Research Article

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

Sebastião Rodrigues Ferreira-Filho, Camila Caetano Cardoso, Luiz Augusto Vieira de Castro, Ricardo Mendes Oliveira, and Renata Rodrigues Sá

Medical School, Federal University of Uberlândia, Uberlândia MG, Brazil

Correspondence should be addressed to Sebastião Rodrigues Ferreira-Filho, ferreirafilho1952@gmail.com

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There are doubts about whether the values obtained from the Cockcroft-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 Crm), 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 Crm. Thirty-six patients who had undergone Nx had their renal filtration analyzed with Cl CG, GFR MDRD and by Cl Crm. 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·m² for Cl Crm, 70.4 ± 24.0 mL·min⁻¹·m² for Cl CG, and 71.2 ± 19.2 mL·min⁻¹·m² for GFR MDRD (with Cl CG > Cl Crm 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 Crm, although Cl CG was more closely associated with Cl Crm 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 (ClCr): creatinine clearance using 24-hour collected urine on two different days (ClCr m) and ClCr by the Cockcroft-Gault formula (ClCrCG) and by the MDRD formula (GFRMDRD). The value obtained for serum creatinine on day 1 was used to calculate the ClCr m, ClCrCG, 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 were obtained for each clearance. The abbreviated GFRMDRD formulas with measured GFRs in individuals with one kidney only were used.

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

| Characteristic                      | Count (%) |
|-------------------------------------|-----------|
| Male gender (n [%])                 | 11 (30.5) |
| Black race (n [%])                  | 14 (38)   |
| Age (years; mean ± SD, range)       | 50.7 ± 10.6 (29–79) |
| Time after nephrectomy (years; mean ± SD, range) | 11.6 ± 9.0 (2–38) |
| 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).

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 ClCr m, 70.4 ± 24.0 mL·min·m⁻² for ClCrCG, and 71.2 ± 19.2 mL·min·m⁻² for GFRMDRD (Figure 1). We obtained significant differences for CrCl m versus CrCl CG (P < .001) and CrCl m versus GFRMDRD (P < .001), but the values for GFRMDRD and CrCl CG were similar (P = .56). The correlation between ClCr m and ClCrCG was positive and significant (r² = 0.62, P < .0001; Figure 2). Additionally, the correlation between ClCr m and GFRMDRD was positive and significant (r² = 0.36; P < .0001; Figure 3). When the slope of CrClCG (0.4456 to 0.6375) was compared with the slope of GFRMDRD (0.2247 to 0.4305) in relation to ClCr m, different values were obtained (F = 9.21718; DF = 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 m, ClCr CG, and GFR MDRD 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 (ClCr CG and GFR MDRD) in single-kidney patients were not different from each other, but both differed from the ClCr m (on the order of −5% for ClCr CG and −4% for GFR MDRD) (Figure 1). When the estimated values were correlated with ClCr m, we observed significant correlations between ClCr CG (Figure 2) and GFR MDRD (Figure 3). Using the determination coefficient ($r^2$) to quantify the correlation between the variables, we could conclude that the $r^2$ value for ClCr CG was larger than the $r^2$ value for GFR MDRD. Accordingly, for the same creatinine levels and the same patient, the ClCr CG was more strongly correlated with ClCr m than with GFR MDRD (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 m both in hyper- and in hypofiltration (slope 0.4 to 0.6; $r^2$: 0.66; $P < .001$), and that the GFR MDRD distances itself more from ClCr m in any situation (slope 0.2 to 0.4; $r^2$: 0.36; $P = .001$). Figure 4 also manifests that there is a common point where the straight lines meet (filtration level $\approx$90 mL-min-m$^{-2}$) evidencing that from this point on there are distinct modifications in the estimated values in relation to the measured clearance values. Both the ClCr CG and the GFR MDRD, if they are over 90 mL-min-m$^{-2}$, they underestimate the values in relation to the ClCr m, and if they are under that, they overestimate them in relation to the values of the ClCr m. It was possible to conclude that ClCr CG is the estimate formula that most closely matches the ClCr m. 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

[1] A. S. Levey, “Measurement of renal function in chronic renal disease,” Kidney International, vol. 38, no. 1, pp. 167–184, 1990.
[2] G. Manjunath, M. J. Sarnak, and A. S. Levey, “Estimating the glomerular filtration rate: Dos and don’ts for assessing kidney function,” Postgraduate Medicine, vol. 110, no. 6, pp. 55–62, 2001.
[3] B. M. Brenner, E. V. Lawler, and H. S. Mackenzie, “The hyperfiltration theory: A paradigm shift in nephrology,” Kidney International, vol. 49, no. 6, pp. 1774–1777, 1996.
[4] B. M. Brenner, “Nephron adaptation to renal injury or ablation,” The American Journal of Physiology, vol. 249, no. 3 Pt 2, pp. F324–337, 1985.
[5] T. Shimamura and A. B. Morrison, “A progressive glomerulosclerosis occurring in partial five sixths nephrectomized rats,” American Journal of Pathology, vol. 79, no. 1, pp. 95–104, 1975.
[6] A. S. Levey, J. Coresh, T. Greene et al., “Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate,” Annals of Internal Medicine, vol. 145, no. 4, pp. 247–254, 2006.
[7] D. W. Cockcroft and M. H. Gault, “Prediction of creatinine clearance from serum creatinine,” Nephron, vol. 16, no. 1, pp. 31–41, 1976.
[8] S. Lavender, P. J. Hilton, and N. F. Jones, “The measurement of glomerular filtration-rate in renal disease,” Lancet, vol. 2, no. 7632, pp. 1216–1218, 1969.
[9] J. C. Verhave, P. Fesler, J. Ribstein, G. Du Cailar, and A. Mimran, “Estimation of renal function in subjects with normal serum creatinine levels: influence of age and body mass index,” American Journal of Kidney Diseases, vol. 46, no. 2, pp. 233–241, 2005.