

# Comparison of 6 equations for estimating glomerular filtration rate in a Chinese benign hypertensive nephrosclerosis population

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## Abstract

Equations to estimate glomerular filtration rate (eGFR) are useful for monitoring the renal status of benign hypertensive nephrosclerosis (BHN). This study aimed to compare the applicability of 6 equations (Cockcroft-Gault [CG] adjusted for body surface area, original modification of diet in renal disease [MDRD], American abbreviated MDRD, Chinese modified MDRD, Chinese abbreviated MDRD, and Chronic Kidney Disease Epidemiology [CKD-EPI]) to estimate GFR in a Chinese BHN population. A total of 179 patients diagnosed with BHN were enrolled. The GFR estimated by each equation was compared to the reference GFR (rGFR) measured using the dual plasma sampling technetium-labeled diethylenetriaminepentaacetic acid method. The Chinese modified and Chinese abbreviated MDRD equations overestimated the rGFR, while the CG, CG adjusted for body surface area, original MDRD, American abbreviated MDRD, and CKD-EPI equations underestimated the rGFR. The difference in performance between estimated GFR (eGFR) based on the American abbreviated MDRD equation and the rGFR was not statistically significant ( $P = .191$ ), while differences in the others were statistically significant ( $P < .05$ ). Furthermore, the advantages in deviation, absolute deviation, deviation degree, precision, and accuracy were also significantly different from those of the other equations. Our findings suggest that eGFR based on the American abbreviated MDRD equation is suitable for the Chinese BHN population.

**Abbreviations:** BHN = benign hypertensive nephrosclerosis, CG = Cockcroft-Gault, CKD = chronic kidney disease, CKD-EPI = Chronic Kidney Disease Epidemiology, eGFR = estimate GFR, ESRD = end-stage renal disease, GFR = glomerular filtration rate, MDRD = modification of diet in renal disease, rGFR = reference GFR.

**Keywords:** benign hypertensive nephrosclerosis, equations, glomerular filtration rate

## 1. Introduction

Chronic kidney disease (CKD) is a global public health problem.<sup>[1]</sup> It is widely accepted that hypertension is one of its main causes.<sup>[2,3]</sup> Hypertensive nephropathy with pathological renal changes may occur in hypertensive patients with CKD for

more than 5 years.<sup>[2,4]</sup> The renal injury responses to hypertension are characterized by tubular hypertrophy, glomerular alterations, and renal fibrosis.<sup>[5]</sup> The pathological manifestation of most cases of hypertensive nephropathy is benign hypertensive nephrosclerosis (BHN).<sup>[2,6]</sup> The progression of BHN shows that the early

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This study was approved by the Human Research Ethics Committee of Guangdong Provincial People's Hospital (GDREC2012099H), Guangzhou, China. All experiments and methods were performed in accordance with the Declaration of Helsinki and the guidelines and regulations of the Human Research Ethics Committee of Guangdong Provincial People's Hospital, which waived the need for informed consent due to the study's retrospective nature.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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kidney injury occurs in the renal tubules, followed by the glomeruli,<sup>[2]</sup> which indicates that the clinical intervention of BHN may differ due to kidney function. Furthermore, the pathophysiology of CKD suggests that the early diagnosis and treatment of CKD may be to delay or prevent its progression to improve patient prognosis. The 2002 Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines suggested that the CKD diagnostic criteria and stage mainly depend on glomerular filtration rate (GFR).<sup>[7]</sup> Thus, the gold standard for estimating renal excretory function remains GFR.<sup>[8]</sup> Therefore, accurately evaluating GFR plays an important role in the prevention and treatment of BHN. Although the clearance rate of inulin or radionuclides such as chromium-labeled ethylenediaminetetraacetic acid (<sup>51</sup>Cr-EDTA) and technetium-labeled diethylenetriaminepentaacetic acid (<sup>99m</sup>Tc-DTPA) accurately reflects GFR, these test methods are expensive and complicated, making their use difficult in clinical practice. Therefore, this study aimed to compare the applicability of 6 equations (Cockcroft-Gault [CG] adjusted for body surface area,<sup>[9]</sup> original modification of diet in renal disease [MDRD],<sup>[10]</sup> American abbreviated MDRD,<sup>[11]</sup> Chinese modified MDRD,<sup>[12]</sup> Chinese abbreviated MDRD,<sup>[12]</sup> and Chronic Kidney Disease Epidemiology [CKD-EPI]<sup>[13]</sup>) to estimate GFR in a Chinese BHN population.

## 2. Methods

### 2.1. Patient population

We retrospectively identified 179 adult patients with BHN treated at Guangdong Provincial People's Hospital between January 2010 and June 2012. All patients underwent the dual-plasma method for the determination of GFR, including those with a hypertension history longer than 8 years or with hypertensive heart disease diagnosed by echocardiography and (or) fundus lesions damaged by hypertension. Exclusion criteria: other kidney disease, ketoacidosis, heart dysfunction (defined as New York Heart Association function stage III or IV), diabetes, acute renal injury, pleural effusion or ascites, edema, limb absence, muscle atrophy, severely malnourishment; and the use of drugs that may interfere with serum creatinine excretion such as diuretics, trimethoprim, or cimetidine. This study was approved by the Human Research Ethics Committee of Guangdong Provincial People's Hospital (GDREC2012099H), Guangzhou, China, which waived the need for informed consent due to the study's retrospective nature. All experiments and

methods were performed in accordance with the Declaration of Helsinki and the guidelines and regulations of the Human Research Ethics Committee of Guangdong Provincial People's Hospital.

### 2.2. Collected data

The collected data included:

1. sex, age, height, weight, body surface area, and body mass index;
2. serum albumin (bromocresol purple method), blood urea nitrogen (urease method), serum creatinine measured by a Beckman DXC800 automatic analyzer (alkaline picric power assay); and
3. routine urinalysis, echocardiography, ophthalmoscopy, and GFR measured by the dual plasma method.

### 2.3. Estimated GFR methods

The 2-sample <sup>99m</sup>Tc-DTPA plasma clearance method was defined as reference GFR (rGFR), and body surface area was calculated as:  $0.0061 \times \text{height (cm)} + 0.0128 \times \text{body weight (kg)} - 0.1529$ . The different equations used to estimate GFR (eGFR) are shown in Table 1.

### 2.4. Statistical analysis

SPSS version 20.0 and Medcalc software were used for data analysis. Data are expressed as mean  $\pm$  SD. The deviation was defined as the difference between eGFR and rGFR; the absolute deviation was defined as the absolute difference between eGFR and rGFR. We used Pearson correlation and linear regression to describe the relationship between eGFR and rGFR. We drew a graph using Bland-Altman between deviation and the mean eGFR and rGFR for regression. The area between the horizontal 0 and the regression line represented the difference between each equation's eGFR and the rGFR. A larger area indicates more bias between each eGFR and the rGFR. The 95% of the distribution of the regression line represents the accuracy of each eGFR equation. The accuracy of the eGFR estimated by each equation is expressed as a percentage of points deviating less than 15%, 30%, or 50% from the rGFR and the Chi-Squared test was used to examine the accuracy of each eGFR. *P* values  $< .05$  were considered statistically significant.

**Table 1**  
Creatinine-based GFR-estimating equations.

Method	Equation
CG[9]	$[(140 - \text{age}) \times \text{weight}] / (72 \times \text{Scr}) \times 0.85$ (if female)
Original MDRD[10]	$170 \times \text{Scr}^{-0.999} \times \text{Age}^{-0.176} \times 0.762$ (if patient is female) $\times 1.180$ (if patient is black) $\times \text{BUN}^{-0.170} \times \text{Alb}^{0.318}$
American abbreviated MDRD[11]	$186 \times \text{Scr}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ (if patient is female)
Chinese modified MDRD[12]	$170 \times \text{Scr}^{-0.999} \times \text{age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{Alb}^{0.318} \times 0.762$ (if patient is female) $\times 1.211$ (Chinese)
Chinese abbreviated MDRD[12]	$186 \times \text{Scr}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ (if patient is female) $\times 1.233$ (Chinese)
CKD-EPI[13]	$144 \times (\text{Scr}/62)^{-0.329} \times 0.993^{\text{age}}$ (female, $\text{Scr} \leq 62$ $\mu\text{mol/L}$ ) $144 \times (\text{Scr}/62)^{-1.209} \times 0.993^{\text{age}}$ (female, $\text{Scr} > 62$ $\mu\text{mol/L}$ ) $141 \times (\text{Scr}/80)^{-0.411} \times 0.993^{\text{age}}$ (male, $\text{Scr} \leq 80$ $\mu\text{mol/L}$ ) $141 \times (\text{Scr}/80)^{-1.209} \times 0.993^{\text{age}}$ (male, $\text{Scr} > 80$ $\mu\text{mol/L}$ )

Cockcroft-Gault formula and creatinine clearance are adjusted for body surface area. Alb = serum albumin concentration (g/L), BUN = serum urea nitrogen concentration (mmol/L), Scr = serum creatinine concentration ( $\mu\text{mol/L}$ ).

**Table 2****Clinical characteristics of the study population.**

Clinical data (n = 179)	
Male	121 (67.60)
Age (years)	66.39 ± 15.06
Weight (kg)	64.44 ± 11.33
Height (cm)	163.36 ± 8.09
Body mass index (kg m <sup>-2</sup> )	24.06 ± 3.39
Body surface area (m <sup>2</sup> )	1.69 ± 0.17
Serum creatinine (μmol L <sup>-1</sup> )	292.67 ± 293.77
Blood urea nitrogen (mmol L <sup>-1</sup> )	12.22 ± 9.30
Serum albumin (g L <sup>-1</sup> )	33.06 ± 4.89
<sup>99m</sup> Tc-DTPA plasma clearance (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )	40.47 ± 25.11

Data expressed as mean ± SD or numbers and proportions. <sup>99m</sup>Tc-DTPA, technetium-labeled diethylenetriaminepentaacetic acid.

**3. Results****3.1. Clinical characteristics**

The patient demographic data are shown in Table 2. A total of 179 patients with BHN were enrolled, including 121 men and 58 women with a mean age of 66.39 ± 15.06 years, mean serum creatinine of 292.67 ± 293.77 μmol/L, mean blood urea nitrogen of 12.22 ± 9.30 mmol/L, mean serum albumin of 33.06 ± 4.89 g/L. The mean rGFR was 40.47 ± 25.11 mL min<sup>-1</sup>·1.73 m<sup>-2</sup>.

**3.2. Comparison of eGFR for each equation with rGFR**

The CG equation, CG equation modified by body surface area, original MDRD equation, American abbreviated MDRD equation, and CKD-EPI equation all underestimated GFR (-3.36, -3.54, -1.74, -1.15, and -2.61 mL min<sup>-1</sup>·1.73 m<sup>-2</sup>, respectively). The difference between eGFR based on the CG equation modified by body surface area and rGFR was the largest among them (3.54 mL min<sup>-1</sup>·1.73 m<sup>-2</sup>). The Chinese modified MDRD equation and the Chinese abbreviated MDRD equation overestimated the GFR. The difference between eGFR based on those equations and the rGFR were 6.43 mL min<sup>-1</sup>·1.73 m<sup>-2</sup> and 8.01 mL min<sup>-1</sup>·1.73 m<sup>-2</sup>, respectively. The difference between eGFR based on the American abbreviated MDRD equation and the rGFR was less than that based on the other equations. The

**Table 3****Comparison of eGFR by each prediction equation with rGFR.**

	mean ± SD (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )
rGFR	40.47 ± 25.11
eGFR of the prediction equation	
CG	37.11 ± 29.35*
Corrected CG	36.93 ± 28.38*
Original MDRD	38.73 ± 28.41*
American abbreviated MDRD	39.32 ± 28.38
Chinese modified MDRD	46.90 ± 34.40*
Chinese abbreviated MDRD	48.49 ± 35.00*
CKD-EPI	37.86 ± 28.57*

\* P < .05 vs rGFR. eGFR = estimated glomerular filtration rate, rGFR = reference glomerular filtration rate.

difference performance between eGFR based on the American abbreviated MDRD equation and the rGFR was not statistically significant (P = .191), while the others were statistically significant (P < .05). Comparisons of the eGFR of each prediction equation with rGFR are shown in Table 3.

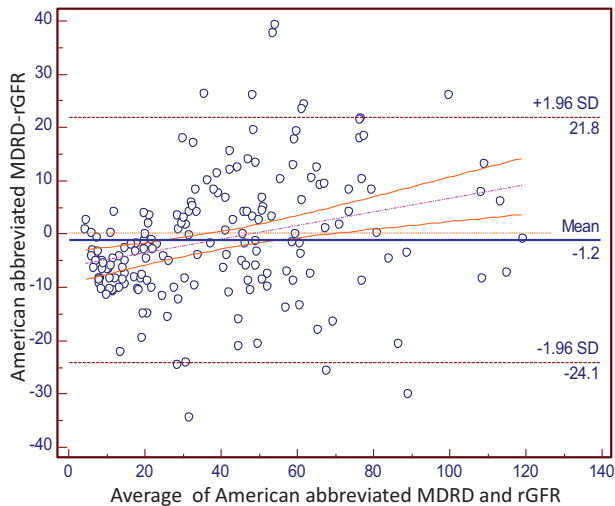
**3.3. Correlation coefficient, determination coefficient, deviation, absolute deviation, deviation degree, precision, and accuracy were compared among the eGFR prediction equations**

The correlation coefficient, determination coefficient, deviation, absolute deviation, deviation degree, precision, and accuracy are compared among the eGFR prediction equations in Table 4. The correlation coefficient of the CG, CG equation modified by body surface area, original MDRD, American abbreviated MDRD, Chinese modified MDRD, Chinese abbreviated MDRD, and CKD-EPI equations fluctuated from 0.90 to 0.92, while the determination coefficient fluctuated from 0.81 to 0.85; neither was statistically significant (P > .05). The deviation of the American abbreviated MDRD equation was significantly less than that of other equations (P < .05). The absolute deviation of the American abbreviated MDRD equation was significantly less than that of the Chinese modified MDRD and Chinese abbreviated MDRD equations (P < .05); however, neither differed significantly from the other equations (P > .05). The

**Table 4****Comparison of correlation coefficient, determination coefficient, median, deviation degree, precision, and accuracy of different eGFR prediction equations.**

	CG	Corrected CG	Original MDRD	American abbreviated MDRD	Chinese modified MDRD	Chinese abbreviated MDRD	CKD-EPI
Correlation coefficient	0.9	0.9	0.92	0.91	0.92	0.91	0.91
Determination coefficient	0.81	0.82	0.85	0.83	0.85	0.83	0.83
Deviation (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )	5.20*	4.54*	3.74*	2.86	-3.10*	-4.52*	4.23*
Deviation (quartile)	13.07	11.43	13.81	12.83	19.74	21.65	11.71
Absolute deviation (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )	8.01	7.37	7.73	7.63	8.14*	9.12*	7.4
Absolute deviation (quartile)	9.72	9.36	8.16	7.78	13.87	14.6	8.04
Deviation degree (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )	745.46	545.16	558.12	574.05	1921.42	2114.47	576.23
Precision (mL min <sup>-1</sup> ·1.73 m <sup>-2</sup> )	52.7	47.9	44.1	45.9	58.9	62.5	45.8
15% accuracy	28.49*	32.4	35.2	38.55	29.05*	22.35*	36.31
30% accuracy	57.54	61.45	62.57	58.66	51.96	45.81*	59.78
50% accuracy	80.45	84.92	83.24	83.24	78.21	76.54	78.77

\* P < .05 vs American abbreviated MDRD equation. eGFR = estimated glomerular filtration rate.



**Figure 1.** Bland-Altman diagram of the American abbreviated MDRD equation and rGFR values. The abscissa is the mean rGFR and American abbreviated MDRD equation values, while the ordinate is the difference between the rGFR and the American abbreviated MDRD. The skew dashed line is the deviation regression equation, and the skew solid line is the 95% prediction interval of the deviation regression line. The mean value of the American abbreviated MDRD equation and the rGFR is  $0\text{--}130\text{ mL}\cdot\text{min}^{-1}\cdot 1.73\text{ m}^{-2}$ , while the proportion between the 0 horizontal line and the dashed line indicates the deviation degree. MDRD = modification of diet in renal disease, rGFR = reference glomerular filtration rate.

15% accuracy of the American abbreviated MDRD equation was significantly higher than those of the CG equation, Chinese modified MDRD equation, and Chinese abbreviated MDRD equation ( $P < .05$ ). The 30% accuracy of the American abbreviated MDRD equation was significantly higher than that of the Chinese abbreviated MDRD equation ( $P < .05$ ). The precision and degree of deviation of the American abbreviated MDRD equation using Bland-Altman analysis were better than those of the CG equation, Chinese modified MDRD equation, and Chinese abbreviated MDRD equation (Fig. 1). Furthermore, the precision and degree of deviation between the American abbreviated MDRD equation and the others were relatively close (Table 4).

#### 4. Discussion

Hypertension is a vital cause of end-stage renal disease in both developing and developed countries.<sup>[3,14]</sup> In fact, hypertensive nephropathy is the second leading cause of end-stage renal disease after diabetes.<sup>[15–17]</sup> As poorly controlled hypertension progresses, an individual's risk of BHN increases.<sup>[18]</sup> The 2002 K/DOQI guidelines suggested that CKD diagnostic criteria and stage mainly depend on GFR.<sup>[7]</sup> The gold standard for estimating renal excretory function remains dependent on GFR.<sup>[8]</sup> Therefore, the accurate evaluation of renal function plays an important role in the diagnosis and treatment of BHN. Since GFR cannot be measured directly, it can only be measured indirectly through the removal of certain markers. Although the clearance rate of inulin or radionuclides such as  $^{51}\text{Cr-EDTA}$  and  $^{99\text{m}}\text{Tc-DTPA}$  accurately reflects the GFR, the test methods are expensive and complicated, making their use difficult in clinical practice.<sup>[19]</sup> Therefore, eGFR prediction equations based on different markers were successively developed.<sup>[20–22]</sup> Numerous clinical studies have shown that

the eGFR equation based on serum creatinine is the most accurate and the detection of serum creatinine is mature and simple, making it widely used in clinical practice.<sup>[22–24]</sup>

In this study, the difference in performance between eGFR based on the American abbreviated MDRD equation and rGFR was not statistically significant ( $P = .191$ ), while those of others were statistically significant ( $P < .05$ ). The CG equation, CG equation modified by body surface area, original MDRD equation, American abbreviated MDRD equation, and CKD-EPI equation all underestimated GFR. The difference between eGFR based on the CG equation modified by body surface area and rGFR was largest among them ( $3.54\text{ mL}\cdot\text{min}^{-1}\cdot 1.73\text{ m}^{-2}$ ). The Chinese modified MDRD equation and the Chinese abbreviated MDRD equation overestimated GFR. The differences between eGFR and rGFR were  $6.43\text{ mL}\cdot\text{min}^{-1}\cdot 1.73\text{ m}^{-2}$ ,  $8.01\text{ mL}\cdot\text{min}^{-1}\cdot 1.73\text{ m}^{-2}$ , respectively. The difference between eGFR based on the American abbreviated MDRD equation and rGFR was not statistically significant as reported by previous studies, while the American abbreviated MDRD equation more closely aligned with isotopic GFR.<sup>[25–27]</sup> The deviation of the American abbreviated MDRD equation was significantly less than that of the other equations ( $P < .05$ ). The absolute deviation of the American abbreviated MDRD equation was significantly less than those of the Chinese modified and Chinese abbreviated MDRD equations ( $P < .05$ ). The 15% accuracy of the American abbreviated MDRD equation was significantly higher than those of the CG equation, Chinese modified MDRD equation, and Chinese abbreviated MDRD equation ( $P < .05$ ). The 30% accuracy of the American abbreviated MDRD equation was significantly higher than that of the Chinese abbreviated MDRD equation ( $P < .05$ ). The precision and degree of deviation of the American abbreviated MDRD equation on Bland-Altman analysis were better than those of the CG equation, Chinese modified MDRD equation, and Chinese abbreviated MDRD equation. Furthermore, the precision and degree of deviation between the American abbreviated MDRD equation and the others were relatively close. Thus, the American abbreviated MDRD equation may be more suitable for estimating GFR in the Chinese BHN population.

The original MDRD equation is highly recommended by the National Kidney Foundation, but it seems unsuitable for Chinese populations.<sup>[28,29]</sup> Ho et al reported that the MDRD equation with modification for the racial coefficient for Asian countries has resulted in substantially different results that may not be due to race alone,<sup>[30]</sup> so the clinical application of the Chinese modified and Chinese abbreviated MDRD equations requires further proof. A previous study demonstrated the superiority of the CG equation in the elderly,<sup>[31]</sup> but this study demonstrated the opposite, possibly due to the specific pathophysiological mechanism of BHN, age, and mean GFR differences between studies. In 2009, Levey et al developed the CKD-EPI equation based on 8254 subjects. Eight equations were established based on race, sex, and serum creatinine level.<sup>[13]</sup> Their results showed that the CKD-EPI equation was superior to the MDRD equation. However, due to the relatively small proportion of patients with early-stage CKD in this study, evaluating some of the equations here might be significantly biased, so it was not studied. Although studies have proven that cystatin C has the advantages of higher sensitivity and non-secretion by the renal tubules, the eGFR equation based on cystatin C requires further clinical studies due to the lack of a unified method for determination and the lack of specificity.<sup>[32–34]</sup> In addition, some studies mentioned that  $^{99\text{m}}\text{Tc-}$

DTPA can bind to proteins, resulting in a 5% to 10% lower actual GFR,<sup>[35,36]</sup> which is also a factor in the bias.

Finally, compared with the other equations, the American abbreviated MDRD equation may be more suitable for use in Chinese BHN populations for estimating GFR due to its advantages in deviation, absolute deviation, deviation degree, precision, and accuracy. High-quality and well-powered evidence is still needed in the future to confirm our results.

#### 4.1. Limitations

Due to its retrospective design, the present study has a few inherent limitations:

1. for comparison of eGFR equations, errors caused by serum creatinine are inevitable;
2. due to the older age of the included population and the proportion of early-stage CKD patients being relatively small, corresponding deviation may occur; and
3. this single-center observational study had a small sample size, and racial and other confounding factors may have influenced our results.

Thus, additional large clinical studies are needed to confirm our results.

#### Author contributions

**Data curation:** Yamei Zhang, Yao Hu, Bohou Li, Nan Jiang, Xueqin Chen.

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