Trends in the prevalence of chronic kidney disease and its risk factors in a general Japanese population: The Hisayama Study

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Abstract

Background. Chronic kidney disease (CKD) is increasingly recognized as a leading public health issue. However, there are limited data assessing secular trends in the prevalence of CKD in general Asian communities.

Methods. We performed three repeated cross-sectional surveys of residents aged ≥40 years in 1974 [2118 subjects (participation rate, 81.2%)], 1988 [2741 subjects (80.9%)] and 2002 [3297 subjects (77.6%)] in a Japanese community. We compared the prevalence of CKD [one or both of proteinuria and estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m2] and potential risk factors among the three surveys.

Results. The prevalence of CKD increased significantly with time in men (13.8% [95% confidence interval (95% CI), 11.4–16.2%] in 1974, 15.9% [95% CI, 13.6–18.2%] in 1988 and 22.1% [95% CI, 19.6–24.6%] in 2002; P for trend < 0.001), but not in women (14.3% [95% CI, 12.2–16.4%], 12.6% [95% CI, 10.9–14.3%] and 15.3% [95% CI, 13.4–17.2%]; P for trend = 0.97). The frequencies of individuals with CKD Stages 3–5 (eGFR < 60 mL/min/1.73 m2) increased over the three decades in both sexes. Despite the widespread use of antihypertensive agents, the proportions of individuals with CKD who reached blood pressure of <130/80 mmHg were only 27.0% in men and 47.5% in women. The frequency of metabolic disorders including diabetes, hypercholesterolaemia and obesity increased over the three decades in both sexes.

Conclusions. The prevalence of CKD increased significantly in men, but not in women over the last three decades in a general Japanese population. Our findings support the requirement for a comprehensive treatment for hypertension and metabolic disorders to reduce the burden of CKD.

Keywords: chronic kidney disease; general population; hypertension; metabolic disorder; prevalence

Introduction

Chronic kidney disease (CKD), most commonly defined by a reduction in kidney function or the presence of proteinuria [1,2], is increasingly recognized as a leading public health issue. The number of patients with end-stage kidney disease has been expanding rapidly and is predicted to exceed 2 million worldwide by the year 2010 [3]. Furthermore, it has been established that CKD is a risk factor not only for progressive kidney failure, but also for cardiovascular morbidity and mortality [4–6].

Several cross-sectional studies have demonstrated that CKD affects 10–15% of the adult population in developed Western countries [7–9]. Recent epidemiological studies have suggested that CKD may be more prevalent in Asian countries than in developed Western countries [10,11]. Furthermore, it has been reported that the number of patients undergoing dialysis in Asian countries such as Malaysia and Japan has been increasing [12,13]. It is likely that the prevalence of CKD would increase over time as a consequence of the accumulation of risk factors such as hypertension, glucose intolerance, obesity and hypercholesterolaemia, probably owing to the westernization of the lifestyle in these Asian countries. However, there are limited data assessing secular trends in the prevalence of CKD in general Asian communities to date. A better understanding of the past and current prevalence of CKD and its potential risk factors may provide useful information for the development of management strategies for CKD.

The Hisayama Study is a community-based cohort study that has been underway since 1961, with a goal of estimating the effects of the remarkable lifestyle changes on the burden of cardiovascular diseases in Japan [14–17]. The aim of the present study is to assess trends in the prevalence of CKD and its risk factors over the last three decades and to examine their relationships.

Subjects and methods

Study population

The town of Hisayama is a suburban community adjacent to Fukuoka City, a metropolitan area on Kyushu Island in southern Japan. The population of the town has been stable for 50 years and was approximately 8000 in 2008. The age and occupational distributions of the Hisayama population are almost identical to those of Japan as a whole. Full commu-
nity surveys of the residents have been repeated from the initiation of the study to date. The study design and characteristics of the subject population have been described in detail elsewhere [14–18]. Briefly, four study cohorts composed of Hisayama residents aged ≥40 years were established in 1961, 1974, 1988 and 2002. For this study, we used data from the cross-sectional surveys conducted at baseline in the latter three cohorts, which included available data on serum creatinine and proteinuria. The full community surveys were conducted as follows. In 1974, we invited all 2629 residents in that age group in the town registry to participate in the survey by the assistance of the town office, and of those, 2135 (participation rate, 81.2%) consented to participate in the health examination. After excluding 17 subjects for whom blood samples were unavailable, 2118 subjects (911 men, 1207 women) were enrolled in this study. In the same manner, 2741 subjects from 2742 participants (participation rate, 80.9%) in 1988 and 3297 subjects from 3298 participants (participation rate, 77.6%) in 2002 were enrolled in the study. A total of 3059 (38%) subjects participated in two or more of the three surveys.

Definition of CKD

Details of the measurement of risk factors in each survey were described previously [15,16,18,19]. Freshly voided urine samples were tested by the dipstick method in all surveys. Proteinuria was defined as 1+ or more. Serum creatinine was measured by the non-compensated Jaffe method in 1974 and 1988 and the enzymatic method in 2002. Serum samples were assayed using a Technicon autoanalyser (Technicon Instruments, Tarrytown, NY) in 1974, a TBA-80S autoanalyser (Toshiba Inc., Tokyo, Japan) in 1988 and an AU-800 autoanalyser (Olympus Corporation, Tokyo, Japan) in 2002. The difference between the serum creatinine levels by the Jaffe method and those by the enzymatic method was calibrated by using 98 serum samples standardized by CRC Corporation (Fukuoka, Japan). The range of creatinine levels in the samples was 0.5 to 15.2 mg/dl by the Jaffe method. The conversion equation was estimated by using a simple linear regression model. The correlation coefficient of this equation was 0.996. The Jaffe method value was converted to an enzymatic method value by using the following equation:

\[
\text{Serum creatinine (enzymatic method [mg/dl])} = 0.9754 \times \text{serum creatinine(Jaffé method[mg/dl])] – 0.2802.}
\]

The estimated glomerular filtration rate (eGFR) was calculated using the isotopic dilution mass spectrometry–traceable creatinine-based four-variable Modification of Diet in Renal Disease (MDRD) Study equation with the Japanese Society of Nephrology Chronic Kidney Disease Initiatives coefficient of 0.741 [20]. eGFR was derived using the following equation:

\[
eGFR(\text{ml/min}/1.73 \text{ m}^2) = 0.741 \times 175 \times \text{serum creatinine(enzymatic method[mg/dl])}^{1.154} \times \text{age(years)}^{-0.203} \times 0.742(\text{if female})
\]

CKD was defined as either the presence of proteinuria or eGFR < 60 ml/min/1.73 m². The clinical stages of CKD were classified according to the recommendations of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines [1]: Stage 1 or 2 (eGFR ≥ 60 ml/min/1.73 m² and the presence of proteinuria), Stage 3 (eGFR 30–59 ml/min/1.73 m²) and Stage 4 or 5 (eGFR < 30 ml/min/1.73 m²).

Risk factors

In each survey, blood pressures were measured three times in a sitting position after at least 5 min of rest, and the mean of the three measurements was used for the analysis. Hypertension was defined as a mean systolic blood pressure ≥140 mmHg or a mean diastolic blood pressure ≥90 mmHg or a current use of antihypertensive agents. Subjects with hypertension were classified as treated or untreated based on whether or not they were currently using antihypertensive agents. Diabetes was defined by fasting glucose concentrations ≥126 mg/dl (7.0 mmol/L) or postprandial glucose concentrations ≥200 mg/dl (11.1 mmol/L) in addition to medical history of diabetes in 1974 and by those methods and a 75-g oral glucose tolerance test in 1988 and 2002. Diabetes was regarded as treated when the subject was under therapy with insulin or hypoglycaemic agents in 1988 and 2002, but the designation of treated or untreated diabetes was not made in 1974 due to an absence of information on treatment status. Serum total cholesterol levels were determined by the Zurkowski method in 1974 and by the enzymatic method in 1988 and 2002. Hypercholesterolaemia was defined as serum total cholesterol ≥220 mg/dl (5.7 mmol/L) or current use of a lipid-modifying agent. Treated hypercholesterolaemia was defined as current use of lipid-modifying agents only in 2002 because information on anti-lipidaemic agents was not available in 1974 and 1988. Body height and weight were measured in light clothing without shoes, and the body mass index (in kilogrammes per square metre) was calculated. Obesity was defined as a body mass index ≥25 kg/m². Metabolic syndrome was defined by using criteria recommended in a joint interim statement of five major scientific organizations [21]. Information on medical history, medical treatment, alcohol intake and smoking habits was obtained through a standard questionnaire by trained interviewers. Alcohol intake and smoking habits were classified as either current habitual use or not.

Results

We compared the age-adjusted prevalence and mean values of risk factors among the three surveys by sex, as shown in Table 1. The prevalence of hypertension was constant in men, but decreased in women from 1974 to 2002. The prevalence of treated hypertension increased over time, whereas the prevalence of untreated hypertension decreased in both sexes. Consequently, mean blood pressure levels decreased over the last three decades. The frequencies of diabetes, hypercholesterolaemia, obesity, metabolic syndrome and alcohol intake increased with time, whereas the frequency of smoking habits decreased in both sexes. The prevalence of diabetes, especially untreated diabetes, increased with time in both sexes.

Figure 1 presents the age-adjusted prevalence of CKD in the three surveys by sex. The age-adjusted prevalence of CKD increased significantly with time in men (13.8% in 1974, 15.9% in 1988 and 22.1% in 2002; P for trend < 0.001), but not in women (14.3%, 12.6% and 15.3%, respectively; P for trend = 0.9). The prevalence of CKD Stages 3–5 increased 3-fold over time in men (4.8%, 9.4% and 15.7%; P for trend < 0.001) and doubled in women (5.8%, 9.9% and 11.7%; P for trend < 0.001). Conversely, the prevalence of CKD Stages 1–2 decreased to two-thirds in men (9.0%, 6.5% and 6.4%; P for trend = 0.02) and by half in women (8.5%, 2.7% and 3.4%; P for trend < 0.001). Similar trends in the prevalence of CKD across the three surveys were also observed in middle-aged and elderly populations in either sex (Figure 2). There was a comparable relationship for the prevalence of...
Table 1. Age-adjusted prevalence and mean values of risk factors in 1974, 1988 and 2002 by sex

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th></th>
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<th>Women</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 911</td>
<td>n = 1165</td>
<td>n = 1414</td>
<td></td>
<td>n = 1207</td>
<td>n = 1576</td>
<td>n = 1883</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>56 ± 11</td>
<td>59 ± 12</td>
<td>61 ± 12</td>
<td>&lt;0.001</td>
<td>57 ± 12</td>
<td>60 ± 12</td>
<td>62 ± 13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>139 ± 21</td>
<td>136 ± 21</td>
<td>134 ± 21</td>
<td>&lt;0.01</td>
<td>141 ± 21</td>
<td>134 ± 21</td>
<td>129 ± 21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>79 ± 12</td>
<td>81 ± 12</td>
<td>81 ± 12</td>
<td>&lt;0.01</td>
<td>78 ± 12</td>
<td>76 ± 12</td>
<td>76 ± 12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>42.0 (39.0–46.0)</td>
<td>44.4 (40.6–48.2)</td>
<td>42.5 (39.0–46.0)</td>
<td>0.90</td>
<td>42.0 (38.4–45.6)</td>
<td>34.7 (31.9–37.5)</td>
<td>31.3 (28.9–33.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treated, %</td>
<td>9.2 (7.2–11.2)</td>
<td>13.8 (11.7–15.9)</td>
<td>19.4 (17.2–21.6)</td>
<td>&lt;0.001</td>
<td>7.9 (6.4–9.4)</td>
<td>13.3 (11.6–15.0)</td>
<td>16.8 (15.1–18.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Untreated, %</td>
<td>32.8 (29.1–36.5)</td>
<td>30.6 (27.4–33.8)</td>
<td>23.1 (20.4–25.8)</td>
<td>&lt;0.001</td>
<td>34.1 (30.9–37.3)</td>
<td>21.3 (19.0–23.6)</td>
<td>14.5 (12.7–16.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>2.5 (1.5–3.5)</td>
<td>14.3 (12.1–16.5)</td>
<td>20.6 (18.2–23.0)</td>
<td>&lt;0.001</td>
<td>2.0 (1.2–2.8)</td>
<td>9.0 (7.6–10.4)</td>
<td>11.5 (10.0–13.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treated, %</td>
<td>–</td>
<td>2.7 (1.8–3.6)</td>
<td>5.6 (4.4–6.8)</td>
<td>&lt;0.001</td>
<td>–</td>
<td>2.6 (1.8–3.4)</td>
<td>2.8 (2.1–3.5)</td>
<td>0.23</td>
</tr>
<tr>
<td>Untreated, %</td>
<td>11.5 (9.5–13.5)</td>
<td>14.9 (12.8–17.0)</td>
<td></td>
<td>0.002</td>
<td>6.4 (5.2–7.6)</td>
<td>8.7 (7.3–10.1)</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Hypercholesterolaemia, %</td>
<td>12.4 (10.1–14.7)</td>
<td>27.1 (24.0–30.2)</td>
<td>26.9 (23.9–29.9)</td>
<td>&lt;0.001</td>
<td>20.3 (17.8–22.8)</td>
<td>41.4 (38.2–44.6)</td>
<td>41.0 (38.0–44.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treated, %</td>
<td>–</td>
<td>–</td>
<td>6.3 (5.0–7.6)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>8.9 (7.7–10.1)</td>
<td>–</td>
</tr>
<tr>
<td>Untreated, %</td>
<td>20.6 (17.9–23.3)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>32.1 (29.3–34.9)</td>
<td>–</td>
<td></td>
<td>–</td>
</tr>
<tr>
<td>Obesity, %</td>
<td>11.3 (9.1–13.5)</td>
<td>24.4 (21.4–27.4)</td>
<td>29.4 (26.2–32.6)</td>
<td>&lt;0.001</td>
<td>21.3 (18.6–24.0)</td>
<td>23.9 (21.4–26.4)</td>
<td>23.8 (21.4–26.2)</td>
<td>0.004</td>
</tr>
<tr>
<td>Metabolic syndrome, %</td>
<td>–</td>
<td>8.1 (6.4–9.8)</td>
<td>13.4 (11.3–15.5)</td>
<td>&lt;0.001</td>
<td>–</td>
<td>16.5 (14.5–18.5)</td>
<td>18.6 (16.7–20.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking habits, %</td>
<td>72.2 (66.6–77.8)</td>
<td>50.6 (46.4–54.8)</td>
<td>46.7 (42.6–50.8)</td>
<td>&lt;0.001</td>
<td>10.2 (8.4–12.0)</td>
<td>6.9 (5.5–8.3)</td>
<td>8.6 (7.0–10.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Alcohol intake, %</td>
<td>63.6 (58.4–68.8)</td>
<td>61.9 (57.2–66.6)</td>
<td>71.2 (66.2–76.2)</td>
<td>&lt;0.001</td>
<td>5.4 (4.1–6.7)</td>
<td>9.8 (8.1–11.5)</td>
<td>29.5 (26.6–32.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Age is not age-adjusted. Values are means ± standard deviations or frequencies. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or current use of antihypertensive agents. Diabetes mellitus was defined by fasting glucose concentrations ≥126 mg/dl (7.0 mmol/L) or postprandial glucose concentrations ≥200 mg/dl (11.1 mmol/L) in 1974 and by a 75-g oral glucose tolerance test in 1988 and 2002 in addition to a medical history of diabetes according to the recommendations of the American Diabetes Association. Hypercholesterolaemia was defined as serum total cholesterol ≥220 mg/dl (5.7 mmol/L) or current use of a lipid-modifying agent. Obesity was defined as body mass index ≥25 kg/m². Treated or untreated statuses were defined as the presence or absence of use of any medication for the treatment. Metabolic syndrome was defined by using criteria recommended in a joint interim statement of five major scientific organizations.
CKD Stages 4–5, but the number of subjects with this stage of CKD was too small to assess reliably according to age or sex [eight subjects (0.4%) in 1974, seven subjects (0.3%) in 1988, 33 subjects (1.0%) in 2002 overall]. The number of subjects undergoing dialysis was zero in 1974, one in 1988 and 10 in 2002. The age-adjusted proportion of subjects with proteinuria did not change across the surveys in men (10.7% in 1974, 7.6% in 1988 and
9.6% in 2002; P for trend = 0.65), but decreased significantly with time in women (10.2% in 1974, 3.8% in 1988 and 5.3% in 2002; P for trend < 0.001).

Next, we estimated the frequencies of well-controlled blood pressure in men and women with CKD in each of the three surveys (Figure 3). Among subjects with CKD, the proportion with blood pressure levels of <140/90 mmHg increased from 46.6% in 1974 to 51.1% in 2002 for men and from 47.0% to 66.6% for women, in parallel with the increment in the proportion of subjects taking antihypertensive agents. The frequency of blood pressure of <130/80 mmHg was <30% in men with CKD in all three surveys, whereas it increased from 24.9% in 1974 to 47.5% in 2002 in women. Among CKD subjects taking antihypertensive agents in 2002, 36.3% of men and 26.3% of women had a blood pressure level <140/90 mmHg, and only 11.1% and 12.8%, respectively, had a blood pressure level <130/80 mmHg. Table 2 shows the age-adjusted prevalence and RR of CKD by the status of hypertension treatment among the three surveys by sex. For men, the RR of presence of CKD increased with time in subjects with untreated hypertension (P for trend = 0.001), but not in subjects with treated hypertension (P for trend = 0.48). For women, there was no evidence of significant differences in the prevalence of CKD over time in any of the hypertension treatment statuses.

Finally, we assessed the relationship between metabolic syndrome and the risk of CKD in 1988 and 2002. Metabolic syndrome was associated with an increased risk of prevalent CKD in either sex (Figure 4). The strength of the relationship did not change over time for men (P for heterogeneity = 0.99), whereas it was attenuated significantly in 2002 compared with 1988 for women (P for heterogeneity = 0.01).

**Discussion**

In the present study, we demonstrated that the prevalence of CKD increased significantly in men, but not in women from the 1970s to the 2000s in a general Japanese population, whereas CKD Stages 3–5 increased progressively with time in both sexes. Importantly, more than half of

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**Table 2. Age-adjusted prevalence of CKD according to hypertension status in 1974, 1988 and 2002 by sex**

<table>
<thead>
<tr>
<th></th>
<th>1974</th>
<th>1988</th>
<th>2002</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-hypertension</td>
<td>10.9 (7.6–14.2)</td>
<td>11.2 (8.5–13.9)</td>
<td>15.5 (12.7–18.3)</td>
<td>0.008</td>
</tr>
<tr>
<td>Prevalence</td>
<td>1.00 (0.76–1.61)</td>
<td>1.11 (1.09–2.17)</td>
<td>1.53 (0.10–2.17)</td>
<td></td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Treated hypertension</td>
<td>18.8 (10.7–26.9)</td>
<td>23.8 (16.7–30.9)</td>
<td>36.1 (23.7–48.5)</td>
<td>0.48</td>
</tr>
<tr>
<td>Prevalence</td>
<td>1.00 (0.70–1.77)</td>
<td>1.10 (0.78–1.81)</td>
<td>1.16 (0.78–1.81)</td>
<td></td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated hypertension</td>
<td>16.6 (11.8–21.4)</td>
<td>17.5 (13.0–22.0)</td>
<td>28.8 (22.6–35.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Prevalence</td>
<td>1.00 (0.70–1.43)</td>
<td>1.00 (1.19–2.30)</td>
<td>1.65 (0.78–1.81)</td>
<td></td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

P for trend < 0.05, **P for trend < 0.001

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Table 3. Age-adjusted frequencies of well-controlled blood pressure in subjects with CKD in 1974, 1988 and 2002 by sex.

<table>
<thead>
<tr>
<th></th>
<th>1974</th>
<th>1988</th>
<th>2002</th>
<th>**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP &lt;140/90 mmHg</td>
<td>46.6</td>
<td>47.8</td>
<td>51.1</td>
<td>*</td>
</tr>
<tr>
<td>BP &lt;130/80 mmHg</td>
<td>28.2</td>
<td>27.4</td>
<td>27.0</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 3. Age-adjusted frequencies of well-controlled blood pressure in subjects with CKD in 1974, 1988 and 2002 by sex.**

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9.6% in 2002; P for trend = 0.65), but decreased significantly with time in women (10.2% in 1974, 3.8% in 1988 and 5.3% in 2002; P for trend < 0.001).

Next, we estimated the frequencies of well-controlled blood pressure in men and women with CKD in each of the three surveys (Figure 3). Among subjects with CKD, the proportion with blood pressure levels of <140/90 mmHg increased from 46.6% in 1974 to 51.1% in 2002 for men and from 47.0% to 66.6% for women, in parallel with the increment in the proportion of subjects taking antihypertensive agents. The frequency of blood pressure of <130/80 mmHg was <30% in men with CKD in all three surveys, whereas it increased from 24.9% in 1974 to 47.5% in 2002 in women. Among CKD subjects taking antihypertensive agents in 2002, 36.3% of men and 26.3% of women had a blood pressure level <140/90 mmHg, and only 11.1% and 12.8%, respectively, had a blood pressure level <130/80 mmHg. Table 2 shows the age-adjusted prevalence and RR of CKD by the status of hypertension treatment among the three surveys by sex. For men, the RR of presence of CKD increased with time in subjects with untreated hypertension (P for trend = 0.001), but not in subjects with treated hypertension (P for trend = 0.48). For women, there was no evidence of significant differences in the prevalence of CKD over time in any of the hypertension treatment statuses.

Finally, we assessed the relationship between metabolic syndrome and the risk of CKD in 1988 and 2002. Metabolic syndrome was associated with an increased risk of prevalent CKD in either sex (Figure 4). The strength of the relationship did not change over time for men (P for heterogeneity = 0.99), whereas it was attenuated significantly in 2002 compared with 1988 for women (P for heterogeneity = 0.01).

**Discussion**

In the present study, we demonstrated that the prevalence of CKD increased significantly in men, but not in women from the 1970s to the 2000s in a general Japanese population, whereas CKD Stages 3–5 increased progressively with time in both sexes. Importantly, more than half of
individuals with CKD did not reach the optimal target levels of blood pressure recommended by the current guidelines [23,24], despite an increment in the proportion of subjects taking antihypertensive agents over the last three decades. Furthermore, our findings implied that the recent increment in the number of subjects with metabolic disorders is linked to the increasing prevalence of CKD. These analyses, therefore, would seem to highlight the importance of the comprehensive management of metabolic disorders in addition to the strict control of blood pressure in order to reduce the burden of CKD in the general Japanese population.

The prevalences of CKD have been reported for several countries. The National Health and Nutrition Examination Surveys reported that the age-adjusted prevalence of CKD Stages 1–4 among subjects aged 20 years or older in the United States increased from 10.0% in 1988–1994 to 13.1% in 1999–2004 [8]. In Nord-Trøndelag, Norway, the prevalence of CKD Stages 3–5 was 4.4% [9]. CKD may be more prevalent in Asian countries than in developed Western countries. A cross-sectional study conducted in 574,024 Japanese subjects over 20 years old demonstrated that the prevalence of CKD Stages 3–5 was 10.6% in Japan [11]. Data from the screenings in Okinawa, Japan showed that the unadjusted prevalence of CKD Stages 3–5 among subjects aged 20 years or older increased between 1993 (10.4%) and 2003 (12.2%) in men, but decreased in women (19.5% in 1993, 17.4% in 2003), although the average serum creatinine levels increased in all age categories during this period in either sex [25]. An increasing trend in the prevalence of CKD in men was thus observed both in our study and Okinawa’s study. The discrepancy observed in women between the two studies may have arisen from a self-selection bias caused by the low participation rate (<20%) in Okinawa’s study, with subjects having an underlying disease (e.g., advanced kidney disease) being less likely to participate in the examination. Importantly, the prevalences of CKD in these studies were estimated on the basis of different eGFR equations, the direct comparison of which might be inappropriate. A nationwide examination will be needed to estimate the burden of CKD in Japan more reliably.

In the present study, the prevalence of metabolic disorders, such as diabetes, hypercholesterolaemia and obesity, was found to have increased dramatically over the last three decades, probably due to the westernization of lifestyle in Japan [26]. In the 2002 survey, diabetes was significantly associated with the likelihood of CKD for both sexes. Diabetes is an especially serious problem in the prevention strategy for CKD because it has been the leading cause of end-stage renal disease since 1998 in Japan [13]. Likewise, hypercholesterolaemia and obesity have been shown to be independent risk factors for CKD [27,28]. Our findings showed a jump in the prevalence of metabolic disorder from 1974 to 1988 ahead of the increment in the prevalence in CKD, possibly suggesting a causal association of metabolic disorder with the risk of CKD. In this study, furthermore, metabolic syndrome, which is defined as the accumulation of three or more risk factors such as elevated blood pressure, glucose intolerance, central obesity and dyslipidaemia, was associated with an increased risk of CKD. Our previous longitudinal study has demonstrated that individuals with metabolic syndrome have 2.1-fold greater risk than those without it [29]. It has also been reported that clusters of multiple metabolic disorders tended to cause CKD in the several epidemiological studies [30,31]. Therefore, it is reasonable to suppose that the increasing prevalence of metabolic disorders has contributed to the increasing trend in CKD, especially CKD Stages 3–5, in our subjects.

Hypertension is well-established as a powerful risk factor for not only cardiovascular disease, but also CKD [32]. In this study, blood pressure levels significantly declined in both sexes over the last three decades, probably because of the widespread use of antihypertensive medication. Nevertheless, about 70% of men with CKD and 50% of women with CKD did not reach the optimal blood pressure levels of <130/80 mmHg even in the latest survey. Several clinical trials have demonstrated that blood pressure lowering was beneficial for the prevention of progressive kidney disease [33,34] and cardiovascular disease in individuals with CKD [35–38]. A recent meta-analysis of Japanese cohort studies also revealed that lower blood pressure level is linearly associated with a lower risk of cardiovascular disease and death in subjects with CKD [39]. These findings, therefore, suggest that blood pressure should be controlled more strictly in individuals with CKD, using the recommendations in the current guidelines [23,24].

Our study showed that the prevalence of CKD Stages 1–2 decreased over the last three decades in both sexes. Importantly, the frequency of women with CKD Stages 1–2 was halved over time, and therefore, the overall prevalence of CKD did not change. In the 2002 survey, blood pressure was well-controlled in women, compared with men (Table 1). It has been established that blood pressure-lowering therapy, particularly the use of renin–angiotensin system inhibitors, reduces the risk of the development of proteinuria and subsequent kidney dysfunction [40–45]. Furthermore, the relationship between metabolic syndrome and the likelihood of CKD for women tended to be attenuated from the 1988 survey to the 2002 survey, possibly due to early interventions, including lifestyle modification or medications against metabolic disorder. Thus, our findings imply that optimal management of blood pressure and metabolic disorder may reduce the prevalence of CKD in women in the next decade.

Several limitations of our study should be noted. First, it is well-known that eGFR values calculated using the MDRD study equation with a single measure of serum creatinine are not fully accurate. In addition, measurement of serum creatinine was not repeated after an interval of at least 3 months. Additionally, the values of serum creatinine were not calibrated using the values from the Cleveland Clinic, although they were calibrated across the three surveys. These matters may have caused some degree of misclassification of eGFR levels. Nevertheless, these limitations may have had little effect on our conclusions because the extent of misclassification of eGFR levels would be similar across the surveys. Second, the method for measuring serum cholesterol could not be calibrated across the surveys in this study. However, we believe that our findings with regard to the trend in the propor-
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References

21. Alberti KG, Eckel RH, Grundy SM et al. Metabolic syndrome was defined by using criteria recommended in a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120: 1640–1645
Ethnic disparities in prevalence and impact of risk factors of chronic kidney disease

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Abstract

Background. There is substantial heterogeneity in literature regarding the epidemiology for chronic kidney disease (CKD) in different Asian populations. We aimed to assess the prevalence and risk factors of CKD in a multi-ethnic Asian population in Singapore.

Methods. We examined 4499 participants of Chinese, Malay and Indian ethnicity, aged 24–95 years, who

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