


to investigate the respective associations between lifestyle and proteinuria and the estimated glomerular filtration rate (eGFR).

Methods: The lifestyle habits of 25,493 middle-aged participants were investigated in a cross-sectional study to find habits that are associated with a low eGFR (<60 mL/min/1.73 m²) and/or the presence of proteinuria. The lifestyle habits of the participants were evaluated using a questionnaire. Unhealthy lifestyle habits were defined as follows: 1. obesity, 2. being a current/former smoker, 3. eating irregular meals, 4. having less than 5 hours sleep, 5. exercising less than once a week, and 6. drinking more than once a week. The associations among unhealthy habits, eGFR, and proteinuria were evaluated using multivariate analysis.

Results: The following lifestyle factors were significantly and independently associated with proteinuria: obesity (odds ratio (OR): 1.18, 95%C.I: 1.04-1.34), being a current/former smoker (OR: 1.26, 95%C.I: 1.11-1.42), eating irregular meals (OR: 1.40, 95%C.I: 1.22-1.61), sleeping less than 5 hours (OR: 1.38, 95%C.I: 1.15-1.65), and exercising less than once a week (OR: 1.18, 95%C.I: 1.05-1.33). In contrast, the following unhealthy lifestyle factors were not clearly associated with a low eGFR: obesity (OR: 1.05, 95%C.I: 0.95-1.17), being a current/former smoker (OR: 0.76, 95%C.I: 0.69-0.84), eating irregular meals (OR: 0.91, 95%C.I: 0.79-1.04), sleeping less than 5 hours (OR: 1.02, 95%C.I: 0.85-1.22), and exercising less than once a week (OR: 0.91, 95%C.I: 0.83-0.99).

Conclusion: Associations between proteinuria and unhealthy lifestyle habits were observed in our cross-sectional study. Unhealthy lifestyles should be monitored during the management of CKD patients with proteinuria.


Keywords: Chronic kidney disease, Lifestyle, Risk factor, Proteinuria, Estimated glomerular filtration rate

Introduction

Chronic kidney disease (CKD) has received considerable attention as an important risk factor for cardiovascular disorders, including ischemic heart disease, heart failure, cerebrovascular disease, and peripheral arterial disease, and all-cause mortality. In addition, CKD patients are likely to develop end-stage kidney disease (ESKD), which can reduce their quality of life (QOL) and has become a socioeconomic concern. It is estimated that more than one million people have CKD in Japan, and early diagnosis and intervention are required in these cases to prevent atherosclerotic cardiovascular complications and/or death.

CKD patients are often affected by diabetes, hypertension, and/or obesity, which are considered to be risk factors for cardiovascular disease in the general population. Conversely, some CKD patients do not display proteinuria or other risk factors for a poor outcome. Also, although proteinuria and the estimated glomerular filtration rate (eGFR) are significantly associated with future kidney function, it is possible
that they are affected by different factors. Several lifestyle factors are associated with CKD. Obesity and a central fat distribution pattern are associated with renal impairment. Furthermore, previous reports have demonstrated that unhealthy lifestyle habits such as smoking, heavy alcohol consumption, and an unhealthy diet (ingesting high amounts of animal fat, salt, and soft drinks) can lead to the development of proteinuria/albuminuria or CKD. However, another study reported that smoking was associated with increased glomerular filtration rate (GFR); thus, the effects of unhealthy lifestyle factors on CKD patients is unclear, and few reports have investigated the relationships between lifestyle habits and proteinuria or eGFR.

The aim of this study was to investigate the characteristics of CKD patients and explore the factors associated with proteinuria and eGFR.

**Materials and Methods**

**Study Population and Data Collection**

This was a cross-sectional study conducted at the Center for Preventive Medicine, NTT Kanto Medical Center, Tokyo, from May 2006 to August 2010. We run a comprehensive medical examination institution that provides health check-up programs, involving several health check-up packages, which include various medical examinations such as blood tests, electrocardiograms, gastrofiberscopy, computed tomography scans, and other tests. Employers in Japan are required by The Industrial Safety and Health Law to commission medical examinations once a year to ensure the health of their employees. NTT, a telecommunications company, entered into a contract in which we provide medical examinations based on the requirements of the abovementioned law to their employees. Our program also includes many types of blood test that are not mandated by the abovementioned law. Almost all of the study subjects were volunteers obtained from among NTT company employees and their families. This large-scale cross-sectional study was conducted as part of the general health check-up program at our center. All examinations were performed by the same trained staff at a single institution. Some of the results for some subjects were used for the employee medical examinations mandated by The Industrial Safety and Health Law of Japan; therefore, the precision of the examination was maintained.

Most participants were male (74.2%) and ranged in age from 40 to 60 years old. The participants completed self-administered questionnaires about their demographic characteristics, medical history (cardiovascular disease, stroke, diabetes, hypertension, dyslipidemia, hyperuricemia/gout, and renal disease), and lifestyle habits (alcohol consumption, smoking status, physical activity, eating habits, and sleeping habits) and then well-trained staff interviewed any participants who had failed to complete their forms. Weight and height were measured after the removal of shoes and heavy clothing. Blood pressure was measured in the sitting position with an automatic monitor. Serum and urine samples were collected from each participant after overnight fasting and immediately subjected to biochemical analysis. Blood was drawn and used to determine the fasting cholesterol level, serum uric acid concentration, glycated hemoglobin (HbA1c) level, and serum creatinine concentration. Blood tests were performed using common enzymatic methods, and serum creatinine concentration was measured with an autoanalyzer “LABOSPECT 008” (Hitachi Corp, Japan). Urinalysis was performed using a Clinitek Atlas XL autoanalyzer (Siemens Healthcare Diagnostics K.K., Japan). The urine test results were classified as (−), (+), (1+), (2+), or (3+). Participants who had missing kidney function or lifestyle data and/or whose eGFR was less than 15 mL/min/1.73 m² were excluded from the study. In the case of participants who underwent several examinations during the study period, the latest data were analyzed.

This survey was conducted according to the Ethics Guidelines for Epidemiological Studies established by the Japanese Government. The participants’ clinical data were retrospectively retrieved from an institutional database. Before each examination, all participants were informed that the clinical data obtained by the program might be retrospectively analyzed and published. All of the examinations included in this study were performed as a routine part of the program, and none were aimed at specifically collecting data for the current study. The study protocol was approved by the institutional ethics committee.

The following parameters were calculated in this study:

1. **eGFR** was calculated using the Japanese GFR inference formula, which was developed by the Japanese Society of Nephrology:

\[
\text{eGFR (mL/min/1.73 m²)} = 194 \times \text{serum creatinine (mg/dL)}^{-1.094} \times \text{age (years)}^{-0.287} \times 0.739 \times \text{gender}
\]

2. **Body mass index (BMI)** = body weight (kg) / height squared (m²).

3. **HbA1c** was measured as the National Glycohemoglobin Standardization Program (NGSP) equivalent value (%), which was developed by the Japan Diabetes Society.

\[\text{HbA1c (Japan Diabetes Society (JDS))} \times \text{gender} + \text{age} \times \text{gender} \times \text{weight} \times \text{gender} + \text{height} \times \text{gender} + \text{education} \times \text{gender} + \text{smoking status} \times \text{gender} + \text{alcohol consumption} \times \text{gender} + \text{physical activity} \times \text{gender} + \text{eating habits} \times \text{gender} + \text{sleeping habits} \times \text{gender} + \text{cardiovascular disease} \times \text{gender} + \text{stroke} \times \text{gender} + \text{diabetes} \times \text{gender} + \text{hypertension} \times \text{gender} + \text{dyslipidemia} \times \text{gender} + \text{hyperuricemia/gout} \times \text{gender} + \text{renal disease} \times \text{gender} \]
As for proteinuria, “−” and “+/−” urine test results were defined as normal; all other results were defined as proteinuria. As for eGFR, an eGFR of <60 mL/min/1.73 m² is generally considered to be indicative of chronic kidney disease; therefore, participants with eGFR of <60 mL/min/1.73 m² (eGFR <60) were defined as having a low eGFR.

With regard to healthy lifestyles, six lifestyle habits were evaluated in this study: (1) Obesity: BMI ≥ 25 kg/m², (2) Sleep: less than 5 hours, (3) Meals: irregular (not eating three times a day), (4) Drinking alcohol: drinking alcohol more than once a week, (5) Smoking: being a current/former smoker, and (6) Physical activity: exercising less than once a week. We defined the six healthy lifestyle habits by consulting “Breslow’s 7 health practices”23) and modifying them according to recent findings. During this process, other previous reports24-26) were also referred to when we were setting the sleep duration and smoking status criteria.

Individuals with metabolic disorders were defined as participants who were receiving pharmacotherapy for diabetes, hypertension, dyslipidemia, and/or hyperuricemia/gout. As for arteriosclerotic diseases, we collected information about the patients’ self-reported clinical histories of cardiovascular disease and/or stroke. In addition, renal diseases were defined as a self-reported clinical history of kidney/urinary calculi, nephritis/nephrosis, kidney cancer, and/or renal insufficiency.

Statistics Analysis

The participants were divided into two categories according to the presence or absence of proteinuria or a low eGFR. Their demographic characteristics were then compared between groups with or without proteinuria or a low eGFR. Subsequently, the participants were stratified into quartiles according to their age at the time of the examination as follows: ≤ 39, 40-47, 48-56, and ≥57. The relationships between these ranks and unhealthy lifestyle habits, proteinuria (+), and low eGFR were then evaluated using Chi square analysis.

The factors that were significantly associated with proteinuria / eGFR <60 mL/min/1.73 m² were then determined using multiple logistic regression analysis. The covariates examined in the multivariate analysis were age, sex, systolic blood pressure, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), triglycerides (TG), HbA1c, uric acid (UA), disease prevalence rates (renal disease, metabolic disorders, and arteriosclerotic disease), and lifestyle habits. The covariates entered into the regression model were categorized as follows: Model 1 (sex, age, and lifestyle habits), Model 2 (sex, systolic pressure, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, triglycerides, HbA1c, uric-acid, the presence of diseases (renal disease, metabolic disorders, arteriosclerotic disease) and lifestyle habits).

All calculations were performed using JMP software, version 8.0 (SAS Institute, Cary, NC, USA). Continuous data are reported as the mean ± SD. P<0.05 were considered significant.

Results

According to the exclusion criteria, candidates who had an eGFR of <15 mL/min/1.73 m² or for whom data was missing were excluded. Thus, 25,493 participants (male: 74.2%; mean age: 48.5 ± 11.2 years) were eligible for the study (inclusion rate=98.5%).

Our subjects were categorized according to the presence or absence of a low eGFR (Table 1: left) or proteinuria (Table 1: right). As a result, we found that 2,748 subjects (10.8 %) had an eGFR of <60 mL/min/1.73 m² (eGFR <60), and 1490 subjects (5.8%) had proteinuria (+).

The mean age of the participants with an eGFR <60 mL/min/1.73 m² was significantly higher than that of individuals with an eGFR ≥60 mL/min/1.73 m². The participants with an eGFR <60 mL/min/1.73 m² displayed significantly higher BMI, systolic and diastolic blood pressure, LDL-C, TG, UA, and HbA1c values than the participants with an eGFR ≥60 mL/min/1.73 m². In addition, their mean HDL-C concentration was significantly lower than that of the latter group. The participants with an eGFR <60 mL/min/1.73 m² also demonstrated a significantly higher prevalences of metabolic disorders, arteriosclerotic disease, and renal disease than subjects with an eGFR ≥60 mL/min/1.73 m². Obesity was more prevalent in the participants with a low eGFR (eGFR <60 mL/min/1.73 m²); however, the prevalence of unhealthy lifestyle habits (having less than 5 hours sleep, eating irregular meals, drinking alcohol more than once a week, and exercising less than once a week) was significantly lower in the participants with a low eGFR.

The proportion of males was significantly higher among subjects with than without proteinuria, and higher BMI, systolic and diastolic blood pressure, LDL-C, TG, UA, and HbA1c values were observed among subjects with than without proteinuria. Moreover, their HDL-C levels were significantly lower than...
Table 1. Demographic characteristics according to estimated glomerular filtration rate (eGFR) and proteinuria

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) or N (%)</th>
<th>ρ</th>
<th>Mean (SD) or N (%)</th>
<th>ρ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>eGFR (mL/min/1.73 m²)</td>
<td>≥60</td>
<td>&lt;60</td>
</tr>
<tr>
<td>Number of participants</td>
<td>25493</td>
<td>22745</td>
<td>2748</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.5 ±11.2</td>
<td>47.4 ±10.9</td>
<td>57.4 ±9.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>18909 (74.2)</td>
<td>16845 (74.1)</td>
<td>2064 (75.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Body mass index (BMI) (kg/m²)</td>
<td>23.1 ±3.3</td>
<td>23.0 ±3.3</td>
<td>23.7 ±3.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Blood pressure measurements (mmHg)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Antihypertensive medication (%)</td>
<td>2963 (11.6)</td>
<td>2239 (9.8)</td>
<td>724 (26.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Systolic</td>
<td>125.0 ±17.3</td>
<td>124.5 ±17.1</td>
<td>129.3 ±18.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Diastolic</td>
<td>79.2 ±10.9</td>
<td>78.9 ±10.9</td>
<td>81.9 ±11.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Lipid metabolism-related measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid-lowering agents (%)</td>
<td>1396 (5.5)</td>
<td>1043 (4.6)</td>
<td>353 (12.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>High density lipoprotein-cholesterol (mg/dL)</td>
<td>59.8 ±15.3</td>
<td>60.0 ±15.2</td>
<td>58.5 ±15.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Low density lipoprotein-cholesterol (mg/dL)</td>
<td>117.8 ±30.1</td>
<td>117.2 ±30.0</td>
<td>123.2 ±29.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>115.6 ±87.2</td>
<td>114.6 ±87.8</td>
<td>123.9 ±82.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Glucose metabolism-related measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoglycemic agents (%)</td>
<td>790 (3.1)</td>
<td>655 (2.9)</td>
<td>135 (4.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>5.67 ±0.66</td>
<td>5.66 ±0.66</td>
<td>5.80 ±0.61</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Uric acid metabolism-related measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid-lowering agents (%)</td>
<td>847 (3.3)</td>
<td>566 (2.5)</td>
<td>281 (10.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Uric acid (mg/dL)</td>
<td>5.8 ±1.4</td>
<td>5.8 ±1.4</td>
<td>6.4 ±1.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Kidney-related items</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatine (mg/dL)</td>
<td>0.84 ±0.16</td>
<td>0.81 ±0.14</td>
<td>1.06 ±0.21</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>74.4 ±12.6</td>
<td>76.8 ±11.0</td>
<td>54.3 ±5.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Clinical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arteriosclerotic disease</td>
<td>566 (2.2)</td>
<td>412 (1.8)</td>
<td>154 (5.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1690 (6.6)</td>
<td>1377 (6.1)</td>
<td>313 (11.4)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Lifestyle-related items</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity (BMI ≥25 kg/m²)</td>
<td>6357 (24.9)</td>
<td>5513 (24.2)</td>
<td>844 (30.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sleep duration (less than 5 hours)</td>
<td>1880 (7.4)</td>
<td>1721 (7.6)</td>
<td>159 (5.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Meals (irregular)</td>
<td>3940 (15.5)</td>
<td>3650 (16.1)</td>
<td>290 (10.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Alcohol intake (more than once a week)</td>
<td>14881 (58.4)</td>
<td>13381 (58.8)</td>
<td>1500 (54.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smoker (current/former smoker)</td>
<td>14074 (55.2)</td>
<td>12592 (55.4)</td>
<td>1482 (53.9)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Exercise (less than once a week)</td>
<td>16560 (65.0)</td>
<td>15011 (66.0)</td>
<td>1549 (56.4)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

p < 0.05: comparisons were made between the eGFR ≥60/proteinuria (−) group and the eGFR < 60/proteinuria (+) group using the t-test or Chi square test.

in subjects without proteinuria. The participants with proteinuria demonstrated a significantly higher prevalence of metabolic disorders, arteriosclerotic disease, and renal disease. Obesity was also more prevalent in the subjects with proteinuria. Furthermore, the prevalence of unhealthy lifestyle habits (eating irregular meals, being a current/former smoker, and exercising less than once a week) was significantly higher among the participants with proteinuria.

The associations detected between specific characteristics and age are shown in Table 2. As the subjects’ age increased, the frequency of unhealthy “meal, exercise, and sleep” habits decreased; however, the proportion of subjects with a low eGFR increased with age.

The factors that were significantly associated with proteinuria are shown in Table 3. We found similar associations between Models 1 and 2. Model 2 included the most covariates. In Model 2: obesity (OR: 1.18, 95%CI: 1.04-1.34), getting less than 5 hours sleep (OR: 1.38, 95%CI: 1.15-1.65), eating irregular meals (OR: 1.40, 95%CI: 1.22-1.61), being
**Table 2.** Percentage of participants with unhealthy lifestyle habits, proteinuria, and a low eGFR stratified according to age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex (male)</th>
<th>eGFR &lt; 60 (mL/min/1.73 m²)</th>
<th>Proteinuria</th>
<th>Obesity (BMI ≥ 25 kg/m²)</th>
<th>Sleep duration (less than 5 hours)</th>
<th>Meals (irregular)</th>
<th>Alcohol intake (more than once a week)</th>
<th>Smoker (current/former)</th>
<th>Exercise (less than once a week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 57</td>
<td>5150 (73.1)</td>
<td>1.05-1.33</td>
<td>1.01 (0.91-1.12)</td>
<td>1.47 (1.32-1.64)</td>
<td>1.82 (1.64-2.04)</td>
<td>1.21 (1.08-1.36)</td>
<td>0.90 (0.80-1.00)</td>
<td>1.40 (1.13-1.44)</td>
<td>1.95 (1.75-2.17)</td>
</tr>
<tr>
<td>≥ 48-56</td>
<td>4463 (70.9)</td>
<td>0.96 (0.80-1.12)</td>
<td>1.41 (1.24-1.61)</td>
<td>1.40 (1.17-1.66)</td>
<td>1.38 (1.15-1.65)</td>
<td>1.27 (1.13-1.44)</td>
<td>0.90 (0.80-1.00)</td>
<td>1.40 (1.22-1.61)</td>
<td>1.49 (1.25-1.77)</td>
</tr>
<tr>
<td>40-47</td>
<td>4502 (76.1)</td>
<td>1.05-1.23</td>
<td>1.49 (1.25-1.77)</td>
<td>1.40 (1.17-1.66)</td>
<td>1.38 (1.15-1.65)</td>
<td>1.27 (1.13-1.44)</td>
<td>0.90 (0.80-1.00)</td>
<td>1.40 (1.22-1.61)</td>
<td>1.95 (1.75-2.17)</td>
</tr>
<tr>
<td>≤ 39</td>
<td>4794 (76.8)</td>
<td>1.05-1.23</td>
<td>1.49 (1.25-1.77)</td>
<td>1.40 (1.17-1.66)</td>
<td>1.38 (1.15-1.65)</td>
<td>1.27 (1.13-1.44)</td>
<td>0.90 (0.80-1.00)</td>
<td>1.40 (1.22-1.61)</td>
<td>1.95 (1.75-2.17)</td>
</tr>
</tbody>
</table>

*Data n (%)*
†: according to Chi square analysis

**Table 3.** Factors associated with proteinuria (Binary logistic regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate odds ratio (95C.I.)</th>
<th>Multivariate Model 1 †</th>
<th>Multivariate Model 2 †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI ≥ 25 kg/m²)</td>
<td>1.95 (1.75-2.17)</td>
<td>1.82 (1.64-2.04)</td>
<td>1.18 (1.04-1.34)</td>
</tr>
<tr>
<td>Sleep duration (less than 5 hours)</td>
<td>1.49 (1.25-1.77)</td>
<td>1.40 (1.17-1.66)</td>
<td>1.38 (1.15-1.65)</td>
</tr>
<tr>
<td>Meals (irregular)</td>
<td>1.41 (1.24-1.61)</td>
<td>1.38 (1.19-1.57)</td>
<td>1.40 (1.22-1.61)</td>
</tr>
<tr>
<td>Alcohol intake (more than once a week)</td>
<td>1.01 (0.91-1.12)</td>
<td>0.90 (0.80-1.00)</td>
<td>0.85 (0.76-0.96)</td>
</tr>
<tr>
<td>Smoker (current/former)</td>
<td>1.47 (1.32-1.64)</td>
<td>1.27 (1.13-1.44)</td>
<td>1.26 (1.11-1.42)</td>
</tr>
<tr>
<td>Exercise (less than once a week)</td>
<td>1.21 (1.08-1.36)</td>
<td>1.19 (1.06-1.33)</td>
<td>1.18 (1.05-1.33)</td>
</tr>
<tr>
<td>R² (p value)</td>
<td>0.02 (&lt;0.01)</td>
<td>0.07 (&lt;0.01)</td>
<td></td>
</tr>
</tbody>
</table>

†: Adjusted for sex and age.
‡: Adjusted for sex, age, systolic pressure, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides, HbA1c, uric-acid, the presence of disease (renal diseases, metabolic disorders, arteriosclerotic diseases)

Table 4 shows the factors that were significantly associated with a low eGFR. Slightly different associations were found between Models 1 and 2; however, it was thought that these differences did not threaten the overall tendency of the findings. In Model 2: drinking alcohol more than once a week (OR: 0.75, 95%CI: 0.68-0.82), being a current/former smoker (OR: 0.76, 95%CI: 0.69-0.84), and exercising less than once a week (OR: 0.91, 95%CI: 0.83-0.99) were associated with a low eGFR. The following factors were also found to be significantly and independently associated with the development of a low eGFR: being female (p < 0.01), higher age (β: 0.088, p < 0.01), LDL-C (β: 0.002, p < 0.01), UA (β: 0.545, p < 0.01), and disease prevalence. HDL-C (p = 0.40) and TG (p = 0.10) were not significantly associated with a low eGFR. Furthermore, systolic blood pressure (β: −0.04, p < 0.01) and HbA1c (β: −0.11, p < 0.01) were found to protect against a low eGFR.

**Discussion and Conclusion**

This large-scale cross-sectional study, which was conducted in one hospital, estimated the frequency of CKD and the risk factors, including lifestyle factors, associated with proteinuria or a low GFR among health check-up participants. To the best of our...
knowledge, this is the first report to elucidate the factors associated with proteinuria or a low GFR and reveal the impact of lifestyle factors on these measures using a large health check-up dataset.

The participants with proteinuria or an eGFR < 60 mL/min/1.73 m² displayed a significantly higher prevalence of atherosclerotic complications and significantly increased metabolic parameters compared with the subjects with an eGFR ≥ 60 mL/min/1.73 m² or proteinuria (−). A previous study in which a Japanese community-based population was followed-up for 10 years also showed that treated hypertension [hazard ratio (HR): males: 1.85, females: 2.28], impaired glucose tolerance [HR: males: 1.21, females: 1.19], treated diabetes [HR: males: 2.48, females: 2.91], and hypercholesterolemia [HR: males: 1.13, females: 1.13] are predictors of CKD stage 1 or 2 [27]. In addition, various atherosclerotic risk factors are significantly associated with the development of CKD [10, 12, 28-30]. These parameters should receive considerable attention as part of the management strategies for preventing CKD.

As for lifestyle factors, several unhealthy lifestyle factors are also significantly associated with the presence of proteinuria. Smoking is associated with the development of albuminuria, which can progress to end-stage renal disease [6, 16, 27, 28, 31]. Physical inactivity indirectly influences CKD development through obesity, diabetes, and hypertension [16, 32]. In addition, several epidemiological studies have suggested that an unhealthy diet is associated with an increased risk of albuminuria and that eating irregular meals may contribute to the development of proteinuria [16, 32]. Getting insufficient sleep has also been found to be associated with the development of obesity, diabetes, and hypertension [15, 34], which are independent risk factors for CKD. As described above, several unhealthy lifestyle factors are suggested to contribute to the development of CKD, and it is possible that these factors have cumulative effects [30]; thus, it is necessary for individuals to comprehensively modify their unhealthy lifestyles to prevent CKD.

On the other hand, our data indicated that smoking and exercising less are factors that protect against a low eGFR. These results seem counterintuitive, but there are several possible explanations for our findings. For example, it is possible that smoking causes hyperfiltration in the early phase of renal dysfunction [19]. As for physical activity, the serum creatinine concentrations of athletes are generally higher than those of sedentary people [36]. In addition, exercise training in obese diabetic patients with chronic kidney disease might decrease proteinuria but not alter GFR [37]. The above mechanisms have the potential to explain the paradoxical relationships between proteinuria/a low eGFR and smoking/physical inactivity observed in this study. Our data also showed that alcohol consumption was a protective factor for both a low eGFR and proteinuria. Previous studies have suggested that appropriate alcohol consumption has a protective effect against cardiovascular disease [38]. In addition, they demonstrated evidence for a dose-response relationship between the level of alcohol consumption and the risk of a variety of physical problems. In “Healthy Japan 21”, the Japanese Ministry of Health and Welfare reported that consuming a mean amount of around 20 g absolute alcohol per day represents “moderate drinking.” [39]. Moderate alcohol consumption has not been shown to be harmful to the kidneys and might have protective effects [40, 41], possibly via similar mechanisms to those reported for cardiovascular disease. Although the detailed effects of alcohol consumption could not be evaluated in our study, our data suggest that appropri-
ate alcohol consumption has a beneficial effect on an individual’s risk of developing CKD.

As stated above, our data suggest that unhealthy lifestyle habits are associated with proteinuria but not eGFR. In other words, our data suggest that there are differences between the risk factors for proteinuria and eGFR. There are several possible explanations for this. The first is that there are fundamental differences between proteinuria and eGFR as indicators of CKD. Proteinuria is a classical and well-established marker of kidney atherosclerosis as well as atherosclerotic disorders. Although a low eGFR has received considerable attention as a risk factor for CKD, eGFR is calculated from an equation and can be affected by several factors, such as renal blood flow, the internal water-electrolytic balance, and muscle mass. In addition, eGFR can be reduced without morbid effects on the kidney. Thus, the presence of proteinuria is particularly indicative of dynamic renal disorders, but cannot be used to quantitatively evaluate renal dysfunction. On the other hand, eGFR can be used to quantitatively estimate renal dysfunction, but does not indicate particular renal disorders. Thus, these factors might indicate different CKD conditions and hence play different roles in the management of CKD. We consider that the abovementioned differences support the idea that they have different risk factors. The second reason for the abovementioned result is age-specific lifestyle characteristics. The frequency of unhealthy lifestyle habits (getting less than 5 hours sleep, physical inactivity, and irregular meals) showed a tendency to decline in accordance with aging in our study. One possible reason for this is that elderly participants often have a greater amount of leisure time and are more anxious about their health than middle-aged participants. On the other hand, eGFR deteriorates with aging in most cases. Conversely, no close relationship was found between proteinuria and aging in our study. Thus, the effects of aging might explain our paradoxical results for the associations between eGFR and unhealthy lifestyle habits. Furthermore, increased systolic blood pressure and HbA1c were found to protect against low eGFR in our multivariate analysis. The effects of aging, sex, and pharmacotherapy might similarly explain our paradoxical results regarding the associations between eGFR and these markers as systolic blood pressure and HbA1c were found to be significantly and independently associated with the development of low eGFR in our other multivariate analysis, which excluded sex, age, and the presence of diseases as covariates (data not shown). Men generally display a higher prevalence of metabolic disorders and arteriosclerotic disease than women; however, men generally display higher eGFR than women. It is widely known that aging and sex influence HbA1c levels. In addition, the administration of drugs for metabolic disorders and atherosclerosis improves blood pressure and HbA1c levels, but might not increase eGFR; therefore, it might be difficult to cross-sectionally determine the effects of lifestyle habits and metabolic markers on eGFR. Further fundamental studies and longitudinal data analyses are required to validate the above hypotheses.

eGFR and proteinuria have been demonstrated to be multiplicatively associated with the risk of adverse outcomes without any evidence of an interaction between them. It is important that as many CKD risk factors as possible are ameliorated in order to prevent the development of CKD and adverse outcomes. Thus, CKD should be comprehensively evaluated using both eGFR and proteinuria.

Limitations

Our study has a few limitations. First, lifestyle habits were evaluated using a self-administered questionnaire and so the participants might have stated that they had more healthy lifestyles than they actually did. Thus, it is possible that the participants were not as healthy as our data suggested, and further evaluations of lifestyle habits based on an established questionnaire are necessary.

Second, our study was affected by selection bias. More than 70% of our participants were healthy male office workers who ranged in age from 40 to 60 years old. Thus, this limited sample might not have accurately represented the whole population; therefore, the investigated cohort was affected by selection bias (the healthy workers effect). The healthy workers effect might have caused the paradoxical associations observed among eGFR and some unhealthy lifestyle habits; thus, a multicenter study involving strict survey monitoring is required.

Lastly, the medications being taken by the participants were unknown. Consequently, the effects of pharmacotherapy on proteinuria and eGFR were not assessed in our study.

As stated above, our study has serious limitations; however, this is the first report to have independently investigated the relationships among lifestyle habits and eGFR/proteinuria.

Conclusion

An association between proteinuria and unhealthy lifestyle habits was observed in our cross-sectional
study. Lifestyle habit modification is important for preventing adverse outcomes in CKD patients, and unhealthy lifestyles should be monitored during the management of CKD patients with proteinuria.

Conflicts of Interest
No.

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