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A study on comparison of Tc-99m DTPA renal dynamic imaging with Mayo quadratic, Cockcroft-Gault, MDRD, and CKD-EPI formulas for estimation of glomerular filtration rate among South Indian live-related kidney donors

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ABSTRACT

Introduction: Glomerular filtration rate (GFR) is calculated using various prediction equations. These equations are derived from the Western population, and extrapolating to our population subgroups may yield inaccurate results.

Objectives: To study the correlation of measured GFR to estimated GFR using four different equations and to analyse how much proximity lies between the GFR calculated by above formulas correlates with DTPA renal scan among South Indian renal donors.

Patients and Methods: An observational study was conducted among prospective renal donors undergoing evaluation. Donors underwent a DTPA scan as per protocol. Downloadable calculators calculated the glomerular filtration rate. Results that were descriptive were presented as mean and standard deviation. Correlation and comparisons were made by calculating Pearson's correlation coefficient and student's t test respectively.

Results: A total of 151 patients were included; 24.5% were males and 75.5% were females. The majority of donors (37.09%) were in the 45-54 years age group. The mean of measured GFR by DTPA was 105.64 mL/min/1.73 m^2 whereas estimated GFR was 100.95, 102.34, 109.35, 97.44 mL/min/1.73 m^2 in MDRD, CKD-EPI, Mayo, and Cockcroft Gault (CG) formulae respectively with a maximum mean difference for CG of 8.2. Weighted kappa agreement between measured and estimated GFR shows 82.96% agreement with CKD-EPI compared to 78.09% agreement with the MDRD formula. Overall, CKD-EPI performed better in GFR estimation in our study subjects.

Conclusion: We found that the CKD-EPI formula performed better in precision, correlation, and accuracy compared to other formulae in GFR estimation among healthy South Indian renal donors. Therefore, the CKD-EPI formula is best suited to pick-up subnormal GFR in clinical practice, as well as in epidemiological studies among the South Asian population.

Implication for health policy/practice/research/medical education:
In an observational study on 151 renal donors, we found, the CKD-EPI GFR performed better in precision, correlation, and accuracy compared to other formulas in estimating GFR among healthy kidney donors.

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Original

Introduction

The rate at which the kidneys filter fluid is known as glomerular filtration rate (GFR). It is a measure to assess kidney functions and is calculated via varied prediction equations using parameters like age, gender and creatinine. It is also essential to know how applicable this may be to the population being studied; since there is a plenty of difference in demography and epidemiology between our country and the West. Hence, extrapolating the data generated in the west for the Indian population will likely yield erroneous results.

We need to assess renal function and morphology in donor kidneys properly. Therefore, GFR estimation is advised for potential renal donors which is considered the best index of overall kidney functions (1,2). Glomerular filtration rate can be measured via different methods, one of them is Tc-99m diethylenetriaminepentaacetic acid (Tc-99m DTPA) plasma clearance mainly because of its simplicity and precision (2-5).

Given this data, this investigation was conducted mainly on the South Indian population to study the correlation of measured GFR to estimated GFR by various equations and to analyse how much proximity lies between the GFR estimation by these formulas and that of measured GFR by DTPA renal scan.

Objectives

1. To study the correlation of measured GFR to estimated GFR by equations like Mayo quadratic, Cockcroft-Gault (CG), modification of diet in renal disease (MDRD), chronic kidney disease-epidemiology collaboration (CKD-EPI).
2. To analyse how much proximity lies between the GFR estimation by these formulas and that of measured GFR by DTPA renal scan. We also aimed to analyse how closely the GFR calculated by these formulas correlates with that of DTPA renal scan.

Patients and Methods

Study design

This is an observational study conducted at the institute of nephrology, Bangalore, from January 2013 to October 2022.

Inclusion criteria

Prospective renal donors.

Exclusion criteria

- Individuals aged less than 20 years or more than 55 years;
- Donors with pre-existing or newly diagnosed hypertension or diabetes mellitus;
- Female donors with a history of gestational diabetes or hypertension during pregnancy;
- Donors with a family history of renal disease.

Prospective renal donors underwent a thorough history, clinical examination, detailed labs, ultrasonogram of the abdomen, and DTPA renal scan. Results were duly collected and documented. GFR is measured by using various formulae, namely (a) Mayo quadratic, (b) CG, (c) MDRD, and (d) CKD-EPI. Downloadable calculators were conducted for calculation and they required only the variables to be substituted. They underwent DTPA renal scan. Preparation of the patient for DTPA; donors were given one litter of water to drink one hour prior to the procedure. Later intravenously Tc 99 labelled DTPA injection was given. Patient lied in a prone position on the table from which films were being taken. After the injection, dye film was taken from 0 minutes to up to 30 minutes. Intravenous infusion of furosemide 20 mg given at the 15th minute. Following that, the patient was asked to void urine, and a post-void film was taken immediately. Four hours later another film was taken. None had any adverse reactions.

Statistical analysis

Descriptive results were expressed in terms of mean, standard deviation. Correlation was made by calculating Pearson's correlation coefficient and comparison was conducted by student *t* test. Simple linear regression was used to obtain R statistics. This reflects the model's predictive ability. A *P* value 0.05 was considered statistically significant.

Results

This study constituted 151 individuals who had work up as prospective renal donors at the Nephrology Department, Institute of Nephrology-Bangalore. There were 37 (24.5%) males and 114 (75.5%) females. The mean age among the donors was 44.68 ± 9.74 years; most of them (37.09%) were 45-54 years (Figure 1).

1. The mean serum creatinine 0.74 ± 0.13 mg/dL. The mean measured GFR by DTPA was 105.64 mL/min/1.73 m^2. In contrast, estimated GFR was 100.95 mL/min/1.73 m^2, 102.34 mL/min/1.73 m^2, 109.35 mL/min/1.73 m^2 and 97.44 mL/min/1.73 m^2 in MDRD, CKD-EPI, Mayo-Quadratic, and CG formulae respectively with the maximum mean difference of 8.2 for the CG formula as shown in Table 1.
2. Correlation between measured GFR by DTPA and estimation of GFR by MDRD, CKD-EPI, Mayo Quadratic, and CG formulae was conducted by Karl Pearson's correlation coefficient that revealed r-value of 0.4354, 0.5372, 0.3678, and 0.4480 respectively with *P* value < 0.0001 (Table 2).
3. The correlation between measured GFR by DTPA and estimated GFR by various formulas is further confirmed by the weighted kappa agreement statistical tool, which showed 78.09%, 82.96%, 80.16%, and 78.47% agreement with MDRD, CKD-EPI, Mayo Quadratic, and CG formula, respectively (Table 3).

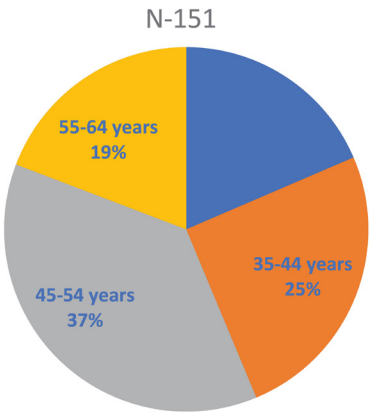

Figure 1. Age distribution of the prospective renal donors (N-151).

Discussion

Since fifty percent decline in GFR is necessary for serum creatinine to raise, the utility of this marker as a measure of GFR is yet to be validated. Hence, the early stages of CKD could go unnoticed. Prediction equations can estimate the GFR, the most crucial measure for evaluating renal functions (6).

In our observational study at the institute of nephrology in Bangalore, 151 potential kidney donors were employed over ten years and varied prediction equations (Mayo Quadratic, CG, MDRD, CKD-EPI) were conducted to estimate GFR and then compare it to the DTPA renal scan. Although lengthy and time-consuming, the clearance of Tc99m-DTPA in timed plasma samples is a reasonably accurate way to assess GFR and correlates very closely with inulin (7,8).

Similar to the observations made by Prasad et al, the majority (37.09%) were in the 45-54 age range, and most of the prospective renal donors were females (9). The mean of measured GFR by DTPA scan was 99.12 mL/min/1.73 m^2 in a study conducted elsewhere, whereas it is 105.64 mL/min/1.73 m^2 in our research.

Mean GFR estimated by the CKD-EPI was 97.44 mL/min/1.73 m^2 was close to GFR measured by the DTPA renal scan. The Mayo Quadratic equation tends to overestimate the GFR, whereas the CG formula underestimates the GFR in our study group. The CG method does not consider the participants' race; most studied donors were female. Further, non-calibration of serum creatinine values with standard measurements may be the cause for the under-performance of the Cockcroft-Gault. The study by Boston et al, which included 109 CKD patients, demonstrated that the MDRD equation was quite exact but should still be used with caution because of the numerous potential sources of inaccuracy (10). In the study conducted by Poggio et al, MDRD overestimated GFR in chronic kidney disease patients (11). At the same time, the GFR in those with normal renal functions was underestimated by both the MDRD and CG equations.

Table 1. Comparison of measured GFR by DTPA with that of estimated GFR by MDRD, CKD-EPI, Mayo Quadratic, and CG formula by dependent *t* test

Formula	Mean	SD	Mean Difference	SD Difference	% Of difference	*T* value	*P* value
GFR measured by DTPA	105.64	9.4					
GFR by MDRD formula	100.95	20.47	4.69	18.44	4.44	3.1267	0.0021 *
GFR measured by DTPA	105.64	9.41					
GFR by CKD-EPI formula	102.34	13.47	3.30	11.56	3.12	3.5032	0.0006*
GFR measured by DTPA	105.64	9.41					
GFR by Mayo Quadratic formula	109.35	11.20	-3.72	11.68	-3.52	-3.9124	0.0001*
GFR measured by DTPA	105.64	9.41					
GFR by CG formula	97.44	23.53	8.20	21.07	7.76	4.7810	0.0001*

GFR, Glomerular filtration rate; DTPA, Diethylenetriamine pentaacetate; MDRD, Modification of diet in renal disease; CKD-EPI, Chronic kidney disease epidemiology collaboration; CG, Cockcroft-Gault.
*$P < 0.05$.

Table 2. Correlation between GFR measured by DTPA with that of MDRD, CKD-EPI, Mayo Quadratic, and CG formula by Karl Pearson's correlation coefficient

Variables	Correlation between measured GFR by DTPA with		
	r value	*T* value	*P* value
GFR by MDRD formula	0.4354	5.9035	0.0001*
GFR by CKD-EPI formula	0.5372	7.7752	0.0001*
GFR by Mayo Quadratic formula	0.3678	4.8281	0.0001*
GFR by CG formula	0.4480	6.1161	0.0001*

GFR, Glomerular filtration rate; DTPA, Diethylenetriamine pentaacetate; MDRD, Modification of diet in renal disease; CKD-EPI, Chronic kidney disease epidemiology collaboration; CG, Cockcroft-Gault.
*$P < 0.05$.

Table 3. Weighted Kappa agreement between measured GFR by DTPA with that of MDRD, CKD-EPI, Mayo Quadratic, and CG formula

Methods	Agreement between GFR measured by DTPA with					
	Agreement	Expected agreement	Kappa	Std. Error	Z value	*P* value
GFR by MDRD formula	78.09%	72.70%	0.1975	0.0359	5.4900	0.0001*
GFR by CKD-EPI formula	82.96%	73.82%	0.3494	0.0441	7.9200	0.0001*
GFR by Mayo Quadratic formula	80.16%	73.49%	0.2515	0.0451	5.5800	0.0001*
GFR by CG formula	78.47%	72.76%	0.2094	0.0321	6.5200	0.0001*

GFR, Glomerular filtration rate; DTPA, Diethylenetriamine pentaacetate; MDRD, Modification of diet in renal disease; CKD-EPI, Chronic kidney disease epidemiology collaboration; CG, Cockcroft-Gault.
*$P < 0.05$.

Our study will be the first study in this regard, in which we compared the estimated GFR using four distinct formulas with the measured GFR using a DTPA scan. Most studies used the MDRD and CG formulas to compare with the DTPA renal scan; however, very few studies employed CKD-EPI equations.

According to a study conducted in Australia, prevalence of CKD in the population older than 25 years using the MDRD equation found to be 13.4%, whereas prevalence using CKD-EPI was 11.5% (12). This difference is due to the fact that 266 study participants who were initially classified as having chronic kidney disease using MDRD equation were later reclassified as not having chronic kidney disease by CKD-EPI due to a better estimation of GFR.

Although all four formulae in our study showed significant *P* values for correlation according to Karl Pearson's coefficient, r-value (0.5372) was highest for the CKD-EPI equation, which was in contrast to the study by Bhuvanakrishna et al, where MDRD performed well (13). The weighted kappa agreement statistical technique was used to confirm the correlation further. It revealed a maximum agreement of 82.96% with CKD EPI equation, supporting the claim that CKD-EPI performs more accurately and precisely than the other three formulas.

Conclusion

The prediction equations cannot substitute the DTPA scan, especially in renal transplant donors. We found that the CKD-EPI GFR performed better in precision, correlation, and accuracy compared to other formulas in estimating GFR among healthy kidney donors. Hence, the CKD-EPI formula is suited to identify subnormal GFR in clinics as well as in epidemiological studies among South Asian population.

Limitations of the study

The majority comprised females and African-Americans were not included in this study.

Authors' contribution

Conceptualization: Bhushan Chandrahasa Shetty, Kishan Aralapuram.
Data curation: Bhushan Chandrahasa Shetty, Kishan Aralapuram.
Formal analysis: Bhushan Chandrahasa Shetty.
Investigation: Bhushan Chandrahasa Shetty, Sreedhara Chikkanayakanahalli Gurusiddaiah.
Methodology: Bhushan Chandrahasa Shetty, Kishan Aralapuram.
Project administration: Sreedhara Chikkanayakanahalli Gurusiddaiah.
Resources: Sreedhara Chikkanayakanahalli Gurusiddaiah.
Software: Bhushan Chandrahasa Shetty.
Supervision: Kishan Aralapuram.
Validation: Kishan Aralapuram.
Visualization: Sreedhara Chikkanayakanahalli Gurusiddaiah.
Writing–original draft: Bhushan Chandrahasa Shetty.
Writing–review & editing: Kishan Aralapuram.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Institute of Nephro-Urology, Bangalore approved this study. Accordingly, written informed consent was taken from all participants before any intervention. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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