Comparison of Creatinine Clearance Estimates With Routine Measured Clearance in Adult Jordanians With a Kidney Transplant

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Abstract

Objectives: There are conflicting data on using the Cockcroft-Gault formula and the Modification of Diet in Renal Disease formula to assess graft function in kidney transplants. This study uses a cohort of Jordanian kidney transplant patients to assess performance of the Cockcroft-Gault formula and the Modification of Diet in Renal Disease equations by using the criterion standard of measured creatinine clearance.

Materials and Methods: Creatinine clearance measured by 24-hour urine creatinine in patients with a kidney transplant was compared with the estimated clearance using the Cockcroft-Gault formula and the Modification of Diet in Renal Disease equations. Correlation, limits of agreement, and concordance analyses were used.

Results: There was a positive correlation between both the Cockcroft-Gault (r=0.878; \( P < .001 \)) and the Modification of Diet in Renal Disease (r=0.732; \( P < .001 \)) equations with creatinine clearance. The former was statistically superior (\( P = .0416 \)). Using Bland-Altman plots, the limits of agreement were wide for both methods. After log transformation, the limits of agreement were -0.06 to +0.27 for the Cockcroft-Gault formula, and -0.21 to + 0.26 for the Modification of Diet in Renal Disease. Concordance analyses showed a correlation coefficient of 0.7384 (95% CI: 0.6134 to 0.8273) when the Cockcroft-Gault formula was used, and 0.7257 (95% CI: 0.5622 to 0.8345) for the Modification of Diet in Renal Disease. Pearson \( P \) coefficient (precision) and bias correction factor \( Cb \) (accuracy) for the Cockcroft-Gault formula and for the Modification of Diet in Renal Disease were 0.8762, 0.8427, 0.7324, and 0.9908.

Conclusions: In Jordanian patients with a renal transplant, although the Cockcroft-Gault formula performed slightly better than the Modification of Diet in Renal Disease equation in estimating creatinine clearance, neither of these equations can accurately predict renal graft function.

Key words: Graft, Glomerular filtration rate, Agreement, Cockcroft-Gault, Modification of diet in renal disease

Introduction

Measuring glomerular filtration rate (GFR) is crucial when following patients who have had a kidney transplant. Relying on serum creatinine alone is not accurate, and measuring creatinine clearance (CrCl) in a timed urine sample is cumbersome, inconvenient, and often difficult to collect a urine sample accurately.\(^1\)\(^-\)\(^4\)

Two study equations, the Cockcroft-Gault formula (CG)\(^5\) and the Modification of Diet in Renal Disease (MDRD),\(^6\)\(^7\) are currently used widely to estimate GFR. The K/DOQI guidelines from the National Kidney Foundation consider the CG formula and the MDRD equations reliable measures of GFR in adults.\(^8\)

There remain conflicting data on applying the CG formula and MDRD formula in a kidney transplant.\(^9\)\(^-\)\(^15\) This study uses a cohort of Jordanian kidney transplant patients to assess the performance of the CG formula and the MDRD equation by using measured CrCl as the criterion standard.
Materials and Methods

We reviewed the charts of 59 patients with a stable kidney transplant, attending the nephrology outpatient clinic at Jordan University Hospital. All protocols were approved by the Institutional Review Board before the study began, and the protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Written, informed consent was obtained from all patients. We gave all patients clear instructions regarding how to collect their urine accurately. Adequacy of the 24-hour urine collection was assessed by comparing total urine creatinine in the sample to the predicted creatinine (22 - [age ÷ 9]) × kilograms of body weight in women, and (28 - [age ÷ 6]) × kilograms of body weight in men. Collections in which the difference between the predicted 24-hour urine creatinine and the measured 24-hour urine creatinine was more than 20% were defined as under collection. Likewise, collections in which the difference between the measured 24-hour urine creatinine and the predicted 24-hour urine creatinine was greater than 20% were defined as over collection. The under and over collections were excluded from the study.

Forty-nine patients (37 men, 12 women; mean age, 40.73 ± 12.81 y) with adequate 24-hour urine collection were ultimately included. The mean serum creatinine at the time of the study was 114 ± 58.3 μmol/L (1.29 ± 0.66 mg/dL). The concentration of serum and urine creatinine was measured by a creatinine picric acid Jaffé reaction using a Roche/Hitachi 917 analyzer (Roche Diagnostics AG, Industriestrasse 7, CH-6343 Rotkreuz, Switzerland). Accurate 24-hour urine collections were used to calculate CrCl according to the CrCl equation: CrCl (mL/min) = (urine creatinine [mL/min] × 24-h urine volume [mL]) ÷ (serum creatinine [mg/dL] × 1440). Four variable MDRD equation was used, where MDRD-GFR (mL/min/1.73 m²) = 186.3 × serum creatinine (mg/dL) -1.154 × age (y) -0.203 × 1.212 (if African-American), × 0.742 (if female). The CG formula, CG-GFR (mL/min) = ([140-age (y)] × weight [kg] ÷ [72 × serum creatinine (mg/dL)]) × 0.85 (if female).

MedCalc statistical software version 10.3.0.0 (MedCalc Software, Acacialaan 22, B-8400 Ostend, Belgium) was used for statistical analysis. Comparisons between 2 correlation coefficients from independent samples were tested using a Fisher z test. The limits of agreement between the 2 methods were analyzed using a Bland-Altman plot. Concordance analyses were performed to look at precision and accuracy of formulas.

Results

The mean creatinine clearance rates for CG, MDRD, and CrCl were 89.0 ± 31.2, 75.0 ± 25.9, and 71.2 ± 28.4. There was a good correlation between CrCl and CG (r=0.876; P < .0001) (Figure 1A). The correlation of MDRD and CrCl was lower than that for CG (r=0.732; P < .0001) (Figure 1B), with significant differences between these correlation coefficients (P = .0416).

Using a Bland-Altman plot, the limits of agreement for the CG were -11.8 to +47.3, whereas the limits of agreement for MDRD were -37.8 to +45.3. After log

\[ r = 0.876, P < .0001 \]

\[ r = 0.732, P < .0001 \]
transformation, the limits of agreement for the CG were -0.06 to +0.27 (Figure 2A), whereas the limits of agreement for MDRD were -0.21 to +0.26 (Figure 2B). For about 95% of the CG formula cases, the CG would be between 0.94 and 1.31 times the measured CrCl values, indicating that CG formula might differ from the measured CrCl by 6% below to 31% above. For MDRD, about 95% of the cases, the MDRD would be between 0.81 and 1.3 times the measured CrCl, indicating that the MDRD formula might differ from the measured CrCl by 19% below to 30% above.

Concordance analyses showed concordance correlation coefficients of 0.7384 (95% CI: 0.6134 to 0.8273) for CG and 0.7257 (95% CI: 0.5622 to 0.8345) for MDRD. Pearson $P$ coefficient (precision) and bias correction factor $C_b$ (accuracy) of CG and of MDRD were 0.8762, 0.8427, 0.7324, and 0.9908.

Discussion

The K/DOQI guidelines of the National Kidney Foundation consider the CG and the MDRD equations reliable measures for GFR in adults.17 Applying MDRD and CG equations has been studied in a normal population18-19 and in chronic kidney disease.19,20 The data are conflicting when applying these formulas to a kidney transplant.9-15 This study showed a positive correlation between CrCl, and CG, and MDRD. To use the 2 tests interchangeably, it is important to show that the 2 methods agree sufficiently. The limits of agreement were wide for both formulas, reflecting the small sample size, and differences in the variation, making the degree of agreement not acceptable clinically, as small changes in GFR are clinically important to a kidney transplant recipient. Recent studies21,22 have highlighted the prediction that the equations are too crude to assess GFR, especially in kidney transplant recipients.

From an analysis of bias, a measure of systematic error, we found that the MDRD overestimated CrCl by 3.8 mL/min/1.73m², and that the CG underestimated CrCl by 17.3 mL/min/1.73m². This is consistent with previous studies where the CG formula overestimates GFR and the MDRD equations slightly overestimate GFR,11,22 or underestimate in different studies.14,23-24

The CG formula shows better concordance in our study, which agrees with the findings of Rodrigo and associates, in which they found better CG concordance among patients with better preserved renal function, while the MDRD and the 4-variable MDRD estimations were more accurate in patients with lower GFR.23

The CG formula has been considered to be one of the least accurate equations.22 According to our data, the CG formula showed slightly better correlation with CrCl, which is consistent with the findings of Büchler and associates.25 Another study by Brown and associates26 showed that the CG formula agreed more closely with 51Cr-EDTA GFR compared with the MDRD.

Conclusions

In a kidney transplant, the predictive performance of CG and MDRD equations is inadequate. Although the CG formula performed better, neither of these equations accurately predicted renal graft function.
The present study has limitations. First, we used CrCl as a criterion standard for estimating GFR. There are many accurate methods of estimating GFR including insulin, $^{51}$Cr-EDETA, $^{27,29}$ 125I-iodohalomate, $^{30,32}$ iohexol clearance, $^{33}$ and $^{99m}$Tc-DTPA. $^{34}$ However, these methods are costly and available mainly in research settings. Second, the CG formula was derived from CrCl measurements, which could explain some of its better correlation over the MDRD equation. Third, the number of patients in this study was small.

There is clearly a need for research to evaluate CG and MDRD prediction equations in larger numbers of kidney transplant patients, using a criterion standard method for comparison.

References


