Renal function and decline in functional capacity in older adults

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Abstract

**Background:** Longitudinal relationship between renal function, disability and mortality has not been evaluated.

**Objective** We investigated the temporal association between renal function and disability, and aimed to identify the influence of disability on mortality according to renal function in a cohort of older Koreans.

**Design/setting:** Korean Longitudinal Study on Health and Aging is a prospective, population-based cohort.

**Subjects:** Community-dwelling Koreans ≥65 years of age.

**Main outcome measures:** Korean version of activities of daily living (ADL), Instrumental activities of daily living (IADL) and all-cause mortality.

**Results:** A total of 984 participants were followed for 5 years with a 70.9% participation rate. The participants were categorized into three groups according to their baseline estimated glomerular filtration rates (eGFRs) (Group I, ≥60; Group II, 45–59; and Group III, <45 ml/min/1.73 m²). Baseline eGFR was higher in participants who maintained functional status compared with participants who died or had disability at follow-up examination. The incidence of ADL/IADL decline was 13, 12.5 and 29.5% in participants who showed improvement, no change, and decline in renal function, respectively (P = 0.01). The hazard ratio for mortality in the subgroup with IADL disability was 1.87 (95% CI: 1.10–3.20, P = 0.022) in Group I, and 2.53 (95% CI: 1.57–4.09, P < 0.001) in Groups II and III after adjustment.

**Conclusions:** Impaired renal function was related to disability and ADL/IADL decline. The effect of ADL/IADL disability on mortality was more prominent in participants with impaired eGFR.

**Keywords:** Chronic kidney disease, disability, older adults, mortality, older people

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Introduction

Maintenance of independent function is a key determinant of successful aging. Many reports show that functional status, as measured by basal activities of daily living (ADL) and/or instrumental activities of daily living (IADL), worsens during the aging process and is an important risk factor for the mortality of the older population [1–4]. Accordingly, the impact of chronic diseases on the functional status of older adults has been one of the main topics in geriatric research.

The prevalence of chronic kidney disease (CKD), defined as persistent kidney damage, usually marked by albuminuria or reduced glomerular filtration rate (GFR < 60 ml/min/1.73 m²), significantly increases with advancing age [5]. CKD was independently associated with mortality regardless of age, whereas relative mortality risk decreased with age. However, absolute mortality risk difference tended to increase with age [6–8].

 Nonetheless, reports are limited regarding the relationship between renal function and disability in older population, and the results of these studies are debatable. In two prospective studies, CKD was an important determinant for the development of walking limitations and ADL/IADL disability [9, 10]. Furthermore, even mild CKD is associated with functional impairment in community-dwelling older adults [11].

However, CKD was not related to ADL impairment in another prospective study [12]. In addition, data from the National Health and Nutrition Examination Survey 1999–2006 in the United States showed that the association between CKD and the ADL/IADL index was attenuated after adjustment for age and other variables [13]. Moreover, the longitudinal relationship between renal functional and disability in older adults has not been evaluated yet.

Thus, we analyzed the status of functional disability by the GFR levels and investigated the temporal association between renal function and disability. We also aimed to show the influence of disability on mortality, according to the estimated GFR (eGFR) level in a community-based prospective cohort study.

Methods

Design of the Korean Longitudinal Study on Health and Aging

This study was conducted as a part of the Korean Longitudinal Study on Health and Aging (KLoSHA), which includes a randomly selected, community-based older population [14, 15]. The KLoSHA protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital (SNUBH) in 2005 and 2010 (IRB No. B-0508/023-003 and B-0912/089-005). This study was performed according to the Declaration of Helsinki.

After obtaining written informed consent from all participants, the assessments were performed at SNUBH. Among the 1,000 original KLoSHA subjects, 984 subjects who were not dependent on renal replacement therapy and had a prerequisite baseline eGFR value were selected for this study. All participants completed a standardized clinical interview consisting of physical and neurological examinations by three clinicians. An additional extensive interview using standardized questionnaires was carried out by three nurses. The duration of the follow-up period was 59.4 ± 6.9 months.

Measurement and definition

Diabetes mellitus (DM) was defined by the use of anti-diabetic medications, a serum fasting glucose level ≥126 mg/dl or haemoglobin A1c level ≥6.5%. Hypertension was defined as a systolic blood pressure ≥140 mmHg, a diastolic blood pressure ≥90 mmHg or the use of anti-hypertensive medication.

The serum creatinine level was measured by the alkaline picrate Jaffe kinetic method using an automatic analyzer (Toshiba 200FR; Tokyo, Japan). Serum creatinine levels were calibrated to an assay traceable by an isotope dilution mass spectrometry (IDMS) device (Roche Diagnostics). The GFR was calculated using the CKD-epidemiology collaboration (CKD-EPI) equation [16].

The participants were categorized into three eGFR groups: Group I, eGFR ≥60 ml/min/1.73 m²; Group II, 45–59 ml/min/1.73 m²; and Group III, <45 ml/min/1.73 m². Impaired eGFR was defined as an eGFR <60 ml/min/1.73 m².

Changes in renal function were defined if participants were categorized into different eGFR groups at the follow-up examination. Accordingly, participants were subdivided into three groups according to the changes in renal function, improved, no change or declined group.

We measured the Cumulative Illness Rating Scale (CIRS) for the evaluation of the general health status [17]. We calculated the overall illness severity represented by the mean of the 13 CIRS items, excluding the psychiatric/behavioral item (CIRS-S). Income was graded by the criterion of the lowest monthly cost of living provided by the Korean government. The designated ‘poor’ income level was less than the lowest cost of living.

Assessment of disability

The functional status was measured by the seven domains contained in the ADL (dressing, washing hands and face, bathing, toileting, eating, ambulating in and out of bed and maintaining control of bowel and/or bladder functions) and by the 10 domains contained in the IADL (decorating, household, preparing meals, laundry, outgoing for a short distance, using transportation, shopping, handling money, using the telephone and taking medicine). For each item, respondents were asked if they were able to perform the activities without any assistance from another person (scored 1), ‘with the assistance of another person (scored 2),’ or ‘with absolute dependence on another person (scored 3).’ Thus, ADL score ranged from 7 to 21 and IADL score ranged from 10 to 30, higher scores representing more dependency.

We calculated the mean score of ADL and IADL by dividing the sum of the scores in all domains by the total number
of domains. ADLs and IADLs were measured using the Korean ADL and IADL scale [18], which has been validated as a reliable tool for quantifying the function of older adults.

Functional outcomes and mortality

We defined disability as answering at least one domain with absolute dependence in either the ADL (ADL disability) or the IADL (IADL disability). ADL/IADL decline was defined as an increase of ≥2 points on total ADL or IADL from baseline to follow-up evaluation [19, 20]. Progression of disability was defined if number of domains answered ‘with absolute dependence’ during a follow-up examination was increased [10].

All participants were flagged for mortality at the National Statistical Office of Korea, which provided the date and cause of all deaths occurring until the end of December 2011.

Statistical analyses

All analyses were performed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Data were presented as the mean ± SD values for continuous variables and as counts and percentages for categorical variables. Differences in continuous variables were analyzed by one-way analysis of variance or Student’s t-test according to the number of subgroups, and differences in categorical variables were analyzed by Pearson’s χ² or Fisher’s exact test.

We analyzed the factors related to the mean scores of ADL or IADL with multiple linear regression analysis and those related to ADL/IADL disability and ADL/IADL decline using multiple logistic regression analysis.

Kaplan–Meier analysis was used for survival curves, and log-rank tests were used to assess significance. Cox’s proportional hazard analysis was used to estimate the hazard ratios (HRs) for mortalities. Formal testing for interactions between the eGFR group and other factors for mortality were conducted by comparing –2 log likelihoods in regression models with and without the interaction term (eGFR group × another factor). P-values of 0.05 were considered statistically significant.

Results

Characteristics and follow-up status of the participants according to eGFR group

There were 747 (75.9%) participants in Group I, 161 (16.4%) participants in Group II and 76 (7.7%) participants in Group III (Supplementary data are available in Age and Ageing online, Table S1). Among the 984 participants, 212 subjects died before the follow-up examination, and 286 subjects were lost to follow-up or refused to participate. Accordingly, 486 participants completed the 5-year follow-up examination and were included in the functional outcome analysis (Supplementary data are available in Age and Ageing online, Figure S1). Although, there was no significant difference in the follow-up loss rate among the three groups; however, the mortality rate was significantly higher in participants with impaired eGFR (16.2, 35.4 and 44.7% in Groups I, II and III, respectively, P < 0.0001).

Renal function and decline in functional capacity

Association between renal function and disability

Renal function was significantly associated with disability or functional status of older adults (Supplementary data are available in Age and Ageing online, Table S1). Especially, the prevalence of ADL/IADL disability increased as the eGFR decreased (ADL/IADL disability: 3.2%/13.9%, 5.0%/26.1% and 13.2%/42.1% in Groups I, II and III, respectively, P < 0.001).

A lower eGFR was related to a higher mean score of ADL and IADL using multiple linear regression analysis, adjusted for covariates (Supplementary data are available in Age and Ageing online, Table S2). Moreover, the odds ratio for ADL disability showed marginal differences among the eGFR groups (P = 0.059); however, for IADL disability, the Group III had a 3.0-fold risk compared with the Group I (P = 0.001) (Table 1).

Finally, baseline eGFR was higher in participants who maintained functional status compared with participants who died or had ADL/IADL disability at follow-up examination (75.0 ± 16.1 versus 68.8 ± 17.5 ml/min/1.73 m², P < 0.001) (Supplementary data are available in Age and Ageing online, Table S2).

Impact of renal function deterioration on functional decline

Among the 413 participants who had follow-up eGFR value, 23 participants (5.6%) showed improvement in renal function, 232 participants (55.3%) showed no change, and 158 participants (39.1%) showed worsening renal function (Table S2).

Table 1. The odds ratio for functional impairment according to GFR levels by multiple logistic regression

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<th>95% CI for OR</th>
<th>P-value</th>
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<td>Group I versus II</td>
<td>0.448</td>
<td>0.64</td>
<td>0.2~2.00</td>
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<td>GFR group</td>
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<td>Group I versus II</td>
<td>0.344</td>
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<td>0.82~2.44</td>
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<tr>
<td>Group I versus III</td>
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<td>3.00</td>
<td>1.57~5.75</td>
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*Disability, functional impairment defined by dependence on another person for any activity in ADL or IADL.

Multiple logistic regression analysis adjusted by age, gender, status of living with spouse, presence of occupation, poor income, year of education, status of smoking and drinking, DM, levels of haemoglobin, albumin, alkaline phosphatase, HDL-cholesterol, CRP, glucose and WBC, and group of GFR for ADL disability.

Multiple linear regression analysis adjusted by age, gender, status of living with spouse, presence of occupation, poor income, year of education, levels of haemoglobin, albumin, alkaline phosphatase, HDL-cholesterol, CRP, glucose and thyroxine, and group of GFR for IADL disability.

GFR group defined as follows; Group I, GFR ≥60 ml/min/1.73 m²; Group II, GFR 45–59 ml/min/1.73 m²; and Group III, GFR <45 ml/min/1.73 m².
function, 44 participants (10.7%) showed decline in renal function and 346 participants (83.8%) showed no change in renal function. There was no significant difference in baseline ADL/IADL scores among the three groups; however, changes in renal function were associated with changes in ADL/IADL (Figure 1). The incidence of ADL/IADL decline was 13, 12.5 and 29.5% in participants who showed improvement, no change and decline in renal function, respectively ($P$ = 0.01).

Influence of disability with respect to renal function on mortality
The mortality rate was higher in participants with ADL disabilities (66.7% versus 20.3%, $P$ < 0.001) and IADL disabilities (54.5% versus 15.1%, $P$ < 0.001) than in those without disabilities. The mean scores of ADL and IADL, or ADL/IADL disability were independent risk factors for mortality by Cox's proportional hazard analysis after adjusting for demographic, socioeconomic or all factors related to mortality and CIRS-S (Supplementary data are available in Age and Ageing online, Table S3).

We evaluated the interactions between disability and age, gender, CIRS-S, eGFR group and factors related to disability. ADL disability showed interactions with age ($P$ for interaction < 0.001), gender ($P$ for interaction < 0.001), eGFR group ($P$ for interaction < 0.001) and serum albumin ($P$ for interaction < 0.001). IADL disability showed interactions with the eGFR group ($P$ for interaction < 0.001), duration of education ($P$ for interaction 0.007) and serum alkaline phosphatase ($P$ for interaction 0.041). When we added the interaction terms ($A \times B$) to Model 3 (Supplementary data are available in Age and Ageing online, Table S3), ADL and IADL disability remained as risk factors for mortality.

The significance of disability as a risk factor for mortality differed according to the renal function (Figure 2). The importance of ADL/IADL disability as a risk factor for mortality was more evident in participants with impaired eGFR. ADL disability was only a significant risk factor for mortality among the participants with impaired eGFR. The HR for the mortality of the subgroup with IADL disabilities was 1.87 (95% CI: 1.10–3.20, $P$ = 0.022) in Group I; however, in Groups II and III, the HR was 2.53 (95% CI: 1.57–4.09, $P$<0.001) after adjustment.

Discussion
Here, we showed that impaired eGFR was related to an increased prevalence of disability, as well as an aggravation of disability. ADL and IADL disability were independent risk factors for all-cause mortality, and their effect on mortality was more prominent in participants with impaired eGFR.

There have been many reports discussing the relationship between renal functional and disability or frailty in a cross-sectional setting. However, very few studies reported the time-dependent influence of renal function on ADL or IADL. The significance of renal function on the prevalence of disability differs from study to study. Possible reasons for these variable results might be that the definition of disability, the scales used and the CKD criteria were different in each study.

In this study, we used stricter criteria for disability, as some level of disability due to aging would be expected in a normal older population. Less strict criteria for disability, such as those adopted by almost all other studies, would be more suitable for populations with a lower prevalence of age-related disability, such as the younger population.

We are the first to notice that the impact of ADL/IADL disability on mortality was more prominent in older participants with renal impairment. Although there was a brief report of the ADL/IADL indexes as risk factors for mortality in an older CKD population, the authors did not demonstrate their results using a sophisticated analysis [21].
possible explanation for this finding is that the risk factors for disability are also risk factors for CKD and mortality. CKD can affect physical function directly or indirectly through atherosclerotic complications [22]. Furthermore, CKD is a well-known risk factor for cardiovascular and all-cause mortality. Therefore, the present interaction analyses indicate that increased disability and decreased renal function in an older population could have an additive impact on mortality, in contrast to populations lacking renal dysfunction.

This study has limitations. First, this study attempted to follow the participants for 5 years, but 29.1% of the initial sample could not be interviewed during a second examination. Furthermore, the substantial mortality difference among the three groups might weaken the functional significance of renal function. Second, the CKD-EPI equation has not been fully validated for use with older Koreans, although a study of 131 CKD patients and healthy volunteers found that the ethnic coefficient of the MDRD equation using IDMS-traceable creatinine values was close to 1 [23]. Third, serum creatinine was measured only once at each examination, which could introduce classification bias. Finally, albuminuria was not measured and quantified. Accordingly, the impact of albuminuria on disability or mortality could not be identified.

In conclusion, impaired eGFR was an important determinant of disability and functional decline in older adults. Furthermore, disability was found to be a more important risk factor for mortality in older adults with impaired eGFR. These findings will be helpful to understand the longitudinal impact of renal functional on functional status. In addition, the interactive influence between renal functional and disability on mortality in older adults suggest that there might be underlying mechanism among them.

**Key points**

- Impaired GFR was related to disability and ADL/IADL decline.
- ADL and IADL disability were independent risk factors for all-cause mortality.
- Effect of disability on mortality was more prominent in CKD patients.
Conflicts of interest

None declared.

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Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References


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