period, consequently limiting the association between dietary diversity and the development of dyslipidemia. Third, we assessed food consumption only at baseline and did not determine whether the participants' dietary patterns changed during the follow-up period. However, the dietary diversity scores in 2012 and 2017 were similar (p value = 0.289, data not shown). Fourth, the follow-up period to assess the outcome changes was short (the cumulative follow-up period being only 3 years). In previous cohort studies in which the association between dietary diversity and dyslipidemia was assessed, the median follow-up periods were from 6 to 16 years [13–15]. The follow-up period in our study might have been too short for determining the associations between diet and outcomes. Fifth, the occupations of participants were not assessed, and we therefore could not determine the effects of specific occupations on dyslipidemia. In previous studies, the effects of occupations and work times on lipid markers and dyslipidemia were assessed [43, 44]. In a study with 5813 participants in the 2013–2016 Korea National Health and Nutrition Examination Survey, an association of night work with dyslipidemia was found in male participants (OR = 1.53, 95% CI: 1.05–2.24) [43]. Another study for 7649 farmers from The China Multi-Ethnic Cohort (CMEC) showed an association between occupational physical activity (OPA) of the farmers and dyslipidemia; the results showed that different OPA levels might lead to differences in the associations with blood lipid levels [44]. Finally, the score in our study is the range of indices, which was narrow. The scores in the top and bottom tertiles were not greatly different, and it was therefore not possible to clearly distinguish differences in dietary patterns, which could confound the association between diet and outcome. In addition, the participants with similar scores showed the same associations, but their scores for food groups were not the same. We assessed the odds ratios and 95% CIs for dyslipidemia according to the QUANTIDD score group with a categorization based on the median value of QUANTIDD scores and we assessed the odds ratios and 95% CIs for dyslipidemia according to a 1 standard deviation increase in the QUANTIDD score, and the results were similar (Supplemental Table 8 and Supplemental Table 9, respectively). Further investigation to identify the relevant individual components contributing to the reduced risk of dyslipidemia may lead to an understanding of diet-specific pathways for dyslipidemia components.

In conclusion, the results of cross-sectional analysis in this study suggest that the higher diversity of diet might reduce the presence of dyslipidemia in men and the results

of longitudinal analysis suggest that a moderate DDS might reduce the risk of dyslipidemia in women. Further studies are needed since the results of cross-sectional and longitudinal analyses were inconsistent.

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Author contributions All of the authors developed the idea for this study and collected the data. Measurements and data analysis were completed by Bui Thi Thuy, Mariko Nakamoto, and Akiko Nakamoto, and Tohru Sakai provided nutritional advice regarding the interpretation of the data. Bui Thi Thuy drafted the manuscript with the help of Mariko Nakamoto. All authors read and approved the final version of the manuscript.

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Data availability The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest All authors state that they have no conflicts of interest.

Ethical standards of disclosure The study was conducted according to the ethical standards of the Declaration of Helsinki, and the protocol was approved by the institutional review board of Tokushima University Hospital (Ethical approval number: 2868). Written consent was obtained from all participants.

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