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Validation of El-Minia Equation for Estimation of Glomerular Filtration Rate in Different Stages of Chronic Kidney Disease

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Original Paper

Introduction. Assessment of glomerular filtration rate (GFR) is the best index of kidney functions. We aimed to determine the accuracy of El-Minia equation for estimation of GFR in different stages of chronic kidney disease (CKD) in the El-Minia population of CKD patients, in comparison to other proposed equations.
Materials and Methods. The study included 320 isotopic GFR measurements by 99m-Tc technetium diethylene triamine pentaacetic acid. Patients were categorized into the five CKD stages based on this measurement, and estimated GFRs based on the El-Minia, Cockroft-Gault, Chronic Kidney Disease Epidemiology Collaboration, Modification of Diet in Renal Disease (MDRD), abbreviated MDRD, Walser, Nankivell, Cockcroft-Gault, and Mayo Clinic equations were validated using the National Kidney Foundation guidelines.
Results. The El-Minia Equation showed the best performance in all 5 stages of CKD, except for stage 1, in which the Cockroft-Gault equation showed the best performance (44% within ± 10% error). In addition, the El-Minia equation provided the best accuracy to classify CKD stages, except for stage 4, in which the MDRD gave the best accuracy (82%). Worsening of the accuracy was documented in all the eight equations with more severe stages of kidney disease. These results were not significantly changed when the analyses were restricted to diabetic patients.
Conclusions. The El-Minia equation represents a better estimation of GFR in all stages of CKD than other published equations for CKD patients in El-Minia, Egypt. This equation was the best one for classification of CKD in these patients.

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INTRODUCTION

Assessment of glomerular filtration rate (GFR) is the best overall index of kidney function. The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation has elaborated a classification of chronic kidney disease (CKD) based on estimated GFR.[1] A number of eGFR equations have been developed for estimation of kidney function, such as the El-Minia equation,[2] Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI),[3] Modification of Diet in Renal Disease (MDRD),[4] abbreviated MDRD,[5] Walser equation,[6] Nankivell equation,[7] Cockcroft-Gault equation,[8] and Mayo Clinic equation.[9] The predictive performance of all these equations warrants assessment in each stage of CKD among different populations with CKD.

A number of compounds labeled with radioisotopes have been employed for assessment of GFR. One of the most available and routinely used agents nowadays is 99m-Tc technetium diethylene triamine pentaacetic acid (^{99m}Tc-DTPA) isotopic clearance. This method was compared with the inulin clearance, based on the single injection technique, and the correlation was 0.97 which is nevertheless impressive.[10] Thus, radionuclidic methods in patients with CKD are reliable and reproducible, closely resembling those of inulin clearance. Among all radionuclidic methods, ^{99m}Tc-DTPA shows the best results,[11] and could be a gold standard measurement of GFR in studies validating estimated GFR based on the proposed equations. Our aim was to determine the accuracy of El-Minia estimated GFR equation in different stages of CKD and the validity of its use for classification of CKD among patients with CKD in El-Minia, Egypt.

MATERIALS AND METHODS

Patients

A comparison of GFR, measured using the gold standard ^{99m}Tc-DTPA method, and estimated GFRs based on different equations (Table 1), including the El-Minia equation, was carried out in 320 CKD patients. The CKD stage was determined according to the National Kidney Foundation's guideline.[1]

Procedures

The patients were hydrated orally at 10 mL water per kilogram body weight before the start of the study. The ^{99m}Tc-DTPA was injected intravenously at a dose of 50 µCi/kg. The patient lied in the supine position and the gamma camera detector was inserted below the patient. Initial rapid sequences of dynamic images were acquired to assess renal perfusion every 4 seconds for 30 minutes to assess the rate of radioactivity accumulation and excretion. Computerized processing was done to perform renography time activity curve to evaluate vascular, secretory, and excretory phases. Sequential static images were therefore acquired 3 hours after intravenous injection of the ^{99m}Tc- DTPA in order to evaluate renal cortical uptake. The acquired GFR was expressed per 1.73 m^2 by multiplying the value by 1.73 and dividing it by the body surface area (BSA) of the patient as estimated by the DuBois and Mosteller formulas.[12,13]

Estimations

The Cockcroft–Gault and Nankivell equations, which are not expressed as mL/min/1.73m2, were adjusted by multiplying the value by 1.73 and dividing by the patients' BSA. Thus, all of the estimated GFRs were normalized to 1.73m^2 BSA except for Wasler equation, which returns results normalized to 3 m^2/height^2.

The stage 1 CKD was defined as a GFR of 90 mL/min/1.73 m^2 and higher; stage 2, between 60 mL/min/1.73 m^2 and 89 mL/min/1.73 m^2; stage 3, between 30 mL/min/1.73 m^2 and 59 mL/min/1.73 m^2; stage 4, between 15 mL/min/1.73 m^2 and 29 mL/min/1.73 m^2; and stage 5, less than 15 mL/min/1.73 m^2.[1] The predictive performance of El-Minia Equation and the other 7 formulas was assessed in every stage of CKD according to the methodology developed in the K/DOQI guidelines[1]; one should consider both the bias and precision of the estimated GFR. Bias expresses the systematic deviation from the gold standard measure of GFR. A prediction equation that consistently overestimates or underestimates the measured GFR

Table 1. Equations for Estimation of Glomerular Filtration Rate*

Name	Equation
El-Minia[2]	GFR (mL/min/1.73 m^2) = 141 × (SCr/0.9)$^{-1.209}$ × 0.993^{age} × BSA$^{0.1}$ × 1.018 for women
CKD-EPI[3]	GFR (mL/min/1.73 m^2) = 141 × (SCr/0.9)$^{-1.209}$ × 0.993^{age} × 1.018 for women
MDRD[4]	GFR (mL/min/1.73 m^2) = 170 × SCr$^{-0.999}$ × age$^{-0.176}$ × BUN-0.170 × serum albumin$^{0.318}$ × 0.762 for women × 1.180 for African-Americans
Abbreviated MDRD[5]	GFR (mL/min/1.73 m^2) = 186 × SCr$^{-1.154}$ × age$^{-0.203}$ × 0.742 for women × 1.212 for African-Americans
Walser[6]	GFR (mL/min/3 m^2) = 7.57 × (SCr × 0.0884)$^{-1}$ - 0.103 × age + 0.096 × weight - 6.66 for men GFR (mL/min/3 m^2) = 6.05 × (SCr × 0.0884)$^{-1}$ - 0.080 × age + 0.080 × weight - 4.81 for women
Nankivell[7]	GFR (mL/min) = 6700/(SCr × 88.4) + body weight/4 - BUN × 0.357/2 - 100/height^2 + 35 for men + 25 for women
Cockcroft-Gault[8]	GFR (mL/min) = [(140 - age) × body weight × 0.85 for women]/(72 × SCr)
Mayo Clinic Formula[9]	GFR (mL/min/1.73 m^2) = exp(1.911 + 5.249/SCr - 2.114/SCr^2 - 0.00686 x age - 0.205 for women) , if SCr < 0.8 mg/dL use 0.8 for SCr

*CKD-EPI indicates Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; Scr, serum creatinine; BSA, body surface area; MDRD, Modification of Diet in Renal Disease; and BUN, blood urea nitrogen.

yields a biased estimate. Precision expresses the variability (or dispersion) of estimated GFR around the gold standard measure. Accuracy combines precision and bias. A useful measure of accuracy is a description of percentiles of the distribution of the differences between estimated and measured GFR. Achieving a high level of accuracy requires both low bias and high precision. Description of the percent of estimates failing within ± 10% of the measured GFR is a useful measure of accuracy.

Statistical Analyses

Continuous variables were shown as mean ± standard deviation. The percent error in GFR prediction was calculated as:

% prediction error = (predicted value-measured value)/(measured value) × 100

Accuracy for each estimated GFR formula was assessed as the proportion of GFR estimates within 10%, 30%, and 50% deviation of the true GFR.[14,15] Precision was determined as root mean square error (standard deviation of the mean difference between real GFR and estimated GFR).

RESULTS

Three hundred and twenty patients were included in this study (202 men and 118 women with CKD; mean age, 46 ± 12 years; body mass index, 29 ± 6 kg/m^2). Their serum creatinine level was 2.2 ± 1.3 mg/dL and their mean GFR was 45 ± 25 mL/min/1.73m^2. One hundred and one of the patients were diabetic. According to the GFR values, stage 1 CKD was documented in 23 patients; stage 2, in 46 patients; stage 3, in 159 patients; stage 4 in 78 patients; and stage 4, in 14 patients (Table 2).

Table 3 demonstrates estimated GFRs based on the studied equations and Table 4 and Figures 1 to 3 summarize percentages within 10%, 30% and 50% error for each GFR estimation equation. In stage 1 CKD, although the Cockroft-Gault equation showed the best performance, its accuracy was 44% within ± 10% error, while the Nankivell equation showed the least performance with only 17% within ± 10% error (Figure 1). Testing the validity of these equations to correctly classify CKD, El-Minia equation as well as Cockroft-Gault equation yielded the best performance (65%), while MDRD provided the least performance (5%; Figure 4). In stage 2 CKD, El-Minia equation showed the best performance, accuracy was 45% within ±10% error while Nankivell formulae showed the least performance with only 23% within ±10% error. On

Table 2. Chronic Kidney Disease (CKD) Stages Based on Glomerular Filtration Rate (GFR)

CKD	Number of Patients	GFR, mL/min/1.73 m^2 Mean	Median	Range
Stage 1 (GFR ≥ 90 mL/min/1.73 m^2)	23	106 ± 13	104	90 to 139
Stage 2 (GFR 60-89 mL/min/1.73 m^2)	46	72 ± 9	71	60 to 89
Stage 3 (GFR 30-59 mL/min/1.73 m^2)	159	42 ± 8	41	30 to 59
Stage 4 (GFR 15-29 mL/min/1.73 m^2)	78	23 ± 4	24	15 to 29
Stage 5 (GFR < 15 mL/min/1.73 m^2)	14	11 ± 3	10	8 to 14

Table 3. Estimation of Glomerular Filtration Rate (GFR) Using 8 Equations Compared With Measured GFR

Method	GFR Mean	Median	Range
Measurement by ^{99m}Tc-DTPA, mL/min/1.73 m^2	45 ± 25	39	8 to 139
Estimations			
El-Minia, mL/min/1.73 m^2	45 ± 23	38	7 to 130
CKD-EPI, mL/min/1.73 m^2	42 ± 22	36	7 to 123
MDRD mL/min/1.73 m^2	40 ± 20	35	8 to 117
Abbreviated MDRD, mL/min/1.73 m^2	41 ± 20	36	8 to 114
Walser, mL/min/3 m^2	44 ± 21	40	7 to 116
Mayo Clinic, mL/min/1.73 m^2	48 ± 29	39	9 to 144
Nankivell, mL/min/1.73 m^2	49 ± 18	47	13 to 115
Cockroft-Gault, mL/min/1.73 m^2	52 ± 24	46	11 to 139

*^{99m}Tc DTPA indicates 99m-Tc technetium diethylene triamine pentaacetic acid; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; and MDRD, Modification of Diet in Renal Disease.

Table 4. Percentage of Prediction Error for Estimated Glomerular Filtration Rates

Method	Within ± 10% Error	Within ± 30% Error	Within ± 50% Error	R^2
El-Minia	49%	76%	85%	0.77
CKD-EPI	35%	73%	85%	0.71
MDRD	33%	73%	83%	0.54
Abbreviated MDRD	32%	71%	83%	0.57
Walser	28%	70%	82%	0.54
Mayo Clinic	31%	71%	81%	0.56
Nankivell	27%	62%	79%	0.55
Cockcroft-Gault	27%	60%	75%	0.54

*CKD-EPI indicates Chronic Kidney Disease Epidemiology Collaboration and MDRD, Modification of Diet in Renal Disease.

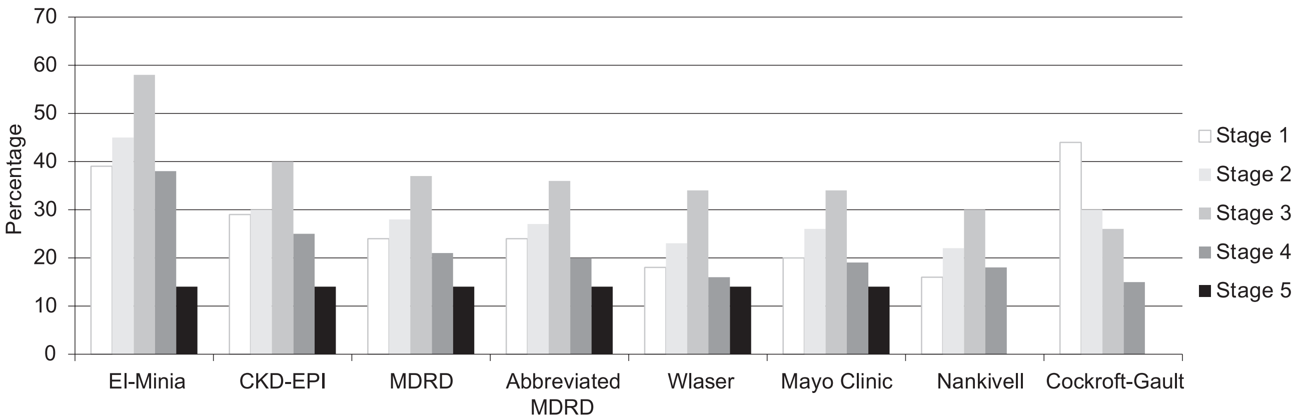

Figure 1. Accuracy of El-Minia equation and other published equations in ± 10% error in chronic kidney disease stages.

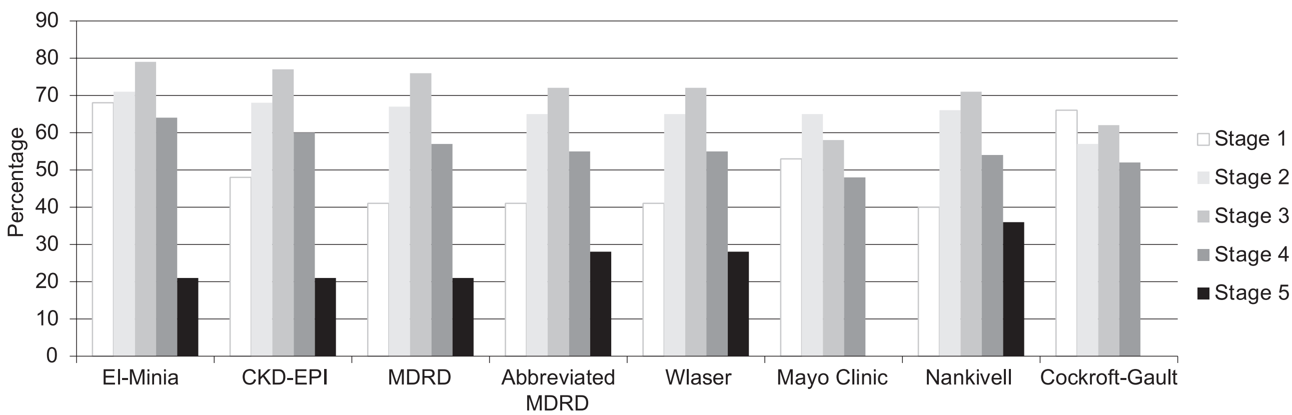

Figure 2. Accuracy of El-Minia Equation and other published equations in ± 30% error in chronic kidney disease stages.

testing the validity of these equations to correctly classify CKD in CKD patients we found that El-Minia equation as well as Nankivell gave the best performance in this stage as they classified 72% of measurements correctly. In stage 3 CKD, El-Minia equation showed the best performance, as its accuracy was 58% within ± 10% error, and Nankivell Formula gave the least performance with accuracy 31% within ± 10% error. Overall, El-Minia equation as well as Nankivell equation classified 79% of measurements correctly (Figure 4). In stage 4 CKD, El-Minia equation gave the best performance with 39% within ± 10% error. In this stage, the MDRD could correctly classify 82% of the patients (Figure 4).

DISCUSSION

Our results illustrated that El-Minia equation

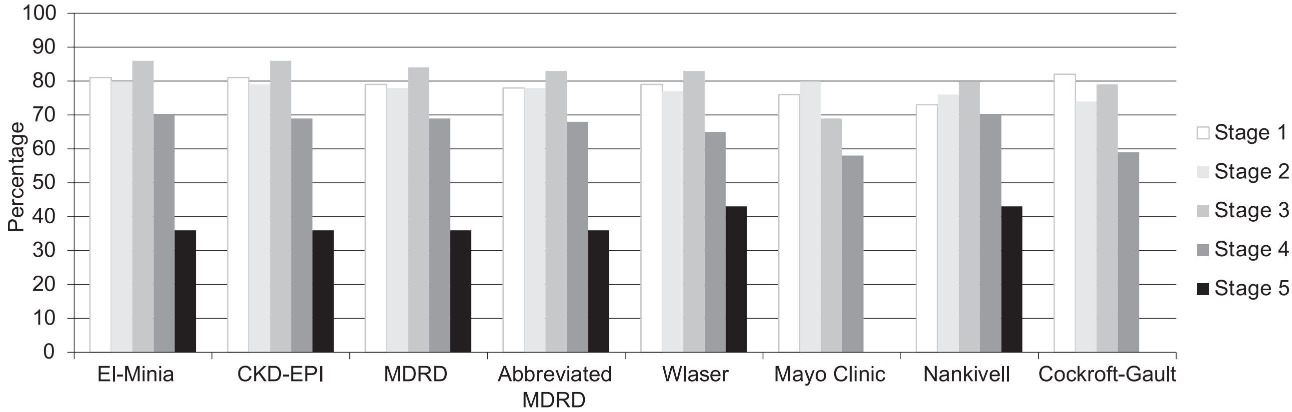

Figure 3. Accuracy of El-Minia Equation & other published equations in ± 50% error in chronic kidney disease stages.

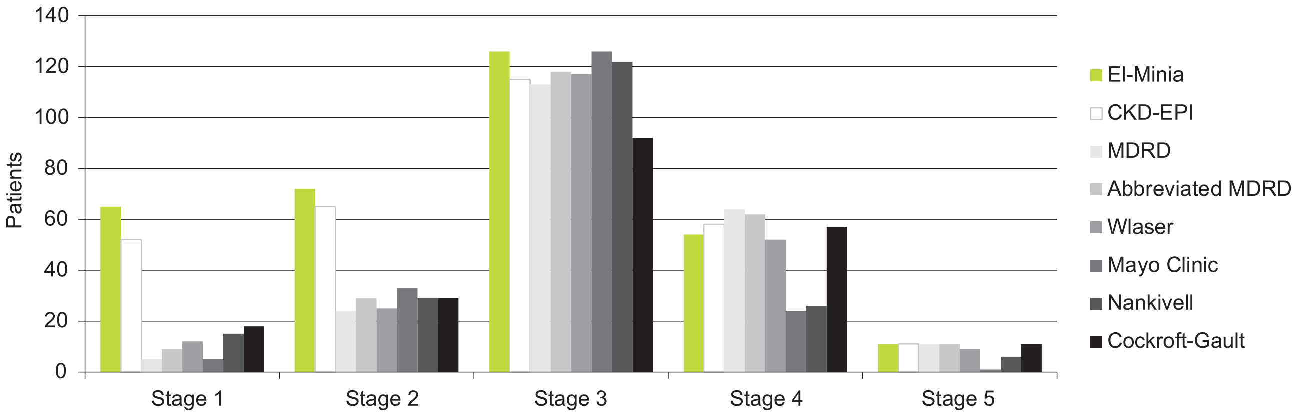

Figure 4. Accuracy of El-Minia equation and other published equations to correctly classify chronic kidney disease stages.

was the best formula to classify CKD in stages 1 to 3, with correctly classifying 65% to 79% of the patients. An ideal GFR equation as suggested by the National Kidney Foundation ought to be expressed as a predictive value within 30% to 50% range of the true GFR in more than 90% of measurements. However, from this point of view, all of the eight tested equations are far from being ideal. We must keep in mind that using a gold standard clearance procedure for classification of CKD cannot be replaced by any one of these equations. Nonetheless, El-Minia equation was the best one to be used in El-Minia CKD patients.

In the current study, the performance of all these eight formulas was tested in the different stages of CKD. The GFR measured using the DTPA was used as a reference method. The relationship between serum creatinine and GFR is variable and depends on factors that may alter, such as muscle mass and muscle catabolic rate. Factors that predict GFR apart from serum creatinine include sex, body mass index, blood urea nitrogen, and medications competing tubular secretion of creatinine. The creatinine clearance actually overestimate GFR but medications such as cimetidine, trimethoprime, triameterene, spironolactone, and amiloride inhibit tubular secretion of creatinine and therefore may cause a falsely low estimate of GFR.

Ross and colleagues[16] reported that the lack of accuracy of estimated GFR in different stages of CKD found in the 8 equations could be explained via several possible mechanisms, including reduction of muscle mass for a given body weight after long-term catabolism with reduced release of serum creatinine. Furthermore, lack of accuracy at stage 5 may be explained by increased tubular creatinine secretion occurring in renal impairment.

In Contrast to our results, White and coworkers[17] reported that Mayo Clinic equation had consistently high accuracy at all CKD stages except for stage 1, where only 56% of estimates were within 30% of the measured GFR. This discrepancy between our results and their results may be attributed to the different ethnicities studied, as 100% of our patients were Middle Eastern, while 92% of their patients were white Caucasian. Also different BSAs can explain discrepancy, as the average BSA of their patients were 1.89 ± 0.23. Reported by White and colleagues,[18] Mariat and colleagues[19] and the current study have demonstrated significant differences in equation performance at different levels of GFR. However, El-Minia equation represented a better estimation and was the best one to classify CKD in El-Minia patients.

Savaj and coworkers[20] revealed that the MDRD equation could provide a closer estimate of GFR to the cystatin C-based equations than other creatinine-based GFR calculations among kidney transplant recipients. This is different to our results as our patients were patients with CKD, and we did not include any kidney transplant recipient in this study. In addition, we used ^{99m}Tc-DTPA as a reference value of GFR.

CONCLUSIONS

None of the proposed equations for GFR estimation provides ideal estimates of kidney function. El-Minia equation, however, represents a better estimation of GFR in all stages of CKD than other published equations for CKD patients in El-Minia, Egypt. This equation was the best one for classification of CKD in these patients.

CONFLICT OF INTEREST

None declared.

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