Table 5 Multivariate analysis of the relationship between weight gain after 20 years of age and the prevalence of chronic kidney disease in subgroups

Gender and subgroup	Number of participants	Odds ratio (95% CI)	*p* value
Women			
Body mass index (kg/m^2)			
<25	22,363	1.13 (0.99–1.27)	0.06
25+	5,788	1.08 (0.88–1.33)	0.44
Waist circumference (cm)			
<90	23,656	1.15 (1.03–1.29)	0.01
90+	4,495	1.23 (0.97–1.55)	0.08
Metabolic syndrome[a]			
No	26,218	1.15 (1.03–1.28)	<0.0001
Yes	1,933	1.55 (1.04–2.31)	0.03
Men			
Body mass index (kg/m^2)			
<25	13,500	1.00 (0.87–1.14)	0.98
25+	7,610	0.90 (0.76–1.07)	0.24
Waist circumference (cm)			
<85	10,247	0.94 (0.79–1.12)	0.50
85+	10,863	1.05 (0.91–1.20)	0.50
Metabolic syndrome[a]			
No	10,979	1.24 (1.07–1.43)	0.01
Yes	10,131	1.04 (0.92–1.18)	0.50

Models adjusted for age, smoking, regular exercise, alcohol intake, history of kidney disease, place of residence, hypertension, diabetes, and hypercholesterolemia

[a] Defined as abdominal obesity (waist circumference ≥90 cm for women and ≥85 cm for men) plus any two of the following three categories: (1) fasting blood glucose ≥100 mg/dl, and/or hemoglobin A_{1c} ≥ 5.2%, and/or the use of insulin, and/or oral antidiabetic medication; (2) triglycerides ≥150 mg/dl, and/or high-density lipoprotein cholesterol <40 mg/dl, and/or cholesterol-lowering medication; and (3) blood pressure ≥130/85 mmHg, and/or use of antihypertensive medication

Table 6 Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of three weight indicators for detecting chronic kidney disease

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Women				
Weight gain after 20 years	0.38 (0.36–0.40)	0.71 (0.70–0.71)	0.12 (0.11–0.13)	0.92 (0.91–0.92)
Body mass index	0.29 (0.27–0.31)	0.80 (0.80–0.81)	0.13 (0.12–0.14)	0.92 (0.91–0.92)
Waist circumference	0.23 (0.22–0.25)	0.85 (0.84–0.85)	0.14 (0.13–0.15)	0.91 (0.91–0.92)
Men				
Weight gain after 20 years	0.57 (0.55–0.59)	0.51 (0.51–0.52)	0.12 (0.12–0.13)	0.91 (0.90–0.91)
Body mass index	0.49 (0.47–0.52)	0.66 (0.65–0.66)	0.15 (0.14–0.16)	0.92 (0.91–0.92)
Waist circumference	0.63 (0.61–0.65)	0.50 (0.49–0.51)	0.13 (0.13–0.14)	0.92 (0.91–0.92)

CI confidence interval

Our study had several limitations. First, the actual body weight gain could not be confirmed, but bias resulting from this factor is not likely because body weight gain is easy to measure. Second, CKD was defined from a single creatinine value and measurements of creatinine can vary among different laboratories. In addition, a single measurement of urinary protein was used because of the nature of an annual health check program. Therefore, it is not possible in this study to confirm whether participants fulfilled CKD criteria for at least a 3-month period. Finally, this was a cross-

sectional study, which makes it difficult to establish causal relationships. Further longitudinal investigations will be needed to clarify whether weight gain after maturity is an independent factor in the development of CKD.

Despite these limitations, there were several strengths to our study. As far as we know, this is the first report about weight gain after maturity and CKD among women from the general population. Our study also had a large sample size, which allowed us to perform stratified subgroup analyses.

Conclusions

Weight gain ≥10 kg after maturity was independently associated with the prevalence of CKD among the Japanese population, even those without metabolic syndrome. Because weight gain is more easily understood by the general population than BMI and can be more accurately measured than waist circumference, advice to limit weight gain to <10 kg after 20 years of age is recommended to avoid an obesity-related increase in the risk of CKD, particularly for women.

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Conflict of interest The authors have declared that no conflict of interest exists.

Appendix

When the participants with a history of kidney disease were excluded, weight gain was independently associated with CKD in both genders (Tables 7 and 8).

Table 7 Multivariate analysis of the relationship between weight gain after 20 years of age and the prevalence of chronic kidney disease among women without history of kidney disease (n = 28,026)

Variable	Age-adjusted (95% CI)	Model 1[a] Odds ratio (95% CI)	Model 2[b] Odds ratio (95% CI)
Weight gain after 20 years			
<10 kg (ref)	1.00	1.00	1.00
≥10 kg	1.43 (1.31–1.55)	1.42 (1.30–1.54)	1.25 (1.14–1.36)
Age			
40–44 (ref)	1.00	1.00	1.00
45–49	1.21 (1.01–1.45)	1.20 (1.00–1.43)	1.14 (0.95–1.36)
50–54	2.04 (1.74–2.40)	2.04 (1.74–2.39)	1.81 (1.53–2.12)
55–59	2.39 (2.06–2.76)	2.38 (2.05–2.76)	1.99 (1.70–2.32)
Current smoker			
No (ref)		1.00	1.00
Yes		1.05 (0.92–1.19)	1.06 (0.93–1.20)
Regular exercise			
No (ref)		1.00	1.00
Yes		1.14 (1.04–1.25)	1.13 (1.04–1.24)
Alcohol intake			
Every day (ref)		1.00	1.00
Sometimes		1.05 (0.91–1.22)	1.06 (0.91–1.22)
Little or never		1.15 (1.01–1.31)	1.14 (1.00–1.30)
Hypertension[c]			
No (ref)			1.00
Yes			1.54 (1.29–1.75)
Diabetes mellitus[d]			
No (ref)			1.00
Yes			1.50 (1.40–1.69)
Hypercholesterolemia[e]			
No (ref)			1.00
Yes			1.16 (1.06–1.26)

[a] Model 1 is adjusted for age, current smoking, regular exercise, alcohol intake, and place of residence

[b] Model 2 is adjusted for the variables in model 1 plus hypertension, diabetes, and hypercholesterolemia

[c] Defined as the use of antihypertensive medication, a systolic blood pressure of ≥140 mmHg, and/or a diastolic blood pressure ≥90 mmHg, or both

[d] Defined as the use of insulin or oral antidiabetic medication, a fasting serum glucose level ≥126 mg/dl, or both

[e] Defined as the use of cholesterol-lowering medication, a low-density lipoprotein cholesterol level ≥140 mg/dl, or both

Table 8 Multivariate analysis of the relationship between weight gain after 20 years of age and the prevalence of chronic kidney disease among men without history of kidney disease (n = 21,027)

Variable	Age-adjusted (95% CI)	Model 1[a] Odds ratio (95% CI)	Model 2[b] Odds ratio (95% CI)
Weight gain after 20 years			
<10 kg (ref)	1.00	1.00	1.00
≥10 kg	1.37 (1.25–1.50)	1.34 (1.23–1.47)	1.15 (1.05–1.26)
Age			
40–44 (ref)	1.00	1.00	1.00
45–49	1.29 (1.11–1.51)	1.31 (1.12–1.53)	1.20 (1.03–1.41)
50–54	1.41 (1.22–1.64)	1.47 (1.26–1.71)	1.22 (1.05–1.42)
55–59	1.80 (1.57–2.06)	1.86 (1.62–2.14)	1.43 (1.24–1.64)
Current smoker			
No (ref)		1.00	1.00
Yes		1.06 (0.96–1.16)	1.05 (0.96–1.16)
Regular exercise			
No (ref)		1.00	1.00
Yes		1.05 (0.95–1.15)	1.03 (0.93–1.14)
Alcohol intake			
Every day (ref)		1.00	1.00
Sometimes		1.20 (1.08–1.35)	1.24 (1.10–1.39)
Little or never		1.40 (1.26–1.56)	1.48 (1.32–1.65)
Hypertension[c]			
No (ref)			1.00
Yes			2.04 (1.85–2.24)
Diabetes mellitus[d]			
No (ref)			1.00
Yes			2.00 (1.78–2.25)
Hypercholesterolemia[e]			
No (ref)			1.00
Yes			1.24 (1.13–1.36)

[a] Model 1 is adjusted for age, current smoking, regular exercise, alcohol intake, and place of residence

[b] Model 2 is adjusted for the variables in model 1 plus hypertension, diabetes, and hypercholesterolemia

[c] Defined as the use of antihypertensive medication, a systolic blood pressure ≥140 mmHg, and/or a diastolic blood pressure ≥90 mmHg, or both

[d] Defined as the use of insulin or oral antidiabetic medication, a fasting serum glucose level ≥126 mg/dl, or both

[e] Defined as the use of cholesterol-lowering medication, a low-density lipoprotein cholesterol level ≥140 mg/dl, or both

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ORIGINAL ARTICLE

Risk factor profiles based on estimated glomerular filtration rate and dipstick proteinuria among participants of the Specific Health Check and Guidance System in Japan 2008

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Abstract
Background Estimated glomerular filtration rate (eGFR) and albuminuria (proteinuria) are both important determinants of the risk of cardiovascular disease (CVD), end-stage renal disease (ESRD), and mortality. Few studies, however, have examined the risk factor profiles based on eGFR and proteinuria among the general population.
Methods Data of the newly developed nationwide screening program of the Specific Health Check-up and Guidance System (Tokutei-Kensin) initiated in 2008 were used in this study. The aim of this screening, targeting people 40–74 years of age, was to detect those with metabolic syndrome and to offer those services regarding lifestyle modifications that will lead to the reduction of diabetes mellitus (DM) and DM-related ESRD. Individual records of 580,000 participants in 69 cities and towns and 3 union cohorts throughout Japan were anonymously provided and included in the present study.
Results Details of 332,174 participants (57.3% of the total) with both serum creatinine and dipstick urine test data were analyzed. Mean (SD) age was 63.6 (8.3) years and 40.6% were men. The mean (SD) eGFR was 75.0 (16.2) ml/min/1.73 m^2 and 5.4% had proteinuria. The prevalence of chronic kidney disease (CKD) stage 3, 4, and 5 was 14.2%, 0.2%, and 0.07%, respectively. The prevalence of DM, hypertension, and history of stroke and heart disease was correlated with the combination of eGFR and degree of proteinuria.
Conclusion The findings of the present study indicate that CKD and risk factors for CVD are quite common among middle-aged Japanese. CKD classification based on eGFR and proteinuria may be useful for predicting CVD, mortality rate, and ESRD in the Japanese population.

Keywords eGFR · CKD · Screening · Proteinuria · Epidemiology

Introduction

Chronic kidney disease (CKD) is a common condition and is a risk factor for developing cardiovascular disease (CVD) and end-stage renal disease (ESRD) [1]. Both the prevalence and incidence of treated ESRD are very high in Japan [2]. Furthermore, the incidence and prevalence continue to increase, despite several preventive strategies aimed at early detection and treatment of CKD. Japan has a long history of universal screening, a program that might facilitate the early detection of CKD [3]. A higher mean age at the start of dialysis can be interpreted as delaying the progression of CKD, but it may also simply reflect the increase in the elderly population and longevity. Dipstick proteinuria is a strong predictor of developing ESRD in a setting of community-based screening [4]. Delayed visits to the nephrology clinic result in an inevitable initiation of

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dialysis with a short duration of follow-ups [5, 6]. Such 'late referral' negatively impacts survival after dialysis is initiated. Preliminary results of the Japanese Society Dialysis Therapy support the notion that the longer the duration of pre-ESRD treatment, the better the survival. Because CKD remains asymptomatic until the late stages, effective strategies for the early detection and treatment of CKD are necessary.

The increasing prevalence of obesity and diabetes mellitus (DM) has become the leading cause of ESRD. A specific nationwide health check-up and guidance system, called Tokutei-Kenshin, was initiated in April 2008 in Japan (The Ministry of Health, Labour and Welfare; http://www-admin@.mhlw.go.jp). The aim of this project is to detect metabolic syndrome and if confirmed, to provide individual instruction to modify lifestyle and the necessary treatment. The target population comprises Japanese citizens between the ages of 40–74 years. Data on the prevalence of risk factors for developing CKD, ESRD, and CVD are limited to the Japanese population. In the present study, we examined the demographics of participants of the newly developed screening system in Japan. Risk factor profiles were examined according to the new CKD classification based on the combination of estimated glomerular filtration rate (eGFR) and dipstick proteinuria findings [7]. Results of dipstick proteinuria were categorized into three groups: (−) and (±), 1+, and ≥2+. The present study provides the baseline characteristics for the future outcome study as the unique identification number was set by the government.

Methods

Individual records for 580,000 participants in 12 communities or prefectures were anonymously provided and included in this analysis. Among these participants, subjects with data for both serum creatinine and dipstick proteinuria were selected for this study. A test was mandatory for dipstick proteinuria, but not for serum creatinine. Therefore, rates of measurement of serum creatinine differ among cohorts or prefectures. Databases included in this study were from Yamagata, Miyagi, Fukushima, Ibaraki, Tokyo, Kanagawa, Niigata, Osaka, Okayama, Kochi, Fukuoka, Miyazaki and Okinawa, and ethical approval was obtained from the respective institute review boards. Data were sent to a data center called the NPO Japan Clinical Research Support Unit to be verified. Outliers were deleted through winsorization and accounted for 0.01–0.1% of the total. Eligible participants visited a pre-assigned clinic or hospital and responded to a questionnaire regarding past history of stroke, cardiac disease, kidney disease, lifestyle habits such as smoking, alcohol intake, walking, etc., and medications for hypertension, DM, and dyslipidemia. Screening participants are eligible for public support for the standard health checks, such as measurement of height, weight, waist circumference, blood pressure, fasting blood glucose, hemoglobin A1c, triglyceride, serum high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, glutamyl oxaloacetic transaminase, glutamate pyruvate transaminase, gamma-glutamyl transpeptidase, hemoglobin, uric acid, serum creatinine, dipstick urine test for proteinuria, hematuria, and glucosuria. Proteinuria was coded as (−), (±), (1+), (2+), and (3+). Serum creatinine was measured using the enzymatic method. Glomerular filtration rate was calculated using the formula of the Japanese Society of Nephrology [8]. Reference levels for triglyceride, HDL cholesterol, LDL cholesterol, uric acid, fasting blood glucose, and hemoglobin A1c were set at 150, 40, 7, 110 mg/dl, and 6.1%, respectively. Blood pressure was measured in all cohorts using a standard sphygmomanometer. Hypertension was defined as ≥140/90 mmHg or on antihypertensive medication. DM was defined as hemoglobin A1c ≥6.1% or on medication for DM. Obesity was defined as body mass index (BMI) ≥25 kg/m^2.

Statistical analysis

Data were analyzed with SAS/STAT software (version 6.03, SAS Institute, Tokyo, Japan). Student's *t* test and the Chi-squared test were performed to compare the significance of discrete variables. A *P* value of less than 0.05 was considered statistically significant in all analyses.

Results

Demographics of the screened subjects are summarized in Table 1. The prevalence of CKD (i.e., eGFR <60 ml/min/1.73 m^2) was as high as 14.2%. Compared to national statistics, smoking rates were lower in both men and women than in the general population. Those with low eGFR comprised 14.2% and proteinuria was distributed as follows: negative and ± 94.55%, 1+ 3.75%, and ≥2+ 1.7%.

The prevalence of obesity, DM, and hypertension is summarized based on the results of eGFR and proteinuria in Table 2. The prevalence of obesity, DM, and hypertension increased in relation to the degree of proteinuria in each eGFR group. Higher levels of proteinuria together with lower levels of eGFR were associated with an increased prevalence of hypertension (Fig. 1).

History of stroke, heart disease, and CVD (either stroke or heart disease) is summarized in Table 3. The prevalence of CVD was highest (25.2%) in those with proteinuria of (1+) and an eGFR of 15–29 ml/min/1.73 m^2, and the prevalence was lowest (6.1%) in those negative and ± for

Table 1 Demographics of the screened cohorts. Screening was performed during April 1, 2008 to March 31, 2009

Number of participants	332,174		
Men (%)	134,751 (40.6)		
Age (years)	63.6 (8.3), 40–74		
Body height (cm)	157.2 (8.5)	Men 164.6 (6.3)[#]	Women 152.2 (5.7)
Body weight (kg)	57.6 (10.5)	Men 64.5 (9.5)[#]	Women 52.8 (8.3)
Body mass index (kg/m^2)	23.2 (3.3)	Men 23.8 (3.1)[#]	Women 22.8 (3.5)
Waist circumference (cm)	84.1 (9.2)	Men 85.7 (8.3)[#]	Women 83 (9.5)
Systolic blood pressure (mmHg)	128.9 (17.4)		
Diastolic blood pressure (mmHg)	76.3 (10.7)		
Fasting blood glucose (mg/dl)	98.2 (21.5)		
Hemoglobin A1c (%)	5.3 (0.7)		
Triglyceride (mg/dl)	122.5 (84.0)		
HDL cholesterol (mg/dl)	62.1 (16.3)		
LDL cholesterol (mg/dl)	125.9 (30.6)		
Hemoglobin (g/dl)	13.6 (1.4)		
Serum creatinine (mg/dl)	0.7 (0.2)	Men 0.8 (0.3)[#]	Women 0.6 (0.2)
eGFR (ml/min/1.73 m^2)	75.0 (16.2)		
<15	240 (0.07%)		
15–29	655 (0.20%)		
30–44	4,300 (1.29%)		
45–59	42,975 (12.94%)		
60–89	225,081 (67.76%)		
≥90	58,923 (17.74%)		
Serum uric acid (mg/dl)	5.2 (1.4)	Men 6.0 (1.3)[#]	Women 4.7 (1.1)
Glucosuria[a]	2.30%		
Proteinuria[a]	5.40%		
Hematuria[a]	7.50%		
Past history (%)			
Stroke	3.30		
Cardiac disease	6.00		
Kidney disease	0.70		
Medication (%)			
Anti-hypertensive drugs	28.80		
Lipid lowering drugs	15.80		
Insulin or hypoglycemic drugs	5.20		
Lifestyle (%)			
Smoking	13.50	Men 25.2%[#]	Women 5.5%
Drinking	44.30	Men 65.2%[#]	Women 30.0%

Data are mean (SD)

[a] Positive urine test denote ≥1+ by dipstick

[#] $P < 0.01$ (vs women)

proteinuria and having an eGFR ≥90 ml/min/1.73 m^2. The combination of higher levels of proteinuria and lower levels of eGFR was associated with an increased prevalence of a history of CVD (Fig. 2).

Mean (SD) levels of BMI and smoking rate are summarized in Table 4. Both BMI and smoking rate were higher in men than in women. The smoking rate tended to decrease in the lower eGFR category.

Discussion

The target population of this screening in Japan comprised participants from 40 to 74 years of age, and the expected turnout was approximately 58 million. In the 2008 screening, the actual participation rate remained low, 20–30%, probably because of the lack of preparation for implementing this new system. The total number of participants in the present study was approximately 0.58 million; therefore, our analysis included at least 1% of the target population in Japan.

The results revealed the current health status among the general Japanese population. The proportion of the population comprising elderly people is high in Japan and its rate of increase is currently the highest in the world. The proportion of those with a low GFR (<60 ml/min/1.73 m^2), regardless of proteinuria, increases with aging. Fortunately, the rate of decline of the GFR in the Japanese is relatively low, 0.36 ml/min/1.73 m^2/year [9]. Elderly people are at risk for CVD and death. Effective strategies to establish a health check and guidance system are necessary to better accommodate the future burden of medical and social costs due to the aging population. Based on the findings of the present study, we propose that a cost–benefit analysis be performed on programs designed for the early detection and treatment of CKD, including education regarding lifestyle modification.

CVD is a recently recognized risk factor for CKD and ESRD [7]. The prevalence of CVD in CKD stage 5 is

Table 2 Prevalence of obesity, DM, and hypertension based on the combination of eGFR and proteinuria

eGFR	Proteinuria	Number (%)	Obesity (%)	DM (%)	Hypertension (%)
<15	Minus, ±	101 (0.03)	22.8	10.2	50.5#
	1+	35 (0.01)	28.6	17.6	88.6*
	≥2+	103 (0.03)	31.1	32.0*	92.2*
15–29	Minus, ±	251 (0.08)	29.1	25.2*	81.1*
	1+	119 (0.04)	31.1	22.7*	85.5*
	≥2+	285 (0.09)	40.3*	38.4*	91.9*
30–44	Minus, ±	3,194 (0.96)	35.8*	13.9*	68.2*
	1+	504 (0.15)	43.8*	24.9*	83.3*
	≥2+	579 (0.17)	46.5*	33.9*	85.9*
45–59	Minus, ±	39,265 (11.82)	30.7*	9.3*	52.7*
	1+	2,408 (0.72)	42.2*	19.6*	71.6*
	≥2+	1,326 (0.40)	49.5*	31.1*	80.2*
60–89	Minus, ±	214,768 (64.66)	25.4*	8.4*	43.3*
	1+	7,579 (2.28)	38.5*	19.3*	62.1*
	≥2+	2,703 (0.81)	46.5*	31.1*	72.0*
≥90	Minus, ±	56,495 (17.01)	24.3	10.6	39.8
	1+	1,812 (0.55)	37.9*	26.5*	57.4*
	≥2+	647 (0.19)	46.5*	36.4*	72.0*

Total number of participants was 332,174. Parentheses are the percentage to the total participants in each column. Obesity, BMI ≥25 kg/m^2; DM, HbA1c ≥6.1% or on treatment; hypertension, 140/90 mmHg or on treatment

* $P < 0.0001$, # $P < 0.05$ (vs. reference value of eGFR ≥90 and proteinuria minus or ±)

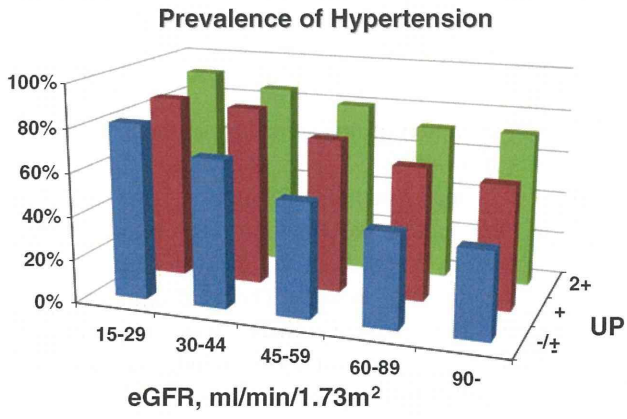

Fig. 1 Prevalence of hypertension by the combination of eGFR and proteinuria. Prevalence of hypertension was significantly ($P < 0.0001$) higher in every column except those with eGFR 15–29 and proteinuria minus or (±) ($P < 0.05$) when compared to the reference value of eGFR ≥90 and proteinuria minus or (±)

Table 3 Prevalence of history of stroke and heart disease based on the combination of eGFR and proteinuria

eGFR	Proteinuria	Stroke	Heart Disease	CVD
<15	Minus, ±	4.0	6.9	10.9*
	1+	5.7	17.1*	22.9
	≥2+	8.7*	12.6	19.4#
15–29	Minus, ±	13.9*	15.9*	25.1*
	1+	15.1*	15.1*	25.2*
	≥2+	11.6*	13.7*	22.5*
30–44	Minus, ±	8.6*	13.1*	19.2*
	1+	9.9*	16.1*	22.4*
	≥2+	10.5*	16.4*	23.7*
45–59	Minus, ±	4.8*	8.5*	12.3*
	1+	6.9*	11.7*	16.2*
	≥2+	8.3*	13.1*	19.2*
60–89	Minus, ±	3.0*	5.6*	8.1*
	1+	4.7*	7.3*	11.1*
	≥2+	5.8*	9.3*	13.8*
≥90	Minus, ±	2.4	4.1	6.1
	1+	3.5†	6.0*	8.8*
	≥2+	4.5†	4.6	8.5†

Total number of participants was 332,174. Cardiovascular disease (CVD) denotes stroke and/or heart disease

* $P < 0.0001$, † $P < 0.02$, # $P < 0.05$ (vs reference value of eGFR ≥90 and proteinuria minus or ±)

approximately 25%; similar to the prevalent dialysis population. Ethnic variations in CVD incidence and subtype are well described in the general population [10, 11]. The stroke mortality rate is high in Japan; however, in the present study, the prevalence of stroke was lower than that of cardiac disease (Table 1). The reasons for this finding are not clear, but many people with stroke are unable to participate in this type of screening program.

Metabolic syndrome is an important risk factor for developing CKD [12], and for DM and hypertension, which are the main causes of ESRD [13]. We previously reported the significance of obesity in the risk for ESRD. Recent societal changes in lifestyle related to motorized transportation and high-calorie intake may have contributed to the

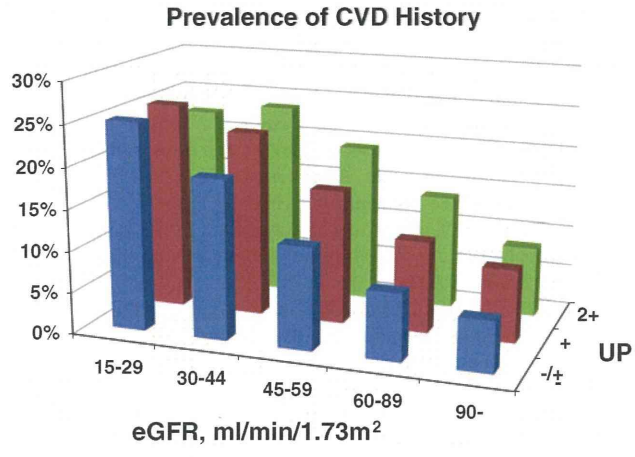

Fig. 2 Prevalence of history of cardiovascular disease (*CVD*) by the combination of eGFR and proteinuria. Prevalence of CVD was significantly ($P < 0.0001$) higher in every column except those with eGFR 15–29; not significant for proteinuria (+), and $P < 0.05$ for proteinuria ≥2+, when compared to the reference value of eGFR ≥90 and proteinuria minus or (±). *P* value was <0.02 for those with eGFR ≥90 and proteinuria ≥2+

Table 4 Mean (SD) levels of body mass index (BMI) and smoking rate in each sex based on the combination of eGFR and proteinuria

eGFR	Proteinuria	Men		Women	
		BMI (kg/m^2)	Smoker (%)	BMI (kg/m^2)	Smoker (%)
<15	Minus, ±	24.1 (2.6)	5.4	22.2 (3.0)	10.9
	1+	24.2 (2.4)	12.5	22.0 (3.4)	5.3
	≥2+	23.3 (2.8)	22.2	24.5 (4.7)	2.5
15–29	Minus, ±	23.6 (3.1)	15.0	23.6 (4.1)	8.0
	1+	24.5 (3.4)	7.0	23.5 (3.8)	6.5
	≥2+	24.2 (3.1)	18.4	25.3 (4.7)	6.0
30–44	Minus, ±	24.3 (2.9)	15.3	23.7 (3.8)	4.4
	1+	24.8 (3.5)	19.5	24.2 (4.5)	6.6
	≥2+	25.2 (3.2)	19.5	24.9 (4.4)	5.9
45–59	Minus, ±	24.1 (2.8)	15.8	23.2 (3.4)	3.9
	1+	24.7 (3.0)	20.6	24.2 (4.2)	5.7
	≥2+	25.2 (3.5)	24.9	25.1 (4.4)	5.7
60–89	Minus, ±	23.7 (3.0)	24.4	22.7 (3.4)	5.1
	1+	24.5 (3.4)	29.4	23.9 (4.3)	6.8
	≥2+	25.1 (3.8)	31.2	24.8 (4.8)	8.1
≥90	Minus, ±	23.4 (3.4)	38.8	22.7 (3.6)	7.2
	1+	24.2 (4.0)	46.5	24.2 (4.5)	8.3
	≥2+	25.0 (4.2)	39.5	25.0 (5.0)	9.4

Total number of participants was 332,174

SD standard deviation

increased prevalence of obesity. Although the prevalence of obesity (BMI ≥30 kg/m^2) is lower in Japan than in the USA [14], complications begin to increase in the Japanese after reaching a BMI of 25 kg/m^2.

Microalbuminuria is suspected when the dipstick test results for proteinuria are (±) and/or 1+ [15]. Routine measurement of microalbuminuria is not feasible for the universal screening of CKD, as the cost is much higher than that of a dipstick urine test for proteinuria. Japan has a long history of universal screening, including dipstick urine testing for both proteinuria and hematuria. A positive proteinuria test result has a strong predictive value for the development of ESRD.

The strengths of the present study are: the number of participants was sufficiently large. It is the first nationwide targeted screening program aimed at determining the prevalence of metabolic syndrome in Japan. People diagnosed with metabolic syndrome are entitled to receive instruction to modify their lifestyles and therefore the risk factors for CKD and CVD can be modified accordingly. The prevalence of metabolic syndrome and obesity, particularly in men, is increasing; therefore, the prevalence of CKD is increasing in Japan [16].The combined eGFR and dipstick proteinuria test results indicate that the prevalence of risk factors for CKD and CVD increasing. Future follow-up studies will provide the predictive value of this CKD stratification on CVD, ESRD, and mortality.

The present study has several limitations. It is a cross-sectional study. Single tests for dipstick proteinuria and serum creatinine might cause misclassification of the true prevalence of CKD. To confirm the existence of CKD, the test should be repeated annually, at least 3 months apart. The current estimation of GFR used in this study is precise (<60 ml/min/1.73 m^2); therefore, the proportion of those with moderately decreased GFR (<45 ml/min/1.73 m^2) seems to be high, 1.56%. We selected patients with data for both serum creatinine and dipstick urine test, which comprised approximately two-thirds of the total participants. A cost–benefit analysis on the best combination of screening tests remains to be performed in Japan. Details of CVD, such as subtype of stroke and heart disease, are not clear. Risk factors may differ among diseases. Information of past medical history, medications, and lifestyle were obtained from a questionnaire, which has not yet been validated. Finally, the elderly population, those aged ≥75 years, was not considered in the present screening. It remains to be determined whether or not risk stratification based on both eGFR and proteinuria is applicable in this age group. CKD also has a role in medical problems commonly seen in elderly people, such as malignancies, pneumonia, sepsis, dementia, and bone fractures.

In conclusion, the risk profiles of CKD and CVD are indicated by the new CKD classification based on eGFR and proteinuria levels in the newly developed screening system used in Japan. Although CKD stratification based on the combined eGFR and proteinuria results seems to be a useful predictor of CVD and mortality in the general

population in Japan, the validity of this finding has yet to be demonstrated in outcome studies, and would be useful for the international comparison of the incidence of ESRD [17].

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Conflict of Interest None.

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●一般演題 1-5

慢性腎臓病(CKD)におけるメタボリックシンドローム(MetS)・脂質異常症の実態と意義
－特定健診受診者コホートにおける横断的解析－

旭　浩一[1]・井関邦敏[2]・鶴屋和彦[3]・山縣邦弘[4]
守山敏樹[5]・藤元昭一[6]・吉田英昭[7]・渡辺　毅[1]

1 背　景

これまでのコホート研究結果から，メタボリックシンドローム(MetS)は慢性腎臓病(CKD)の発症要因であること，CKDではMetSに類似の脂質異常(高中性脂肪(TG)血症，低HDL-コレステロール(HDL-C)血症，small dense LDLやレムナントなど質的に異常なリポ蛋白の増加)が存在し，心血管イベント(CVD)発症(心腎連関)との関連が示唆されている。しかし，全国的規模の一般住民レベルでのCKDにおけるMetSと脂質異常の実態およびそれらの相互関連の研究はない。

2 方　法

全国69自治体国保・3健保組合のコホート群から平成20年度の約58万人分の特定健康診査(特定健診)データを収集，血清Cr値が測定された332,174名について日本人の推定GFR推算式[1]に基づくeGFRと試験紙法による尿蛋白レベルで層別化し，血清脂質異常との関連を横断的に解析した。また，各保険者(国保)において特定健診データに基づいてMetS(該当群，予備群，非該当群)ならびに特定保健指導レベルが判定された65,476名につき，CKDステージとの関連を検討した。

MetSの判定は内臓脂肪蓄積(腹囲：男性85cm，女性90cm以上)を満たし，追加リスクすなわち①血糖(空腹時血糖値110mg/dL以上，HbA1c(JDS)5.5%以上，糖尿病に対する薬剤治療中のいずれかに該当)，②脂質(TG 150mg/dL以上，HDL-C 40mg/dL未満，脂質異常症に対する薬剤治療中のいずれかに該当)，③血圧(収縮期血圧130mmHg以上，拡張期血圧85mmHg以上，高血圧症に対する薬剤治療中のいずれかに該当)のうち2項目以上満たす者を該当者，1項目を満たす者を予備群，いずれも当てはまらない者ならびに追加リスクに当てはまっても内臓脂肪蓄積のない者を非該当者とした。

特定保健指導レベルは，標準的な健診・保健指導プログラム(確定版)(平成19年4月厚生労働省健康局http://www.mhlw.go.jp/bunya/shakaihosho/iryouseido01/info03a. html)に基づき，内臓脂肪蓄積(腹囲：男性85cm，女性90cm以上または上記以外でBMI 25kg/m^2以上)，追加リスク①血糖(空腹時血糖値100mg/dL以上，HbA1c(JDS)5.2%以上，糖尿病に対す

Koichi Asahi, *et al.*：Metabolic syndrome and dyslipidemia in a population with chronic kidney disease: a cross-sectional study among participants of the Specific Health Check and Guidance System in Japan

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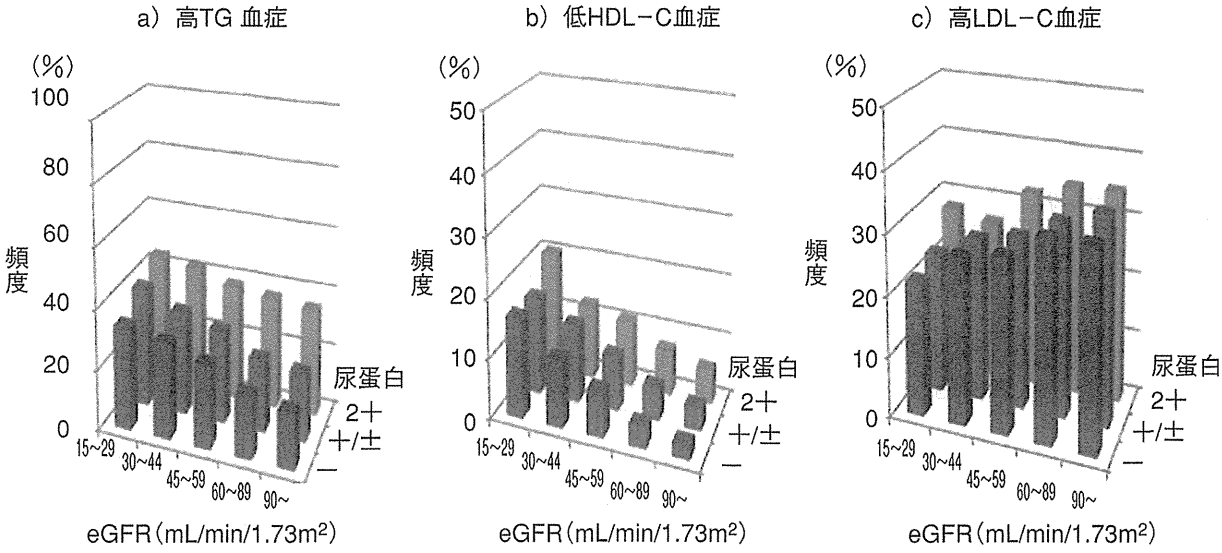

図1　特定健診における脂質異常症の頻度とCKD(eGFRと尿蛋白)の関連

る薬剤治療中のいずれかに該当)，②脂質(TG 150mg/dL以上，HDL−C 40mg/dL未満，脂質異常症に対する薬剤治療中のいずれかに該当)，③血圧(収縮期血圧130mmHg以上，拡張期血圧85mmHg以上，高血圧症に対する薬剤治療中のいずれかに該当)に加え，喫煙歴(6ヵ月以上かつ最近1ヵ月)，年齢に基づき「積極的支援」，「動機付け支援」，「情報提供のみ」の各保健指導レベルに階層化された。すなわち，内臓脂肪蓄積(腹囲：男性85cm，女性90cm以上：腹囲条項)ありで追加リスク2項目以上該当，または追加リスク1項目該当かつ喫煙歴ありは「積極的支援」，追加リスク1項目該当かつ喫煙歴なしは「動機付け支援」，内臓脂肪蓄積(腹囲条項非該当だがBMI 25kg/m^{2}以上)ありで追加リスク3項目該当または2項目該当かつ喫煙歴ありは「積極的支援」，追加リスク2項目該当かつ喫煙歴なしまたは1項目該当は「動機付け支援」と判定された。この判定で「積極的支援」と判定される者のうち65歳以上の者は「動機付け支援」にdown gradeされ，糖尿病，高血圧症または脂質異常症(高脂血症)の治療にかかわる薬剤を服用している者は支援対象から除外された。

3　結　　果

尿蛋白(定性：試験紙法)と腎機能低下(eGFR)はそれぞれ独立して，その程度が進行するとともにCVDの既往歴ならびに肥満(BMI 25kg/m^{2}以上)を有する割合(頻度)が増加(正相関)した。また，尿蛋白と腎機能低下はその程度が進行するとともに，高TG血症，低HDL−C血症を有する割合(頻度)が増加(正相関)し，高LDL−C血症を有する割合が減少(負相関)した(**図1**)。

MetS該当者またはMetS予備群の割合は，CKDでない者が27.3%であるのに対し，CKDステージ1または2で40.2%，CKDステージ3以上かつ尿蛋白陰性の者で36.4%，CKDステージ3以上かつ尿蛋白陽性の者で51.1%であった。また，保健指導レベルが「積極的支援」または「動機付け支援」レベルと判定された者の割合は，CKDのない者が12.9%であるのに対し，CKDステージ1または2で11.4%，CKDステージ3以上かつ尿蛋白陰性の者で12.4%，CKDステージ3以上かつ尿蛋白陽性の者で8.5%であった(**表1**)。

4　考　　察

日本人の一般住民においてCKDにおける脂質異常症の特徴は，MetS類似の高TG血症，低HDL−C血症の頻度の増加であり，高LDL−C血症についてはCKDの進行に伴いその頻度が

表1　特定健診におけるメタボリックシンドロームならびに特定保健指導レベルとCKDの関連

1）メタボリックシンドロームとCKD

MetS判定（国保）	CKDなし	CKDステージ1, 2（eGFR≧60, 尿蛋白陽性）	CKDステージ3以上（eGFR＜60, 尿蛋白陰性）	CKDステージ3以上（eGFR＜60, 尿蛋白陽性）	合　計
MetS該当（%）	8505（15.9）	1323（27.7）	1380（23.4）	456（39.1）	11664（17.8）
MetS予備群（%）	6114（11.4）	598（12.5）	763（13.0）	140（12.0）	7615（11.6）
MetS非該当（%）	38572（71.9）	2792（58.4）	3715（63.1）	562（48.2）	45641（69.7）
判定不能（%）	447（0.8）	69（1.4）	32（0.5）	8（0.7）	556（0.9）
合計（%）	53638（100.0）	4782（100.0）	5890（100.0）	1166（100.0）	65476（100.0）

2）特定保健指導レベルとCKD

保健指導レベル判定（国保）	CKDなし	CKDステージ1, 2（eGFR≧60, 尿蛋白陽性）	CKDステージ3以上（eGFR＜60, 尿蛋白陰性）	CKDステージ3以上（eGFR＜60, 尿蛋白陽性）	合　計
積極的支援（%）	2104（3.9）	197（4.1）	125（2.1）	14（1.2）	2440（3.7）
動機付け支援（%）	4833（9.0）	347（7.3）	607（10.3）	85（7.3）	5872（9.0）
情報提供のみ（%）	45943（85.7）	4132（86.4）	5095（86.5）	1049（90.0）	56219（85.9）
判定不能（%）	758（1.4）	106（2.2）	63（1.1）	18（1.5）	945（1.4）
合計（%）	53638（100.0）	4782（100.0）	5890（100.0）	1166（100.0）	65476（100.0）

低下することが確認された。少なくとも低HDL血症は腎機能低下の要因である可能性があるが，今後この特徴と心腎連関の因果関係を検討するとともに，それを踏まえた治療が望まれる。

また今回の検討でCKDステージの進行に伴いMetSと判定される者の割合は増加するが，全体としては一般住民のCKDのおおむね半数以上はMetS該当者およびその予備群とは判定されないことも明らかになった。さらに，内臓脂肪蓄積と追加リスクに加え喫煙習慣，年齢，服薬状況を加味した保健指導レベル判定では，CKDステージの進行とともに「積極的支援」レベルまたは「動機付け支援」レベルの保健指導の対象となる者はむしろ減少し，よりCVDリスクの高いCKDステージ3以上かつ尿蛋白陽性の者でもこれに該当する者が10%に満たなかった。

CKD進行例ではすでに何らかの薬物治療中であるために，特定保健指導における支援対象から除外されたことが考えられるが，特定健診受診者における腎疾患の既往に関する検討では，特定健診問診項目「医師から，慢性の腎不全にかかっているといわれたり，治療（人工透析）を受けたことがありますか。」に対し「はい」と回答したものは，ステージ1以上の全CKDの1.57%であり，CKDステージ3以上でeGFR 45mL/min/1.73m^{2}未満の者に限ってもその8.9%にすぎないことが判明している[2]。このことは受診者のみならず医療機関におけるCKDの認知度も極めて低いことを予想させる成績であり，薬物治療中のため特定保健指導で支援対象とならない者に対するCVD予防のための啓蒙の実態の把握も必要と考えられる。

以上よりMetSに視点をおいた現行の特定健診・保健指導では，CKDが盲点となる可能性が示唆され，CVD高危険群の効率的な把握の観点からは制度改善の余地があると考えられる。今後は血清Cr値の特定健診検査項目への採用と蛋白尿を含めた受診勧奨基準の設定ならびにCKD発症・進展予防のための保健指導プログラムの策定が必要となると考えられる。

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