Modified Glomerular Filtration Rate Estimating Equation for Chinese Patients with Chronic Kidney Disease

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The Modification of Diet in Renal Disease (MDRD) equations provide a rapid method of assessing GFR in patients with chronic kidney disease (CKD). However, previous research indicated that modification of these equations is necessary for application in Chinese patients with CKD. The objective of this study was to modify MDRD equations on the basis of the data from the Chinese CKD population and compare the diagnostic performance of the modified MDRD equations with that of the original MDRD equations across CKD stages in a multicenter, cross-sectional study of GFR estimation from plasma creatinine, demographic data, and clinical characteristics. A total of 684 adult patients with CKD, from nine geographic regions of China were selected. A random sample of 454 of these patients were included in the training sample set, and the remaining 230 patients were included in the testing sample set. With the use of the dual plasma sampling ^{99m}Tc-DTPA plasma clearance method as a reference for GFR measurement, the original MDRD equations were modified by two methods: First, by adding a racial factor for Chinese in the original MDRD equations, and, second, by applying multiple linear regression to the training sample and modifying the coefficient that is associated with each variable in the original MDRD equations and then validating in the testing sample and comparing it with the original MDRD equations. All modified MDRD equations showed significant performance improvement in bias, precision, and accuracy compared with the original MDRD equations, and the percentage of estimated GFR that did not deviate >30% from the reference GFR was >75%. The modified MDRD equations that were based on the Chinese patients with CKD offered significant advantages in different CKD stages and could be applied in clinical practice, at least in Chinese patients with CKD.

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GFR is one of the commonly used indexes for early detection of chronic kidney disease (CKD). An accurate, convenient, and reproductive GFR estimating method is important for clinical practice. Earlier studies focused on plasma creatinine (Pcr) and creatinine clearance as markers of GFR, but Pcr usually does not increase until GFR has decreased by 50% or more, and many patients with normal Pcr levels frequently have lower GFR (1). Also, creatinine clearance usually overestimates true GFR (2).

Creatinine-based estimating equations overcame some of these limitations and offered a rapid method for GFR estimation. In the Modification of Diet in Renal Disease (MDRD) Study, using renal clearance of ^{125}I-iothalamate as a reference GFR (rGFR), Levey *et al.* (3) published a series of creatinine-based GFR estimating equations (MDRD equations). The abbreviated MDRD equation, which includes only four variables—Pcr, gender, age, and ethnicity (4)—has been the most widely used in clinical practice, becoming a powerful screening tool for early detection of CKD. It provided an acceptable level of accuracy (at least 70% of estimated GFR [eGFR] within a 30% deviation from the rGFR) in advanced stages of CKD (5) and was recommended by Kidney Disease Outcome Quality Initiative (K/DOQI) clinical practice guidelines (5).

Race is an important determinant of GFR estimation. For example, when the MDRD equations are applied to black individuals, a coefficient should be used (3). In our previous study (6), the performance of MDRD equation 7 and the abbreviated MDRD equation was tested in a group of Chinese patients with

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CKD. The results showed that both equations underestimated rGFR in near-normal renal function and overestimated rGFR in advanced renal failure. We concluded that careful modification of these equations was necessary to improve their performance when used to identify Chinese patients with CKD.

In our study, an attempt was made to improve the performance of the original MDRD equations by modifying the original MDRD equation 7 and abbreviated MDRD equation. The diagnostic performance of the modified equations was compared with the original ones in various stages of CKD.

Materials and Methods

Patients and Design

Nine renal institutes of university hospitals located in nine geographic regions of China participated in this study from June 2004 to September 2005. The same inclusion and exclusion criteria were used in all participating renal institutes: Patients who were older than 18 yr and had CKD were eligible for inclusion. CKD was diagnosed and classified according to K/DOQI clinical practice guideline (5). Patients with acute kidney function deterioration, edema, skeletal muscle atrophy, pleural effusion or ascites, malnutrition, amputation, heart failure, or ketoacidosis were excluded. Patients who were taking cimetidine or trimethoprim or who were on any kind of renal replacement therapy also were excluded.

The nine participating renal institutes used the same data collecting methods and the same data collecting forms. The collected data included gender, age, body height, body weight, BP, and rGFR. Fasting plasma was taken from selected patients for analysis of creatinine, urea nitrogen, and albumin in a single laboratory at the First Hospital, Peking University.

GFR Measurement

Unlike Pcr, ^{99m}Tc-DTPA plasma clearance was measured in the nine participating renal institutes. Efforts had been made to make the inter-institute variance as small as possible, including staff training, ^{99m}Tc-DTPA drug selection (radiochemical purity >95% and percentage of ^{99m}Tc-DTPA bound to plasma protein <5%). The identical operational procedures were followed by all nine participating centers, including patients' preparation, intravenous injection, plasma sampling time points and procedure, and radioactivity measurement (6).

rGFR was measured by the dual plasma sampling method (7,8), standardized by body surface area (BSA) (9), and resulted in the rGFR: rGFR (ml/min per 1.73 m^2) = [Dln $(P_1/P_2)/(T_2\text{-}T_1)$] exp $\{[(T_1 \ln P_2) - (T_2 \ln P_1)]/(T_2 - T_1)\} \times 0.93 \times 1.73/\text{BSA}$, where D is dosage of drug injected, T_1 is time of first blood sampling (approximately 2 h), P_1 is plasma activity at T_1, T_2 is time of second blood sampling (approximately 4 h), and P_2 is plasma activity at T_2. The units of measurement were counts per minute per milliliter for D, P_1, and P_2 and minutes for T_1 and T_2.

Pcr Assay and Calibration

Pcr levels were measured in a single laboratory on a Hitachi 7600 analyzer using the Jaffe's kinetic method, which was described elsewhere (6). To ensure that our Pcr values were calibrated equally to the MDRD study, we randomly selected 57 fresh-frozen plasma samples (range 0.72 to 12.64 mg/dl [64 to 1118 μmol/L] of Jaffe's kinetic method Pcr values measured in our laboratory) from our specimens and analyzed them in both our laboratory and the Cleveland Clinic Laboratory. The Pcr value that was measured by our laboratory can be calibrated to the Pcr value that was measured by the Cleveland Clinic Laboratory, which used a CX3 analyzer (Beckman Coulter Inc., Fullerton, CA), using a linear regression equation: CX3 Pcr (mg/dl) = $-15.91 + 1.32 \times$ Hitachi Pcr (mg/dl) ($R^2 = 0.999$; $P < 0.001$).

Other Analyses

Plasma urea was measured by the urease method. The normal reference range was 3.20 to 7.10 mmol/L [8.96 to 19.88 mg/dl] blood urea nitrogen (BUN). Plasma albumin was measured using the bromcresol green method. The normal reference range was 3.5 to 5.5 g/dl (35 to 55 g/L).

Estimation of GFR from Original MDRD Equations

Calibrated CX3 Pcr was put into the MDRD equation 7 and abbreviated MDRD equation to estimate GFR (7GFR and aGFR, respectively):

$$\text{7GFR (ml/min per 1.73 m}^2) = 170 \times \text{Pcr}^{-0.999} \times \text{age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{albumin}^{0.318} \times 0.762 \text{ (if female)} \quad (1)$$

$$\text{aGFR (ml/min per 1.73m}^2) = 186 \times \text{Pcr}^{-1.154} \times \text{age}^{-0.203} \times 0.742 \text{ (if female)} \quad (2)$$

where Pcr is in mg/dl, BUN is in mg/dl, albumin is in g/dl, and age is in years.

Modification of Original MDRD Equations

A total of 720 participants were included, and 36 outliers were deleted. The remaining 684 patients were used for further analysis. From these patients, 454 were randomly selected and used for the training model, and the remaining 230 patients were used to test the performance of the modified equations.

We assumed that the performances of MDRD equations could be improved in Chinese patients with CKD by adding a racial factor, so 7GFR and aGFR were calculated on the basis of data from the 454 training samples; using 7GFR and aGFR as dependent variables, respectively, two linear regression models were established to predict rGFR from 7GFR or aGFR. It was decided that if the intercepts of the two models were not significantly different from zero, then the models should be simplified by forcing the intercepts to be zero.

In the former two models, the Pcr value that was calibrated to the MDRD laboratory was used to estimate 7GFR and aGFR, so when the two modified equations are used, Pcr value that is calibrated to the MDRD laboratory should be used. This was inconvenient in clinical practice in China. In the above concern, we reconstructed another two regression models, using an approach similar to that used in the development of the original MDRD equations. In these two models, log transformation was applied before the linear regression, and linearity and equal variance test were satisfactory. In the concern that retransforming back to the usual scale might induce bias, the predicted eGFR was adjusted using the smearing method (10). The smearing coefficients for these two models were calculated to be 1.05.

eGFR was compared with rGFR using Bland-Altman analysis of the validation set. The difference between eGFR and rGFR was defined as eGFR minus rGFR; the absolute difference between eGFR and rGFR was defined as the absolute value of difference. The regression of the difference between eGFR and rGFR against the average of the two methods was measured. The bias for eGFR was expressed as the area between the regression line and a common distance along the zero difference line. Ninety-five percent limits of agreement then were constructed around this linear regression line. The precision was expressed as the width between the 95% limits of agreement. Accuracy was measured as the percentage of eGFR that did not deviate >15, 30, and 50% from the rGFR.

Table 1. Basic characteristics of the patients[a]

Characteristic (n = 684)	Mean ± SD (Median) or n (%)
Female (n [%])	332 (48.53)
Age (yr)	49.9 ± 15.8 (49.0)
Height (cm)	164.7 ± 8.3 (165.0)
Weight (kg)	64.5 ± 12.4 (63.0)
BSA (m^2)	1.7 ± 0.18 (1.7)
BMI (kg/m^2)	23.6 ± 3.6 (23.4)
Plasma creatinine (mg/dl)	2.0 ± 1.8 (1.3)
Plasma urea nitrogen (mg/dl)	28.4 ± 19.9 (21.5)
Plasma albumin (g/dl)	3.99 ± 0.6 (4.1)
rGFR (ml/min per 1.73 m^2)	55.1 ± 35.1 (49.9)
Causes of CKD	
primary or secondary glomerular disease	264 (38.6)
hypertension	102 (14.9)
obstructive kidney disease	92 (13.5)
renovascular disease	89 (13.0)
chronic tubulointerstitial disease	44 (6.4)
diabetic nephropathy	37 (5.4)
polycystic kidney disease	18 (2.6)
other causes or causes unknown	38 (5.6)
CKD stages	
1	125 (18.3)
2	161 (23.6)
3	197 (28.8)
4	101 (14.7)
5	100 (14.6)

[a]BMI, body mass index; BSA, body surface area; CKD, chronic kidney disease; rGFR, reference GFR.

Statistical Analyses

Quantitative variables of patient's age, height, weight, BSA, body mass index, Pcr, plasma urea, plasma albumin, and rGFR were described as mean ± SD or as median (Table 1). The accuracy of the equations was compared in certain stages of CKD with χ^2 test. Because of skewed distribution, Spearman correlation and linear regression were used to describe the relationship between eGFR and rGFR. The Wilcoxon signed ranks test was used to compare the difference and absolute difference in a certain stage of CKD. The results were considered to be significant at $P < 0.05$. Medcalc for Windows, version 8.0 (Medcalc Software, Mariekerke, Belgium) was used for data analysis.

Results

Patient Characteristics

A total of 684 patients with CKD were included in the final analysis, including 352 men and 332 women, and the average age was 49.98 ± 15.8 yr. Causes and stages of CKD are listed in Table 1.

Modification of MDRD Equations

In the first two linear regression, the intercepts of the modified MDRD equation 7 (−0.383; 95% confidence interval [CI] −3.104 to 2.337) and of the modified abbreviated MDRD equation (0.311; 95% CI −2.526 to 3.149) were not significantly different from 0 ($P = 0.78$ and $P = 0.83$, respectively). By forcing the two intercepts to be zero, the form of two models was reduced and got the following equations ($n = 454$, $R^2 = 0.95$ and 0.94 respectively):

$$\text{c-7GFR}_1\ (\text{ml/min per 1.73 m}^2) = 170 \times \text{Pcr}^{-0.999} \times \text{age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{albumin}^{0.318} \times 0.762\ (\text{if female}) \times 1.202\ (\text{if Chinese}) \quad (3)$$

$$\text{c-aGFR}_1\ (\text{ml/min per1.73 m}^2) = 186 \times \text{Pcr}^{-1.154} \times \text{age}^{-0.203} \times 0.742\ (\text{if female}) \times 1.227\ (\text{if Chinese}) \quad (4)$$

Development of New Equations

Calibrated CX3 Pcr was needed in equations 3 and 4, which were not convenient for clinical application in Chinese, so we tried to reconstruct another two regression models, using Pcr values measured with the Jaffe's kinetic method on a Hitachi 7600 analyzer. The first model used the same variables as MDRD equation 7, and the second used the same variables as the abbreviated MDRD equation. The two resulted in equations

Table 2. Overall performance of eGFR equations compared with rGFR: Difference, absolute difference, bias, precision, and accuracy[a]

Parameter	Equation 1	Equation 2	Equation 3	Equation 4	Equation 5	Equation 6
Intercept (95% CI)	6.45 (3.78 to 9.84)	6.58 (3.75 to 9.39)	7.76 (4.54 to 10.98)	8.06 (4.61 to 11.53)	8.55 (5.45 to 11.64)	9.54 (6.26 to 12.81)
Slope (95% CI)	0.69 (0.65 to 0.74)	0.68 (0.64 to 0.72)	0.84[b] (0.78 to 0.88)	0.83[b] (0.78 to 0.88)	0.82[b] (0.77 to 0.87)	0.81[b] (0.76 to 0.85)
R	0.91	0.90	0.91	0.90	0.92	0.91
R^2	0.84	0.81	0.84	0.81	0.84	0.82
Median of difference (ml/min per 1.73 m^2; 25%, 75% percentile)	−7.4 (−19.5, −1.3)	−7.8 (−21.5, −1.8)	−0.3[b] (−8.5, 6.3)	−0.9[b] (−9.6, 7.4)	−0.8[b] (−9.7, 7.4)	−0.8[b] (−9.7, 7.4)
Median of absolute difference (ml/min per 1.73 m^2; 25%, 75% percentile)	8.7 (3.7, 19.5)	9.4 (4.2, 21.5)	7.3[b] (2.7, 15.1)	8.8[b] (3.3, 15.2)	7.1[b] (2.7, 15.6)	7.9[b] (3.3, 15.6)
Bias (arbitrary units)	2133.9	2175.0	605.8	543.0	685.6	677.2
Precision (ml/min per 1.73 m^2; %)	57.6	60.7	54	57.5	53.2	56.5
15% accuracy	32.6	30.0	50.4[b]	48.7[b]	47.4[b]	46.9[b]
30% accuracy	70.4	66.1	76.1	77.8[b]	79.6[b]	79.6[b]
50% accuracy	95.2	93.9	93.9	92.2	93.5	93.0

[a]The estimated GFR (eGFR) that resulted from these six equations all were significantly correlated with rGFR. Linear regressions were made using eGFR against rGFR. The six intercepts were much similar, but the slopes of equations 3 through 6 were significantly closer to the identical line compared with the slopes of equations 1 and 2. CI, confidence interval.
[b]$P < 0.05$ compared with equations 1 and 2.

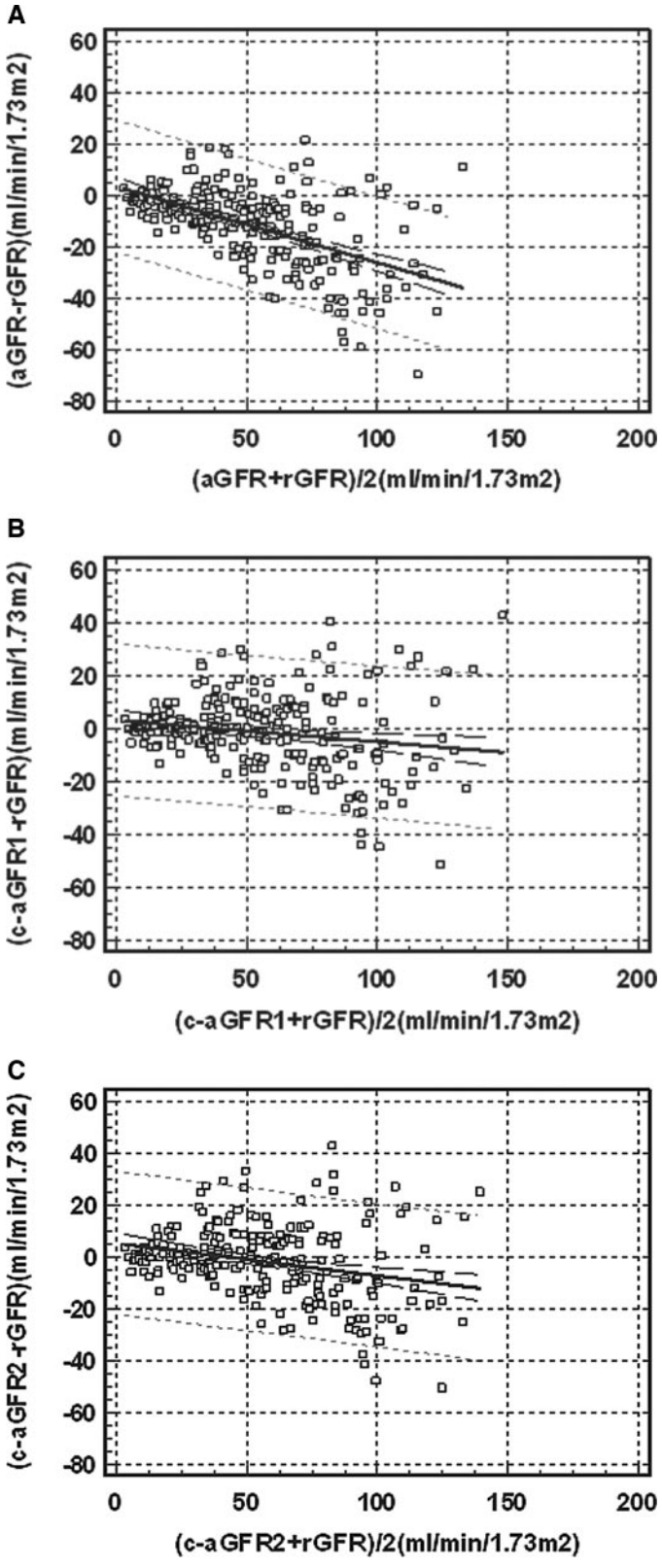

Figure 1. Bland-Altman plot showing the disagreement between estimated GFR (eGFR; including aGFR, c-aGFR1, and c-aGFR2) and reference GFR (rGFR). Solid line represents the regression line of difference between methods against average of methods, dashed lines represent 95% confidence intervals for the regression line, and dotted lines represent 95% limits of agreement. aGFR, eGFR (ml/min per 1.73 m^2) by original abbreviated Modification of Diet in Renal Disease (MDRD) equation; c-aGFR1, eGFR (ml/min per 1.73 m^2) by modified abbreviated MDRD equation by adding a racial factor for Chinese; c-aGFR2, eGFR (ml/min per 1.73 m^2) by modified abbreviated MDRD equation based on the result of multiple linear regression from data of Chinese patients with chronic kidney disease (CKD). (A) Disagreement between aGFR and average of aGFR and rGFR. (B) Disagreement between c-aGFR1 and average of c-aGFR1 and rGFR. (C) Disagreement between c-aGFR2 and average of c-aGFR2 and rGFR.

5 and 6 after adjustment using the smearing method, presented in the Appendix ($n = 454$; $R^2 = 0.86$ for both).

Diagnostic Performance of the Equations

First, the overall diagnostic performance was compared among equations 1 through 6. Linear regressions were made using eGFR against rGFR. The six intercepts were much similar, but the slopes of equations 3 through 6 were significantly closer to the identical line compared with the slopes of equations 1 and 2). On the Bland-Altman plot, compared with equations 1 and 2, the biases of equations 3 through 6 were much less, and precision of equations 3 through 6 were slightly higher (Table 2, Figure 1). The differences between eGFR resulted from equations 3 through 6, and rGFR were significantly less than the differences that resulted from the other two. Equations 3 and 5 showed fewer absolute differences than equation 1; so did equations 4 and 6 than equation 2. The 15% accuracy of equations 3 through 6 was significantly higher compared with equations 1 and 2, 30% accuracy of equations 4 through 6 was significantly higher than equations 1 and 2; there also was some improvement in the 30% accuracy of equation 3 but without statistically significant. The 50% accuracy was comparable for the six equations. There was no significant difference among equations 3 through 6 in 15 to 50% accuracy (Table 2).

The performance of the six equations in various stages of CKD was analyzed. In CKD stages 1, 2, 3, 4, and 5, the differences between equations 3 through 6 and rGFR were significantly less than the differences that resulted from the other two equations ($P < 0.05$ for all; Figure 2). Equations 3 through 6 also resulted in lower absolute differences compared with the other two equations in CKD stages 1 and 2 ($P < 0.05$ for all). The absolute differences of equations 3 through 6 also were less than those of equations 1 and 2 in CKD stage 3 but without statistical significance. The absolute differences of the six equations were similar in stages 4 and 5 (Figure 3).

In CKD stages 1 and 2, equations 3 through 6 showed significant improvements in 15 and 30% accuracy compared with equations 1 and 2 ($P < 0.05$ for all); in CKD stage 3, significant 15% accuracy was achieved comparing equations 3 and 5 with equations 1 and 2 ($P < 0.05$ for both). Some improvement was achieved comparing equations 4 and 6 with equations 1 and 2 without statistical significance; in CKD stages 4 and 5, 15% accuracy improvements of equations 3 through 6 was gained without statistical significance. The 15 and 30% accuracy among equations 3 through 6 was not significantly different.

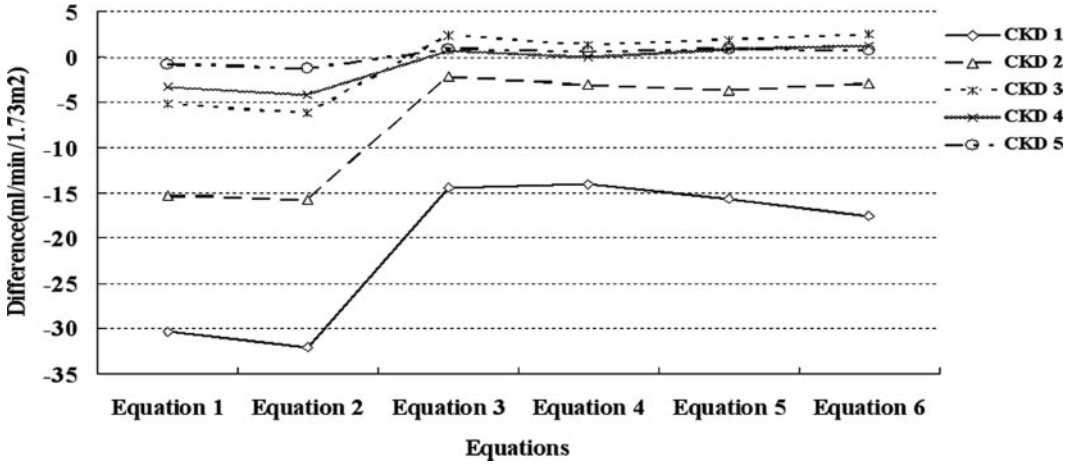

Figure 2. Comparison of equations: Difference between eGFR and rGFR. The differences between equations 3 through 6 eGFR and rGFR were significantly less than those between equations 1 and 2 eGFR and rGFR in each CKD stage ($P < 0.05$ for all).

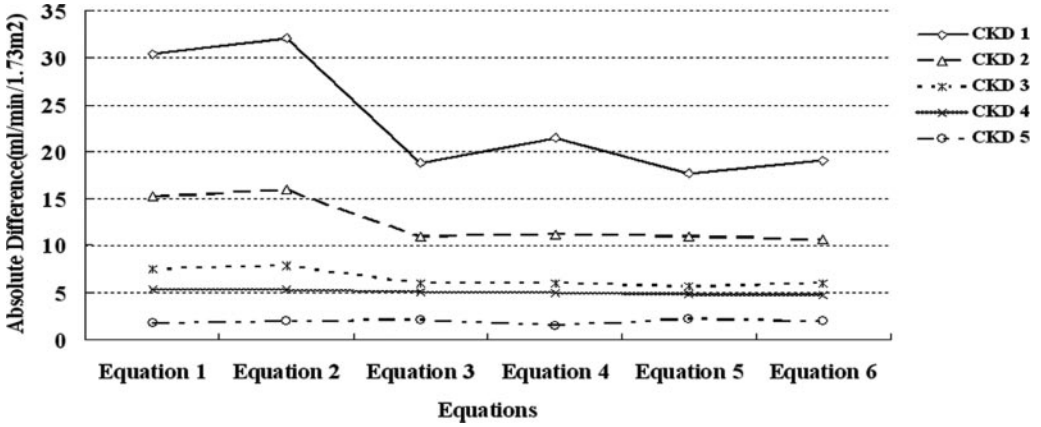

Figure 3. Comparison of equations: Absolute difference between eGFR and rGFR. The absolute differences between equations 3 through 6 eGFR and rGFR were significantly less than those between equations 1 and 2 eGFR and rGFR in CKD stages 1 and 2 ($P < 0.05$ for all). The absolute differences of equations 3 through 6 were also less than those of equations 1 and 2 in CKD stage 3 but without statistical significance. The absolute differences of the six equations were similar in stages 4 and 5.

The 50% accuracy of the six equations was not significantly different in each stage of CKD (Figure 4).

CKD Stage Misclassification by the Equations

We also evaluated CKD stage misclassification by the original MDRD equations and the modified MDRD equations. In CKD stage 1, 71.4 and 73.8% of patients were misclassified as in CKD stage 2 by equations 1 and 2; the percentages were 47.6, 45.2, 54.8, and 52.4% for equations 3 through 6, respectively. In CKD stage 2, compared with the modified MDRD equations, more patients were misclassified as in CKD stage 3 by equations 1 and 2; the percentages of incorrect stage were 60.0, 68.3, 30.0, 31.7, 31.7, and 31.7% for equations 1 through 6, respectively (χ^2 test, $P < 0.05$; Table 3). In CKD stages 3 through 5, there was no significant difference in the percentages of misclassification among the six equations (χ^2 test, $P > 0.05$).

Final Equations

For more precise GFR prediction, we modified original MDRD equations on the basis of data from all 684 patients with CKD, using the similar methods in equations 3 through 6. The final equations by adding racial coefficients were re-expressed as follows ($n = 684$ for both, $R^2 = 0.95$):

$$\text{c-7GFR}_3\ (\text{ml/min per 1.73 m}^2) = 170 \times \text{Pcr}^{-0.999} \times \text{age}^{-0.176} \times \text{BUN}^{-0.170} \times \text{albumin}^{0.318} \times 0.762\ (\text{if female}) \times 1.211\ (\text{if Chinese}) \quad (7)$$

$$\text{c-aGFR}_3\ (\text{ml/min per 1.73 m}^2) = 186 \times \text{Pcr}^{-1.154} \times \text{age}^{-0.203} \times 0.742\ (\text{if female}) \times 1.233\ (\text{if Chinese}) \quad (8)$$

The final equations 9 and 10, based on the values of Pcr measured with a Hitachi 7600 analyzer from our laboratory after smearing adjustment, also are described in the Appendix ($n = 684$ for both; $R^2 = 0.86$).

Discussion

With the increasing emphasis on the earlier detection and management of CKD, estimation of urine albumin excretion and GFR has assumed greater importance. The MDRD equations were developed on the basis of white and black patients

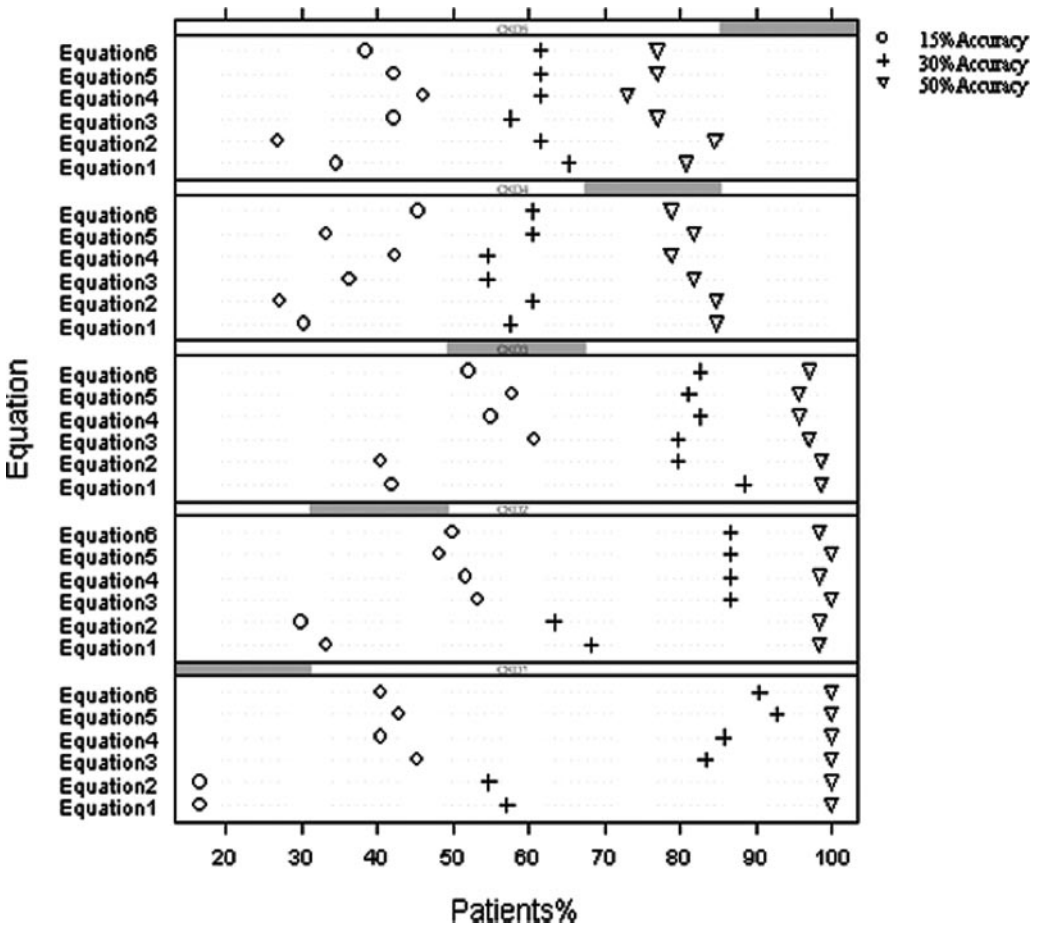

Figure 4. Comparison of equations: 15, 30, and 50% accuracy of equations in various stages of CKD. In CKD stages 1 and 2, equations 3 through 6 showed significant improvements in 15 and 30% accuracy compared with equations 1 and 2 ($P < 0.05$ for all); significant 15% accuracy were achieved comparing equations 3 and 5 with equations 1 and 2 in CKD stage 3 ($P < 0.05$ for both); some improvement was achieved comparing equations 4 and 6 with equations 1 and 2 in CKD stage 3 without statistical significance. In CKD stages 4 and 5, 15% accuracy improvements of equations 3 through 6 was gained without statistical significance. The 15 and 30% accuracy among equations 3 through 6 were not significantly different. The 50% accuracy of the six equations was not significantly different in each stage of CKD.

and were not suitable for Asian individuals (6,11): Both original MDRD equation 7 and the abbreviated MDRD equation underestimated rGFR in patients with nearly normal kidney function (6,12,13). Underestimation of GFR in near-normal kidney function causes misclassification and results in unnecessary interventions, such as referral to nephrologists and/or excessive monitoring or other interventions (14,15). Therefore, we tried to fill a major void in the international classification of the stage of renal insufficiency by modifying the original MDRD equations for the estimation of GFR in Chinese patients.

In our study, all the modified MDRD equations showed lower bias and higher accuracy than the original MDRD equations in each stage of CKD when applied to Chinese patients; particularly in patients with near-normal kidney function, cases of CKD stage 2 that were misdiagnosed as CKD stage 3 by modified equations were less by approximately 40% than those of original MDRD equations. This will help nephrologists to figure out a relatively correct prevalence of CKD and ensure that clinicians make a proper clinical action plan for patients with CKD and avoid unnecessary clinical intervention.

Because there were no significant performance difference among equations 3 through 6 and because the final equations 7 through 10 were based on all patients, which were assumed to be more accurate than equations 3 through 6, we recommend that equations 7 through 10 be used. Because equations 8 and 10 require only one laboratory variable, Pcr, and the GFR estimating process is simplified without decreasing accuracy, for easier application, especially in population screening, equations 8 and 10 are recommended.

There are several methods to measure Pcr in clinical laboratories. Jaffe's kinetic method on a Hitachi analyzer is the most widely used method in Chinese clinical laboratories. For better practicability, the Jaffe's kinetic method on a Hitachi analyzer was used our study. For patients with Pcr value as measured on a Hitachi analyzer using the Jaffe's kinetic method, equation 10 could be used; for patients with Pcr as measured on Beckman analyzers using the Jaffe's kinetic method, equation 8 could be used.

Recently, some studies (16,17) emphasized the importance of calibration of Pcr. Use of Pcr in MDRD equations requires that

Table 3. Percentages of CKD stage misclassification by original and modified equations in CKD stages 1 and 2[a]

Classification Based on:	CKD Stage Based on rGFR	
	1	2
Equation 1		
CKD stage 1	28.6	0
CKD stage 2	71.4	40
CKD stage 3	0	60
Equation 2		
CKD stage 1	26.2	1.7
CKD stage 2	73.8	31.7
CKD stage 3	0	66.6
Equation 3		
CKD stage 1	52.4	8.3
CKD stage 2	47.6	70
CKD stage 3	0	21.7
Equation 4		
CKD stage 1	54.8	13.3
CKD stage 2	45.2	68.3
CKD stage 3	0	18.4
Equation 5		
CKD stage 1	45.2	10
CKD stage 2	54.8	68.3
CKD stage 3	0	21.7
Equation 6		
CKD stage 1	47.6	11.7
CKD stage 2	52.4	68.3
CKD stage 3	0	20

[a]In CKD stage 1, equations 3 through 6 showed lower percentages of misclassification than equations 1 and 2 ($P < 0.05$ for equations 3 and 4; NS for equations 5 and 6). In CKD stage 2, equations 3 through 6 achieved lower percentages of misclassification than equations 1 and 2 ($P < 0.05$ for all).

the Pcr value be calibrated to the Cleveland Clinic Laboratory value. Failure to do so can introduce a systemic bias in the eGFR, so we think that it is important to calibrate Pcr to the Cleveland Clinic Laboratory value in equation 8; for equation 10, Pcr calibration could be performed in the laboratory at the First Hospital, Beijing University.

There are several reasons for why the modified equations outperformed the original equations. First, there were racial differences, and addition of the Chinese racial factor certainly allowed performance improvement. Furthermore, the rGFR method that was used in our study—plasma clearance of ^{99m}Tc-DTPA—was different from that used in the MDRD study—renal clearance of ^{125}I-iothalamate. These two methods may differ from each other compared with inulin clearance (18–20). Therefore, GFR estimation equations that are derived from different rGFR might differ from each other, even in the same group of patients.

Several limitations in our study should be noted. First, according to Levey *et al.* (16), the Pcr-based equations were derived from the results of multiple regression analysis, their performance best fitted around the observed mean. The original MDRD equations were developed in patients with average GFR of 39.8 ml/min per 1.73 m^2; the eGFR would underestimate rGFR in individuals with a higher range of GFR and overestimate rGFR in a group with advanced kidney failure. Although great improvement was achieved, equations 3 through 6 still underestimate GFR when GFR is nearly normal. We modified MDRD equations on the basis of the original MDRD equations and used the same variables and a similar method so that it would not inevitably inherit the same shortcomings of the original equations.

Second, in the modified MDRD equations, Pcr still was the important GFR-predicting variable, so the main, unavoidable pitfall of Pcr-based GFR estimation equations will contribute to the inaccuracy of each equation. It is a fundamentally different relationship between Pcr and GFR in populations with different levels of GFR (16); therefore, different levels of Pcr were not necessarily reflecting the true variation of GFR (21). In near-normal GFR levels, there was no significant decrease of Pcr with the increment of true GFR. However, in advanced kidney failure, with the prominent increment of Pcr, only a slight GFR decrease was detected. Some other potential GFR-predicting variables, such as plasma cystatin C, might be included to improve the performance of GFR-estimating equations, especially in early stages of CKD (22).

Third, because the percentage of patients with CKD that was caused by hypertension and/or diabetes was relatively small in our studied population, the modified equations' performance in patients with hypertension and/or diabetes needs to be examined further.

Conclusion

The importance of being able to assess GFR accurately without complex procedures is especially important in China, a vast, developing country with a population of 1.3 billion—almost one fifth of the world's population—and the prevalence of CKD in this country seems to be increasing. From our study, we concluded that the accuracy of these modified MDRD equations on the basis of data that were obtained from Chinese patients with CKD was better than that of the original MDRD equations in Chinese patients with CKD and provide clinicians with the opportunity to estimate GFR more accurately using simple Pcr and demographic variables. It will be interesting to know whether these modified MDRD equations will have the same performance in patients with CKD in other Asian individuals.

Appendix

The equations that are based on the result of multiple linear regression from data of 454 Chinese patients with CKD, as well as the final equations that were derived from data of 684 Chinese patients with CKD, after smearing adjustment, are as follows ($R^2 = 0.86$ for all):

$$\text{c-7GFR}_2 \text{ (ml/min per 1.73 m}^2) = 184 \times \text{Pcr}^{-1.091} \times \text{age}^{-0.203} \times \text{BUN}^{-0.161} \times \text{albumin}^{0.33} \times 0.816 \text{ (if female)} \quad (5)$$

$$\text{c-aGFR}_2 \text{ (ml/min per 1.73 m}^2) = 206 \times \text{Pcr}^{-1.234} \times \text{age}^{-0.227} \times 0.803 \text{ (if female)} \quad (6)$$

$$\text{c-7GFR}_4\ (\text{ml/min per } 1.73\ \text{m}^2) = 193 \times \text{Pcr}^{-1.064} \times \text{age}^{-0.161} \times \text{BUN}^{-0.197} \times \text{albumin}^{0.274} \times 0.80\ (\text{if female}) \quad (9)$$

$$\text{c-aGFR}_4\ (\text{ml/min per } 1.73\ \text{m}^2) = 175 \times \text{Pcr}^{-1.234} \times \text{age}^{-0.179} \times 0.79\ (\text{if female}) \quad (10)$$

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Erratum

Correction

Erratum for Ma *et al*.: Modified Glomerular Filtration Rate Estimating Equation for Chinese Patients with Chronic Kidney Disease. *J Am Soc Nephrol* 17: 2937–2944, 2006.

The authors regretfully report an error in the linear progression equation used with a CX3 analyzer by the Cleveland Clinic Laboratory to measure plasma creatine (Pcr). The published value of −15.91 μmol/L should have been presented in the units of mg/dl, or −0.18 mg/dl. The corrected equation is shown below.

CX3 Pcr (mg/dl) = −0.18 + 1.32 × Hitachi Pcr (mg/dl)