Comparison of MDRD and CKD-EPI Formulas for Estimating Glomerular Filtration Rate in Elderly Preoperative Patients

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ABSTRACT

Objective: The best indicator of kidney function is the glomerular filtration rate (GFR). For estimating the GFR, calculation of creatinine based Modification of Diet in Renal Disease (MDRD), Cockroft and Gault (CG) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) are emloyed. In this study we aimed to compare GFR approximations in preoperative elderly patients using MDRD and CKD-EPI formulas.

Methods: Age, gender, and serum creatinine levels of patients who were older than 65 years of age and underwent surgery in the year 2015 at our hospital were retrospectively evaluated. GFR was estimated using MDRD and CKD-EPI formulas. The results of both the formulas used were compared.

Results: Average GFR values were measured as 77.1 mL/min/1.73 m2 using the MDRD equation and as 71.1 mL/min/1.73 m2 using the CKD-EPI equation. A positive correlation was observed between the groups ($r=0.974$, $p<0.05$).

Conclusion: Measurement of GFR using the MDRD and CKD-EPI equations is easy, simple, and cost-effective. In this study, we demonstrated that in preoperative elderly patients, evaluating renal function using the CKD-EPI formula is better in describing stage 2 renal failure in patients than using the MDRD formula is.

Keywords: Glomerular filtration rate, modification of diet in renal disease, chronic kidney disease epidemiology collaboration

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INTRODUCTION

Chronic kidney disease (CKD) occurs as a result of an irreversible damage in the nephrons (1). The incidence of CKD in adults is 10%–15% (2).

The glomerular filtration rate (GFR) is the best indicator in both the diagnosis and follow-up of renal disease to assess renal function (3). When measuring GFR in a 24-hour urine, analysis of creatinine clearance is troublesome and difficult in geriatric and pediatric patients, especially in the outpatient clinics (4).

The optimal GFR should be independent of age, weight, and muscle mass. It should not be secreted or reabsorbed from the tubules, and the production should be endogenous at a constant rate. Since exogenous substances, such as Cr-EDTA and inulin, provide these conditions, they are accepted as the gold standard in GFR measurement. However, they are not frequently used due to high cost and difficulty of implementation. Creatinine is the most commonly used marker for GFR measurement (5). Unfortunately, creatinine levels are affected by age, gender, race, protein intake, muscle mass, and chronic diseases (6–8). In addition, a small amount of tubular secretion occurs. Errors arise from uncertainties in calibration that occur during measurement. To avoid these errors, several formulas have been developed to evaluate renal function (9).

For this purpose, the classic Cockcroft–Gault (CG) formula, Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD–EPI) equation are used (10, 11).

If the serum creatinine level is measured, it is recommended to report GFR in the same report (12, 13). In the United States, the reporting rate of GFR is 84% (14). For the measurement of GFR, the MDRD formula is usually used (15, 16). Recently, however, the use of the CKD–EPI equation in predicting GFR has also been suggested (10). It has been indicated that compared with MDRD, more accurate and definite results are obtained with this formula (1, 10, 17, 18). However, whereas the rate is only 4% for CKD–EPI used in US laboratories, it is 92% for MDRD (14).

A 24-hour urine collection is difficult and impractical for patients. In addition, creatinine levels do not correctly reflect GFR since

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muscle mass decreases in the elderly. Small increases in creatinine levels in elderly patients indicate a significant decrease in GFR. That is, serum creatinine values alone are not sufficient to assess the frequency and stages of renal disease in elderly patients. For these reasons, it is important to use the correct formulas in GFR measurement to assess the frequency and stages of renal disease in elderly patients.

The aim of the present study was to compare the MDRD and CKD–EPI formulas used in GFR measurements in preoperative patients aged >65 years old.

METHODS

Data on age, gender, and creatinine values of 500 (260 male and 240 female) patients who had been operated between January 1, 2015 and December 31, 2015 were obtained from the University of Health Sciences, Ümraniye Training and Research Hospital automation system. For all patients, race was chosen as "not African-American". The estimated GFR was calculated using the MDRD and CKD–EPI formulas. Patients were divided into five subgroups of CKD according to their MDRD and CKD–EPI values.

MDRD Calculation:
GFR=175×([serum creatinine]−1.154)×([age]−0.203)×(0.742 for females)×(1.212 for African-Americans).

CKD–EPI Calculation:

GFR=141×min (Scr/κ,1) α×max (Scr/κ,1)−1.209×0.993 age×1.018 (female)×1.159 (African-American).
Where:
Scr=serum creatinine (mg/dL),
κ=0.7 for females and 0.9 for males,
α=−0.329 for females and −0.411 for males,
min=minimum Scr/k or 1,
max=maximum Scr/k or 1.

Stages of CKD:
Group 1: GFR ≥90 mL/min/1.73 m^2.
Group 2: GFR=60–89 mL/min/1.73 m^2.
Group 3: GFR=30–59 mL/min/1.73 m^2.
Group 4: GFR=15–29 mL/min/1.73 m^2.
Group 5: GFR<15 mL/min/1.73 m^2.

The University of Health Sciences, Ümraniye Training and Research Hospital Ethics Review Board approved (project approval no. 13761) our study on September 9, 2016. Verbal consent was obtained from the patients.

Statistical Analysis
Descriptive statistics were used to define continuous variables (mean, standard deviation, median, minimum, and maximum).

Student's t test was used for the comparison of two continuous variables with independent and normally distributed data. Mann–Whitney U test was used for the comparison of two independent and non-normally distributed data.

On the other hand, Pearson's correlation coefficient was used for normally distributed continuous variables, and Spearman's rho correlation coefficient was used for the determination of the relationship between two independent and non-normally distributed variables.

Statistical significance level was determined as 0.05. The MedCalc statistical software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013) was used for statistical analysis.

RESULTS

A total of 500 elderly (≥65 years old) patients were included in the study. There were 240 female and 260 male patients. Data (mean, median, standard deviation, minimum, and maximum) regarding their age and creatinine and GFR values calculated using two different formulas (MDRD and CKD–EPI) are shown in Table 1.

When all patients were analyzed according to gender, there was a significant difference in terms of age and creatinine distribution. Age was found to be higher in female patients. Creatinine levels were found to be higher in males than in females ($p<0.05$, for both). There was no significant difference in the distribution of GFR values as calculated by the MDRD and CKD–EPI formulas according to sex (Table 2).

Patients included in the study were divided into two age groups: patients between 65 and 74 and ≥75 years old. There were 333 patients in the 65–74 age group and 167 in the ≥75 age group. When the patients were analyzed according to age groups, there was no significant difference in terms of distribution of creatinine values, but there was a significant difference both in the distribution of GFR values calculated with MDRD ($p=0.001$) and in the distribution of GFR values calculated with CKD–EPI ($p<0.05$) (Table 3).

The GFR values of the patients were calculated using two different formulas, and the stages of their CKD were determined according to these values. The distribution of the patients according to their stages is shown in Table 4 as number and percentage.

When we divided the patients according their CKD stages as determined by their GFR values that were calculated using the MDRD and CKD–EPI formulas, 168 (33.6%) patients were diag-

Table 1. Demographic data of the patients

	N	Mean	Median	St. deviation	Min	Max
Age (year)	500	72.7	71	6.5	65	96
Creatinine (mg/dL)	500	1.1	0.9	0.9	0.4	13.3
MDRD (mL/min/1.73 m^2)	500	77.1	79.2	25.8	3.9	147.4
CKD–EPİ (mL/min/ 1.73 m^2)	500	71.1	77.7	21.5	3.3	104.8

MDRD: Modification of Diet in Renal Disease; CKD–EPI: Chronic Kidney Disease Epidemiology Collaboration; St.: standard; Min: minimum; Max: maximum

Table 2. Comparison of parameters according to sex

	Sex	N	Mean	Median	St. deviation	Min	Max	p
Age (year)	Male	260	71.8	71	5.6	65	91	0.026
	Female	240	73.6	72	7.2	65	96	
Creatinine (mg/dL)	Male	260	1.2	0.9	0.9	0.6	13.3	<0.05
	Female	240	0.9	0.8	0.7	0.4	8.2	
MDRD (mL/min/1.73 m^2)	Male	260	78.2	80.1	27.1	3.9	147.4	0.308
	Female	240	75.9	78.3	24.2	5.2	145.6	
CKD–EPI	Male	260	71.2	77.8	22.1	3.3	104.8	0.469
(mL/min/1.73 m^2)	Female	240	71.0	77.5	20.8	4.5	100.9	

MDRD: Modification of Diet in Renal Disease; CKD–EPI: Chronic Kidney Disease Epidemiology Collaboration; St.: standard; Min: minimum; Max: maximum

Table 3. Comparison of parameters according to age groups

	Age (year)	N	Mean	Median	St. deviation	Min	Max	p
Creatinine (mg/dL)	65-74	333	1.1	0.9	0.9	0.4	13.3	0.381
	>75	167	1.1	0.9	0.6	0.5	4.1	
MDRD (mL/min/1.73 m^2)	65-74	333	79.8	80.8	24.6	3.9	145.6	0.001
	>75	167	71.7	73.3	27.3	11.1	147.4	
CKD–EPI (mL/max/1.73 m^2)	65-74	333	74.8	80.1	20.3	3.3	104.8	<0.05
	>75	167	63.7	69.3	21.9	9.7	96.3	

MDRD: Modification of Diet in Renal Disease; CKD–EPI: Chronic Kidney Disease Epidemiology Collaboration; St.: standard; Min: minimum; Max: maximum

Table 4. Patient distribution of CKD stages according to GFR values calculated by the MDRD and CKD–EPI formulas

	CKD stage	N	%
MDRD	Stage V (<15)	10	2.0
(mL/min/1.73 m^2)	Stage IV (15–29)	17	3.4
	Stage III (30–59)	84	16.8
	Stage II (60–89)	221	44.2
	Stage I (≥90)	168	33.6
CKD-EPİ	Stage V (<15)	10	2.0
(mL/min/1.73 m^2)	Stage IV (15–29)	20	4.0
	Stage III (30–59)	100	20.0
	Stage II (60–89)	274	54.8
	Stage I (≥90)	96	19.2

MDRD: Modification of Diet in Renal Disease; CKD–EPI: Chronic Kidney Disease Epidemiology Collaboration; GFR: glomerular filtration rate; CKD: chronic kidney disease

Table 5. Correlation analysis of the MDRD and CKD–EPI formulas used to calculate GFR values

		MDRD–CKD–EPI
Total		0.974 (<0.05*)
Sex	Male	0.981 (<0.05*)
	Female	0.966 (<0.05*)
Age (year)	65-74	0.989 (<0.05*)
	>75	0.988 (<0.05*)

*Spearman's Rho Correlation p

MDRD: Modification of Diet in Renal Disease; CKD–EPI: Chronic Kidney Disease Epidemiology Collaboration; GFR: glomerular filtration rate

nosed with stage I, and 332 (66.4%) patients were diagnosed with stages II–V. According to CKD–EPI, there were 96 (19.2%) patients with stage I and 404 (81.8%) patients with stages II–V (p<0.05) (Table 4). When both formulas were compared, the rates of patients with stage I and stage II were significantly different (p<0.05). There were more patients with stage II when the CKD–EPI formula was used.

When Spearman correlation analysis was performed, there was a strong positive correlation between the MDRD and CKD–EPI formulas (p<0.05) (Table 5, Figure 1) that we used to calculate the GFR values of the patients.

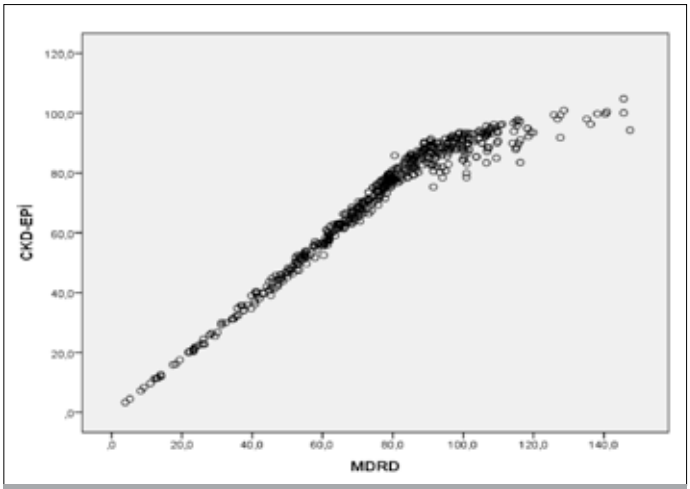

Figure 1. Correlation graph of MDRD and CKD-EPI formulas that are used for calculating GFR values
MDRD: Modification of diet in renal disease; CKD-EPI: Chronic Kidney Disease-Epidemiology Collaboration; GFR: Glomerular filtration rate

DISCUSSION

When the MDRD and CKD–EPI formulas are compared to calculate GFR in elderly preoperative patients, both formulas yield similar results. However, the rate of patients with stage II CKD with CKD–EPI is higher than that with MDRD. The MDRD formula classifies the majority of these patients as stage II. There is a strong relationship between these two formulas. Although creatinine values did not change despite the age in elderly patients, there was a significant decrease in GFR values calculated by both MDRD and CKD–EPI. This suggests that evaluation, diagnosis, and classification of CKD only by considering the creatinine values will yield incorrect results in elderly patients. Therefore, it is necessary to calculate GFR using MDRD and CKD–EPI when evaluating, diagnosing, and classifying CKD in elderly patients.

Chronic kidney disease is an important public health problem. It may be asymptomatic in the early stages; however, when symptoms develop, renal function loss might already be up to 90%. Progression of CKD can be stopped or delayed with the help of early diagnosis. Otherwise, the patient will end up with end-stage renal failure.

It is important to correctly assess CKD especially in elderly patients. Aging is an inevitable biological process involving all organs, and the kidneys are significantly affected by this phenomenon. Aging leads to progressive nephron loss, glomerular and tubulointerstitial damage, and decreased renal function in the kidneys. These changes begin in the fourth decade of life and increase in the fifth and sixth decades; the glomerular–tubular functions, systemic hemodynamics, and homeostasis of the body are all affected by these changes. During an illness or stress, structural and functional changes in the kidneys with aging reduce the adaptation capability of the kidneys to changing conditions. Thus, the conditions that can be easily overcome by younger individuals can lead to fluid–electrolyte disorders and renal failure in the elderly.

Glomerular filtration rate plays an essential role in the evaluation, diagnosis, and classification of CKD (12, 19). The decrease in GFR in the elderly can be masked by the decrease in muscle mass. Despite the decrease in GFR, serum creatinine level remains normal. For this reason, small increases in serum creatinine in the elderly show severe decreases in renal function. That is, serum creatinine values alone are not sufficient to assess the frequency and the stage of renal disease in elderly patients. At this point, evaluation and monitoring of renal function with GFR are of great importance in the early diagnosis and follow-up of CKD.

Methods, such as inulin clearance, ^{51}Cr-EDTA, ^{99}mTC-DTPA, ^{125}I-iothalamate, and iohexol clearances, that are considered as the gold and silver standards and are used to measure GFR are costly and difficult to apply in clinical practice. Since the tubule is secreted, creatinine clearance does not show the complete status of renal functions (20, 21).

The CG formula is based on a 24-hour creatinine clearance. To calculate GFR more accurately, the MDRD and CKD–EPI formulas have been developed with reference to the ^{125}I-iothalamate methods. Both "The Kidney Disease Outcomes Quality Initiative (K/DOQI)" and "Kidney Disease: Improving Global Outcomes (K/DIGO)" also recommend the use of these formulas (15).

Chronic kidney disease is divided into five different stages according to GFR values. According to these stages, the approach, the type of treatment, the complications that may develop, and the precautions to be taken before any probable surgical intervention differ. Therefore, GFR calculations should be performed in the most accurate way while patients are evaluated for CKD.

Studies comparing "the CKD–EPI equations" with "the Modification of Diet in Renal Disease" indicate that CKD–EPI yields more accurate results in estimating GFR and recommends the use of this equation in clinical practice (1, 22). Although both formulas were mainly developed in patients with CKD, different population data were also taken into account in the CKD–EPI equation (11, 23).

With the CKD–EPI formula, GFR can also be calculated as >90 mL/min/1.73 m^2. However, the MDRD formula states that a numerical value of <60 mL/min GFR can be given, and higher values should be given as 60 (24).

In our study, when we grouped our patients into CKD stages according to their GFR values as calculated using the MDRD and CKD–EPI formulas, there were 168 (33.6%) patients with stage I according to MDRD and 332 (66.4%) patients with stages II–V. According to CKD–EPI, there were 96 (19.2%) patients with stage I and 404 (81.8%) patients with stages II–V. In the light of this data, when we evaluate patients with CKD–EPI, more patients appear to be in stage II and above. That is, compared with MDRD, the CKD–EPI formula captures more patients with CKD. Although whether the CKD–EPI formula determines real patients with CKD or that it shows GFR lower than its actual value is still a question, the CKD–EPI formula has proven to be more accurate and precise than the MDRD formula in the literature (10, 17, 18).

In a study comparing creatinine clearance with the "Modification of Diet in Renal Disease", similar results were obtained with both methods in patients >65 years old (25).

In another study conducted by Öztürk et al. (26), the GFR values were calculated in patients with type 2 diabetes mellitus (DM) using the CG, MDRD, and CKD–EPI formulas. In their study, they determined an advanced positive correlation among these three methods.

Since patients <65 years old were not included in our study, we could not obtain any result for patients in this group, but when we looked at patients >65 years old, we found a strong positive correlation between CKD–EPI and MDRD similar to the previous study.

Özdemir et al. (27) compared creatinine clearance, MDRD, and CKD–EPI formulas in one of their studies. When the cases were analyzed according to gender, there was a significant difference between GFR values in women. Whereas there was a statistically significant difference between creatinine clearance and MDRD, there was no significant difference between CKD–EPI with creatinine clearance and CKD–EPI and MDRD. In males, whereas there was a statistically significant difference between creatinine clearance and MDRD, no significant difference between CKD–EPI with creatinine clearance and MDRD with CKD–EPI was determined.

Similarly, when we performed sex-based correlation analysis in our study, we also found a strong positive correlation between MDRD and CKD–EPI in both men and women. Given this information, we believe that both formulas can be used in place of each other in elderly patients to calculate GFR without considering sex parameter.

Jeong et al. (28) compared the accuracy of the CKD–EPI and MDRD equations by performing GFR measurements with ^{51}Cr-EDTA. In their study, GFR ≥60 mL/min/1.73 m^2 had significantly higher results with the CKD–EPI equation.

Chronic kidney disease often affects the elderly. The prevalence of CKD increases with aging. The prevalence of CKD in our country is reported at 15.7%. Whereas the prevalence of CKD is 11.5% among individuals <60 years old, the percentage increases as high as 38.3% in individuals 60 years old and above. The prevalence of CKD in the United States is 13%. Of these patients, 37% were >70 years old with stage III and above CKD (29). The increasing incidence of diseases, such as hypertension, obesity, and DM, that constitute a risk for CKD in our country makes the early diagnosis and follow-up of CKD more important (30).

The increase in the elderly population in our country and the decrease in renal function with aging are indicators of an increase in the prevalence of CKD in the coming years. For this reason, we believe that we have shown the importance of calculating GFR to make a more accurate assessment since creatinine values alone in the early diagnosis and management of CKD in elderly patients are not enough.

Calculation of GFR using the MDRD and CKD–EPI equations is cheap and simple. There is also an advanced positive correlation between the two formulas. Based on all of this, the use of these formulas in practice is of great importance in the evaluation of renal function.

CONCLUSION

Although there is a strong association between these two formulas, our study results show that the CKD–EPI formula in preoperative elderly patients defines stage II renal failure earlier. For this reason, for this group of patients, it seems more appropriate to suggest the use of the CKD–EPI formula primarily to prevent possible complications.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University of Health Sciences Ümraniye Training and Research Hospital

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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