Table 2 continued

	BMI_8	BMI_9	BMI_10	BMI_11	Total	*P* value
Drugs taken						
Antihypertensive, (%)	3,538 (34.8)	2,923 (39.0)	2,298 (42.5)	5,720 (48.3)	34,371 (27.0)	<0.001
Antidiabetic, (%)	475 (4.7)	430 (5.7)	342 (6.3)	1,159 (9.8)	4,922 (3.9)	<0.001
Antihyperlipidemic, (%)	2,540 (25.0)	2,008 (26.8)	1,388 (25.7)	3,234 (27.3)	27,107 (21.3)	<0.001
Chemistry data						
Proteinuria, (%)	422 (4.1)	344 (4.6)	343 (6.3)	1,008 (8.5)	4,960 (3.9)	<0.001
eGFR, ml/min/1.73 m^2	74.4 (63.4–86.7)	74.4 (63.4–85.8)	74.4 (63.1–85.2)	74.4 (63.4–89.0)	74.7 (63.9–88.9)	<0.001
sCr, mg/dl	0.60 (0.56–0.70)	0.60 (0.60–0.70)	0.60 (0.59–0.70)	0.60 (0.50–0.70)	0.60 (0.53–0.70)	<0.001
FPG, mg/dl	94 (88–101)	95 (89–103)	95 (89–103)	97 (90–107)	92 (86–99)	<0.001
TG, mg/dl	106 (78–145)	108 (82–147)	112 (84–153)	118 (88–159)	93 (69–129)	<0.001
LDL, mg/dl	132 (113–153)	133 (113–153)	133 (113–153)	132 (114–153)	128 (109–149)	<0.001

Data are expressed as median (interquartile range) or percentage. Differences were evaluated using Kruskal–Wallis test or Chi-squared test as appropriate

BMI body mass index, *eGFR* estimated glomerular filtration rate, *FPG* fasting plasma glucose, *TG* triglyceride, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

active [22]. VAT is reported to have a higher association with proteinuria; however, this has not been found consistently [23]. Our study did not assess SAT or VAT condition; therefore, we cannot shed any further light on this issue.

A new finding in this study is that the subjects with a BMI <20.4 kg/m^2 in men and <18.4 kg/m^2 in women were significantly associated with proteinuria; however, the reason for this is not clear. Few papers have described an association between lowest BMI subjects and proteinuria [24]. According to our data, there was no strong association by univariate analysis, but significant associations were found between the lowest BMI subjects and proteinuria by multivariate analysis in both genders. Therefore, lowest BMI is not thought to have a strong influence on the presence of proteinuria, but it has significant power. There was no definitive explanation, but we would like to put forward some suggestions for consideration as to why these subjects had a significant association with proteinuria.

Firstly, postural proteinuria is thought to be related to renal ptosis or wandering kidney, which is often found in thinner people [25]. This condition might be included in subjects with the lowest BMI. Secondly, another risk of low BMI on proteinuria could be related to age. The OR for proteinuria was analyzed for age groups—in younger subjects, a larger OR was particularly prominent in the subjects with the lowest BMI; on the other hand, no clear age relationship was found in the higher BMI group. This suggested the possibility of more glomerulonephritis than nephrosclerosis or more postural proteinuria in the lowest BMI subjects. Thirdly, we could see that current smokers were more prevalent in the lower BMI groups in both genders, and causal relationships between cigarette smoking and proteinuria have been reported via the hyperfiltration mechanism [26].

Some epidemiological studies revealed that subjects with chronic lung disease or with malignancies were frequently seen among those with a lower BMI [27, 28]. In addition, a significant relationship between the presence of proteinuria and chronic obstructive lung disease has been reported [29], and its cause was speculated to be endovascular dysfunction [30]. In our study, the presence of lung disease or malignancies was not surveyed, so we could not clarify this issue; therefore, we were unable to rule out the contribution of lung diseases or malignancies to the presence of proteinuria, especially in view of the high frequency of smoking in the lower BMI participants.

Overall mortality analysis showed a U-shape with high mortality in both lower and higher BMI subjects [28]; however, because our study was cross-sectional, mortality analysis was not feasible. Other considered

Table 3 Univariate and multivariate logistic analyses for proteinuria

	Univariate			Multivariate		
	OR	95 % CI		OR	95 % CI	
		Lowest	Highest		Lowest	Highest
Men						
BMI subgroup (kg/m^2)						
≤18.4	1.160	0.974	1.382	1.756	1.455	2.118
8.5–19.5	1.109	0.937	1.312	1.429	1.199	1.703
19.5–20.4	1.038	0.901	1.195	1.261	1.090	1.459
20.5–21.4	0.894	0.786	1.017	0.980	0.858	1.118
21.5–22.4	1 (reference)			1 (reference)		
22.5–23.4	1.079	0.967	1.204	0.978	0.875	1.095
23.5–24.4	1.259	1.131	1.401	1.034	0.925	1.156
24.5–25.4	1.383	1.240	1.542	1.066	0.950	1.197
25.5–26.4	1.639	1.464	1.834	1.187	1.050	1.342
26.5–27.4	1.855	1.646	2.092	1.234	1.079	1.410
≥27.5	2.490	2.249	2.756	1.422	1.245	1.624
Age, +10 years	1.151	1.120	1.182	0.952	0.922	0.984
Waist circumference, +10 cm	1.393	1.355	1.432	1.113	1.064	1.165
SBP, +10 mmHg	1.246	1.229	1.264	1.176	1.158	1.194
FPG, + 10 mg/dl	1.134	1.126	1.142	1.109	1.099	1.118
TG, +50 mg/dl	1.075	1.064	1.086	1.029	1.017	1.042
LDL, +10 mg/dl	1.004	0.994	1.011	1.003	0.995	1.012
eGFR, +10 ml/min/1.73 m^2	0.822	0.809	0.836	0.822	0.808	0.837
Antihypertensive	2.316	2.201	2.436	1.731	1.635	1.833
Antidiabetic	2.773	2.576	2.985	1.481	1.357	1.615
Antihyperlipidemic	1.645	1.533	1.766	1.112	1.031	1.201
Current smoking	1.217	1.151	1.286	1.433	1.350	1.521
Daily drinking	0.950	0.903	1.000	0.899	0.852	0.949
Women						
BMI subgroup (kg/m^2)						
≤18.4	1.335	1.158	1.538	1.717	1.473	2.002
18.5–19.5	0.963	0.823	1.127	1.168	0.993	1.374
19.5–20.4	0.977	0.848	1.125	1.132	0.980	1.308
20.5–21.4	0.974	0.851	1.116	1.047	0.913	1.201
21.5–22.4	1 (reference)			1 (reference)		
22.5–23.4	1.282	1.127	1.457	1.205	1.059	1.372
23.5–24.4	1.402	1.230	1.599	1.259	1.101	1.439
24.5–25.4	1.529	1.335	1.752	1.275	1.108	1.467
25.5–26.4	1.699	1.471	1.961	1.334	1.147	1.550
26.5–27.4	2.394	2.071	2.766	1.799	1.541	2.099
≥27.5	3.288	2.933	3.687	2.203	1.917	2.532
Age, +10 years	1.129	1.093	1.167	0.869	0.837	0.902
Waist circumference, +10 cm	1.338	1.303	1.374	0.989	0.948	1.032
SBP, +10 mmHg	1.261	1.242	1.280	1.179	1.160	1.199
FPG, + 10 mg/dl	1.156	1.145	1.167	1.112	1.100	1.125
TG, +50 mg/dl	1.156	1.137	1.175	1.066	1.046	1.087
LDL, +10 mg/dl	1.012	1.002	1.021	0.999	0.990	1.009
eGFR, +10 ml/min/1.73 m^2	0.843	0.828	0.859	0.847	0.831	0.864
Antihypertensive	2.304	2.176	2.440	1.608	1.507	1.716

Table 3 continued

	Univariate			Multivariate		
	OR	95 % CI		OR	95 % CI	
		Lowest	Highest		Lowest	Highest
Antidiabetic	2.802	2.538	3.094	1.248	1.108	1.405
Antihyperlipidemic	1.383	1.297	1.474	1.040	0.969	1.115
Current smoking	1.215	1.086	1.358	1.373	1.219	1.546
Daily drinking	0.867	0.776	0.968	0.926	0.826	1.038

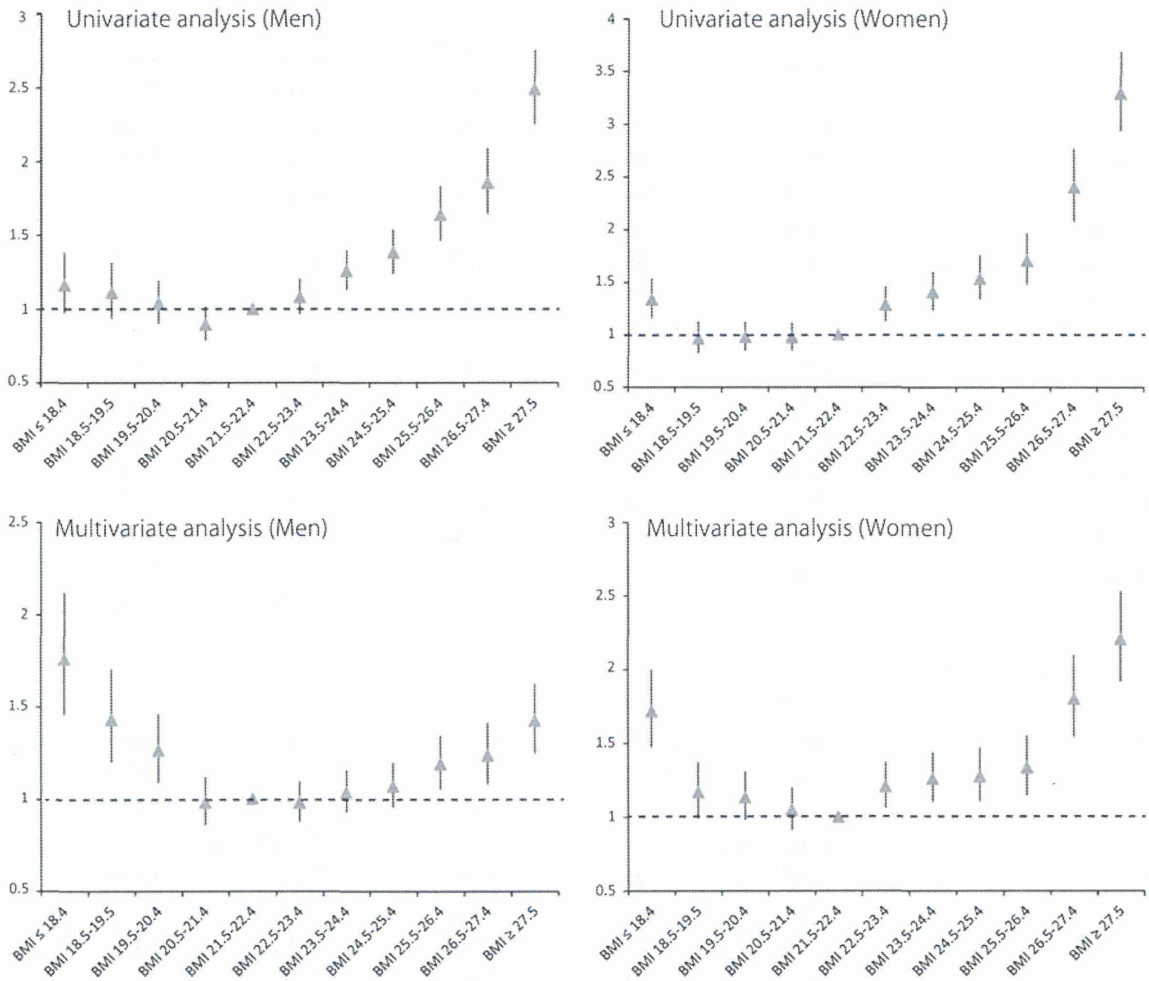

Fig. 1 OR and 95 % CI for proteinuria (urine dipstick protein ≥1+) by grading BMI. Subjects were divided by BMI grading as shown on the *x* axis. The OR for proteinuria of each subgroup was calculated by univariate (*upper panels*) and multivariate (*lower panels*) logistic analyses with the subgroup BMI range of 21.5–22.4 as a reference. Multivariate analysis was conducted by adjusting for age, waist circumference, eGFR, SBP, FPG, TG, LDL cholesterol, use of antihypertensive, antidiabetic, or antihyperlipidemic medication, and lifestyle factors (drinking, smoking)

reasons for this finding are that subjects with proteinuria and undetected kidney disease might have a lower BMI, or that low BMI subjects who might have had low birth weight and a smaller number of nephrons [31, 32] had an increased risk for hyperfiltration, resulting in kidney damage and proteinuria. This hypothesis could not be clarified because of the cross-sectional nature of this study.

Some studies have focused on the influence of alcohol intake on proteinuria. Analyzing the autopsy data of

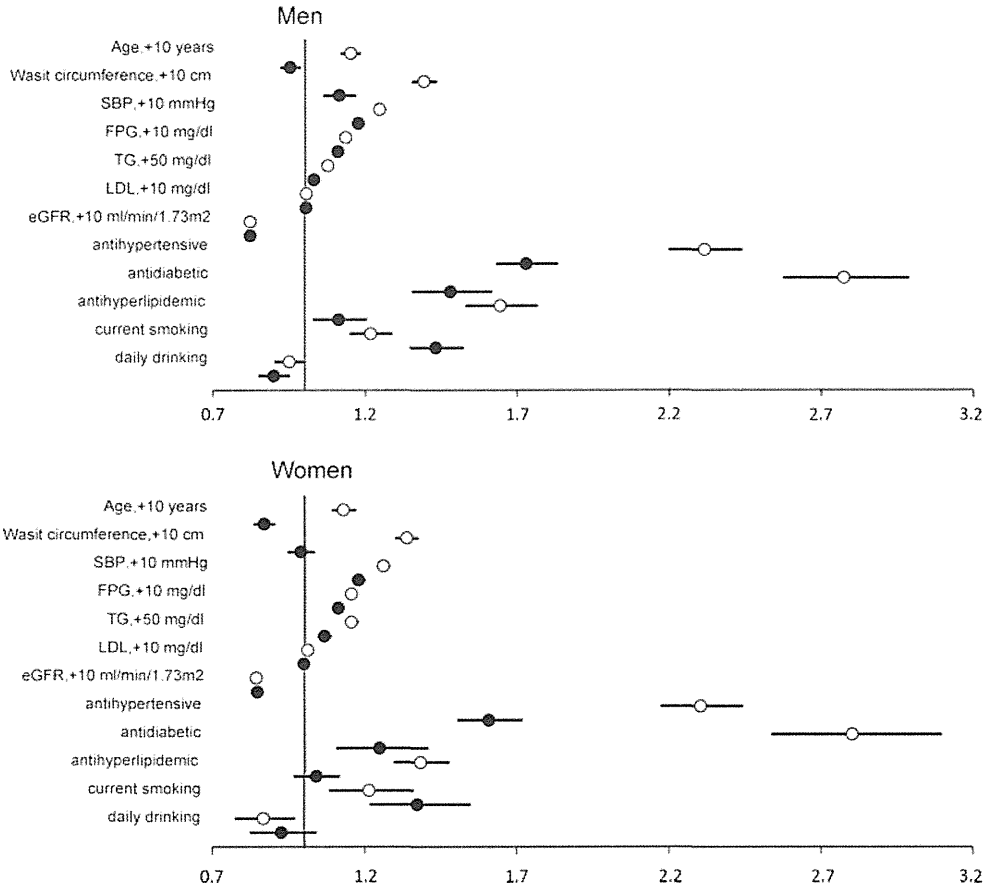

Fig. 2 OR and 95 % CI for proteinuria (urine dipstick protein ≥1+). The OR for proteinuria of each covariate was calculated by univariate (*open circles*, OR and 95 % CI) and multivariate (*closed circles* OR and 95 % CI) logistic analyses. Multivariate analysis was conducted by adjusting for the grading of BMI, age, waist circumference, eGFR, SBP, FPG, TG, LDL cholsterol, use of antihypertensive, antidiabetic, or antihyperlipidemic medication, and lifestyle factors (drinking, smoking)

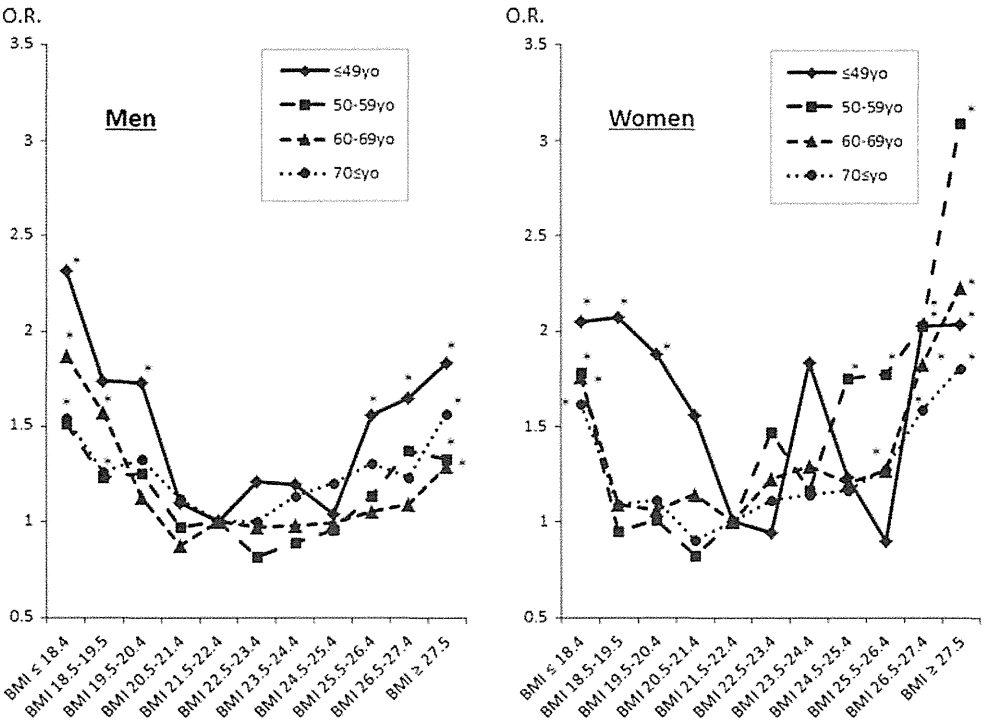

Fig. 3 Effect of age on the association between BMI and proteinuria. To examine whether age affects the association between BMI and proteinuria, ORs by age groups for proteinuria were calculated according to the degree of BMI after adjustment by waist circumference, SBP, FPG, TG, LDL, eGFR, antihypertensive medication, antidiabetic medication, antihyperlipidemic medication, current smoking and daily drinking. In the lowest BMI groups in both genders, there was a trend for the younger subjects to have a greater OR for proteinuria. Lowest BMI groups showed significant ORs relative to the reference, except in the 50–59 year age group in men; on the other hand, all age groups in the lowest BMI groups in women revealed significant ORs for proteinuria

Japanese–Americans in Hawaii revealed less renal arteriolar hyalinization in subjects taking alcohol at 30 ml/day than in those without alcohol intake [33]. Alcohol intake at least once a week has been reported to be a significant inverse risk factor for proteinuria in Japanese people [34]. On the other hand, moderate to heavy alcohol intake was reported to be a significant risk factor for albuminuria in Australians [35]. Our data only refer to 'daily drinking,' so we are unable to assess the level of alcohol intake; however, it is not an unusual finding that daily drinking is an inverse risk factor for proteinuria.

Limitations

This study was cross-sectional, so we are unable to infer causality related to proteinuria. There might have been some biases towards participants who were particularly motivated to undergo a health examination. Many subjects were excluded because of missing data. Urine dipstick analyses were also performed manually. The visual judgment associated with this analysis can thus be considered as another limitation. In particular, some of the cases of dipstick-positive proteinuria could have been transient, and the presence of persisting proteinuria was not confirmed. Physiological proteinuria could not be ruled out because the dipstick test for detecting proteinuria was only carried out once. Urine specific gravity and pH were not recorded; therefore, the effect of urine concentration on test performance was not assessed. Furthermore, a relatively high false-positive rate for proteinuria by judging isolated dipstick test results was reported [36].

Summary

We examined the association between BMI and proteinuria, and compared the risk of proteinuria among those classified into different levels of BMI in a large (>200,000) Japanese database of health check-up data of adults with no pre-existing cardiovascular diseases. We found that BMI levels were associated with proteinuria in a U-shape and that there were remarkable gender differences in this regard. Health guidance should not only focus on higher BMI subjects but also on the thinnest subjects in terms of the prevention of CKD.

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Conflict of interest None.

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Association of the triglycerides to high-density lipoprotein cholesterol ratio with the risk of chronic kidney disease: Analysis in a large Japanese population

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ABSTRACT

Objectives: To investigate the relationship between triglycerides to high-density lipoprotein cholesterol ratio (TG/HDL-C) and chronic kidney disease (CKD).
Methods: We used data from 216,007 Japanese adults who participated in a nationwide health checkup program. Men (n = 88,516) and women (n = 127,491) were grouped into quartiles based on their TG/HDL-C levels (<1.26, 1.26–1.98, 1.99–3.18, and >3.18 in men; <0.96, 0.96–1.44, 1.45–2.22, and >2.22 in women). We cross-sectionally assessed the association of TG/HDL-C levels with CKD [defined as an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2 (low eGFR) and/or proteinuria (defined as urinary protein ≥1+ on dipstick testing)], low eGFR, and proteinuria.
Results: The prevalence of CKD, low eGFR, and proteinuria increased significantly with elevating quartiles of TG/HDL-C in both genders (all P for trend <0.001). Participants in the highest quartile of TG/HDL-C had a significantly greater risk of CKD than those in the lowest quartile after adjustment for the relevant confounding factors (odds ratio: 1.57, 95% confidence interval: 1.49–1.65 in men; 1.41, 1.34–1.48 in women, respectively). Furthermore, there were significant associations with low eGFR and proteinuria. In stratified analysis, the risk of CKD increased linearly with greater TG/HDL-C levels in participants with and without hypertension, diabetes, and obesity. Moreover, higher TG/HDL-C levels were relevant for CKD, especially in participants with hypertension and diabetes (P for interaction <0.001, respectively).
Conclusions: An elevated TG/HDL-C is associated with the risk of CKD in the Japanese population.

1. Introduction

Chronic kidney disease (CKD) is a global public health problem and a major risk factor for progressive kidney failure and cardiovascular morbidity and mortality [1]. Identifying and managing the risk factors associated with mild CKD may well be the best strategy to prevent and delay advanced outcomes of CKD [1].

Abnormal lipoprotein metabolism has been identified as a possible cause of CKD [2,3], and moderate CKD is associated with

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elevated levels of triglycerides (TG) and a decreased level of high-density lipoprotein cholesterol (HDL-C) [2–7].

Recent studies have shown that there is an association between TG/HDL-C and insulin resistance and that TG/HDL-C may be a better predictor of cardiovascular events than other lipid parameters, including TG, low-density lipoprotein-cholesterol (LDL-C), or the total cholesterol/HDL-C ratio [8–11]. In addition, TG/HDL-C has also been shown to predict the LDL particle size [12–14]. However, little is known about the association between TG/HDL-C and CKD. In the present study, we investigated the association between TG/HDL-C and CKD in a nationally representative group of Japanese adults.

2. Methods

2.1. Study population

This cross-sectional cohort study was conducted as a part of the prospective ongoing project entitled "Research on the Positioning of Chronic Kidney Disease in Specific Health Check and Guidance in Japan", and it was based on data obtained from the Japanese Specific Health Check and Guidance System. This annual health check program was initiated in 2008 by the Japanese government and it promotes the early diagnosis of metabolic syndrome and intervention strategies for the prevention of this disease. In 2008 and 2009, data were collected from 676,905 individuals participated in the health checkups. Men ($n = 278,017$) and women ($n = 383,586$) involved were between 20 and 101 years of age. For our study, data from 216,007 of the participants (88,516 men and 127,491 women) aged between 20 and 88 years were used for statistical analyses. (We excluded 460,898 participants because essential data, including information on proteinuria and serum creatinine levels, were unavailable.) This study was conducted in accordance with the Private Information Protection Law and ethical guidelines for epidemiology research published by the Ministry of Health, Labour and Welfare in 2005.

Table 1
Clinical features of all subjects.

Variables	Men ($n = 88,516$)	Women ($n = 127,491$)	P value
Age, years	63.8 ± 8.9	63.8 ± 8.5	0.77
Body mass index, kg/m^2	23.7 ± 3.0	22.8 ± 3.5	<0.001
Waist circumference, cm	85.3 ± 8.2	82.6 ± 9.8	<0.001
Systolic blood pressure, mmHg	131 ± 17	128 ± 18	<0.001
Diastolic blood pressure, mmHg	78 ± 11	75 ± 11	<0.001
Fasting blood glucose, g/dL	102 ± 25	95 ± 18	<0.001
Hemoglobin A1c, %	5.4 ± 0.8	5.3 ± 0.6	<0.001
LDL-C, mg/dL	121 ± 30	130 ± 30	<0.001
HDL-C, mg/dL	57 ± 15	66 ± 16	<0.001
TG, mg/dL	133 ± 96	107 ± 61	<0.001
TG/HDL-C	2.66 ± 2.59	1.83 ± 1.50	<0.001
Serum creatinine, mg/dL	0.84 ± 0.27	0.63 ± 0.19	<0.001
Estimated GFR, mL/min/1.73 m^2	74.7 ± 16.6	76.1 ± 16.3	<0.001
Low eGFR, %	17.7	11.4	<0.001
Proteinuria, %	8.2	4.0	<0.001
Chronic kidney disease, %	23.3	14.5	<0.001
Hypertension, %	51.4	42.7	<0.001
Diabetes mellitus, %	15.7	8.4	<0.001
Obesity, %	31.0	23.0	<0.001
Current smoker, %	25.3	5.9	<0.001
Daily drinker, %	44.9	8.3	<0.001
Regular exercise, %	47.6	39.8	<0.001
History of stroke, %	5.3	2.8	<0.001
History of heart disease, %	8.3	5.2	<0.001
Medication for hypertension, %	34.2	29.0	<0.001
Medication for diabetes mellitus, %	7.5	4.1	<0.001
Medication for dyslipidemia, %	12.9	22.9	<0.001

Low eGFR was defined as eGFR <60 mL/min/1.73 m^2. Proteinuria was defined as urinary protein of ≥1+ on dipstick testing. Chronic kidney disease was defined as low eGFR and/or proteinuria. Hypertension was defined as a systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or self-reported use of antihypertensive drugs. Diabetes was defined in accordance with American Diabetes Association guidelines as a fasting glucose concentration of ≥126 mg/dL, hemoglobin A1c concentration of ≥6.5%, or self-reported use of antihyperglycemic drugs. TG/HDL-C was calculated as TG (mg/dL) divided by HDL-C (mg/dL).
Abbreviations: LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; GFR, glomerular filtration rate; eGFR, estimated GFR.

2.2. Clinical evaluation and laboratory measurements

All participants completed a self-administered questionnaire that documented their medical history, current medications, smoking habits (current smoker or not), alcohol consumption (daily drinker or not), and regular exercise habits. A study physician physically examined every participant and checked the participants' reported medical history to ensure the accuracy of the information. The height and weight of participants were measured, and their body mass index (BMI) was calculated (kg/m^2). For these measurements, participants wore light clothing without shoes. Blood pressures were measured and blood as well as urine sampling was done at each participant's local medical institute, as stipulated by the health check program.

Blood samples were collected after participants fasted overnight and the blood was analyzed using an automated clinical chemical analyzer within 24 h of sampling. All blood analyses were conducted at a local, rather than a central, laboratory. Although the methods used for blood analyses were not calibrated between laboratories, the Japan Society of Clinical Chemistry-recommended methods for laboratory tests several years ago, and these recommendations have been widely adopted by laboratories across Japan. The enzymatic method was used to measure serum creatinine levels in fresh blood samples. Levels of LDL-C, HDL-C, and TG were determined enzymatically. Hemoglobin A1c (HbA1c) values were expressed as a National Glycohemoglobin Standardization Program equivalent value, which was calculated according to the following formula:

$$\mathrm{HbA1c}(\%) = \mathrm{HbA1c\ (Japan\ Diabetes\ Society)}\ (\%) + 0.4\%.$$

2.3. Definition of CKD, diabetes mellitus, obesity, hypertension, and TG/HDL-C

The estimated glomerular filtration rate (eGFR) was calculated using the following equation; eGFR (mL/min/1.73 m^2) = 194 × serum creatinine (mg/dL)$^{-1.094}$ × age (years)$^{-0287}$ × 0.739 (for women) [15]. Proteinuria was defined as urinary protein value of ≥1+ with dipstick testing. CKD was defined as an eGFR <60 mL/min/1.73 m^2 (low eGFR) and/or the presence of proteinuria. Hypertension was defined as a systolic blood pressure (SBP) of ≥140 mmHg, and/or a diastolic blood pressure (DBP) of ≥90 mmHg, or self-reported use of antihypertensive drugs. Diabetes mellitus was defined in accordance with the guidelines of the American Diabetes Association [16]; fasting glucose concentration ≥126 mg/dL, HbA1c concentration ≥6.5%, or self-reported use of antihyperglycemic drugs. TG/HDL-C was calculated as TG (mg/dL) divided by HDL-C (mg/dL). Male and female participants were separately grouped into quartiles based on their TG/HDL-C levels. TG/HDL-C levels for the quartile groups (Q) were as follows: $Q_1 < 1.26$, Q_2 1.26–1.98, Q_3 1.99–3.18, and $Q_4 > 3.18$ for men and $Q_1 < 0.96$, Q_2 0.96–1.44, Q_3 1.45–2.22, and $Q_4 > 2.22$ for women.

Table 2
Mean values or frequencies of relevant factors according to the quartiles of TG/HDL-C.

(A) Men

	TG/HDL-C				*P* for trend
	Q_1	Q_2	Q_3	Q_4	
	<1.26	1.26–1.98	1.99–3.18	>3.18	
	(n = 22,126)	(n = 22,126)	(n = 22,142)	(n = 22,122)	
Age, years	64.4 ± 8.7	64.4 ± 8.5	63.9 ± 8.8	62.3 ± 9.5	<0.001
Body mass index, kg/m^2	22.3 ± 2.8	23.4 ± 2.8	24.2 ± 2.9	24.9 ± 3	<0.001
Waist circumference, cm	81.2 ± 7.8	84.6 ± 7.8	86.7 ± 7.7	88.7 ± 7.7	<0.001
Systolic blood pressure, mmHg	129 ± 17	130 ± 17	131 ± 17	132 ± 17	<0.001
Diastolic blood pressure, mmHg	77 ± 11	78 ± 11	78 ± 11	79 ± 11	<0.001
Fasting blood glucose, g/dL	99 ± 21	101 ± 22	102 ± 24	106 ± 31	<0.001
Hemoglobin A1c,%	5.7 ± 0.7	5.7 ± 0.7	5.8 ± 0.8	5.9 ± 0.9	<0.001
LDL-C, mg/dL	110 ± 27	122 ± 28	128 ± 29	125 ± 33	<0.001
HDL-C, mg/dL	73 ± 15	60 ± 11	53 ± 10	45 ± 9	<0.001
TG, mg/dL	64 ± 16	95 ± 19	131 ± 27	242 ± 131	<0.001
TG/HDL-C	0.91 ± 0.23	1.60 ± 0.20	2.51 ± 0.34	5.61 ± 3.69	<0.001
Hypertension, %	45.3	50.9	53.7	55.5	<0.001
Diabetes mellitus, %	12.4	14.0	15.9	20.4	<0.001
Obesity, %	15.8	27.0	35.6	45.6	<0.001
Current smoker, %	19.1	23.2	25.9	32.8	<0.001
Daily drinker, %	52.1	45.5	41.4	40.5	<0.001
Regular exercise, %	53.3	49.7	46.4	40.8	<0.001
History of stroke, %	4.9	5.6	5.5	5.1	0.41
History of heart disease, %	7.9	8.5	9.0	7.8	0.95
Medication for hypertension, %	29.5	34.5	37	35.8	<0.001
Medication for diabetes mellitus, %	7.1	7.3	7.4	8.1	<0.001
Medication for dyslipidemia, %	9.2	12.8	14.6	15.1	<0.001

(B) Women

	TG/HDL-C				*P* for trend
	Q_1	Q_2	Q_3	Q_4	
	<0.96	0.96–1.44	1.45–2.22	>2.22	
	(n = 31,894)	(n = 31,817)	(n = 31,918)	(n = 31,862)	
Age, years	61.7 ± 9.7	63.7 ± 8.5	64.7 ± 7.7	64.9 ± 7.5	<0.001
Body mass index, kg/m^2	21.2 ± 2.9	22.3 ± 3.2	23.3 ± 3.4	24.3 ± 3.5	<0.001
Waist circumference, cm	77.8 ± 9.1	81.6 ± 9.4	84.3 ± 9.4	86.8 ± 9	<0.001
Systolic blood pressure, mmHg	124 ± 18	127 ± 17	129 ± 17	131 ± 17	<0.001
Diastolic blood pressure, mmHg	73 ± 11	74 ± 10	75 ± 10	76 ± 10	<0.001
Fasting blood glucose, g/dL	92 ± 14	94 ± 16	96 ± 17	99 ± 22	<0.001
Hemoglobin A1c, %	5.6 ± 0.5	5.7 ± 0.5	5.7 ± 0.6	5.9 ± 0.7	<0.001
LDL-C, mg/dL	118 ± 27	128 ± 28	135 ± 30	138 ± 32	<0.001
HDL-C, mg/dL	82 ± 15	70 ± 11	62 ± 10	51 ± 9	<0.001
TG, mg/dL	57 ± 13	82 ± 15	109 ± 20	180 ± 74	<0.001
TG/HDL-C	0.71 ± 0.16	1.18 ± 0.14	1.78 ± 0.22	3.66 ± 1.97	<0.001
Hypertension, %	31.5	40.1	46.3	53.0	<0.001
Diabetes mellitus, %	4.8	6.5	8.9	13.4	<0.001
Obesity, %	9.7	18.3	27.3	36.8	<0.001
Current smoker, %	5.1	5.2	5.7	7.5	<0.001
Daily drinker, %	12	8.6	6.6	5.9	<0.001
Regular exercise, %	40.5	40.3	40	38.5	<0.001
History of stroke, %	2.2	2.7	3.1	3.3	<0.001
History of heart disease, %	4.2	5.2	5.3	6.0	<0.001
Medication for hypertension, %	19.6	26.6	32.4	37.5	<0.001
Medication for diabetes mellitus, %	2.7	3.4	4.2	6.1	<0.001
Medication for dyslipidemia, %	17	21.9	25.8	27	<0.001

Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or self-reported use of antihypertensive drugs. Diabetes was defined in accordance with American Diabetes Association guidelines as a fasting glucose concentration of ≥126 mg/dL, hemoglobin A1c concentration of ≥6.5%, or self-reported use of antihyperglycemic drugs. TG/HDL-C was calculated as TG (mg/dL) divided by HDL-C (mg/dL).
Abbreviations: LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

2.4. Statistical analyses

Independent two-tailed *t*-tests and chi-square tests were used for the analysis of continuous and categorical variables, respectively. We used a linear regression model to compare the mean values of possible risk factors between the quartile groups in each gender. The age- or multivariate-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for CKD, low eGFR, and proteinuria were determined by logistic regression model adjusted for potential confounding covariates. The confounding covariates used for adjustment included waist circumference, hypertension, obesity, diabetes, a current smoking habit, daily alcohol consumption, regular exercise habits, history of stroke and heart disease, and medication for dyslipidemia. We tested for heterogeneity in the relationship between subgroups by adding a multiplicative interaction term in our statistical model. All statistical analyses were

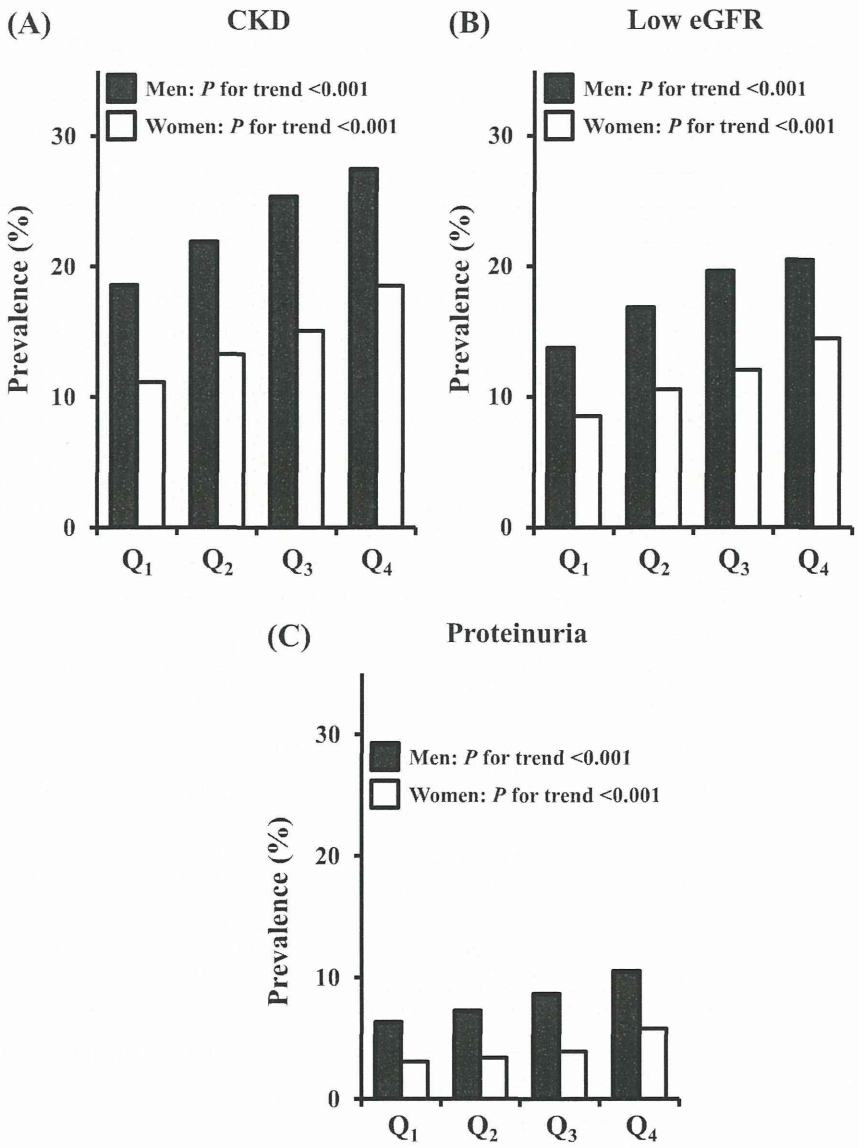

Fig. 1. The prevalence of CKD, low eGFR and proteinuria in participants with different TG/HDL-C. The prevalence of CKD (A), low eGFR (B) and proteinuria (C) increased as TG/HDL-C in men (closed bars) and women (open bars) increased. Low eGFR was defined as eGFR <60 mL/min/1.73 m^2. Proteinuria was defined as urinary protein value of ≥1+ as measured by dipstick testing. CKD was defined as a low eGFR and/or proteinuria. Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; TG/HDL; triglycerides/high-density lipoprotein cholesterol.

performed with JMP version 9.0 software (SAS Institute, Inc., Cary, NC, USA).

3. Results

Table 1 shows the characteristics of the 216,007 participants (88,516 men and 127,491 women). The mean age of men and women was similar. Compared with women, a significantly higher percentage of men had proteinuria (as indicated by a value of ≥1+ on dipstick testing) and CKD. The mean serum levels of LDL-C and HDL-C, and the percentage of participants who took medication for dyslipidemia in women were significantly higher than those in men.

Table 2 shows the mean values or frequencies of potential risk factors in the quartile groups for men (Table 2A) and women (Table 2B). The frequency of hypertension, diabetes mellitus, obesity, a current smoking habit, and medication for hypertension, diabetes, and dyslipidemia also increased with higher TG/HDL-C levels in both genders. On the other hand, the mean values for HDL-C level as well as the frequencies for daily alcohol consumption and regular exercise habits decreased in both men and women. We observed opposite trends with regards to the association between age and TG/HDL-C; there was an inverse association between age and TG/HDL-C among men and a positive association between age and TG/HDL-C among women.

Fig. 1 presents the prevalence of CKD, low eGFR, and proteinuria among men and women according to TG/HDL-C levels. The prevalence of CKD increased 1.5–fold higher in the highest TG/HDL-C quartile group than in the lowest group in men (18.6% in Q_1, 21.9% in Q_2, 25.4% in Q_3, and 27.5% in Q_4, P for trend <0.001) and doubled in women (11.1%, 13.3%, 15.1%, and 18.5%, respectively, P for trend <0.001). Similar trends in the prevalence of low eGFR and proteinuria were also observed in both genders.

The age-adjusted or multivariate-adjusted ORs and 95% CIs for the presence of CKD, low eGFR, and proteinuria according to TG/HDL-C levels are shown in Table 3. The age-adjusted ORs for CKD,