Original Article

Modification of diet in renal disease and Cockraft-Gaultformula accuracy in glomerular filtration rate estimation in Iranian adults

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Abstract

Introduction: The aim of this study was to evaluate the accuracy of modification of diet in renal disease (MDRD) and Cockraft-Gault (C-G) formulas for estimating GFR in a sample of Iranian adult.

Materials and Methods: This study was an analytic cross-sectional study on 54 patients with chronic kidney disease. Glomerular filtration rate was measured by kidney scan via TC99m-labeled diethylenetriaminepentaacetic acid, and it was estimated by MDRD and Cockraft-Gault formulas.

Results: The mean of measured GFR and estimated GFR by MDRD and C-G formulas was 61.64 ± 34.26 ml/min, 51.80 ± 25.47, and 54.29 ± 24 ml/min respectively (*P*-value < 0.001, $r = 0.818$ and *P*-value < 0.001, $r = 0.847$, respectively). Pearson correlation test showed direct linear relationship between sGFR and GFR as estimated by the Cockraft-Gault and MDRD formulas.

Conclusion: Based on our results, modification of diet in renal disease (MDRD) and Cockraf-Gault (C-G) formulas are accurate formulas in Iranian adults but they need a correction factor.

Key words: Cockraft-Gault formula, chronic kidney disease, glomerular filtration rate, modification of diet in renal disease, TC99m-Labeled diethylene triamine penta acetic acid

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INTRODUCTION

Chronic kidney disease (CKD) is a worldwide health problem with progressively increasing mortality and morbidity and measurement of renal function is very important in managing CKD patients.[1] Serum creatinine concentration is not a reliable and sensitive indicator of renal function.[2] In clinical practice, glomerular filtration rate (GFR) is frequently used for evaluation of kidney function.[3,4] Direct measurement of GFR is considered impractical because it is a difficult and time-consuming test, and thus, GFR is estimated by many formulas and recent guidelines have suggested evaluating renal function based on these formulas.[5] Most of these formulas are creatinin-based equations for estimating GFR.[6] Two of them (modification of diet in renal disease (MDRD) and Cockraft-Gault (C-G) formulas) estimate the GFR based on creatinine measurements and are commonly used in clinical practice. Of the two, MDRD is more complicated and takes more biochemical as well as demographic parameters into account (albumin, urea, creatinin, age, sex, race), and studies have shown that as a result it can estimate GFR more accurately than

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the C-G formula.[7] Cockraft-Gault formula usually overestimates GFR in young adults and underestimates it in elders (>70 years old).[8] Furthermore, the accuracy of both formulas varies with different races which may be due to differences in the body mass and diet;[8,9] In Chinese and Japanese population, MDRD is more accurate when a correction coefficient is taken into consideration but such a coefficient did not increase the accuracy for other Asian races.[10,11] Due to the importance of accurate estimation of GFR in clinical management of CKD patients, this study was designed to evaluate the accuracy of MDRD and C-G formulas in a sample of Iranian adult.

MATERIALS AND METHODS

This study was an analytic cross-sectional study on 60 patients with CKD, who were assigned to four different stages based on the kidney disease outcome quality initiative (KDOQI) criteria with 15 patients in each stage. This study was conducted in two years from the beginning of 2008 until the end of 2009.[12] Inclusion criteria consisted of the following: Patients with confirmed chronic kidney disease who were older than 18 years. All patients with stage 5 CKD according to the KDOQI criteria were excluded,[13] presence of edema, limb amputation, any recent change in serum creatinin, acute febrile disease, pregnancy, administration of drugs which interfered with tubular creatinin secretion[14,15] and any new change in intravascular volume (diarrhea, vomiting, bleeding) during the last 1 month were the other exclusion criteria. Sixty patients who met the inclusion criteria were randomly sampled to be included in the study, from these 60 patients who met the inclusion criteria, 54 patients had none of the exclusion criteria and finished the study.

Demographic data collection and anthropometric examinations were performed by trained general physicians. Weight was measured with a Seca 707® scale (range 0.1–150 kg) with an accuracy of up to 100 g. Height was measured without shoes, using a tape Stadiometer with a minimum measurement of 1 mm. A fasting blood sample was taken for serum albumin g/dl (Alb), creatinin (Cr), and blood urea nitrogen (BUN) measurement. Serum Cr (mg/dl) was measured via modified kinetic Jaffe´ colorimetric method and BUN (mg/dl) via enzymatic Method by Technicon RA-1000 analyzer.

Glomerular filtration rate (ml/min) was measured by kidney Scan via TC99m-Labeled DTPA (diethylene triamine penta acetic acid) and it was estimated by both MDRD and Cockraft-Gault formulas. Correction for body surface area is necessary for GC formula and body surface area was calculated by the Du bios formula (BSA =weight (kg)0.425×height (m)0.725 ×0.20247.[16]

Glomerular filtration rate was measured by kidney scan via GATES method using ADAC single head genesis machines in a Nuclear Medicine Center.[17] In kidney scan, the patient lies in supine position on a bed with the detector moving beneath the bed; the detector scans the kidneys immediately after injection of TC99m-Labeled DTPA prepared by Kavoshgar Company. After the scan, a syringe is placed at a 30 cm distance from the detector and a one-minute count is performed (Post injection count). Patients' height and weight measurements were inserted in the scanner's software which would then provide a measurement of GFR based on height, weight and pre and post injection count (Standard GFR).

Written informed consents were obtained from all of the participants. This study was approved by Ethics Committee of Isfahan University of Medical Sciences (Research project number: 187030).

Statistical analysis

Statistical analysis was done by SPSS-16 and *P*-value less than 0.05 was signifiicant *T*-paired test was used for comparison of the estimated and the standard GFR measurements. Pearson correlation coefficient was used for determining the correlation between the standard GFR and the GFR measure estimated by both MDRD and Cockraft-Gault formulas. Regression analysis was used for determination of an equation for correction of estimations of GFR by MDRD and Cockraft-Gault formulas.

RESULTS

Fifty-five patients with CKD who met the inclusion criteria and had none of the exclusion criteria were enrolled in this study. From them, 33 patients were male and 21 patients were female. The demographic data and biochemical measurements are shown in

Table 1: Demographic and baseline clinical characteristics of the patients

Characteristic	
Age (year)	54.01 ± 15.26 (mean ± SD)
Sex	
Male	33 (61%)
Female	21 (39%)
Weight (kg)	66.87 ± 11.42 (mean ± SD)
Hight (cm)	165.8 ± 8.50 (mean ± SD)
Body surface area (m[2])	1.63 ± 0.16 (mean ± SD)
Serum Creatinin (mg/dl)	1.76 ± 0.89 (mean ± SD)
Serum Albumin (g/dl)	4.04 ± 0.45 (mean ± SD)
Blood urea nitrogen (mg/dl)	27.38 ± 16.30 (mean ± SD)

Table 2: Mean of GFR[1] according to MDRD2, Cockraft-Gault formula and T99 –DTPA3 scan

Mean	MDRD (ml/min/1.73m2)	SGFR (ml/min)	C-G (ml/min/1.73m2)
Stage 1	79.30 ± 17.29	109.57 ± 15.05	80.06 ± 20.30
Stage 2	65.21 ± 13.60	71.33 ± 8.92	65.90 ± 14.03
Stage 3	40.85 ± 14.60	43.22 ± 11.25	45.12 ± 13.76
Stage 4	23.28 ± 7.58	23.78 ± 4.96	27.10 ± 10.49
Total	51.80 ± 25.47	61.64 ± 34.26	54.29 ± 24

GFR: Standard glomerular filtration rate. MDRD: Modification of diet in renal disease. T99 –DTPA: TC99m-Labeled diethylenetriaminepentaacetic acid.

Table 3: Comparison of GFR, calculated by MDRD, cockraft-gault and T99DTPA scan.

P value	MDRD-SGFR	C-G-SGFR	D-MDRD-D-C-G
Total	<0.001	0.008	0.944
Stage 1	<0.001	<0.001	0.952
Stage 2	0.168	0.280	0.606
Stage 3	0.539	0.524	0.140
Stage 4	0.858	0.360	0.117

Table 1.

The mean values of the estimated and standard GFR measurements in CKD stages 1 to 4 are shown in Table 2. Table 3 compares the mean values of GFR as calculated by MDRD and Cockraft-Gault formulas and measured by T99DTPA scan. Pearson correlation test showed direct linear relationship between the standard GFR (sGFR) and the estimated GFR, calculated by MDRD (*P* value < 0.001, r = 0.847).

Linear regression analysis shows that eGFR as calculated by the MDRD formula should be corrected with the following equation:

GFR = 2.62 + (1.14 × MDRD)

Figure 1 shows the distribution and linear regression of sGFR values relative to eGFR values as estimated by the MDRD formula.

Pearson correlation test also showed direct linear relationship sGFR and eGFR as calculated by the C-G formula (*P*-value < 0.001, *r* = 0.818).

For correction of estimated GFR based on the C-G formula, the following equation was produced by linear regression:

GFR = 0.594 + (1.124 × C-G formula)

Figure 2 shows the distribution and linear regression of sGFR values relative to eGFR values as estimated by the C-G formula.

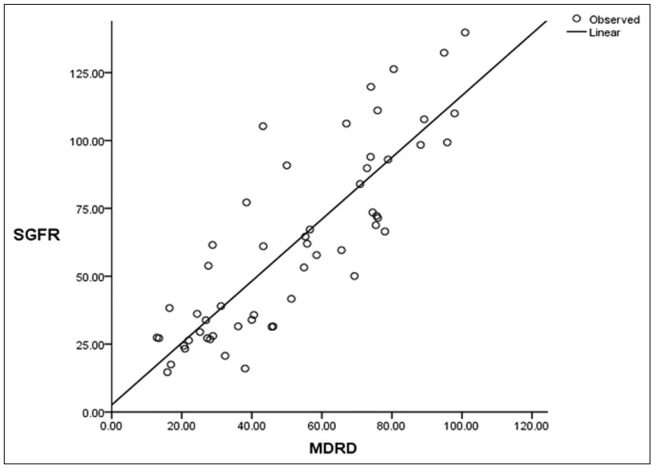

Figure 1: Distribution and linear regression of SGFR according to MDRD.

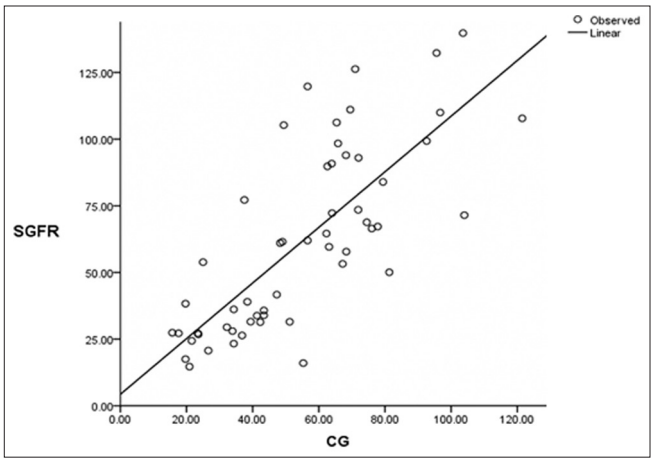

Figure 2: Distribution and linear regression of SGFR according to C-G formula

DISCUSSION

Early stages of CKD are asymptomatic conditions and as such accurate estimation of GFR is necessary for early diagnosis and epidemiologic studies. Creatinine clearance usually overestimates GFR in healthy subjects and is significantly correlated with body mass index (BMI), which is due to higher fractional excretion of creatinine in subjects with higher BMI.[18]

In clinical practice MDRD and Cockraft-Gault formulas are the two main formulas used for estimating GFR.[19] Incorrect estimation of GFR, leads to incorrect estimation of CKD stage and presence. Studies have shown that ethnicity is a very important parameter in MDRD formula and its accuracy for different races depends on using different correction coefficients for

each race; such correction coefficients for Asian races, have only been determined for Chinese and Japanese races so far.[10,11]

There are many studies on prevalence of CKD in Iran. Hosseinpanah *et al.* estimated that the overall prevalence of CKD in Iran is 18.9% with 99.2% of the patients in the stage 3 CKD which is significantly higher than reports from developed countries.[3] Najafi and colleagues investigated risk factors and the prevalence of moderate to severe CKD in Golestan Province, Iran; they filled questionnaire and estimated GFR using the MDRD formula. The prevalence of CKD–Stage 3-5 in their study was similar to the rates reported by National Health and Nutrition Examination Surveys (NHANES; 1988–1994), which was reported at 4.7%.[20,21] Ghafari *et al.* screened high-risk groups for CKD by measuring serum Cr and urinary protein excretion.[22] According to the study of Nafar and colleagues in 2004, Over 700 000 people were estimated to have CKD in Iran. The prevalence rate of CKD was estimated to be 1083 and its incidence rate was estimated at 173.5 per year per 100 000 population.[23]

In our study, there were no significant differences between the standard GFR and the estimated GFR measurements based on CKD stage, except for stage I, in which both formulas underestimated GFR. Zou *et al.* study has also showed that both MDRD and Cockraft-Gault formulas underestimate GFR in CKD stage 1 and overestimate the GFR in CKD stage 3 and 4.[8] Froissart *et al.* study on Europeans demonstrated that GFR calculated by the Cockraft-Gault formula overestimates and MDRD underestimates GFR.[19] Our study, however, showed that both MDRD and Cockraft-Gault formulas have similar accuracy in estimating GFR in the Iranian adult with both underestimating GFR and neither being reliable for estimating the GFR in the health population ($\mathbf{r}_{MDRD} = 0.847$, $\mathbf{r}_{C\text{-}G} = 0.81$).

In conclusion based on our results, modification of diet in renal disease (MDRD) and Cockraf Gault (C-G) formulas are accurate formulas in Iranian adults but they need a correction factor.

Suggestions and limitations

This study was performed on a small sample size in Isfahan. Further studies should be performed on a larger sample so that a far more accurate correction coefficient for MDRD and C-G formulas in Iranian adult can be provided.

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