Determination of glomerular filtration rate with radionuclide renography and direct urinary activity quantitation

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Objective. The direct urinary activity quantitation method is quick (approximately 40 minutes), requires only a single blood sample, is performed as part of standard renal scanning and shows high accuracy compared with 24-hour creatinine clearance. The purpose was to evaluate the practical application and accuracy of this technique at our clinic.

Design. Direct urinary activity quantitation was done in patients scheduled for routine radionuclide renography and compared to standard multiple-blood-sample techniques by means of Cr-51-EDTA and Tc-99m-DTPA.

Setting. Academic Medical Complex, Department of Nuclear Medicine, Universitas Hospital, Bloemfontein.

Participants. Fifteen patients scheduled for routine radionuclide renography (glomerular filtration rate (GFR) determination) were voluntarily enrolled in the study. The GFRs of selected patients varied over a wide range. Possible obstructive uropathy was excluded.

Main outcome measures. GFRs obtained by the direct urinary method were compared with GFRs determined by multisample Cr-51-EDTA and Tc-99m DTPA.

Results. GFRs from the direct urinary method compared with multisample Tc-99m-DTPA showed differences from –19,85 to 22,95 ml/min with a mean of 0,2 (± 12,25) ml/min (r = 0,93). When compared with multisample Cr-51 EDTA, differences ranged from –34,35 to 21,05 ml/min with a mean of –4,25 (± 16,08) ml/min (r = 0,90).

Conclusion. The direct urinary activity technique is easily applied and highly accurate compared with previous standardised multisample radionuclide techniques for determination of GFR.

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Measurement of total glomerular filtration rate (GFR) of both kidneys provides a sensitive and commonly employed index of overall renal excretory function.[1] It is usually measured by creatinine clearance. This method is generally accepted because of the constant endogenous production of creatinine, which is completely filtered down by the glomeruli and only secreted by the tubules to a small extent.[2] Several nuclear medicine techniques for measuring GFR using Cr-51-EDTA (diethylene triamine penta-acetic acid) and Tc-99m-DTPA (ethylene diamine tetra-acetic acid) are in use today.[3] Among these, determination of GFR by means of the direct urinary method with Tc-99m-DTPA was reported by Jackson *et al.*[4] to have specific advantages. It is quick (approximately 40 minutes), requires only one blood sample, is performed as part of standard radionuclide renography and shows high accuracy compared with 24-hour creatinine clearance. The purpose of this study was to evaluate the practical application of this technique at our clinic and to compare it with multiple blood sample techniques using Tc-99m-DTPA and Cr-51-EDTA, the latter having been accepted as an accurate method for many years.

Patients and methods

Nine male and 6 female patients aged 18 - 69 years (mean 37 years) and referred for radionuclide renography were studied. Kidney functions varied over a wide range. Patients with possible urinary obstruction were excluded. Informed consent was obtained in each case. The study was also approved by the local ethics and radiation control committees.

The studies were performed with a dual-headed scintillation camera fitted with low-energy high-resolution collimators. The patients were given 250 - 500 ml water to drink before being positioned supine to include the heart and kidneys in the field of view; 111 - 296 MBq (3 - 8 mCi) Tc-99m-DTPA (AEC, Pelindaba) and 3,7 MBq (100 µCi) Cr-51-EDTA (Amersham, UK) were administered intravenously. Dynamic imaging was performed for 30 minutes with a 128 x 128 word matrix and for 15 seconds per image. Only the posterior views of the heart were used for calculation. Blood samples were drawn at 6, 12, 18, 24, 30, 60, 120, 180 and 240 minutes after injection. On completion of the dynamic acquisition, each patient was requested to stand upright for a few seconds in order to enhance drainage of activity from the renal calices. This is important and has not been emphasised previously. The patient was then repositioned for a 60-second pre-void anterior bladder image. After voiding, a similar post-void anterior image was obtained. The volume and radioactive concentration of the voided urine were subsequently determined.

The total urinary activity (TUA) excreted from injection to time of completion of post-void image (time t) was calculated as described by Jackson *et al.*:[4]

$$TUA = \frac{Pre\text{-void counts} \times U \times Vu}{Pre\text{-void} - \text{post-void counts}}$$

where U is the radioactive concentration and Vu the volume of the voided urine.

The kidney clearance (Cl) was then determined as:

$$Cl = \frac{TUA}{P \times t}$$

with P the mean plasma activity concentration from injection to time t obtained from a region of interest over the heart and a plasma sample taken at 30 minutes.[4]

In the multiple blood sample technique Tc-99m-DTPA and Cr-51-EDTA plasma activity from all blood samples was determined and clearance calculated by means of a dual compartmental-fitting algorithm for each radionuclide.[5] The methods were compared by calculations of 95% confidence intervals and linear regression analysis.

Results

The GFR values of the 15 patients are shown in Table I as well as the differences between the direct urinary method and the two multisample methods. GFR as determined with the direct urinary method had a mean value of 84,28 (± 35,84) ml/min. The multisample method with Tc-99m-DTPA (MSTc) and Cr-51-EDTA (MSCr) yielded mean values of 84,07 (± 33,74) ml/min and 88,52 (± 34,70) ml/min respectively. The differences between the direct urinary method and MSTc ranged from –19,85 ml/min to 22,95 ml/min with a mean of 0,21 (± 12,25) ml/min. The differences obtained when MSCr measurements were compared with the direct method ranged from –34,35 ml/min to 21,05 ml/min with a mean of –4,24 (± 16,08) ml/min.

Table I. GFR values obtained with the different radionuclide methods

Patient	Direct method (DU) (ml/min)	Tc-99m DTPA (MSTc) (ml/min)	Difference (DU-MSTc)	Cr-51 EDTA (MSCr) (ml/min)	Difference (DU-MSCr)
1	90,07	97,30	–7,23	107,80	–17,73
2	106,18	109,80	–3,62	98,50	7,68
3	104,54	121,70	–17,16	96,80	7,74
4	73,92	65,80	8,12	66,10	7,82
5	122,08	109,60	12,48	139,70	–17,62
6	94,45	114,30	–19,85	128,80	–34,35
7	123,14	124,90	–1,76	138,10	–14,96
8	114,85	91,90	22,95	93,80	21,05
9	88,04	90,40	–2,36	71,50	16,54
10	98,52	85,40	13,12	102,20	–3,68
11	8,69	12,70	–4,01	12,90	–4,21
12	23,83	24,50	–0,67	52,30	–28,47
13	111,71	92,40	19,31	100,80	10,91
14	82,44	85,60	–3,16	80,70	1,74
15	21,67	34,70	–13,03	37,80	–16,13
Mean	84,28	84,07	0,21	88,52	–4,24
SD	35,84	33,74	12,25	34,70	16,08

The 95% confidence intervals for the different parameters were as follows: direct urinary method 64,4 to 104 ml/min; MSTc 65,4 to 103 ml/min; MSCr 69,3 to 108 ml/min; direct urinary method-MSTc –6,57 to 6,99 ml/min and direct urinary method-MSCr –13,1 to 4,66 ml/min. These data indicate good agreement between the different methods for obtaining GFR.

Figs 1 and 2 demonstrate the curves obtained with regression analysis when the direct urinary method was compared to the MSTc and MSCr methods respectively. The regression equations were direct urinary method = 0,998 MSTc + 0,35 (r = 0,93) and direct urinary method = 0,926 MSCr + 2,30 (r = 0,90) respectively, indicating good agreement between the direct method and GFR obtained from multisample determinations.

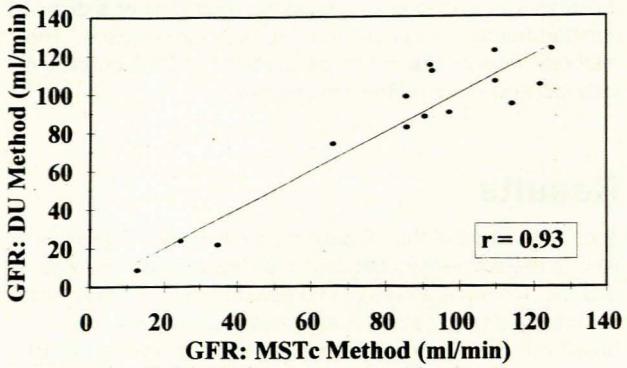

Fig. 1. Linear regression analysis of GFR obtained via the direct urinary (DU) method v. GFR from multiple blood samples using Tc-99m-DTPA (MSTc) (DU = 0,998 MSTc + 0,35).

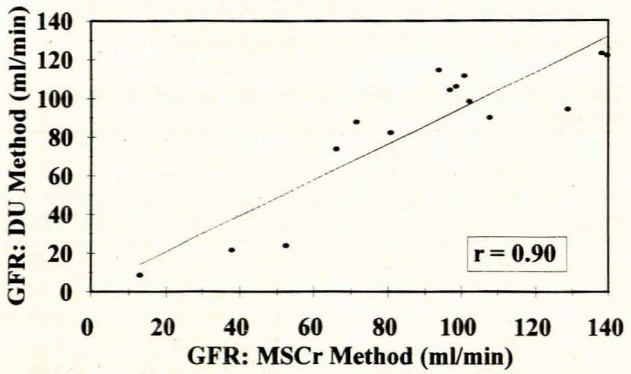

Fig. 2. Linear regression analysis of GFR obtained via the direct urinary (DU) method v. GFR from multiple blood samples using Cr-51-EDTA (MSCr) (DU = 0,926 MSCr + 2,30).

Discussion

Determination of GFR is clinically used to quantify kidney function. It is affected mainly by arterial blood pressure, colloid osmotic pressure and glomerular afferent and efferent arteriolar resistance. The GFR is relatively stable in the physiological range of arterial pressure (80 - 180 mmHg) by adaptation of the other variables through autoregulation.[6] Conventional methods of GFR measurement that use radioactive tracer and creatinine clearance may be accurate but are often tedious. With creatinine clearance the 24-hour urine collection should be accurate for precise results.[7] Different radioactive tracer techniques for the determination of GFR are usually based on one or more of the following: measurement of activity in one, two or multiple blood samples to determine plasma clearance, rate of removal of activity from blood or tissue, rate of appearance of tracer in the urine and rate of renal tracer uptake.[3] Of these techniques, the measurement of GFR by the direct urinary method reported by Jackson *et al.*,[4] showed a high correlation with creatinine clearance (r = 0,96). Similar accuracy was reported when the direct method was compared with different radionuclide methods of multiple blood sample techniques to determine DTPA clearance.[3] In our study a good level of accuracy and precision were found according to the 95% confidence intervals when the direct method was compared with multiple blood sample techniques using Tc-99m-DTPA and Cr-51-EDTA clearance.

The advantages of the direct urinary method can be summarised as follows.[3,4] It decreases the problem of DTPA protein-binding which becomes more important when blood samples have to be taken over several hours. As the DTPA concentration in the plasma decreases the protein-bound fraction becomes more significant.[8] It overcomes the problem of volume of distribution which varies with different commercial products of DTPA. Volume of distribution is also important when early renal uptake of tracer is used to determine GFR and could influence this significantly. It overcomes the problems of creatinine clearance of 24-hour urine collection, varying endogenous creatinine production and tubular secretion of creatinine; the latter becomes more important with lower values of GFR. Measurement of syringe activity before and after administration becomes unnecessary, as is the case with the indirect methods. These are based on blood sampling to determine plasma clearance or rate of renal tracer uptake. The problem of multiple blood samples is also overcome thus, since only one sample is necessary.

The disadvantages of the direct urinary method centre on two aspects, viz. the inaccuracy of vesical activity with renal outflow obstruction and the relative inconvenience of sampling and handling of urine. Errors as a result of stasis can be reduced by the patient's being in the upright position to enhance drainage of activity to the bladder before imaging.

We found the direct urinary method easy to implement in combination with Tc-99m-DTPA renography. In comparison with the multiple blood sample techniques using Cr-51-EDTA and Tc-99m-DTPA, accuracy was maintained over a wide range of kidney function.

REFERENCES

1. Braunwald E, Isselbacher KJ, Petersdorf RG, Wilson JD, Martin JB, Fauci AS. *Harrison's Principles of Internal Medicine.* 11th ed. New York: McGraw-Hill, 1987: 1143-1144.
2. Hladky SB, Rink TJ. *Body Fluid and Kidney Physiology.* London: Edward Arnold, 1986: 36-57.
3. Mulligan JS, Blue PW, Hasbargen JA. Methods for measuring GFR with technetium-99m-DTPA: an analysis of several common methods. *J Nucl Med* 1990; **31:** 1211-1219.
4. Jackson JH, Blue PW, Ghaed N. Glomerular filtration rate determined in conjunction with routine renal scanning. *Radiology* 1985; **154:** 203-205.
5. Cohen ML. Radionuclide clearance techniques. *Semin Nucl Med* 1974; **4:** 23-38.
6. Bray JJ, Cragg PA, Macknight ADC, Mills RG, Taylor DW. *Lecture Notes on Human Physiology.* London: Blackwell Scientific Publications, 1989: 520.
7. Gates GF. Glomerular filtration rate; Estimation from fractional renal accumulation of ^{99m}Tc-DTPA. *AJR* 1982; **138:** 565-570.
8. Klopper JF, Hauser W, Atkins HC, Eckelman UC, Richards P. Evaluation of Tc-99m-DTPA for the measurement of glomerular filtration rate. *J Nucl Med* 1972; **13:** 107-110.

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