
A Simple Method for Measuring Severely Reduced Glomerular Filtration Rate

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Objective: The purpose of this study was to develop a simpler method to measure severely reduced glomerular filtration rate (GFR) for patients with a GFR below 30 mL/min.

Method: The GFR was measured in 24 patients using both the ^{51}Cr EDTA slope-intercept method (the conventional method) and $^{99\text{m}}\text{Tc}$ -DTPA with our proposed simpler GFRn method.

Results: The correlation coefficient was 0.92 between the 2 methods, with a slope of 0.97 and an intercept of 2 mL/min.

Conclusion: Our simplified method for measuring GFR is accurate for most patients with severely reduced GFR. Errors are acceptably small in patients with severely reduced GFR when edema or dehydration are present. If extrarenal (liver) clearance is significant, however, a urine sampling method is required for an accurate GFR measurement.

Key Words: severely reduced renal function; glomerular filtration rate; technetium-99m-DTPA; chromium-51 EDTA

J Nucl Med Technol 2000; 28:173-175

The method we use for routine glomerular filtration rate (GFR) measurements with $^{99\text{m}}\text{Tc}$ DTPA is by a single-sample (1-3) method. When used as an adjunct to renography, the preparation of a standard from the high radioactive concentrations used for imaging requires accurate weighing technique and isotope dilution for dead-time free counting. A new standard must be made each time a GFR measurement is undertaken because of the short half-life of $^{99\text{m}}\text{Tc}$. Accurate timing of blood sampling is necessary and the method is unreliable (3,4) for GFRs below 30 mL/min.

The recommended technique for determining severely reduced GFR (less than 30 mL/min) (3) is a lengthy and complex process that requires counting 2 plasma samples, 2 accurately timed urine samples, and an estimation of residual urine.

We showed earlier (4) that:

$$\text{GFRn} = K\lambda, \quad (1)$$

where:

$$K = 13893.$$

The plasma clearance constant, λ , was a reliable method of measuring body surface area (BSA) normalized GFR in the presence of a normal size extracellular volume (ECV). The method is inaccurate in the presence of an enlarged or reduced ECV. This can be explained theoretically by assuming that GFR, as measured by the conventional slope-intercept technique, remains unchanged in the presence of an increased or decreased ECV, due, for example, to edema or dehydration. In other words:

$$\text{GFR} = \lambda_n \text{ECV} = \lambda_m (\text{ECV} + \Delta \text{ECV}), \quad (2)$$

where λ_n and ECV are the theoretically normal values and λ_m is the clearance constant, measured in the presence of an ECV increased by ΔECV .

Rearrange Equation 2 as:

$$\begin{aligned} \lambda_m &= \lambda_n \text{ECV} / (\text{ECV} + \Delta \text{ECV}) \\ &= \lambda_n / (1 + \Delta \text{ECV} / \text{ECV}) \end{aligned}$$

Take the first 2 terms of the binomial expansion:

$$\lambda_m = \lambda_n (1 - \Delta \text{ECV} / \text{ECV})$$

Incorporate this into Equation 1:

$$\text{GFRn} = K\lambda_n (1 - \Delta \text{ECV} / \text{ECV}) \quad (3)$$

Equation 3 demonstrates that there is a fractional error in GFRn measurement due to ΔECV , which is independent of GFR size. This implies that for low-GFR values, measurement by the GFRn method will be acceptably accurate in the presence of enlarged or reduced ECV. For a true GFR of 20 mL/min and a $\Delta \text{ECV} / \text{ECV}$ of 0.1, the GFRn measurement would be 18 mL/min. This small error would not cause a problem in the quantification of severely impaired renal function.

METHODS AND MATERIALS

Simultaneous measurements of GFR and GFRn were made on patients referred for conventional $^{99\text{m}}\text{Tc}$ -DTPA renography and a GFR measurement. Of these, 24 patients were selected for

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this study, where the GFR was less than 50 mL/min. The BSA-normalized GFR measurements were made with 0.1 mCi ⁵¹Cr EDTA by the Russell 2-sample, slope intercept method (5) with the Brochner-Mortensen correction (6). GFRn was measured using 3 mCi ^{99m}Tc-DTPA and Equation 1:

$$\text{GFRn} = -13893(\ln(P2) - \ln(P1))/(T2 - T1), \quad (4)$$

where Ln is the natural logarithm and P(1) and P(2) are the 3-mL plasma samples' activities taken at times T(1) and T(2) after ^{99m}Tc-DTPA injection.

The first sample must be taken when isotope equilibrium is established between the vascular and extravascular space, in other words T(1) = 90 min. Sampling time T(2) should be as reasonably long after T(1) as departmental conditions will allow. In our department, T(2) is 180 min, after injection. Note that when isotope equilibrium is established, the isotope clearance curve is monoexponential and, thus, the Ln (clearance curve) is linear. This means that sampling need not be accurately timed but sampling times are accurately known. Also note that it is the time difference (T2-T1) that is required in the calculation so that the time of injection is not needed. The ^{99m}Tc content of the plasma was counted immediately and the ⁵¹Cr was counted 3 d later after the ^{99m}Tc had decayed.

RESULTS

Figure 1 shows the regression fit, with 95% prediction limits, between GFR and GFRn for 24 patients whose GFR was less than 50 mL/min. The correlation coefficient was 0.92, slope 0.97, and intercept 2 mL/min. The GFRn errors are small, below 30 mL/min.

To quantify the GFRn error with abnormal ECV size, the following variables were calculated:

$$\% \text{ GFR Error} = (\text{GFRn} - \text{GFR}) \times 100/\text{GFR}$$

and

$$\% \text{ ECV Error} = \Delta \text{ECV} \times 100/\text{ECV} = (\text{ECVm} - \text{ECVc}) \times 100/\text{ECVc},$$

where ECVm is the patient's ECV, as measured by the GFR method, corrected for the 1-compartment assumption, and ECVc is the patient's expected ECV, as calculated using the formula of Christensen (1), in other words:

$$\text{ECVc} = 8116.6 \times \text{BSA} - 28.2.$$

Figure 2 shows the regression fit of these variables with 95% prediction limits. The correlation coefficient was 0.89, slope 0.9, and intercept 14. It is clear that as ECV increases above that expected from the patient's dimensions, GFRn proportionally decreases below GFR and vice versa. The near-unity slope confirms the derivation and validity of Equation 3.

DISCUSSION

The GFRn = Kλ method of measuring GFR will be in error when edema or dehydration is present, but these errors are acceptably small in severely reduced GFR. A useful application of the method would be to measure GFR after a renogram acquisition during which poor function is noticed and the already injected ^{99m}Tc-DTPA is sampled to measure λ. Since the first plasma sample must be taken at least 90 min after injection, ample time is available to arrange for the measurement.

The GFRn method will overestimate GFR, however, when extrarenal (e.g., liver) clearance is significant. A urine sampling method will be needed in this case for an accurate GFR.

CONCLUSION

The GFRn method has been shown to accurately measure severely reduced GFR, even in the presence of enlarged or

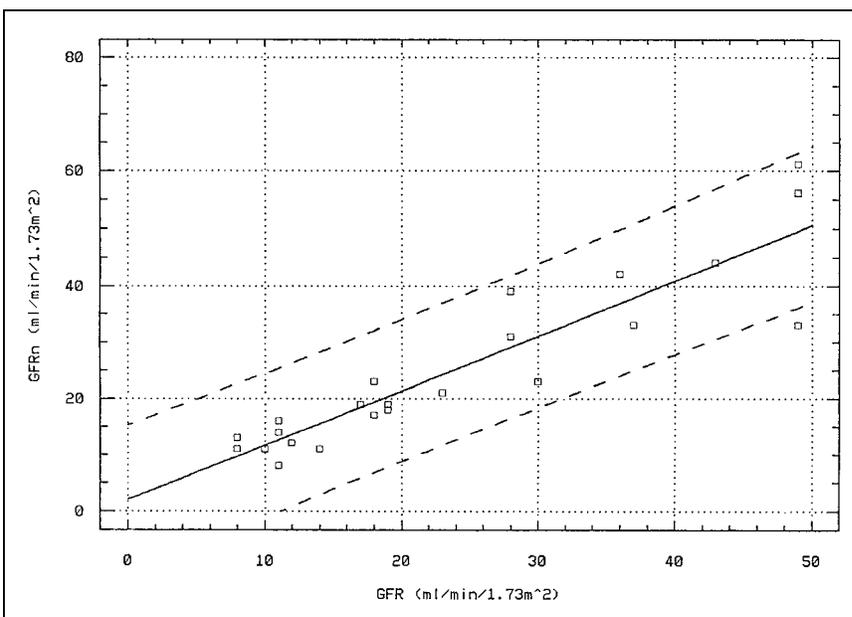


FIGURE 1. The regression fit, with 95% prediction limits, for simultaneous measurements of GFR and GFRn for 24 patients whose GFR was less than 50 mL/min. GFR was measured by the conventional slope-intercept method, with ⁵¹Cr-EDTA, and GFRn was measured by the Kλ method, using ^{99m}Tc-DTPA.

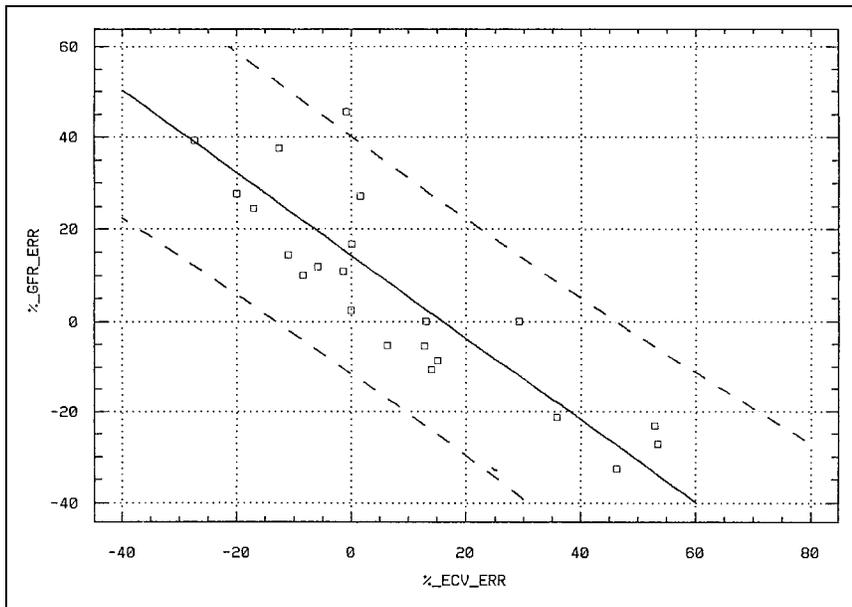


FIGURE 2. This regression curve was created to quantify the error in GFRn estimation when enlarged or reduced ECV is present in the patient. The curve demonstrates how an enlarged ECV will result in a reduced GFRn estimation compared with a GFR measurement and vice versa.

reduced ECV. Its application is simpler and, therefore, probably less prone to technical errors than urine collection techniques.

ACKNOWLEDGMENT

The poster version of this paper won first place at the 1998 biannual congress of the South African Society of Nuclear Medicine.

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