

# Blood Pressure Control in a Japanese Population With Chronic Kidney Disease: A Baseline Survey of a Nationwide Cohort

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## BACKGROUND

Hypertension is a key risk factor for adverse renal outcomes in chronic kidney disease (CKD), and strict blood pressure control is recommended to halt its progression. This study assessed blood pressure control in the Japanese CKD population.

## METHODS

We used a nationwide database of 250,130 subjects (aged 20–88), including 45,845 CKD subjects (18.3%), participated in an annual health check, “The Specific Health Check and Guidance in Japan,” and examined the relationship between CKD status and blood pressure. Blood pressures were measured in sitting position by trained staff, and target blood pressure for CKD subjects was defined as systolic (SBP)/diastolic blood pressure (DBP) <130/80 mm Hg.

## RESULTS

In total population, CKD subjects had a higher prevalence of hypertension (58.0% vs. 41.8%,  $P < 0.001$ ) and a higher proportion with antihypertensive medication (42.4% vs. 26.7%,  $P < 0.001$ ), compared with non-CKD subjects. The proportion of subjects

achieving target blood pressure was significantly lower among total CKD subjects than among total non-CKD subjects (34.6% vs. 43.8%,  $P \leq 0.001$ ). Among CKD subjects, these proportions were especially low in those with stage 4–5 (24.3–27.5%), those on antihypertensive medication (21.6%) and those with proteinuria  $\geq 2\pm$  (21.3%).

Logistic regression analysis showed that independent factors for high-blood pressure in CKD subjects were age, male gender, alcohol consumption, nonsmoking, diabetes, dyslipidemia, obesity, proteinuria, and antihypertensive medication.

## CONCLUSIONS

Blood pressure control was inadequate in the majority of Japanese CKD subjects, despite antihypertensive treatment. More aggressive efforts to achieve target blood pressures among CKD subjects are recommended.

**Keywords:** blood pressure; chronic kidney disease; epidemiology; hypertension

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In recent years, chronic kidney disease (CKD) has received attention as a risk factor for end-stage renal disease, cardiovascular events, and all-cause mortality. Measures to prevent the development and progression of CKD are urgently required worldwide.

Various factors are associated with the development of CKD, including age, hypertension, diabetes, dyslipidemia, obesity, smoking, proteinuria, and hematuria.<sup>1</sup> Among these, the most

prevalent and strongest risk factor for adverse renal outcomes is hypertension.<sup>2</sup> In the United States, the prevalence of hypertension is reported to be much higher in CKD subjects than in non-CKD subjects (50.9–70.9% vs. 21.9–48.3%).<sup>3</sup> In Japan, the prevalence of hypertension was documented to be 91.9% in a hospital-based CKD population<sup>4</sup> and 80.3% in high-risk CKD subjects.<sup>5</sup>

According to the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High-Blood Pressure (JNC 7)<sup>6</sup> and the Japanese guidelines for CKD,<sup>7</sup> the target blood pressure for subjects with CKD is a systolic blood pressure (SBP) <130 mm Hg and diastolic blood pressure (DBP) <80 mm Hg. Furthermore, for those CKD subjects with proteinuria of 1 g/day or greater, tighter control of blood pressure (SBP <125 mm Hg, DBP <75 mm Hg) is recommended.<sup>7</sup>

Although the significance of blood pressure in the development of vascular disease, including CKD, is well-recognized,

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blood pressure control in patients with CKD is currently unsatisfactory. There are several reasons for this, including the fact that many hypertensive subjects do not receive antihypertensive medication, and that blood pressure control is poor due to insufficient treatment. A report based on the nationwide National Health and Nutrition Examination Survey (NHANES) survey in the United States indicated that within the hypertensive CKD population, the proportion of subjects using antihypertensive medication was 49.7–68.3%, and the majority (70.7–78.7%) of CKD subjects using antihypertensive medication did not achieve sufficient blood pressure control, with a low proportion of subjects (39.1–48.3%) achieving the target blood pressure.<sup>8</sup> Achievement of target blood pressure is affected by individual characteristics, including age, gender, and ethnicity.<sup>9</sup> However, there has been no study examining blood pressure control in the context of CKD in an Asian population.

To address this issue, a cross-sectional study was conducted using the nationwide annual health check database of “The Specific Health Check and Guidance in Japan”.

## METHODS

**Study population.** This study formed part of the ongoing “Research on the Positioning of Chronic Kidney Disease in Specific Health Check and Guidance in Japan” project. A new annual health check program, “The Specific Health Check and Guidance in Japan” was started by Japanese government in 2008, targeting early diagnosis and intervention for metabolic syndrome. This health check program includes all inhabitants over the age of 20 years in Japan, who are covered by national insurance. In 2009, the total number of subjects invited and participating were about 52 million and 21 million, respectively (response rate 40.5%).

In Japan there are 47 administrative districts (prefectures), each with a population of between 0.6 and 13 million. In this study, 13 prefectures (Yamagata, Miyagi, Fukushima, Niigata, Tokyo, Kanagawa, Ibaraki, Osaka, Okayama, Kochi, Fukuoka, Miyazaki, and Okinawa) that agreed with our study aim and were randomly distributed across Japan were selected. Data for these prefectures was obtained from the nationwide database, and data was collected on 278,017 men and 383,586 women (total population 676,905, aged from 20 to 101 years), who participated in the health checks in 2008 and 2009. The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the institutional ethics committee.

In this health check, measurement of creatinine is optional and serum creatinine was not determined in half of the regions in Japan. Among the 676,905 participants, 426,775 were excluded from the present analysis because essential data, including blood pressure measurements, and data on proteinuria, and serum creatinine levels were incomplete. Therefore, data for 101,147 males and 148,983 females (a total of 250,130 subjects, aged 20 to 88 years) were used in the final statistical analyses. Comparison between those with and those without complete data did not show significant differences in

baseline characteristics such as age, gender, or the proportion of subjects using antihypertensive medication.

**Measurements.** Subjects used a self-report questionnaire to document their medical history, current medications, smoking habit (smoker or nonsmoker), and alcohol intake (drinker or nondrinker). SBP and DBP were measured by trained staff, using a standard sphygmomanometer or an automated device, with subjects in the sitting position for at least 5 min before the measurement. Hypertension was defined as a SBP  $\geq 140$  mm Hg, or a DBP  $\geq 90$  mm Hg, or use of antihypertensive medication. Body mass index was calculated as weight (kg) divided by height squared ( $m^2$ ). For both men and women, obesity was defined as a body mass index  $\geq 25.0$  kg/ $m^2$ . Plasma glucose levels were measured by the hexokinase enzymatic reference method. Subjects with diabetes were identified either by self-reported physical diagnosis, or by a fasting plasma glucose concentration  $\geq 126$  mg/dl, or a hemoglobin A<sub>1c</sub> value  $\geq 6.5\%$ . Triglyceride and low-density lipoprotein cholesterol concentrations were measured by enzymatic methods. High-density lipoprotein cholesterol concentration was measured directly. Dyslipidemia was defined as a triglyceride concentration  $\geq 150$  mg/dl, or low-density lipoprotein cholesterol concentration  $\geq 140$  mg/dl, or high-density lipoprotein cholesterol concentration  $< 40$  mg/dl, or use of antilipidemic medication.

Dipstick urinalysis was performed on a single spot urine specimen, collected in the early morning after overnight fasting. The results of the urine test were recorded as (–), trace, (1+), (2+), or (3+). A positive proteinuria test was defined as (1+) or greater. Serum creatinine was measured by an enzymatic method and estimated glomerular filtration rate (eGFR) was obtained using the Japanese equation for eGFR.<sup>10</sup> In keeping with the universal definition, CKD was defined as proteinuria and/or reduced renal function (eGFR  $< 60$  ml/min/1.73  $m^2$ ), and was further categorized into five stages: stage 1, eGFR  $\geq 90$  ml/min/1.73  $m^2$  with proteinuria; stage 2, eGFR 60–89 with proteinuria; stage 3, eGFR 30–59; stage 4, eGFR 15–29; and stage 5, eGFR  $< 15$ .<sup>11</sup> To investigate the relationship between CKD stage and blood pressure in detail, stage 3 was further divided into stage 3A (eGFR 45–59) and stage 3B (eGFR 30–44).

**Statistical analyses.** The unpaired *t*-test and one-factor analysis of variance were used to compare mean values, and the  $\chi^2$ -test was used to evaluate differences in proportions. To examine the correlation between blood pressure and various parameters, including age, gender, alcohol consumption, smoking, diabetes, dyslipidemia, obesity, use of antihypertensive medication, eGFR, and proteinuria in subjects with CKD, a multiple linear regression analysis was performed. To examine the factors related to insufficient blood pressure control in subjects with CKD (SBP  $\geq 130$  mm Hg or DBP  $\geq 80$  mm Hg), multivariate logistic regression analyses that included age, gender, alcohol consumption, smoking, dyslipidemia, obesity, use of antihypertensive medication, renal function, and proteinuria, were performed. Continuous data are expressed as mean  $\pm$  s.d.

All statistical analyses were performed using JMP version 8 software (SAS Institute Inc., Cary, NC). A significant difference was defined as  $P < 0.05$ .

## RESULTS

### Baseline characteristics of the participants

Among a total of 250,130 participants, there were 45,845 CKD subjects (18.3%) and 204,285 non-CKD subjects (81.7%). The CKD subjects were more likely to be males and older, had a higher prevalence of, diabetes, dyslipidemia and obesity, were more likely to have a past history of kidney or cardiovascular disease, and had a lower prevalence of smoking (Table 1).

### Prevalence of hypertension in subjects with CKD

Blood pressure was first compared between CKD and non-CKD subjects. Hypertension was significantly more prevalent in CKD subjects than in non-CKD subjects (58.0% vs. 41.8%,  $P < 0.001$ ) (Figure 1). Among the CKD subjects, the prevalence of hypertension was higher in males, the elderly, and

in those with a higher grade of proteinuria. The prevalence of hypertension was also increased in the advanced stages of CKD: 60.3% in stage 1 ( $n = 1,936$ ), 64.1% in stage 2 ( $n = 8,061$ ), 56.0% in stage 3 ( $n = 35,256$ ), 88.3% in stage 4 ( $n = 461$ ), and 84.0% in stage 5 ( $n = 131$ ) ( $P$  for trend  $< 0.001$ ) (Figure 1).

Blood pressure was significantly higher in CKD subjects than in non-CKD subjects (SBP  $132 \pm 18$  vs.  $128 \pm 17$  mm Hg,  $P < 0.001$ ; DBP  $78 \pm 11$  vs.  $76 \pm 11$  mm Hg,  $P < 0.001$ ). CKD subjects in the advanced stages of disease had higher SBP and lower DBP, compared with those in the early stages of disease (Figure 2).

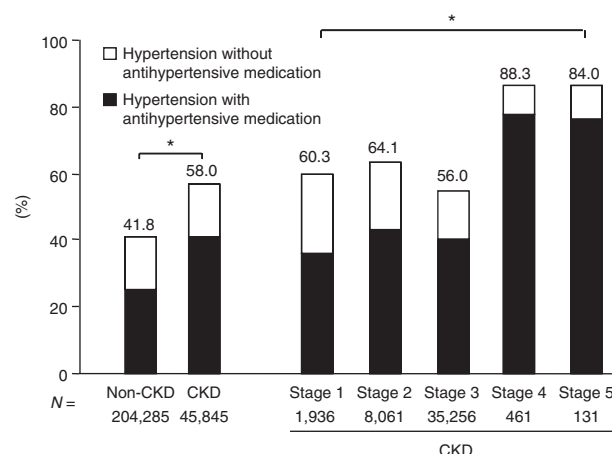
In the multiple regression analysis that included age, gender, alcohol consumption, smoking, diabetes, dyslipidemia, obesity, use of antihypertensive medication, eGFR and proteinuria, SBP was positively associated with all parameters except smoking. In contrast, DBP was positively associated with male gender, alcohol consumption, dyslipidemia, obesity, use of antihypertensive medication, eGFR and proteinuria, and negatively associated with age, smoking, and diabetes (Table 2).

**Table 1 | Basal characteristics of the study participants**

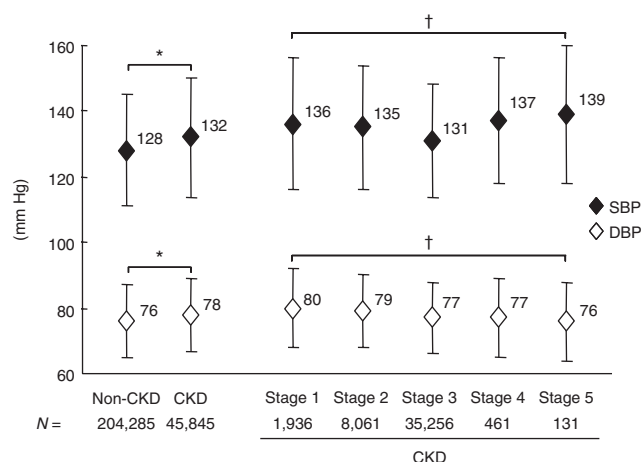
	Total population	Non-CKD population	CKD population
Number (%)	250,130	204,285 (81.7)	45,845 (18.3)
Age, years	63.6 $\pm$ 8.7	63.0 $\pm$ 9.0	66.3 $\pm$ 6.9*
Male gender, $n$ (%)	101,147 (40.4)	77,349 (37.9)	23,798 (51.9)*
Hypertension, $n$ (%)	112,002 (44.8)	85,396 (41.8)	26,606 (58.0)*
Using antihypertensive medication, $n$ (%)	73,929 (29.6)	54,492 (26.7)	19,437 (42.4)*
Not using antihypertensive medication, $n$ (%)	38,073 (15.2)	30,904 (15.1)	7,169 (15.6)*
Alcohol consumption, $n$ (%)	113,317 (45.3)	92,438 (45.3)	20,879 (45.5)
Smoker, $n$ (%)	34,185 (13.7)	28,356 (13.9)	5,829 (12.7)*
Diabetes, $n$ (%)	34,403 (9.4)	17,119 (8.4)	6,284 (13.7)*
Dyslipidemia, $n$ (%)	138,535 (55.4)	110,258 (54.0)	28,277 (61.7)*
Obesity, $n$ (%)	63,899 (25.5)	48,903 (23.9)	14,996 (32.7)*
eGFR, ml/min/1.73 m <sup>2</sup>	75.1 $\pm$ 16.2	78.9 $\pm$ 14.0	58.2 $\pm$ 14.3*
Systolic blood pressure, mm Hg	129 $\pm$ 17	128 $\pm$ 17	132 $\pm$ 18*
Diastolic blood pressure, mm Hg	76 $\pm$ 11	76 $\pm$ 11	78 $\pm$ 11*
Body mass index (kg/m <sup>2</sup> )	23.1 $\pm$ 3.3	22.9 $\pm$ 3.3	23.8 $\pm$ 3.4*
Past history of kidney disease, $n$ (%)	1,400 (0.6)	692 (0.3)	708 (1.5)*
Past history of CVD, $n$ (%)	22,838 (9.1)	16,493 (8.1)	6,345 (13.8)*
Proteinuria $\geq 1+$ , $n$ (%)	13,999 (5.6)	—	13,999 (30.5)

CVD, cardiovascular diseases; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

\* $P < 0.05$  by unpaired  $t$ -test, comparing non-CKD subjects with CKD subjects.



**Figure 1 |** The prevalence of hypertension in CKD and non-CKD subjects. \* $P < 0.001$  by  $\chi^2$ -test. CKD, chronic kidney disease.



**Figure 2 |** Blood pressures levels in CKD and non-CKD subjects. \* $P < 0.001$  by unpaired  $t$ -test; † $P < 0.001$  by analysis of variance. Data are mean  $\pm$  s.d. CKD, chronic kidney disease; DBP, diastolic blood pressure; SBP, systolic blood pressure.

**Table 2 | Multivariate linear regression coefficients for the association of systolic and diastolic blood pressures with clinical parameters**

	Systolic blood pressure		Diastolic blood pressure	
	Coefficient	P value	Coefficient	P value
Age	0.34	<0.001	−0.09	<0.001
Male gender	1.09	<0.001	2.38	<0.001
Alcohol consumption	1.81	<0.001	1.28	<0.001
Smoker	−0.8	0.001	−1.07	<0.001
Diabetes	2.23	<0.001	−1.68	<0.001
Dyslipidemia	1.57	<0.001	0.92	<0.001
Obesity	3.83	<0.001	2.59	<0.001
Use of antihypertensive medication	6.14	<0.001	2.26	<0.001
eGFR, ml/min/1.73 m <sup>2</sup>	0.03	<0.001	0.01	0.022
Proteinuria, ≥1+	4.55	<0.001	1.73	<0.001

Adjusted for age, gender, alcohol consumption, smoking, diabetes, dyslipidemia, obesity, use of antihypertensive medication, eGFR, and proteinuria.  
eGFR, estimated glomerular filtration rate.

### The proportion of subjects using antihypertensive medication

Among the total population, the proportion of subjects using antihypertensive medication was higher in CKD subjects than in non-CKD subjects (42.4% vs. 26.7%,  $P \leq 0.001$ ) (Table 1). In contrast, the proportion of subjects not using antihypertensive medication was almost identical in total CKD subjects (15.6%) and total non-CKD subjects (15.1%). Among those with hypertension, a higher proportion of CKD subjects than non-CKD subjects used antihypertensive medication (73.1% vs. 63.8%,  $P \leq 0.001$ ). Among the CKD subjects, those proportions were especially high in subjects in the advanced stages of CKD (63.2–69.9% in stage 1–2, 74.1% in stage 3, and 86.3–90.4% in stage 4–5), and in the older population (57.6% in those <60 years, 69.4% in those between 60 and 64 years, 72.3% in those between 65 and 69 years, and 78.3% in those ≥70 years).

### The proportion of subjects achieving the target blood pressure

The proportion of subjects achieving the target blood pressure ( $\leq 130/80$  mm Hg) was significantly lower among CKD subjects than non-CKD subjects (34.6% vs. 43.8%,  $P \leq 0.001$ ). Among CKD subjects, this proportion was especially low in those using antihypertensive treatment (21.6%) (Table 3).

Among the CKD population, a higher proportion of those who achieved the target blood pressure were in stage 3 (36.5%), and especially stage 3A (37.0%), than in the advanced stages (stage 4–5, 24.3–27.5%). In contrast, among CKD subjects using antihypertensive treatment, the proportion of those who achieved the target blood pressure was higher in stage 4–5 (23.9–27.4%) and lower in stages 1–2 (15.3–16.3%). Similarly, among the older population, attainment of target blood pressure was low

**Table 3 | Blood pressure control in the CKD population**

Variable (n)	BP <130/80 among total CKD subjects, n (%)	BP <130/80 among CKD subjects using antihypertensive medication, n (%)
CKD (45,845)	15,824 (34.6)	4,197 (21.6)
<i>CKD</i>		
Stage 1 (1,936)	562 (29.0)*	113 (15.3)*
Stage 2 (8,061)	2,255 (28.0)	588 (16.3)
Stage 3 (35,256)	12,877 (36.5)	3,382 (23.1)
Stage 3a (32,102)	11,879 (37.0)	2,880 (22.8)
Stage 3b (3,154)	998 (31.6)	502 (25.1)
Stage 4 (461)	112 (24.3)	88 (23.9)
Stage 5 (131)	36 (27.5)	26 (27.4)
<i>Proteinuria</i>		
−/± (31,846)	12,101 (38.0)*	3,031 (24.2)*
1+ (9,669)	2,816 (29.1)	798 (18.0)
≥ 2+ (4,330)	924 (21.3)	368 (14.9)
<i>Gender</i>		
Male (23,798)	7,139 (30.0)*	2,246 (20.6)*
Female (22,047)	8,709 (39.5)	1,951 (22.9)
<i>Age, years</i>		
<60 (6,283)	2,771 (44.1)*	287 (19.6)*
60–64 (7,470)	2,659 (35.6)	555 (21.4)
65–69 (14,606)	4,981 (34.1)	1,298 (21.1)
≥70 (17,486)	5,438 (31.1)	2,057 (22.8)

BP, blood pressure; CKD, chronic kidney disease.

\* $P < 0.05$  across categories by  $\chi^2$ -test.

for all subjects but high in those subjects using antihypertensive drugs. Lower proportions of subjects with a high grade of proteinuria, as well as males, achieved the target blood pressure, both among the total population, and the subpopulation receiving antihypertensive treatment (Table 3).

For subjects with high-grade proteinuria ( $\geq 1$  g/day), tighter control of blood pressure ( $<125/75$  mm Hg) is recommended. In this study, no information was available on urinary protein and creatinine concentrations; therefore proteinuria  $\geq 2+$  by dipstick was used as a proxy for proteinuria  $\geq 1$  g/day. The proportions of CKD subjects achieving tighter blood pressure control were 14.4% for those with proteinuria  $\geq 2\pm$ , 9.1% for those with proteinuria  $\geq 2\pm$  who were receiving antihypertensive treatment, and 21.4% for those with proteinuria  $\geq 2\pm$  who were not receiving antihypertensive treatment.

In addition, to investigate the factors associated with inadequate blood pressure control (SBP  $\geq 130$  mm Hg or DBP  $\geq 80$  mm Hg), logistic regression analysis was performed. Older age, male gender, alcohol consumption, being a nonsmoker, diabetes, dyslipidemia, obesity, use of antihypertensive treatment, and proteinuria were all independent factors predisposing to poor blood pressure control among subjects with CKD (Table 4).



**Table 4 | Multiple logistic regression analysis of predictive factors associated with suboptimal blood pressure control (SBP  $\geq$ 130 mm Hg or DBP  $\geq$ 80 mm Hg) in subjects with CKD**

	Odds ratio	95% CI	P value
Age (per 10 year increase)	1.21	1.17–1.24	<0.001
Male gender	1.25	1.20–1.31	<0.001
Alcohol consumption	1.27	1.21–1.32	<0.001
Smoker	0.86	0.81–0.92	<0.001
Diabetes	1.13	1.06–1.21	<0.001
Dyslipidemia	1.18	1.14–1.23	<0.001
Obesity	1.63	1.56–1.71	<0.001
Use of antihypertensive medication	2.36	2.26–2.47	<0.001
eGFR <60 ml/min/1.73 m <sup>2</sup>	0.97	0.89–1.06	0.539
Proteinuria $\geq$ 1+	1.52	1.40–1.64	<0.001

CI, confidence interval; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

## DISCUSSION

This study, which was based on a large-scale nationwide database of the Japanese population, revealed for the first time that blood pressure levels did not meet the target in the majority of subjects with CKD, and especially in those with advanced CKD and high-grade proteinuria. This poor blood pressure control may be partly attributable to inadequate use of medication.

This study showed that there was a higher prevalence of hypertension (58.0%), a higher proportion of subjects using antihypertensive treatment (42.4%), and a lower proportion of subjects achieving the target blood pressure (34.6%) among the total CKD population than among the total non-CKD population. Although the characteristics of the participants were different, these percentages were slightly better than those from the NHANES 1999–2006 study in the United States (63.9–80.5% prevalence of hypertension, 10.6–20.0% of subjects achieving the target blood pressure, and 49.7–68.3% receiving antihypertensive treatment).<sup>8</sup> Other studies in Western countries have documented the proportion of subjects among the CKD population that achieved target blood pressure as 12–46%.<sup>12</sup> Previous Japanese studies targeting a high-risk CKD population showed a much higher prevalence of hypertension; 91.9% in hospital-based CKD patients,<sup>4</sup> and 80.3% in a CKD population with past and family histories of hypertension, diabetes, and kidney disease.<sup>5</sup> This suggests that the prevalence of hypertension among subjects with CKD varies, depending on the characteristics of the study population. Overall, the severity of hypertension in this study appeared to be less than in previous studies.

Among the total population, the proportions of subjects not using antihypertensive medication was almost identical for all CKD subjects and all non-CKD subjects. In contrast, among subjects with hypertension, it was significantly lower in the CKD subjects than in the non-CKD subjects. Based on this observation, it might be speculated that the main reason for the high proportion of CKD subjects with inadequate blood pressure control appears to be under-treatment rather

than nontreatment. Although there were high percentages of subjects receiving antihypertensive treatment among those with advanced CKD, those with proteinuria  $\geq$ 2+, and among the older subjects, these groups had low proportions achieving target blood pressure. This suggests that intervention with antihypertensive medication is especially inadequate in these populations. In contrast, the proportion of CKD subjects in the early stages of disease that was using antihypertensive medication was lower, and the administration of antihypertensive treatment should be promoted in this group.

According to the CKD guidelines,<sup>7</sup> tighter control of blood pressure (<125/75 mm Hg) is recommended for subjects with proteinuria  $\geq$ 2+. However, the proportion of these subjects with well controlled blood pressure was very low. Thus, meeting this target range of blood pressure does not appear to be feasible with current medications, and a more intense and comprehensive approach that includes the use of antihypertensive drugs is recommended. These findings suggest that different countermeasures need to be taken to achieve target blood pressure, depending on the status of subjects with CKD.

Of note, among CKD subjects with stage 3 disease, and especially those with stage 3A disease (eGFR 45–59 ml/min/1.73 m<sup>2</sup>), there was a relatively lower prevalence of hypertension and a higher proportion achieving target blood pressure control. This finding is in keeping with a Japanese report on a high-risk CKD population, which indicated that there was a lower proportion of subjects with high-blood pressure ( $\geq$ 140/90 mm Hg) among those with stage 3–4 disease than among those with stage 1–2 disease.<sup>5</sup> However, American studies have shown that blood pressure control deteriorates with advancing CKD stage, both in the general and high-risk populations.<sup>9</sup> Although differences in the backgrounds of participants may contribute to this discrepancy, it is possible that the effect of stage 3 CKD on blood pressure may differ, depending on the ethnicity of the population.

Multiple linear regression and logistic regression analyses suggested that multiple risk factors, including older age, gender, alcohol consumption, obesity, diabetes, and dyslipidemia, were associated with blood pressure and poor blood pressure control. This finding is consistent with a previous report that subjects with diabetes and high-grade albuminuria, among a cohort with chronic renal insufficiency, were likely to have inadequate blood pressure control.<sup>13</sup> These findings highlight the importance of lifestyle modifications in order to achieve target blood pressure.

Although a target blood pressure of <130/80 mm Hg is recommended for subjects with CKD, a recent study showed that the beneficial effect of intensive blood pressure control may be limited to CKD subjects with proteinuria.<sup>14</sup> Therefore, caution is required in applying this target blood pressure to CKD subjects without proteinuria.

The strengths of this study were the use of a large-scale nationwide database and the fact that the hypertensive status of this population reflected the current situation in the entire Japanese population. This study could provide useful clinical information for the treatment of subjects with CKD in Japan.

There are, however, several limitations to this study. First, single measurements of blood pressure, serum creatinine and proteinuria may have led to some misclassification of CKD and blood pressure categories. Such misclassification would probably have been nondifferential and would have biased the relationship toward the null. Therefore, there is a possibility that the observed relationship between blood pressure and CKD status may have been underestimated. Second, no detailed information was available on the antihypertensive treatments, such as the types of blood pressure-lowering drugs that were used. Third, blood pressure was measured in the morning after overnight fasting, and the values obtained in this study may differ from those measured in an outpatient clinic. Fourth, the response rate for this Specific Health Check and Guidance program was not high. This may have resulted in selection bias. Caution is required in generalizing these results to the entire Japanese population. Fifth, due to the cross-sectional nature of this study, we cannot infer the causality between blood pressure and related factors.

In conclusion, this study revealed that the majority of Japanese subjects with CKD had inadequate blood pressure control, despite using antihypertensive treatment. More aggressive efforts should be recommended in order to achieve target blood pressures in subjects with CKD.

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