Original Paper

Comparison of the MDRD Study and CKD-EPI Equations for the Estimation of the Glomerular Filtration Rate in the Korean General Population: The Fifth Korea National Health and Nutrition Examination Survey (KNHANES V-1), 2010

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Key Words

Chronic kidney disease • Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation • Modification of Diet in Renal Disease (MDRD) study equation • Performance

Abstract

Background: We compared the accuracy of the Modification of Diet in Renal Disease (MDRD) study and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations in Korean patients and evaluated the difference in CKD prevalence determined using the two equations in the Korean general population. **Methods:** The accuracy of the two equations was evaluated in 607 patients who underwent a chromium-51-ethylenediaminetetraacetic acid GFR measurement. Additionally, we compared the difference in CKD prevalence determined by the two equations among 5,822 participants in the fifth Korea National Health and Nutrition Examination Survey, 2010. **Results:** Among the 607 subjects, the median bias of the CKD-EPI equation was significantly lower than that of the MDRD study equation (0.9 vs. 2.2, $p=0.020$). The accuracy of the two equations was not significantly different in patients with $\text{mGFR} < 60 \text{ mL/min/1.73m}^2$; however, the accuracy of the CKD-EPI equation was significantly higher than that of the MDRD study equation in patients with $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$. The prevalences of the CKD stages 1, 2 and 3 in the Korean general population were 47.56, 49.23, and 3.07%, respectively, for the MDRD study equation; and were 68.48, 28.89, and 2.49%, respectively, for the CKD-EPI equation. **Conclusions:** These data suggest that the CKD-EPI equation might be more useful in clinical practice than the MDRD study equation in Koreans.

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Introduction

The estimated glomerular filtration rate (eGFR) calculated using the Modification of Diet in Renal Disease (MDRD) study equation is a representative index for the prediction of the glomerular filtration rate (GFR). Because the $eGFR_{MDRD}$ is underestimated at $GFR \geq 60$ mL/min/1.73m², the National Kidney Disease Education Program (NKDEP) recommends reporting $eGFR_{MDRD}$ values equal or greater than 60 mL/min/1.73m² as ≥ 60 mL/min/1.73m² instead of the calculated eGFR value [1]. Recently, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was developed, and the $eGFR_{CKD-EPI}$ was more accurately calculated at $GFR \geq 60$ mL/min/1.73m² than that calculated using the MDRD study equation [2-6]; the result was validated in a group of patients aged 80 years or older [7].

Previous studies that compared the MDRD study equation with the CKD-EPI equation in Korea targeted patients with specific diseases such as acute myocardial infarction and acute heart failure. In addition, the eGFR was not compared with the measured GFR (mGFR) [8, 9].

In this study, we evaluated the accuracy of the MDRD study and CKD-EPI equations in Korea based on the mGFR. Additionally, the difference in the prevalence of CKD stage was analyzed in a large-scale Korean general population.

Materials and Methods

Study population

A total of 835 Korean patients underwent chromium 51 ethylenediaminetetraacetic acid (⁵¹Cr-EDTA) GFR measurement at the Asan Medical Center in 2012. In total, 607 patients aged 20 or older were selected for this study. Blood samples were collected for the measurement of serum creatinine concentration on the same day that the ⁵¹Cr-EDTA GFR was measured. The accuracy of the two equations was evaluated in 607 patients.

To compare the performance of the two equations in the Korean general population, data from the fifth Korea National Health and Nutrition Examination Survey (KNHANES V-1), 2010 were used. Of the 8,958 survey participants, 6,665 were 20 years old or older. Of the 6,665 adult participants, 788 who did not undergo the test of serum creatinine concentration and 55 who did not indicate their comorbid medical conditions in their health surveys were excluded from this study. Therefore, 5,822 subjects were selected for this study. All subjects included in the present study were Korean ethnic group. This study was approved by the Institutional Review Board of the Asan Medical Center (approval number: 2013-0318).

Measurement of the GFR

The mGFR was assessed using the two-sample plasma clearance rate of ⁵¹Cr-EDTA, calculated by the slope-intercept method with corrections for the body surface area and the fast exponential curve using the methods recommended in the British Nuclear Medicine Society GFR guidelines [10].

Estimation of the GFR

Each eGFR was calculated using the four-variable MDRD study equation [11], $GFR = 175 \times \text{standardized serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ [if female] and the CKD-EPI equation [2]: For female with a serum creatinine level ≤ 0.7 mg/dL, $GFR = 144 \times (\text{Serum creatinine}/0.7)^{-0.329} \times (0.993)^{\text{Age}}$; for female with a serum creatinine level > 0.7 mg/dL, $GFR = 144 \times (\text{Serum creatinine}/0.7)^{-1.209} \times (0.993)^{\text{Age}}$; for male with a serum creatinine level ≤ 0.9 mg/dL, $GFR = 141 \times (\text{Serum creatinine}/0.9)^{-0.411} \times (0.993)^{\text{Age}}$; for male with a serum creatinine level > 0.9 mg/dL, $GFR = 141 \times (\text{Serum creatinine}/0.9)^{-1.209} \times (0.993)^{\text{Age}}$. In the 607-subject mGFR group and the 5,822-subject KNHANES V-1 group, the serum creatinine concentration measurements were performed using the Toshiba 200-FR Neo (Toshiba Medical Systems Co., Tokyo, Japan) and the Hitachi Automatic Analyzer 7600 (Hitachi High-Technologies Co., Tokyo, Japan), respectively. For both instruments, isotope-dilution mass spectrometry traceable calibration was conducted daily using the Roche multicalibrator (Roche Diagnostics, Indianapolis, IN, USA), and the serum creatinine concentration was measured using the rate-blanked compensated kinetic Jaffe method.

Fig. 1. Comparison of measured to estimated glomerular filtration rate (GFR) in 607 patients who underwent GFR measurement using ⁵¹Cr-EDTA. Solid circle represents female subjects and open circle depicts male subjects. Scatter plots in (A) Modification of Diet in Renal Disease (MDRD) study equation and (B) Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation versus measured GFR. The solid line represents linear regression and dashed line depicts 95% confidential interval for slope. Bland-Altman plots in (C) MDRD study equation and (D) CKD-EPI equation versus measured GFR. Solid line represents mean difference and dashed line depicts ± 1.96 standard deviation (SD). A positive difference suggests an underestimation by each equation and vice versa.

GFR categories

Based on the clinical practice guidelines of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative, CKD was classified into five stages [12]. However, the GFR group in this study was subdivided into eight categories by GFR increments of 15 mL/min/1.73m²: GFR <15, 15–29, 30–44, 45–59, 60–74, 75–89, 90–104 and ≥ 105 mL/min/1.73m².

Statistical analyses

To compare the accuracies of the MDRD study and CKD-EPI equations, the mGFR was defined as the reference GFR. In the 607 subjects whose mGFR was measured, the scatter plot and Bland-Altman bias plot of two equations were drawn. The bias was defined as mGFR minus eGFR. The accuracy was evaluated as a percentage of the eGFR that was within ± 10 , ± 20 and $\pm 30\%$ of the mGFR. The concordance rate between mGFR and eGFR was investigated in the eight GFR groups. The concordance rate was defined when the mGFR and eGFR were in the same GFR group.

The CKD stage distributions determined using the two equations in the Korean general population were compared in terms of age, gender and body mass index (BMI). Continuous variables were expressed

Fig. 2. Concordance between measured and estimated glomerular filtration rate (GFR) in 607 patients who underwent GFR measurement using ^{51}Cr -EDTA. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease; mGFR, measured glomerular filtration rate.

as means $\pm$ SD. The statistical analyses were performed using SPSS version 19.0 (SPSS, Inc., Chicago, IL, USA), and MedCalc version 11.5.1.0 (MedCalc Statistical Software, Ostend, Belgium). The $p < 0.05$ indicated statistical significance.

Results

Performance of the MDRD study and CKD-EPI equations

The scatter plots and Bland-Altman plots for estimated versus measured GFR were shown in Fig. 1. Among the 607 subjects, the mean bias of the CKD-EPI and MDRD study equation was 4.4 and 2.6 mL/min/1.73m², respectively. And the median bias of the CKD-EPI equation was 0.9 mL/min/1.73m² (95% CI, -0.3 to 2.1; range, -6.6 to 18.6), which was significantly lower than that of the MDRD equation of 2.2 mL/min/1.73m² (95% CI, 0.8 to 3.5; range, -5.7 to 19.9; $p = 0.020$). Among 607 subjects, the percentages of eGFR_{MDRD} that were within ± 10 , ± 20 and $\pm 30\%$ of mGFR were 31.6, 60.0 and 80.7%, respectively; and those of the eGFR_{CKD-EPI} were 35.4, 64.6 and 81.7%. The accuracies of the two equations were not significantly different in patients with mGFR < 60 mL/min/1.73m², however, the accuracy of the CKD-EPI equation was significantly higher than that of the MDRD study equation in patients with mGFR ≥ 60 mL/min/1.73m² ($p < 0.05$).

Concordance rate of eGFR and mGFR

The eGFR distributions based on the MDRD study and CKD-EPI equations in the eight mGFR groups are presented in Fig. 2. The overall concordance rate of the eGFR and mGFR had a mean of 44.2% (range, 29.9–67.3%) for the MDRD study equation and 48.0% (range, 40.3–67.3%) for the CKD-EPI equation ($p = 0.2493$). The concordance rate between eGFR and mGFR in the four GFR groups with mGFR < 60 mL/min/1.73m² (< 15 , 15–29, 30–44 and

45–59) showed a mean of 53.3% for the MDRD study equation and 50.8% for the CKD-EPI equation ($p=0.6478$). And the concordance rate in the four GFR groups with $\text{mGFR} \geq 60 \text{ mL/min/1.73m}^2$ (60–74, 75–89, 90–104 and ≥ 105) showed a mean of 38.1% for the MDRD study equation and 45.5% for the CKD-EPI equation ($p=0.0517$). Both equations underestimated or overestimated the GFR between 15–105 mL/min/1.73m^2 . The overestimation of GFR observed mainly in $\text{mGFR} < 60 \text{ mL/min/1.73m}^2$ groups. Whereas, the underestimation was noticeable in $\text{mGFR} \geq 60 \text{ mL/min/1.73m}^2$ groups, especially in MDRD study equation than CKD-EPI equation.

CKD stage distribution in the Korean general population

The baseline characteristics of the 5,822 subjects who participated in the KNHANES V-1 are shown in Table 1. The frequencies of the CKD stages 1, 2, 3, 4 and 5 by the MDRD study equation were 47.56, 49.23, 3.07, 0.12 and 0.02%, respectively; and those by the CKD-EPI equation were 68.48, 28.89, 2.49, 0.12 and 0.02% (Table 1). In the stratified analysis by gender and BMI, the prevalence of CKD stage 1 by the CKD-EPI equation was higher than that of MDRD study equation. And the prevalence of CKD stage 3 by the CKD-EPI equation was decreased by 0.51% for male, 0.64% for female, 0.62% for BMI 20–25 and 0.80% for BMI 26–30 participants, respectively, compared to MDRD study equation (Table 2).

Discussion

The CKD-EPI equation was confirmed to have less bias than the MDRD study equation, and provided more precise GFR estimations at $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$ [2]. Stevens *et al.* reported that the biases ($\text{mGFR}-\text{eGFR}$) in the MDRD study and CKD-EPI equations at $\text{GFR} < 60 \text{ mL/min/1.73m}^2$ among Caucasians were 3.4 and 1.9 mL/min/1.73m^2 , respectively; these biases at $\text{GFR} 60\text{--}89 \text{ mL/min/1.73m}^2$ were 11.9 and 4.2 mL/min/1.73m^2 [5]. According to Teo *et al.*, the median biases (converted to $\text{mGFR}-\text{eGFR}$) in the MDRD study and CKD-EPI equations among Asians at $\text{GFR} < 60 \text{ mL/min/1.73m}^2$ were 2.4 and 1.5 mL/min/1.73m^2 , respectively; these biases at $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$ were 5.3 and $-0.9 \text{ mL/min/1.73m}^2$ [4]. Previous studies showed that the bias of the CKD-EPI equation was less than that of the MDRD study equation, not only at $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$ but also at $\text{GFR} < 60 \text{ mL/min/1.73m}^2$. However, in the present study, although the difference between the two equations was not statistically significant, the bias of the CKD-EPI equation was greater than that of the MDRD study equation at $\text{GFR} < 60 \text{ mL/min/1.73m}^2$. A different study population could explain this difference. In the present study, although the differences were small, a greater bias was observed at $\text{GFR} < 45 \text{ mL/min/1.73m}^2$. The median biases of the MDRD study and CKD-EPI equations at $\text{GFR} 45\text{--}59 \text{ mL/min/1.73m}^2$ were -0.6 and $-2.4 \text{ mL/min/1.73m}^2$, respectively; whereas those at $\text{GFR} < 45 \text{ mL/min/1.73m}^2$ were -4.5 and $-4.4 \text{ mL/min/1.73m}^2$.

In the present study, the bias and accuracy of the two equations at $\text{GFR} < 60 \text{ mL/min/1.73m}^2$ were not significantly different. However, at $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$, the bias of the CKD-EPI equation was significantly less than that of the MDRD study equation. In addition, the MDRD study equation pronouncedly underestimated GFR at $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$ than CKD-EPI equation. Therefore, the CKD-EPI equation was confirmed to provide a more precise estimate of the $\text{GFR} \geq 60 \text{ mL/min/1.73m}^2$ than the MDRD study equation in Koreans.

Shafi *et al.* reported that the prevalences of CKD stages 1, 2 and 3 in Caucasians were 58.3, 35.0 and 6.3%, respectively using the MDRD study equation; the prevalences of these stages were 69.0, 24.6 and 6.0%, respectively, using the CKD-EPI equation [13]. Our data indicated similar distributions of CKD stage prevalence compared to Caucasians. The MDRD study equation is known to overestimate the prevalence of CKD stage 3 compared to the CKD-EPI equation [14, 15]. Similar to the previous study, the prevalence of CKD stage 3 decreased by 0.58% based on the CKD-EPI equation in the Korean general population.

Table 1. Baseline subject characteristics and the prevalence of chronic kidney disease based on estimated glomerular filtration rate calculated using the MDRD study and CKD-EPI equations of the fifth Korea National Health and Nutrition Examination Survey (KNHANES V-1), 2010 – stratified by age

Variables	< 40 years n=1,873	40-49 years n=1,124	50-59 years n=1,134	60-69 years n=968	≥ 70 years n=723	Total n=5,822
Male, n (%)	773 (41.3)	519 (46.2)	462 (40.7)	448 (46.3)	332 (45.9)	2534 (43.5)
Age (years)	31.5±5.5	44.2±2.9	54.2±2.8	64.5±2.9	74.6±3.9	49.2±15.7
Systolic BP (mmHg)	107.9±12.0	114.8±14.8	122.1±17.1	128.4±17.0	131.2±17.3	118.3±17.5
Diastolic BP (mmHg)	71.2±9.9	76.2±10.8	78.3±10.6	76.5±9.5	73.2±9.7	74.7±10.5
Waist circumference (cm)	77.3±10.3	80.8±9.4	82.4±8.7	84.3±9.0	84.1±9.7	81.0±9.9
BMI (kg/m ²) ^a	22.9±3.6	23.9±3.1	24.1±3.0	24.2±3.0	23.6±3.4	23.6±3.3
HbA1c (%)	7.6±2.3	8.0±2.1	7.3±1.3	7.2±1.3	7.1±1.3	7.3±1.5
Total cholesterol (mmol/L)	4.62±0.9	4.9±1.0	5.2±1.0	5.0±0.9	4.9±1.0	4.9±1.0
HDL (mmol/L)	1.42±0.3	1.4±0.3	1.4±0.3	1.3±0.3	1.3±0.3	1.4±0.3
TG (mmol/L)	1.29±1.2	1.5±1.3	1.7±1.6	1.6±1.1	1.6±1.0	1.5±1.3
LDL (mmol/L)	2.61±0.8	2.9±0.9	3.0±1.0	2.9±0.9	2.9±0.9	2.8±0.9
eGFR _{MDRD} (mL/min/1.73m ²)	99.2±16.2	91.0±14.2	88.2±15.4	83.9±15.7	77.3±18.1	90.2±17.5
eGFR _{CKD-EPI} (mL/min/1.73m ²)	110.5±12.3	100.1±11.2	93.5±11.7	85.8±11.8	75.9±14.5	96.8±17.0
CKD stage based on eGFR _{MDRD} (mL/min/1.73m ²)						
≥105	569 (30.38)	207 (18.42)	136 (11.99)	76 (7.85)	41 (5.67)	1,029 (17.67)
90-104	745 (39.78)	399 (35.50)	259 (22.84)	209 (21.59)	128 (17.70)	1,740 (29.89)
75-89	485 (25.89)	399 (35.50)	541 (47.71)	408 (42.15)	212 (29.32)	2,045 (35.13)
60-74	74 (3.95)	116 (10.32)	167 (14.73)	233 (24.07)	231 (31.95)	821 (14.10)
45-59	0 (.00)	2 (.18)	26 (2.29)	37 (3.82)	88 (12.17)	153 (2.63)
30-44	0 (.00)	1 (.09)	4 (.35)	4 (.41)	17 (2.35)	26 (.45)
15-29	0 (.00)	0 (.00)	1 (.09)	0 (.00)	6 (.83)	7 (.12)
<15	0 (.00)	0 (.00)	0 (.00)	1 (.10)	0 (.00)	1 (.02)
CKD stage based on eGFR _{CKD-EPI} (mL/min/1.73m ²)						
≥105	1,310 (69.94)	487 (43.33)	122 (10.76)	6 (.62)	0 (.00)	1,925 (33.06)
90-104	437 (23.33)	412 (36.65)	648 (57.14)	473 (48.86)	92 (12.72)	2,062 (35.42)
75-89	119 (6.35)	192 (17.08)	268 (23.63)	339 (35.02)	314 (43.43)	1,232 (21.16)
60-74	7 (.37)	31 (2.76)	83 (7.32)	118 (12.19)	211 (29.18)	450 (7.73)
45-59	0 (.00)	1 (.09)	9 (.79)	28 (2.89)	79 (10.93)	117 (2.01)
30-44	0 (.00)	1 (.09)	3 (.26)	3 (.31)	21 (2.90)	28 (.48)
15-29	0 (.00)	0 (.00)	1 (.09)	0 (.00)	6 (.83)	7 (.12)
<15	0 (.00)	0 (.00)	0 (.00)	1 (.10)	0 (.00)	1 (.02)
Concordance between eGFR _{MDRD} and eGFR _{CKD-EPI} group						
Cohen's κ	0.043	0.221	0.338	0.423	0.706	0.322
p value for Cohen's κ	0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Data are expressed as number (percent), mean ± standard deviation. ^a Twelve of 5,822 participants were excluded due to missing data. Abbreviations: BMI, body mass index; BP, blood pressure; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein; MDRD, Modification of Diet in Renal Disease; TG, triglyceride

The prevalence of CKD stage 1 increased by 20.92% based on the CKD-EPI equation; this increase was almost twofold that in Caucasians [13]. Although the clinical significance of CKD stage 1 is not critical, this difference suggests that the prevalence of CKD stage 1 differs significantly according to the equation used to calculate eGFR in the Korean general population, compared to Caucasians. Oh et al. reported that the prevalence of CKD stage 1 in Korean general population (KNHANES IV) was 32.6% using MDRD study equation [16]. With our results, the prevalence of CKD stage 1 (47.56%) by MDRD study equation was higher

Table 2. The prevalence chronic kidney disease based on estimated glomerular filtration rate calculated using the MDRD study and CKD-EPI equations of the fifth Korea National Health and Nutrition Examination Survey (KNHANES V-1), 2010 – stratified by gender and body mass index

Group	Gender		Body mass index (kg/m ²) ^a					
	Male	Female	<20		20-25		26-30	
	No. (%)	No. (%)	No.	(%)	No.	(%)	No.	(%)
CKD stage based on eGFR _{MDRD} (mL/min/1.73m ²)								
≥105	303 (11.96)	726 (22.08)	168 (29.22)		635 (17.17)		188 (13.67)	36 (22.36)
90-104	729 (28.77)	1,011 (30.75)	204 (35.48)		1,141 (30.85)		349 (25.38)	41 (25.47)
75-89	956 (37.73)	1,089 (33.12)	157 (27.30)		1,326 (35.85)		517 (37.60)	42 (26.09)
60-74	451 (17.80)	370 (11.25)	35 (6.09)		487 (13.17)		265 (19.27)	32 (19.88)
45-59	74 (2.92)	79 (2.40)	8 (1.39)		94 (2.54)		44 (3.20)	7 (4.35)
30-44	15 (.59)	11 (.33)	2 (.35)		13 (.35)		8 (.58)	3 (1.86)
15-29	5 (.20)	2 (.06)	0 (.00)		3 (.08)		4 (.29)	0 (.00)
<15	1 (.04)	0 (.00)	1 (.17)		0 (.00)		0 (.00)	0 (.00)
CKD stage based on eGFR _{CKD-EPI} (mL/min/1.73m ²)								
≥105	613 (24.19)	1,312 (39.90)	306 (53.22)		1,213 (32.79)		337 (24.51)	63 (39.13)
90-104	909 (35.87)	1,153 (35.07)	155 (26.96)		1,346 (36.39)		518 (37.67)	40 (24.84)
75-89	679 (26.80)	553 (16.82)	80 (13.91)		784 (21.19)		336 (24.44)	30 (18.63)
60-74	251 (9.91)	199 (6.05)	23 (4.00)		269 (7.27)		139 (10.11)	18 (11.18)
45-59	57 (2.25)	60 (1.82)	9 (1.57)		68 (1.84)		33 (2.40)	7 (4.35)
30-44	19 (.75)	9 (.27)	1 (.17)		16 (.43)		8 (.58)	3 (1.86)
15-29	5 (.20)	2 (.06)	0 (.00)		3 (.08)		4 (.29)	0 (.00)
<15	1 (.04)	0 (.00)	1 (.17)		0 (.00)		0 (.00)	0 (.00)

Abbreviations: see the Table 1. ^a Twelve of 5,822 participants were excluded due to missing data

than the previous study [16]. Since the prevalences of CKD stage 3 or more in Korean general population has decreased [17], the prevalences of CKD stage 1 or 2 are expected to increase like our data.

The serum concentrations of creatinine are affected by several factors such as age, gender, race, body mass, chronic illness and diet [18]. With our results, the differences in prevalence of CKD stage 1 by two equations were higher in female gender, 40-59 years old and BMI 26-30 kg/m² in KNHANES V-1 participants. Since gender and body mass are also major contributing factors for creatinine generation, it should be considered to compare the performance of creatinine-based eGFR equation.

Conclusion

Both the MDRD study and CKD-EPI equations showed an equivalent performance at GFR <60 mL/min/1.73m² in the general Korean population; however, the CKD-EPI equation estimated the GFR more precisely than the MDRD study equation at GFR ≥60 mL/min/1.73m². Therefore, the CKD-EPI equation might be more useful in clinical practice than the MDRD study equation in Koreans.

Conflict of Interests

The authors have no conflicts of interest.

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