Increased risk of mortality in the elderly population with late-stage chronic kidney disease: a cohort study in Taiwan

Shang-Jyh Hwang, Ming-Yen Lin, Hung-Chun Chen, Su-Chen Hwang, Wu-Chang Yang, Chih-Cheng Hsu, Herng-Chia Chiu and Lih-Wen Mau

Abstract

Background. Taiwan has the world’s highest incidence and second highest prevalence of end-stage renal disease (ESRD), particularly in older age groups. However, the transition from chronic kidney disease (CKD) to death or ESRD remains unclear. This study aimed to identify the impact of late-stage CKD on all-cause and cause-specific mortality by identifying the CKD population.

Methods. This was an observational cohort study (n = 35,529), mean age 75.7 years (SD = 5.3), of participants in the Elderly Health Examination Program (EHEP) in Kaohsiung City, Taiwan, between 2002 and 2004. Estimated glomerular filtration rate (eGFR) was calculated by the simplified modified diet in renal disease equation. Proportional hazard ratios (HR) of mortality associated with late-stage CKD were assessed by Cox regression.

Results. The crude prevalence rate of CKD stages 3–5 was 39.4%; 1840 participants (5.18%) died within 2-year follow-up, a mortality rate of 20.3 per 1000 person-years overall and 16.4 per 1000 person-years in the reference group. Higher HR for all-cause and cause-specific mortality were found in the groups with decreased eGFR. Compared with the reference group (eGFR > 60 mL/min/1.73 m²), adjusted HR for all-cause mortality were 1.5, 2.1 and 2.6 for groups with eGFR 30–44, 15–29 and < 15 mL/min/1.73 m², respectively (P < 0.001). Higher HR of mortality due to cardiovascular or renal diseases were also significantly associated with decreased eGFR (P < 0.05).

Conclusion. Late-stage CKD is a significant risk factor for mortality, especially due to cardiovascular and renal diseases, in elderly Taiwanese. Given the higher prevalence rate of late-stage CKD in the study area, CKD patient mortality was relatively lower, which might reflect underestimation of renal function for patients at early stages of CKD, or partly explain the high ESRD population.

Keywords: chronic kidney disease; elderly population; epidemiology and outcomes; glomerular filtration rate; mortality risk

Introduction

The growth of end-stage renal disease (ESRD) populations worldwide has been a concern for many countries, as ESRD consumes increasing proportions of health care budgets [1]. In Taiwan, the incidence and prevalence of ESRD are among the highest in the world. The ESRD population, 0.15% of the total population, spends 7% of the total annual budget for the National Health Insurance (NHI) Program on dialysis in Taiwan [2]. The burden of ESRD also increases with the growth of the elderly population. The chronic kidney disease (CKD) prevalence was ~11% to 14% in the USA, with 75% of the CKD population aged 65 years and older, and that segment of the population growing [3,4].

Taiwan is one of the rapidly ageing countries in the world. The population aged 65 years and older was > 7% of the total population (World Health Organization definition of an ageing country) in 1993, reached 9.01% in 2002, and increases at a rate of 0.2% annually [5]. This increasing elderly population may contribute to Taiwan’s high incidence and prevalence of ESRD in age groups 65–75 years and 76 years and older [4]. However, whether the high incidence and prevalence of ESRD in the elderly population are due to the high prevalence of advanced CKD or lower death rates of CKD patients is still unknown.

Based on data from the Taiwanese Survey on Blood Sugar, Lipid, and Pressure (TW3H), in 2002, Yang and colleagues reported a point prevalence of 6.43% for CKD...
stages 3–5 in the general population aged 16 years and older in Taiwan; the prevalence of late CKD among those aged 65 years and older reached 30% [6,7]. Both rates are higher than the corresponding CKD prevalence in the USA. The Third National Health and Nutrition Examination Survey estimated the prevalence of all-stage CKD in US adults at 10.9%, and 4.6% for stages 3–5. The prevalence of moderate or severe CKD was estimated at 25% for Americans older than 70 years [8].

Only a small proportion of elderly CKD patients progress to ESRD; many more die before reaching the end stage [9–16]. The aims of this study were to examine the prevalence of late-stage CKD in a community-dwelling elderly population, and the association of late-stage CKD with all-cause and cause-specific mortality. We tested the hypothesis that risk of mortality in the elderly population increases with late-stage CKD.

**Subjects and methods**

**Study design and population**

The study design was a retrospective cohort study in Kaohsiung City in southern Taiwan. Kaohsiung City is the second largest metropolitan area in Taiwan, with a total population of 1.51 million, with 7.63% aged older than 65 years in 2002 [5] and the highest incidence and prevalence of ESRD in the country. The study cohort comprised residents aged 65 years or older dwelling in Kaohsiung City who participated in the Elderly Health Examination Program (EHEP) in 2002 and continuously through 2004. EHEP is a free annual physical examination program, which originated as a social service program in Kaohsiung City in 1983. After implementation of Taiwan’s NHI Program in 1995, EHEP expenses have been shared by the Health Department of Kaohsiung City and the NHI program.

At baseline 36 983 elderly subjects participated in EHEP in 2002. Participants with missing data for the estimation of glomerular filtration rate (GFR) \((n = 1428)\) or who began renal replacement therapy treatments before the examination date \((n = 26)\) were excluded. A cohort including 35 529 elderly participants \((\sim 30.8\% \text{ of the elderly population in Kaohsiung City})\) was established in 2002 and followed through 31 December 2004, or to the date of death.

**Data sources**

We used two data sources: (1) EHEP data from the Bureau of Health in Kaohsiung City; (2) mortality data from the death registrations of the National Department of Health (DOH). The EHEP checklist included weight, height and blood pressure measurements, and laboratory tests evaluating functioning of various systems. Blood biochemistry, urinalysis and stool occult blood were examined at laboratory units in each contracting hospital. The results of the health examinations generated by each hospital were transmitted electronically to the Bureau of Health, Kaohsiung City.

Deaths during follow-up (2002–2004) were identified from the DOH mortality data released by the DOH. To examine cause-specific mortality, causes of death were classified by International Classification of Diseases, Ninth Edition, Clinical Modification codes as follows: malignant tumours, 140–239; cardiovascular disease, 401–448; diabetes mellitus, 250; renal disease, 580–588 [17].

**Measures of kidney function, classification of CKD and study covariates**

Kidney function was calculated by the simplified Modification of Diet in Renal Diseases Study (MDRD) equation for estimating GFR (eGFR ml/min/1.73 m² = \(186.3 \times [\text{serum creatinine, } \text{mg/dL}]^{-1.154} \times \text{age}^{-0.203} \times \left[0.742 \text{ for women}\right]\)) [18]. The CKD classifications defined by the US National Kidney Foundation (NKF) in 2002 were modified in the present study because > 97% of the total sample were classified as CKD stages 1–3 and, of these, almost 40% were at stage 3 by US NKF classification criteria.

To prevent underestimating renal function for patients with CKD stages 1–3, especially stage 3, stage 3 was subclassified into stages 3a (eGFR 45–59 ml/min/1.73 m²) and 3b (30–44 ml/min/1.73 m²), as in the study by Go et al. [9] Participants with estimated glomerular filtration rate (eGFR) > 60 ml/min/1.73 m² were defined as the reference group, instead of being traditionally classified as non-CKD and CKD stages 1 and 2, because the simplified MDRD equation tends to underestimate GFR in near-normal cases [19]. Criteria for CKD stage 4 (15–29 ml/min/1.73 m²) and stage 5 (< 15 ml/min/1.73 m²) remain the same as the NKF classification. Stages 3a–5 were defined as late-stage CKD. Overall, the mean follow-up time was 30.8 (SD, 3.6) months for the reference group (eGFR > 60); 30.8 months (SD, 3.8) for stage 3a; 30.2 months (SD, 4.7) for stage 3b; 29.2 months (SD, 6.1) for stage 4 and 27.7 months (SD, 8.3) for stage 5.

**Adjustment variables for the risk of death**

Demographic covariates included age and sex. Biochemical data included blood pressure (systolic and diastolic), fasting blood sugar, serum cholesterol, serum triglycerides, serum albumin, haemoglobin and the number of metabolic syndrome components. The physical examination data are limited in that they contain no comorbidity information. Thus, we used lab data to identify patients with metabolic syndrome [20]. The definition of metabolic syndrome was based on the National Cholesterol Education Program Third Adult Treatment Panel guidelines, including (1) triglycerides ≥ 150 mg/dL, (2) blood pressure ≥ 130/85 mmHg, (3) fasting glucose ≥ 110 mg/dL and (4) body mass index (BMI) ≥ 27 kg/m² [20].

**Statistical techniques**

All analyses were performed using SPSS software (version 12.0). Basic demographics and laboratory data in each CKD stage were described and mean differences analysed by one-way analysis of variance (ANOVA) and distributions of metabolic syndromes were compared by chi-square tests. The prevalence of each CKD stage was calculated and
further compared to the mortality per 1000 person-years of the reference group. Cox regression analysis was applied to compute proportional HR for all-cause and cause-specific mortality associated with late-stage CKD, after controlling for age, sex, haemoglobin, serum albumin, hypertension, dyslipidaemia, obesity and diabetes. However, the differences were smaller after adjustment.

Proportional hazard ratios of mortality

Proportional hazards ratios (HR) for all-cause and cause-specific mortality were generated by Cox regression models (Table 3). For all-cause mortality \( (N = 1840) \), the results indicated the group with eGFR < 15 mL/min/1.73 m\(^2\) had the highest HR of mortality \( [2.55; 95\% \text{ CI}, 1.8–3.6] \) compared to the reference group eGFR \( \geq 60 \text{ mL/min/1.73 m}^2 \). The groups with eGFR 30–44 (HR, 1.52; CI, 1.3–1.8) and 15–29 mL/min/1.73 m\(^2\) (HR, 2.10; CI, 1.7–2.6) had significantly higher HR of mortality compared with the reference group \( (P < 0.001) \). The results are also shown in Figure 2a.

Late-stage CKD significantly increased the risk of mortality due to cardiovascular and renal disease (Table 3). The hazard ratio of cardiovascular mortality was 3.22 times higher for eGFR < 15 mL/min/1.73 m\(^2\) \( (CI, 1.3–8.3) \); 3.62 for eGFR 15–29 \( (CI, 2.3–5.8) \) and 2.42 for eGFR 30–44 \( (CI, 1.7–3.4) \) compared with the reference group. The hazard ratio of mortality due to renal diseases dramatically increased with lower eGFR: 44.56 for eGFR < 15 mL/min/1.73 m\(^2\) \( (CI, 11.4–173.5) \); 17.86 for eGFR 15–29 \( (CI, 4.9–64.7) \) and 9.58 for eGFR 30–44 \( (CI, 2.9–31.6) \). The risks of mortality due to malignant tumours or diabetes mellitus were not significantly associated with graded decreases of eGFR (Figure 2).

Discussion

The present study aimed to examine the hypothesis that declining renal function is associated with increasing risk of mortality in elderly Taiwanese. The findings support this hypothesis and confirm that mortality cases due to cardiovascular and renal disease are associated with late-stage CKD [9–13]. The present findings also reveal a relatively higher prevalence rate of CKD compared to the rest of Taiwan and to the US [6,8], with lower mortality rates in the elderly population [9,10,13], possibly indicating a reason for the higher ESRD incidence rate in southern Taiwan, or underestimation of actual renal function for patients classified with CKD stages 1–3.

CKD has been found to be an important risk factor for cardiovascular events and death in African American and in white American patients [13], and in elderly patients [8,14]. Compared with populations in western countries [12,14,15], cardiovascular disease occurs less frequently among Asians, possibly resulting in a higher likelihood of Asian CKD patients progressing to ESRD rather than dying of cardiovascular disease. Along with a higher incidence and prevalence of ESRD in Taiwan, however, our study found a higher hazard of cardiovascular mortality in an Asian late-stage CKD population. Future research analysing competing effects of cardiovascular disease on death versus ESRD may provide a better picture of the progression from CKD to ESRD in cardiovascular disease patients.
Table 1. Basic demographics and laboratory data by estimated glomerular filtration rate (eGFR) groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>eGFR Groups (mL/min/1.73 m²)</th>
<th>All</th>
<th>≥ 60</th>
<th>45–59</th>
<th>30–44</th>
<th>15–29</th>
<th>&lt; 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td></td>
<td>35,529</td>
<td>21,528</td>
<td>9,841</td>
<td>3,135</td>
<td>785</td>
<td>240</td>
</tr>
<tr>
<td>Percent (%)</td>
<td></td>
<td>100</td>
<td>60.6</td>
<td>27.7</td>
<td>8.8</td>
<td>2.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>75.7 (5.3)</td>
<td>75.2 (5.2)</td>
<td>76.2 (5.2)</td>
<td>76.9 (5.7)</td>
<td>77.9 (5.8)</td>
<td>76.6 (5.7)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td></td>
<td>21,121 (59.4)</td>
<td>12,103 (56.2)</td>
<td>6,453 (65.6)</td>
<td>1,884 (60.1)</td>
<td>531 (67.6)</td>
<td>150 (57.3)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td>24.5 (3.6)</td>
<td>24.4 (3.6)</td>
<td>24.6 (3.6)</td>
<td>24.8 (3.7)</td>
<td>24.4 (3.7)</td>
<td>24.1 (3.5)</td>
</tr>
<tr>
<td>Systolic pressure (mmHg)</td>
<td></td>
<td>137.2 (20.6)</td>
<td>135.9 (20.2)</td>
<td>138.6 (20.7)</td>
<td>140.7 (21.7)</td>
<td>140.1 (23.0)</td>
<td>139.0 (22.5)</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td></td>
<td>80.1 (13.1)</td>
<td>79.9 (72.9)</td>
<td>80.5 (13.2)</td>
<td>80.0 (13.9)</td>
<td>79.7 (14.7)</td>
<td>77.1 (12.8)</td>
</tr>
<tr>
<td>Fasting blood sugar (mg/dL)</td>
<td></td>
<td>111.3 (44.6)</td>
<td>111.0 (37.6)</td>
<td>110.9 (37.5)</td>
<td>114.6 (88.6)</td>
<td>114.4 (41.6)</td>
<td>109.3 (40.0)</td>
</tr>
<tr>
<td>Serum cholesterol (mg/dL)</td>
<td></td>
<td>202.7 (45.0)</td>
<td>200.6 (40.0)</td>
<td>204.7 (40.6)</td>
<td>207.4 (43.5)</td>
<td>208.0 (49.4)</td>
<td>196.0 (50.6)</td>
</tr>
<tr>
<td>Serum triglycerides (mg/dL)</td>
<td></td>
<td>136.4 (83.7)</td>
<td>130.6 (81.2)</td>
<td>140.4 (82.3)</td>
<td>140.1 (85.9)</td>
<td>146.9 (105.9)</td>
<td>156.7 (106.9)</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td></td>
<td>4.4 (0.9)</td>
<td>4.4 (1.0)</td>
<td>4.4 (0.8)</td>
<td>4.3 (1.0)</td>
<td>4.3 (0.3)</td>
<td>4.2 (0.4)</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td></td>
<td>4.1 (1.5)</td>
<td>4.1 (1.5)</td>
<td>4.1 (1.5)</td>
<td>4.1 (1.5)</td>
<td>4.1 (1.5)</td>
<td>4.1 (1.5)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td></td>
<td>10,394 (29.3)</td>
<td>6,186 (28.7)</td>
<td>2,961 (30.1)</td>
<td>962 (30.7)</td>
<td>231 (29.4)</td>
<td>169 (10.5)</td>
</tr>
<tr>
<td>Hyperglycaemia, n (%)</td>
<td></td>
<td>9,942 (29.8)</td>
<td>6,553 (28.4)</td>
<td>2,995 (30.4)</td>
<td>1,044 (33.3)</td>
<td>268 (34.1)</td>
<td>82 (34.2)</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td></td>
<td>9,981 (29.0)</td>
<td>6,074 (28.2)</td>
<td>3,235 (32.9)</td>
<td>1,220 (38.9)</td>
<td>363 (46.3)</td>
<td>89 (37.1)</td>
</tr>
<tr>
<td>Obesity, n (%)</td>
<td></td>
<td>10,992 (30.8)</td>
<td>6,447 (26.3)</td>
<td>3,145 (32.0)</td>
<td>1,063 (33.9)</td>
<td>220 (80.0)</td>
<td>67 (27.9)</td>
</tr>
<tr>
<td>Number of metabolic syndrome components, n (%)</td>
<td></td>
<td>3,650 (10.5)</td>
<td>2,547 (11.8)</td>
<td>1,296 (13.1)</td>
<td>462 (14.8)</td>
<td>123 (4.4)</td>
<td>26 (10.8)</td>
</tr>
</tbody>
</table>

Note: Data are expressed as mean (standard deviation) unless otherwise noted.  
*Mean difference reached the significance level P < 0.001 by ANOVA.  
*Distribution of each variable statistically varied by the level of eGFR (P < 0.001) by χ² tests.

Table 2. Mortality in estimated glomerular filtration (eGFR) groups in the observation period, 2002–2004

<table>
<thead>
<tr>
<th>eGFR Groups</th>
<th>N at risk</th>
<th>Person-years of follow-up</th>
<th>Deaths during follow-up</th>
<th>Mortality per 1000 person-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>35,529</td>
<td>90,599</td>
<td>1,840</td>
<td>20.3 (19.4–21.2)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>21,528</td>
<td>55,195</td>
<td>905</td>
<td>16.4 (15.3–17.5)</td>
</tr>
<tr>
<td>45–59</td>
<td>9,841</td>
<td>25,232</td>
<td>494</td>
<td>19.5 (17.8–21.2)</td>
</tr>
<tr>
<td>30–44</td>
<td>3,135</td>
<td>7,896</td>
<td>268</td>
<td>33.9 (29.8–37.0)</td>
</tr>
<tr>
<td>15–29</td>
<td>785</td>
<td>1,906</td>
<td>123</td>
<td>64.5 (53.1–75.9)</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>240</td>
<td>558</td>
<td>50</td>
<td>89.6 (64.8–114.4)</td>
</tr>
</tbody>
</table>

Note: CI, confidence interval.  
P < 0.001.

Table 3. Hazard ratios of all-cause mortality and specific-cause mortality by estimated glomerular filtration rate (eGFR) groups

<table>
<thead>
<tr>
<th>Mortality</th>
<th>All-cause N = 1,840</th>
<th>Malignancy N = 634</th>
<th>Diabetes N = 1,46</th>
<th>Cardiovascular disease N = 328</th>
<th>Renal disease N = 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 60 (Reference)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>45–59</td>
<td>1.10 (1.0–1.2)</td>
<td>1.09 (0.9–1.3)</td>
<td>1.20 (0.7–1.9)</td>
<td>1.30 (1.0–1.7)</td>
<td>2.22 (0.6–8.3)</td>
</tr>
<tr>
<td>30–44</td>
<td>1.52 (1.3–1.8)</td>
<td>0.94 (0.7–1.3)</td>
<td>1.41 (0.8–2.4)</td>
<td>2.49 (1.7–3.4)</td>
<td>9.58 (2.9–31.6)</td>
</tr>
<tr>
<td>15–29</td>
<td>2.10 (1.7–2.6)</td>
<td>1.14 (0.8–1.7)</td>
<td>1.50 (0.7–3.0)</td>
<td>3.62 (2.3–5.8)</td>
<td>17.86 (4.9–64.7)</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>2.55 (1.8–3.6)</td>
<td>1.67 (0.9–3.0)</td>
<td>1.89 (0.7–5.1)</td>
<td>3.22 (1.3–8.3)</td>
<td>44.56 (11.4–173.5)</td>
</tr>
</tbody>
</table>

Note: Data are calculated by Cox proportional model and expressed as hazard ratios (95% confidence intervals). All models are adjusted for age, sex, haemoglobin, albumin, hypertension, dyslipidaemia, obesity and diabetes. Estimated glomerular filtration rate was calculated by the simplified Modified Diet in Renal Disease equation.  
P < 0.001.  
P < 0.05.
Fig. 1. Unadjusted and Adjusted probabilities for all-cause death by estimated glomerular filtration rate (eGFR). The survival probability was calculated by Cox regression analysis, unadjusted (left panel) and adjusted for age, sex and existence of metabolic syndrome components (right panel).

Expected higher relative risk of diabetic mortality was not found in late-CKD patients in our study. A possible explanation is that a significant proportion of elderly diabetic patients die from complications of diabetes other than diabetic nephropathy [16]. As shown in Table 3, only 146 out of 1840 mortality cases were due to diabetes. However, diabetic patients could die of cardiovascular disease or renal disease and the death could be classified as non-diabetic mortality because the ICD-9-CM coding system for national Registration of Death Data is comprehensive for cardiovascular mortality, but very specific for diabetic mortality. Several additional Cox regression models (not shown) were established to examine the effects of metabolic syndrome on relative risk of diabetic mortality. Compared to late CKD, hyperglycaemia appears to be a stronger consistent predictor of diabetic mortality. In other words, blood sugar control is more strongly related to risk of diabetic mortality.

Similarly, malignancy mortality, the leading cause of death for the general population and for elderly people in Taiwan [17], is not significantly associated with late-stage CKD. This could be because seriously ill cancer patients are distributed among different eGFR groups, and cancer patients may die before developing renal failure. Overall, additional research is needed to investigate competing death risk factors affecting CKD progression, such as treatment regimens, socioeconomic status, frequency of medical care use and health insurance. Further cross-national comparison is also critical to examine ecologic risk associated with the progression from CKD to ESRD or mortality.

Our study is unique because the study cohort is derived from a national health insurance system with the highest incidence and prevalence of ESRD in the world [4]. Within Taiwan, the study area, Kaohsiung City, has a much higher incidence and prevalence of ESRD than other areas of Taiwan [21]. Possibly, the high ESRD incidence in elderly Kaohsiung residents results from the high CKD prevalence. However, few studies have focused on the CKD prevalence in Taiwan, except for the national TW3H survey conducted in 2002 [6]. Compared with the 30% CKD prevalence among elderly participants in the TW3H Survey, our study found a 39.4% late-stage CKD prevalence in the elderly population of Kaohsiung City. It should be noted that the current study dataset was derived from the annual EHEP in Kaohsiung City. The nature of voluntary participation in physical health examination programs tends to favour those with better health status and hinder those who are disabled or bedridden, or who have severe physical or mental illnesses compared to a community-based survey like TW3H. However, we found that the prevalence of late-stage CKD in the Kaohsiung study cohort was higher compared to the rest of Taiwan [6] and to the USA [8], with relatively higher survival rates for all-cause mortality [9]. These findings suggest two perspectives regarding implications. First, the large pool of CKD patients may be increasing the ESRD population in Kaohsiung City. Second, the higher reported prevalence of renal disease and the better survival might be due to underestimation of renal function in patients classified with CKD stages 1–3 based on the current eGFR classification [19].

The classification of CKD, originally proposed by the US NKF, was based on Third National Health and Nutrition Examination Survey data [18], and the simplified MDRD equation was used to calculate eGFR [22]. Racial differences in adaptation of the criteria for CKD classification or in application of the equation for estimating GFR may result in misclassification of CKD and affect the results and implications [23]. Careful modification of MDRD equations might be necessary in the Chinese population with CKD because the MDRD equation could underestimate GFR in cases of near-normal eGFR and
Mortality risk with late-stage chronic kidney disease

Fig. 2. Adjusted hazard ratios for all-cause (a) and cause-specific mortality by estimated glomerular filtration rate (eGFR). Malignancy (b); diabetes mellitus (c); cardiovascular diseases (d) and renal diseases (e). Data are expressed as hazard ratio ± 95% confidence interval. *P < 0.05 **P < 0.001.

overestimated eGFR in cases of advanced kidney failure [19]. Therefore, we used a modified NKF classification of CKD as did in the study of Go et al. [9] and divided CKD stage 3 (eGFR 30–59 mL/min/1.73 m²) into CKD stages 3a (eGFR 45–59 mL/min/1.73 m²) and 3b (eGFR 30–44 mL/min/1.73 m²). The present findings are similar to the study of Go et al., but more sensitive to the subclassification of stage 3 (stages 3a and 3b). Compared to the reference group (eGFR ≥ 60), mortality HR for patients at stage 3a (eGFR 45–59 mL/min/1.73 m²) were not significantly higher for all-cause mortality or any cause-specific mortality. On the other hand, stage 3b (eGFR 30–44 mL/min/1.73 m²) was associated with a higher risk of all-cause mortality or specific mortality due to cardiovascular disease and renal disease. As O’Hare et al. point out [24], the inconsistency in mortality in relationship with eGFR in various age groups may suggest a finer categorization of CKD is needed. A larger sample size survey in the general population is critical to evaluate the appropriateness of GFR cut-points for the classification of CKD stages in Asian populations or the Chinese population specifically.

Potential limitations of our study should be noted. First, the elderly study sample was younger and included more men than the general elderly population in Kaohsiung, possibly due the younger elderly men having better mobility and being more able to participate in the physical examination program. Second, the physical health examination datasets did not provide sufficient information on subjects’ past histories of comorbid conditions and medications, and thus health conditions can be judged only through laboratory data. Instead of studying the relationship between specific existing diseases and mortality, the present study considered the effect of metabolic syndromes on mortality because of its associated risk for mortality in relation to CKD [25,26]. Third, laboratory data were measured at different medical institutions and by different laboratory equipment. As a result, there was no calibration or standardization of creatinine measurements. Non-standardized
methods of serum creatinine measurement and the subsequent calculated results of eGFR from serum creatinine may lead to misclassification of the CKD staging. However, measurement bias of creatinine or other lab data was assumed to be minimized by the accreditation of the contracting hospitals that provided the annual health examination services. Finally, there is a possibility of misclassification of cause of death, which might interfere with the association of late-CKD and expected mortality.

In conclusion, late-stage CKD is a risk factor for mortality in elderly Taiwanese, especially for higher mortality rates due to cardiovascular and renal diseases. Given the higher prevalence rate of late-stage CKD in the study area, and the relatively low mortality of CKD patients, our results might reflect underestimation of renal function for patients at early stages of CKD, or partly explain the high ESRD population.

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