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 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 ($ClCr_m$), 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 $ClCr_m$. Thirty-six patients who had undergone Nx had their renal filtration analyzed with Cl_{CG} , GFR_{MDRD} and by $ClCr_m$. 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 ($X \pm SD$). The results of three clearances were $81.1 \pm 35.6 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ for $ClCr_m$, $70.4 \pm 24.0 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ for $ClCr_{CG}$, and $71.2 \pm 19.2 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ for GFR_{MDRD} (with $ClCr_m > ClCr_{CG}$ and GFR_{MDRD} ; $P < .001$). No difference was found between the $ClCr_{CG}$ and GFR_{MDRD} values ($P = .72$). The data demonstrated that both estimate formulas were strongly correlated with $ClCr_m$, although $ClCr_{CG}$ was more closely associated with $ClCr_m$ than GFR_{MDRD} ($ClCr_{CG}$ with $r^2 : 0.64$ and GFR_{MDRD} with $r^2 : 0.34$; $P < .001$). In conclusion, for people with only one kidney remaining after NX, our data showed that glomerular filtration rate estimation by $ClCr_{CG}$ 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. 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

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

Male gender (n [%])	11 (30.5)
Black race (n [%])	14 (38)
Age (years; mean $\pm$ SD, range)	50.7 $\pm$ 10.6 (29–79)
Time after nephrectomy (years; mean $\pm$ SD, range)	11.6 $\pm$ 9.0 (2 m–38 y)
Body weight (kg; mean $\pm$ SD, range)	72.8 $\pm$ 16.4 (43–119)
BSA (m^2 ; mean $\pm$ SD, range)	1.74 $\pm$ 0.22 (1.27–2.24)
Plasma creatinine (mg/dL; mean $\pm$ SD, range)	1.3 $\pm$ 0.67 (0.8–4.1)
Plasma creatinine >2 mg% (n [%])	3 (8.3%)
Measured creatinine clearance:	
First day ($mL \cdot min \cdot m^{-2}$)	79.8 $\pm$ 4.4
Second day ($mL \cdot min \cdot m^{-2}$)	81.6 $\pm$ 4.4

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

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 (ClCr_{CG}) and by the MDRD formula (GFR_{MDRD}). The value obtained for serum creatinine on day 1 was used to calculate the ClCr_m, ClCr_{CG}, and GFR_{MDRD}. 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 GFR_{MDRD} was calculated with the following formula: $175 \times \text{plasma creatinine}^{-1.154} \times \text{age}^{-0.203}$ ($\times 0.742$ if female; $\times 1.21$ if black) [6]. The ClCr_{CG} was calculated with the following formula: $(140 - \text{age}) \times \text{body weight} / \text{plasma creatinine} \times 72$ ($\times 0.85$ for females) [7]. The measured creatinine clearance was calculated with the traditional equation: $U \cdot V / P$; where U is urine creatinine levels, V is the volume of urine by minute, and P is the plasma levels of creatinine [8]. The patients were orientated to rid themselves of the first urine on the first day of the test and then to collect in appropriate containers all the diuresis volume of the next 24 hours. The diuresis collected in the morning of the following morning was included in the total volume. This orientation was given by the doctor and referred to all the specimens. Values of expected creatinine

FIGURE 1: A comparison of the measured (ClCr_m) and estimated (ClCr_{CG}) creatinine clearances and glomerular filtration rate (GFR_{MDRD}) in patients with a single kidney.

excretion in the 24 h urine were considered to be from 20 to 25 mg/kg/24 hs (men), and from 15 to 20 mg/kg/24 hs (women). All measurements and estimation formulas were corrected for body surface area ($mL \cdot min$ per $1.73 m^2$).

2.1. Statistics. All values were evaluated for normality using D'Agostino 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 $\pm$ standard error ($X \pm SD$).

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 $81.1 \pm 35.6 mL \cdot min \cdot m^{-2}$ for ClCr_m, $70.4 \pm 24.0 mL \cdot min \cdot m^{-2}$ for ClCr_{CG}, and $71.2 \pm 19.2 mL \cdot min \cdot m^{-2}$ for GFR_{MDRD} (Figure 1). We obtained significant differences for CrCl_m versus CrCl_{CG} ($P < .001$) and CrCl_m versus GFR_{MDRD} ($P < .001$), but the values for GFR_{MDRD} and CrCl_{CG} were similar ($P = .56$). The correlation between ClCr_m and ClCr_{CG} was positive and significant ($r^2 = 0.62$, $P < .0001$; Figure 2). Additionally, the correlation between ClCr_m and GFR_{MDRD} was positive and significant ($r^2 = .36$; $P < .0001$; Figure 3). When the slope of CrCl_{CG} (0.4456 to 0.6375) was compared with the slope of GFR_{MDRD} (0.2247 to 0.4305) in relation to ClCr_m, different values were obtained ($F = 9.21718$; $DFn = 1$; $DFd = 140$; $P = .00286$; 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,

FIGURE 2: The correlation between measured (ClCr_m) and estimated (ClCr_{CG}) creatinine clearances in patients with a single kidney.

FIGURE 3: The correlation between measured creatinine clearance (ClCr_m) and the estimated GFR_{MDRD} formula in patients with a single kidney.

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

FIGURE 4: The ClCr_{CG} and GFR_{MDRD} slopes in relation to measured creatinine clearance (ClCr_m).

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 $\approx 90 \text{ mL} \cdot \text{min} \cdot \text{m}^{-2}$) 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 $90 \text{ mL} \cdot \text{min} \cdot \text{m}^{-2}$, 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.

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