Determination of Glomerular Filtration Rate by Using Gamma Camera

H.I. Mansour* , M. A. Mohamed** , Mona A .Koshlaf***

Faculty of Education - Janzoor , Tripoli University*
Physics Department
Libyan Academy for Graduate Studies**
School of Medical Science
Libyan medical Research Center AL Zawya***
Mohamed.Amer@academy.edu.Ly

الية تقنيةِ آلةِ تصوير جاما كَانتْ حوالي 16 % , 12 % و8 % لقِيَمِ معدل الترشيحِ الكُبيبيِ (GFR) 30 , 60 و100 مل لكل دقيقة , لذا، فإن ثقة آلةِ تصوير جاما وطريقةَ العيّنةِ المتعدّدةِ المُبَسَّطةِ لتنبؤِ بمعدل الترشيحِ الكُبيبيِ (GFR) كَانتْ تقريباً متساوية.

ABSTRACT

Glomerular filtration rate (GFR) is a commonly accepted standard measure of renal function. It is routinely measured using tracers that are cleared exclusively by glomerular filtration.

The aim of this study was to apply new nuclear medicine technique based on direct determination of clearance of a radioactive tracer provided that all the uptake compartments of the radioactive tracer should be included in the field of the view of the gamma camera.

A total of 10 men and 7 women range from 27 to 64 years old were studied using dual head gamma camera. The data for clearance calculation comprises : (1) a transmission scan of part of the body using water phantom with a uniform distribution of the radioisotope , (2) the background corrected activity curves in the anterior and posterior views over all uptake compartments following the injection of radioactive tracer, and (3) the activity of radioactive tracer in two blood samples drawn during the examination. The results for GFR above 30 ml min^{-1}, the regression line of GFR by using simplified multiple sample method versus GFR in gamma camera method were not significantly different from the line of identity.

The reliability of the gamma camera method was about 16%, 12 % and 8% for GFR values of 30, 60 and 100 ml min^{-1}. Therefore, the reliability of the gamma camera and the simplified multiple sample method for prediction of GFR were almost the same.

Introduction

Determination of clearance in nuclear medicine are predominantly indirect methods, i.e, the decline of plasma concentration curve of the radioactive indicator is interpreted as both uptake of the indicator by an organ and exchange of the indicator with large extravascular space. The determination of glomerular filtration rate (GFR) with ^{51}Cr-EDTA is for example, one of the most widely used indirect clearance methods in nuclear medicine. Until about 12 years ago the simplified multiples sample method (MSM), with blood samples drawn 3-5 h following the injection of ^{51}Cr-EDTA, was the method of the choice in routine clinical work [1]. In recent years several alternative indirect methods based on the single sample method have appeared [2-5]. They rely only on a single blood sample taken within a certain time interval following the injection of the radioactive indicator. The single sample method is faster than the MSM but it is less reliable, in particular at very low GFR.

The calculation of GFR in renography with ^{99m}Tc diethylenetriaminepetaacetic acid (^{99m}Tc- DTPA) method is yet another example of direct clearance method which has been used for many years [6]. Determined the single kidney GFR as the ratio of the derivative with time of the renogram at about 2 min to plasma concentration of ^{99m}Tc- DTPA at this time, this method has some similarities to the method described in this study. Gates'method [7-8] gained widespread use for estimation GFR without the need for drawing plasma samples. GFR was estimated as ration of the sum of the net left and right renal count rates at times before the first disappearance of ^{99m}Tc- DTPA from the kidneys to the injected dose in the kidney measurement geometry. Kidney depth was estimated based on weight and height. The standard error of the estimate (SEE) of the calculated GFR versus GFR taken as the creatinine clearance was 8.4 ml.min^{-1}. During the last two decades many modified version of Gates' method have been published for determination of GFR with ^{99m}Tc-DTPA [8-10] and with markedly different SEE values when predicted GFR. Rehling *et al* [9] report SEEs of 8.3 and 11.8 ml.min^{-1} for GFR 50 and 100 ml.min^{-1} while Carlsen *et al* [10] find an SEE as high as 19.1 ml.min^{-1} in Gate's method.
The present study gamma camera is used for clearance determination, dual head camera is used to compensate for different depths of the uptake compartments and a flood field phantom for determination of the absolute transmission of radioisotope through the body at the level of uptake compartments. In addition , a few blood samples are drawn during the examination. Hence, the gamma camera technique for direct determination of clearance is somewhat more cumbersome than, for example routine renography alone. The recording of transmission scan and of the renal images in posterior and interior views replace the measurement of kidney depths in lateral view from scintigraphic images or

by CT methods. Further, the drawing of a few blood samples during the examination converts the gamma camera into a device for absolute measurements.

Material and methods

A total number of 17 patients (10 males, 7 females: age range 27-64 years, mean age = 57.53) were studied. Patients both with normal and with increased plasma concentration of creatinine were included in order to cover a wide range of GFRs.

The determination of GFR was made according to the simplified multiple samples method with ^{51}Cr-EDTA and with four blood samples drawn 3 h post-injection with a time interval of 20 min [1]. The plasma clearance of ^{51}Cr-EDTA was corrected for one compartment model, extra-renal clearance and for the underestimation of the renal of EDTA by 10% in comparison inulin clearance [1]. If the estimated endogenous creatinine clearance was below 30 ml.min^{-1}, five blood samples were drawn 3 h post-injection with time interval of 30 min. the radioactive indicator was injected through a catheter into an arm vein while the blood samples were drawn from a venous catheter of the same type in the contralateral arm. Plasma samples of 2 ml each were counted together with 2 ml ^{51}Cr-EDTA standard samples in the well counter.

Imaging protocol with flood phantom

The patient lay in supine position on the imaging table with the detectors of dual head gamma camera (Sophy DXE-2) in the posterior and anterior views at the level of the kidneys and bladder. The gamma camera was mounted with a set of low energy, high resolution collimators. A large water filled flood field phantom with bout 300 MBq $^{99m}TcO_4$ uniformly mixed in water was laced between the imaging table and the lower detector. The upper and lower detectors were close to patient and the flood field phantom, respectively. A set of two static images was recorded for 3 min. The flood field was removed from the examination room and the lower detector was positioned just below the imaging table. As a preparation before the start of the renographic examination, the patient was asked to void the bladder.

Renographic imaging protocol

The catheter used for injection of ^{51}Cr-EDTA was also used for the bolus injection of about 200 MBq of ^{99m}Tc- DTPA. Dynamic images of size 64 x 64 pixel were acquired simultaneously in the posterior and anterior view for 40 min with a sampling time of 10 sec. The energy window setting around the ^{99m}Tc photon peak was 20%. At times about 10, 20, and 30 min post injection blood samples were drawn from the venous catheter in the contralateral arm.

Generation of time-activity curves in the renography

Region of interest (ROIs) were drawn around the left and right kidney and bladder in posterior view. Subsequently, background ROIs were drawn around the kidneys and the bladder (fig.1). The images in the anterior view were mirrored and the six ROIs from the posterior images were overlaid the anterior images. The posterior ROIs were either accepted for use in the interior view or slightly adjusted manually to fit the anterior images series.

The six time-activity curves (TACs) corresponding to the two kidneys and the bladder in the posterior and anterior views were generated and corrected for

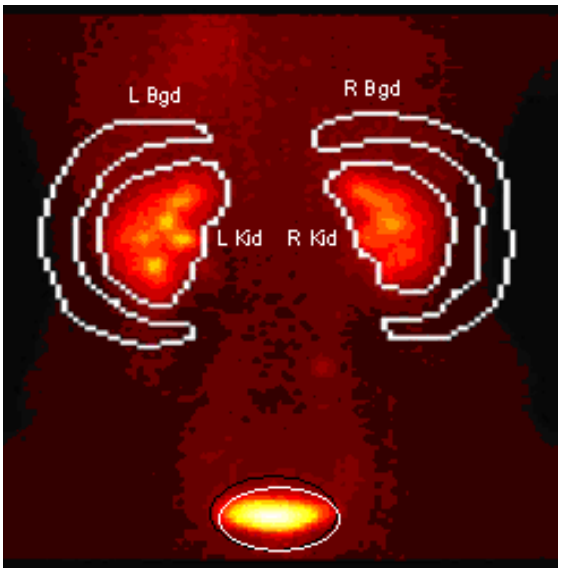

Fig. 1 Creation of ROI over the kidneys , the bladder, and the background areas in the posterior view.

background radiation using the TACs generated from the background ROIs, and finally, the net activity curves were corrected for the decay of ^{99m} Tc.

Methods

Let $K_{post}(t)$ and $K_{ant}(t)$ denote the background corrected count rates from the left or right kidney in posterior and anterior views, respectively. Then $K_{post}(t)$ can be expressed as:

$$K_{post}(t) = TF_{it} \cdot \exp(-\mu \cdot KCD_{post}) \cdot K(t) \quad (1)$$

Where TF_{it} is the transmission factor of the imaging table and **μ** is the linear attenuation coefficient of ^{99m}Tc in the body (0.12 cm^{-1}). KCD_{post}, denotes the kidney center distance in the posterior view and K(t) represents the net renal count rate at time t corrected for attenuation. For $K_{ant}(t)$ we obtain a similar expression:

$$K_{ant}(t) = \exp(-\boldsymbol{\mu}.KCD_{ant}) \cdot K(t). \quad (2)$$

Solution of Equation 1 and 2 with respect to K(t) yields

$$K(t)2 = K_{post}(t) \cdot K_{ant}(t) / [TF_{it} \cdot \exp(\mu \cdot PT_k)] \quad (3)$$

Where PT_k represents the patients thickness at the level of kidneys, i.e , the sum of KCD_{post} and KCD_{ant}. The denominator of Equation 3 is equal to the transmission factor of TF_k of ^{99m}Tc for the left or right kidney region and the imaging table:

$$TF_k = TF_{it} \cdot \exp(-\boldsymbol{\mu}.PT_K) \quad (4)$$

Using the counts determinations by the two detectors within the whole kidney ROIs of the flood field phantom, the transmission factor TF_k for left or right kidney region can be calculated as

$$TF_k = CTS_{k,pat} / CTS_{k,dir} \quad (5)$$

Define S_{gc} as the sensitivity of the gamma camera in, for example, cps.MBq^{-1} at the surface of the collimator.
Then we have:

$$KC(t) = (1/S_{gc}) \cdot K(t) \quad (6)$$

Where KC(t) denotes the kidney contents of ^{99m}Tc-DTPA (in MBq) at time t. After insertion of KC(t) from Equation 6 and TF_k from Equation 4 into Equation 3 we obtain:

$$KC(t) = (1/S_{gc}) \cdot [K_{post}(t) \cdot K_{ant}(t) / TF_k]^{½} \quad (7)$$

A formula similar to Equation 7 holds for bladder contents BC(t) of ^{99m}Tc-DTPA (in MBq) at time t.

$$BC(t) = (1/S_{gc}) \cdot [B_{post}(t) \cdot B_{ant}(t) / TF_b]^{½} \quad (8)$$

Where the transmission factor TF_b for the bladder region is determined as

$$TF_b = CTS_{b,pat} / CTS_{b,dir} \quad (9)$$

The total kidney uptake TKU(t), i.e, the quantity of ^{99m}Tc-DTPA (in MBq) taken up by the two kidneys at time t is calculated as:

$$TKU(t) = KC_{lk}(t) + KC_{rk}(t) + BC(t) \quad (10)$$

Where lk and rk refer to the left kidney and right kidney, respectively. The total kidney uptake curve always monotonically increase with time and, theoretically, with the net injected dose as the asymptotic value.
The plasma samples of ^{99m}Tc-DTPA drawn, for example, at 10,20 and 30 min post-injection are converted into plasma concentration Cp (in MBq.ml^{-1}) as follows:

$$C_p = DF.S_{wc} .CPM_{ps} \quad (11)$$

Wher CPM_{ps} denotes the count rate (in cpm) in the well counter of a 1ml plasma sample, and S_{wc} is the sensitivity of the well counter (in MBq /cpm) calibrated using the nuclear medicine dose calibrator. DF is the decay factor of ^{99m}Tc from injection time to the measurement time.
Let CLR denote the clearance of ^{99m}Tc-DTPA (in ml.min^{-1}). The total kidney uptake (in MBq) at time t can be expressed as follows:

$$TKU(t) = CLR\int_{t1}^{t} C_p(T)dt + TKU(t_1) \quad (12)$$

Where $C_p(t)$ denotes C_p at time t and $TKU(t_1)$ is the value of TKU at time t_1.

The set of plasma concentration in Equation 11 is exposed to a monoexponential curve fit:

$$Cp(t) = \alpha \cdot (\exp \beta t) \quad (13)$$

Where α and β have the dimensions MBq .ml^{-1} , respectively.

Let f(t) denote the integral of Cp(t) from time t_1 to time t. For monoexponential fit for Cp(t) as in Equation 13 we obtain:

$$F(t) = (\alpha / \beta) . [\exp(\beta t) - \exp(\beta t_1)] \quad (14)$$

Substitution of this expression for the integral of Cp(t) in Equation 12 gives

$$TKU(t) = CLR . f(t) + TKu(t_1) \quad (15)$$

Linear regression with constant term of TKU(t) versus f(t) for values of t in an interval from time t2 to t1 yield values for CLR and TKU(t1). Since the monoexponential fit in Equation 13 is not valid at times much earlier than the first sampling time of to min or much later than the last sampling time of 30 min, the linear regression in Equation 15 will be made for t_1 equal to 7.5 min and t_2 equal to 32.5 min.
Since the clearance of ^{51}Cr-EDTA underestimates the clearance of inulin by 10% [1] , GFR is calculated as:

$$GFR = 1.1 . CLR \quad (16)$$

Recall that, since the present gamma camera technique is direct method, there are no extra-renal contribution to be accounted for CLR. The renal plasma clearance of ^{99m}Tc-DTPA is assumed to be identical to that of ^{51}Cr-EDTA [14]

Figure 2 shows the final results of an example from a patient with total and single kidney GFR values based on the gamma camera technique. We chose an example with normal renal outflow from one kidney and very delayed outflow.

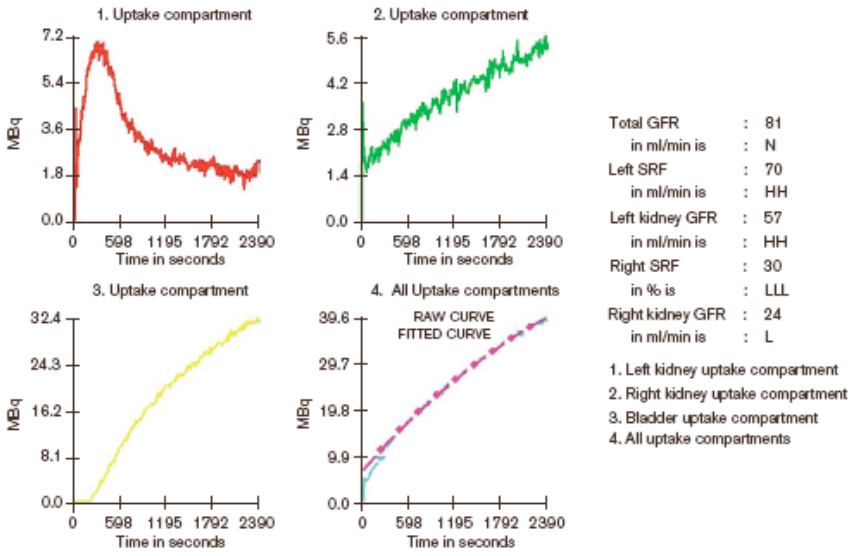

Fig.2 Example of final results of the gamma camera method applied to a ^{99m}Tc-DTPA renography examination.

Results and Discussion

The results of weighted linear regression of the multiple samples method GFR_{msm} versus the gamma camera method GFR_{gm} in the patient material are shown graphically in Fig.3. The regression line can be expressed as:

$$GFR_{msm} = (0.863 \pm 0.042) \, . \, GFR_{gm} + (8.03 \pm 2.42) \qquad (17)$$

Where GFR_{msm} is in $ml.min^{-1}$, and the mean ± 1 SD are indicated for the slope and intercept. The slope and the intercept are significantly different from unity and zero , respectively.

The SEE of GFR_{msm} around the regression line was:

$$SEE = 0.953 \, . \, (GFR_{gm})^{½} \qquad (18)$$

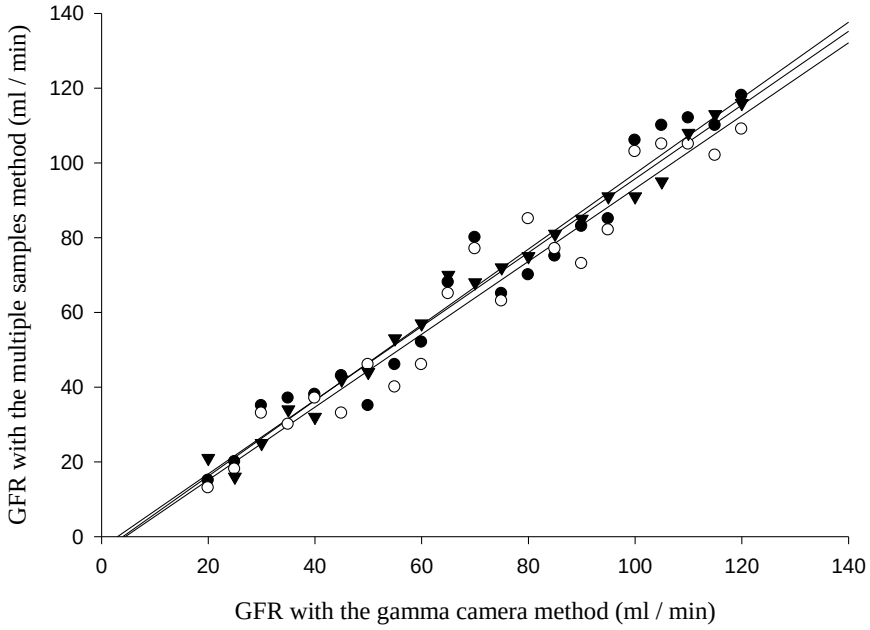

Fig.3 Linear regression of GFR determined with the sampling method using ^{51}Cr-EDTA versus GFR determined with the gamma camera method in ^{99m}Tc-DTPA renography.

For values of GFR_{gm} of , for example, 30 ,60 and 120 ml-min^{-1}. the mean ± 1 SD of the estimated GFR by sampling method based on Equation 17 and 18 were 31.45 ± 5.3 ml.min^{-1} , 58.2 ± 7.6 ml.min^{-1}, and 113.5 ± 10.2 ml.min^{-1} corresponding to values of coefficient of variation of 17.0% , 13.0% and 9.5%.

The reliabilities of gamma camera method alone were calculated as 13.5% , 10.4% and 5.4% for GFR_{gm} of 30 ,60 and 120 ml.min^{-1}. These reliabilities should be compared with corresponding values of the sampling method, i.e , 10% 7.5% and 7.7%.
The reliabilities of gamma camera method and sampling methods are of the same magnitude. From a practical point of view the two methods may be regarded as equally good for the prediction of GFR when GFR is about 30 ml.min^{-1} or higher.

The results for the total patient show a regression line of GFR_{msm} versus GFR_{gm} significantly different from the line of identity. The simplified multiple samples method has an essential limitation : it becomes increasingly more accurate at GFR values below 30 $ml.min^{-1}$, a phenomenon caused by the extraction renal clearance of ^{51}Cr-EDTA and to the fact that the terminal exponential of the plasma clearance curve may not be reached during the plasma sampling period. This will lead to an overestimation of GFR at low GFR values for GFR_{gm} below 30 $ml.min^{-1}$ were above the regression line in Equation 17 when these subjects were excluded from the regression analysis, although thy were not above the upper 95% significance limit.

In other study by Moore *et al*.[11] it was concluded that the plasma clearance curve did not reach the true terminal exponential by 2 h as usually assumed. As a matter of fact , they presented evidence that the true terminal exponential is not reached until times later than 4h. Therefore, the conventional multiple samples method with ^{51}Cr-EDTA overestimated true renal clearance by 10%.

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