Original Article

Impact of Body Mass Index on Gates Method of Glomerular Filtration Rate Estimation: A Comparative Study with Single Plasma Sample Method

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Abstract

Purpose of the Study: This study aims to compare glomerular filtration rate (GFR) estimated by Gates method using gamma camera (GC) with single plasma sample method (SPSM) in people with normal and abnormal body mass index (BMI) using SPSM as gold standard. **Materials and Methods:** It was single-center prospective study including 60 voluntary kidney donors. Technetium-99m labeled Diethylene Triamine Pentaacetic Acid (^{99m}Tc-DTPA) was administered intravenous under GC. GFR was calculated using Gates Method. After the scan, the subjects were called again after 180 min of injection of ^{99m} Tc-DTPA. Then, a 3 ml venous blood sample was obtained from the contralateral arm. Russell's formula was used to determine the GFR by SPSM. **Results:** Mean GFR calculated by SPSM and Gates' method, was 94.0 ± 15.2 ml/min/1.73 m^2 and 87.3 ± 16 ml/min/1.73 m^2 respectively. Moderate correlation noted between two methods (r = 0.71, P < 0.0001). Significant correlation noted between GFR calculated by SPSM and Gates method in people with normal BMI (r = 0.92) with no significant statistical difference (P = 0.8). However, only moderate correlation noted between GFR calculated by SPSM and Gates method in people with BMI outside normal range (r = 0.71) with a significant statistical difference (P = 0.0002). **Conclusion:** Gates method of GFR estimation using GC shows significant correlation with plasma sample technique in people with normal BMI. In people with BMI outside normal range, it significantly underestimates GFR.

Keywords: *Body mass index, gates method, glomerular filtration rate, single plasma sample method*

Introduction

Glomerular filtration rate (GFR) is the rate at which fluid is filtered by the kidneys. It is a measure commonly used to assess renal function, especially in donors for renal transplant.[1]

GFR is usually assessed by measuring blood urea nitrogen and serum creatinine. Although widely used, these endogenous markers are not ideal and depend on lots of other factors, hence not reliable. The other methods for determining GFR is to measure the clearance of exogenous substances such as inulin, iohexol, chromium- 51-ethylenediaminetetraacetic acid, Technetium-99m labeled Diethylene Triamine Pentaacetic Acid (^{99m}Tc-DTPA) or I-125 labeled iothalamate.[2] Estimation of GFR by Tc-99m DTPA plasma clearance has gained significant popularity due to its simplicity and precision.[3] Good correlation between ^{99m}Tc-DTPA plasma clearance and inulin clearances when measuring GFR in clinical applications has been reported.[4] Various techniques of plasma clearance of ^{99m}Tc-DTPA have been employed to estimate GFR. Multisample technique in which blood samples are taken at 5, 10, 15, 30, 45, 60, 120, 180, and 240 min was introduced initially. A time-activity curve is plotted, and GFR is calculated from dose divided by the area under the curve. Since it is exhaustive and difficult to perform in routine clinical practice, single plasma sample method (SPSM) and double plasma sample method of GFR estimation were derived from the multi-sample technique. Multi, double, and single sample techniques were observed to have a significant correlation.[5] Apart from plasma sample technique, few computer-based methods have also been developed among which gamma camera (GC)-based method became highly popular as it can provide an immediate calculation of individual kidney function as well as of global renal function. Gary Gates first computed GFR from the scintigraphic determination of ^{99m}Tc-DTPA uptake within the kidneys, and since then

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this method has become universal and versatile, but its accuracy is debated.[6] Many studies in the past reported lower accuracy of the GC method in determining GFR as compared to plasma sample technique.[7-10] One of the potential sources of error while calculating GFR by Gates method is the calculation of renal depth which is done by Tonnesen equation. However, few studies have shown that Tonnesen equation is reliable when body mass index (BMI) is within the normal range. It significantly underestimates renal depth in people whose BMI is out of the normal range.[11-13] However, no study till date evaluates the effect of BMI on GFR estimation by Gates method. Therefore, we designed our study to compare GFR estimated by SPSM method with the GFR calculated by Gates method using GC in people with normal and abnormal BMI using SPSM as gold standard.

Materials and Methods

Study population

This was a prospective, single-center study included 60 voluntary kidney donors from October 20, 2014, to November 21, 2015. The study was approved by the Institute's Ethics Committee, and informed consent was taken from all patients.

Healthy voluntary kidney donors advised nuclear diagnostic tests for preoperative screening having age group between 18 and 60 years with normal serum creatinine level (serum creatinine <1.3 mg/dl) and willing to give written informed consent was included in the study. Child, pregnant woman, and individuals with any kind of renal pathology were excluded from the study.

Patient preparation

After explaining the procedure and taking informed consent, healthy donors were advised to avoid excessive intake of tea, coffee, coke, and protein-rich diet before the study. Then they were advised to drink around 500 ml of water 30 min before the study for optimum hydration. Just before the study, they were advised to void to avoid reservoir effect. Then, height and weight of the subjects were measured.

Glomerular filtration rate calculation by gates method

^{99m}Tc-DTPA was administered intravenous under GC and transit of tracer through the kidneys was recorded for 7 min. The sequential dynamic flow frames were acquired with 30 frames of 2 s and 25 frames of 15 s in a 128 × 128 matrix. Administered dose of Tc-DTPA was calculated from pre- and postinjection counting of the syringe under the camera. The renal region of interest (ROI) and semilunar background ROI were drawn at the inferior pole of the kidney avoiding the liver, spleen, and iliac vessels in all frames of the dynamic study to obtain time-activity curves. GFR was calculated, starting from renal uptake during 2–3 min period after injection, corrected for background activity, linear attenuation, and depth (the distance estimated on the basis of body height and weight). The background curve was multiplied by each side to intersect the renal curve 120 s after the rise in kidney activity. The area subtended by the relative kidney function curve between 120 and 180 s, corrected for the background curve, was taken for the total renal counts. To calculate quantitative GFR values, the total counts were then normalized with regards to the injected activity dose and time interval. Resulting values were defined as clearance equivalent and converted to individual and total quantitative renal clearance values expressed in ml/min. The quantitative GFR was obtained by multiplying the regression coefficient (9.81270) with the total renal uptake percent subtracting the intercept value (6.82519) used in the Gates method.

- GFR= (% renal uptake of ^{99m} Tc-DTPA) (9.81270)−(6.82519)

$$\%\ \text{renal uptake} = \frac{\left(\text{Rt kidney count} - \text{bkg counts}\right)/e^{-uxr} + \left(\text{Lt kidney cnts} - \text{bkg counts}\right)/e^{-uxl}}{\left(\text{pre syringe cnts} - \text{post syringe cnts}\right)}$$

Glomerular filtration rate calculation by plasma sample method

After the scan, the subjects were called after 180 min of injection of ^{99m}Tc-DTPA. A 3ml venous blood sample was obtained from the arm contralateral to the injection site. The sample was centrifuged, and 1ml of plasma was separated and measured after 48 h in a well counter with a gamma-ray spectrometer. At the same time, 1 ml of the standard was withdrawn and counted after 48 h. Russell's formula was used to determine the GFR.

- GFR (ml/min) = A × In (D/P) + B

Where A = −0.278 × T + 119.1 + 2450/T

B = 2.886 × T − 1222.9 − 16,820/T

D = Total injected dose counts (CPM)

P = plasma activity (CPM/ml)

T = sampling time.

Statistical analysis

All statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). The data were expressed as the mean ± standard deviation of the mean. Correlation analysis was performed using Pearsons correlation test. Student's *t*-test was used to compare GFR between SPSM and Gates method.

Results

Out of 60 donors included in the study, 31 were male and 29 were female. Mean age of donors was 46.3 ± 5.5 years (37–59 years). Mean height was 1.64 ± 0.1 m (1.45–1.8 m).

Mean weight and BMI was 64.6 ± 15.4 kg (37–100.1 kg) and 23.8 ± 4.8 (16.3–33.1), respectively. Mean GFR value, calculated by SPSM, was 94.0 ± 15.2 ml/min/1.73 m^2. The mean GFR value as calculated by Gates' method was 87.3 ± 16 ml/min/1.73 m^2. No significant correlation noted between GFR calculated by SPSM and age (r = −0.008, P = 0.95), height (r = −0.11, P = 0.38), weight (r = − 0.1, P = 0.41), and BMI (r = −0.04, P = 0.71). No significant difference noted in GFR calculated by SPSM method between female (93.5 ± 15.4 ml/min/1.73 m^2) and male (94.5 ± 15.3 ml/min/1.73 m^2) (P = 0.78).

Moderate correlation noted between GFR estimated by SPSM and Gates' method (r = 0.71, P < 0.0001) [Figure 1]. Significant difference noted between GFR calculated by SPSM and Gates method (94.0 ± 15.2 ml/min/1.73 m^2 vs. 87.3 ± 16 ml/min/1.73 m^2, P = 0.02).

We further evaluate the role of BMI in the estimation of GFR by Gates method using SPSM GFR as gold standard. For this, we have subdivided our study population into two groups, Group 1 consist of people with normal BMI (18.5–24.9) and Group 2 consist of people with BMI outside the normal range (<18.5 and ≥25). Each group consists of 30 people. No significant difference noted in GFR calculated by SPSM method between Group 1 and Group 2 (93.2 ± 15.3 ml/min/1.73 m^2 vs. 94.9 ± 15.3 ml/min/1.73 m^2, P = 0.66). However, significant difference noted in GFR calculated by Gates method between Group 1 and Group 2 (94.7 ± 15.7 ml/min/1.73 m^2 vs. 80.4 ± 13.3 ml/min/1.73 m^2, P = 0.0006). Significant correlation noted between GFR calculated by SPSM and Gates method in people with normal BMI (r = 0.92, P < 0.0001). No significant difference noted in GFR calculated between SPSM and Gates method in people with normal BMI (93.2 ± 15.3 ml/min/1.73 m^2 vs. 94.7 ± 15.7 ml/min/1.73 m^2, P = 0.8) [Figure 2]. However, only moderate correlation noted between GFR calculated by SPSM and Gates method in people with BMI outside normal range (r = 0.71, P < 0.0001). Significant difference noted in GFR calculated between SPSM and Gates method in people with BMI outside the normal range (94.9 ± 15.3 ml/min/1.73 m^2 vs. 80.4 ± 13.3 ml/min/1.73 m^2, P = 0.0002) [Figure 3].

Discussion

GFR is the most important parameter for the assessment of renal function particularly in case of potential kidney donor for a transplant where the renal function assessment becomes even more important due to its direct influence on the success of the transplant. The exact estimation of GFR still remains a challenging task despite the presence of innumerable equations and methods. Moreover, none of the methods shows an exact correlation with other. Therefore, the quest for search continues to find out the most reliable yet simple method for estimation of GFR in clinical practice.

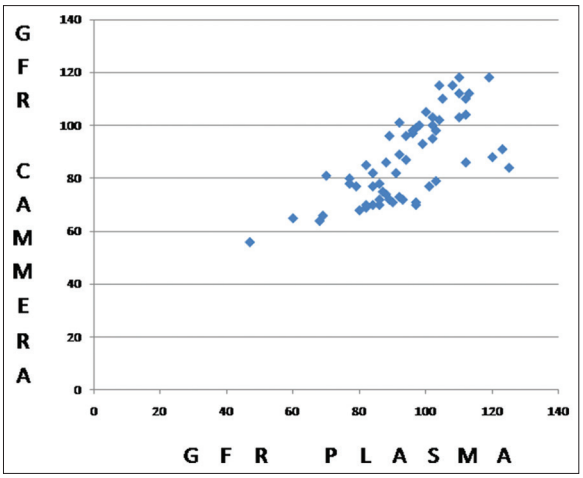

Figure 1: Scatter diagram revealed moderate correlation between glomerular filtration rate estimated by Gates method and single plasma sample method

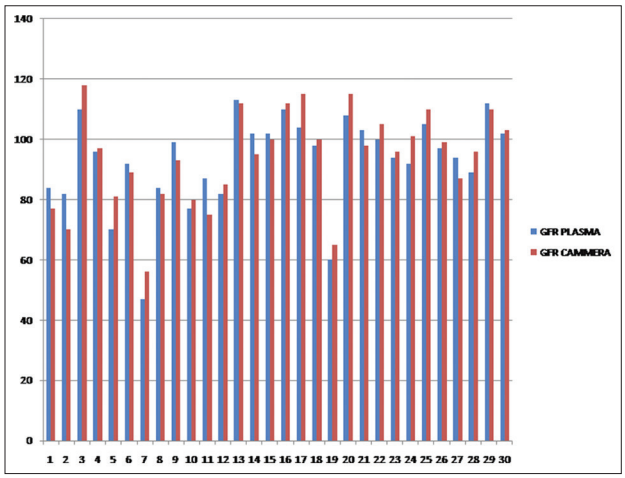

Figure 2: Bar diagram showing comparison of glomerular filtration rate values estimated by Gates method and single plasma sample method in people with normal body mass index

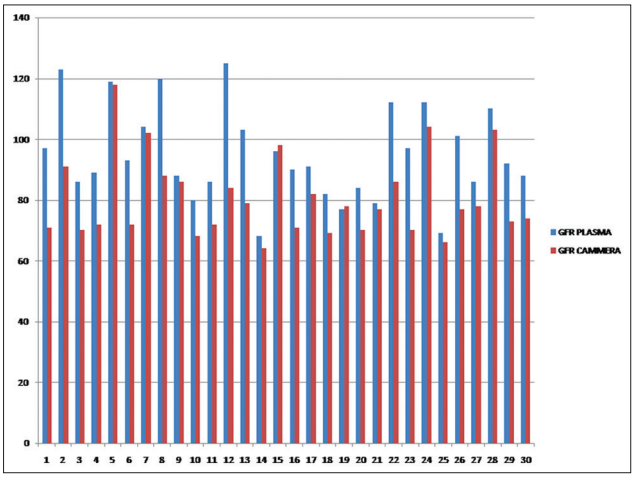

Figure 3: Bar diagram showing comparison of glomerular filtration rate values estimated by Gates method and single plasma sample method in people with body mass index outside normal range. It clearly demonstrates that Gates method significantly underestimates glomerular filtration rate in this group

Among the various methods of GFR estimation, plasma sample technique is the most reliable method. Statistically, the more the number of samples the better the estimate. However, multi-sample technique, used earlier is time-consuming and tedious. Furthermore, these are associated with several potential errors such as errors in pipetting, sample timing, and preparation of the standard. Additional errors include measurement of administered indicator, failure to completely inject the syringe contents and unintentional partial extravascular injection of indicator and errors in measurement of the patient's height and weight, etc.[14] Later, camera-based techniques of GFR estimation were proposed that are easier and faster.[15] Since then various studies have been conducted to test the reliability of these methods [Table 1]. These methods use age, weight, and highly gender- and ethnicity-biased. While most of the studies have been done in the western population, the data on the Asian population is limited.

However, most of these studies have reported lower reliability of GFR estimation by Gates method as compared to plasma sample technique. Several studies suggested the most potential source of error in GFR estimation by plasma sample technique is the calculation of renal depth by Tonnesen equation which significantly underestimates renal depth in people with BMI outside the normal range.[11-13] Therefore, in this study, we tried to compare GFR estimated by SPSM method with the GFR calculated by Gates method using GC in people with normal and abnormal BMI using SPSM as gold standard.

In our study, we have noted no significant correlation between GFR estimated by SPSM method with age, sex, height, weight, and BMI. Zhao *et al*.[16] in their study of 212 kidney donors also noted no significant correlation between GFR with age and sex.

In our study, we found moderate correlation between GFR estimated by Gates method and SPSM method. This is similar to findings by Kumar *et al*.[10] who also noted moderate correlation between GFR estimated by Gates method and SPSM method. However, in contrast to their study, we noted significant difference between GFR estimated by two methods. This is in agreement with another study by Hephzibah *et al*.[2] on Indian population who noted significant difference between GFR estimated by plasma sample method and GC method with low correlation coefficient.

We further divided our study population into two groups to study the effect of BMI on GFR estimation by Gates method. Significant correlation noted between GFR calculated by SPSM and Gates method in people with normal BMI ($r = 0.92$, $P < 0.0001$). No significant difference noted in GFR calculated between SPSM and Gates method in people with normal BMI ($P = 0.8$). However, only moderate correlation noted between GFR calculated by SPSM and Gates method in people with BMI outside the normal range ($r = 0.71$, $P < 0.0001$). Significant difference noted in GFR calculated between SPSM and Gates method in people with BMI outside the normal range ($P = 0.0002$) with significant underestimation of GFR by Gates method. This finding can be explained by the erroneous calculation of renal depth in people with BMI outside the normal range by Tonnesen equation. In a study by Shuguang *et al*.[12] on 123 patients they have noted that renal depth calculation by Tonnesen formula is accurate in people whose BMI is in normal range. However, it significantly underestimates renal depth in people with BMI outside normal range. This is in accordance to the findings of our study. Our findings is further supported by the fact that Zhang *et al*.[17] in their study noted the significant correlation between GFR estimated by GC method and plasma sample method for most of the patients except for three patients who were either too thin or too fat.

These findings are important since Gates method of GFR estimation by GC is easier and simpler to perform than plasma sample method. Furthermore, it is only method which gives a differential renal function which is important in voluntary kidney donors to determine which kidney to be donated. Hence, in people with normal BMI, Gates method should be an investigation of choice for estimation of GFR. While in people with BMI outside normal range computed tomography (CT)-based renal depth calculation should be done for estimation of GFR to avoid underestimation of GFR by conventional Gates method. Since most of the GC is now equipped with single-photon emission CT-CT, it could be performed routinely for accurate estimation of GFR by Gates method.

Table 1: Various studies showing correlation between GFR estimated by gates method and plasma sample method

Author	No. of patients	Plasma sample method used	Correlation coefficient	Conclusion
Itoh K [7]	133	Single/double	0.79	Gates tend to overestimate GFR
Zhang *et al*.[16]	54	double	0.88	Gates correlated well with PS method
Aydin F [8]	115	Single	0.49	Gates is not suitable for estimation of GFR in clinical practice
Assadi M *et al*. [9]	36	Single	0.9	Gates tend to underestimate GFR
Hephzibah *et al*. [2]	88	Single	0.22	Gates did not correlated well with PS method
		Double	0.27	Gates did not correlated well with PS method
Kumar M *et al*. [10]	66	Double	0.69	Gates is not suitable for estimation of GFR in clinical practice

Conclusion

Gates method of GFR estimation using GC shows significant correlation with plasma sample technique in people with normal BMI and should be the investigation of choice for estimation of GFR in this group. In people with BMI outside normal range, it significantly underestimates GFR and CT based renal depth calculation to be performed for better accuracy in this group.

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Conflicts of interest

There are no conflicts of interest.

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