

Applicability of various estimation formulas to assess renal function in Chinese children

Yue Du, Ting-Ting Sun, Ling Hou, Jin-Jie Guo, Xiu-Li Wang, Yu-Bin Wu

Shenyang, China

Background: This study was to evaluate the relative applicability of the most commonly used estimation formulas for renal glomerular filtration rate (GFR) of Chinese children with chronic kidney disease (CKD).

Methods: One hundred CKD patients of less than 17 years old were divided into two groups by sex which was further categorized into five subgroups based on CKD staging according to the "reference" GFR (rGFR) determined by Tc-99m-DTPA renal dynamic imaging. Four GFR markers including serum cystatin C (CysC), β 2-microglobulin, creatinine, and blood urea nitrogen were measured.

Results: Among all four markers, CysC best reflected the extent of glomerular damages for CKD stage 1. The value for estimation of GFR (eGFR) was derived from five different formulas either over-estimated or underestimated GFR as referenced to rGFR, and the extent of deviations was dependent on gender, age and CKD stage. The Counahan-Barratt formula and the Schwartz formula gave the most accurate estimations of GFR for CKD stages 1 and 2-3, respectively regardless of gender and age differences. Receiver operating characteristic analyses indicated that the Counahan-Barratt formula has the highest diagnostic accuracy.

Conclusion: The Counahan-Barratt formula provides the best approximation to rGFR, thereby the highest applicability to Chinese children with CKD of different genders, ages and CKD stages.

World J Pediatr 2015;11(4):346-351

Key words: chronic kidney disease;
Counahan-Barratt formula;
cystatin C;
renal glomerular filtration rate;
Schwartz formula

Author Affiliations: Pediatric Nephrology, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110004, China (Du Y, Sun TT, Hou L, Guo JJ, Wang XL, Wu YB)

Corresponding Author: Yue Du, MD, PhD, Pediatric Nephrology, Shengjing Hospital of China Medical University, Shenyang 110004, China (Tel: +86-024-96615-56411; Fax: +86-024-96615-56411; Email: ydu_cmu@163.com)

doi: 10.1007/s12519-014-0532-7
Online First November 2014

©Children's Hospital, Zhejiang University School of Medicine, China and Springer-Verlag Berlin Heidelberg 2014. All rights reserved.

Introduction

Chronic renal insufficiency in children is a serious problem which can eventually result in end-stage renal failure requiring renal replacement therapy and increased risk of cardiovascular disease, metabolic syndrome, and other complications. With rapid increase in the incidence of kidney disease in children in recent years, an urgent need has been prompted for more accurate means of determining glomerular filtration rate (GFR), which is critical for better diagnosis of acute and chronic renal insufficiency, early intervention to prevent development into end-stage renal failure, and monitoring for nephrotoxicity caused by antibiotics and chemotherapeutic agents.^[1,2] In children with chronic kidney disease (CKD), measured GFR is the best indicator of global kidney dysfunction. Especially in CKD children with a well-maintained fluid and electrolyte balance thereby entirely normal urinalysis, a reduced GFR serves as the only clinical sign of kidney damage in these individuals.

The methods of evaluating GFR include direct measurement and formula estimation. Direct detection method (such as inulin) and exogenous radioactive markers (such as the rate of renal excretion of Tc-99m-DTPA) are considered the "reference" for measurement of GFR (rGFR). However, the method involves complicated operating procedures and is costly and time-consuming; thus its clinical applications have certain limitations.^[3] Serum creatinine, blood urea nitrogen, and other traditional markers have been clinically used to detect kidney dysfunction over the years. Nowadays, the new markers like serum cystatin C have been used worldwide in replacement with the traditional indicators. In particular, cystatin C has been emerged as an endogenous marker of GFR is superior to serum creatinine for the detection of mild to moderate chronic kidney dysfunction.^[4] In the past decades, researchers have developed a fair number of GFR estimation formulas based on serum creatinine and serum cystatin C (CysC), of which Schwartz formula,^[5] the Modification of Diet in Renal Disease (MDRD) formula,^[6] the Cockcroft-Gault formula,^[7] Counahan-Barratt formula,^[8] and CysC-based GFR assessment

equation^[7,9] have been widely used for children GFR assessment in Western countries. However, the potential application of these formulas for Chinese children has not been validated. This study aimed to evaluate the applicability of various indicators and formulas, using the measured GFR by means of Tc-99m-DTPA renal dynamic imaging as a reference approach, and to assess renal function in Chinese children with kidney disease.

Methods

Patient information

One hundred patients from the Department of Pediatric Nephrology, Shengjing Hospital affiliated to the China Medical University were recruited from January to December 2011. The inclusion criteria included CKD at ages ≥ 1 year but ≤ 16 years with complete post-admission Tc-99m-DTPA renal dynamic imaging, abnormal serum creatinine, urea nitrogen, serum cystatin C and serum $\beta 2$ -microglobulin, and height, according to the Clinical Practice Guidelines of the United States of Kidney Disease and Dialysis (K/DOQ I).^[10] The exclusion criteria included heart failure, dehydration, limb deficiencies, and use of drugs that may influence the level of serum creatinine and its determination. The protocols for human studies were approved by the Institutional Review Board of Shengjing Hospital and informed written consent was obtained from the caregivers of the participants.

In 100 CKD patients, 67 were males (age, 9.4 ± 3.3 years; height, 140.3 ± 23.7 cm; weight, 39.0 ± 17.4 kg) and 33 females (age, 8.9 ± 3.4 years; height, 136.5 ± 22.6 cm; weight, 34.1 ± 16.1). Among them, 22 patients were diagnosed with nephrotic syndrome, 34 with glomerulonephritis, 6 with lupus nephritis, 15 with purpura nephritis, 4 with IgM nephropathy, 14 with IgA nephropathy, 2 with hemolytic uremic syndrome, 1 with renal agenesis, and 2 with renal dysplasia. The patients were divided into two groups by sex, and each group was subdivided into five groups based on rGFR values: stage 1 (64%): rGFR ≥ 90 mL/(min/1.73 m²); stage 2 (23%): rGFR=60-89 mL/(min/1.73 m²); stage 3 (8%): rGFR=30-59 mL/(min/1.73 m²); stage 4 (4%): rGFR=15-29 mL/(min/1.73 m²); and stage 5 (1%): rGFR ≤ 15 mL/(min/1.73 m²).

Tc-99m-DTPA renal dynamic imaging

Twenty minutes prior to Tc-99m-DTPA, the patients were allowed to drink 300-500 mL water and then emptied the bladder. The basal radioactivity in a syringe for loading with Tc-99m-DTPA was counted for 6 seconds. The patients were allowed to lie in a supine position, and the probe was aligned to midline of the spine where the kidney and bladder could be

visualized. Immediately after intravenous injection of Tc-99m-DTPA through the cubital vein, dynamic image acquisition was conducted at an interval of one frame per 2 seconds for consecutive 30 frames, followed by one frame per acquisition of 30, followed by one frame per 15 seconds for consecutive 80 frames. The residual radioactivity in a syringe was counted for 6 seconds. The levels of Tc-99m-DTPA in the body of the patients were calculated. Finally, the patients' height and weight together with the Tc-99m-DTPA levels were input into the computer to generate the renal time-radioactivity curve and acquire the values of renal GFR, which were designated as the "reference" GFR (rGFR) as recommended by the Nephrology Committee of the Society of Nuclear Medicine, because of the satisfactory accuracy and relative simplicity.^[11-13]

Estimation of GFR by various formulas

The following formulas were evaluated for their accuracy in the estimation of GFR (eGFR); (1) The Schwartz formula: $eGFR = K \times \text{height (cm)} / \text{serum creatinine } (\mu\text{mol/L})$, where K is a constant (K is 49 for girls of 2-16 year-old and boys of 2-13 year-old; K is 49 for boys of 13 -16 year-old);^[3] (2) The Cockcroft-Gault formula: $eGFR = (140 - \text{age}) \times \text{weight (kg)} \times (0.85, \text{female}) / \text{Scr (mg/dL)} \times 72$;^[14] (3) The MDRD formula: $eGFR = 186 \times \text{Scr}^{-1.154} \times \text{age}^{-0.203} \times (0.724, \text{women})$;^[15] (4) The Counahan-Barratt formula: $eGFR = 0.43 \times \text{height (cm)} \times [\text{Scr } (\mu\text{mol/L}) / 88.4]^{-1}$;^[16] and (5) the formula based on CysC: $eGFR = 84.69 \times \text{CysC (mg/L)}^{-1.680} \times 1.384$ (<14-year-old).^[7,8]

Measurement of serum CysC and $\beta 2$ -microglobulin

Serum CysC and $\beta 2$ -microglobulin were measured using RANDOX enzymatic creatinine assay (Randox Laboratories Limited, Crumlin, County Antrim, UK) with calibration traceable to the international standard reference material as recently recommended by the National Kidney Foundation (KDIGO 2012, Kidney international 2013). The correlation between their levels and the rGFR values determined by Tc-99m-DTPA was analyzed.

Statistical analysis

The data from the study were presented as mean \pm SD. The correlation between serum cystatin C, $\beta 2$ -microglobulin and rGFR was analyzed using SPSS18.0 software. The accuracy of eGFR from different formulas was comparatively assessed against rGFR $\pm 30\%$: eGFR falling within this range was considered accurate and the closer eGFR is to rGFR, the more accurate it is. Receiver operating characteristic (ROC) analysis was performed with sensitivity plotted against 1-specificity. The area under ROC curve (AUC) was estimated to assess the diagnostic accuracy.

Results

Correlation analysis of different indicators with rGFR

We first performed logistic analysis of correlation of rGFR with serum CysC or serum β 2-microglobulin, two commonly used markers for renal dysfunction or GFR in female and male patients, separately. As illustrated in Fig. 1, there was a good negative correlation between rGFR and CysC in both female and male patients, but rGFR was correlated with β 2-microglobulin only in male patients. Overall, CysC seemed to be a better marker for GFR and the markers appeared to have better correlations in male patients than in female patients.

Comparison of eGFR derived from various formulas with rGFR in different CKD stages

We then measured the serum levels of several indicators including CysC, β 2-microglobulin, creatinine (Scr), and urea nitrogen (BUN), and computed the values of eGFR using five different formulas, in females and males of varying CKD stages (Tables 1 and 2). As expected, all measured values showed a negative relationship with the rGFR, whereas the computed values showed a positive relationship with the rGFR. Based on these data, we sorted out the relative accuracy or applicability of the eGFR derived from five different formulas by comparing their relative proximities to the rGFR. To yield a quantitative comparison, we calculated the difference between rGFR and eGFR and the accuracy of estimation, the percentage of patients falling into the range of $rGFR \pm 30\%$, at different CKD stages in female and male patients, separately. As shown in Tables 3 and 4, the eGFR either over- or under-estimated GFR values, as opposed to the rGFR. For females (Table 3), the magnitude of difference

was in the order of Counahan-Barratt<CysC-based<Schwartz<Cockcroft-Gault<MDRD and the accuracy was in the opposite order Counahan-Barratt>CysC-based>Schwartz>Cockcroft-Gault>MDRD, for CKD stage 1. For CKD stage 2-3, however, the order of magnitude of difference became Schwartz<Cockcroft-Gault<Counahan-Barratt<MDRD<CysC-based with the accuracy order of Schwartz>Cockcroft-Gault> MDRD>Counahan-Barratt>CysC-based. For males in CKD stage 1 (Table 4), the magnitude of difference was in the order of Counahan-

Table 1. rGFR and eGFR values in female and male patients of various CKD stages

Variables	CKD stages		
	Stage 1	Stage 2	Stage 3
Female			
Scr (μ mol/L)	53.1 \pm 23.7	87.2 \pm 33.1	560.1 \pm 456.0
BUN (mmol/L)	5.3 \pm 1.8	11.3 \pm 7.6	56.0 \pm 44.0
β 2-MG (mg/L)	2.0 \pm 0.9	10.3 \pm 13.1	-
CysC (mg/L)	1.0 \pm 0.4	1.7 \pm 0.7	5.4 \pm 2.8
Schwartz formula	139.6 \pm 38.5	85.0 \pm 31.2	38.3 \pm 53.8
MDRD formula	193.3 \pm 82.9	104.2 \pm 37.7	38.4 \pm 52.0
Cockcroft-Gault formula	90.2 \pm 47.8	71.0 \pm 39.5	36.5 \pm 56.8
Counahan-Barratt formula	108.3 \pm 29.3	65.9 \pm 24.2	29.7 \pm 41.7
CysC-based formula	124.4 \pm 52.5	66.3 \pm 44.1	12.2 \pm 13.0
rGFR	121.0 \pm 29.5	78.7 \pm 8.8	44.2 \pm 12.7
Male			
Scr (μ mol/L)	48.0 \pm 12.8	73.2 \pm 34.6	470.2 \pm 518.3
BUN (mmol/L)	4.6 \pm 1.7	7.7 \pm 3.9	24.2 \pm 15.6
β 2-MG (mg/L)	1.9 \pm 0.6	2.8 \pm 1.1	2.7 \pm 0.6
CysC (mg/L)	0.9 \pm 0.2	1.6 \pm 0.6	3.4 \pm 2.4
Schwartz formula	160.2 \pm 39.6	108.4 \pm 41.3	59.3 \pm 48.4
MDRD formula	86.8 \pm 119.5	79.0 \pm 106.8	58.2 \pm 73.8
Cockcroft-Gault formula	132.8 \pm 46.4	108.1 \pm 84.1	44.9 \pm 36.8
Counahan-Barratt formula	118.0 \pm 29.4	80.7 \pm 28.2	46.0 \pm 37.5
CysC-based formula	168.0 \pm 89.0	72.1 \pm 41.6	53.6 \pm 50.3
rGFR	118.7 \pm 17.1	77.2 \pm 8.3	42.1 \pm 12.2

rGFR: "reference" glomerular filtration rate determined by Tc-99m-DTPA; eGFR: estimated GFR by formulas; CKD: chronic kidney disease; Scr: serum creatinine; BUN: blood urea nitrogen; CysC: cystatin C; β 2-MG: β 2-microglobulin.

Table 2. Comparison of rGFR and eGFR values in female and male patients of various chronic kidney disease stages

Formulas	Stage 1 (n=21)			Stage 2~3 (n=11)		
	Mean Δ	Δ SD	Accuracy	Mean Δ	Δ SD	Accuracy
Female						
Schwartz formula	-24.4	43.7	42	-2.6	29.2	45
MDRD formula	-78.2	84.5	19	-16.0	36.2	36
Cockcroft-Gault formula	24.9	51.9	23	8.0	37.7	18
Counahan-Barratt formula	6.8	35.6	61	13.2	20.8	40
CysC-based formula	-9.3	54.4	47	18.2	31.9	16
Male						
Schwartz formula	-41.4	39.1	44	-27.6	40.4	70
MDRD formula	118.7	-152.2	6	-102.2	94.7	10
Cockcroft-Gault formula	-14.0	44.0	60	-23.3	75.1	47
Counahan-Barratt formula	-0.02	29.1	81	-22.7	75.3	61
CysC-based formula	-49.2	89.5	51	-4.0	46.0	38

rGFR: "reference" glomerular filtration rate determined by Tc-99m-DTPA; eGFR: estimated GFR by formulas; CysC: cystatin C; Mean Δ : averaged difference between eGFR and rGFR (mL/(min.1.73 m²)); Δ SD: standard deviation of difference between eGFR and rGFR (mL/(min.1.73 m²)); Accuracy: percentage of eGFR values within the range of $rGFR \pm 30\%$.

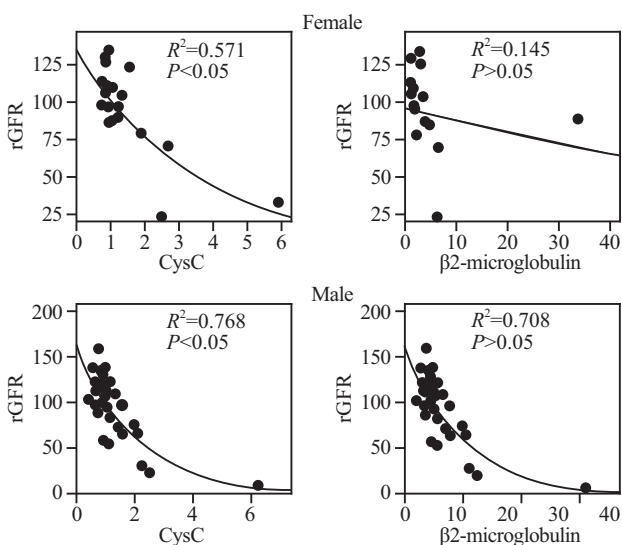


Fig. 1. Correlation between the "reference" glomerular filtration rate (rGFR) determined by Tc-99m-DTPA with serum cystatin C (CysC) and β 2-microglobulin. Dots are experimental data and lines represent the curve regression for correlation. R^2 : correlation coefficient.

Barratt<Cockcroft-Gault <Schwartz<CysC-based<MDRD with an opposite order for accuracy. And for males in CKD stage 2-3, the magnitude of difference was in the order of CysC-based<Counahan-Barratt<Cockcroft-Gault<Schwartz <MDRD, but the order of accuracy was Schwartz> Counahan-Barratt>Cockcroft-Gault>CysC-based> MDRD. Taken together, it appeared that the Counahan-Barratt formula yielded the best estimation of GFR for both females and males in CKD stage 1, and the Schwartz formula provided the highest accuracy for young CKD patients in stage 2-3. On the other hand, the MDRD formula seemed to give rise to least valuable estimation in all cases and conditions.

Comparisons of eGFR derived from various formulas with rGFR at different ages

We divided the participants first by gender into female and male groups and then subdivided them based on ages. We then computed eGFR with the five different formulas and

Table 3. Comparison of rGFR and eGFR values in female and male patients of different ages

Formulas	<10 y (n=16)			≥10 y (n=16)		
	MeanΔ	ΔSD	Accuracy	MeanΔ	ΔSD	Accuracy
Female						
Schwartz formula	-15.3	41.5	50	-22.6	36.8	16
MDRD formula	-81.8	95.3	12.5	-31.0	42.4	37.5
Cockcroft-Gault formula	40.0	36.5	6	-2.7	48.1	37.5
Counahan-Barratt formula	10.0	29.9	62.5	4.1	30.2	50
CysC-based formula	-8.7	44.5	37.5	7.8	52.7	43.7
Male						
Schwartz formula	-30.1	37.8	50	-41.6	40.7	32
MDRD formula	-184.0	131.0	3	-83.4	64.2	2
Cockcroft-Gault formula	-6.0	60.8	56.2	-27.0	47.3	47
Counahan-Barratt formula	-2.4	29.8	75	-0.05	26.7	79
CysC-based formula	-48.7	97.6	31.2	-18.3	55.0	61

rGFR: "reference" glomerular filtration rate determined by Tc-99m-DTPA; eGFR: estimated GFR by formulas; CysC: cystatin C; MeanΔ: averaged difference between eGFR and rGFR (mL/(min.1.73 m²)); ΔSD: standard deviation of difference between eGFR and rGFR (mL/(min.1.73 m²)); Accuracy: percentage of eGFR values within the range of rGFR±30%.

compared with the rGFR. For females under 10 years old, the proximity was in the order of CysC-based>Counahan-Barratt>Schwartz>Cockcroft-Gault>MDRD, whereas the accuracy was in the order of Counahan-Barratt >Schwartz>CysC-based>MDRD> Cockcroft-Gault. For females ≥10 years old, the accuracy was in the order of Counahan-Barratt>CysC-based>MDRD=Cockcroft-Gault>Schwartz. For male patients of both <10 and ≥10 years old, the Counahan-Barratt formula stood out the most accurate estimation method for GFR, which was consistent with the results from the female patients.

Comparison of diagnostic accuracy of various formulas

ROC analysis was performed to compare the diagnostic accuracy of various formulas for estimation of GFR. The results are presented in Fig. 2. Since the mean level of measured GFR in the present study was relatively high, high cut-offs of GFR were used for analysis. We found that either at >120 mL/min or at <90 mL/min, the area under ROC curve (AUC) for the Counahan-Barratt formula was larger than other formulas, indicating that this formula has the highest diagnostic accuracy among the five formulas examined.

Table 4. Receiver-operator characteristic (ROC) curve analysis for precision and diagnostic accuracy of various formulas

Formulas	AUC	SEM	P value	95% CI
Cut-off >120 mL/min				
Schwartz formula	0.766	0.063	0.01	0.643-0.889
MDRD formula	0.699	0.071	0.017	0.560-0.838
Cockcroft-Gault formula	0.769	0.062	0.001	0.646-0.891
Counahan-Barratt formula	0.792	0.060	0.000	0.674-0.911
CysC-based formula	0.738	0.062	0.004	0.617-0.860
Cut-off <90 mL/min				
Schwartz formula	0.869	0.049	0.000	0.772-0.965
MDRD formula	0.779	0.064	0.000	0.652-0.905
Cockcroft-Gault formula	0.840	0.060	0.000	0.724-0.957
Counahan-Barratt formula	0.876	0.047	0.000	0.784-0.967
CysC-based formula	0.862	0.050	0.000	0.765-0.960

AUC: area under ROC curve; SEM: standard error of mean; CI: confidence interval.

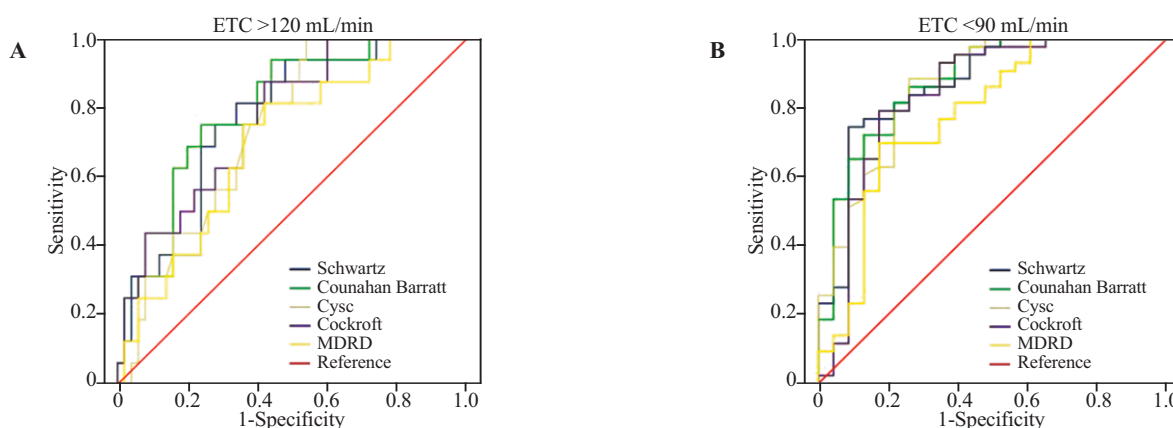


Fig. 2. Receiver-operator characteristic (ROC) curve analysis for precision and diagnostic accuracy of various formulas. **A:** ROC curves with ETC >120 mL/min; **B:** ROC curves with ETC <90 mL/min.

Discussion

In this study, we identified a GFR estimation method most appropriate for children with CKD. The main findings were as follows: (1) Among all four markers tested, CysC best reflected the extent of glomerular damages in young patients at CKD stage 1, when the GFR was still within the normal range and the serum creatinine and urea nitrogen levels remained unaltered, indicating that CysC was the most sensible marker for early stage of CKD; (2) The eGFR values derived from five different formulas either over-estimated or underestimated GFR as referenced to rGFR, and the extent of deviations varied depending on gender, age and CKD stage; (3) The Counahan-Barratt formula and the Schwartz formula gave the most accurate estimations of GFR for patients of CKD stages 1 and 2-3, respectively, regardless of gender and age differences, whereas the accuracy of the MDRD formula and CysC-based formula were the lowest among all five formulas for males and females, respectively. It is noted that none of the GFR formulas tested in this study reached the accuracy level of the KDOQI recommendations to be validated in Chinese children.^[10] Based on these findings, we concluded that the Counahan-Barratt formula provides the best approximation to rGFR thereby the highest applicability to Chinese children with stages 1-3 CKD of varying genders, ages and CKD stages, and the MDRD formula and CysC-based formula are not suitable for Chinese children.

GFR is the best indicator of kidney filtration or renal function, and the main basis for the diagnosis and staging of CKD, as well as for the evaluation of the severity of kidney disease and the therapeutic outcomes. It is also pivotal to the adjustment of drug dosage for the treatment of renal dysfunction and the determination of the optimal window for commencing renal replacement therapy. Therefore, it is critical to work out a method of determining GFR with high accuracy, reproducibility and simplicity. However, since measuring GFR remains relatively cumbersome and costly, estimating GFR using renal biomarkers remains highly desirable and relevant for daily practice.

Our results on the relative values of four different markers for GFR were in general in good agreement with the consensus that CysC is a superior marker to other contemporary makers and traditional markers as well.^[17-19] The advantages were reflected by its ability to detect the minor changes of GFR in the early stage of renal disease with higher sensitivity and greater accuracy for the extent of renal dysfunction and GFR.^[20-24] In our study, β_2 microglobulin also demonstrated its reasonable value for detecting minor to moderate changes of GFR thereby kidney dysfunction.

The Schwartz formula is recommended, by the

American Kidney Foundation, as the best mathematical model for the evaluation of GFR in children, which has gained its recognition as a formula reflecting children's renal function in the Western countries.^[25] The Schwartz formula has been also tested in European children according to age and sex and proposed for its routine use in children and adolescents.^[26-28] Nonetheless, in our study, the Schwartz formula tended to over-estimate GFR for CKD stage 1 of both females and males, which was inconsistent with the reports in the literature. For CKD stage 2, the Schwartz formula seemed to be able to better reflect the true GFR value relative to other formulas. This CKD stage-dependent accuracy of GFR estimation might be ascribed to the constant K in the Schwartz formula; the K value in the current form of the Schwartz formula was derived from children in the United States. This K value may not be applicable to Chinese children with kidney disease; thus, the accuracy of the Schwartz formula for Chinese children is impaired.

The Counahan-Barratt formula is another commonly used mathematical model for estimating GFR in children,^[8] which also incorporates height, SCr, and other measurements. In the present study, this formula was found to be best suited to stage 1 patients with mild kidney disease.

The MDRD and Cockcroft-Gault formulas are recommend by K/DOQI guidelines for use in adults, and they are not suitable for children.^[14] Consistently, in the present study, the MDRD formula yielded the least accurate estimation of GFR in the patients of different genders and CKD stages. Similarly, based on our results the Cockcroft-Gault formula seems to be not suitable for assessing renal function in children.

In summary, this study showed that in the assessment of children's renal function, CysC is the best marker for kidney function, followed by β_2 -microglobulin, and SCr and BUN may not offer good assessment of renal function of children in the early stage of CKD. Among the five most commonly used eGFR formulas in clinical practice, the Counahan-Barratt formula can accurately estimate GFR in young patients at the CKD stage 1. The Schwartz formula may be used for young patients at the CDK stages 2-3. One important limitation of this study is that the number of study group is small and only two cases of CKD stage 4 and one case of CKD stage 5 were enrolled; thus the application of our findings is limited to young patients with relatively mild renal dysfunction, but not more advanced stages. Moreover, a recent study suggested that Tc-99m-DTPA renal dynamic imaging method may be used as the reference method in investigating the validity of CDK-EPI equation for determining glomerular filtration rate.^[29] Though this study was performed in adults, precaution must be taken in interpreting our findings from children using Tc-99m-DTPA as a reference.

Funding: None.

Ethical approval: The protocols for human studies were approved by the Institutional Review Board of Shengjing Hospital and informed written consent was obtained from the caregivers of the participants.

Competing interest: All authors declare no conflict of interest.

Contributors: Du Y conceived and designed this study. Sun TT did data analysis and wrote the draft. Hou L revised the manuscript and acted as the guarantor of the study. Guo JJ reviewed critically the article. Wang XL and Wu YB conducted data collection. All authors approved the final version of the article for publication.

References

- Delanaye P, Ebert N. Assessment of kidney function: Estimating GFR in children. *Nat Rev Nephrol* 2012;8:503-504.
- Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. *Clin J Am Soc Nephrol* 2009;4:1832-1843.
- Schwartz GJ, Munoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 2009;20:629-637.
- Grubb AO. Cystatin C—properties and use as diagnostic marker. *Adv Clin Chem* 2000;35:63-99.
- Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants children and adolescents. *Pediatr Clin North Am* 1987;34:571-590.
- Grootendorst DC, Michels WM, Richardson JD, Jager KJ, Boeschoten EW, Dekker FW, et al. The MDRD formula dose not reflect GFR in ESRD patients. *Nephrol Dial Transplant* 2011;26:1932-1937.
- Qutb A, Syed G, Tamim HM, Al Jondeby M, Jaradat M, Tamimi W, et al. Cystatin C-based formula is superior to MDRD, Cockcroft-Gault and Nankivell formulae in estimating the glomerular filtration rate in renal allografts. *Exp Clin Transplant* 2009;7:197-202.
- Lee CK, Swinford RD, Cerda RD, Portman RJ, Hwang W, Furth SL. Evaluation of serum creatinine concentration-based glomerular filtration rate equations in pediatric patients with chronic kidney disease. *Pharmacotherapy* 2012;32:642-648.
- Bevc S, Hojs R, Ekart R, Gorenjak M, Puklavac L. Simple cystatin C formula compared to sophisticated CKD-EPI formulas for estimation of glomerular filtration rate in the elderly. *Ther Apher Dial* 2011;15:261-268.
- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis* 2002;39(Suppl 1):S1-246.
- Blaufox MD, Aurell M, Bubeck B, Fommei E, Piepsz A, Russell C, et al. Report of the radionuclides in nephrourology committee on renal clearance. *J Nucl Med* 1996;37:1883-1890.
- Vivier PH, Storey P, Rusinek H, Zhang JL, Yamamoto A, Tantilto K, et al. Kidney function: glomerular filtration rate measurement with MR renography in patients with cirrhosis. *Radiology* 2011;259:462-470.
- Prigent A, Cosgriff P, Gates GF, Granerus G, Fine EJ, Itoh K, et al. Consensus report on quality control of quantitative measurements of renal function obtained from the renogram: International Consensus Committee from the Scientific Committee of Radionuclides in Nephrourology. *Semin Nucl Med* 1999;29:146-159.
- Filler G, Foster J, Acker A, Lepage N, Akbari A, Ehrlich JH. The Cockcroft-Gault formula should not be used in children. *Kidney Int* 2005;67:2321-2324.
- Levey AS, Bosch JP, Lewis JB, Greene T, Rogers NL, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 1999;130:461-470.
- Counahan R, Chantler C, Ghazali S, Kirkwood B, Rose F, Barratt TM. Estimation of glomerular filtration rate from plasma creatinine concentration in children. *Arch Intern Med* 1976;51:875-878.
- Abraham BP, Frazier EA, Morrow WR, Blaszkak RT, Devarajan P, Mitsnefes M, et al. Cystatin C and neutrophil gelatinase-associated lipocalin as markers of renal function in pediatric heart transplant recipients. *Pediatr Transplant* 2011;15:564-569.
- Bacchetta J, Cochat P, Rognant N, Ranchin B, Hadj-Aissa A, Dubourg L. Which creatinine and cystatin C equations can be reliably used in children? *Clin J Am Soc Nephrol* 2011;6:552-560.
- Vupputuri S, Fox CS, Coresh J, Woodward M, Muntner P. Differential estimation of CKD using creatinine-versus cystatin C-based estimating equations by category of body mass index. *Am J Kidney Dis* 2009;53:993-1001.
- Blufpand HN, Tromp J, Abbink FC, Stoffel-Wagner B, Bouman AA, Schouten-van Meeteren AY, et al. Cystatin C more accurately detects mildly impaired renal function than creatinine in children receiving treatment for malignancy. *Pediatr Blood Cancer* 2011;57:262-267. [In Chinese]
- Ruan YY, Feng JT, Huang ZQ, Qin WL, Mou JF. Diagnostic value of serum cystatin C in renal function impairments in children with viral encephalitis. *Zhongguo Dang Dai Er Ke Za Zhi* 2011;13:119-122.
- Herrero-Morín JD, Málaga S, Fernández N, Rey C, Diéguez MA, Solís G, et al. Cystatin C and beta2-microglobulin: markers of glomerular filtration in critically ill children. *Crit Care* 2007;11:R59.
- Filler G, Priem F, Lepage N, Sinha P, Vollmer I, Clark H, et al. β -Trace Protein, cystatin C, β 2-microglobulin, and creatinine compared for detecting impaired glomerular filtration rates in children. *Clin Chem* 2002;48:729-736.
- Donadio C, Lucchesi A, Ardini M, Donadio E, Giordani R. Serum levels of beta-trace protein and glomerular filtration rate—preliminary results. *J Pharm Biomed Anal* 2003;32:1099-1104.
- Zappitelli M, Joseph L, Gupta IR, Bell L, Paradis G. Validation of child serum creatinine-based prediction equations for glomerular filtration rate. *Pediatr Nephrol* 2007;22:272-281.
- Bacchetta J, Cochat P, Rognant N, Ranchin B, Hadj-Aissa A, Dubourg L. Which creatinine and cystatin C equations can be reliably used in children? *Clin J Am Soc Nephrol* 2011;6:552-560.
- Selistre L, De Souza V, Cochat P, Antonello IC, Hadj-Aissa A, Ranchin B, et al. GFR estimation in adolescents and young adults. *J Am Soc Nephrol* 2012;23:989-996.
- De Souza VC, Rabilloud M, Cochat P, Selistre L, Hadj-Aissa A, Kassai B, et al. Schwartz formula: is one k-coefficient adequate for all children? *PLoS One* 2012;7:e53439.
- Xie P, Huang JM, Liu XM, Wu WJ, Pan LP, Lin HY. (99m)Tc-DTPA renal dynamic imaging method may be unsuitable to be used as the reference method in investigating the validity of CDK-EPI equation for determining glomerular filtration rate. *PLoS One* 2013;8:e62328.

Received July 23, 2013

Accepted after revision November 27, 2013