Assessment of the Plasma Volume Product to Calculate Glomerular Filtration Rate

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To further validate the rate of renal uptake of the ^{99m}Tc-DTPA-plasma volume product (RUPV) method to estimate glomerular filtration rate (GFR), 104 determinations were performed and compared to blood sample of GFR assays. The interassay consistency was also studied in 42 patients. **Methods:** The studies were performed with 370–550 MBq (10–15 mCi) of ^{99m}Tc-DTPA and a gamma camera. The 3-min cumulative renal uptake was calculated from the renogram curves and expressed as the rate of renal uptake in min^{-1}. The plasma volume, in milliliters, was estimated from the patient's body weight. The GFR (ml/min) was calculated from [RU] × [PV] and by using two blood samples. To study interassay consistency, two determinations of GFR were performed on separate days. **Results:** The regression equation relating the rate of renal uptake (RU) in the abscissa and the GFR obtained from plasma samples in the ordinate is: $y = 3.13 + 10.5x$ ($n = 104$; $r = 0.90$). The regression equation of RUPV estimated GFR (x) compared to the GFR calculated from blood samples (y) is: $y = 6.9 + 0.91x$ ($n = 104$; $r = 0.94$). The interassay consistency study showed no statistically significant difference between measurements obtained on Days 1 and 2. The mean ± s.e.m. GFR for each determination were 84.3 ± 6.12 and 81.9 ± 6.21. For the blood sample method, the mean s.e.m. for each day were 87.26 ± 6.69 and 96.86 ± 6.58 ($p < 0.05$). The percent variation coefficient for the RUPV method was: CV% = 6.8 ± 2.7 and 12.1 ± 3.3 ($p < 0.03$) for the blood sample method. **Conclusion:** The observed accuracy of the determination is comparable to that in our previous study of a separate patient population at another hospital. This method would be suitable for interinstitutional comparison and for longitudinal patient studies.

Key Words: glomerular filtration rate; renal uptake; technetium-99m-DTPA

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We have previously shown that the product of the rate of renal uptake, RU (min^{-1}) of ^{99m}Tc-DTPA and the plasma volume, PV (ml), of the patient gives a measure of the glomerular filtration rate, GFR (ml/min) (*1*). The RUPV relationship is valid when:

1. The rate of renal uptake is obtained during the initial 180 sec before urinary excretion of the tracer.
2. The tracer is confined to the vascular compartment and the kidneys at the time of measurement.
3. The tracer within the kidneys is filtered and there is no tubular reabsorption.
4. The average volume of distribution of the tracer during the measurement approximates the subject's plasma volume.

To further validate the RUPV method in a clinical setting, the GFR was calculated in 104 patients undergoing radiorenography and the results were compared to GFR calculated with a blood sample technique. In addition, the interassay consistency was studied in 42 patients who had two RUPV GFR measurements within 72 hr as part of a baseline captopril renography study.

METHODS

Patients

The patients were referred for renography or captopril renography. One hundred and four renal studies were performed with 10–15 mCi (370–555 MBq) ^{99m}Tc-DTPA on a 15-in. field of view gamma camera. The detector was positioned under the imaging table with the patient supine and data were acquired at a rate of one frame every 20 sec onto a computer for 20 min. Daily camera sensitivity measurements were performed using 1.0 mCi of ^{99m}Tc contained in a syringe on the examining table maintaining the same geometry used for clinical studies.

Data Analysis

Renal regions of interest (ROIs) and background ROIs placed inferior to the lower pole of each kidney were used to generate background-corrected time-activity renogram curves. A point on the curve 180 sec after injection was selected to calculate cumulative renal uptake.

GFR is calculated using the RUPV method as previously described (*1*). Briefly, the rate of renal uptake (RU), expressed in min^{-1}, is obtained from cumulative renal uptake at 3 min $(K_b/e^{-\mu x})/D$ divided by time (t), during which renal uptake was observed. The rate of renal uptake is:

$$RU = [(Kb/e^{-\mu x})/D]/t, \qquad \text{Eq. 1}$$

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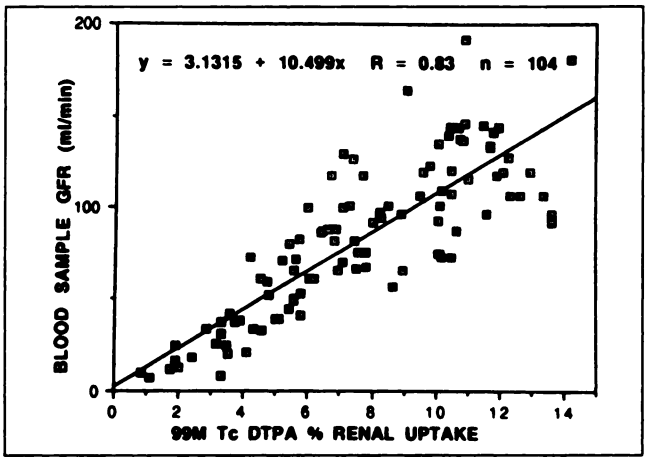

FIGURE 1. Percent renal uptake of ^{99m}Tc-DTPA at 3 min plotted against the GFR (ml/min) obtained from two blood samples.

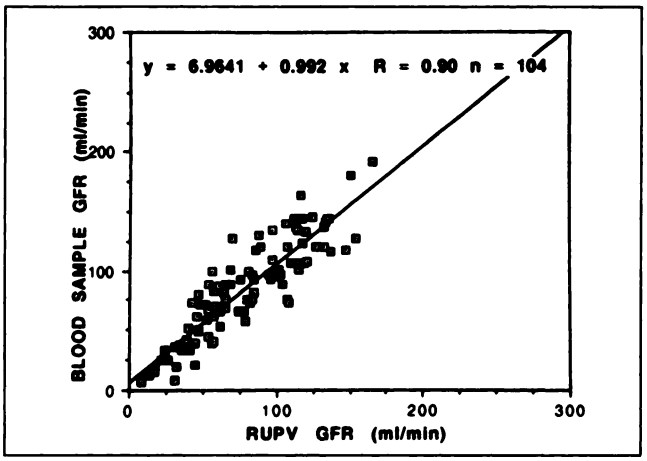

FIGURE 2. GFR calculated from the clearance of ^{99m}Tc-DTPA with the RUPV method plotted against results obtained from the two blood samples.

where K_b = the activity in the kidney expressed in microcuries, μ = the attenuation coefficient for ^{99m}Tc (0.153 cm^{-1}), x = the kidney depth according to Tønnensen (*2*) and D = the total injected dose in microcuries.

Direct plasma volume estimation was obtained from:

$$PV3 = 84.5W^{0.80635}, \quad \text{Eq. 2}$$

where W = body weight in kilograms (*3,4*).

The GFR for each kidney is obtained from the product of the rate of uptake RU and the patient's plasma volume. The total GFR is the sum of the individual kidney GFR.

An independent calculation of GFR (milliliter/minute) is performed for each patient from two blood samples at 45 and 240 min after administration of the radionuclide. Duplicate plasma samples are counted in a scintillation well counter. The total injected dose is determined from a dilution of an aliquot of the ^{99m}Tc-DTPA preparation used for the study. The plasma activity at time zero (A_0) is obtained by extrapolation and the disappearance rate (k) is obtained from the logarithmic slope. The total blood sample GFR is:

$$GFR = [TID/A_0]^* k \text{ (ml/min)}. \quad \text{Eq. 3}$$

The consistency of the RUPV method was studied in 42 patients, thus giving a measure of the intrasubject variability due to measurement error variation. These patients, who had no evidence of renovascular hypertension, had a baseline renogram followed by a post-Captopril renogram 24–72 hr later.

A two-tailed t-test was used for statistical analysis. Differences are reported as significant when $p < 0.05$.

RESULTS

The regression equation relating the rate of renal uptake and blood sample GFR (Fig. 1) is: $y = 3.13 + 10.5x$ ($r = 0.83$; $n = 104$). In Figure 2 the RUPV data are shown in the x-axis as a predictor of plasma clearance of ^{99m}Tc-DTPA measured from blood samples. A direct calculation of plasma volume and the rate of renal uptake was used to provide a good prediction of DTPA clearance as indicated by a slope of 0.99 and an intercept of 6.96 ml/min.

The mean ± s.e.m. for RUPV calculated clearance is 76.85 ± 6.15 ml/min and 83.20 ± 6.46 ml/min ($p < 0.001$) for the blood sample method.

The comparison of GFR obtained in two separate determinations in 42 subjects is shown in Figure 3 together with the 95% confidence limits. The Day 1 versus Day 2 plot has a slope of 0.91 and an intercept of 9.76 ml/min. The percent coefficient of variation (CV%) for RUPV is 6.8 ± 2.7; for the plasma clearance method, is 12.1 ± 3.3.

The mean ± s.e.m. GFR for Days 1 and 2 are 84.3 ± 6.12 and 81.90 ± 6.21 ml/min (p = ns) with the RUPV method, respectively. For the blood sample method, they are 87.26 ± 6.69 and 96.86 ± 6.58 ml/min ($p < 0.05$). The mean Day 1-Day 2 difference ± s.e.m. is −2.95 ± 4.64 ml/min for the RUPV method and −14.96 ± 4.48 ml/min for the blood sample method ($p < 0.05$).

There was no significant difference between the renal uptakes obtained on Days 1 and 2 (0.0276 ± 0.0001 and 0.0268 ± 0.0001) or between Days 1 and 2 for plasma volume estimations (3001 ± 22 and 2991 ± 22 ml).

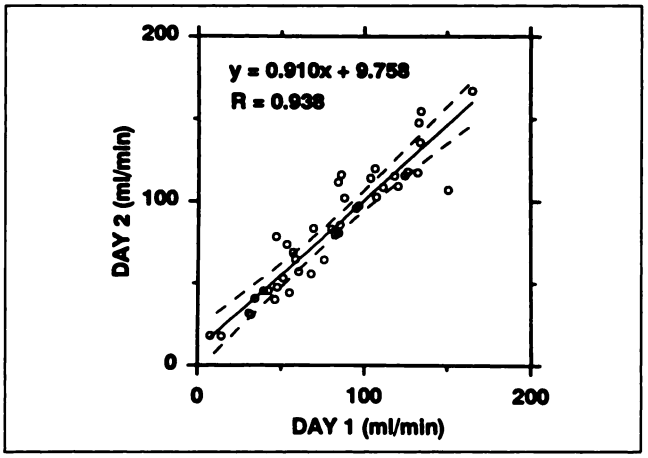

FIGURE 3. Comparison of GFR results in two separate studies obtained from 42 patients undergoing a baseline (Day 1) and a captopril (Day 2) renogram. The 99% confidence limit is shown by the dotted line.

DISCUSSION

The calculation of GFR from gamma camera images is based on the assumption that the cumulative uptake of the tracer represents the tracer filtered during the time of measurement, providing there is no urinary excretion during that time (*5,6*). These requisites define a measurement window equal to the mean renal parenchyma transit time, somewhere between 100 and 240 sec (*7*).

The ratio between cumulative renal uptake (counts accumulated during the acquisition) and plasma concentration of tracer (counts per milliliter) is the volume of plasma (milliliters) cleared during the acquisition time (3 min). The rate of clearance is the volume cleared per unit time (milliliters per minute).

The plasma concentration of the tracer is given by the dilution of the total tracer injected into the distribution volume. It is not possible, however, to obtain an accurate estimate of the distribution volume from a single blood sample because the concentration progressively declines with time. This is particularly true during the initial few minutes that follow the administration of the tracer, in which the tracer both mixes within and leaves the intravascular compartment, resulting in variable nonhomogeneous plasma concentrations. An average volume of distribution for the initial 3 min of the study was used to solve the RUPV equation, assuming that this volume approximates the plasma volume of the subject.

Other methods incorporate some estimate of plasma or blood concentration using external counting over the heart or other body regions and a blood sample to calibrate the scintigraphic data.

A simpler method would provide an estimate of the plasma clearance by correlating the renal uptake of ^{99m}Tc-DTPA to an independent measurement of GFR (i.e., inulin or creatinine clearance) (*8,9*) and applying regression equations to these two independent measurements. The latter does not require blood samples and the results are derived without the need to know the distribution volume. An improved approach (*1,5,6,10*) is to estimate the volume of distribution of the tracer to provide a direct GFR measurement in milliliters per minute. This is preferred because the results are related to individual patients and are not drawn from a regression equation obtained from an unrelated group of patients.

This study correlates well with the results of an earlier report (*1*). The accuracy of the test is essential to allow interinstitutional comparison of test results. To achieve this objective before adopting the RUPV or any other scintigraphic method, an effort should be made to relate the results to the blood sample calculated clearance of the tracer. This relatively simple validation will reinforce the confidence about test performance and interpretation.

The consistency of the test is critical to evaluate temporal changes in renal function in an individual. We have found a good correlation between two separate determinations in 42 patients ($r = 0.94$). The %CV of 6.8 ± 2.7 is well within the accepted range for most GFR methods (*10*). Gates has also found excellent reproducibility ($r = 0.99$) with scintigraphic GFR calculation in 15 individual kidneys (*8*). In comparison, the more cumbersome blood sample technique is commonly performed by different technologists, and requires proper collection and handling of the samples, preparation of standards and counting, which has, in our hands, a %CV of 12.1 ± 3.3.

Factors that can affect the consistency of scintigraphic measurements are: camera sensitivity, calculation of the net injected dose, selection of renal and background ROIs and the accurate choice of the 3-min mark on the background-corrected time-activity curves. Dedicated software that provide automatic ROI outlines and background correction with minimal operator intervention may be helpful to ensure better results by reducing intra- and interoperator variability.

Although there are errors associated with the use of a nomogram to estimate plasma volume from the patient's weight, the plasma volume calculation is not prone to significant operator errors.

CONCLUSION

The reproducibility of these scintigraphic techniques makes the method suitable for routine clinical application. Because the scintigraphic calculation of GFR is simple, we suggest, even for those institutions where blood samples are routinely obtained for GFR calculation, to perform a simultaneous gamma camera calculation of GFR as an additional control of measurement accuracy.

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