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Assessment of Four Different eGFR Equations in Older Turkish Adults

Yaşlı Türk Bireylerde Dört Farklı eGFR Formülünün Değerlendirilmesi

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Abstract: Age-related physiologic changes and comorbidities make it difficult to estimate the glomerular filtration rate (GFR) in older adults. Although inulin clearance is accepted as the gold standard for measuring GFR, it is impractical in clinical practice. A total of 228 patients who underwent a 24-hour creatinine clearance test for the measured GFR (mGFR) were included in the study. The estimated GFR (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-epi), Berlin Initiative Study-1 (BIS-1) and Full Age Spectrum (FAS) formula. The medians of the differences between mGFR and each eGFR equation were used for assessing the bias, and the interquartile range (IQR) of the differences was used for expressing the precision of each equation. The mean age was 76.98±7.83 years and the frequency of female patients was 58.20%. In all patients, FAS [bias=0.40 (1.09%), IQR= 26.55 (%52.49)] and BIS-1 [bias=1.36 (4.27%), IQR=26.71 (%55.28)] were less biased. In the mGFR≥60 mL/min/1.73 m² subgroup, MDRD was the most precise [bias= -1.73 (-1.69%), IQR=25.14 (%49.75)], in four equations. In patients younger than 75 years, MDRD and CKD-epi equations were less biased, and the CKD-epi equation had the smallest IQR [bias=2.80 (4.52%), bias= -2.93 (-4.29%), IQR=32.97 (49.94%)], whereas, in those older than 75 years, BIS-1 and FAS equations were less biased. However, for the patients 30≤mGFR<60 and mGFR<30 mL/min/1.73 m², BIS-1 had the lowest bias and smallest IQRs [bias=3.49 (7.81%), IQR=14.28 (33.20%) and bias=7.60 (40.11%), IQR=13.81 (39.59%)]. In conclusion, BIS-1 and FAS equations were less biased in older patients with mGFR<60 mL/min/1.73 m², and MDRD and CKD-epi were less biased in patients with mGFR≥60 mL/min/1.73 m².

Keywords: Glomerular filtration rate; Older adults; Creatinine clearance; Glomerular filtration rate equation.

Ethics Committee Approval: This study was conducted in conformity with the Declaration of Helsinki and was approved by the local ethics committee (IRB number: 2023/01-13).

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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Özet: Yaşla ilişkili fizyolojik değişiklikler ve eşlik eden hastalıklar, yaşlı bireylerde glomerüler filtrasyon hızının (GFH) tahmin edilmesini güçleştirmektedir. Klinik uygulamada altın standart olarak kabul edilen inülin klirensi, pratikte kullanımı zor olduğundan tercih edilmemektedir. Bu çalışmada, ölçülen GFH (mGFH) için 24 saatlik kreatinin klirens testi uygulanan toplam 228 hasta değerlendirilmiştir. Tahmini GFH (eGFH), Modification of Diet in Renal Disease (MDRD), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI Berlin Initiative Study-1 (BIS-1) ve Full Age Spectrum (FAS) formüllerine göre hesaplanmıştır. mGFH ile her bir eGFH formülü arasındaki farkların medyanı yanlılığı, interkuartil aralığı (IQR) ise her formülün hassasiyetini göstermek amacıyla kullanılmıştır. Hastaların ortalama yaşı 76.98±7.83 yıl olup, kadın hasta sıklığı %58.20'dir. Tüm hastalarda FAS [yanlılık=0.40 (1.09%) IQR=26.55 (%52.49)] ve BIS-1 [yanlılık=1.36 (4.27%) IQR=26.71 (%55.28)], formülleri daha az yanlılık göstermiştir. mGFH ≥60 mL/dk/1.73 m² alt grubunda, MDRD formülü dört formül arasında en hassas olanıdır [yanlılık= -1.73 (-1.69%), IQR=25.14 (%49.75)]. 75 yaş altı hastalarda MDRD ve CKD-EPI formülleri daha az yanlılık göstermiş, CKD-EPI formülü en dar IQR değerine sahip olmuştur [yanlılık=2.80 (4.52%), yanlılık= -2.93 (-4.29%), IQR=32.97 (49.94%)]. Ayrıca, 75 yaş üzerindeki bireylerde BIS-1 ve FAS formülleri daha az yanlılık göstermiştir. mGFH 30≤mGFH<60 ve mGFH<30 mL/dk/1.73 m² olan hastalarda ise, BIS-1 formülü en düşük yanlılık ve en dar IQR değerleriyle öne çıkmıştır [sırasıyla yanlılık=3.49 (7.81%), IQR=14.28 (33.20%) ve yanlılık=7.60 (40.11%), IQR=13.81 (39.59%)]. Sonuç olarak, mGFH <60 mL/dk/1.73 m² olan yaşlı hastalarda BIS-1 ve FAS formülleri daha az yanlılık gösterirken, mGFH ≥60 mL/dk/1.73 m² olan hastalarda MDRD ve CKD-EPI formülleri daha doğru sonuçlar vermektedir.

Anahtar Kelimeler: Glomerüler filtrasyon hızı; Yaşlı bireyler; Kreatinin klirensi; Glomerüler filtrasyon hızı formülleri

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1. Introduction

Age-related changes occur in the urinary system, as in all systems. The number of nephrons decreases by 50%, and compensatory hypertrophy develops in the remaining nephrons [1]. After the age of 40 years, creatinine clearance decreases by 1 mL/min/1.73 m² each year [2]. In addition, comorbidities such as chronic kidney disease (CKD), type 2 diabetes mellitus (T2DM), hypertension (HT), and the number of drugs increase with aging [3]. Among individuals with advanced CKD, older adults form the most significant demographic. These changes make it difficult to evaluate the glomerular filtration rate (GFR), the key to the diagnosis of CKD, the adjustment of drug dosage, and the administration of intravenous contrast in older adults [4–6].

Various procedures for measured GFR (mGFR) are available. In the assessment of renal function, inulin clearance is the gold standard measurement; however, it is too complicated for clinical practice [7]. Creatinine, one of the most commonly used markers, is the end product of creatine phosphate in muscle [8]. It is freely filtered from the glomeruli, whereas it is actively secreted from the peritubular capillaries [9]. This appears as an excess of 10–20% in the GFR calculation. Despite this situation, creatinine is frequently the preferred marker for GFR calculation because of its ease of measurement and use. Also, the 24-hour creatinine clearance test is expensive and urine collection is difficult due to mobility, gait and balance problems, and cognitive impairment in older adults. Urinary tract catheterization to collect urine is impractical because of the many complications in older patients [10]. Due to these challenging issues, estimated GFR (eGFR) is more prominent in older adults than mGFR.

Accurate estimation of GFR is important for drug dose adjustment and rationalization of pharmacotherapy in older adults. Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-epi) are the most used creatinine-based equations for estimating GFR [11,12]. Additionally, Berlin Initiative Study (BIS) and Full Age Spectrum (FAS) are other systems based on creatinine equations [13,14]. However, which equation is optimal for accurate assessment of GFR in Turkish older adults has not yet been studied in detail. In this study, we aimed to define the most precise equation among MDRD, CKD-EPI, BIS-1, and FAS, at various GFR ranges in Turkish older adults.

2. Materials and Methods

2.1. Participants and Study Design

This is a retrospective and cross-sectional study. Between January 2013 and October 2021, patients who were hospitalized in our geriatric clinic for any reason were screened. A total of 228 patients who underwent a 24-hour creatinine clearance test were included in the study (Figure 1). The 24-hour urine collection process was conducted under the supervision of nurses and doctors for hospitalized patients. All data were collected retrospectively from the patients' medical records, including descriptive information, comorbidities, Charlson Comorbidity Index (CCI), blood tests, and 24-hour creatinine clearance test results. Exclusion criteria included undergoing kidney replacement therapy, acute kidney failure, acute glomerulonephritis, cirrhosis, congestive heart failure, hypovolemia, cachexia, muscle disease, and sepsis.

2.2. Measurement of GFR

The 24-hour urinary creatinine clearance test was performed to evaluate hypertensive nephropathy, diabetic nephropathy, and stage of chronic kidney disease, and to adjust the drug dose. Creatinine levels were measured using a Diagnostic Modular System AutoAnalyzer (Roche E170 and P 800, Switzerland) immunoassay (IUD).

mGFR was calculated using the following formula:

$$\text{Creatinine clearance} = \frac{\text{urinary creatinine (mg/dL)} \times \text{24-hour urinary volume (mL)}}{\text{plasma creatinine (mg/dL)} \times 1440}$$

2.2.1. Estimation of GFR

The GFR was estimated according to the MDRD, CKD-epi, BIS-1, and FAS formulas. The formulas are as follows:

$$\text{MDRD} = 175 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 0.742 \text{ (if female)} [11]$$

$$\text{CKD-epi} = 141 \times \min(\text{serum creatinine /k, 1})^{\alpha} \times \max(\text{serum creatinine /k, 1})^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ (if female)}$$

($k=0.7$ for females and 0.9 for males, $\alpha=0.329$ for females and 0.411 for males)[12]

$$\text{BIS-1 GFR} = 3736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95} \times 0.82 \text{ (if female)} [13]$$

$FAS-eGFR = (107.3 / (\text{serum creatinine} / Q)) \times 0.988^{(\text{Age}-40)}$ for age >40 years where Q is 0.70 mg/dL for females and 0.90 mg/dL for males.[14]

2.3. Statistical Analysis

The data were analyzed using the IBM SPSS software. For quantitative data, descriptive measures are given as means \pm standard deviations and the proportions for qualitative data are provided. For normally distributed data, t-tests were employed. The differences between eGFR and mGFR were tested using the Wilcoxon signed-rank test for matched pairs because normality was violated. The medians of the differences between mGFR and each eGFR equation are used for assessing bias and the interquartile range (IQR) of the differences was used for expressing the precision of each equation. The IQR of the difference was calculated as the difference between the 75th and 25th percentiles. GFR and positive values indicate cases of overestimating. A bias close to zero is therefore preferred and smaller IQRs indicate better precision. Bland-Altman plots for the differences against the means were produced for both the raw and percentage differences. Simple linear regression models between the differences between each eGFR and mGFR and the respective means were built to evaluate proportional bias. Subgroup analyses were conducted for age groups (<75 years and \geq 75 years) and different mGFR (mGFR \geq 60, 30 \leq mGFR<60, mGFR<30 mL/min/1.73 m²) ranges. A significance level of p<0.05 was applied in all analyses.

3. Results

A total of 228 consecutive patients were included in the study. The mean age was 76.98 \pm 7.83 years and the frequency of female patients was 58.20%. The demographic features of the patients measured and eGFR results are shown in Table 1.

3.1. Overall patients

The comparison of mGFR and four equations showed that BIS-1 and FAS were not significantly different (p=0.853 and p=0.582, respectively), but the MDRD and CKD-epi were significantly different (p<0.001 for each) (Table 2). Bland-Altman plots of four equations against mGFR are given in Figures 1 and 2 for the differences and percentage differences, respectively. We observed that the spread of differences varied strongly with the averages when raw differences were plotted as in Figure 1; therefore, the percentage differences in Bland-Altman plots in both age groups were also considered and plotted in Figure 2. Using the one-sample t-test, mean differences between the four

equations and mGFR were tested and the differences between BIS-1 and mGFR and FAS and mGFR were not statistically significant (p=0.199 and p=0.189 respectively) (Table 4). Regression analysis of the differences between mGFR and each eGFR was conducted using the means of the mGFR and eGFR as predictors to investigate proportional bias (Table 3). The bias and precision were investigated separately for the subgroups with respect to mGFR levels in addition to the overall assessments because all models yielded significant coefficients. In all patients and various mGFR ranges, FAS [bias=0.40 (1.09%)] and BIS-1 [bias=1.36 (4.27%)] were less biased. Regarding precision, the MDRD equation had the smallest IQR in all patients [IQR=25.14 (49.75%)]. In the mGFR \geq 60 mL/min/1.73 m² subgroup, MDRD was better in the estimation of GFR than other equations [bias= -1.73 (-1.69%)]; FAS had the smallest IQR [25.35 (29.38%)]. For estimating the mGFR in 30 \leq mGFR<60 mL/min/1.73 m² and mGFR <30 mL/min/1.73 m², FAS had less bias than the other equations [bias= 3.72 and 8.43 (8.21% and 43.35%)] and BIS-1 was more precise [IQR=16.53 and 16.07 (32.89% and 36.46%)] (Table 5).

3.2. Participants aged <75 years

In patients younger than 75 years (n=89) and various mGFR ranges, MDRD and CKD-epi equations were less biased, and the CKD-epi equation had the smallest IQR (bias=2.80 (4.52%), bias=-2.93 (-4.29%), IQR=32.97 (49.94%) respectively). For the subgroup 30 \leq mGFR<60 mL/min/1.73 m², BIS-1, and FAS were less biased, and BIS-1 had the smallest IQR (bias=9.32 (17.86%) and bias=7.60 (14.81%), and IQR=22.76 (44.96%) respectively) (Table 5). For patients with mGFR<30 mL/min/1.73 m², the FAS equation was less biased [bias=21.49 (56.76%)], and the BIS-1 equation had the smallest IQR [IQR=27.50 (76.74%)]. For the subgroup mGFR \geq 60 mL/min/1.73 m², MDRD was less biased [bias= -7.33 (-7.06%)] and FAS was more precise [IQR=26.30 (28.18%)].

3.3. Participants aged \geq 75 years

In patients older than 75 years (n= 139) and various mGFR ranges, BIS-1 and FAS equations were less biased, but the IQRs of the equations were similar. For the mGFR>60 mL/min/1.73 m² subgroup, MDRD, and CKD-epi equations were less biased, but BIS-1 and FAS had the smallest IQRs [bias=5.75 (5.86%), bias= -1.89 (-2.87%), IQR=23.24 (30.04%) and IQR=23.48 (30.92%), respectively]. For the patients with 30 \leq mGFR<60 mL/min/1.73 m², BIS-1 and FAS were less biased and had the smallest IQRs

[bias=4.23 (8.63%), bias=3.49 (7.81%), IQR=14.07 (28.89%), and IQR=14.28 (33.20%), respectively]. For the remaining patients with mGFR<30, FAS had the least bias [bias=7.60 (40.11%)], whereas BIS-1

had the smallest IQR [IQR=12.32 (35.75%)]. Table 5 summarizes the bias and precision of the equations.

Table 1. Patient characteristics of the study.

Parameter	All (n=228)
Sex (female) (%)	58.20
Age (year)*	76.98±7.83
Serum creatinine	1.17±0.70
HT (%)	82.00
DM (%)	76.30
CKD (%)	30.70
CCI	2.38±1.26
mGFR (CrCl-24h) mL/min/1.73 m ² *	58.15±34.02
eGFR mL/min/1.73 m ² *	
CKD-epi*	62.81±24.93
MDRD*	68.61±29.71
FAS*	56.17±23.06
BIS-1*	56.02±20.79

CCI: Charlson Comorbidity Index; BIS-1: Berlin Initiative Study 1; CKD: Chronic kidney disease; CKD-epi: The Chronic Kidney Disease Epidemiology Collaboration; CrCl-24h: Creatinine Clearance from a 24-hour urine collection; DM: Diabetes Mellitus; eGFR: Estimated glomerular filtration rate; Fas: Full Age Spectrum; HT: Hypertension; MDRD: The original Modification of Diet in Renal Disease; mGFR: Measured glomerular filtration rate.

*mean±SD

Table 2. Comparison of measured GFR and estimated GFR values

Comparison	P value	Wilcoxon signed-rank statistic
mGFR-MDRD	<0.001	-6.603
mGFR-CKD-epi	<0.001	-3.814
mGFR-BIS-1	0.853	-0.186
mGFR-FAS	0.582	-0.550

BIS-1: Berlin Initiative Study 1; CKD-epi: The Chronic Kidney Disease Epidemiology Collaboration; FAS: Full Age Spectrum; MDRD: The original Modification of Diet in Renal Disease; mGFR: Measured glomerular filtration rate.

Table 3. Regression analysis between the differences and the means and the differences (percentage) and the means

Variable	The differences and the means		The differences (percentage) and the means	
	Beta	p	Beta	p
Mean (MDRD, mGFR)	-0.153	0.005	-0.452	< 0.001
Mean (CKD-epi, mGFR)	-0.354	< 0.001	-0.582	< 0.001
Mean (BIS-1, mGFR)	-0.544	< 0.001	-0.887	< 0.001
Mean (FAS, mGFR)	-0.436	< 0.001	-0.671	< 0.001

BIS-1: Berlin Initiative Study 1; CKD-epi: The Chronic Kidney Disease Epidemiology Collaboration; FAS: Full Age Spectrum; MDRD: The original Modification of Diet in Renal Disease; mGFR: Measured glomerular filtration rate.

Table 4. One-sample tests for the mean differences

	Mean Difference	95% CI	p
MDRD-mGFR	10.69	7.49-13.88	< 0.001
CKD-EPI-mGFR	4.83	1.78-7.88	< 0.001
BIS-1-mGFR	-1.94	-4.93-1.03	0.199
FAS-mGFR	-1.97	-4.93-0.98	0.189

BIS-1: Berlin Initiative Study 1; CKD-epi: The Chronic Kidney Disease Epidemiology Collaboration; FAS: Full Age Spectrum; MDRD: The original Modification of Diet in Renal Disease; mGFR: Measured glomerular filtration rate.

Table 5. Bias and precisions of equations compared with measured GFR

	Overall (n=228)	mGFR\geq60 (n=93)	30\leqmGFR<60 (n=83)	mGFR<30 (n=52)
All Participants				
Bias (median differences)				
MDRD	9.42	-1.73	15.23	13.17
CKD-epi	5.39	-9.39	11.59	11.40
BIS-1	1.36	-17.41	4.93	10.90
FAS	0.40	-15.44	3.72	8.43
Precision (IQR of differences)				
MDRD	25.14	30.50	24.94	22.68
CKD-epi	26.31	30.24	24.24	24.81
BIS-1	26.71	25.52	16.53	16.07
FAS	26.55	25.35	18.06	18.11
Bias (median percentage difference)				
MDRD	18.91	-1.69	31.38	57.21
CKD-epi	13.14	-11.16	24.83	43.62
BIS-1	4.27	-23.69	12.13	46.45
FAS	1.09	-22.57	8.21	43.35
Precision (IQR of percentage differences)				
MDRD	49.75	32.55	43.72	42.21
CKD-epi	52.66	36.92	42.07	53.07
BIS-1	55.28	28.47	32.89	36.46
FAS	52.49	29.38	36.47	42.33
Participants <75 years				
Bias (median differences)				
MDRD	2.80	-7.33	13.72	27.63
CKD-epi	-2.93	-13.55	13.47	25.88
BIS-1	-5.90	-22.01	9.32	23.38
FAS	-5.61	-18.92	7.60	21.49
Precision (IQR of differences)				
MDRD	34.30	31.92	30.86	36.78
CKD-epi	32.97	31.71	31.57	34.34
BIS-1	38.58	27.33	22.76	27.50
FAS	36.50	26.30	25.10	29.50
Bias (median percentage difference)				
MDRD	4.52	-7.06	25.22	48.90
CKD-epi	-4.29	-15.88	24.83	64.61
BIS-1	-8.40	-24.02	17.86	60.26
FAS	-9.72	-22.57	14.81	56.76
Precision (IQR of percentage differences)				
MDRD	55.43	32.42	50.94	91.97
CKD-epi	49.94	31.08	51.31	94.78
BIS-1	52.09	27.98	44.96	76.74
FAS	53.23	28.18	47.31	85.74
Participants \geq75 years				
Bias (median differences)				
MDRD	11.04	5.75	16.24	11.32
CKD-epi	8.12	-1.89	11.41	8.76
BIS-1	4.93	-12.95	4.23	10.08
FAS	3.32	-12.91	3.49	7.60
Precision (IQR of differences)				

MDRD	20.14	27.60	21.56	18.47
CKD-epi	19.53	25.98	21.27	16.90
BIS-1	20.20	23.24	14.07	12.32
FAS	19.44	23.48	14.28	13.81
Bias (median percentage difference)				
MDRD	31.38	5.86	31.40	52.41
CKD-epi	18.76	-2.87	24.41	40.80
BIS-1	14.18	-22.35	8.63	46.36
FAS	9.30	-21.54	7.81	40.11
Precision (IQR of percentage differences)				
MDRD	44.15	33.65	36.09	38.73
CKD-epi	43.40	38.41	39.81	48.49
BIS-1	45.77	30.04	28.89	35.75
FAS	46.64	30.92	33.20	39.59

BIS-1: Berlin Initiative Study 1; CKD-epi: The Chronic Kidney Disease Epidemiology Collaboration; CrCl-24h: Creatinine Clearance from a 24-hour urine collection; Fas: Full Age Spectrum; MDRD: The original Modification of Diet in Renal Disease; mGFR: Measured glomerular filtration rate.

Figure-1 The differences between eGFR using FAS, BIS-1, CKD-EPI, and MDRD equations and mGFR.

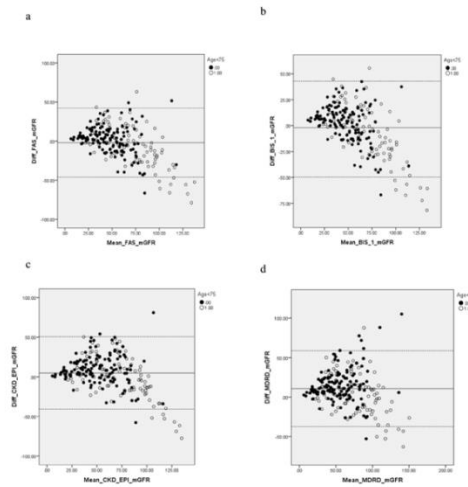


Fig. 1 Bland–Altman plots reveal the differences between estimated glomerular filtration rate (eGFR) using a FAS equation, b BIS-1 equation, c CKD-EPI equation, and d MDRD equation, and measured GFR (mGFR), plotted against the mean of mGFR and eGFR. All values are expressed in ml/min/1.73 m². Horizontal solid lines stand for the mean of bias, and horizontal dash lines represent the 95% confidence interval of bias. Participants <75 years are represented by a hollow circle and those ≥75 years by a filled square.

Figure-2 The percentage differences between eGFR using FAS, BIS-1, CKD-EPI, and MDRD equations, and mGFR.

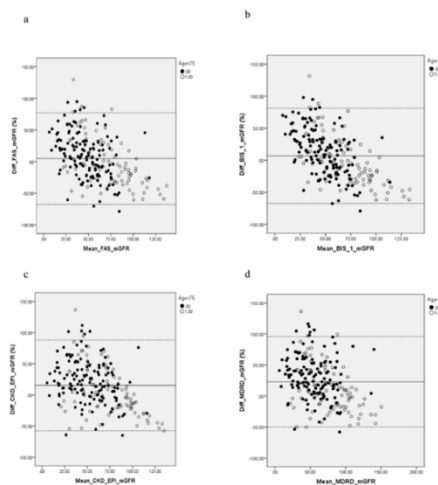


Fig. 2 Bland–Altman plots reveal the percentage differences between estimated glomerular filtration rate (eGFR) using a FAS equation, b BIS-1 equation, c CKD-EPI equation, and d MDRD equation, and measured GFR (mGFR), plotted against the mean of mGFR and eGFR. All values are expressed in ml/min/1.73 m². Horizontal solid lines stand for the mean of bias, and horizontal dash lines represent the 95% confidence interval of bias. Participants <75 years are represented by a hollow circle and those ≥75 years by a filled square

4. Discussion

This cross-sectional and retrospective study evaluating the capacity of BIS-1, FAS, MDRD, and CKD-epi to accurately assess GFR in older adults found that BIS-1 and FAS equations were less biased in the patients. Patients with $mGFR \geq 60$ mL/min/1.73 m², MDRD, and CKD-epi equations were less biased, and for those with $mGFR < 60$ mL/min/1.73 m², BIS-1, and FAS were less biased. Nevertheless, in those older than 75 years, however, MDRD and CKD-epi equations were less biased, and BIS-1 and FAS had the smallest IQRs in $mGFR \geq 60$ mL/min/1.73 m².

It is known that after the age of 40 years, there is a decrease in creatinine clearance every year (7.5 to 10 mL per minute per decade). In addition to physiologic changes, other comorbidities, as well as CKD, are common in older adults [15]. The management of CKD is closely related to renal functions [6,16,17], and most antibiotics require dose adjustment based on renal function [18]. Considering all these situations, accurate and practical GFR measurement becomes even more crucial for these patients. The limited applicability of the 24-hour urine collecting methods increases the importance of estimated GFR methods. Accordingly, although cystatin-based measurement methods are considered more reliable, creatinine-based eGFR equations are the most commonly used worldwide. Within this context, the organization Kidney Disease: Improving Global Outcomes (KDIGO) recommends using CKD-epi as an eGFR equation for the entire population, and if eGFR is below 60 mL/min/1.73 m², it recommends cystatin C measurements [19]. However, it is worth noting that only 13% of patients were aged 65 years or older in the study conducted for the CKD-epi equation [20]. Moreover, patients older than 70 years were excluded from the MDRD equation study [21]. This may be why those equations are poorly related to mGFR in older adults, especially those with lower GFR.

Apart from age-related changes in the kidney system, changes in the muscle and diet can affect serum creatinine, thus measurement methods in older individuals may differ from those in younger individuals. Therefore, the BIS-1 and BIS-2 equations were developed for patients older than 70 years; BIS-2 was reported to be a reliable equation in patients with eGFR greater than 30 mL/min per 1.73 m², and the BIS-1 equation was reported as an acceptable alternative in older patients with normal or mild-to-moderately reduced kidney function [13,22]. Also, the FAS equation was developed to

eliminate the effect of age and sex on creatinine clearance [23]. The FAS and BIS-1 equations were recommended as accurate equations to estimate GFR in older patients, especially for those with moderately reduced kidney function [24]. Nevertheless, the present study demonstrated that the BIS-1 and FAS equations were less biased in older adults with $mGFR < 60$ mL/min/1.73 m².

In a study, Guan et al. found that the BIS-2 might be optimal for Chinese older adults (≥ 75 years) with $mGFR \geq 30$ mL/min/1.73 m², and CKD-epi could yield better performance than the BIS-2 equation, especially in those aged < 75 years with $mGFR < 30$ mL/min/1.73 m². In that study, mGFR was evaluated using a renal dynamic imaging method, with 99 m Tc-diethylene-tri-amine pentaacetic acid (99m Tc-DTPA).[15] In our study, we could perform neither 99 m Tc-DTPA nor cystatin-based equations, but both studies showed that most used equations (MDRD and CKD-epi) might not be optimal for all ages and in various mGFR subgroups. Another recent study reported that MDRD, CKD-epi, and BIS-1 could not be considered interchangeable for assessing eGFR in Chinese centenarians [25].

Scarr et al. reported an unexpected finding in a study. In their study, MDRD, CKD-epi creatinine (CKD-epi-cr), CKD-epi cystatin C (CKD-epi-cys), CKD-EPI-cr-cys, and β_2 microglobulin were performed for eGFR in Canadian older adults with type 1 diabetes. All these equations underestimated mGFR and were related to greater negative bias and lower accuracy in higher mGFR [26].

In an older multi-ethnic group, MDRD and Cockcroft–Gault (CG) had discordant results in 60% of patients [27]. Although CG is not the most reliable and used equation, it is an important study in that it showed that measurement methods could be inconsistent with each other in older patients and the study was conducted on a multi-ethnic group. In accordance with the present study, the BIS-1 equation was reported to be most accurate in Chinese older adults among CKD-epi, Lund-Malmö Revised (LMR), BIS-1, and FAS equations based on serum creatinine when GFR was measured using the dual plasma sample clearance method with Technetium-99 m-diethylenetriamine-pentaacetic acid (Tc-99 m-DTPA) [28]. Another study concluded that the BIS-1 equation was more accurate than the MDRD and CKD-epi in patients older than 80 years with a $GFR < 60$ mL/min/1.73 m² [29].

When the literature is reviewed, there is no consensus on a gold standard equation for GFR in older individuals. Different results in groups with different characteristics suggest that biomarkers used in equations also relate to age, sex, comorbid conditions, various mGFRs, and ethnicity. In our study, we evaluated the various mGFR values in older adults by dividing by age, those older than 75 years, and those who were aged 75 years and younger, using four different equations. Compatible with the literature, this study showed that BIS-1 and FAS equations were suitable for older adults with moderately reduced kidney function.

4.1. Strengths and limitations

This study is the first study on Turkish older adults to define the most precise eGFR equation. Four of the most commonly used equations were assessed for this purpose, and the GFR was measured using 24-hour creatinine clearance. Also, this study had

some limitations. First, it was a cross-sectional and retrospective study. After that, a single laboratory measurement was used to calculate the mGFR and eGFR equations, and muscle mass was not evaluated. The next issue, inulin clearance, the gold standard method, was not measured. Finally, all participants were hospitalized, and the results might not reflect the entire population. Prospective studies with a larger population are needed.

5. Conclusion

BIS-1 and FAS equations were found to be less biased in older patients with $\text{mGFR} < 60 \text{ mL/min/1.73 m}^2$, and MDRD and CKD-epi were less biased in patients with $\text{mGFR} \geq 60 \text{ mL/min/1.73 m}^2$. These equations may become valuable in older adults for the estimation of GFR. Moreover, equations may be combined to obtain accurate eGFR.

REFERENCES

- Denic A, Lieske JC, Chakkerla HA, Poggio ED, Alexander MP, Singh P, Kremers WK, Lerman LO, Rule AD. The Substantial Loss of Nephrons in Healthy Human Kidneys with Aging. *J Am Soc Nephrol* [Internet]. 2017 Jan 1 [cited 2022 Apr 21];28(1):313–20.
- Lindeman RD. Overview: renal physiology and pathophysiology of aging. *American Journal of Kidney Diseases*. 1990;16(4):275–82.
- Ates Bulut E, Soysal P, Isik AT. Frequency and coincidence of geriatric syndromes according to age groups: single-center experience in Turkey between 2013 and 2017. *Clin Interv Aging*. 2018;13:1899–905.
- Jessani S, Levey AS, Bux R, Inker LA, Islam M, Chaturvedi N, Mariat C, Schmid CH, Jafar TH. Estimation of GFR in South Asians: A Study From the General Population in Pakistan. *Am J Kidney Dis* [Internet]. 2014 [cited 2022 Apr 21];63(1):49.
- Gurm HS, Dixon SR, Smith DE, Share D, Lalonde T, Greenbaum A, Moscucci M. Renal function-based contrast dosing to define safe limits of radiographic contrast media in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol* [Internet]. 2011 Aug 23 [cited 2022 Apr 21];58(9):907–14.
- Canaslan K, Ates Bulut E, Kocyigit SE, Aydin AE, Isik AT. Predictivity of the comorbidity indices for geriatric syndromes. *BMC Geriatr* [Internet]. 2022 Dec 19 [cited 2022 Jul 2];22(1):440.
- Delanaye P, Souvignet M, Dubourg L, Thibaudin L, Maillard N, Krzesinski JM, Cavalier E, Mariat C. [Measurement of inulin: development]. *Ann Biol Clin (Paris)* [Internet]. 2011 May [cited 2022 Apr 21];69(3):273–84.
- Hosten AO. BUN and Creatinine. *Clinical Methods: The History, Physical, and Laboratory Examinations* [Internet]. 1990 [cited 2022 Apr 21]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK305/>
- Wyss M, Kaddurah-Daouk R. Creatine and creatinine metabolism. *Physiol Rev* [Internet]. 2000 [cited 2022 Apr 21];80(3):1107–213.
- Bo M, Porrino P, di Santo SG, Mazzone A, Cherubini A, Mossello E, Bianchetti A, Musicco M, Ferrari A, Ferrara N, Filippini C, Trabucchi M, Morandi A, Bellelli G. The association of indwelling urinary catheter with delirium in hospitalized patients and nursing home residents: an explorative analysis from the “Delirium Day 2015.” *Aging Clin Exp Res* [Internet]. 2019 Mar 14 [cited 2022 Apr 21];31(3):411–20.
- Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW, van Lente F. Expressing the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate with Standardized Serum Creatinine Values. *Clin Chem* [Internet]. 2007 Apr 1;53(4):766–72.
- Levey AS, Stevens LA. Estimating GFR Using the CKD Epidemiology Collaboration (CKD-EPI) Creatinine Equation: More Accurate GFR Estimates, Lower CKD Prevalence Estimates, and Better Risk Predictions. Vol. 55, *American Journal of Kidney Diseases*. 2010. p. 622–7.
- Schaeffner ES, Ebert N, Delanaye P, Frei U, Gaedeke J, Jakob O, Kuhlmann MK, Schuchardt M, Tölle M, Ziebig R, van der Giet M, Martus P. Two Novel Equations to Estimate Kidney Function in Persons Aged 70 Years or Older. *Ann Intern Med* [Internet]. 2012 Oct 2;157(7):471–81.
- Hoste L, Dubourg L, Selistre L, de Souza VC, Ranchin B, Hadj-Aïssa A, Cochat P, Martens F, Pottel H. A new equation to estimate the glomerular filtration rate in children, adolescents and young adults. *Nephrology Dialysis Transplantation* [Internet]. 2014 May 1;29(5):1082–91.

15. Guan C, Liang M, Liu R, Qin S, He F, Li J, Zhu X, Dai H, Fu J. Assessment of creatinine and cystatin C-based eGFR equations in Chinese older adults with chronic kidney disease. *Int Urol Nephrol*. 2018 Dec 1;50(12):2229–38.
16. Reid IR, Billington EO. Drug therapy for osteoporosis in older adults. *The Lancet*. 2022 Mar 12;399(10329):1080–92.
17. Inker LA, Titan S. Measurement and Estimation of GFR for Use in Clinical Practice: Core Curriculum 2021. *American Journal of Kidney Diseases*. 2021 Nov 1;78(5):736–49.
18. Fahimi F, Emami S, Farokhi FR. The Rate of Antibiotic Dosage Adjustment in Renal Dysfunction. *Iran J Pharm Res [Internet]*. 2012 Mar [cited 2022 Jun 13];11(1):157.
19. Levin A, Stevens PE, Bilous RW, Coresh J, de Francisco ALM, de Jong PE, Griffith KE, Hemmelgarn BR, Iseki K, Lamb EJ, Levey AS, Riella MC, Shlipak MG, Wang H, White CT, Winearls CG. Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl (2011) [Internet]*. 2013 Jan 1 [cited 2022 Jun 13];3(1):1–150.
20. Levey AS, Stevens LA, Schmid CH, Zhang Y (Lucy), Castro AF, Feldman HI, Kusek JW, Eggers P, van Lente F, Greene T, Coresh J. A New Equation to Estimate Glomerular Filtration Rate. *Ann Intern Med [Internet]*. 2009 May 5;150(9):604–12.
21. Levey AS, Coresh J, Greene T, Stevens LA, Zhang Y, Hendriksen S, Kusek JW, van Lente F. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med [Internet]*. 2006 Aug 15 [cited 2022 Dec 7];145(4):247–54.
22. Koppe L, Klich A, Dubourg L, Ecochard R, Hadj-Aissa A. Performance of creatinine-based equations compared in older patients. *J Nephrol [Internet]*. 2013 Jul [cited 2022 Dec 7];26(4):716–23.
23. Pottel H, Hoste L, Dubourg L, Ebert N, Schaeffner E, Eriksen BO, Melsom T, Lamb EJ, Rule AD, Turner ST, Glasscock RJ, de Souza V, Selistre L, Mariat C, Martens F, Delanaye P. An estimated glomerular filtration rate equation for the full age spectrum. *Nephrol Dial Transplant [Internet]*. 2016 May 1 [cited 2022 Dec 7];31(5):798–806.
24. Chen A, Sun Y, Li W, Yang J, Yao Z, Shi L, Jia J. Application of GFR estimation equations in elderly patients with measured GFR below 60 mL/min/1.73 m². *Aging Clin Exp Res [Internet]*. 2020 Mar 1 [cited 2022 Dec 7];32(3):415–22.
25. Han QX, Zhang D, Zhao YL, Liu L, Li J, Zhang F, Luan FX, Duan JY, Liu ZS, Cai GY, Chen XM, Zhu HY. Analysis of chronic kidney disease staging with different estimated glomerular filtration rate equations in Chinese centenarians. *Chin Med J (Engl)*. 2019 Mar 5;132(5):512–8.
26. Scarr D, Bjornstad P, Lovblom LE, Lovshin JA, Boulet G, Lytvyn Y, Farooqi MA, Lai V, Orszag A, Weisman A, Keenan HA, Brent MH, Paul N, Bril V, Cherney DZI, Perkins BA. Estimating GFR by Serum Creatinine, Cystatin C, and β 2-Microglobulin in Older Adults: Results From the Canadian Study of Longevity in Type 1 Diabetes. *Kidney Int Rep*. 2019 Jun 1;4(6):786–96.
27. Gill J, Malyuk R, Djurdjev O, Levin A. Use of GFR equations to adjust drug doses in an elderly multi-ethnic group - A cautionary tale. *Nephrology Dialysis Transplantation*. 2007 Oct;22(10):2894–9.
28. Xia F, Hao W, Liang J, Wu Y, Yu F, Hu W, Zhao Z, Liu W. Applicability of Creatinine-based equations for estimating glomerular filtration rate in elderly Chinese patients. *BMC Geriatr [Internet]*. 2021 Dec 1 [cited 2022 Dec 7];21(1).
29. Lopes MB, Araújo LQ, Passos MT, Nishida SK, Kirsztajn GM, Cendoroglo MS, Sesso RC. Estimation of glomerular filtration rate from serum creatinine and cystatin C in octogenarians and nonagenarians. *BMC Nephrol [Internet]*. 2013 Dec 2 [cited 2022 Dec 7];14(1).