British Journal of Nutrition (2014), **112**, 2010–2017
doi:10.1017/S0007114514003109

Dietary glycaemic index and glycaemic load in relation to all-cause and cause-specific mortality in a Japanese community: the Takayama study

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(Submitted 12 May 2014 – Final revision received 8 August 2014 – Accepted 26 August 2014 – First published online 20 October 2014)

Abstract

Diets with a high glycaemic index (GI) or glycaemic load (GL) have been hypothesised to increase the risk of diabetes, CVD and some cancers. In the present study, the associations of dietary GI and GL with the risk of all-cause and cause-specific mortality were prospectively examined in a general population in Japan, where white rice is the main contributor of dietary GI and GL. A total of 28 356 residents of Takayama City, Japan, who responded to a self-administered questionnaire in 1992 were included in the present analyses. Dietary intake was assessed using a validated FFQ. Mortality was ascertained over 16 years. In men, dietary GI was found to be significantly inversely associated with the risk of all-cause and non-cancer, non-cardiovascular mortality; the hazard ratios (HR) for the highest *v.* lowest quartile were 0·80 (95 % CI 0·68, 0·95) and 0·64 (95 % CI 0·49, 0·84), respectively. Dietary GL was found to be significantly inversely associated with the risk of all-cause, cancer, and non-cancer, non-cardiovascular mortality; the HR for the highest *v.* lowest quartile were 0·71 (95 % CI 0·59, 0·86), 0·71 (95 % CI 0·52, 0·99) and 0·64 (95 % CI 0·48, 0·87), respectively. The results obtained for the GL derived from white rice, but not from other foods, closely mirrored those obtained for overall GL. In women, dietary GI was found to be significantly positively associated with the risk of cardiovascular mortality; the HR for the highest *v.* lowest quartile was 1·56 (95 % CI 1·15, 2·13). The results of the present study suggest potential favourable effects of dietary GI and GL on mortality in men, but an association between high GI and an increased risk of cardiovascular mortality in women.

Key words: Glycaemic index: Glycaemic load: Mortality: Prospective cohort studies

The concept of glycaemic index (GI) was introduced by Jenkins *et al.*[1] to quantify the glycaemic response to carbohydrates in different foods. High-GI foods result in high postprandial glucose concentrations that decline rapidly, whereas low-GI foods result in lower postprandial glucose concentrations that decline more gradually[1]. Glycaemic load (GL), calculated by summing both the GI value and the amount of carbohydrates in a food, has been proposed as a global indicator that represents both the quality and quantity of carbohydrates[2]. High-GI and -GL food consumption may result in a chronic elevation of blood glucose concentrations. Epidemiological studies have suggested that high-GI or -GL diets may increase the risk of diabetes[3], CVD[4] and some cancers[5], although most of these studies have been conducted in Western populations. CVD and cancer are the leading causes of death in developed countries, and in addition to cardiovascular death, diabetes has been reported to be associated with premature death from several cancers and other non-CVD[6,7]. Therefore, dietary GI or GL is suspected to increase the risk of total mortality as well as mortality from relevant diseases. To our knowledge, only one study, the Nurses' Health Study[8], has reported the association of dietary GL with total mortality; dietary GL has been found to be significantly associated with an increased mortality risk (hazard ratio (HR) per 41 units = 1·22). No study has been carried out on this association in men. In Japan, white rice, a food with a high GI, is consumed as a staple food and is the main contributor of dietary GI and GL. In spite of its high GI value, a high intake of rice has been found to be associated with a decreased risk of death from CVD among Japanese men in a prospective study[9]. Dietary GI and GL have never been studied in relation to CVD (except stroke[10]) or cancer in Japan. Especially in rice-consuming populations, it is important to evaluate the associations of dietary GI or GL with the risk of death from a broad range of causes. In the present study, the associations of dietary GI and GL with the risk of all-cause and cause-specific mortality were examined in a

Abbreviations: GI, glycaemic index; GL, glycaemic load; HR, hazard ratios; ICD, International Classification of Diseases.

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population-based cohort of Japanese men and women (the Takayama study).

Methods

The Takayama study

The Takayama study was initiated in 1992 to identify dietary and lifestyle factors that are associated with the morbidity of cancer and various other diseases. A total of 31 552 residents, aged ≥35 years, of Takayama City, Gifu Prefecture, Japan, completed a baseline self-administered questionnaire that included questions on demographic characteristics, smoking status, diet, physical activity, and medical and reproductive histories, yielding a participation rate of 85·3 %. The rationale and design of the Takayama study have been described in detail elsewhere[11]. Subjects who reported having or having had cancer during baseline questionnaire administration (186 men and 540 women), stroke or CHD (886 men and 861 women) were excluded from the present analyses. Subjects who died during the first 3 years of follow-up (402 men and 321 women) were also excluded. In total, 28 356 subjects (12 953 men and 15 403 women) were included in the present analyses.

Dietary intake was assessed using a validated 169-item semi-quantitative FFQ. The subjects were asked to report how often, on average, they consumed each of the food items listed in the questionnaire and what was the usual serving size of each item consumed during the previous year. The intakes of nutrients and foods were estimated from the frequency of consumption and portion size using the Japanese Standard Tables of Food Composition, 5th revised and enlarged edition, published by the Science and Technology Agency of Japan. Fatty acid composition was evaluated using data published by Sasaki *et al.*[12]. A detailed description of the FFQ, its reliability and validity, and the method used for calculating nutrient intakes has been published previously[13,14]. The Spearman correlation coefficients between the questionnaire and twelve daily diet records kept over a 1-year period for the intakes of total energy, carbohydrates and dietary fibre were 0·44, 0·34 and 0·63, respectively, in men and 0·53, 0·45 and 0·60, respectively, in women.

Details regarding the methods used for assessing the GI of individual foods and mixed meals have been reported elsewhere[10]. Briefly, GI values were assigned based on the International Table of GI[15] and published data from studies carried out in Japan[16]. Values for foods for which only the white rice-based GI was available were transformed into glucose-based GI values. Foods containing ≤3·5 g of carbohydrates per serving were assigned a value of 0. Values obtained for the amount of carbohydrates available after subtracting the amount of dietary fibre from that of total carbohydrates were used to calculate the GI and GL. Dietary GL was computed by adding the products of the available carbohydrates of each food consumed multiplied by the GI of individual foods and dividing the products by 100. Dietary GI was calculated by dividing the dietary GL by the amount of total carbohydrate consumed and multiplying by 100. GL derived from white rice and other foods were also assessed separately. White rice with germs, but not brown rice, was considered as white rice.

Physical activity was assessed from the average hours per week spent performing various kinds of activities during the previous year. The time spent per week performing an activity of specific intensity was multiplied by its corresponding energy expenditure requirements, expressed as a metabolic equivalent, and summed to obtain a score (metabolic equivalents-h/week). Details including the validity of this method have been described elsewhere[17].

Follow-up and endpoints

Information regarding subjects who died or moved out of Takayama City between the baseline and 1 October 2008 was obtained from residential registers or family registers. Causes of death were identified from death certificates provided by the Legal Affairs Bureau. They were coded according to the International Classification of Diseases (ICD), 10th revision. The endpoints were all-cause mortality and disease-specific mortality including mortality from cancer (ICD-10: C00–D48), CVD (ICD-10: I00–I99), and all other causes (non-cancer, non-CVD). As dietary GI and GL were significantly associated with non-cancer, non-cardiovascular mortality in men, major causes of deaths in this category, such as infections (ICD-10: A00–A99 and B00–B99), endocrine, nutritional, and metabolic diseases (ICD-10: E00–E90), respiratory diseases (ICD-10: J00–J99), digestive diseases (ICD-10: K00–K93), genitourinary diseases (ICD-10: N00–N99), and external causes of injury and poisoning (ICD-10: S00–T98), were further assessed. During the study period, 941 (6·5 %) men and 971 (5·7 %) women moved out of Takayama City. The date of moving out of the city was not known for 104 (0·7 %) men and 147 (0·9 %) women. They were censored at the latest date when they were known to reside in the city. The present study was approved by the Ethics Committee of the Gifu University Graduate School of Medicine.

Statistical analyses

For each subject, person-years of follow-up were calculated from the date of responding to the baseline questionnaire to the date of death, the date of moving out of Takayama City or 1 October 2008, whichever occurred first. The mean duration of follow-up was 14·4 years (409 198 person-years). The subjects were divided into four groups according to the quartile of dietary GI, dietary GL, GL derived from white rice and GL derived from other foods. Using the Cox proportional-hazards model, the HR and their 95 % CI for all-cause mortality and cause-specific mortality for each category were calculated in comparison with the lowest intake category. The median value obtained for each category was used to assess linear trend. Dietary GI, GL and the intakes of all nutrients and foods were adjusted for total energy using the residual method[18]. First, age and total energy were included in the models as covariates. Additional adjustments were made for non-dietary factors including marital

status (married, not married or missing), education (≤11, 12–14, ≥15 years, or missing), height (in quartile or missing), BMI (in quartile or missing), physical activity (metabolic equivalents-h/week), alcohol consumption (in quartile for men and non-drinkers and drinkers below or above the median alcohol level for women), smoking status (never, former, current with ≤30 years of smoking, current with >30 years of smoking, or missing for men and never, former, current, or missing for women), histories of diabetes and hypertension (yes or no) and menopausal status (premenopausal, postmenopausal or missing; only women) and dietary factors including saturated fat, polyunsaturated fat, salt, vegetables and fruits. All the statistical analyses were performed using SAS programs. Significance was defined as two-sided $P<0{\cdot}05$.

Results

The baseline characteristics of the study population by sex and quartile of dietary GI and GL are summarised in Table 1. Men with greater dietary GI were found to more likely be physically active and less educated and to less likely have reported histories of hypertension and diabetes. They were also found to have a higher intake of carbohydrates and lower intakes of alcohol, fats, salt, fruits and vegetables. Women with greater dietary GI were found to more likely be married, premenopausal, and less educated and to less likely have reported a history of diabetes. They were also found to have a higher intake of carbohydrates and lower intakes of alcohol, total energy, fats, salt, fruits and vegetables. These characteristics were also observed in relation to dietary GL, except that it was found that men with higher dietary GL were more likely to be never smokers and have a higher intake of fruits and that women with higher dietary GL were more likely to be never smokers and their menopausal status was irrelevant. The questionnaire used in the present study was designed to measure an individual's relative intakes of nutrients or foods rather than absolute values. Although the mean values for dietary intakes are given in the table, some of them may be overestimated by the questionnaire.

During the follow-up period excluding the first 3 years, there were 2499 male deaths and 2117 female deaths. When compared with the lowest quartiles, the highest quartiles of dietary GI, dietary GL, and GL derived from white rice were found to be significantly associated with a decrease in all-cause mortality in men after controlling for covariates (Table 2). The trends towards a greater reduction in the risk of mortality were also statistically significant. The HR for all-cause mortality in men in the highest quartile of GL derived from white rice was significantly lower than that in men in the highest quartile of GL derived from other foods ($P=0{\cdot}01$). Dietary GL was significantly inversely associated with the risk of cancer mortality. The results obtained for GL derived from white rice mirrored those obtained for overall GL. Dietary GI, dietary GL, and GL derived from white rice were significantly inversely associated with the risk of non-cancer, non-cardiovascular mortality. Among non-cancer, non-cardiovascular causes of death, a significant or suggestive inverse association with dietary GI or GL was observed for endocrine, nutritional, and metabolic diseases, respiratory diseases, and digestive diseases. The HR for the highest *v.* lowest quartile of GI and GL were as follows: endocrine, nutritional, and metabolic diseases, GI, 0·29 (95% CI 0·21, 1·21; $P_{trend}=0{\cdot}03$); GL, 0·14 (95% CI 0·04, 0·54; $P_{trend}=0{\cdot}003$); respiratory diseases, GI, 0·74 (95% CI 0·48, 1·13; $P_{trend}=0{\cdot}09$); GL, 0·63 (95% CI 0·38, 1·05; $P_{trend}=0{\cdot}04$); digestive diseases, GI, 0·40 (95% CI 0·16, 1·04; $P_{trend}=0{\cdot}10$); GL, 0·44 (95% CI 0·16, 1·25; $P_{trend}=0{\cdot}10$).

In women, dietary GI was significantly positively associated with the risk of cardiovascular mortality after controlling for covariates (Table 3). The GL derived from white rice was significantly inversely associated with the risk of cancer mortality.

Additional adjustments made for the intakes of dietary fibre, vitamins, and minerals, vitamin use, and history of cancer screenings did not alter the results. For example, the HR for all-cause mortality in men in the highest *v.* lowest quartile of dietary GL was 0·71 (95% CI 0·59, 0·86; $P_{trend}=0{\cdot}0001$) and that for cardiovascular mortality in women in the highest *v.* lowest quartile of dietary GI was 1·61 (95% CI 1·17, 2·21; $P_{trend}=0{\cdot}004$) after additionally controlling for the intakes of dietary fibre and Ca, vitamin use, and attendance at stomach cancer screenings. Adjustments made for the intakes of traditional Japanese foods, such as fish, tofu, miso, soya sauce and seaweed, did not alter the results substantially. Adjustments made for the intakes of red meat, poultry and fish did not alter the results. Dairy food intake was neither a confounder nor a modifier of the associations. The inverse association observed between vegetable intake and dietary GI as well as GL in the present study may lead to a concern that vegetable intake may be associated with an increased risk of mortality in men. However, vegetable intake was independently significantly associated with a decreased risk of mortality; the HR for all-cause mortality for every 100 g increase in vegetable intake was 0·96 (95% CI 0·95, 0·99) in the multivariate model for dietary GI. On the other hand, salt intake was significantly associated with an increased risk of all-cause mortality (HR for every 1 g increase in salt intake was 1·04, 95% CI 1·02, 1·06).

Exclusion of subjects who reported a history of diabetes did not alter the results; for example, the multivariate HR for all-cause mortality in men in the highest *v.* lowest quartile of dietary GL were 0·74 (95% CI 0·60, 0·90; $P_{trend}=0{\cdot}0007$) and the HR for cardiovascular mortality in women in the highest *v.* lowest quartile of dietary GI was 1·47 (95% CI 1·06, 2·02; $P_{trend}=0{\cdot}03$) after controlling for covariates. Exclusion of subjects who died during the first 6 years also did not alter the results substantially; for example, the HR for all-cause mortality in men in the highest *v.* lowest quartile of dietary GL was 0·72 (95% CI 0·58, 0·89; $P_{trend}=0{\cdot}001$) and that for cardiovascular mortality in women in the highest *v.* lowest quartile of dietary GI was 1·45 (95% CI 1·03, 2·04; $P_{trend}=0{\cdot}03$). Inclusion of subjects who died during the first 3 years also did not alter the results substantially.

Discussion

In the present prospective study, dietary GI and GL were found to be associated with a decreased risk of all-cause

Table 1. Baseline characteristics of the study population by sex and quartile (Q) of dietary glycaemic index (GI) and glycaemic load (GL)*

	GI				GL			
Characteristics	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Men								
Age (years)	53·9	54·0	52·9	53·1	53·6	55·4	52·6	52·3
Married (%)	91·8	92·6	93·0	89·9	91·9	91·9	93·0	90·4
Years of education (%)								
≤11	52·1	56·5	57·2	59·9	52·4	57·3	56·7	59·2
12–14	33·3	30·9	31·1	30·9	33·5	30·3	31·4	31·1
≥15	14·6	12·6	11·7	9·2	14·1	12·4	11·9	9·7
Smoking (%)								
Never	17·0	18·5	14·9	16·9	14·7	18·6	14·7	19·3
Former	27·0	28·3	27·3	26·1	28·5	30·0	27·9	25·7
Current	53·0	53·1	57·8	57·1	56·8	51·7	57·4	55·0
History of hypertension (%)	21·4	18·9	18·4	15·7	21·6	20·2	18·0	14·6
History of diabetes mellitus (%)	7·7	6·0	5·3	4·5	7·6	6·7	4·9	4·1
Height (cm)	165·3	164·8	164·9	164·4	165·2	164·4	165·0	164·7
BMI (kg/m^2)	22·6	22·6	22·6	22·4	22·6	22·4	22·6	22·5
Alcohol intake (mg/d)	57·1	47·5	40·0	24·9	67·9	43·1	39·7	18·8
Exercise (MET-h/week)	25·0	28·4	28·3	28·1	25·9	25·6	29·2	29·1
Dietary intake								
Total energy (kJ/d)	10 619	11 422	11 632	10 368	11 242	10 301	11 305	11 196
Saturated fat (g/d)	18·4	18·3	17·4	13·7	15·0	16·0	16·8	15·4
Polyunsaturated fat (g/d)	16·2	16·5	16·0	13·2	17·7	15·0	15·3	13·9
Vegetables (g/d)	435	413	372	268	434	368	361	326
Fruits (g/d)	136	142	126	83·8	119	112	115	142
Red meat (g/d)	44·0	44·8	43·9	34·8	50·7	39·9	41·6	35·3
Poultry (g/d)	17·7	18·5	18·1	14·9	21·4	16·7	17·0	14·1
Fish and shellfish (g/d)	113·8	113·8	106·9	85·6	129·3	103·1	102·4	85·2
Tofu (g/d)	77·2	75·8	72·7	59·1	84·9	69·5	72·2	58·2
Miso (g/d)	16·9	18·0	17·7	15·9	17·8	17·3	17·8	15·6
Soya sauce (g/d)	25·6	25·3	23·8	19·3	27·6	23·0	23·1	20·2
Seaweed (g/d)	27·0	25·9	23·9	18·3	27·4	24·2	23·5	20·1
Salts (g/d)	15·7	15·4	14·4	11·3	16·4	14·0	13·9	12·5
Women								
Age (years)	54·7	54·7	55·2	54·3	53·1	54·9	57·3	53·6
Married (%)	74·9	76·6	75·0	77·9	77·0	77·1	71·0	79·3
Years of education (%)								
≤11	63·7	62·5	66·9	69·6	59·3	63·7	71·2	68·6
12–14	30·2	32·8	28·7	26·7	34·0	31·3	25·4	27·6
≥15	6·2	4·7	4·5	3·8	6·8	5·1	3·5	3·8
Smoking (%)								
Never	79·4	84·0	84·4	82·7	78·4	83·9	84·9	83·3
Former	4·9	4·3	3·6	4·2	4·6	4·2	4·2	3·9
Current	15·7	11·8	12·1	13·1	17·0	11·9	10·9	12·9
History of hypertension (%)	17·4	17·1	17·5	16·4	21·6	20·2	18·0	14·6
History of diabetes mellitus (%)	3·5	2·7	2·4	1·7	7·6	6·7	4·9	4·1
Postmenopausal (%)	60·4	57·6	58·5	56·1	54·7	58·4	64·1	55·5
Height (cm)	152·4	152·4	151·9	152·0	152·8	152·3	151·3	152·3
BMI (kg/m^2)	22·0	22·0	22·0	21·9	22·0	22·0	22·0	22·0
Alcohol intake (mg/d)	13·0	6·7	6·3	5·2	15·3	6·1	4·9	5·0
Exercise (MET-h/week)	18·7	19·3	19·4	19·0	19·3	19·9	17·7	19·5
Dietary intake								
Total energy (kJ/d)	9389	8447	8611	9376	9941	7887	7895	10 104
Saturated fat (g/d)	19·0	15·9	14·7	13·6	20·9	14·6	13·2	14·5
Polyunsaturated fat (g/d)	16·3	14·3	13·5	13·1	18·3	13·3	12·0	13·6
Vegetables (g/d)	532	385	359	307	520	369	335	359
Fruits (g/d)	182	134	123	99·6	156	121	125	136
Red meat (g/d)	35·3	31·2	28·8	27·5	43·3	28·2	23·8	27·5
Poultry (g/d)	17·4	15·8	14·5	13·9	22·3	14·1	11·9	13·4
Fish and shellfish (g/d)	96·7	83·5	77·2	75·1	113·5	75·4	68·0	75·5
Tofu (g/d)	74·0	64·7	61·5	57·9	81·8	62·6	53·2	60·4
Miso (g/d)	15·9	14·9	14·7	14·4	16·3	15·2	13·0	15·3
Soya sauce (g/d)	25·5	22·0	20·6	20·2	27·8	20·5	18·6	21·3
Seaweed (g/d)	32·2	25·3	23·0	20·6	31·9	25·2	21·0	23·0
Salts (g/d)	15·8	13·0	12·2	11·3	16·6	12·3	11·2	12·3

MET, metabolic equivalent.

* Values are means for continuous variables and percentages for categorical variables.

Table 2. All-cause and cause-specific mortality in men by quartiles (Q) of dietary glycaemic index (GI) and glycaemic load (GL) (Hazard ratios (HR) and 95 % confidence intervals; medians and number of deaths)

	Q1	Q2		Q3		Q4		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	P_{trend}
All-cause mortality								
Dietary GI								
Median	56·4		62·4		66·3		69·7	
No. of deaths	688		688		553		570	
Age- and energy-adjusted HR	1·0	0·98	0·88, 1·08	0·86	0·77, 0·97	0·88	0·79, 0·98	0·005
Multivariate HR*	1·0	0·97	0·86, 1·08	0·83	0·72, 0·95	0·80	0·68, 0·95	0·004
Dietary GL								
Median	169·6		208·8		245·0		275·9	
No. of deaths	660		777		522		540	
Age- and energy-adjusted HR	1·0	0·99	0·89, 1·09	0·84	0·75, 0·94	0·87	0·78, 0·98	0·002
Multivariate HR*	1·0	0·93	0·83, 1·05	0·78	0·68, 0·91	0·71	0·59, 0·86	0·001
GL derived from white rice								
Median	89·6		122·9		168·0		187·7	
No. of deaths	681		777		485		556	
Multivariate HR*	1·0	1·01	0·90, 1·13	0·87	0·75, 1·00	0·77	0·66, 0·91	0·001
GL derived from other foods								
Median	55·9		73·0		85·4		105·9	
No. of deaths	532		592		706		669	
Multivariate HR*	1·0	0·98	0·87, 1·12	1·11	0·97, 1·27	1·04	0·90, 1·20	0·43
Cancer mortality								
Dietary GI								
No. of deaths	228		240		196		182	
Age- and energy-adjusted HR	1·0	1·03	0·86, 1·23	0·90	0·74, 1·09	0·83	0·68, 1·01	0·04
Multivariate HR*	1·0	1·10	0·90, 1·34	0·96	0·76, 1·21	0·93	0·70, 1·23	0·58
Dietary GL								
No. of deaths	236		255		189		166	
Age- and energy-adjusted HR	1·0	0·94	0·79, 1·13	0·83	0·69, 1·01	0·74	0·60, 0·90	0·001
Multivariate HR*	1·0	0·99	0·81, 1·21	0·81	0·64, 1·04	0·71	0·52, 0·99	0·02
GL derived from white rice								
No. of deaths	226		257		183		180	
Multivariate HR*	1·0	1·10	0·91, 1·35	0·95	0·75, 1·21	0·84	0·64, 1·11	0·17
GL derived from other foods								
No. of deaths	224		197		222		203	
Multivariate HR*	1·0	0·83	0·67, 1·02	0·98	0·79, 1·22	0·89	0·70, 1·13	0·57
Cardiovascular mortality								
Dietary GI								
No. of deaths	198		170		141		156	
Age- and energy-adjusted HR	1·0	0·84	0·68, 1·03	0·79	0·63, 0·98	0·86	0·69, 1·06	0·07
Multivariate HR*	1·0	0·87	0·70, 1·09	0·85	0·65, 1·11	0·93	0·67, 1·28	0·42
Dietary GL								
No. of deaths	179		215		138		133	
Age- and energy-adjusted HR	1·0	0·97	0·80, 1·19	0·84	0·67, 1·05	0·80	0·64, 1·01	0·03
Multivariate HR*	1·0	0·97	0·76, 1·22	0·94	0·70, 1·27	0·86	0·58, 1·27	0·49
GL derived from white rice								
No. of deaths	205		206		110		144	
Multivariate HR*	1·0	0·88	0·71, 1·09	0·78	0·58, 1·03	0·77	0·55, 1·06	0·07
GL derived from other foods								
No. of deaths	118		159		206		182	
Multivariate HR*	1·0	1·18	0·91, 1·53	1·38	1·05, 1·80	1·22	0·92, 1·64	0·24
Non-cancer, non-cardiovascular mortality								
Dietary GI								
No. of deaths	262		278		215		232	
Age- and energy-adjusted HR	1·0	1·03	0·87, 1·22	0·89	0·74, 1·07	0·95	0·80, 1·13	0·30
Multivariate HR*	1·0	0·92	0·77, 1·11	0·72	0·58, 0·89	0·64	0·49, 0·84	0·0004
Dietary GL								
No. of deaths	245		307		194		241	
Age- and energy-adjusted HR	1·0	1·04	0·87, 1·22	0·85	0·70, 1·03	1·06	0·88, 1·26	0·86
Multivariate HR*	1·0	0·86	0·71, 1·05	0·68	0·53, 0·86	0·64	0·48, 0·87	0·001
GL derived from white rice								
No. of deaths	250		314		192		231	
Multivariate HR*	1·0	1·01	0·83, 1·21	0·86	0·68, 1·08	0·73	0·56, 0·95	0·01
GL derived from other foods								
No of deaths	190		235		278		284	
Multivariate HR*	1·0	1·05	0·85, 1·29	1·11	0·89, 1·38	1·11	0·88, 1·40	0·37

* Adjusted for age, energy, height, BMI, physical activity, smoking status, education, marital status, histories of diabetes and hypertension, and intakes of alcohol, saturated fat, polyunsaturated fat, salt, vegetables and fruits.

Table 3. All-cause and cause-specific mortality in women by quartiles (Q) of dietary glycaemic index (GI) and glycaemic load (GL) (Hazard ratios (HR) and 95 % confidence intervals)

	Q1	Q2		Q3		Q4		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	P_{trend}
All-cause mortality								
Dietary GI								
Median	58·3		62·3		65·6		70·1	
No. of deaths	485		504		593		535	
Age- and energy-adjusted HR	1·0	0·99	0·88, 1·12	1·10	0·97, 1·24	1·07	0·95, 1·22	0·12
Multivariate HR*	1·0	1·00	0·87, 1·14	1·06	0·92, 1·22	1·10	0·91, 1·31	0·26
Dietary GL								
Median	154·1		179·0		196·3		241·1	
No. of deaths	385		567		711		454	
Age- and energy-adjusted HR	1·0	1·18	1·04, 1·35	1·17	1·03, 1·33	1·06	0·93, 1·21	0·87
Multivariate HR*	1·0	1·15	1·00, 1·32	1·09	0·93, 1·28	1·03	0·82, 1·30	0·99
GL derived from white rice								
Median	87·5		111·7		126·1		182·9	
No. of deaths	417		493		768		439	
Multivariate HR*	1·0	0·94	0·81, 1·08	1·01	0·88, 1·17	0·85	0·69, 1·03	0·11
GL derived from other foods								
Median	80·7		93·6		102·9		117·2	
No. of deaths	415		573		587		542	
Multivariate HR*	1·0	1·12	0·98, 1·28	1·18	1·03, 1·34	1·08	0·94, 1·23	0·36
Cancer mortality								
GI								
No. of deaths	135		138		146		136	
Age- and energy-adjusted HR	1·0	1·01	0·80, 1·29	1·05	0·83, 1·33	1·02	0·80, 1·29	0·83
Multivariate HR*	1·0	1·00	0·78, 1·28	0·97	0·74, 1·28	0·86	0·61, 1·21	0·41
GL								
No. of deaths	116		140		165		134	
Age- and energy-adjusted HR	1·0	1·09	0·85, 1·39	1·13	0·89, 1·43	1·10	0·86, 1·41	0·51
Multivariate HR*	1·0	1·07	0·82, 1·39	1·04	0·77, 1·40	0·88	0·59, 1·33	0·47
GL derived from white rice								
No. of deaths	130		130		168		127	
Multivariate HR*	1·0	0·87	0·67, 1·13	0·89	0·68, 1·16	0·67	0·47, 0·95	0·03
GL derived from other foods								
No. of deaths	121		134		146		154	
Multivariate HR*	1·0	0·83	0·67, 1·02	0·98	0·79, 1·22	1·25	0·96, 1·61	0·57
Cardiovascular mortality								
GI								
No. of deaths	158		192		218		196	
Age- and energy-adjusted HR	1·0	1·13	0·91, 1·39	1·17	0·95, 1·43	1·17	0·95, 1·44	0·15
Multivariate HR*	1·0	1·19	0·95, 1·50	1·26	0·98, 1·60	1·56	1·15, 2·13	0·007
GL								
No. of deaths	134		217		266		147	
Age- and energy-adjusted HR	1·0	1·22	0·99, 1·52	1·11	0·90, 1·37	0·95	0·75, 1·20	0·26
Multivariate HR*	1·0	1·19	0·94, 1·51	1·06	0·81, 1·40	1·10	0·73, 1·64	0·80
GL derived from white rice								
No. of deaths	139		189		295		141	
Multivariate HR*	1·0	0·99	0·78, 1·25	1·02	0·79, 1·31	0·88	0·62, 1·25	0·46
GL derived from other foods								
No. of deaths	151		223		206		184	
Multivariate HR*	1·0	1·08	0·87, 1·34	1·03	0·82, 1·28	0·92	0·73, 1·16	0·33
Non-cancer, non-cardiovascular mortality								
Dietary GI								
No. of deaths	192		173		229		203	
Age- and energy-adjusted HR	1·0	0·85	0·69, 1·04	1·04	0·85, 1·26	1·01	0·83, 1·23	0·49
Multivariate HR*	1·0	0·83	0·67, 1·04	0·94	0·75, 1·17	0·93	0·70, 1·24	0·83
Dietary GL								
No. of deaths	135		210		279		173	
Age- and energy-adjusted HR	1·0	1·20	0·97, 1·50	1·22	0·98, 1·50	1·12	0·90, 1·41	0·54
Multivariate HR*	1·0	1·17	0·92, 1·48	1·13	0·87, 1·48	1·10	0·76, 1·61	0·73
GL derived from white rice								
No. of deaths	148		174		304		171	
Multivariate HR*	1·0	0·93	0·74, 1·18	1·07	0·84, 1·36	0·97	0·70, 1·35	0·98
GL derived from other foods								
No. of deaths	143		216		234		204	
Multivariate HR*	1·0	1·20	0·97, 1·50	1·36	1·09, 1·70	1·13	0·90, 1·42	0·34

* Adjusted for age, energy, height, BMI, physical activity, smoking status, education, marital status, menopausal status, histories of diabetes and hypertension, and intakes of alcohol, saturated fat, polyunsaturated fat, salt, vegetables and fruits.

and non-cancer, non-cardiovascular mortality in men. Dietary GL was found to be also associated with a decreased risk of cancer mortality in men. Dietary GI was found to be associated with an increased risk of cardiovascular mortality in women. Several reviews of previous studies on dietary GI or GL and the risk of CVD have been published, and most of them have concluded that a high GI or GL increases the risk of CVD in women but not in men. Our findings concerning cardiovascular mortality in both men and women do not contradict the results of previous studies[4,19–21]. However, the significant inverse associations observed between dietary GI and GL and non-cancer, non-cardiovascular mortality and between dietary GL and cancer mortality in men were unexpected. These inverse associations contributed to the reduction of all-cause mortality in relation to dietary GI and GL in men.

Numerous epidemiological studies have assessed the associations of dietary GI and GL with the risk of cancers, but the results were less consistent when compared with those obtained for CVD. A recent meta-analysis of prospective studies has revealed a weak association of diabetes-related cancers (bladder, breast, colorectal, endometrial, liver, pancreatic and prostate cancers) with dietary GI (relative risk = 1·07) or GL (relative risk = 1·02)[22]. The results were interpreted to indicate that GI or GL may not ideally predict insulin secretion, which is more relevant than hyperglycaemia to the development of cancer[22].

No study has examined the association of dietary GI or GL with the risk of non-cancer, non-cardiovascular mortality in men as a whole. The association between dietary GI and mortality from inflammatory diseases was examined in one study carried out in Australia[23]. The association was almost null in men, although a significant positive association was observed in women. In the present study, among non-cancer, non-cardiovascular causes, mortality from digestive diseases, respiratory diseases, and endocrine, nutritional, and metabolic diseases was found to exhibit a suggestive inverse association with dietary GL. Considering these results, dietary GI or GL may be favoured as a nutritional support for improving the prognosis of various diseases rather than as a risk determinant of diseases in men. It is also possible that certain dietary components in white rice, rather than GL, may have beneficial effects on all-cause and cause-specific mortality in men because the GL derived from white rice contributed to the inverse associations of overall GL with mortality. The GL derived from white rice was also associated with a decreased risk of cancer mortality in women. Howarth *et al.*[24] found that a higher GL was associated with a decreased risk of colorectal cancer in women in the Multiethnic Cohort Study. They suggested that this might be because, in this population, a major source of dietary GL is white rice. Given the results of the present and other studies, application of the GI to white rice in the Japanese diet can lead to misinformation and counterproductive dietary guidance.

The strengths of the present study include the prospective design, validation of dietary questionnaire, representation of the general population, information on potential confounders, a high rate of participation and the length of follow-up. The study also has several limitations. Although adjustments for numerous potential confounders were made, confounding due to unknown factors or residual confounding cannot be ruled out. The sample size was limited, which precluded analyses on causes leading to small numbers of deaths. The results of the study may have been affected by the misclassification of dietary GI or GL. It has been shown that GI values obtained for the same foods are roughly similar in an ethnically and physically wide variety of subjects[25]. However, the GI of a food may vary when it is eaten with different foods. It has been reported that dairy foods reduce the GI of white rice when consumed together[26]. Although dairy food intake was found to be neither a confounder nor a modifier of the associations of dietary GI and GL with the risk of mortality, the statistical handling followed in the present study would not be sufficient to disentangle the relative roles of these dietary components. Some degree of misclassification of dietary intake is also expected, just as in other nutritional epidemiological studies. However, it is unlikely that measurement errors in the estimation of dietary GI and GL and the intakes of nutrients at the baseline were dependent on the subsequent deaths. Usual dietary intake was estimated through a single dietary intake assessment. According to the National Health and Nutrition Survey in Japan[27], rice intake was 33·9 % of energy in 1992 and 30·7 % of energy in 2008. The corresponding values for fat and protein intakes were 25·5 and 15·6 % of energy, respectively, in 1992 and 25·1 and 14·6 % of energy, respectively, in 2008. Although these data indicate that dietary intake during the follow-up period did not change greatly at the population level, dietary intake change at the individual level cannot be ruled out. Underlying diseases or preclinical signs at the baseline may have affected dietary intake assessment. However, the exclusion of those who died during the first 6 years of follow-up did not alter the results substantially. The question of generalisability is also relevant. Our findings were recorded in a population that is leaner, similar to other Japanese populations, when compared with Western populations and that consumes rice as the main contributor of dietary GI and GL. Foods that contribute to dietary GI and GL can differ across populations and may have different health implications.

In conclusion, the results of the present study do not support the associations of dietary GI and GL with an increased risk of all-cause or cause-specific mortality in men. Rather, potential favourable effects were observed in men. On the other hand, a high GI was found to be associated with an increased risk of cardiovascular mortality in women. Further studies are needed to confirm or refute these findings. As these associations appear to be dependent on the food sources of dietary GI and GL and sex, studies among various populations are encouraged.

Acknowledgements

The authors thank Dr Shougen Matsushita and Mr Takehiko Minaguchi for their help with data collection.

The present study was supported in part by grants from the Ministry of Education, Culture, Sports, Science, and

Technology and the National Cancer Center Research and Development Fund, Japan. The Ministry of Education, Culture, Sports, Science, and Technology and the National Cancer Center had no role in the design and analysis of the study or in the writing of this article.

The authors' contributions were as follows: C. N. organised the study and wrote the manuscript; K. W., M. T. and T. K. conducted the data analysis; K. N. helped supervise the field activities and interpret the data. All the authors read and approved the final manuscript.

None of the authors has any conflicts of interest to declare.

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