# Full age spectrum equation versus CKD-EPI and MDRD equations to estimate glomerular filtration rate in adults with obstructive nephropathy 

Kedan Cai © ${ }^{\text {© }}$ Lingxiong Chai, Qun Luo, Zhiwei Dai, Lingping Wu and Yue Hong


#### Abstract

Objective: To compare the full age spectrum (FAS) equation with the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations in predicting glomerular filtration rate (GFR) in patients with obstructive nephropathy. Methods: Adult patients with obstructive nephropathy who had undergone a GFR measurement using technetium-99m diethylenetriaminepentaacetic acid radioisotope renography were enrolled in the study. The measured GFR was taken as the reference value. Bias, precision and accuracy were compared between the three equations. Kappa test and the Bland-Altman method were used to evaluate the classification and the agreement. Receiver operating characteristic (ROC) curve analysis was used to describe the diagnostic accuracy of each equation. Results: A total of 327 patients were enrolled. The P30 value for the FAS equation was $60.2 \%$ in the overall study cohort. The FAS equation had the highest diagnostic accuracy $\left(R^{\prime} C^{A U C}=0.87\right.$, $95 \%$ confidence interval [CI] $0.84,0.91$ ) compared with the MDRD equation $\left(R O C^{A U C}=0.86\right.$, $95 \% \mathrm{CI} 0.82,0.89$ ). The median bias of the FAS equation was significantly higher than that of the MDRD equation ( 8.7 versus $7.6 \mathrm{ml} / \mathrm{min} / \mathrm{I} .73 \mathrm{~m}^{2}$, respectively). Conclusions: Despite the drawbacks associated with each equation, the FAS equation was probably closer to ideal to estimate GFR in patients with obstructive nephropathy.


Department of Nephrology, Ningbo No. 2 Hospital, Ningbo University School of Medicine, Ningbo, Zhejiang Province, China

## Corresponding author:

Qun Luo, Department of Nephrology, Ningbo No. 2
Hospital, Ningbo University School of Medicine, 4I Xibei Street, Ningbo 3I50I0, Zhejiang Province, China.
Email: luoqun@nbu.edu.cn

## Keywords

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## Introduction

Obstructive nephropathy is one of the most common causes of chronic kidney disease (CKD). ${ }^{1}$ It is often caused by kidney stones, cancer or prostatic hyperplasia. ${ }^{2}$ Obstruction of the urinary tract may lower renal blood flow and the glomerular filtration rate (GFR), ${ }^{1}$ leading to renal fibrosis. ${ }^{3}$ To optimize patient outcomes, it has been suggested that renal function should be monitored during follow-up to estimate the condition of the disease and the effects of treatment. ${ }^{4}$

Glomerular filtration rate is considered the ideal indicator to evaluate renal function in patients with CKD. ${ }^{5}$ There are several newly developed equations to evaluate GFR, which are much more convenient and cheaper than the conventional methods that use renal clearance of exogenous inulin or other alternative exogenous markers. For example, the Modification of Diet in Renal Disease (MDRD) equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation are the most commonly used equations worldwide. ${ }^{6,7}$

Recently, a new equation, full age spectrum (FAS), was developed and validated in a purely Caucasian population based on normalized serum creatinine. ${ }^{8}$ The FAS equation showed less bias and a better performance than the CKD-EPI equation in studies in which reference GFR values were obtained by various methods, but none of the studies used radioisotope renography with technetium-99m diethylenetriaminepentaacetic acid ( 99 mTc -DTPA). ${ }^{8,9}$ However, the FAS equation has not been validated in Chinese patients with
obstructive nephropathy compared with 99 mTc -DTPA radioisotope renography as the standard method for measuring GFR.

The objective of this study was to estimate the performance of the FAS equation in patients with obstructive nephropathy and to compare this equation with the MDRD and CKD-EPI equations. To the best of our knowledge, few studies have validated these equations in a cohort of patients who only have obstructive nephropathy. ${ }^{2}$

## Patients and methods

## Patient population

This retrospective study enrolled consecutive adult patients with obstructive nephropathy who had undergone a GFR measurement using 99 mTc -DTPA radioisotope renography at the Department of Nephrology, Ningbo No. 2 Hospital, Ningbo University School of Medicine, Ningbo, Zhejiang Province, China, between 1 January 2011 and 30 April 2016. Demographic data were recorded for each patient, including age, sex, height and weight. Exclusion criteria included the following: (i) acute kidney injury; (ii) treatment with dialysis; (iii) prior renal transplantation; (iv) severe malnutrition; (v) infection; (vi) severe liver or cardiac dysfunction; (vii) pleural or abdominal effusion: (viii) treatment with medication that can affect renal function, such as vitamin C or a large dose of steroids.

Based on the measured GFR (mGFR) value from the 99 mTc -DTPA radioisotope renography, patients were divided into four groups according to the Kidney Disease

Improvement Global Outcomes guidelines as follows: ${ }^{10}$ group 1 , eGFR $\geq 90 \mathrm{ml} / \mathrm{min} /$ $1.73 \mathrm{~m}^{2}$ (stage 1 CKD ); group 2, eGFR $60-89 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ (stage 2 CKD); group 3 , eGFR $30-59 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ (stage 3 CKD); group 4, eGFR $15-29 \mathrm{ml} /$ $\min / 1.73 \mathrm{~m}^{2}$ (stage 4 CKD).

The study was approved by the Ethics Committee of Ningbo No. 2 Hospital, Ningbo University School of Medicine, Ningbo, Zhejiang Province, China (No. PJ-NBEY-KY-2016-021-01). Due to the retrospective design of this current study, written informed consent was not required from the participants.

## Measurement of GFR

The mGFR was measured using 99 mTc DTPA radioisotope renography on a Siemens e.cam single gamma camera with high dynamic range detector technology as described previously (Siemens Healthcare, Erlangen, Germany). ${ }^{11} 5 \mathrm{mCi} 99 \mathrm{mTc}-$ DTPA (purity 95-99\%; Atom-Hitech Isotope Limited Company, Hangzhou, China) was injected into the patient after their height and weight measurements had been taken, and they had consumed 500 ml of drinking water and had emptied their bladder. mGFR was calculated using a personal computer using the Gates method and corrected by body surface area with the Du Bios equation.

## Measurement of serum creatinine

All whole blood samples were drawn from the median cubital vein in the morning following a minimum 8-h fast. Approximately 5 ml of whole blood was added to a test tube containing no anticoagulant as required for the production of serum and stored at room temperature for 1 h . The blood samples were centrifuged at 4128 g for 5 min at 4 C in a Thermo Scientific ${ }^{\mathrm{TM}}$ Heraeus $^{\text {TM }}$ Multifuge ${ }^{\text {TM }}$ X1 Centrifuge
(ThermoFisher Scientific, Rockford, IL, USA). Serum creatinine was measured using the sarcosine oxidase method (Purebio Biotechnology, Ningbo, China) on an ADVIA ${ }^{\circledR} 2400$ Clinical Chemistry System (Siemens Healthcare).

## Estimation of GFR

All three equations, MDRD, CKD-EPI and FAS, were used to estimate the GFR for each patient. The three equations are presented in Table 1.

## Statistical analyses

All statistical analyses were performed using SPSS software, version 19.0 (IBM Corp, Armonk, NY, USA) and MedCalc software, version 15.2.2 (MedCalc ${ }^{\circledR}$, Ostend, Belgium). The data are presented as mean $\pm$ SD for normally distributed continuous variables, median (interquartile range) for not normally distributed continuous variables, and frequencies and percentages for categorical variables. Confidence intervals (CIs) were calculated using the Bootstrap method. The subjects were stratified by $\mathrm{mGFR}(<60$ versus $\geq 60 \mathrm{ml} / \mathrm{min} /$ $1.73 \mathrm{~m}^{2}$ ) and age ( $<70$ versus $\geq 70$ years).

Bias, precision and accuracy were analysed to compare the performance of the three equations. Bias was calculated by determining the eGFR value minus the mGFR value. Precision was expressed as the root mean square error (RMSE). The accuracy of each equation was defined as P30, the percentage of eGFR values within $30 \%$ deviation of the mGFR.

Paired $t$-test was used to compare the bias. McNemar's test and Kappa test were employed for accuracy and classification agreement between eGFR and mGFR. The Bland-Altman method was used to evaluate the agreement between eGFR and mGFR. Additionally, correlations between eGFR and mGFR were assessed

Table I. The equations used to estimate glomerular filtration rate (eGFR) based on serum creatinine (SCr) levels, age and sex in a study that compared three equations: Modification of Diet in Renal Disease (MDRD) equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and the full age spectrum (FAS). ${ }^{6-8}$

| eGFR equation |  | Equation |
| :---: | :---: | :---: |
| MDRD |  | $175 \times(\mathrm{SCr})^{-1.154} \times(\mathrm{Age})^{-0.203} \times 0.742$ (if female) |
| CKD-EPI |  |  |
| Female: $\mathrm{SCr} \leq 0.7 \mathrm{mg} / \mathrm{dl}$ |  | $144 \times(\mathrm{SCr} / 0.7)^{-0.329} \times 0.993^{\text {Age }}$ |
| Female: $\mathrm{SCr}>0.7 \mathrm{mg} / \mathrm{dl}$ |  | $144 \times(\mathrm{SCr} / 0.7)^{-1.209} \times 0.993^{\text {Age }}$ |
| Male: $\mathrm{SCr} \leq 0.9 \mathrm{mg} / \mathrm{dl}$ |  | $141 \times(\mathrm{SCr} / 0.9)^{-0.411} \times 0.993^{\text {Age }}$ |
| Male: $\mathrm{SCr}>0.9 \mathrm{mg} / \mathrm{dl}$ |  | $14 \mathrm{I} \times(\mathrm{SCr} / 0.9)^{-1.209} \times 0.993^{\text {Age }}$ |
| FAS |  |  |
| Female: $18 \leq$ age $\leq 40$ years | $\mathrm{Q}=0.70 \mathrm{mg} / \mathrm{dl}$ | 107.3/(SCr/Q) |
| Female: age $>40$ years |  | $[107.3 /(\mathrm{SCr} / \mathrm{Q})]^{* 0.988}{ }^{(\text {age }-40)}$ |
| Male: $18 \leq$ age $\leq 40$ years | $\mathrm{Q}=0.90 \mathrm{mg} / \mathrm{dl}$ | 107.3/(SCr/Q) |
| Male: age $>40$ years |  | $[107.3 /(\mathrm{SCr} / \mathrm{Q})]^{*} 0.988^{(\mathrm{age}-40)}$ |

using Pearson's correlation analysis. Area under the receiver operating characteristic (ROC) curve was used to describe the diagnostic efficacy of the equations. The cut-off for GFR stratification was $<60 \mathrm{ml} / \mathrm{min} /$ $1.73 \mathrm{~m}^{2}$. A $P$-value $<0.05$ was considered statistically significant.

## Results

This study enrolled 327 adult patients with obstructive nephropathy who had undergone a GFR measurement using 99 mTc DTPA radioisotope renography. The detailed demographic and clinical characteristics of the patients are presented in Table 2. There were 133 females and 194 males, with a mean $\pm$ SD age of 56.25 $\pm 14.19$ years. A total of 51 of 327 (15.60\%) patients had bilateral obstructions and 276 of 327 ( $84.40 \%$ ) patients had unilateral obstructions. The main aetiology was urinary tract stones, accounting for $69.42 \%$ of the total (227 of 327 patients). The mean $\pm$ SD mGFR was $69.58 \pm 21.15 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ and the mean $\pm$ SD eGFR of the three methods were GFRmdrd $\quad 77.18 \pm 33.627 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$, GFRepi $78.50 \pm 30.627 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ and

GFRfas $\quad 78.33 \pm 33.17 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$. Based on the mGFR value, there were 54 (16.51\%), 166 (50.76\%), 97 (29.66\%) and $10(3.06 \%)$ patients with stages $1,2,3$ and 4 CKD, respectively.

The performance of the FAS equation compared with the MDRD and CKD-EPI equations is summarized in Table 3. The FAS equation produced a higher eGFR compared with mGFR and there was an obvious positive bias of $8.7 \mathrm{ml} / \mathrm{min} .1 .73 \mathrm{~m}^{2}$, which was not significantly different to that of the CKD-EPI equation (bias, $8.9 \mathrm{ml} / \mathrm{min} /$ $1.73 \mathrm{~m}^{2}$ ), but significantly higher than that of the MDRD equation (bias, $7.6 \mathrm{ml} / \mathrm{min} /$ $1.73 \mathrm{~m}^{2} ; P=0.01$ ). The P30 value for the FAS equation was $60.2 \%$ in the overall study cohort, a little lower than the MDRD equation, but this was not significantly different compared with the CKDEPI equation. In terms of precision, the RMSEs showed no statistically significant difference among the three equations.

There was a significant correlation between the mGFR and eGFRfas by Pearson's correlation analysis ( $r=0.707$, $P<0.05$ ). Similar correlations between mGFR and eGFR using the other two equations were observed $\quad\left(r_{\mathrm{mdrd}}=0.672\right.$,

Table 2. Demographic and clinical characteristics of patients $(n=327)$ with obstructive nephropathy that participated in this study to compare three equations used to estimate glomerular filtration rate (eGFR) compared with measured GFR.

|  | Total cohort $n=327$ | Females $n=133$ | Males $n=194$ |
| :---: | :---: | :---: | :---: |
| Age, years | $56.25 \pm 14.19$ | $56.07 \pm 14.20$ | $56.38 \pm 14.23$ |
| Weight, kg | $61.85 \pm 10.43$ | $56.82 \pm 8.41$ | $65.31 \pm 10.30$ |
| Height, cm | $164.72 \pm 7.07$ | $158.95 \pm 5.07$ | $168.68 \pm 5.32$ |
| Body mass index, $\mathrm{kg} / \mathrm{m}^{2}$ | $22.73 \pm 3.12$ | $22.48 \pm 3.14$ | $22.90 \pm 3.10$ |
| Body surface area, $\mathrm{m}^{2}$ | $1.77 \pm 0.15$ | $1.67 \pm 0.12$ | $1.84 \pm 0.14$ |
| Serum albumin, g/l | $38.07 \pm 6.00$ | $38.82 \pm 5.34$ | $37.56 \pm 7.37$ |
| Serum creatinine, $\mu \mathrm{mol} / \mathrm{l}$ | 80.00 (63.10-110.10) | 64.60 (56.20-82.60) | 89.40 (73.70-128.02) |
| Serum urea nitrogen, mmol/l | $5.92 \pm 3.77$ | $5.13 \pm 2.81$ | $6.46 \pm 4.22$ |
| Measured GFR, ml/min/ $/ .73 \mathrm{~m}^{2}$ | $69.58 \pm 21.15$ | $70.41 \pm 20.31$ | $69.02 \pm 21.74$ |
| Chronic kidney disease stage |  |  |  |
| I | 54 (16.51) | 23 (17.29) | 31 (15.98) |
| 2 | 166 (50.76) | 70 (52.63) | 96 (49.48) |
| 3 | 97 (29.66) | 36 (27.07) | 61 (31.44) |
| 4 | 10 (3.06) | 4 (3.01) | 6 (3.09) |

Data presented as mean $\pm$ SD, median (interquartile range) and $n$ of patients (\%).
$\left.P<0.05 ; r_{\text {epi }}=0.709, P<0.05\right)$. The BlandAltman plots of the three eGFR equations against mGFR are shown in Figure 1. Compared with mGFR, the agreement with eGFRfas $\left(-37.5,55.0 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}\right.$; $P<0.01$ ) and eGFRepi ( $-33.4,51.2 \mathrm{ml} /$ $\mathrm{min} / 1.73 \mathrm{~m}^{2} ; P<0.01$ ) was narrower than that between eGFRmdrd and mGFR $\left(-41.3,56.5 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2} ; P<0.01\right)$. The Kappa coefficient of the FAS equation for staging consistency was 0.426 (Table 3), while the other two groups had poor agreement. Table 4 presents the diagnostic values of the three equations to identify patients with $\mathrm{mGFR}<60 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$. The FAS equation gave the best diagnostic accuracy $\left(\mathrm{ROC}^{\mathrm{AUC}}=0.87 ; 95 \%\right.$ CI $\left.0.84,0.91\right)$ and was significantly superior to the MDRD equation $\left(\mathrm{ROC}^{\mathrm{AUC}}=0.86 ; 95 \%\right.$ CI 0.82 , $0.89 ; P=0.036$; Figure 2).

In the subgroup stratified by age $(\geq 70$ years), the FAS equation showed the lowest bias compared with mGFR with a mean difference of $-1.9(95 \%$ CI -6.6 , $3.1) \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$. The value showed no statistical difference from 0 , indicating
that the FAS equation showed no bias in this setting (Table 3). The FAS equation was significantly superior to the other two equations in this age group in terms of bias ( $P<0.05$ for both comparisons). The highest P30 value was $66.0 \%$ for the FAS equation, although there was no significant difference among the three equations. The precision of eGFR as calculated by the FAS equation was similar to that of the other two equations without there being a statistically significant difference in the RMSEs. There was poor consistency between eGFRfas and mGFR based on the correlation and the Kappa values, which were similar to the other eGFR equations.

In the subgroup stratified by mGFR $\left(<60 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}\right)$, the FAS equation had a significantly lower bias compared with the eGFRepi equation ( $P=0.009$ ). In terms of P30 accuracy and RMSE precision, these were highest with the FAS equation, but there were no significant differences between the three equations. As for the Kappa values, there was a poor staging consistency between eGFRfas and mGFR values.
Table 3. The performance of three different equations used to estimate glomerular filtration rate (eGFR) compared with measured GFR (mGFR) according to age and mGFR groups in patients ( $n=327$ ) with obstructive nephropathy.

| Analytical groups | $\begin{aligned} & \mathrm{mGFR}, \mathrm{ml} / \mathrm{min} / \\ & \mathrm{I} .73 \mathrm{~m}^{2} \end{aligned}$ | eGFR <br> equation | Root mean square error | $\begin{aligned} & \text { Bias, } \mathrm{ml} / \\ & \mathrm{min} / 1.73 \mathrm{~m}^{2} \\ & (95 \% \mathrm{Cl}) \end{aligned}$ | $\begin{aligned} & \text { P30, \% } \\ & \text { (95\% CI) } \end{aligned}$ | Pearson's correlation analysis ( $95 \% \mathrm{CI}$ ) | Kappa |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Overall study cohort | $69.58 \pm 21.15$ |  |  |  |  |  |  |
|  |  | MDRD | 26.0 (24.2, 28.2) | $7.6(4.6,10.4)^{\text {a }}$ | 60.6 (54.7,65.7) | 0.672 (0.603, 0.736)* | 0.401 |
|  |  | CKD-EPI | 23.3 (21.7, 25.3) | 8.9 (6.7, II.3) | 56.3 (51.1,62.1) | 0.709 (0.645, 0.766)* | 0.351 |
|  |  | FAS | 25.1 (23.3, 27.2) | 8.7 (6.1, I 1.3) | 60.2 (55.1, 65.7) | 0.707 (0.646, 0.768)* | 0.426 |
| Adults 18-70 years | $72.49 \pm 20.77$ |  |  |  |  |  |  |
|  |  | MDRD | 26.7 (24.6, 29.1) | $7.9(4.8,11.25)^{\text {a }}$ | 62.1 (56.3, 67.5) | 0.666 (0.585, 0.739)* | 0.390 |
|  |  | CKD-EPI | 23.9 (22.1, 26.1) | 9.9 (7.3, 12.5) | 56.7 (50.5, 62.5) | 0.669 (0.622, 0.769)* | 0.325 |
|  |  | FAS | 26.3 (24.2, 28.6) | 10.7 (7.9, 13.5) | 59.2 (53.1, 65.0) | 0.686 (0.610, 0.758)* | 0.376 |
| Older adults $\geq 70$ years | $53.46 \pm 15.21$ |  |  |  |  |  |  |
|  |  | MDRD | 22.4 (18.7, 27.8) | $5.9(-0.1,12.0)^{\text {a }}$ | 52.0 (38.0, 66.0) | 0.473 (0.160, 0.701)* | 0.284 |
|  |  | CKD-EPI | 19.8 (16.5, 24.6) | 3.5 (-2.1, 8.9) ${ }^{\text {b }}$ | 54.0 (40.0, 68.0) | 0.445 (0.1 18, 0.685)* | 0.270 |
|  |  | FAS | 17.5 (14.7, 21.8) | -1.9 (-6.6, 3.1) | 66.0 (52.0, 78.0) | 0.468 (0.168, 0.706)* | 0.375 |
| $\mathrm{mGFR}<60 \mathrm{ml} / \mathrm{min} / \mathrm{I} .73 \mathrm{~m}^{2}$ | $45.49 \pm 10.40$ |  |  |  |  |  |  |
|  |  | MDRD | 22.3 (19.7, 25.8) | 4.5 (0.4, 8.5) | 47.7 (38.3, 57.0) | 0.538 (0.393, 0.680)* | 0.117 |
|  |  | CKD-EPI | 22.8 (20.1, 26.3) | $5.9(1.9,10.6)^{\text {b }}$ | 43.0 (33.6, 52.3) | 0.566 (0.403, 0.687)* | 0.093 |
|  |  | FAS | 20.8 (18.3, 24.0) | 4.6 (I.I, 8.8) | 53.3 (43.0, 62.6) | 0.588 (0.403, 0.685)* | 0.138 |
| $\mathrm{mGFR} \geq 60 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ | $81.30 \pm 13.86$ |  |  |  |  |  |  |
|  |  | MDRD | 27.7 (25.3, 30.5) | $9.1(5.5,12.5)^{\text {a }}$ | 66.8 (60.5, 72.7) | 0.417 (0.286, 0.532)* | 0.177 |
|  |  | CKD-EPI | 23.6 (21.6,26.0) | 10.4 (7.5, 13.2) | 62.7 (55.9, 69.1) | 0.425 (0.289, 0.533)* | 0.110 |
|  |  | FAS | 27.0 (24.7, 29.8) | 10.8 (7.4, 14.0) | 63.6 (57.7, 70.0) | 0.457 (0.32I, 0.565)* | 0.169 |

${ }^{\mathrm{a}} \mathrm{P}<0.05$ GFRfas compared with GFRmdrd; ${ }^{\mathrm{b}} \mathrm{P}<0.05$ GFRfas compared with GFRepi.
*p $<0.05$ Pearson's correlation analysis.
CI, confidence interval; MDRD, Modification of Diet in Renal Disease equation, CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation; FAS, full age spectrum.


Figure I. Bland-Altman plots of the estimated glomerular filtration rate (eGFR) and measured GFR (mGFR) for the three eGFR equations: Modification of Diet in Renal Disease (MDRD) equation (A), the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (B) and the full age spectrum (FAS) equation (C). A positive difference in 'eGFR - mGFR' indicates an overestimation by the eGFR equation, whereas a negative difference indicates an underestimation. The solid lines indicate the mean difference; the dashed lines indicate the lines of agreement, calculated as the mean difference $\pm$ I. 96 SD of this difference. The colour version of this figure is available at: http://imr.sagepub.com.

## Discussion

It is necessary to periodically monitor kidney function using convenient and accurate methods in order to facilitate an early diagnosis of kidney problems and to improve patient outcomes. ${ }^{4}$ This current study demonstrated that the FAS equation was nearly equivalent to the MDRD and CKD-EPI equations in terms of bias, accuracy and precision, and also positively correlated with the mGFR. The FAS equation gave the best diagnostic efficiency among the three equations. Especially in older patients and patients with $\mathrm{GFR}<60 \mathrm{ml} /$ $\mathrm{min} / 1.73 \mathrm{~m}^{2}$, the FAS equation was superior to the other two equations in terms of bias and it was as good in other aspects.

Until now, over 10 equations to estimate the GFR have been developed. The MDRD and CKD-EPI equations are the most widely used equations worldwide. ${ }^{12}$ A previous study suggested that the MDRD and CKD-EPI equations were validated to estimate GFR in patients with obstructive nephropathy, despite the pathogenetic, pathological and physiological changes associated with obstructive nephropathy being different from those in diffuse renal diseases. ${ }^{2}$ In 2016, a novel eGFR equation, the FAS equation, was developed based on the concept of population-normalized serum creatinine, denoted as $\mathrm{SCr} / \mathrm{Q} .{ }^{8}$ To the best of our knowledge, this current study is the first to compare the FAS equation with the CKD-EPI and MDRD equations in the patients with obstructive nephropathy in China.

Bias, precision and accuracy are the most important indicators to evaluate the validity of the method used to determine the GFR. ${ }^{13}$ In this current study, the values of these indices for the MDRD and CKD-EPI equations were consistent with those demonstrated previously. ${ }^{2}$ The FAS equation was nearly equivalent to the other two equations in terms of bias, accuracy and

Table 4. Diagnostic measures of three different equations used to estimate glomerular filtration rate (GFR) using a cut-off of $60 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$.

|  | Equations used to estimate GFR |  |  |
| :--- | :--- | :--- | :--- |
| Diagnostic measures | MDRD | CKD-EPI | FAS |
| AUC $(95 \% \mathrm{CI})$ | $0.86(0.82,0.89)^{*}$ | $0.87(0.83,0.91)$ | $0.87(0.84,0.91)$ |
| Standard error | 0.02 | 0.02 | 0.02 |
| Sensitivity, $\%$ | 84.11 | 80.37 | 89.72 |
| Specificity, \% | 80.00 | 82.73 | 72.73 |
| Youden | 0.64 | 0.63 | 0.62 |

*P $=0.036$ GFRfas compared with GFRmdrd.
MDRD, Modification of Diet in Renal Disease equation, CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation; FAS, full age spectrum; AUC, area under the curve; Cl , confidence interval.


Figure 2. Receiver operating characteristics curve analysis for the diagnostic ability of the three equations: Modification of Diet in Renal Disease (MDRD) equation, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and the full age spectrum (FAS) equation. The values of the areas under the curve are listed in Table 4. The colour version of this figure is available at: http://imr.sagepub.com.
precision. And among these three equations, the FAS equation gave the best diagnostic efficiency, significantly surpassing the MDRD equation.

In the subgroup of older patients $(\geq 70$ years), the mean bias of the FAS equation was nearest to zero and lower than that of the MDRD and CKD-EPI equations. The FAS equation showed the highest accuracy and precision compared with the MDRD and CKD-EPI equations, although without reaching a statistically significant difference. This finding was consistent with previous research that validated the FAS
equation in 14 databases. ${ }^{8}$ Some studies demonstrated that the MDRD and CKDEPI equations were not very suitable for elderly patients. ${ }^{14,15}$ These current findings suggest that the FAS equation may be suitable for older patients with obstructive nephropathy.

The agreement and staging consistency between eGFRfas and mGFR were not ideal. The kappa value was only 0.426 in the overall study cohort and it was poorer in the subgroups stratified by age or mGFR. The agreement between eGFRfas and mGFR was wider than that between
eGFRepi and mGFR, but narrower than that between eGFRmdrd and mGFR, with all exceeding the acceptable limits of consistency defined as $\pm 30 \mathrm{ml} / \mathrm{min} / 1.73 \mathrm{~m}^{2}$ among these three equations. This result was consistent a previous study that validated the FAS equation in diffuse renal disease. ${ }^{11}$ All of these findings suggest that the FAS equation may not be ideal for the direct estimation of GFR in the patients with obstructive nephropathy in China. However, in adults and the older subgroups, the previous study demonstrated that the FAS equation showed a higher accuracy rate in correctly classifying subjects into matched GFR categories than that of CKD-EPI equation with a statistical difference. ${ }^{8}$

The possible reasons of these differences might be as follows: (i) an appropriate Qvalue for the FAS equation is crucial. The Q-value for the FAS equation was derived from a Belgian population, ${ }^{16}$ which was lower than that of Korean males; ${ }^{9}$ (ii) in addition, the performance of the eGFR equation could be improved by using coefficients specific for local ethnic groups. ${ }^{7,17}$ Therefore, it is better to obtain the Qvalue of the serum creatinine specifically for different ethnicities; ${ }^{18}$ (iii) the only aetiology was obstructive nephropathy in this current study, which was different to a previous study, ${ }^{8}$ in which the main aetiology was diffuse renal diseases; (iv) the difference in the serum creatinine measuring methods and the different reference measurements should be taken into consideration when evaluating the different equations. In this current study, serum creatinine was measured using an enzymatic assay, rather than using an isotope dilution mass spectrometry traceable creatinine method; (v) mGFR was obtained using 99 mTc -DTPA radioisotope renography in this current study, while iothalamate was applied for the CKD-EPI equation, ${ }^{19}$ and iohexol,
inulin and iothalamate measurements were used for the FAS equation. ${ }^{8}$

This current study had several limitations. First, the study population was from a single centre with a small sample size and with no patients at with stage 5 CKD, so the study cohort is not representative of the general population. Secondly, the study did not estimate eGFR using the cystatin $C$ equation or the combination of plasma creatinine and cystatin $C$, which may be more reliable predictors of GFR.

In conclusion, despite the drawbacks associated with each eGFR equation, the FAS equation was probably closer to the measured GFR in patients with obstructive nephropathy.

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## Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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## ORCID iD

Kedan Cai (D) http://orcid.org/0000-0003-3169-5143

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