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Full Age Spectrum Equation in Evaluation of Glomerular Filtration Rate in Elderly Patients with Chronic Kidney Disease

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Abstract

Objective: To evaluate the utility and significance of the Full Age Spectrum (FAS) equations for estimating glomerular filtration rate (GFR) in elderly patients with chronic kidney disease (CKD). *Methods:* A total of 191 elderly CKD patients diagnosed at the First Affiliated Hospital of Hainan Medical University were included. GFR was measured using the standard 99mTc-DTPA renal dynamic imaging method (TcGFR). GFR was estimated (eGFR) using the FAS equations based on serum creatinine (SCr) and cystatin C (CysC) levels, as well as the CKD Epidemiology Collaboration (CKD-EPI) equations. The results were recorded as eGFR1, eGFR2, eGFR3, and eGFR4. The correlation and bias between each equation-derived eGFR and TcGFR were compared. Stratified analyses were performed based on gender, age groups, and CKD stages. The applicability, sensitivity, specificity, precision, and accuracy within 15% and 30% (P15, P30) of the four equations were evaluated. *Results:* All eGFR equations showed significant positive correlations with TcGFR. Among them, eGFR4 had the strongest correlation with TcGFR (r = 0.786), followed by eGFR3. The least biased equation was eGFR2, with eGFR3 ranking second. The highest precision was observed with eGFR3, followed by eGFR2. For P15 accuracy, the order was eGFR3 > eGFR2 > eGFR4 > eGFR1, while for P30 accuracy, it was eGFR2 > eGFR3 > eGFR4 > eGFR1. The Bland-Altman plots indicated that eGFR4 had the smallest 95% confidence interval, followed by eGFR3, eGFR2, and eGFR1. The area under the curve (AUC) for the equations ranked as follows: eGFR2 > eGFR4 > eGFR3 > eGFR1. Stratified analyses revealed that: (1) For female CKD stages 1–3, eGFR2 was the most suitable; for stages 4–5, eGFR1 and eGFR3 were preferable. (2) For females aged ≥ 70 years, eGFR3 was optimal. (3) For male CKD stages 1–3, eGFR2 was recommended, and eGFR4 was an alternative for those aged ≥ 70 years. (4) For male CKD stages 4–5, eGFR1, eGFR3, and eGFR4 were all appropriate, with eGFR3 being particularly suitable for those aged ≥ 70 years. *Conclusion:* The FAS equations for estimating eGFR in elderly CKD patients are superior to the CKD-EPI equations. The optimal choice of equation varies based on age, gender, and CKD stage, allowing for tailored equation selection as an alternative to renal dynamic imaging for hospitalized patients.

Keywords

Full Age Spectrum equations
Chronic kidney disease
Glomerular filtration rate
Serum creatinine
Serum cystatin C

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1. Introduction

The accurate estimation of glomerular filtration rate (eGFR) plays a crucial role in the diagnosis, staging, and prognosis of chronic kidney disease (CKD). With the increasing prevalence of an aging population, precise assessment of kidney function in elderly individuals has significant clinical implications. According to the World Health Organization, elderly individuals are defined as those aged 60 years and older. In 2016, Pottel *et al.* [1] developed the Full Age Spectrum (FAS) equations for estimating eGFR, based on data from 6,870 subjects. Compared with the CKD Epidemiology Collaboration (CKD-EPI) equations recommended by the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guidelines [2], the FAS equations demonstrate reduced bias and higher accuracy in elderly populations.

As the FAS equations were developed based on data from Caucasian individuals, it remains uncertain whether these equations are equally applicable to elderly CKD patients in China, where body composition differs from that of Caucasians. Few studies have addressed whether the FAS equations outperform CKD-EPI equations for estimating GFR in elderly Chinese CKD patients. This study validates the FAS equations using 99mTc-DTPA renal dynamic imaging (TcGFR) as the gold standard and compares them to CKD-EPI equations to evaluate their applicability.

2. Materials and methods

2.1. General data

This study included elderly CKD patients treated at the First Affiliated Hospital of Hainan Medical College between December 2018 and December 2019.

Inclusion criteria: (1) Diagnosis consistent with KDIGO CKD diagnostic criteria; (2) Age ≥ 60 years; (3) Complete data on gender, age, height, and weight; (4) Serum creatinine (SCr) and serum cystatin C (CysC) measured within three days before or after hospital admission; (5) TcGFR measured using 99mTc-DTPA renal dynamic imaging within one week of admission; (6) Stable creatinine and urea nitrogen levels, with no CKD stage changes within three months.

Exclusion criteria: (1) Acute kidney injury during the disease course; (2) Severe malnutrition, edema, or pleural effusions; (3) Dialysis within one week before GFR measurement; (4) Coexisting hyperthyroidism or hypothyroidism; (5) Malignant tumors or incomplete clinical data.

2.2. Study methods

SCr and CysC were measured using a Siemens ADVIA 2400 automated biochemical analyzer. SCr was assessed using enzymatic methods, with kits provided by Mike Biotechnology Co., Ltd., while CysC was measured using latex immunoturbidimetry, with reagents and calibrators supplied by Meikang Biotechnology Co., Ltd. Quality control materials were sourced from Bio-Rad Laboratories.

TcGFR was measured using a Millennium MG/MyoSIGHT SPECT system (GE Healthcare), employing a low-energy general-purpose collimator and 99mTc-DTPA as the imaging agent. The Gates method was used to calculate GFR, recorded as TcGFR.

eGFR values were calculated as follows:

(1) eGFR1: FAS-SCr equation.

(2) eGFR2: FAS-CysC equation.

(3) eGFR3: FAS-SCr-CysC equation.

(4) eGFR4: CKD-EPI equation.

The formulas used for eGFR estimation are provided in **Table 1**.

2.3. Statistical analysis

Statistical analysis was conducted using SPSS 25.0 and MedCalc 19.3.1. Categorical data were expressed as percentages (%), while continuous data were tested for normality using the Kolmogorov-Smirnov test. Data with a normal distribution were presented as mean ± standard deviation (SD), whereas non-normally distributed data were expressed as medians with interquartile ranges. Pearson correlation analysis was used to assess the

Table 1. eGFR calculation formulas

Name	Formula
FAS-SCr	For ages 2–40, eGFR = 107.3 / (SCr / 88.4 / QScr) For ages > 40, eGFR = [107.3 / (SCr / 88.4 / QScr)] × 0.988(Age - 40) QScr = 0.90 (Male), 0.70 (Female)
FAS-CysC	For ages > 40, eGFR = [107.3 / (CysC / QCysC)] × 0.988(Age - 40) QCysC = 0.82 (< 70 years old), 0.95 (> 70 years old)
FAS-SCr-CysC	For ages > 40, eGFR = 107.3 / [0.5 × (SCr / 88.4 / QScr) + 0.5 × (CysC / QCysC)] × 0.988(Age - 40) QScr = 0.90 (Male), 0.70 (Female); QCysC = 0.82 (< 70 years old), 0.95 (> 70 years old)
CKD-EPI	eGFR = 135 × Min (SCr/κ, 1)α × Max(SCr/κ, 1)-0.601 × Min (CysC/0.8, 1)-0.375 × Max (CysC/0.8, 1)-0.711 × 0.995Age × 0.969(Female) κ = 0.9 (Male), 0.7 (Female); α = -0.207 (Male), -0.248 (Female)

Definition and notes: FAS-SCr, Full-age spectrum equation using serum creatinine as a variable; FAS-CysC, Full-age spectrum equation using serum cystatin C as a variable; FAS-SCr-CysC, Full-age spectrum equation using both serum creatinine and cystatin C as variables; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation using serum creatinine and cystatin C; SCr, Serum creatinine; CysC, Serum cystatin C; eGFR, Estimated glomerular filtration rate; Q_{Scr}, Correction coefficient for serum creatinine; Q_{CysC}, Correction coefficient for serum cystatin C; Min/Max, Minimum or maximum value; κ, α, Correction factors for gender.

relationship between each eGFR equation and the TcGFR. The accuracy of the equations was evaluated by calculating the proportion of eGFR values falling within 15% (P15) or 30% (P30) of the TcGFR and comparing these using the χ^2 test. Precision was represented by the standard error, with smaller values indicating greater precision, while absolute bias, defined as the absolute difference between eGFR and TcGFR, was analyzed using the Wilcoxon rank-sum test. Bland-Altman scatter plots were generated to evaluate the deviation and agreement limits between eGFR and TcGFR. Finally, receiver operating characteristic (ROC) curves were employed to compare the diagnostic performance of the equations for detecting kidney dysfunction, defined as a TcGFR of less than 60 mL/min/1.73 m². A *P*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. General information

This study included 191 patients, comprising 108 males and 83 females, with an average age of 70.71 ± 7.24 years (range: 60–87 years). The average height was 160.46 ± 7.94 cm, and the average weight was 60.14 ± 10.07 kg. Serum creatinine (SCr) levels were 232.49 (141.38, 465.86) μmol/L, and serum cystatin C (CysC) levels were 2.38 (1.51, 3.32) mg/L. True clearance-based glomerular filtration rate (TcGFR) was 26.86 (18.50, 43.39) mL/min/1.73 m². Estimated GFR (eGFR) values were as follows:

(1) eGFR1: 23.49 (11.69, 37.71) mL/min/1.73 m²
(2) eGFR2: 27.01 (19.30, 43.56) mL/min/1.73 m²
(3) eGFR3: 25.69 (14.62, 39.98) mL/min/1.73 m²
(4) eGFR4: 22.10 (11.19, 39.36)mL/min/1.73 m²

3.2. Correlation with TcGFR

All eGFR equations showed a significant positive correlation with TcGFR. Among them, eGFR4 had the highest correlation (r = 0.786, P < 0.001), followed by eGFR3 (r = 0.782, P < 0.001), eGFR1 (r = 0.755, P < 0.001), and eGFR2 (r = 0.750, P < 0.001), as shown in **Table 2**.

3.3. Bias of the equations

eGFR2 had the least bias, followed by eGFR3 and eGFR4. eGFR1 had the greatest bias. No significant difference was found between eGFR2 and eGFR3 (P > 0.05). Comparisons between eGFR4 and eGFR2 or

eGFR3 showed statistically significant differences ($P < 0.05$), while the difference between eGFR4 and eGFR1 was not significant ($P > 0.05$), as shown in **Table 2**.

3.4. Accuracy and precision

eGFR3 had the highest P15 accuracy, followed by eGFR2 and eGFR4, with no statistically significant differences between them. For P30 accuracy, eGFR2 performed best, followed by eGFR3 and eGFR4, with no significant differences. eGFR1 showed the lowest accuracy in both P15 and P30. In terms of precision, eGFR3 was the most precise, followed by eGFR2, eGFR4, and eGFR1 (**Table 2**).

3.5. Limits of agreement

Bland-Altman plots indicated that eGFR4 had the narrowest 95% confidence interval, followed by eGFR3, eGFR2, and eGFR1 (**Table 2**, **Figure 1**).

3.6. Diagnostic performance

The area under the curve (AUC) was highest for eGFR2 (0.926). At an optimal cutoff value of 45.59 mL/min/1.73 m², eGFR2 had a positive predictive value of 0.956, sensitivity of 0.929, and Youden index of 0.77. eGFR3 and eGFR4 had similar sensitivity and Youden index, with comparable positive predictive values to eGFR2. Differences between eGFR2, eGFR3, and eGFR4

Table 2. Performance comparison of different eGFR equations in CKD patients

Category	Correlation coefficient	P15 (%)	P30 (%)	Precision	Absolute bias (median, range)	Consistency limits (95% CI)
eGFR1 (FAS-SCr)	0.755	26.18	49.74	12.718	7.76 (3.83, 13.58)	(-17.1, 28.0)
eGFR2 (FAS-CysC)	0.750	34.55	62.30	11.452	6.27 (2.88, 12.36)	(-23.0, 21.8)
eGFR3 (FAS-SCr-CysC)	0.782	36.13	60.21	11.067	6.92 (2.68, 10.35)	(-16.6, 24.0)
eGFR4 (CKD-EPI)	0.786	29.32	52.88	12.171	6.98 (3.35, 11.83)	(-16.9, 26.7)

Abbreviations: eGFR, Estimated glomerular filtration rate; TcGFR, True clearance-based glomerular filtration rate (standard measure); P15, Percentage of eGFR within 15% of TcGFR; P30, Percentage of eGFR within 30% of TcGFR.

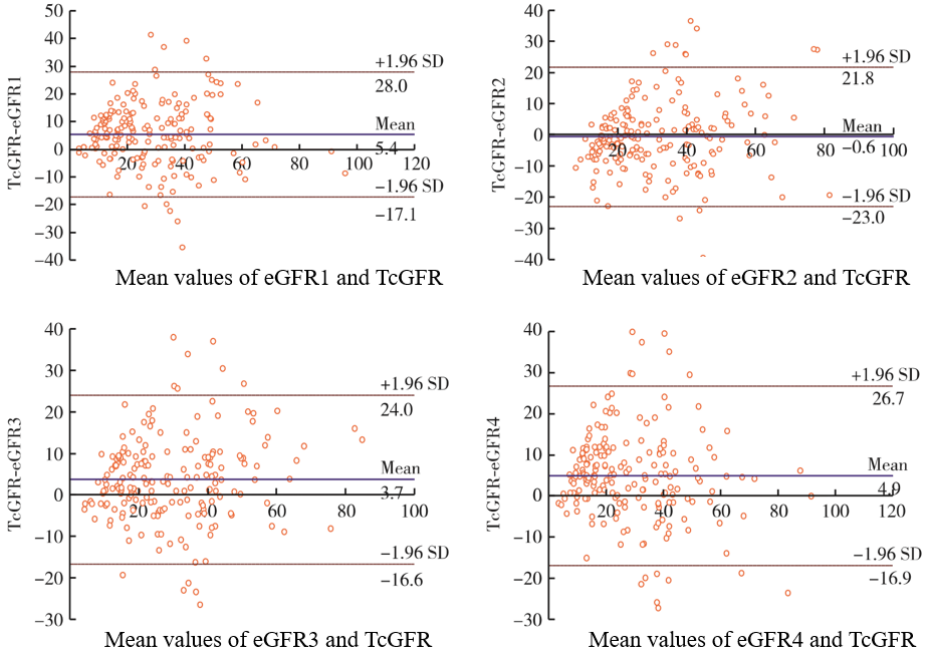

Figure 1. Bland-Altman scatter plot

Table 3. Evaluation of diagnostic efficacy of eGFR equations

Equation	AUC (95% CI)	Optimal cutoff	Jordon's index	Specificity (%)	Sensitivity (%)	Positive predictive value (%)	Negative predictive value (%)
eGFR1	0.868 (0.786–0.950)	34.84	0.61	0.757	0.857	0.951	0.623
eGFR2	0.926 (0.856–0.996)	45.59	0.77	0.836	0.929	0.956	0.600
eGFR3	0.910 (0.837–0.982)	41.71	0.71	0.853	0.857	0.956	0.750
eGFR4	0.917 (0.845–0.989)	41.54	0.71	0.847	0.857	0.956	0.670

Abbreviations: eGFR, Estimated glomerular filtration rate; AUC, Area under the receiver operating characteristic curve; 95% CI, 95% confidence interval; FAS-SCr (eGFR1), FAS equation using serum creatinine; FAS-CysC (eGFR2), FAS equation using cystatin C; FAS-SCr-CysC (eGFR3), FAS equation using both serum creatinine and cystatin C; CKD-EPI (eGFR4), Chronic Kidney Disease Epidemiology Collaboration equation.

were not statistically significant, but all were significantly different from eGFR1 (**Table 3**, **Figure 2**).

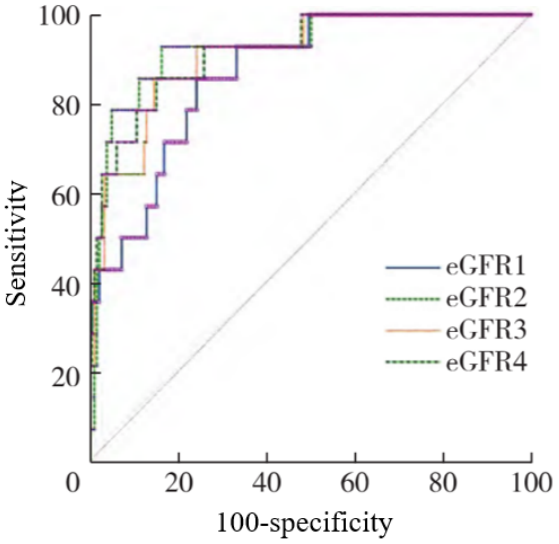

Figure 2. Receiver operating characteristic (ROC) curve

3.7. Stratification by CKD stage and age

3.7.1. Male patients

(1) CKD stages 1–3, age < 70 years (30 cases): eGFR2 estimates were closest to TcGFR (P = 0.131); all other equations showed significant differences (P < 0.05).

(2) CKD stages 1–3, age ≥ 70 years (28 cases): eGFR2 and eGFR4 were closest to TcGFR (P = 0.838, P = 0.08), with no significant differences between them (P = 0.062).

(3) CKD stages 4–5, age < 70 years (27 cases): eGFR1, eGFR3, and eGFR4 were closest to TcGFR (P = 0.755, 0.792, 0.259). For age ≥ 70 years (23 cases), the same equations showed similarity to TcGFR, but significant differences were found between eGFR1 and eGFR3, and between GFR4 and eGFR3 (P < 0.001). No significant differences were observed between eGFR1 and GFR4 (P = 0.693).

3.7.2. Female patients

(1) CKD stages 1–3, age < 70 years (16 cases) and age ≥ 70 years (13 cases): eGFR2 estimates were closest to TcGFR (P = 0.07, P = 0.101); all other equations showed significant differences (P < 0.05).

(2) CKD stages 4–5, age < 70 years (24 cases): eGFR1 and eGFR3 estimates were closer to TcGFR (P = 0.137, 0.797), with significant differences between them (P = 0.005). Comparisons between eGFR1 and eGFR4 showed no significant differences (P = 0.331). For age ≥ 70 years (30 cases), eGFR3 was closest to TcGFR (P = 0.066); all other equations had significant differences (P < 0.05).

4. Discussion

A meta-analysis in 2018 revealed that the prevalence of chronic kidney disease (CKD) among Chinese adults is approximately 13.4%, while the prevalence in individuals

aged 60 years and older reaches 19.25% [3]. CKD has become the 11th leading cause of death worldwide, making accurate diagnosis and proper staging critically important. Glomerular filtration rate (GFR) serves as the primary clinical basis for diagnosing and staging CKD. Utilizing 99mTc-DTPA renal dynamic imaging through single-photon emission computed tomography not only assesses renal perfusion but also accurately measures global and segmental GFR. However, this method is relatively expensive, requires specialized equipment and personnel, and poses radiation exposure risks to patients, limiting its widespread application, particularly in resource-limited primary care settings. Consequently, simplified estimation equations remain more commonly used in clinical practice than renal dynamic imaging.

In 2009, the CKD-EPI equation was developed. Initially, the equation based on serum creatinine (SCr) was criticized for underestimating actual GFR due to issues with study populations and racial inclusion [4]. Subsequently, an equation based on cystatin C (CysC) was introduced [5], but its application has been limited due to standardization issues and higher costs, making it a supplementary tool. In 2012, the CKD-EPI group developed a combined equation, which demonstrated reduced bias and improved accuracy and precision compared to single-variable equations, leading to its widespread clinical adoption [6]. Several studies have validated the CKD-EPI combined equation in the Chinese population [7,8], confirming its suitability for estimating GFR compared to single-variable equations. However, the CKD-EPI equation does not cover all age groups. To address this gap, the FAS equation was developed, showing reduced bias and higher accuracy in elderly patients [9]. Previous analyses of adult populations found that the FAS-CysC equation had the lowest bias, the highest precision, and the largest area under the curve, consistent with international studies [10]. However, other research indicated that the FAS equation may not be suitable for elderly patients with GFR < 30 mL/(min·1.73 m²) [11]. This study aimed to evaluate the applicability of the FAS equation in elderly patients in the local population.

Results showed that eGFR3 exhibited the highest accuracy. A possible reason is that the FAS equation, developed by Pottel *et al.* [12], incorporated a larger sample size, broader age range, and normalized average values for biomarkers, effectively reducing gender differences and age-related effects on SCr. This normalization method also mitigated the influence of non-GFR factors affecting SCr and CysC in patients with obesity, smoking, thyroid dysfunction, or inflammation. In contrast, eGFR4 did not standardize SCr and CysC or differentiate by age, which may have contributed to discrepancies. The target population for this study comprised individuals aged ≥ 60 years, most of whom were in the later stages of CKD (stages 3–5) and had other chronic conditions. Factors such as reduced protein intake and increased catabolism [13] may have caused deviations in SCr or CysC levels, thereby impacting the equation's results. Additionally, only 1% of participants in the eGFR4 validation cohort were of Asian descent, highlighting potential racial influences.

The study found that both eGFR3 and eGFR4 performed slightly worse than the CysC-based eGFR2 equation in P30 accuracy and absolute bias but were superior to the SCr-based eGFR1 equation. These findings are consistent with results from a multicenter study in China [14]. Moreover, eGFR2 demonstrated the smallest bias, the largest area under the curve (0.926), and the highest Youden index, sensitivity, and positive predictive value. This indicates that CysC is more stable than SCr, a phenomenon more pronounced in elderly patients. The eGFR2 equation does not include a gender variable, unlike the other three equations, suggesting that gender adjustments may not be as critical for elderly populations.

Stratified analysis by gender, age, and CKD stage revealed the following recommendations:

(1) For CKD stages 1–3, the eGFR2 equation is recommended for females, while eGFR3 is suggested for males aged ≥ 70 years.

(2) For CKD stages 4–5, eGFR1 and eGFR3 are suitable for females, while eGFR1, eGFR3, and eGFR4 are recommended for males aged

< 70 years. However, with an expanded sample size, eGFR3 may become more applicable. For individuals aged ≥ 70 years, the eGFR3 equation is preferred.

(3) International studies evaluating the FAS equation in patients with renal impairment have also suggested that it outperforms the CKD-EPI equation [15].

5. Conclusion

The FAS equation demonstrates superior performance compared to the CKD-EPI equation for estimating eGFR in elderly patients within the local population. However, the optimal equation varies by age group, gender, and CKD stage. The FAS equation, while normalized, was initially constructed based on Caucasian populations, and the potential bias due to racial differences cannot be ruled out. Therefore, further large-sample, multicenter studies involving Chinese CKD patients are needed to refine the FAS equation. Expanding the sample size and age range in future research will provide more comprehensive validation and improvement of the FAS equation, ultimately offering greater clinical utility and guidance.

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Disclosure statement

The authors declare no conflict of interest.

References

[1] Pottel H, Hoste L, Dubourg L, et al., 2016, An Estimated Glomerular Filtration Rate Equation for the Full Age Spectrum. Nephrol Dial Transplant, 31(5): 798–806. https://doi.org/10.1093/ndt/gfv454

[2] Inker LA, Schmid CH, Tighiouart H, et al., 2012, Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. N Engl J Med, 367(1): 20–29. https://doi.org/10.1056/NEJMoa1114248. Erratum in N Engl J Med, 367(7): 681. Erratum in N Engl J Med, 367(21): 2060.

[3] Wang SZ, Zhu YJ, Li GQ, et al., 2018, Meta-Analysis of the Prevalence of Chronic Kidney Disease in Chinese Adults and Its Comparison. Chinese Journal of Nephrology, 34(8): 579–586.

[4] Raman M, Middleton RJ, Kalra PA, et al., 2017, Estimating Renal Function in Old People: An In-Depth Review. Int Urol Nephrol, 49(11): 1979–1988. https://doi.org/10.1007/s11255-017-1682-z

[5] Björk J, Grubb A, Gudnason V, et al., 2018, Comparison of Glomerular Filtration Rate Estimating Equations Derived from Creatinine and Cystatin C: Validation in the Age, Gene/Environment Susceptibility-Reykjavik Elderly Cohort. Nephrol Dial Transplant, 33(8): 1380–1388. https://doi.org/10.1093/ndt/gfx272

[6] Alaini A, Malhotra D, Rondon-Berrios H, et al., 2017, Establishing the Presence or Absence of Chronic Kidney Disease: Uses and Limitations of Formulas Estimating the Glomerular Filtration Rate. World J Methodol, 7(3): 73–92. https://doi.org/10.5662/wjm.v7.i3.73

[7] Song J, Yao HX, Sun SY, 2016, Comparison of Applicability Between the Newly Published CKD-EPI Equation in 2012 and the Other Two Equations. Chinese Journal of Laboratory Diagnosis, 2016(2): 255–259.

[8] Zhu WW, Zheng M, Wang XF, 2017, Comparison of the Efficacy of Three CKD-EPI Equations in Estimating GFR in

Elderly Patients with Chronic Kidney Disease. Shandong Medical Journal, 57(14): 80–83.

[9] Huang SH, Wu XX, 2018, Clinical Application of a New Creatinine-Based Equation for Estimating Glomerular Filtration Rate in Patients with Chronic Kidney Disease Across the Full Age Spectrum. Chinese Critical Care Medicine, 30(9): 877–881.

[10] Sun W, Xie Q, Chen HY, et al., 2021, Application of Chronic Kidney Disease Epidemiology Collaboration Equation and Full Age Spectrum Equation in Adults with Chronic Kidney Disease. Chinese Journal of Medical Imaging Technology, 37(1): 113–117.

[11] Chen A, Sun Y, Li W, et al., 2020, Application of GFR Estimation Equations in Elderly Patients with Measured GFR Below 60 mL/min/1.73 m². Aging Clin Exp Res, 32(3): 415–422. https://doi.org/10.1007/s40520-019-01218-2

[12] Pottel H, Delanaye P, Schaeffner E, et al., 2017, Estimating Glomerular Filtration Rate for the Full Age Spectrum from Serum Creatinine and Cystatin C. Nephrol Dial Transplant, 32(3): 497–507. https://doi.org/10.1093/ndt/gfw425

[13] Chen J, Zhang Q, 2019, Nutrition Management in Elderly Patients with Chronic Kidney Disease. Chinese Journal of Nephrology, Dialysis & Transplantation, 28(6): 548–549.

[14] Yong Z, Li F, Pei X, et al., 2019, A Comparison Between 2017 FAS and 2012 CKD-EPI Equations: A Multi-Center Validation Study in Chinese Adult Population. Int Urol Nephrol, 51(1): 139–146. https://doi.org/10.1007/s11255-018-1997-4

[15] Trocchi P, Girndt M, Scheidt-Nave C, et al., 2017, Impact of the Estimation Equation for GFR on Population-Based Prevalence Estimates of Kidney Dysfunction. BMC Nephrol, 18(1): 341. https://doi.org/10.1186/s12882-017-0749-5