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Letter to the editor

Small but non-negligible discrepancy between subgroup and single CKD-EPI equation to calculate the estimated glomerular filtration rate

To the Editor

The Kidney Disease: Improving Global Outcomes (KDIGO) initiative recommends that doctors calculate the estimated glomerular filtration rate (eGFR) in adults using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation [1]. The 2009 CKD-EPI creatinine equation has been expressed in 2 different ways, i.e., as a "subgroup equation" based on sex, creatinine concentration and race (white/other or black), and as a "single equation" that combines all of the variables into one equation [1,2]. Although the 2009 CKD-EPI creatinine equation can be expressed in these different ways, the eGFR values calculated should be the same for both. In rare cases, however, the eGFR values may differ between the 2 equations [3]. For example, when calculated using the subgroup CKD-EPI, a 48-y-old white female with a serum creatinine concentration of 1.10 mg/dl (97.24 μmol/l) has an eGFR of 60 ml/min/1.73 m^2 [$144 \times (1.10/0.7)^{-1.209} \times 0.933^{48}$], which corresponds to stage 2 CKD (GFR category), while the single CKD-EPI yields an eGFR of 59 ml/min/1.73m^2 [$141 \times \min(1.10/0.7,1)^{-0.329} \times \max(1.10/0.7,1)^{-1.209} \times 1.018$ (if female)], which corresponds to stage 3A CKD. Of course, in addition to the eGFR category, causes of CKD and albuminuria should be evaluated to determine the CKD stage as recommended by KDIGO [1]. In another example, a 71-y black male with a creatinine concentration of 0.98 mg/dl (86.63 μmol/l) had a subgroup CKD-EPI of 89 ml/min/1.73 m^2 [$163 \times (0.98/0.9)^{-1.209} \times 0.933^{71}$] and a single CKD-EPI of 90 ml/min/1.73 m^2 [$141 \times \min(0.98/0.9,1)^{-0.411} \times \max(0.98/0.9,1)^{-1.209} \times 1.159$ (if black)]; these eGFR values differ by 1 ml/min/1.73 m^2.

This difference can be explained by the constants applied to the single CKD-EPI equation [3]. To overcome this difference, we previously proposed to change the values of the constants used in the sex and race variables of the single CKD-EPI equation [3]. In the previous study, we focused only on Asians, especially Koreans. Thus, we aimed to evaluate the modified single CKD-EPI equation when applied to various races in this study.

We analyzed the differences between the subgroup CKD-EPI and the single CKD-EPI using United States National Health and Nutrition Examination Survey (NHANES) data from 2009 to 2016. The eGFR was calculated using the subgroup and single CKD-EPI equations, and the calculated eGFR values were rounded to integers as recommended by KDIGO [1]. We classified the CKD stage (eGFR category) based on the eGFR values, as suggested in the KDIGO 2012 guidelines [1]. Between 2009 and 2016, we were able to calculate the eGFR of 25,644 subjects in total, based on demographic and laboratory data. The gender distribution of the subjects was 50.9% (n = 13,064) female and 49.1% (n = 12,580) male. The ethnic distribution was 78.9% (n = 20,235) white/other and 21.1% (n = 5409) black.

In the whole dataset, the difference in eGFR values between the subgroup and original single CKD-EPI equation was 19.1% (4892/25,644), and the GFR categories were different in 0.26% of cases (66/25,644; Table 1). Applying the modified single CKD-EPI (scenario 1) proposed in the previous study [3], made all of the GFR categories agree between the two equations, but there were 37 cases in which the eGFR value calculated using the modified single CKD-EPI equation (scenario 1) was 1 ml/min/1.73m^2 higher than that of the subgroup CKD-EPI equation. If the decimal places of the constant applied to the original single CKD-EPI equation is extended to six digits (scenario 2), both the eGFR values and the GFR categories become equal to each other. Extending the number of decimal places to 6 digits makes the calculation more complicated. However, since most clinical laboratories automatically calculate and report creatinine-based eGFR through a laboratory information system, hospital information system, or an instrument interface, the complexity of the calculation is not a problem.

Although we analyzed large scale population-based data, applying the modified single CKD-EPI equation (scenario 2) to other datasets may yield different eGFR values and GFR categories. With our results, we would like to emphasize that although the currently used subgroup and single CKD-EPI equations are the same formula, but with different calculation methods, these different methods may lead to discrepancies in the eGFR values as well as GFR category in some cases. The discrepancy is certainly very minor compared with the uncertainty in terms of the creatinine measurement [3]. However, since the laboratory results are intended to aid medical decision making [4], correctable errors must be corrected, even for very small errors, to increase the value of the laboratory results. In addition to the current 2009 CKD-EPI creatinine equation, the 2012 CKD-EPI creatinine-cystatin C equation is also represented by both subgroup and single equations [5]. Regardless of the calculation methods, the eGFR values and GFR categories must be equal to each other.

In conclusion, the constants applied to the currently used single 2009 CKD-EPI creatinine equation need to be revised or re-expressed appropriately. Clinicians should be aware of the differences in eGFR values according to the equation type used.

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Table 1
Comparison between subgroup CKD-EPI and single CKD-EPI equations.

Variables	NHANES dataset				
	2009–2010 (n = 6860)	2011–2012 (n = 5976)	2013–2014 (n = 6553)	2015–2016 (n = 6255)	All (n = 25,644)
Original single CKD-EPI compared to subgroup CKD-EPI (1)					
GFR = 141 × min (Scr/κ, 1)$^{\alpha}$ × max (Scr/κ, 1)$^{-1.209}$ × (0.993)^{Age} × 1.018 [if female] × 1.159 [if black]					
eGFR value					
Same, n (%)	5572 (81.2)	4804 (80.4)	5327 (81.3)	5049 (80.7)	20,752 (80.9)
Different, n (%)	1288 (18.8)	1172 (19.6)	1226 (18.7)	1206 (19.3)	4892 (19.1)
GFR category					
Same, n (%)	6834 (99.6)	5966 (99.8)	6533 (99.7)	6245 (99.8)	25,578 (99.7)
Different, n (%)	26 (0.4)	10 (0.2)	20 (0.3)	10 (0.2)	66 (0.3)
Modification of single CKD-EPI equation compared to subgroup CKD-EPI					
Senario 1, single CKD-EPI-version 1 (3)					
GFR = 141 × min (Scr/κ, 1)$^{\alpha}$ × max (Scr/κ, 1)$^{-1.209}$ × (0.993)^{Age} × 1.0213 [if female] × 1.15603 [if black male] × 1.15278 [if black female]					
eGFR value					
Same, n (%)	6850 (99.9)	5972 (99.9)	6542 (99.8)	6243 (99.8)	25,607 (99.9)
Different, n (%)	10 (0.1)	4 (0.1)	11 (0.2)	12 (0.2)	37 (0.1)
GFR category					
Same, n (%)	6860 (100)	5976 (100)	6553 (100)	6255 (100)	25,644 (100)
Different, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Senario 2, single CKD-EPI-version 2					
GFR = 141 × min (Scr/κ, 1)$^{\alpha}$ × max (Scr/κ, 1)$^{-1.209}$ × (0.993)^{Age} × 1.021277 [if female] × 1.156028 [if black male] × 1.152778 [if black female]					
eGFR value					
Same, n (%)	6860 (100)	5976 (100)	6553 (100)	6255 (100)	25,644 (100)
Different, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
GFR category					
Same, n (%)	6860 (100)	5976 (100)	6553 (100)	6255 (100)	25,644 (100)
Different, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

CKD-EPI, chronic kidney disease epidemiology collaboration; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey.

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