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Original Investigation

CKD and Health-Related Quality of Life: The Korea National Health and Nutrition Examination Survey

Ji In Park, MD, *Hyunjeong Baek, MD, PhD,* *and Hae Hyuk Jung, MD, PhD*

Background: Quality of life is increasingly viewed as an important health outcome. However, the association of chronic kidney disease (CKD) and its severity with health-related quality of life is uncertain.

Study Design: Nationwide population-based cross-sectional study.

Setting & Participants: 46,676 adults participating in the Korea National Health and Nutrition Examination Survey (KNHANES) 2005 to 2013.

Predictor: CKD ascertained as dipstick-positive proteinuria or estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2. 5 eGFR categories of CKD were compared: ≥ 90 (with proteinuria), 60 to 89 (with proteinuria), 45 to 59, 30 to 44, and <30 mL/min/1.73 m^2.

Outcomes: The EQ-5D index for health status (range, 0 [death] to 1 [optimal health]).

Results: The total crude CKD prevalence estimate for adults 20 years or older in Korea was 5.5%. After adjustments for age, sex, risk factors, and comorbid conditions, the EQ-5D index was lower in those with versus without CKD, with mean differences of -0.004 (95% CI, -0.015 to 0.007), -0.016 (95% CI, -0.032 to -0.000), -0.020 (95% CI, -0.029 to -0.011), -0.052 (95% CI, -0.072 to -0.032), and -0.067 (95% CI, -0.101 to -0.032), respectively, for CKD eGFR categories of ≥ 90, 60 to 89, 45 to 59, 30 to 44, and <30 mL/min/1.73 m^2. In the subgroup of older (≥ 60 years) individuals, the adjusted mean difference in the EQ-5D index was lower in the CKD eGFR category of 60 to 89 mL/min/1.73 m^2, but not in the eGFR category of 45 to 59 mL/min/1.73 m^2, compared to non-CKD.

Limitations: The survey was conducted on noninstitutionalized civilians, and the chronicity of kidney disease was not verified. Caution is required if our results are applied to special settings and specific populations.

Conclusions: There was a graded but complex association between CKD and poor health-related quality of life in this large community-based population.

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INDEX WORDS: Health-related quality of life (HRQoL); health status; chronic kidney disease (CKD); estimated glomerular filtration rate (eGFR); renal function; proteinuria; kidney failure; chronic; health surveys; Korea.

More and more, health-related quality of life (HRQoL) is being acknowledged to be an important health outcome. It provides a comprehensive appraisal of disease burden, incorporating assessment of symptoms, functional capacity, and well-being in relation to treatment effectiveness and health care policy. The concept of HRQoL builds on the International Classification of Functioning, Disability and Health, which is the basis of the World Health Organization's methodology for determining health and disability at the individual and population levels.[1]

Chronic kidney disease (CKD) is an important cause of morbidity and mortality worldwide. Patients with CKD have an increased risk for death, particularly from cardiovascular causes.[2,3] Graded associations between reduced estimated glomerular filtration rate (eGFR) and risks for death and cardiovascular events have been reported.[4] In addition to death and cardiovascular diseases, other complications of CKD, such as hypertension, anemia, and bone diseases, are also more prevalent with the progressive loss of kidney function.[5] Thus, HRQoL may be impaired along with the development of complications as kidney function declines.

There have been a number of studies evaluating the effect of eGFR on HRQoL. In patients with CKD with a mean eGFR of 23.6 mL/min/1.73 m^2, HRQoL was reported to be notably impaired compared to that in a general population.[6] Moreover, in several studies using a cutoff of either 45 or 60 mL/min/1.73 m^2, HRQoL was found to be impaired in patients with reduced eGFRs.[7-10] However, other studies reported that these associations disappeared after adjusting for confounders such as anemia and cardiovascular

diseases.[11,12] Because CKD highly associates with various coexisting conditions and patient characteristics, including aging, female sex, hypertension, diabetes, anemia, bone disorders, and cardiovascular diseases, the deterioration in HRQoL in patients with CKD should be considered a complex and multifactorial process. Previous studies on the topic have been limited by the inclusion of relatively small numbers of participants and the use of dichotomous eGFR groups. A small sample size might limit statistical power to detect associations in models with sufficient variables and to examine the different levels of reduced kidney function.

In this large community-based population study, we examined the effect of decreased kidney function on impairment in HRQoL. We hypothesized that there would be an independent graded association between severity of CKD and degree of HRQoL impairment.

METHODS

Participants

The Korea National Health and Nutrition Examination Survey (KNHANES) is a nationwide population-based cross-sectional study of the health and nutritional status of the noninstitutionalized Korean population. It comprises a health questionnaire, physical/laboratory examinations, and nutrition survey; to date, phase I (1998), II (2001), III (2005), IV (2007-2009), V (2010-2012), and VI (2013-2015) surveys have been conducted by the Korean Ministry of Health and Welfare. Written informed consent was obtained from each participant in KNHANES at the time of enrollment.

The present study was based on data obtained from KNHANES 2005 to 2013 because the EQ-5D (EuroQol Research Foundation) questionnaire was used to measure HRQoL since 2005, and complete data from KNHANES 2014 to 2015 had not yet been released when these analyses were conducted. Of 61,435 participants in the health questionnaire and physical/laboratory examination of KNHANES 2005 to 2013, we excluded participants younger than 20 years (n = 14,759), resulting in 46,676 participants being included in the analysis (Fig 1).

The study protocol was approved by our institutional review board (file no. KNUH-2015-03-001).

Health-Related Quality of Life

HRQoL was assessed using the Korean version of the EQ-5D health questionnaire. The EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 levels: no problem, some problem, and extreme problem. The combination of all possible dimensions and levels results in 243 unique health states. A multiattribute value function is used to map preferences for each of these health states. From this scoring algorithm, EQ-5D index scores are calculated based on responses to the 5-item questionnaire. The scoring algorithm for the EQ-5D index used in this research is based on the Korean value set.[13] Scores of 1 and 0 correspond to optimal health and the worst health state, judged to be equivalent to death, respectively.

The EQ-5D index has been used regarding a wide variety of diseases and conditions in more than 4,000 publications to date.[14] The validity, reliability, and responsiveness of this instrument have been documented extensively in both general and specific disease populations.[15,16] The EQ-5D has also been used in previous studies of CKD populations,[17] and its validity and reliability have been demonstrated in Koreans.[18,19]
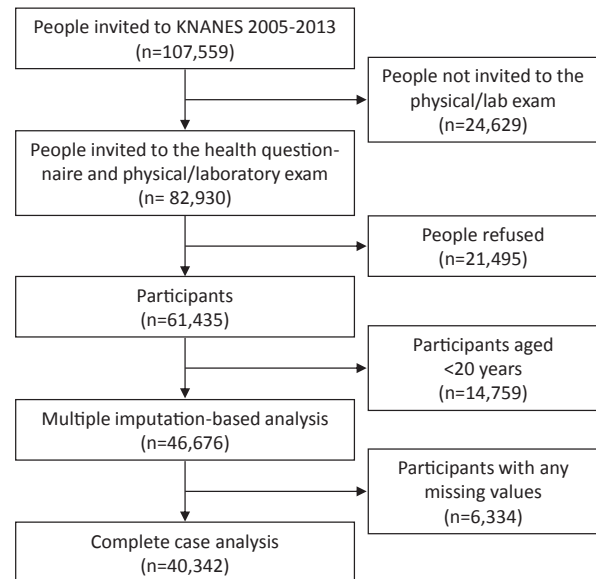

Figure 1. Flow chart of study participants. To mitigate the loss of information and investigate possible bias related to missing data, we performed multiple imputation for handling missing data. We also performed complete-case analysis, which used only participants for whom all analyzed variables were available. The survey sample weight was introduced in our analyses to provide representative estimates of the Korean population. Mean values for age, EQ-5D index, and estimated glomerular filtration rate (eGFR) were 49.9 years, 0.932, and 92.1 mL/min/1.73 m^2 in complete cases and 50.0 years, 0.928, and 92.1 mL/min/1.73 m^2 in the multiple imputation data sets, respectively. Weighted mean estimates of age, EQ-5D index, and eGFR were 45.4 years, 0.943, and 94.9 mL/min/1.73 m^2, respectively. Abbreviation: KNHANES, Korea National Health and Nutrition Examination Survey.

Anthropometric and Laboratory Data

Trained medical staff performed physical examinations following standardized procedures. Blood pressure was measured manually 3 times at 30-second intervals after a minimum of 5 minutes of rest in a seated position and recorded as the average value of the 2nd and 3rd measurements.

Blood samples were collected after at least an 8-hour fast, properly processed, immediately refrigerated, and transported in cold storage to the central laboratory within 24 hours. Serum creatinine was measured by the colorimetric method using the ADVIA 1650 (Siemens) in KNHANES 2005 and 2007 or the Automatic Analyzer 7600 (Hitachi) in KNHANES 2008–2013. Serum glucose was measured by the enzymatic method. Blood hemoglobin was measured by the impedance method in KNHANES 2005 and 2007 or the sodium lauryl sulfate hemoglobin method in KNHANES 2008 to 2013.

Kidney Function

In KNHANES 2008 to 2013, eGFR was calculated from serum creatinine level calibrated to an isotope-dilution mass spectrometry–traceable standard using the CKD-EPI (CKD Epidemiology Collaboration) equation.[20] In KNHANES 2005 and 2007, in which creatinine measurements were not standardized, we reduced creatinine levels by 5%, which is the calibration factor used to adjust nonstandardized samples.[21]

The CKD-EPI equation for estimating GFR more accurately categorizes risk for death than the MDRD (Modification of Diet in Renal Disease) Study equation.[22] The accuracy of the CKD-EPI