Cardiovascular disease (CVD) is one of the most serious complications of kidney disease, yet studies of CVD in early stage of chronic kidney disease (CKD) in Asian patients are very limited. Therefore, this study determined the prevalence and the spectrum of CVD in individuals with early-stage CKD and compared them with data of individuals without CKD. Compared with individuals with estimated GFR (eGFR) >90 ml/min per 1.73 m², the prevalence of myocardial infarction, stroke, and total CVD of individuals with eGFR 60 to 89 ml/min per 1.73 m² was increased by 91.4, 71.7, and 67.6%, respectively. For individuals with eGFR 30 to 59 ml/min per 1.73 m², the percentage was 105.2, 289.1, and 200.7%, respectively. For each eGFR category, stroke was more prevalent than myocardial infarction. Compared with individuals with eGFR >90 ml/min per 1.73 m², participants with eGFR 60 to 89 and 30 to 59 ml/min per 1.73 m² tended to have more cardiovascular risk factors, and there were strong unadjusted and adjusted associations between CVD with different stages of eGFR (eGFR >90 ml/min per 1.73 m² as reference). This is the first report on the prevalence and the spectrum of CVD in early stages of CKD in a community-based Chinese population. The spectrum of CVD in this Chinese population is different from reports of Western countries. Individuals with subtle decreased renal function seem much more likely to have multiple cardiovascular risk factors and have higher prevalence of CVD than those without CKD.
Estimated GFR (eGFR) was calculated with an abbreviated MDRD equation (14) by calibrated Scr. eGFR was stratified into >90 (as reference group), 60 to 89, and 30 to 59 ml/min per 1.73 m². Spot urinary albumin-to-creatinine ratio (ACR) >30 mg/g was introduced to define albuminuria from a practical point of view. Albuminuria was measured by immunoturbidimetric methods (Audit Diagnostics, Cork, Ireland).

**Other Variables**

Sociodemographic characteristics, personal health history (e.g., hypertension, diabetes), and lifestyle behavior (e.g., smoking) were obtained by questionnaire. BP was measured according to the guidelines presented in Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (15). Fasting blood glucose, serum total cholesterol, LDL cholesterol, and HDL cholesterol also were measured.

**Statistical Analyses**

Data entry and management were performed on Epidata software. All analyses and calculations were performed by SPSS statistical package, version 10.0 (SPSS, Inc., Chicago, IL). Data were presented as mean ± SD for continuous variables and as proportions for categorical variables. Descriptive analyses were used to characterize the participant population by sociodemographic data (age and gender) and health status (e.g., hypertension, diabetes). Prevalence and mean values of selected conditions were examined using χ² statistics for categorical variables and Wilcoxon’s rank sum for continuous values. The unadjusted odds ratios (OR) between different eGFR staging (>90, 60 to 89, and 30 to 59 ml/min per 1.73 m²; >90 ml/min per 1.73 m² as the reference) and CVD were determined by univariate logistic regression analysis. The association between staging of eGFR and CVD then was determined after adjustment for age and gender. Next, the association was assessed after adjustment for traditional risk factors (obesity, hypercholesteremia, low HDL cholesterol, diabetes, and systolic BP level) and/or nontraditional CVD risk factors.

**Results**

**General Characteristics**

Complete information was available for 98.2% (n = 2310) of participants examined. Participants who could not provide history of CVD and did not have results of Scr and/or ACR were excluded from further analysis. Two participants with eGFR <30 ml/min per 1.73 m² were excluded from analysis. All participants were Chinese. General characteristics are given in Table 1. The mean age was 60.68 yr (range 42 to 85), and 49.5% were men. Forty-seven percent (n = 1086) of participants were categorized as hypertensive. Among them, 87.4% reported a history of hypertension. Twenty-eight percent (n = 646) of participants were categorized as having diabetes, and 71.5% of them reported a history of diabetes.

**Indicators of Kidney Damage**

Overall prevalence of albuminuria was 6.2% (n = 142). A total of 754 (32.7%) individuals had a eGFR of 60 to 89 ml/min per 1.73 m², with the mean eGFR being 78.7 ml/min per 1.73 m². A total of 67 (2.9%) individuals had an eGFR of 30 to 59 ml/min per 1.73 m², with the mean eGFR being 52.3 ml/min per 1.73 m².

**Prevalence of CVD**

The overall prevalence of self-reported myocardial infarction (MI) and stroke was 7.7% (n = 178) and 12.1% (n = 280), respectively. Twelve percent of participants with albuminuria reported history of MI compared with 7.4% of those without albuminuria (P = 0.071; Figure 1). The prevalence of stroke among participants with albuminuria was higher than those without albuminuria (20.4 versus 11.6%; P = 0.003). The overall prevalence of CVD in participants with albuminuria was 26.8% (n = 38) and in participants without albuminuria was 17.2% (n = 372; P = 0.006).

When analyzed by different stage of eGFR, participants with lower eGFR had a higher prevalence of MI, stroke, and CVD (Figure 2). Even for eGFR between 60 and 89 ml/min per 1.73 m², there was a marked increase in prevalence of MI, stroke, and CVD. Compared with participants with eGFR >90 ml/min per 1.73 m², the prevalence of MI, stroke, and total CVD of

**Table 1. General characteristics of the study population**

<table>
<thead>
<tr>
<th>General Characteristics</th>
<th>Total (n = 2,308)</th>
<th>eGFR &gt;90b (n = 1,487)</th>
<th>eGFR 60 to 89b (n = 754)</th>
<th>eGFR 30 to 59b (n = 67)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>60.68 ± 9.94</td>
<td>58.26 ± 9.67</td>
<td>64.70 ± 8.93</td>
<td>69.03 ± 7.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>49.5</td>
<td>48.5</td>
<td>52.0</td>
<td>44.8</td>
<td>0.215</td>
</tr>
<tr>
<td>Obesity (%)c</td>
<td>29.1</td>
<td>27.0</td>
<td>32.8</td>
<td>34.3</td>
<td>0.012</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>28.0</td>
<td>29.2</td>
<td>25.2</td>
<td>32.8</td>
<td>0.093</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>47.1</td>
<td>42.0</td>
<td>55.3</td>
<td>65.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>125.86 ± 18.57</td>
<td>124.60 ± 18.33</td>
<td>127.81 ± 18.59</td>
<td>131.89 ± 20.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>76.65 ± 10.30</td>
<td>76.88 ± 10.33</td>
<td>76.28 ± 10.12</td>
<td>75.61 ± 11.53</td>
<td>0.308</td>
</tr>
<tr>
<td>Albuminuria¹</td>
<td>6.2</td>
<td>5.9</td>
<td>5.8</td>
<td>14.9</td>
<td>0.010</td>
</tr>
<tr>
<td>Hypercholesteremiae⁷</td>
<td>30.8</td>
<td>28.0</td>
<td>34.7</td>
<td>47.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low HDL cholesterol²</td>
<td>5.5</td>
<td>5.4</td>
<td>5.3</td>
<td>9.0</td>
<td>0.449</td>
</tr>
</tbody>
</table>

*a* eGFR, estimated GFR.

*b* Calculated with abbreviated Modification of Diet in Renal Disease (MDRD) equation (ml/min per 1.73 m²).

*c* Defined as body mass index >25 kg/m².

¹Defined as urinary albumin-to-creatinine ratio >30 mg/g.

²Defined as serum cholesterol >5.72 mmol/L.

³Defined as serum HDL <0.91 mmol/L.
participants with eGFR 60 to 89 ml/min per 1.73 m² was higher with 91.4, 71.7, and 67.6%, respectively. For participants with eGFR 30 to 59 ml/min per 1.73 m², the number was 105.2, 289.1, and 200.7%, respectively. For each eGFR category, stroke was more prevalent than MI.

**Risk Factors for CVD**

Compared with participants with eGFR >90 ml/min per m², participants with eGFR 60 to 89 and 30 to 59 ml/min per 1.73 m² tended to have more cardiovascular risk factors (Table 1), such as older age, obesity, diabetes, hypertension, hypercholesterolemia, and albuminuria. There were strong unadjusted associations between CVD with different stages of eGFR (eGFR >90 ml/min per 1.73 m² as reference; Table 2). After adjustment for age and gender, the OR of different stages of eGFR decreased but still existed. OR remained similar in magnitude after further adjustment for traditional (age, gender, obesity, hypercholesterolemia, low HDL cholesterol, diabetes, and systolic BP level) and/or nontraditional risk factor (albuminuria) for CVD (Table 2). After adjustment for all risk factors and risk markers for CVD, OR of eGFR 60 to 89 and 30 to 59 ml/min per 1.73 m² were statistically significant: 1.315 (95% confidence interval 1.031 to 1.677) and 2.398 (95% confidence interval 1.396 to 4.120).

**Discussion**

Our study demonstrated that in a Chinese population of individuals who were older than 40 yr, prevalence of CVD was markedly increased in early stage of CKD, and mildly decreased eGFR was independently associated with CVD in this population; the spectrum of CVD was different from that in Western countries. By reviewing relevant publications that covered an 18-yr period (1986 through 2003), Vanholder et al. (16) concluded that there is an undeniable link between kidney dysfunction and cardiovascular risk, and the process of cardiovascular damage starts long before the dialysis stage is reached. For general or community-based population, however, the relationship has not been conclusive. In both the Framingham Study and the First National Health and Nutrition Examination Survey (NHANES I), the level of kidney function was not an independent risk factor for CVD outcomes (8,9), whereas in the Atherosclerosis Risk in Communities (ARIC) study and NHANES II, it was a risk factor for both CVD and all-cause mortality (10,11). One possible explanation might be related to different measures to ascertain the level of kidney function. Scr is less sensitive than eGFR for detecting small differences in level of kidney function and therefore may be less likely to detect an association. Besides, differences in the study populations might contribute to the discrepancy (e.g., black individuals were part of the ARIC study but not the Framingham studies), so it is relevant to investigate the relationship between CVD and kidney function stage in different races.

Our study indicated for the first time in a community-based Chinese population if individuals who were older than 40 yr that for individuals with mildly decreased renal function (eGFR 60 to 89 and 30 to 59 ml/min per 1.73 m²), there was a markedly increased prevalence of CVD. Further analysis indicated that individuals with mildly decreased eGFR tended to have more traditional CVD risk factors (e.g., older age, obesity, hypertension). Although adjustments for these factors were made, mildly decreased renal function still was independently correlated with CVD. Albuminuria is an alternative marker for the presence of CKD (14), and there is a strong association between microalbuminuria and CVD in several cross-sectional studies (17–21). In our study, albuminuria was associated with elevated prevalence of CVD. After adjustment for presence of albuminuria, however, an independent association between mildly decreased kidney function and CVD still existed. Also, there might be other markers and factors than albuminuria (e.g., homocysteine, oxidative stress) that were not assessed in this study and contribute to the increased prevalence of CVD.

In our study, stroke was the predominant form of CVD, both...
in all participants and in those with mildly decreased renal function, which was different from data of white individuals (12,13). Reports from the general population also indicated that cerebrovascular disease predominates in Asian individuals, and the number who die from stroke is more than three times of that for coronary heart disease (12,22). However, the exact mechanism of the difference is unclear, but at least the prevalence or the magnitude of the traditional risk factors seems unlikely to explain the differing spectrum of CVD among the specific defined included Asian individuals (23).

There are certain limitations of our study. First, only self-reported prevalence of CVD was determined. The validity of self-reported MI and stroke events by questionnaire was between 70 and 80% in previous studies (24,25). This would tend to miss some cases of CVD and cause a bias toward the null. Second, when used in a Chinese population, the MDRD equation underestimated GFR in cases of near-normal GFR (26), thereby affecting the strength of the study.

We believe that our study has useful features and raises important questions. The majority of studies that have evaluated associations between CVD and CKD come from Europe and North America (16). Our study extends the observation of link between CVD and CKD to an Asian population that is characterized by a relatively lower risk for CVD (12,13). Our study indicated that individuals with subtle decreased renal function seem much more likely to have multiple cardiovascular risk factors and have a higher prevalence of CVD than those without CKD, which is consistent with studies from white populations (16) and provide important information for the recognition of the relation between CVD and CKD. Furthermore, whereas mortality rates from CVD have been halved in many developed countries since the 1980s (27), they are still rising in most developing counties, including China (28). In Beijing, age-adjusted coronary heart disease mortality rates increased by 50% in men and 27% in women from 1984 to 1999 (29). Our study identified a specific population of individuals who have relatively higher prevalence of CKD and need multiple cardiovascular risk factor interventions and thus has significant meaning for prevention and treatment of CVD in China. Additional intervention studies to evaluate potential treatments of CVD in CKD are necessary.

Table 2. Unadjusted and adjusted OR and 95% CI of cardiovascular diseases associated with different stages of eGFR

<table>
<thead>
<tr>
<th>Adjusted Factors</th>
<th>eGFR 60 to 89 ml/min per 1.73 m² (OR [95% CI])</th>
<th>eGFR 30 to 59 ml/min per 1.73 m² (OR [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>1.894 (1.514 to 2.369)</td>
<td>4.465 (2.688 to 7.415)</td>
</tr>
<tr>
<td>Adjusted for age and gender</td>
<td>1.273 (1.002 to 1.617)</td>
<td>2.479 (1.451 to 4.236)</td>
</tr>
<tr>
<td>Adjusted for age, gender, obesity, hypercholesteremia, low HDL cholesterol, diabetes, and systolic BP level b</td>
<td>1.324 (1.039 to 1.686)</td>
<td>2.512 (1.465 to 4.306)</td>
</tr>
<tr>
<td>Adjusted for age, gender, and albuminuria</td>
<td>1.281 (1.008 to 1.628)</td>
<td>2.418 (1.415 to 4.131)</td>
</tr>
<tr>
<td>Adjusted for all of the above</td>
<td>1.315 (1.031 to 1.677)</td>
<td>2.398 (1.396 to 4.120)</td>
</tr>
</tbody>
</table>

aCI, confidence interval; OR, odds ratio.
b<130 (reference), 130 to 159, 140 to 159, and >160 mmHg.

Acknowledgments

We thank the Department of Clinical Laboratory, Peking University First Hospital, for performing tests of albuminuria.

References


Access to UpToDate on-line is available for additional clinical information at [http://www.jasn.org/](http://www.jasn.org/)