The association of moderate renal dysfunction with impaired preference-based health-related quality of life: 3rd Korean national health and nutritional examination survey

Hajeong Lee¹, Yun Jung Oh¹, Myounghee Kim², Ho Kim², Jung Pyo Lee³, Sejoong Kim⁴, Kook-Hwan Oh¹, Ho Jun Chin⁴, Kwon Wook Joo¹,³, Chun Soo Lim³,⁵, Suhnggwon Kim¹,³, Yon Su Kim¹,³ and Dong Ki Kim¹,⁶*

Abstract

Background: Only a few large-scale studies have investigated the association between health-related quality of life (HRQOL) and renal function. Moreover, the HRQOL of patients with moderate renal dysfunction is frequently underestimated by healthcare providers. This study assessed the impact of renal function on preference-based HRQOL in Korean adult population.

Methods: We analyzed data for 5,555 adults from the 3rd Korean National Health and Nutritional Examination Survey 2005. The EuroQol-5D (EQ-5D) utility score was used to evaluate HRQOL. The study subjects were stratified into three groups based on their estimated glomerular filtration rates (eGFRs): ≥ 90.0, 60.0-89.9 and 30.0-59.9 mL/min/1.73 m². Individuals with advanced renal dysfunction were excluded from the analysis.

Results: The proportions of participants who reported problems in each of the five EQ-5D dimensions increased significantly with decreasing eGFR. However, a significant decrease in the EQ-5D utility score was observed among participants with an eGFR of 30.0-59.9 mL/min/1.73 m². Participants with an eGFR of 30.0-59.9 mL/min/1.73 m² had an almost 1.5-fold higher risk of impaired health utility (the lowest quartile of EQ-5D utility score) compared with those participants with eGFRs ≥ 90.0 mL/min/1.73 m², after adjustment for age, gender, health-related behaviors, socioeconomic and psychological variables, and other comorbidities. Among the five dimensions of the EQ-5D, an eGFR of 30.0-59.9 mL/min/1.73 m² was an independent determinant of self-reported problems in the mobility and pain/discomfort dimensions.

Conclusions: Although age affects the association between renal dysfunction and the EQ-5D, moderate renal dysfunction seems to be an important determinant of impaired health utility in a general population and may affect the mobility and pain/discomfort dimensions of health utility.

Keywords: Chronic kidney disease, EuroQol-5D, Preference-based health utility

Background

Generic preference-based health-related quality of life (HRQOL) instruments, which generate health state values as a single numerical index, have been proposed for use in health-economic analyses for comparing HRQOL across different diseases and allocating proper healthcare resources [1,2]. Because chronic kidney disease (CKD) is highly interactive with various comorbidities including diabetes, cardiovascular and cerebrovascular diseases, the substantial healthcare expenditure for patients with CKD cannot be directly attributed to CKD itself [3]. Indeed, an inadequate financial policy for pre-dialysis CKD is one of the barriers preventing improved patients outcomes [4]. Thus, preference-based HRQOL measurement based on renal function is needed for proper allocation of healthcare resources to CKD patients.
Although CKD is a progressive and life-long condition with multiple medical comorbidities, its implications for HRQOL have only been studied, for the most part, in the advanced stages of CKD (stage 4-5) [5]. The HRQOL in patients with advanced CKD is significantly impaired and is an important indicator of future mortality [6]. More recently, however, the high mortality rate and prevalence of comorbid conditions even in patients in the earlier stages of CKD [7] has raised concerns that HRQOL could also be reduced in these patients. Indeed, there is considerable evidence of decreased HRQOL among patients with mild-to-moderate renal dysfunction compared with the population with normal renal function [8-11]. However, only limited information is currently available regarding estimates of the relative impact of renal dysfunction on HRQOL and predictors of HRQOL as targets of intervention. Previous studies have demonstrated that various comorbid conditions, such as anemia, hypertension, frailty, symptom burden, and depression, negatively affect HRQOL in pre-dialysis CKD patients [12]. However, these studies have limited generalizability because they either are based on a non-representative sample [9,13-16] or do not allow for integration of HRQOL measures into health-economic analyses because of the use of non-preference-based models [11].

Therefore, a population-based study of the relationship between renal function and preference-based health utility measures may contribute to a comprehensive public health strategy for the management of CKD. In the present study, we analyzed population-based data from a nationwide cross-sectional health survey to determine the association of health utility with mild-to-moderate renal dysfunction.

**Methods**

**Participants**

The data analyzed in this study were obtained from the 3rd Korean National Health and Nutritional Examination Survey (KNHANES) 2005, which included a population-based random sampling of 34,145 individuals in households across 600 national districts. The survey was conducted with a stratified, multi-stage, clustered probability design in order to select a representative nationwide sample of the non-institutionalized Korean population. A total of 28,590 subjects were excluded from this study because they were age < 18 years (n = 8,292), did not complete either the EQ-5D questionnaire (n = 9,720) or blood test (n = 27,731), or had advanced renal dysfunction (n = 12). After the above exclusion criteria were applied, 5,555 individuals aged 18 years or older who had an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m² were included in this investigation. Because the analyzed survey data are publicly available, ethical approval was not required for this study.

**Health-related quality of life**

HRQOL was measured using the EuroQol-5D (EQ-5D) questionnaire, a widely used generic preference-based instrument [17,18]. The EQ-5D consists of five questions regarding current health status in terms of mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each question has three possible responses: “no problems”, “some problems”, and “extreme problems”. The EQ-5D health states are defined as a combination of the responses for each item and the survey can therefore yield $3^5$ (= 243) possible combinations of responses. These responses were converted into weighted values according to the Korean value set [19], and the average was calculated as a quality adjustment weight for each health state. The EQ-5D instrument has been translated into Korean, and its validity (Spearman correlation coefficient with the first question of the Health Survey Short-Form 36: 0.51 in EQ-5D) and reliability (test-retest reliability) have been demonstrated previously [19,20].

**Laboratory parameters**

Blood samples were collected after a 12-hour overnight fast; they were properly processed, immediately refrigerated, and transported in cold storage to the central laboratory (Seoul Medical Science Institute, Seoul, Korea) within 24 hours. Serum creatinine, glucose, and lipid levels were measured using the ADVIA 1650 system (Bayer Health Care, Tarrytown, NY). The serum creatinine concentration was measured using the kinetic Jaffe method, and the inter-assay coefficient of variation was less than 5%. Because the creatinine assay was not calibrated to be traceable to an isotope dilution mass spectrometry (IDMS), eGFR was calculated using the original Modification of Diet in Renal Disease (MDRD) equation as follows: eGFR = 186.3 × (serum creatinine)$^{1.154}$ × (age)$^{-0.203}$ × 0.742 (if female) [21]. Proteinuria was measured by the urine dipstick test.

**Demographic and clinical characteristics**

Demographic characteristics included age, gender, marital status (living with/without a spouse), education level (no education or elementary school graduate/middle or high school graduate/university graduate or higher), occupational status (white collar/blue collar/student, soldier or housewife/no occupation), residential area (rural/urban), and monthly individual income (lowest quartile/2nd and 3rd quartile/highest quartile) in US dollars. Individuals who were legally married or cohabiting were considered to have a spouse; single, divorced, or separated individuals were categorized as not having a spouse. Information about various comorbidities was also collected. Hypertension was identified in individuals who met at least one of the following three criteria: physician diagnosis of hypertension, self-report of antihypertensive drug intake, and...
systolic blood pressure (SBP) \( \geq 140 \text{ mmHg} \) or diastolic blood pressure (DBP) \( \geq 90 \text{ mmHg} \). Blood pressure was measured manually twice at 30-second intervals after a minimum of five minutes of rest in a seated position, and the mean values were used to identify hypertensive participants. Diabetes was diagnosed in subjects with a fasting plasma glucose \( \geq 126 \text{ mg/dL} \) or those patients who were identified in the health interview survey as actively using an oral hypoglycemic agent or insulin. Diagnosis of metabolic syndrome was based on the presence of three or more of the following: (1) waist circumference \( \geq 90 \text{ cm} \) for men or \( \geq 80 \text{ cm} \) for women [22], (2) triglyceride levels \( \geq 150 \text{ mg/dL} \), (3) high-density lipoprotein cholesterol levels < 40 mg/dL for men or < 50 mg/dL for women, (4) SBP \( \geq 130 \text{ mmHg} \) or DBP \( \geq 85 \text{ mmHg} \) or self-report of antihypertensive drug therapy, and (5) fasting plasma glucose level \( \geq 100 \text{ mg/dL} \) or self-report of ongoing treatment with an oral hypoglycemic agent or insulin. Anemia was defined as a hemoglobin level of < 13 g/dL for men and < 12 g/dL for women. Information regarding ischemic heart disease and cerebrovascular accidents was acquired from self-reported history. Ischemic heart disease included angina pectoris and myocardial infarction. Proteinuria was categorized into 3 groups according to the degree of proteinuria measured by the dipstick as negative, mild (trace), and heavy (2+ to 4+).

Information on health-related behaviors such as smoking status (life-time smoker/non-smoker), alcohol intake (less than once per month/more than once per month), and regular physical activity of moderate intensity (more/less than three times per week) was obtained from the health questionnaire. Life-time smokers included those adults who reported that they had smoked at least 100 cigarettes in their lifetime, and non-smokers included respondents who had smoked fewer than 100 cigarettes in their lifetime and did not smoke at the time of the survey. Moderate-intensity activities were defined as those lasting at least 10 minutes and causing a slight increase in the individual’s heart rate compared with sedentary activities; table tennis, swimming, yoga and badminton were included as moderate-intensity activities, but walking was excluded. Psychological variables from questionnaires included self-reported stress (none or small amount/some or extreme) and sleep quality (sufficient/insufficient).

Results
Characteristics of the study population
The demographic characteristics of the participants, stratified by eGFR, are shown in Table 1. The mean age of the study subjects was 46.5 ± 15.7 years, and 42.8% were male. A total of 716 participants had an eGFR of \( \geq 90.0 \text{ mL/min/1.73 m}^2 \), 4,353 had an eGFR of 60.0-89.9 \text{ mL/min/1.73 m}^2, and 486 had an eGFR of 30.0-59.9 \text{ mL/min/1.73 m}^2. The mean eGFR of each group was as follows: 96.7 \text{ mL/min/1.73 m}^2 in the group with eGFRs of \( \geq 90.0 \text{ mL/min/1.73 m}^2 \); 75.3 \text{ mL/min/1.73 m}^2 in the group with eGFRs of 60.0-89.9 \text{ mL/min/1.73 m}^2; and 55.9 \text{ mL/min/1.73 m}^2 in the group with eGFRs of 30.0-59.9 \text{ mL/min/1.73 m}^2. Subjects with a lower eGFR were older, predominantly women, and more likely to have comorbidities, including diabetes, hypertension, metabolic syndrome, anemia, ischemic heart disease and cerebrovascular accidents.

Table 2 shows the variables associated with health-related behaviors, socioeconomic status, and psychological variables. Subjects with a lower eGFR showed better health-related behavioral patterns, including lower rates of smoking and alcohol consumption. On the other hand, the proportion of subjects living in a rural area, having no occupation, or with less education was significantly higher as the eGFR decreased. In addition, household income also decreased with decreasing eGFR. Although the degree of stress did not differ between eGFR groups, the proportion of participants experiencing poor sleep quality increased significantly with decreasing eGFR and
was particularly low in the group with eGFRs of 30.0-59.9 mL/min/1.73 m².

HRQOL: EQ-5D dimensions and health utility score
The proportions of participants reporting problems (some problem/extreme problem) in each dimension of the EQ-5D questionnaire are shown in Figure 1. There was a significant increase in reported problems in all dimensions of the EQ-5D with decreasing eGFR. In total, 46.1% of participants with eGFRs of 30.0-59.9 mL/min/1.73 m² had problems with mobility, 9.6% had problems with self-care, 32.6% had problems with usual activity, 70.5% had problems with pain/discomfort, and 37.8% had problems with anxiety/depression.

Table 1 Demographic characteristics of participants by eGFR

| eGFR (mL/min/1.73 m²) | All (n = 5,555) | ≥ 90.0 (n = 716) | 60.0-89.9 (n = 4,353) | 30.0-59.9 (n = 486) | P for trend |
|-----------------------|----------------|-----------------|----------------------|-------------------|-------------|
| Age                   | 46.5 ± 15.7    | 32.3 ± 12.1     | 46.5 ± 14.0          | 67.7 ± 9.9        | < 0.001     |
| Male                  | 2,379 (100)    | 456 (19.2)      | 1,835 (77.1)         | 88 (3.7)          |             |
| Female                | 3,176 (100)    | 260 (8.2)       | 2,518 (79.3)         | 398 (12.5)        |             |
| eGFR                  | 76.4 ± 12.2    | 96.7 ± 5.6      | 75.3 ± 8.2           | 55.9 ± 5.5        | < 0.001     |
| Proteinuria (%)       |                |                 |                      |                   | 0.141       |
| Negative              | 94.4           | 93.3            | 94.9                 | 91.6              |             |
| Mild                  | 4.8            | 5.9             | 4.5                  | 6.1               |             |
| Heavy                 | 0.8            | 0.7             | 0.6                  | 2.3               |             |
| Co-morbidities (%)    |                |                 |                      |                   |             |
| Diabetes mellitus     | 7.6            | 3.7             | 7.0                  | 190               | < 0.001     |
| Hypertension          | 25.3           | 11.0            | 24.1                 | 55.3              | < 0.001     |
| Metabolic syndrome    | 29.4           | 13.8            | 28.4                 | 600               | < 0.001     |
| Anemia                | 11.2           | 9.5             | 11.0                 | 160               | 0.001       |
| Ischemic heart disease| 2.2            | 0.4             | 2.0                  | 6.0               | < 0.001     |
| Cerebrovascular disease| 2.2            | 0.5             | 1.8                  | 8.2               | < 0.001     |

Data are expressed as the mean ± standard deviation or a percentage. eGFR calculated using the modified MDRD formula [21]. Ischemic heart disease included angina pectoris and myocardial infarction. eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.

Table 2 Socioeconomic status, psychological factors, and health-related behavioral patterns of participants stratified to eGFR

| eGFR (mL/min/1.73 m²) | All (n = 5,555) | ≥ 90.0 (n = 716) | 60.0-89.9 (n = 4,353) | 30.0-59.9 (n = 486) | P for trend |
|-----------------------|----------------|-----------------|----------------------|-------------------|-------------|
| Marital status: living without a spouse (%) | 28.5 | 48.6 | 23.2 | 46.8 | 0.001 |
| Occupation (%)        |                |                 |                      |                   | < 0.001     |
| White collar          | 31.9           | 34.2            | 34.0                 | 95                |             |
| Blue collar           | 26.6           | 26.1            | 27.1                 | 22.1              |             |
| Student/soldier/housewife | 25.9 | 30.2 | 25.2 | 26.1 |             |
| No occupation         | 15.6           | 9.5             | 13.6                 | 42.0              |             |
| Education (%)         |                |                 |                      |                   | < 0.001     |
| University or higher  | 25.3           | 33.1            | 26.2                 | 4.9               |             |
| Upper secondary level | 49.9           | 58.8            | 51.6                 | 21.4              |             |
| Compulsory education  | 24.9           | 8.1             | 22.2                 | 73.8              |             |
| Income (US $)         | 2,090.9 ± 1,489.0 | 2,221.5 ± 1,326.5 | 2,166.5 ± 1,509.5 | 1,298.9 ± 1280.8 | < 0.001     |
| Rural residence (%)   | 22.7           | 19.0            | 21.9                 | 35.4              | < 0.001     |
| Some or extreme degree of stress (%) | 33.9 | 33.4 | 33.8 | 33.6 | 0.778 |
| Sleep quality: insufficient sleep (%) | 35.6 | 41.1 | 35.5 | 29.0 | < 0.001 |
| Physical activity: ≤ 3 times per week (%) | 13.4 | 16.2 | 13.5 | 5.8 | 0.145 |
| Smoking: life-time smoker (%) | 37.9 | 46.2 | 37.9 | 26.0 | < 0.001 |
| Alcohol intake: ≥ once a month (%) | 31.2 | 39.5 | 32.1 | 11.6 | < 0.001 |

Data expressed a as a percentage or the mean ± standard deviation. eGFR was calculated using the modified MDRD formula [21]. Upper secondary level of education included middle and high school graduate. Compulsory education meant elementary school graduate or less. eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.
The crude EQ-5D utility score significantly decreased with decreasing eGFR (Figure 2A). The mean age-adjusted EQ-5D utility score for all participants was 0.845 ± 0.004 (standard error of the mean). The age-adjusted EQ-5D utility score was significantly lower among participants with an eGFR of 30.0-59.9 mL/min/1.73 m² (0.807 ± 0.009) compared with those participants with an eGFR of ≥90.0 mL/min/1.73 m² (0.857 ± 0.003) or 60.0-89.9 mL/min/1.73 m² (0.870 ± 0.003) (Figure 2B). Figure 3 shows data from a nationally representative catalogue of age-adjusted mean EQ-5D utility scores for major chronic diseases, as derived from data from the 3rd KNHANES [24]. When our results were integrated with the data from that catalogue, we found that individuals with an eGFR of 30.0-59.9 mL/min/1.73 m² had lower utility scores than those individuals with chronic obstructive pulmonary disease, asthma, hypertension, or diabetes.

Correlates of impaired health utility
A logistic regression model was built to assess factors that were significantly associated with impaired health utility, defined as an EQ-5D utility score in the lowest quartile. To perform logistic regression analysis, certain continuous values were transformed into categorical values, as previously described. Subjects were divided into three age groups, as follows: < 40 years old, 40-60 years old, and ≥ 60 years old. Body mass index and lipid levels were considered as components of metabolic syndrome. Table 3 displays the results of univariate and multivariate analyses for impaired HRQOL. In the univariate regression analysis, variables including age, gender, health-related behaviors (smoking, alcohol intake), socioeconomic factors (marital status, area of residence, occupation, education, and household income), psychological factors (stress, sleep quality), and other co-morbidities (e.g., hypertension, diabetes, metabolic syndrome, ischemic heart disease and cerebrovascular disease) showed significant association with impaired health utility. However, the degree of proteinuria failed to prove its association with health utility in the univariate regression analysis.

In the multivariate analysis, an eGFR of 30.0-59.9 mL/min/1.73 m² was one of the independent risk factors predicting impaired health utility (odds ratio (OR) 1.531; 95% confidence interval (CI) 1.077-2.176; P = 0.018) after adjustment for age, sex, comorbidities (diabetes, hypertension, metabolic syndrome, ischemic heart disease, and cerebrovascular accidents) health-related behaviors (alcohol intake, smoking, and physical activity), socioeconomic factors (marital status, occupation, education, rural residence, and income) and psychological factors (stress and sleep quality).

In the binary multivariate logistic regression on EQ-5D responses, an eGFR of 30.0-59.9 mL/min/1.73 m² was
significantly associated with reported problems in the mobility (OR, 2.192; 95% CI, 1.178-4.077; \(P = 0.013\)) and pain/discomfort dimensions (OR, 1.574; 95% CI, 1.113-2.225; \(P = 0.010\)). Although impaired renal function was significantly associated with the self-care, usual activities, and anxiety/depression dimensions in the univariate analyses, these associations lost statistical significance after adjustment for covariates (Table 4).

Discussion

This is the first population-based analysis of the impact of renal dysfunction on preference-based health utility using a generic preference-based instrument. In this cross-sectional study, we found that moderate renal dysfunction is independently associated with reduced health utility, particularly in the domains of mobility and pain/discomfort.

Until recently, increasing comorbidities, along with the progression of CKD, was thought to play an important role in reduced HRQOL in patients with renal dysfunction [12]. There are, however, conflicting data on the association between HRQOL and renal function itself, especially among patients with mild-to-moderate renal dysfunction. In the Renal Research Institute-CKD study [25], eGFR had no linear association with HRQOL, and low eGFR was not an independent determinant of reduced HRQOL. Similarly, Odden et al. [9] found that age-adjusted HRQOL is significantly associated with renal dysfunction but that the effect is attenuated by demographic and socioeconomic variables. However, these studies were performed using subjects who had either profound renal dysfunction [25] or a history of cardiovascular events [9], both of which are major confounders in a HRQOL analysis. Therefore, these data may not be applicable to population with mild-to-moderate renal dysfunction. On the contrary, Chin et al. [14] reported that an eGFR value of 45 mL/min/1.73 m\(^2\) or lower is an independent determinant of impaired HRQOL in the elderly Korean population. Similarly, in a population-based study in Australia, Chow et al. [11] reported that an eGFR lower than 60 mL/min/1.73 m\(^2\) is significantly associated with an impaired HRQOL after adjusting for comorbidities associated with CKD. In accordance with previous population-based studies, we also demonstrated that an eGFR of 30.0-59.9 mL/min/1.73 m\(^2\) remains an independent predictor of impaired HRQOL after adjustment for demographic, socioeconomic and psychological factors, and major comorbidities associated with CKD. We hypothesize that the conflicting findings regarding the impact of renal function on preference based health utility are largely due to the differences in study subjects in terms of their renal function and comorbidities. Because the number and severity of comorbidities increase with the
progression of CKD, it can be assumed that GFR is a more important determinant of health utility in mild-to-moderate renal dysfunction. Thus, early detection of renal dysfunction and proper therapeutic intervention are important to public health efforts aimed at improving health utility.

In this study, the dimensions of EQ-5D that were particularly affected by moderate renal dysfunction were mobility and pain/discomfort, suggesting that these two components are responsible for the reduction in health utility scores that is associated with declining renal function. Although physical inactivity or functional limitations are frequently observed even in patients with mild-to-moderate renal dysfunction and are also a modifiable risk factor for mortality [26-29], there are conflicting data regarding the impact of renal function on physical activity in these patients. Data from a community-based survey of the US adult population showed that impairment in physical function among CKD patients is related to comorbidities and old age rather than to renal function itself [26]. However, other reports have suggested that renal dysfunction is directly associated with impaired physical function in elderly persons, independent of comorbidities [14,30]. Similarly, the prevalence of frailty, of which loss of mobility is a key component, increases with decreasing renal function in elderly cohorts, independent of comorbidities. Although the reasons for the association are unclear, unmeasured confounding variables such as sarcopenia [31], inflammation [32], malnutrition, or other co-morbidities may play a role [12].

In addition to impaired mobility, we found that more than 70% of the participants with an eGFR of 30.0-59.9 mL/min/1.73 m$^2$ reported that they had some or extreme pain or discomfort, and an eGFR of 30-59.9 mL/min/1.73 m$^2$ remained an independent risk factor for self-reported problems in the pain/discomfort dimension after adjusting for covariates. Similarly, the Renal Research Institute-CKD study showed that the presence of physical pain among patients with CKD

![Figure 3 EQ-5D utility scores for chronic diseases in Korea][24]. The black bar indicates patients with eGFR 30.0-59.9 mL/min/1.73 m$^2$ who were investigated in this study.
stages 3-5 was associated with lower HRQOL [25]. Unfortunately, chronic pain is often not only unrecognized, but also inadequately treated in the CKD population [33]. Therefore, regular screening for pain and the development of safe and effective treatments for chronic pain are necessary to improve HRQOL in the CKD population.

The EQ-5D is a useful preference-based measurement of HRQOL that incorporates values or utilities for health status and can be used in health-economic analyses to optimize resource allocation [34,35]. In this study, we found that age-adjusted EQ-5D utility scores in participants with moderate renal dysfunction are lower than in patients with diabetes, hypertension, asthma or chronic obstructive pulmonary disease. Despite the substantially lower health utility of these patients and the chronicity of the disease, CKD awareness is extremely low in both high- and low-income countries [36]. Indeed, the awareness rate

| Table 3 Univariate and multivariate logistic regression analyses for impaired HRQOL |
|-----------------------------------------------|----------------|----------------|----------------|
|                                              | Unadjusted OR (95% CI) | P   | Adjusted OR (95% CI) | P   |
| Age (year)                                   | < 40 Reference       |      |      |      |
|                                              | 40-60 2.205 (1.910-2.545) | < 0.001 | 1.598 (1.345-1.879) | < 0.001 |
|                                              | ≥ 60 9.573 (8.117-11.289) | < 0.001 | 3.337 (2.598-4.287) | < 0.001 |
| Male                                         | Male 0.569 (0.508-0.638) | < 0.001 | 0.569 (0.487-0.666) | < 0.001 |
| eGFR  ≥ 90.0                                 | Reference Reference |
|                                              | 60.0-89.9 1.994 (1.639-2.426) | < 0.001 | 1.168 (0.929-1.469) | 0.185 |
|                                              | 30.0-59.9 10.372 (7.868-13.672) | < 0.001 | 1.531 (1.077-2.176) | 0.011 |
| Diabetes mellitus                            | Yes 2.140 (1.747-2.622) | < 0.001 |       |
| Hypertension                                  | Yes 2.554 (2.252-2.895) | < 0.001 | 1.231 (1.048-1.445) |       |
| Metabolic syndrome                           | Yes 2.091 (1.853-2.358) | < 0.001 |       |
| Ischemic heart disease                       | Yes 8.419 (5.184-13.675) | < 0.001 | 3.730 (2.169-6.415) | < 0.001 |
| Cerebrovascular accident                     | yes 3.349 (3.505-8.164) | < 0.001 | 1.971 (1.194-3.256) | 0.008 |
| Alcohol intake                                | ≥ 1/week 0.652 (0.576-0.737) | < 0.001 |       |
| Smoking status                                | life-time smoker 0.789 (0.703-0.886) | < 0.001 |       |
| Marital status                                | without spouse 1.290 (1.141-1.458) | < 0.001 |       |
| Occupation                                    | white collar Reference Reference |
| Education                                     | ≥ university Reference Reference |
|                                              | blue collar 2.545 (2.184-2.965) | < 0.001 | 1.400 (1.154-1.689) | 0.001 |
|                                              | other† 1.944 (1.661-2.275) | < 0.001 | 1.328 (1.097-1.608) | 0.004 |
|                                              | no occupation 4.953 (4.148-5.914) | < 0.001 | 1.741 (1.378-2.199) | < 0.001 |
| Education                                     | Reference Reference |
|                                              | upper 2ndary‡ 1.886 (1.608-2.213) | < 0.001 | 1.294 (1.076-1.555) | 0.006 |
|                                              | ≤ compulsory§ 9.607 (8.035-11.488) | < 0.001 | 2.515 (1.970-3.212) | < 0.001 |
| Income                                        | highest quartile Reference Reference |
|                                              | 2nd-3rd quartile 1.432 (1.224-1.674) | < 0.001 | 1.139 (0.953-1.360) | 0.152 |
|                                              | lowest quartile 4.735 (3.986-5.625) | < 0.001 | 1.676 (1.356-2.072) | < 0.001 |
|                                              | rural residence 2.056 (1.808-2.339) | < 0.001 | 1.190 (1.011-1.401) | 0.036 |
| Stress                                        | some or extreme 1.752 (1.559-1.968) | < 0.001 | 1.753 (1.525-2.016) | < 0.001 |
| Sleep quality                                 | insufficient 1.276 (1.137-1.432) | < 0.001 | 1.606 (1.396-1.848) | < 0.001 |

Values shown are OR (95% CI). Impaired HRQOL was defined as the lowest quartile of EQ-5D weighted values. Potential risk factors in the unadjusted analysis (P < 0.05) were included in the adjusted analysis. The multivariate logistic regression analysis model was derived using the backward conditional method.

†Students, soldiers and housewives; ‡middle and high school graduates; §elementary school or no education. HRQOL, health-related quality of life; eGFR, estimated glomerular filtration rate (mL/min/1.73 m²); OR, odds ratio; CI, confidence interval.
of CKD (stage I to III) has been reported to be lower than 10%, whereas the awareness rates of diabetes and hypertension are 55.8% and 51% respectively in Korea [37]. Moreover, the World Health Organization (WHO) does not yet recognize CKD as a major chronic disease that must be prevented to reduce mortality. Even though it seems apparent that early CKD detection and proper intervention can vastly reduce healthcare expenses for end-stage renal disease, these preventive strategies are implemented less frequently than recommended, even in developed countries. In addition, according to the budget expenditure report of the Centers for Disease Control and Prevention, CKD was allotted the smallest budget considering the burden of the disease [38]. Taken together, these findings suggest that healthcare resource allocation for CKD is inadequate. Under such circumstances, the results of this study provide evidence that moderate renal dysfunction may be worthy of a proportionate allotment of the available healthcare resources.

This cross-sectional study has several limitations that needed to be addressed. First, the present data showed skewed distributions of gender and eGFR groups. In this study, the proportion of the subjects in the normal renal function (eGFR ≥ 90.0 mL/min/1.73 m²) group was lower than that of the mildly decreased renal function group (eGFR 60.0-89.9 mL/min/1.73 m²). In addition, the proportion of women was higher compared with men, especially in the stage III CKD group compared with other population-based studies [39]. Although these deviant distributions may be partly explained by the inaccuracy of the MDRD equations in Asian populations [40], and an incorrect coefficient factor for female gender, which

| Table 4 Binary multivariate logistic regression of the EQ-5D dimensions | EQ-SD dimensions |
| --- | --- | --- | --- | --- | --- |
| **Age** | **Reference** | **Reference** | **Reference** | **Reference** | **Reference** |
| < 40 | – | – | – | – | – |
| 40-60 | 2.706 (1.196-4.354)* | 9.205 (2.148-39.441)** | 3.137 (1.986-4.955)* | 1.601 (1.347-1.903)* | 1.347 (1.118-1.623)** |
| ≥ 60 | 7.230 (4.462-11.716)* | 13.686 (3.095-60.511)** | 5.788 (3.529-9.494)* | 3.254 (2.537-14.174)* | 1.603 (1.243-2.068)** |
| **Sex** | **Reference** | – | – | – | – |
| Male | 0.452 (0.354-0.578)* | – | 0.565 (0.440-0.727)** | 0.543 (0.464-0.635)* | 0.461 (0.364-0.584)* |
| Female | – | – | – | – | – |
| **eGFR** | **Reference** | – | – | – | – |
| ≥ 90.0 | – | – | – | – | – |
| 60.0-89.9 | 1.863 (1.053-3.296)* | – | – | – | – |
| 30.0-59.9 | 1.219 (1.178-4.077)* | – | – | – | – |
| **Diabetes mellitus** | – | – | – | – | – |
| **Hypertension** | – | – | – | – | – |
| **Metabolic syndrome** | – | – | – | – | – |
| **Ischemic heart disease** | 2.403 (1.523-3.791)* | – | 1.968 (1.245-3.110)** | 2.515 (1.558-4.058)* | 1.987 (1.316-2.999)** |
| **Cerebrovascular disease** | 3.056 (1.886-4.953)* | 5.326 (3.091-9.179)* | 3.018 (1.907-4.777)* | 1.578 (0.987-2.524) | 1.833 (1.188-2.827)** |
| **Anemia** | – | – | – | – | – |
| **Alcohol intake** | – | 0.518 (0.306-0.877)* | – | – | – |
| **Smoking** | – | – | – | – | – |
| **Physical inactivity** | 1.246 (0.978-1.589) | 1.978 (1.098-3.564)* | 1.435 (1.098-1.875)* | – | 1.158 (0.978-1.372) |
| **Marital status** | – | – | – | – | – |
| **Occupation** | – | – | – | – | – |
| White collar | 1.412 (1.419-1.735)* | – | – | – | – |
| Blue collar | 1.401 (0.987-1.988) | 0.935 (0.436-2.005) | 1.336 (0.920-1.939) | 1.540 (1.272-1.863)* | 1.194 (0.960-1.486) |
| Other† | 1.403 (0.985-1.998) | 1.318 (0.619-2.808) | 1.355 (0.926-1.983) | 1.342 (1.108-1.625)** | 1.213 (0.981-1.499) |
| No occupation | 2.293 (1.600-3.287)* | 2.369 (1.146-4.898)* | 2.148 (1.464-3.149)* | 1.637 (1.280-2.605)* | 1.581 (1.234-2.026)** |
| **Education** | – | – | – | – | – |
| Upper 2ndary‡ | 1.976 (1.226-3.187)** | 1.830 (0.618-5.423) | 1.680 (1.026-2.751)* | 1.235 (1.027-1.486)* | 1.276 (1.032-1.578)* |
| ≤ compulsory§ | 4.347 (2.631-7.181)* | 3.468 (1.154-10.421)* | 3.221 (1.907-5.440)* | 2.306 (1.810-2.938)* | 1.697 (1.286-2.240)* |
| **Income** | – | – | – | – | – |
| Highest quartile | 1.383 (1.107-1.727)** | – | 1.581 (1.255-1.992)* | – | 0.854 (0.714-1.021) |
| Lowest quartile | 1.215 (0.857-1.722) | 1.534 (0.662-3.554) | 1.563 (1.048-2.322)* | 1.121 (0.938-1.339) | 1.209 (0.983-1.488) |
| **Residence** | – | – | – | – | – |
| Rural | 1.941 (1.367-2.758)* | 3.005 (1.324-6.825)** | 2.442 (1.632-3.654)* | 1.590 (1.288-1.963)** | 1.879 (1.483-2.381)** |
| Urban | – | – | – | – | – |
| **Stress** | – | – | – | – | – |
| Some/extreme | 1.455 (1.186-1.785)* | – | 1.496 (1.208-1.852)* | 1.739 (1.514-1.997)** | 3.041 (2.633-3.513)* |
| Insufficient | – | – | – | – | – |

Values shown are OR (95% CI). Cells with a dash indicate that the variable was not included in the model. Cells with two dashes indicate that the variable was included in the multivariate model but excluded after the multivariate analysis. The multivariate logistic regression analysis model was derived using the backward conditional method. * Students, soldiers and housewives; † middle and high school graduates; § elementary school or no education; **P < 0.001; **P < 0.001. eGFR, estimated glomerular filtration rate (mL/min/1.73 m²); OR, odd ratio; CI, confidence interval.
underestimates true GFR [41], the possibility of potential selection bias cannot be ruled out in this study. Second, the possible confounding effect of age which is strongly associated with both CKD and health utility could also affect the results. Furthermore, the associations we observed were only inferred from this analysis, and unmeasured residual confounding should be considered in when interpreting our results. Third, the method for serum creatinine measurement was not calibrated to be traceable to IDMS. Thus, there is the possibility of under-estimating the GFR in participants with GFR over 60 mL/min/1.73 m² [42]. Finally, no longitudinal data were available on the associations between health utility and mortality or progression to end stage renal disease among CKD participants. The precise reason why renal impairment contributes to decreased health utility was not investigated in this cross-sectional analysis, and the interventions that could positively affect CKD patients’ health utility remain unknown.

Conclusions
In this study, moderate renal dysfunction was independently associated with impaired health utility in a Korean adult population, even though age had substantial influence on the association. Reduced mobility and increased pain or discomfort were the two dimensions significantly that were affected by moderate renal dysfunction. In addition, subjects with moderate renal dysfunction showed lower age-adjusted health preference scores than those subjects with major chronic diseases including diabetes and hypertension. These results indicate that more careful assessment of preference-based utility and proper healthcare resource allocation are required for patients with moderate renal dysfunction to improve clinical outcomes.

Acknowledgements
This work was supported by a grant from the Korean Healthcare Technology R&D Project, Ministry of Health, Welfare and Family Affairs, Republic of Korea (A084001).

Author details
1Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea. 2Department of Epidemiology and Biostatistics, School of Public Health, Seoul National University Hospital, Seoul, South Korea. 3Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, South Korea. 4Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea. 5Kidney Research Institute, Seoul National University Hospital, Seoul, South Korea. 6Department of Internal Medicine, Seoul National University Hospital, 101 Daehakro, Jongno-gu, 110-744 Seoul, Republic of Korea.

Authors’ contributions
All authors contributed extensively to the work presented in this paper at all stage. HL, YSK and DKK conceived the design of this research and wrote the manuscript. DKK supervised this project. YJD and JPL assembled the input data. MK and HK performed the statistical analyses. KHO and KWJ interpreted the data analyses. SK provided critical revision of the manuscript. HJC, CSL and SK gave conceptual advice and commented on the manuscript. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 16 August 2011 Accepted: 24 April 2012 Published: 24 April 2012

References
1. Neumann PJ, Goldie SJ, Weinstein MC. Preference-based measures in economic evaluation in health care. Annu Rev Public Health 2000, 21:587-611.
2. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-effectiveness in Health and Medicine. JAMA 1996, 276:1253-1258.
3. Collins AJ, Foley RN, Herzog C, Chavers B, Gilberston D, Ishani A, Kasiske B, Liu J, Mau LW, McBean M, Murray A, St Peter W, Guo H, Gustafson S, Li Q, Li S, Li S, Peng Y, Ou Y, Roberts T, Skeans M, Snyder J, Solid C, Wang C, Weinhandl E, Zaun D, Arko C, Chen SC, Dalleska F, Daniels F, Dunning S, Ebben J, Frazier E, Hantlik C, Johnson R, Sheets D, Wang X, Forest B, Constantini E, Eversen S, Eggers P, Agudoa L. US Renal Data System 2010 Annual Data Report. Am J Kidney Dis 2011, 57A8:e1-526.
4. Rettig RA, Norris K, Nissenson AR. Chronic kidney disease in the United States: a public policy imperative. Clin J Am Soc Nephrol 2008, 3:1902-1910.
5. Mapes DL, Bragg-Gresham JL, Bommer J, Fukuhara S, McKevitt P, Wikstrom B, Lopes AA. Health-related quality of life in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis 2004, 44:554-560.
6. Mapes DL, Lopes AA, Satayuth S, McCullough KP, Goodkin DA, Locatelli F, Fukuhara S, Young EW, Kurokawa K, Saito A, Bommer J, Wolfe RA, Held PJ, Port FK. Health-related quality of life as a predictor of mortality and hospitalization: the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2003, 64:339-349.
7. Go AS, Chertow GM, Fan D, McCulloch CE, Hus C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2006, 351:1296-1305.
8. Kalender B, Ozdemir AC, Dervisoglu E, Ozdemir O. Quality of life in chronic kidney disease: effects of treatment modality, depression, malnutrition and inflammation. Int J Clin Pract 2007, 61:569-576.
9. Odden MC, Wooley MA, Shlipak MG. Depression, stress, and quality of life in persons with chronic kidney disease: the Heart and Soul Study. Nephron Clin Pract 2006, 103:c1-c7.
10. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, Hebert P, Hunsicker LG, Jaber BL, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raij L, Robbins J, Spivak M, Tallarico JM, Tubul SS, Wei W, Wiebe N, Zoccali C. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Hypertension. Hypertension 2003, 42:1050-1065.
11. Chow FY, Briganti EM, Kerr PG, Chadban SJ, Zimmer PZ, Atkins RC. Health-related quality of life in Australian adults with renal insufficiency: a population-based study. Am J Kidney Dis 2003, 41:596-604.
12. Soni RK, Weisbord SD, Unruh ML. Health-related quality of life outcomes in chronic kidney disease.Curr Opin Nephrol Hypertens 2010, 19:153-159.
13. Tajima R, Kondo M, Kai H, Saito C, Okada M, Takahashi H, Doi M, Tsuukou S, Yamaga K. Measurement of health-related quality of life in patients with chronic kidney disease in Japan with EuroQol (EQ-5D). Clin Exp Nephrol 2010, 14:340-348.
14. Chin HY, Song YR, Lee JI, Lee SB, Kim KW, Na KY, Kim S, Chae DW. Moderately decreased renal function negatively affects the health-related quality of life among the elderly Korean population: a population-based study. Nephrol Dial Transplant 2008, 23:2810-2817.
15. Shelip MK, Stenhman-Breen C, Fried LF, Song X, Siscovick D, Fried LP, Psaty BM, Newman AB. The presence of frailty in elderly persons with chronic renal insufficiency. Am J Kidney Dis 2004, 43:861-867.
16. Mujais SK, Stone K, Braultette J, Takano T, Soroka S, Franek C, Mendelssohn D, Finkelstein FO. Health-related quality of life in CKD Patients: correlates and evolution over time. Clin J Am Soc Nephrol 2009, 4:1299-1301.
17. Dolan P: Modeling valuations for EuroQol health states. Med Care 1997, 35:1095-1108.
18. EuroQol—a new facility for the measurement of health-related quality of life. The EuroQol Group. Health Policy 1990, 16:199-208.
19. Kang EJ, Shin HS, Park HJ: A valuation of health status using EQ-SD. Korean J Health Econ Policy 2006, 12:19-42.
20. Kim MH, Cho YS, Uhm WS, Kim S, Bae SC: Cross-cultural adaptation and validation of the Korean version of the EQ-SD in patients with rheumatic diseases. Qual Life Res 2005, 14:1401-1406.
21. Leeve AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Peronne RD, Lau J, Eknoyan G: National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003, 139:137-147.
22. Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GL, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ: Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007, 75:72-80.
23. Park SS, Yoon YS, Oh SW: Health-related quality of life in metabolic syndrome: The Korea National Health and Nutrition Examination Survey 2005. Diabetes Res Clin Pract 2009, 85:31-38.
24. Kang EJ, No SK: A Catalogue of EQ-SD Utility Weights for Chronic Diseases among Noninstitutionalized Community Residents in Korea. Value Health 2009, 12:S114-S117.
25. Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G, Burrows-Hudson S, Messana JM, Levin N, Rajagopalan S, Port FK, Wolfe RA, Saran R: Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. Am J Kidney Dis 2005, 45:658-666.
26. Plantinga LC, Johansen K, Crews DC, Shahinian VB, Robinson BM, Saran R, Burrows NR, Williams DE, Powe NR: Association of CKD with disability in the United States. Am J Kidney Dis 2011, 57:212-227.
27. Padilla J, Krasnoff J, Da Silva M, Hsu CY, Frassetto L, Johansen KL, Painter P: Physical functioning in patients with chronic kidney disease. J Nephrol 2008, 21:550-559.
28. Wilhelm-Leen ER, Hall YN, Tamura M, Chertow GM: Frailty and chronic kidney disease: the Third National Health and Nutrition Evaluation Survey. Am J Med 2009, 122:664-671.
29. Beddhu S, Bard BC, Zitterkoph J, Neilson J, Greene T: Physical Activity and Mortality in Chronic Kidney Disease (NHANES III). Curr Opin Nephrol Hypertens 2009, 18:1901-1908.
30. Fried LF, Lee JS, Shlipak M, Chertow GM, Green C, Ding J, Harris T, Newman AB: Chronic kidney disease and functional limitation in older people: health, aging and body composition study. J Gerontol A Biol Sci Med Sci 2006, 61A:750-756.
31. Foley RN, Wang C, Ishani A, Collins AJ, Murray AM: Kidney function and sarcopenia in the United States general population: NHANES III. Am J Kidney Dis 2007, 49:279-286.
32. Fried LF, Lee JS, Shlipak M, Chertow GM, Green C, Ding J, Harris T, Newman AB: Association of metabolic syndrome with inflammation in CKD: results From the Third National Health and Nutrition Examination Survey (NHANES III). Am J Kidney Dis 2005, 46:577-586.
33. Pham PCT, Toscano E, Pham PMT, Pham PAT, Pham SV, Pham PTT: Pain management in patients with chronic kidney disease. NDT Plus 2009, 4:111-118.
34. Torrance GW: Measurement of health state utilities for economic appraisal. J Health Econ 1996, 5:1-30.
35. Sullivan PW, Lawrence WF, Gushchtyan V: A national catalog of preference-based scores for chronic conditions in the United States. Med Care 2005, 43:736-740.
36. Obrador GT, Mahdavi-Mazdeh M, Collins AJ: Establishing the Global Kidney Disease Prevention Network (KDPN): a position statement from the National Kidney Foundation. Am J Kidney Dis 2011, 57:361-370.
37. Chin HJ, Ahn JM, Na KY, Chae DW, Lee TW, Heo NJ, Kim S: The effect of the World Kidney Day campaign on the awareness of chronic kidney disease and the status of risk factors for cardiovascular disease and renal progression. Nephrol Dial Transplant 2010, 25:413-419.
38. Curry CW, De AK, Ikeda RM, Thacker SB: Health burden and funding at the Centers for Disease Control and Prevention. Am J Prev Med 2006, 30:269-276.
39. Zhang QL, Rothenbacher D: Prevalence of chronic kidney disease in population-based studies: systematic review. BMC Public Health 2008, 8:117.
40. Chen J, Wildman RP, Gu D, Kusek JW, Spruill M, Reynolds K: Prevalence of decreased kidney function in Chinese adults aged 35 to 74 years. Kidney Int 2005, 68:2837-2845.
41. Grillo M, Anastasio P, De Santo NG: Relationship of gender, age, and body mass index to errors in predicted kidney function. Nephrol Dial Transplant 2005, 20:1791-1798.
42. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Costis FG: Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. Ann Intern Med 2004, 141:929-937.

Pre-publication history
The pre-publication history for this paper can be accessed here: http://www.biomedcentral.com/1471-2369/13/19/prepub

doi:10.1186/1471-2369-13-19
Cite this article as: Lee et al. The association of moderate renal dysfunction with impaired preference-based health-related quality of life: 3rd Korean national health and nutritional examination survey. BMC Nephrology 2012 13:19.