Sultan Qaboos University Med J, February 2014, Vol. 14, Iss. 1, pp. e72-79, Epub. 27TH Jan 14
Submitted 8TH May 13
Revision Req. 21ST Jun 13; Revision recd. 30TH Jul 13
Accepted 25TH Aug 13

CLINICAL & BASIC RESEARCH

Assessment of Glomerular Filtration Rates by Cockcroft-Gault and Modification of Diet in Renal Disease Equations in a Cohort of Omani Patients

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تقييم سرعة الترشيح الكبيبي فى المرضى العمانيين باستخدام معادلة كوككروفت–جولت و معادلة تعديل النظام الغذائى لمرضى الكلى

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ABSTRACT: ***Objectives***: Glomerular filtration rate (GFR) is the best index of renal function and is frequently assessed by corrected creatinine clearance (CCL_{cr}). The limitations of CCL_{cr} have inspired researchers to derive easy formulas to estimate GFR, with Cockcroft-Gault (C-G) and the modification of diet in renal disease (MDRD) being the most widely used. This study aimed to evaluate the validity of these equations by finding the relation between CCL_{cr} and estimated GFR (eGFR) by C-G, modified C-G and MDRD equations. ***Methods:*** From 2007 to 2011, 158 subjects were analysed for serum creatinine and CCL_{cr} at Bowsher Polyclinic, Muscat, Oman. The C-G equation was used to obtain $eGFR_{C-G}$ which was adjusted to body surface area (BSA) to obtain $eGFR_{mC-G}$, and the MDRD equation was used to obtain $eGFR_{MDRD}$. The $eGFR_{MDRD}$, $eGFR_{mC-G}$ and $eGFR_{C-G}$ were then compared to CCL_{cr}. ***Results:*** The $eGFR_{MDRD}$, $eGFR_{mC-G}$ and $eGFR_{C-G}$ significantly correlated with CCL_{cr}, with a slightly stronger correlation with $eGFR_{MDRD}$ (r = 0.701, 0.658 and 0.605, respectively). A receiver operating characteristic curve analysis showed that the diagnostic accuracy of $eGFR_{MDRD}$ for diagnosing chronic kidney disease (CKD) was higher than that of $eGFR_{mC-G}$, which in turn was higher than that of $eGFR_{C-G}$ (area under the curve was 0.846, 0.831, and 0.791; cut-off limits were 61.9, 58.3 and 59.5, respectively). ***Conclusion:*** C-G and MDRD equations can be an alternative to the CCL_{cr} test for assessing GFR, thus avoiding the need for the cumbersome and expensive GFR test. The MDRD formula had greater validity than the C-G equation and the C-G equation validity was improved by an adjustment to BSA.

Keywords: Creatinine; Glomerular Filtration Rate; Diet Modification; Chronic Kidney Disease; Oman.

الملخص: **الهدف**: يعد حساب سرعة الترشيح الكبيبي والذي يقاس عن طريق استخلاص الكرياتينين من أفضل المؤشرات لوظائف الكليتين. ونظرا لسلبيات طريقة استخلاص الكرياتينين، اضطرالباحثون لاشتقاق معادلات لحساب سرعة الترشيح الكبيبي لا تعتمد على استخلاص الكرياتينين. و تعد معادلة كوككروفت–جولت ومعادلة تعديل النظام الغذائي لمرضى الكلى من أكثر هذه المعادلات شيوعا. الغرض من هذه الدراسة هو تقييم هذه المعادلات عن طريق إيجاد العلاقة بين استخلاص الكرياتينين وكل من سرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت و سرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت المعدلة لمساحة سطح الجسم و سرعة الترشيح الكبيبي عن طريق معادلة تعديل النظام الغذائي لمرضى الكلى. **الطريقة**: لقد أجريت هذه الدراسة في مجمع بوشر التخصصي في محافظة مسقط في عمان (الفترة من عام 2007و حتى عام 2011). و تم قياس نسبة الكرياتينين بالدم و كمية استخلاص الكرياتينين في بول 24 ساعة في المرضى المشاركين في الدراسة و عددهم مائة و ثمانية و خمسون مريضا. تم حساب سرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت وسرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت المعدلة لمساحة سطح الجسم و سرعة الترشيح الكبيبي عن طريق معادلة تعديل النظام الغذائي لمرضى الكلى لجميع المرضى ثم تم دراسة العلاقة بين استخلاص الكرياتينين و بين و سرعة الترشيح الكبيبي عن طريق المعادلات الثلاثة. **النتائج**: تبين انه يوجد ارتباط كبيربين كل من سرعة الترشيح الكبيبي عن طريق معادلة تعديل النظام الغذائي لمرضى الكلى وسرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت المعدلة وسرعة الترشيح الكبيبي عن طريق معادلة كوككروفت–جولت و بين استخلاص الكرياتينين(معامل الارتباط= 0.701 و0.658 و0.605 بالترتيب) و أظهر منحنى خصائص التشغيل أن قدرة سرعة الترشيح الكبيبي عن طريق معادلة تعديل النظام الغذائى لمرضى الكلى لتشخيص مرض الكلى المزمن أعلى من قدرة سرعة الترشيح الكبيبّ عن طريق معادلة كوككروفت–جولت المعدلة لمساحة سطح الجسم و الذي بدوره أعلى من سرعة الترشيح الكبيبي عن طريق معادلة كوككروفت– جولت (المنطقه تحت المنحنى كانت 0.846و 0.831و0.791و حدود القطع كانت 61.9 و58.3 و59.5 بالترتيب) **الخلاصة**: تعد معادلة كوككروفت–جولت و معادلة تعديل النظام الغذائى لمرضى الكلى بديل عن اختبار استخلاص الكرياتينين لقياس سرعة الترشيح الكبيبي مما يؤدي إلى تجنب صعوبة و تكلفة هذا الاختبار. وتعد معادلة تعديل النظام الغذائى لمرضى الكلى أكثر دقة من معادلة كوككروفت–جولت المعدلة لمساحة سطح الجسم و التي بدورها أكثر دقة من معادلة كوككروفت–جولت الأصلية.

مفتاح الكلمات: الكرياتينين؛ سرعة الترشيح الكبيبي؛ تعديل النظام الغذائي؛ مرض الكليتين المزمن؛ عمان.

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Advances in Knowledge

- *Methods using exogenous substances to assess renal function are expensive, time-consuming, risky and cannot be easily implemented in clinical practice. Additionally, creatinine clearance (CL_{cr}) has some limitations. Due to the limitations of the clearance tests, they are frequently replaced by estimation equations such as Cockcroft-Gault (C-G) and the modification of diet in renal disease (MDRD) formulas.*
- *In this study, the MDRD formula had greater validity than the C-G equation and the C-G equation validity was improved by an adjustment to body surface area.*

Applications to Patient Care

- *The knowledge that C-G and MDRD equations can be used as an alternative to the CL_{cr} test for assessing GFR will enable the patient to avoid the time-consuming, cumbersome and expensive CL_{cr} test.*
- *It will be easier for the clinician to follow the progress of kidney disease by assessing eGFR with these equations, depending on patient age, weight and serum creatinine. It will also circumvent the need for 24-hour urine collection.*
- *The MDRD formula is recommended to assess eGFR in patients with chronic kidney disease as it has greater validity than the C-G equation.*

Glomerular filtration rate (GFR) is considered the best index of renal function as it assesses the progression of kidney dysfunction. The normal value is ~130 and 120 ml/min/1.73 m² for men and women, respectively, depending on age, sex and body size.[1] GFR can be determined by measuring the clearance of exogenous (inulin, 125-iothalamate, 51 Cr-ethylene diamine tetra acetic acid [EDTA], 99mTc-diethylene triamine penta acetic acid [DTPA] and iohexol) or endogenous (creatinine) substances.[2] Methods using exogenous substances are expensive, time-consuming, risky and cannot be easily implemented in clinical practice. Nevertheless, inulin clearance is the gold standard test for GFR as it is freely filtered and is not secreted, reabsorbed, synthesised or metabolised by the kidney.[3]

Creatine clearance (CL_{cr}) is an alternative to inulin clearance. Creatinine is freely filtered and is not metabolised by the kidney; however, it is secreted by the renal tubules.[4] If the effect of secretion is ignored, then all of the filtered creatinine will be excreted and this will reflect the GFR. Thus the GFR and CL_{cr} will be equal: [UCr x V]/SCr,[5] where UCr is urine creatinine, V is the 24-hour urine volume and SCr is the serum creatinine. However, CL_{cr} tends to exceed the true GFR due to tubular secretion.[5] It should therefore be adjusted to body surface area (BSA) so as to obtain the corrected creatinine clearance (CCL_{cr}) in ml/min/1.73 m² by the following equation:[6]

The normal value of CCL_{cr} is 95 ± 20 ml/min per 1.73 m² in women and 120 ± 25 ml/min per 1.73 m² in men.[5]

$$CCL_{cr} = \frac{(CL_{cr} \times 1.73)}{BSA}$$

SCr varies inversely with GFR and is used to assess stable kidney function, as a rise in SCr represents a reduction in GFR. However, in acute renal failure, GFR is markedly reduced and there is no time for creatinine to accumulate.[6] The mean SCr values for men and women are 100 and 82 µmol/L, respectively. These values vary by race and differ according to its production, secretion, extrarenal excretion and assay.[7,8]

The limitations of CL_{cr} and inulin clearance have inspired researchers to seek out easy formulas to estimate GFR (eGFR).[9] The most widely used formulas are Cockcroft-Gault (C-G)[10] and the modification of diet in renal disease (MDRD).[11] These formulas include variables such as age, sex, race, weight and SCr. In adults, normal eGFR is ≥90 ml/min/1.73m². Chronic kidney disease (CKD) is defined by an eGFR of <60 ml/min/1.73 m².[9] As for SCr, the proper interpretation of these equations requires stable kidney function, and its accuracy is also limited as SCr is affected by factors other than creatinine filtration.[12,13]

In the C-G equation, CL_{cr} can be estimated by the following formula:[10]

CL_{cr} (ml/min) = (140 - age in years) x (weight in Kg) x 1.23 if male (1.04 if female)/SCr in µmol/L

This formula should be adjusted for BSA to increase its accuracy and compare normal values.[14] It appears to be less accurate in the obese, those of different ethnicities, different age groups, children and pregnant women.[1]

The original MDRD equation has six variables, including urea and albumin which was a limitation

for the added cost and analytical variation.[13] Recognising this, the MDRD-4 variable equation was developed based on SCr, age, gender and ethnicity by the following formula:[15]

eGFR (ml/min per 1.73 m^2) = 1.75 x $SCr^{-1.154}$ x $age^{-0.203}$ x 1.212 (if of African descent) x 0.742 (if female), where SCr is in µmol/L and age in years

This study was conducted primarily to evaluate the performance of C-G and MDRD equations in Omani patients by finding out the relation between CCL_{cr} and eGFR by using C-G ($eGFR_{C-G}$), modified C-G ($eGFR_{mC-G}$) and MDRD ($eGFR_{MDRD}$) equations. Secondly, we sought to replace the CL_{cr} test with eGFR for the assessment of kidney function in clinical practice, thereby avoiding the need for the time-consuming, cumbersome and expensive CL_{cr} test.

Methods

This cross-sectional analytical study was carried out at Bowsher Polyclinic, Muscat, Oman, by auditing the files of subjects reporting to the Internal Medicine Clinic for a CL_{cr} test to assess kidney function from 1 January 2007 to 30 April 2011. Ethical approval was received from the Regional Research & Ethics Committee of the Directorate General & Health Services of the Muscat Region.

The inclusion criteria included adult patients who reported to the Internal Medicine Clinic at Polyclinic for a CL_{cr} test. However, patients who had incomplete data or dialysis therapy were excluded; thus 97 of the 255 files reviewed could not be considered, leaving a total of 158 subjects. Demographic data, such as age, gender, weight, height, body mass index (BMI) and BSA, were recorded.

All subjects were analysed for SCr and subjected to 24-hour urine collection to estimate urine volume (V) and urine creatinine (UCr). The CL_{cr} was calculated by the following equation:[5]

$$CCL_{cr}\ (ml/min) = \frac{(UCr \times V)}{SCr}$$

The CL_{cr} was then adjusted to BSA to get CCL_{cr} in ml/min per 1.73 m^2 by the following formula, where BSA equals the square root ([height in cm x weight in Kg]/3600):[8,16]

$$CCL_{cr} = \frac{(CL_{cr} \times 1.73)}{BSA}$$

Depending on a patient's gender, age and SCr, C-G was used to obtain the predicted CL_{cr}, which was abbreviated as $eGFR_{C-G}$, as in the following formula:[10]

$eGFR_{C-G}$ (ml/min) = (140 - age in years) x (weight in Kg) x 1.23 if male (1.04 if female)/SCr in µmol/L.

The $eGFR_{C-G}$ (ml/min) was adjusted to BSA (modified C-G) to obtain $eGFR_{mC-G}$ (ml/min per 1.73 m^2): $eGFR_{mC-G} = eGFR_{C-G} \times 1.73/BSA$.

The MDRD-4 variable equation was used to obtain $eGFR_{MDRD}$ in ml/min per 1.73 m^2 by the following formula:[15]

$eGFR_{MDRD} = 175 \times SCr^{-1.154} \times age^{-0.203})$ x 1.212 (if of African descent) x 0.742 (if female), where SCr is in µmol/L and age in years. None of our patients were of African descent.

The $eGFR_{C-G}$, $eGFR_{mC-G}$ and $eGFR_{MDRD}$ were compared to CCL_{cr} and statistical analysis was done to find out the correlation between them and to estimate an agreement between them. Data were coded using the Statistical Package for the Social Sciences (SPSS), Version 15 (IBM, Corp., Chicago, Illinois, USA) and summarised using the mean, standard deviation (SD), minimal and maximum values for quantitative variables and number and percentage for qualitative values. Correlations were done to test for linear relations between variables. Logistic regression analysis was done to test for significant predictors of dependent variables. A receiver operating characteristic (ROC) curve was used to test the validity of scores calculated by regression equations. A *P* value of ≤ 0.05 was considered statistically significant.

Results

The subjects in the study (N = 158) were predominantly <70 years of age (n = 115), although 43 were ≥70 years. The gender distribution was nearly equal (85 males and 73 females) and 42 were obese while 116 were not considered obese. Of those included in the study, 99 had diabetes (DM) and 59 were non-diabetic. The mean ± SD (range) age was 61.65 ± 10.46 (34.0–82.0); BMI was 27.93 ± 5.89 (16.6–54.6); SCr was 108.23 ± 47.12 (28.0–373.0); CCL_{cr} was 69.52 ± 37.28 (10.30–196.5); $eGFR_{MDRD}$ was 62.89 ± 27.52 (14.0–206.0); $eGFR_{mC-G}$ was 66.37 ± 28.09 (18.3–154.3), and $eGFR_{C-G}$ was 66.87 ±

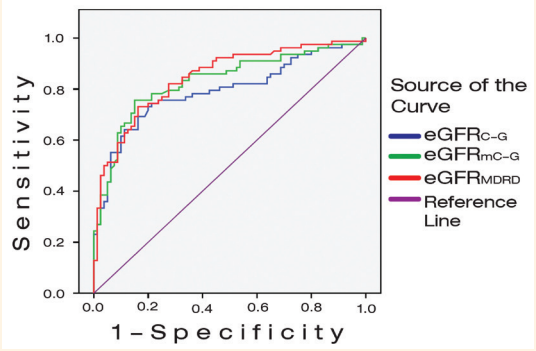

Figure 1: The validity of $eGFR_{C\text{-}G}$, $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ as a diagnostic tool for renal impairment after receiver operating characteristic curve analysis.

$eGFR_{C\text{-}G}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; $eGFR_{mC\text{-}G}$ = estimated glomerular filtration rate by modified Cockcroft-Gault equation; $eGFR_{MDRD}$ = estimated glomerular filtration rate by modification of diet in renal disease.

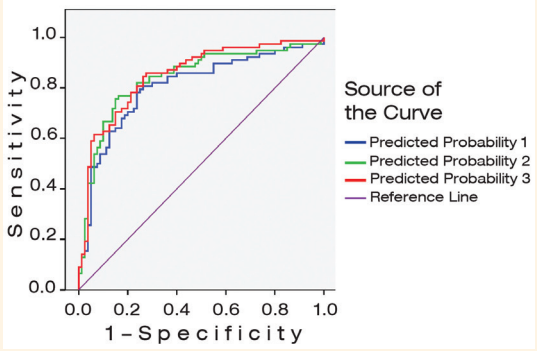

Figure 2: Receiver operating characteristic curve for $eGFR_{C\text{-}G}$, $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ for the assessment of kidney function after adjustment for age, sex, weight and diabetes mellitus*.

$eGFR_{C\text{-}G}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; $eGFR_{mC\text{-}G}$ = estimated glomerular filtration rate by modified Cockcroft-Gault equation; $eGFR_{MDRD}$ = estimated glomerular filtration rate by modification of diet in renal disease.

**Predicted probability 1 by $eGFR_{C\text{-}G}$; predicted probability 2 by $eGFR_{mC\text{-}G}$; predicted probability 3 by $eGFR_{MDRD}$.*

30.54 (20.21–163.92) of the studied subjects.

The $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ correlated significantly with CCL_{cr}, with a slightly stronger correlation with $eGFR_{MDRD}$ (r = 0.701, 0.658 and 0.605, respectively; P <0.001).

Studying $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ at a known cut-off value of 90 found that $eGFR_{mC\text{-}G}$ had a higher validity than $eGFR_{C\text{-}G}$ and that $eGFR_{MDRD}$ had a higher sensitivity and lower specificity than either $eGFR_{mC\text{-}G}$ or $eGFR_{C\text{-}G}$ (sensitivity = 97.4, 93.6 and 92.3; specificity = 22.5%, 27.5% and 26.3%, respectively).

The ROC curve analysis showed that the diagnostic accuracy of $eGFR_{mC\text{-}G}$ for a diagnosis of CKD was higher than that of $eGFR_{C\text{-}G}$. The $eGFR_{MDRD}$ had a higher area under the curve (AUC) and higher sensitivity and lower specificity than either $eGFR_{C\text{-}G}$ or $eGFR_{mC\text{-}G}$ [Figure 1 and Table 1].

Regression analysis was performed to predict renal impairment by using $eGFR_{C\text{-}G}$ adjusted for age, sex, obesity and DM. A regression equation was applied to calculate the predicted score for each patient (ranging from 0–100). The predicted score was entered in a ROC curve to detect its validity as well as to determine the best cut-off value for diagnosing renal impairment. The same was done for $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ for comparison. A ROC curve analysis showed that the $eGFR_{mC\text{-}G}$ score had a higher AUC, sensitivity, negative predictive value (NPV) and total accuracy (TA), and lower specificity and positive predictive value (PPV) than the $eGFR_{C\text{-}G}$ score. Additionally, the $eGFR_{MDRD}$ score had a higher validity than the $eGFR_{mC\text{-}G}$ score [Figure 2 and Table 2].

Regarding the validity among the studied groups, the $eGFR_{MDRD}$ had a higher validity than either $eGFR_{C\text{-}G}$ or $eGFR_{mC\text{-}G}$ in the obese, diabetic, male or the ≥70-year-old subjects. Comparing the validity of $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$, this study also showed that $eGFR_{mC\text{-}G}$ had higher validity in the

Table 1: The validity of $eGFR_{C\text{-}G}$, $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ as a diagnostic tool for renal impairment after receiver operating characteristic curve analysis

	AUC	*P* value	Cut-off values*	Sensitivity	Specificity	PPV	NPV	TA
$eGFR_{C\text{-}G}$	0.791	<0.001	≤59.5	73.1	80.0	78.1	75.3	76.6
$eGFR_{mC\text{-}G}$	0.831	<0.001	≤58.3	75.6	85.0	83.1	78.2	80.4
$eGFR_{MDRD}$	0.846	<0.001	≤61.9	82.1	72.5	74.4	80.6	77.2

AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value; TA = total accuracy; $eGFR_{C\text{-}G}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; $eGFR_{mC\text{-}G}$ = estimated glomerular filtration rate by modified Cockcroft-Gault equation; $eGFR_{MDRD}$ = estimated glomerular filtration rate by modification of diet in renal disease.

**mg/min for $eGFR_{C\text{-}G}$ and mg/min/1.73 m^2 for $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$.*

Table 2: The validity of $eGFR_{C\text{-}G}$, $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ as a diagnostic tool for the assessment of kidney function after adjustment for age, sex, weight and diabetes

	AUC	*P* value	Cut-off values*	Sensitivity	Specificity	PPV	NPV	TA
$eGFR_{C\text{-}G}$	0.806	<0.001	≥48.7	80.8	73.8	75.0	79.7	77.2
$eGFR_{mC\text{-}G}$	0.841	<0.001	≥46.3	84.6	71.3	74.2	82.6	77.8
$eGFR_{MDRD}$	0.853	<0.001	≥48.4	84.6	73.8	75.9	83.1	79.1

AUC = area under the curve; PPV = positive predictive value; NPV = negative predictive value; TA = total accuracy; $eGFR_{C\text{-}G}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; $eGFR_{mC\text{-}G}$ = estimated glomerular filtration rate by modified Cockcroft-Gault equation; $eGFR_{MDRD}$ = estimated glomerular filtration rate by modification of diet in renal disease.

**mg/min for $eGFR_{C\text{-}G}$ and mg/min/1.73 m2 for $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$.*

≥70-year-old, male and diabetic subjects; however, in the obese subjects, $eGFR_{mC\text{-}G}$ was more sensitive but had less specificity, PPV, NPV and TA than in $eGFR_{C\text{-}G}$ [Table 3].

Discussion

GFR is the best index of renal function in health and disease. It can be estimated by measuring the renal clearance of certain substances using exogenous (radioisotopic and non-radioisotopic) filtration markers. However, these methods are impractical and expensive.[17] Endogenous markers such as creatinine have also been used to assess GFR. The accuracy of CL_{cr} may be limited by inaccurate urine collection and creatinine secretion. Not only is urine collection time-consuming and cumbersome, but incomplete collection leads to a reduced CL_{cr} while over-collection leads to an increased CL_{cr}.[8] Moreover, CL_{cr} overestimates the GFR due to tubular creatinine secretion.[5] To compensate for these previous limitations, investigators have devised equations that predict GFR based on SCr, gender, body size, race and age. The most widely used equations are the C-G equation, which produces GFR values in ml/min, and the MDRD equation, which produces GFR values in ml/min per 1.73 m².[18] The C-G equation should be adjusted for BSA to increase its accuracy and enable a comparison with normal values.[14]

In this study, we evaluated the performance of the C-G and MDRD equations for estimating the GFR in a cohort of 158 subjects. An important characteristic of the cohort is that it included subjects whose CCL_{cr} ranged from 10.3–196.5 ml/min per 1.73 m² with sufficient numbers of subjects having CCL_{cr} >60 and <60 (84 and 74, respectively). Thus, the performance of these equations could be assessed over a wide range of kidney function. Furthermore, because all patients included in this study were Arab, the performances of the C-G and MDRD equations could be assessed in a group of subjects whose anthropometric characteristics are slightly different from those of American or European subjects.

With these different anthropometric characteristics in mind, we compared $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ with CCL_{cr}. It was found that these equations underestimated GFR in comparison to CCL_{cr} (mean CCL_{cr}, $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and eGFRC-G were 69.52, 62.89, 66.37 and 66.87, respectively). This can be explained by the fact that CCL_{cr} exceeds the true GFR by 19% because of tubular secretion.[5] In their study, Froissart *et al.* showed that there was a very good global agreement between measured GFR and both $eGFR_{MDRD}$ and $eGFR_{mC\text{-}G}$. On average, $eGFR_{MDRD}$ was only 1.0 ml/min per 1.73 m² less than measured GFR; $eGFR_{mC\text{-}G}$ was only 1.9 ml/min per 1.73 m² greater than measured GFR. However, Froissart *et al.*'s study compared $eGFR_{MDRD}$ and $eGFR_{mC\text{-}G}$ against GFR measured by 51Cr-EDTA renal clearance, and not CCL_{cr}, and did not evaluate $eGFR_{C\text{-}G}$.[19] Similarly, in 1999, Levey *et al.* documented that the C-G formula largely overestimated measured GFR.[13]

The current study demonstrated that $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ can replace CCL_{cr} in practice, avoiding the limitations of CCL_{cr}, as evidenced by the significant correlation between them, with a stronger correlation with $eGFR_{MDRD}$ (r = 0.701, 0.658 and 0.605, respectively; *P* <0.001). These results are supported by a Pakistani study which compared $eGFR_{MDRD}$ and $eGFR_{C\text{-}G}$ with CCL_{cr} in 369 cases, revealing a significant correlation between them, with a stronger correlation with $eGFR_{MDRD}$ (r = 0.788 for $eGFR_{MDRD}$ and r = 0.775 for $eGFR_{C\text{-}G}$). However, that study did not evaluate $eGFR_{mC\text{-}G}$.[18] In 2006, Shoker *et al.* compared

Table 3: The validity of $eGFR_{C\text{-}G}$, $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$ in diagnosing renal impairment among different studied groups

Variable	eGFR	Group	Sensitivity	Specificity	PPV	NPV	TA
Age	$eGFR_{C\text{-}G}$	<70	76.5	84.4	79.6	81.8	80.9
	$eGFR_{mC\text{-}G}$	<70	82.4	81.3	77.8	85.2	81.7
	$eGFR_{MDRD}$	<70	82.4	79.7	76.4	85.0	80.9
	$eGFR_{C\text{-}G}$	≥70	88.9	31.3	68.6	62.5	67.4
	$eGFR_{mC\text{-}G}$	≥70	88.9	31.3	68.6	62.5	67.4
	$eGFR_{MDRD}$	≥70	88.9	50.0	75.0	72.7	74.4
Sex	$eGFR_{C\text{-}G}$	F	83.8	72.2	75.6	81.3	78.1
	$eGFR_{mC\text{-}G}$	F	83.8	72.2	75.6	81.3	78.1
	$eGFR_{MDRD}$	F	83.8	72.2	75.6	81.3	78.1
	$eGFR_{C\text{-}G}$	M	78.0	75.0	74.4	78.6	76.5
	$eGFR_{mC\text{-}G}$	M	85.4	70.5	72.9	83.8	77.6
	$eGFR_{MDRD}$	M	85.4	75.0	76.1	84.6	80.0
BMI	$eGFR_{C\text{-}G}$	Not	81.8	78.7	77.6	82.8	80.2
	$eGFR_{mC\text{-}G}$	Not	85.5	77.0	77.0	85.5	81.0
	$eGFR_{MDRD}$	Not	83.6	77.0	76.7	83.9	80.2
	$eGFR_{C\text{-}G}$	Obese	78.3	57.9	69.2	68.8	69.0
	$eGFR_{mC\text{-}G}$	Obese	82.6	52.6	67.9	71.4	69.0
	$eGFR_{MDRD}$	Obese	87.0	63.2	74.1	80.0	76.2
DM	$eGFR_{C\text{-}G}$	DM	87.3	56.8	71.6	78.1	73.7
	$eGFR_{mC\text{-}G}$	DM	89.1	56.8	72.1	80.6	74.7
	$eGFR_{MDRD}$	DM	89.1	61.4	74.2	81.8	76.8
	$eGFR_{C\text{-}G}$	No DM	65.2	94.4	88.2	81.0	83.1
	$eGFR_{mC\text{-}G}$	No DM	73.9	88.9	81.0	84.2	83.1
	$eGFR_{MDRD}$	No DM	73.9	88.9	81.0	84.2	83.1

eGFR = estimated glomerular filtration rate; PPV = positive predictive values; NPV = negative predictive value; TA = total accuracy; $eGFR_{C\text{-}G}$ = estimated glomerular filtration rate by Cockcroft-Gault equation; $eGFR_{mC\text{-}G}$ = estimated glomerular filtration rate by modified Cockcroft-Gault equation; $eGFR_{MDRD}$ = estimated glomerular filtration rate by modification of diet in renal disease; BMI = body mass index; F = female; M = male; DM = diabetes mellitus.

$eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ with CCL_{cr}, documenting that $eGFR_{mC\text{-}G}$ gave superior results compared to $eGFR_{C\text{-}G}$, with an overall accuracy in the general and subgroup analysis.[14] Similarly, our results showed that $eGFR_{mC\text{-}G}$ had a stronger correlation with CCL_{cr} than $eGFR_{C\text{-}G}$ emphasising that the correction for BSA increases the validity of the C-G equation. The difference between the two studies is that $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ were compared with CL_{cr} in the Shoker *et al.* study, but in our study they were compared with CCL_{cr}, which is more accurate. In 2012, Alcântara *et al.* compared $eGFR_{C\text{-}G}$ with CCL_{cr} and no significant difference was found between the mean $eGFR_{C\text{-}G}$ (64.7 ± 27.4) and the mean CCL_{cr} (68.4 ± 32.6) and a correlation between them was found (r = 0.68; P <0.001). Using lean body weight instead of total body weight to obtain the $eGFR_{C\text{-}G}$, the correlation coefficient was increased to 0.75 (P <0.001).[20] However, Alcântara *et al.'s* study did not evaluate $eGFR_{mC\text{-}G}$ and $eGFR_{MDRD}$, as in our study.

In studying $eGFR_{MDRD}$, $eGFR_{mC\text{-}G}$ and $eGFR_{C\text{-}G}$ as a diagnostic tool for renal impairment, as

detected by CCL_{cr} and at a known cut-off value of 90, it was found that $eGFR_{mC-G}$ had a higher validity than $eGFR_{C-G}$. This emphasises that correction for BSA increases the validity of the C-G equation and that $eGFR_{MDRD}$ had a higher sensitivity and lower specificity than either $eGFR_{mC-G}$ or $eGFR_{C-G}$. A ROC curve analysis showed that the diagnostic accuracy of $eGFR_{mC-G}$ for diagnosing CKD was higher than that of $eGFR_{C-G}$, and that $eGFR_{MDRD}$ had a higher sensitivity, higher AUC and a lower specificity than either $eGFR_{C-G}$ or $eGFR_{mC-G}$. By doing a regression analysis to predict renal impairment, using $eGFR_{C-G}$, $eGFR_{mC-G}$ and $eGFR_{MDRD}$ adjusted for age, sex, obesity and DM, the ROC curve analysis showed that the $eGFR_{mC-G}$ score had a higher AUC, sensitivity, NPV and TA, and a lower specificity and PPV than that of the $eGFR_{C-G}$ score. Additionally, it showed that the $eGFR_{MDRD}$ score had a higher validity than the $eGFR_{mC-G}$ score. Our results supported those of Srinivas *et al.*, whose study compared $eGFR_{MDRD}$ and $eGFR_{mC-G}$ with GFR measured by 99mTc-DTPA renal clearance in 599 renal donors; this study demonstrated that $eGFR_{MDRD}$ performed better in terms of global bias, precision, correlation and accuracy than $eGFR_{mC-G}$.[21]

Regarding the validity among studied groups, our study showed that $eGFR_{MDRD}$ had a higher validity than either $eGFR_{C-G}$ or $eGFR_{mC-G}$ in males, those with DM, individuals ≥70 years of age and those who were obese. The $eGFR_{mC-G}$ had higher validity in diabetics, males and those ≥70 years of age than $eGFR_{C-G}$; however, in the obese subjects, $eGFR_{mC-G}$ was more sensitive but had less specificity, PPV, NPV and TA than $eGFR_{C-G}$. This was similar to Froissart *et al.'s* study, which showed that $eGFR_{mC-G}$ had the lowest level of precision for obese subjects.[19]

In 2005, Rigalleau *et al.* compared $eGFR_{MDRD}$ and $eGFR_{mC-G}$ with measured GFR in 160 diabetic patients, and revealed that $eGFR_{MDRD}$ and $eGFR_{mC-G}$ correlated well with measured GFR, while $eGFR_{MDRD}$ underestimated and $eGFR_{mC-G}$ overestimated it. The ROC curve analysis showed that the maximum diagnostic accuracy of $eGFR_{mC-G}$ for diagnosing CKD was lower than that of $eGFR_{MDRD}$. It was concluded that the MDRD equation is more accurate for the diagnosis of renal failure in diabetic patients.[22] However, $eGFR_{MDRD}$ and $eGFR_{mC-G}$ were evaluated against measured GFR by 51Cr-EDTA clearance and not against CCL_{cr}. The $eGFR_{C-G}$ was not evaluated.

Based on the current study, as well as other studies, it is clear that the measurement of CL_{cr} using a 24-hour urine collection system does not improve the estimate of GFR compared to that provided by the C-G and MDRD equations. Nevertheless, this system provides useful information for the estimation of GFR in individuals with unsual dietary intake (for example in subjects with vegetarian diets or those taking creatine supplements), or abnormal muscle mass (for instance as a result of amputation, malnutrition or muscle wasting). It is also useful for the assessment of diet and nutritional status, and for assessing the patient's status when there is a need to start dialysis.[9]

There are several limitations to this study. First, CL_{cr} was used as the reference method for GFR although the measurement of CL_{cr} has many theoretical and practical difficulties. Ideally it should be substituted by inulin or isotope clearances as a reference to verify the accuracy of the results. Second, it would be more relevant to compare C-G and MDRD formulas in a multicentre environment.

Conclusion

C-G and MDRD equations can be used as an alternative to the CL_{cr} test for assessing GFR, thereby avoiding the cumbersome, time-consuming and expensive GFR test. The MDRD formula had better validity in this study than the C-G equation and the validity of the C-G equation was improved by an adjustment to the BSA.

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