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ORIGINAL ARTICLE

Weight gain after 20 years of age is associated with prevalence of chronic kidney disease

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Abstract
Background Weight gain after maturity is a risk factor for diabetes, coronary heart disease, and stroke, even in individuals with a normal body mass index; however, there is little information about the influence of weight gain after maturity on chronic kidney disease (CKD). Therefore, we examined the association between weight gain after 20 years of age and the prevalence of CKD.
Methods A cross-sectional study was performed on 28,151 women and 21,110 men aged between 40 and 59 years who participated in the specific health check and guidance system of Japan in 2008. We compared prevalence of CKD between participants with and without weight gain of at least 10 kg after 20 years of age. Multivariate logistic regression models and stratified analyses were used to adjust for possible confounding factors.
Results The prevalence of CKD among participants with weight gain was significantly higher than among those without weight gain both in women (11.8 vs 8.3%, $p < 0.0001$) and in men (12.2 vs 9.2%, $p < 0.0001$). After adjustment for age, smoking, regular exercise, alcohol intake, history of kidney disease, hypertension, diabetes, and hypercholesterolemia, the odds ratio (95% confidence interval) for CKD was 1.24 (1.14–1.36) in women and 1.15 (1.05–1.26) in men with weight gain of at least 10 kg after the age of 20 years. Even in participants without metabolic syndrome, weight gain was independently associated with CKD in both genders.
Conclusions Weight gain after 20 years of age is associated with CKD among Japanese, even those without metabolic syndrome.

Keywords Weight gain · Chronic kidney disease · Obesity · General population · Cross-sectional study

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Introduction

The prevalence of obesity in Japan has increased over the past several decades [1], and is a worldwide public health problem of growing importance. Obesity is an established risk factor for several chronic diseases, including hypertension and diabetes mellitus. Even in individuals with a normal body mass index (BMI), weight gain after maturity is an important risk factor for diabetes [2, 3], coronary heart disease [4, 5], and stroke [6].

Obesity has also been recognized as a risk factor for chronic kidney disease (CKD). Weight gain has been reported to be associated with the incidence of CKD among Korean men, even when BMI remained within the normal range [7]. However, information is lacking about the influence of weight gain after maturity on CKD among

women, because previous studies of the association between obesity and CKD defined obesity by the BMI or waist circumference [8, 9]. An increase of weight after maturity largely reflects increased fat mass, so such an increase may be more closely associated with the risk of CKD, especially among participants with a normal BMI or waist circumference. The average BMI of Asian populations is lower than that of non-Asian populations, although the tendency for abdominal obesity might be greater than in non-Asian populations [10]. Weight gain after maturity might be a basis for recommendations on lifestyle modification, and it may be especially attractive to use this measure for Asian populations. Measures such as weight and weight gain are also attractive from a public education perspective, because they are much easier for the general population to understand than BMI and can be measured more accurately than waist circumference.

In this study, we examined the effect of weight gain after maturity on the prevalence of CKD among Japanese. We hypothesized that the prevalence of CKD might be associated with weight gain after maturity, even for individuals within the normal range of BMI or waist circumference.

Methods

Study population

We used data from 68 areas of 7 prefectures obtained by the Japanese specific health check and guidance system (SHC) in 2008; the SHC has been described elsewhere [11]. In brief, participants answered a self-administered questionnaire that covered their medical history, smoking habits, alcohol intake, and exercise pattern. Trained staff then measured the height, weight, blood pressure, and waist circumference of each participant, after which serum and spot urine samples were collected. We only included participants aged between 40 and 59 years in this study, because previous reports have indicated that metabolic syndrome was a risk factor for CKD only for younger participants (≤60 years) among men [12, 13] and because body weight might decrease due to comorbidities >60 years. Participants with missing information were also excluded. All of the participants remained anonymous and the study was conducted according to Japanese privacy protection laws and the ethical guidelines for epidemiological studies published by the Ministry of Education, Science and Culture and the Ministry of Health, Labor and Welfare in 2005.

Proteinuria and CKD

Proteinuria was defined by a dipstick urinalysis score of ≥1+ proteinuria (equivalent to ≥30 mg/dl) because of poor discrimination between negative and trace positive dipstick readings [14]. The primary endpoint was the prevalence of CKD, which was defined as ≥1+ proteinuria on urinalysis, a glomerular filtration rate (GFR) <60 ml/min/1.73 m^2 as calculated by using the estimated GFR (eGFR) formula shown below for Japanese [15], or both [16].

$$\text{eGFR} = 194 \times (\text{serum creatinine}^{-1.094}) \times (\text{age}^{-0.287}) \times (0.739 \text{ for females}).$$

Weight gain, obesity, and metabolic syndrome

Information about weight gain was collected from the self-administered questionnaire, which included the following item: "Have you gained more than 10 kg since 20 years of age?" Participants answered yes or no. Using BMI values (calculated as weight in kilograms/(height in meters)^2), the subjects were categorized as non-obese (<25 kg/m^2) or obese (≥25 kg/m^2). Using waist circumference measured at the umbilicus, they were categorized as having abdominal obesity (≥90 cm for women and ≥85 cm for men) or not (<90 cm for women and ≤85 cm for men) according to the definition of the metabolic syndrome in the SHC [11]. The SHC definition of the metabolic syndrome is not the same as that used by the World Health Organization or the Japanese Society of Internal Medicine [17, 18]. Instead, metabolic syndrome is defined as abdominal obesity (waist circumference ≥90 cm in women and ≥85 cm in men) and/or obese (BMI ≥25 kg/m^2) plus any two of the following three categories: (1) fasting blood glucose ≥100 mg/dl, hemoglobin A_{1c} ≥5.2%, use of insulin, and/or oral antidiabetic medication; (2) triglycerides ≥150 mg/dl, high-density lipoprotein cholesterol <40 mg/dl, and/or the use of cholesterol-lowering medication; or (3) blood pressure ≥130/85 mmHg and/or use of antihypertensive medication.

Covariates

Information about current smoking, alcohol, and exercise habits, a history of stroke, heart disease, CKD, or dialysis, and use of medication for diabetes mellitus, hypertension, or hypercholesterolemia was collected from the questionnaire. Diabetes mellitus was defined as the use of insulin or oral antidiabetic medication, a fasting serum glucose ≥126 mg/dl, or both. Hypertension was defined as the use of antihypertensive medication, a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg, or both. Hypercholesterolemia was defined as the use of cholesterol-lowering medication, a low-density lipoprotein cholesterol level ≥140 mg/dl, or both.

Statistical analysis

We analyzed the data separately by gender, because previous reports have indicated that the influence of BMI or

metabolic syndrome on CKD differs between men and women [12, 13, 19]. We used the Chi-squared test, Student's t test, and the Mann–Whitney U test to assess differences among the characteristics of the study participants in relation to weight gain. We conducted multivariate analyses using logistic regression models. The data were initially adjusted for age alone, and then for multiple covariates. In the multivariate models, we included the following covariates that might confound the relationship between weight and CKD: age, current smoking, regular exercise, alcohol intake, a history of kidney disease, and current hypertension, diabetes, and hypercholesterolemia. Because hypertension, diabetes, and hypercholesterolemia are likely to be intermediate factors on the pathway between weight gain and CKD, we did not adjust for these variables in the primary analyses, but we added them sequentially to multivariate models in the secondary analyses. We also performed analyses stratified by presence or absence of metabolic syndrome, abdominal obesity, and obesity or non-obesity. We compared the sensitivity and specificity of weight gain, BMI, and waist circumference for identifying CKD. We calculated 95% confidence intervals (CI) using Wilson's method [20]. A p value of <0.05 was considered to indicate statistical significance and all tests were two-tailed. All statistical analyses were performed with the SPSS for Windows statistical package (Version 18.0; SPSS, Chicago, IL, USA).

Results

A total of 189,709 residents and workers of the target districts aged between 40 and 59 years participated in the SHC. Among them, complete data were available for 28,151 women (27.1%) and 21,111 men (24.6% of participants in this age range). There were no differences between the included and excluded subjects with regard to characteristics such as age, BMI, and waist circumference. Among the 28,151 women and 21,111 men, 8,494 women (30.2%) and 10,485 men (49.7%) answered that their weight had increased by at least 10 kg since 20 years of age.

Table 1 Clinical characteristics of 28,151 women stratified by weight gain after 20 years of age

Variable	Weight gain		p value
	<10 kg (n = 19,657)	≥10 kg (n = 8,494)	
Age [years; mean (SD)]	51.9 (5.9)	52.4 (5.7)	<0.0001
BMI [kg/m^2; mean (SD)]	20.9 (2.5)	25.9 (3.6)	<0.0001
Waist circumference [cm; mean (SD)]	76.5 (7.8)	88.7 (9.1)	<0.0001
Current smoker (%)	13.2	13.3	0.73
Regular exercise, yes (%)	26.8	25.0	0.002
Alcohol intake (%)			
Every day	14.1	10.8	<0.0001
Sometimes	26.7	24.2	
Never	59.3	65.0	
History of stroke (%)	1.0	1.6	<0.0001
History of cardiac disease (%)	1.8	2.9	<0.0001
History of kidney disease (%)	0.4	0.5	0.24
Systolic blood pressure [mmHg; mean (SD)]	118.1 (16.8)	125.7 (17.5)	<0.0001
Diastolic blood pressure [mmHg; mean (SD)]	71.9 (11.0)	76.6 (11.2)	<0.0001
Antihypertensive medication, yes (%)	9.2	20.9	<0.0001
Fasting blood glucose [mg/dl; mean (SD)]	90.3 (15.3)	97.2 (21.3)	<0.0001
Hemoglobin A_{1c} [%; mean (SD)]	5.1 (0.5)	5.3 (0.7)	<0.0001
Antidiabetic medication, yes (%)	1.3	3.5	<0.0001
Low-density lipoprotein cholesterol [mg/dl; mean (SD)]	122.8 (31.7)	134.5 (32.4)	<0.0001
Medication for hypercholesterolemia, yes (%)	6.8	12.3	<0.0001
Triglycerides [mg/dl; median (IQR)]	77 (57, 107)	108 (77, 155)	<0.0001
High-density lipoprotein cholesterol [mg/dl; mean (SD)]	71.4 (16.5)	61.5 (14.4)	<0.0001
Creatinine [mg/dl; mean (SD)]	0.61 (0.15)	0.61 (0.13)	0.66
eGFR [ml/min/1.73 m^2; mean (SD)]	82.4 (16.2)	82.5 (16.8)	0.71
Proteinuria[a] (%)	2.9	5.6	<0.0001
Chronic kidney disease[b] (%)	8.3	11.8	<0.0001

SD standard deviation, *IQR* interquartile range

[a] Defined as the presence of ≥1+ proteinuria on urinalysis

[b] Defined as an estimated glomerular filtration rate <60 ml/min per 1.73 m^2 or as proteinuria on urinalysis

Table 2 Clinical characteristics of 21,110 men stratified by weight gain after 20 years of age

Variable	Weight gain		*p* value
	<10 kg (n = 10,625)	≥10 kg (n = 10,485)	
Age [years; mean (SD)]	50.9 (6.0)	51.3 (5.8)	0.31
BMI [kg/m^2; mean (SD)]	22.3 (2.6)	26.0 (3.1)	<0.0001
Waist circumference [cm; mean (SD)]	80.7 (7.1)	90.5 (7.9)	<0.0001
Current smoker (%)	40.1	37.5	<0.0001
Regular exercise, yes (%)	31.6	27.6	<0.0001
Alcohol intake (%)			
Every day	44.2	39.9	<0.0001
Sometimes	27.6	30.7	
Never	28.2	29.4	
History of stroke (%)	1.9	2.1	0.24
History of cardiac disease (%)	2.7	3.5	<0.0001
History of kidney disease (%)	0.3	0.5	0.06
Systolic blood pressure [mmHg; mean (SD)]	123.1 (16.6)	127.9 (16.1)	<0.0001
Diastolic blood pressure [mmHg; mean (SD)]	72.6 (11.5)	80.5 (11.3)	<0.0001
Antihypertensive medication, yes (%)	11.7	19.9	<0.0001
Fasting blood glucose [mg/dl; mean (SD)]	98.1 (26.2)	102.7 (26.5)	<0.0001
Hemoglobin A_{1c} [%; mean (SD)]	5.2 (0.8)	5.4 (0.8)	<0.0001
Antidiabetic medication, yes (%)	3.5	4.4	0.0001
Low-density lipoprotein cholesterol [mg/dl; mean (SD)]	119.6 (31.4)	129.8 (31.9)	<0.0001
Medication for hypercholesterolemia, yes (%)	4.8	9.0	<0.0001
Triglycerides [mg/dl; median (IQR)]	103 (73, 156)	142 (99, 211)	<0.0001
High-density lipoprotein cholesterol [mg/dl; mean (SD)]	61.0 (16.4)	53.0 (13.1)	<0.0001
Creatinine [mg/dl; mean (SD)]	0.80 (0.26)	0.83 (0.37)	<0.0001
eGFR [ml/min/1.73 m^2; mean (SD)]	83.4 (17.0)	80.6 (16.2)	<0.0001
Proteinuria[a] (%)	5.9	8.2	<0.0001
Chronic kidney disease[b] (%)	9.2	12.2	<0.0001

SD standard deviation, *IQR* interquartile range

[a] Defined as the presence of ≥1+ proteinuria on urinalysis

[b] Defined as an estimated glomerular filtration rate <60 ml/min per 1.73 m^2 or as proteinuria on urinalysis

Clinical characteristics of the participants stratified by weight gain status are listed in Tables 1 and 2. As expected, both women and men with at least 10 kg of weight gain had a higher BMI, larger waist circumference, higher blood pressure, higher blood glucose, and higher low-density lipoprotein cholesterol and triglyceride levels. They were also more likely to have a history of cardiac disease, lower alcohol consumption, and less physical activity in both genders. The prevalence of CKD among the participants with weight gain was significantly higher than among those without weight gain both in women (11.8 vs 8.3%, $p \leq 0.0001$) and in men (12.2 vs 9.2%, $p \leq 0.0001$). The prevalence of proteinuria among the participants with weight gain was also significantly higher than among those without weight gain both in women (5.6 vs 2.9%, $p \leq 0.0001$) and in men (8.2 vs 5.9%, $p \leq 0.0001$).

In the age-adjusted analysis, the odds ratios for CKD increased along with increasing age in both genders (Tables 3, 4). Multivariate analysis revealed that weight gain was significantly associated with the prevalence of CKD, even after adjusting for hypertension, diabetes, and hypercholesterolemia. Thus, weight gain was independently associated with CKD in both genders. When the participants with a history of kidney disease were excluded, the results of the models also remained similar (Appendix). When proteinuria was replaced by the prevalence of CKD, multivariate analysis revealed that weight gain was significantly associated with proteinuria, even after adjusting for hypertension, diabetes, and hypercholesterolemia [the odds ratio (95% CI) 1.43 (1.25–1.63) in women and 1.16 (1.04–1.30) in men].

Stratified analysis showed that weight gain was independently associated with the prevalence of CKD among the subgroup without metabolic syndrome in both genders (Table 5). Among women, weight gain was also independently associated with the prevalence of CKD in the subgroup without abdominal obesity (waist circumference ≤90 cm).

The sensitivity and specificity of weight gain, BMI, and waist circumference for identifying CKD are shown in Table 6. Weight gain among women showed highest sensitivity (38%), but lowest specificity (71%), among the

Table 3 Multivariate analysis of the relationship between weight gain after 20 years of age and the prevalence of chronic kidney disease among women

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 (1.32–1.56)	1.43 (1.31–1.55)	1.24 (1.14–1.36)
Age			
40–44 (ref)	1.00	1.00	1.00
45–49	1.22 (1.02–1.46)	1.21 (1.01–1.45)	1.14 (0.95–1.37)
50–54	2.06 (1.76–2.42)	2.04 (1.74–2.39)	1.82 (1.54–2.13)
55–59	2.40 (2.07–2.78)	2.35 (2.03–2.73)	1.99 (1.71–2.32)
Current smoker			
No (ref)		1.00	1.00
Yes		1.05 (0.93–1.19)	1.05 (0.93–1.19)
Regular exercise			
No (ref)		1.00	1.00
Yes		0.88 (0.81–0.96)	0.88 (0.81–0.97)
Alcohol intake			
Every day (ref)		1.00	1.00
Sometimes		1.07 (0.92–1.23)	1.07 (0.92–1.24)
Little or never		1.14 (1.00–1.30)	1.15 (1.00–1.31)
History of kidney disease			
No (ref)		1.00	1.00
Yes		3.34 (2.18–5.13)	3.07 (1.99–4.72)
Hypertension[c]			
No (ref)			1.00
Yes			1.57 (1.43–1.72)
Diabetes mellitus[d]			
No (ref)			1.00
Yes			1.47 (1.26–1.71)
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, history of kidney disease, 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

three variables, while weight gain showed middle-level sensitivity (57%) and specificity (51%) among men.

Discussion

The present study demonstrated that weight gain of at least 10 kg after 20 years of age was independently associated with the prevalence of CKD. This association was recognized even in the subgroup of participants without metabolic syndrome in both genders. The present study also showed that weight gain was independently associated with the prevalence of CKD in the subgroup of women without abdominal obesity (waist circumference ≤90 cm). These results suggest that using the assessment of weight gain for prevention of obesity may protect individuals who are within the current guidelines from potentially avoidable risks related with obesity to CKD, particularly for women.

Obesity is not only indirectly associated with CKD through various risk factors, such as hypertension and diabetes, but has also been recognized to directly influence the development of kidney dysfunction [9, 21–24]. Although the exact mechanism by which obesity is associated with CKD has not yet been elucidated, intra-abdominal fat mass plays a key role in metabolic syndrome. Weight gain after maturity largely reflects an increased fat mass, and thus may be a more direct (i.e., better) predictor of CKD than BMI or waist circumference. In addition, because the median BMI of Asians is lower than that of non-Asians [10], weight gain may be a more effective predictor of CKD in Asian populations. In fact, weight gain has been reported to be associated with the incidence of CKD among Korean men, even when BMI remained within the normal range [7].

Table 4 Multivariate analysis of the relationship between weight gain after 20 years of age and the prevalence of chronic kidney disease among men

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 (1.26–1.49)	1.34 (1.23–1.47)	1.15 (1.05–1.26)
Age			
40–44 (ref)	1.00	1.00	1.00
45–49	1.30 (1.11–1.52)	1.31 (1.12–1.53)	1.20 (1.02–1.40)
50–54	1.44 (1.24–1.67)	1.47 (1.27–1.71)	1.22 (1.05–1.42)
55–59	1.83 (1.60–2.09)	1.87 (1.63–2.15)	1.43 (1.27–1.64)
Current smoker			
No (ref)		1.00	1.00
Yes		1.05 (0.96–1.15)	1.05 (0.96–1.15)
Regular exercise			
No (ref)		1.00	1.00
Yes		1.05 (0.96–1.16)	1.04 (0.94–1.14)
Alcohol intake			
Every day (ref)		1.00	1.00
Sometimes		1.21 (1.08–1.35)	1.24 (1.11–1.39)
Little or never		1.40 (1.26–1.56)	1.48 (1.33–1.65)
History of kidney disease			
No (ref)		1.00	1.00
Yes		9.43 (6.05–14.69)	8.11 (5.15–12.77)
Hypertension[c]			
No (ref)			1.00
Yes			2.07 (1.88–2.27)
Diabetes mellitus[d]			
No (ref)			1.00
Yes			2.00 (1.78–2.25)
Hypercholesterolemia[e]			
No (ref)			1.00
Yes			1.24 (1.13–1.37)

[a] Model 1 is adjusted for age, current smoking, regular exercise, alcohol intake, history of kidney disease, 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

The present study also found weight gain was independently associated with the prevalence of CKD among both genders, even individuals without metabolic syndrome. To our knowledge, this is the first study to demonstrate a relationship between weight gain after maturity and CKD among women.

The present study also showed that weight gain among women had the highest sensitivity, but the lowest specificity, for CKD among the three measurements used to evaluate obesity. It is theoretically desirable for a screening test to be both highly sensitive and highly specific, but it is difficult to achieve this because of a trade-off between sensitivity and specificity. For public health activities aimed at preventing obesity, a test with high sensitivity may be more useful than one with high specificity. Thus, using the assessment of weight gain for prevention of obesity and CKD is attractive from a public health perspective, particularly for women.

Several studies revealed that the clinical implication of CKD and obesity or metabolic syndrome may be different according to gender. [12, 13, 19] Menopausal status has been suggested to be one of the candidates in determining the gender differences, because metabolic syndrome was a risk factor for CKD in postmenopausal women, but not in premenopausal women [13]. Because the mean age at menopause was reported to be 48.3 years and 80% of females had their menopause between 45 and 54 years of age in Japan [25], our study must include both premenopausal and postmenopausal women. Some differences between men and women in this study might be associated with menopausal status, whereas the information regarding menopausal status of participants was lacking in this study.

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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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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