Research Article

Comparison of Measured Creatinine Clearance and Clearances Estimated by Cockcroft-Gault and MDRD Formulas in Patients with a Single Kidney

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There are doubts about whether the values obtained from the Cockroft-Gault (CL_CG) and Modification of Diet in Renal Disease (GFR_MDRD) formulas are comparable to the more traditional formula used to obtain the creatinine clearance from a 24-hour urine collection (CL_Cr), particularly in patients with only one kidney. The present study aimed to compare these formulas in individuals with one remaining kidney after previous nephrectomy (Nx) and to verify which estimated formula correlates more closely with CL_Cr. Thirty-six patients who had undergone Nx had their renal filtration analyzed with CL_CG, GFR_MDRD, and by CL_Cr. The average time after Nx was 11.6 ± 9.0 years, and the average age at the time of the study was 50.7 ± 10.6 years old (X ± SD). The results of three clearances were 81.1 ± 35.6 mL·min⁻¹·m⁻² for CL_Cr, 70.4 ± 24.0 mL·min⁻¹·m⁻² for CL_CG, and 71.2 ± 19.2 mL·min⁻¹·m⁻² for GFR_MDRD (with CL_Cr > CL_CG and GFR_MDRD; P < .001). No difference was found between the CL_CG and GFR_MDRD values (P = .72). The data demonstrated that both estimate formulas were strongly correlated with CL_Cr, although CL_CG was more closely associated with CL_Cr than GFR_MDRD (CL_CG with r² : 0.64 and GFR_MDRD with r² : 0.34; P < .001). In conclusion, for people with only one kidney remaining after NX, our data showed that glomerular filtration rate estimation by CL_CG is more related to the values obtained with the traditional clearance measurement based on a 24-hour urine collection test.

1. Introduction

The Kidney Disease Outcomes Quality Initiative guidelines from the National Kidney Foundation classify stages of Chronic Kidney Disease according to the estimated glomerular filtration rate (GFR), which is considered the best index of function in both healthy and diseased kidneys [1]. GFR is a direct measurement of kidney function; it is reduced before the onset of kidney failure symptoms [2]. Healthy individuals who submitted to unilateral nephrectomy for donation or other causes experience an abrupt 50% reduction in total kidney mass; theoretically, their initial GFR could decrease by the same percentage. This fact is supported by the concept that GFR levels are the product of the single nephron filtration rate multiplied by the number of functioning nephrons in the remaining kidney. It is important to recognize that the GFR can be insensitive in detecting the number of lost nephron number because of compensatory increases in the single-nephron GFR secondary to increased glomerular capillary pressure or glomerular hypertrophy [3]. Experimental and clinical studies of solitary kidneys have detected such modifications in glomerular function after renal mass is reduced [4, 5].

Numerous formulas have been developed to estimate GFR or creatinine clearance from serum creatinine and other sources. One widely used formula for predicting creatinine clearance was proposed by Cockcroft and Gault Gault. More recently, the Modification of Diet in Renal Disease (MDRD) study formula, which uses four or six variable equations, has been used to evaluate GFR in clinical practice. However, there are concerns about whether the values obtained from the CG and MDRD formulas are comparable to the measured
creatinine clearance values obtained traditionally from a 24-hour urine collection test, particularly in patients with only one kidney. The present study aimed to compare these formulas with measured GFRs in individuals with one kidney remaining after unilateral nephrectomy.

2. Patients and Methods

In this cross-sectional study, thirty-six individuals who underwent unilateral nephrectomy were enrolled. The mean age was 50.7 ± 10.6 years. Overall, 11 subjects were male and 15 were female. Other clinical characteristics are presented in Table 1. The reasons for unilateral nephrectomy were organ donation (n = 28) and treatment of renal stones with hydronephrosis (n = 8). Three methods were used to measure and estimate glomerular filtration rates (GFR) and creatinine clearances (CICr): creatinine clearance using 24-hour collected urine on two different days (CICr_m) and CICr by the Cockcroft-Gault formula (CICrCG) and by the MDRD formula (GFRMDRD). The value obtained for serum creatinine on day 1 was used to calculate the CICr_m, CICrCG, and GFRMDRD. The same was performed for day 2. Because all measurements and formulas were conducted in duplicate (on day 1 and day 2) for each individual, a total of 72 results were obtained for each clearance. The abbreviated GFRMDRD (on day 1 and day 2) for each individual, a total of 72 results all measurements and formulas were conducted in duplicate.

Time after nephrectomy (years; mean ± SD, range) 11.6 ± 9.0 (2 m–38 y)

Body weight (kg; mean ± SD, range) 72.8 ± 16.4 (43–119)

BSA (m²; mean ± SD, range) 1.74 ± 0.22 (1.27–2.24)

Plasma creatinine (mg/dL; mean ± SD, range) 1.3 ± 0.67 (0.8–4.1)

Plasma creatinine >2 mg% (n [%]) 3 (8.3%)

Measured creatinine clearance:

First day (mL·min·m⁻²) 79.8 ± 4.4

Second day (mL·min·m⁻²) 81.6 ± 4.4

BSA: Body surface area; first versus second day (P > .07).

Table 1: Characteristics of the studied population (n = 36).

<table>
<thead>
<tr>
<th>Male gender (n [%])</th>
<th>11 (30.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black race (n [%])</td>
<td>14 (38)</td>
</tr>
<tr>
<td>Age (years; mean ± SD, range)</td>
<td>50.7 ± 10.6 (29–79)</td>
</tr>
<tr>
<td>Time after nephrectomy (years; mean ± SD, range)</td>
<td>11.6 ± 9.0 (2 m–38 y)</td>
</tr>
<tr>
<td>Body weight (kg; mean ± SD, range)</td>
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</tr>
<tr>
<td>Plasma creatinine &gt;2 mg% (n [%])</td>
<td>3 (8.3%)</td>
</tr>
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2.1. Statistics. All values were evaluated for normality using D’Agostinho and Pearson tests. If a Gaussian distribution was confirmed, ANOVA and Tukey post tests were applied. Linear regression was calculated between the variables. The slopes of each curve were compared for equality using the F-test. P < .05 was considered significant. Results were reported as mean ± standard error (X ± SD).

3. Results

The participants’ clinical characteristics are shown in Table 1. The urinary excretion of creatinine in the samples did not indicate any inadequacy in the 24 h collection of urine. When the three clearances were compared, we obtained 81.1 ± 35.6 mL·min·m⁻² for CICr_m, 70.4 ± 24.0 mL·min·m⁻² for CICrCG, and 71.2 ± 19.2 mL·min·m⁻² for GFRMDRD (Figure 1). We obtained significant differences for CrCl_m versus CrClCG (P < .001) and CrCl_m versus GFRMDRD (P < .001), but the values for GFRMDRD and CrClCG were similar (P = .56). The correlation between CICr_m and CICrCG was positive and significant (r² = 0.62, P < .0001; Figure 2). Additionally, the correlation between CICr_m and GFRMDRD was positive and significant (r² = 0.36; P < .0001; Figure 3). When the slope of CrClMDRD (0.4456 to 0.6735) was compared with the slope of GFRMDRD (0.2247 to 0.4305) in relation to CICr_m, different values were obtained (F = 9.21718; DFD = 1DFd = 140; P = .00286; Figure 4).

4. Discussion

The most commonly used formulas to calculate creatinine clearance and glomerular filtration rate are the Cockcroft-Gault and Modification of Diet in Renal Disease formulas,
which tend to underestimate renal function by approximately 25% to 30% at its upper limit in normal individuals as well as patients with CKD [9]. It is important to recognize that each of these simplified methods has its own limitations and only provides reliable estimates if all variables and techniques are performed exactly as stipulated. On the other hand, the creatinine clearance measured by 24-hour urine collection is associated with problems in determining glomerular filtration. Improper urine collection is one of the factors that can affect the final result; nonetheless, this method is commonly used in many clinical centers and hospitals to investigate renal function. The present study compared the ClCr, ClCrCG, and GFRMDRD for the same patient using the same serum creatinine values. This work is not aimed to establish the clearance measured by 24-hour urine collection as the gold standard because, as described above, this method has inherent errors. Rather, we aimed to determine which of the formulas produces results closest to those obtained via the traditional method (i.e., 24-hour urine collection) in patients with a single kidney.

The results of this study showed that the estimated clearance values (ClCrCG and GFRMDRD) in single-kidney patients were not different from each other, but both differed from the ClCr (on the order of −5% for ClCrCG and −4% for GFRMDRD) (Figure 1). When the estimated values were correlated with ClCr, we observed significant correlations between ClCrCG (Figure 2) and GFRMDRD (Figure 3). Using the determination coefficient (r²) to quantify the correlation between the variables, we could conclude that the r² value for ClCrCG was larger than the r² value for GFRMDRD. Accordingly, for the same creatinine levels and the same patient, the ClCrCG was more strongly correlated with ClCr than with GFRMDRD (0.67 versus 0.34; P < .001) in single-kidney patients.

In Figure 4, we can see that the clearance values estimated by the CG equation are nearer to the values of the ClCr in any situation (slope 0.2 to 0.4; r² : 0.36; P = .001). Figure 4 also manifests that there is a common point where the straight lines meet (filtration level ≈90 mL·min⁻¹·m²²) evidencing that from this point on there are distinct modifications in the estimated values in relation to the measured clearance values. Both the ClCrCG and the GFRMDRD, if they are over 90 mL·min⁻¹·m²², they underestimate the values in relation to the ClCr, and if they are under that, they overestimate them in relation to the values of the ClCr. It was possible to conclude that ClCrCG is the estimate formula that most closely matches the ClCr. It should be noted that our data included a large range of values for age, BSA, and time after nephrectomy (Table 1). The correlations demonstrated by our data may not be the same for specific subgroups of single-kidney patients, including the obese or very young or elderly people. More studies with large sample should be completed to permit more precise conclusions.
References


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