

MDRD ve CKD-EPI eGFR Arasındaki Uyum: Bir Büyük Popülasyona Dayalı Yöntem Karşılaştırma

Agreement Between MDRD and CKD-EPI eGFR Results: A Large Population-Based Method Comparison

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ABSTRACT

Aim: Since glomerular filtration rate (GFR) determined by 24 hours urine is cumbersome, nephrologists recommend using an estimated GFR (eGFR). This study aimed to investigate the agreement between Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR in high case numbers.

Materials and Methods: 56228 eGFR results were included in the study. For agreement between MDRD and CKD-EPI eGFR results, kappa analysis was used. Additionally, the two methods were compared according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.

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Results: The category agreement between the two eGFR methods was 84.4%, while the discordance was 15.6%. Incompatibility was found as 3.0%, 33.2%, 13.0%, 7.2% and 1.1% from (GFR category) G1 to G5, respectively. CKD-EPI eGFR results were average 4.4% higher than MDRD. When Chronic Kidney Disease (CKD) stage transition limits were taken as the medical decision limit, the highest difference% was determined to be 9.8% at stage 1-2 transition.

Conclusion: Although the difference between the two methods is <9.8%, the 15.6% categorical discordance will create a follow-up problem in patient monitoring; it also shows that it is not appropriate to use it in a healthy population, given that MDRD produces higher results in low serum creatinine.

Keywords: eGFR, CKD-EPI, MDRD, Method Comparison

ÖZET

Amaç: 24 saatlik idrarla belirlenen glomerüler filtrasyon hızı (GFR) külfetli ve hataya yatkın olduğundan, günümüzde nefrologlar tahmini bir GFR (eGFR) kullanılmasını önermektedir. Bu çalışma, yüksek vaka sayılarında Renal Hastalıkta Diyet Modifikasyonu (MDRD) ve Kronik Böbrek Hastalığı Epidemiyolojisi Birliği (KBH-EPI) eGFR arasındaki uyumu araştırmayı amaçladık.

Gereç ve Yöntem: Dışlama kriterleri sonrasında 56228 eGFR sonucu çalışmaya dahil edildi. MDRD ve KBH-EPI eGFR sonuçları arasındaki uyum için kappa analizi kullanıldı. Ek olarak, iki yöntem Klinik ve Laboratuvar Standartları Enstitüsü (CLSI) standardına göre karşılaştırıldı.

Bulgular: İki eGFR yöntemin arasındaki uyum %84.4, uyumsuzluk ise %15.6 saptandı. Kronik Böbrek Hastalığı (KBH) Evre 1'den 5'e göre sınıflandırıldığında uyumsuzluk sırasıyla %3.0, %33.2, %13.0, %7.2 ve %1.1 olarak bulundu. KBH-EPI eGFR sonuçları, MDRD'denortalama %4.4 daha yüksekti. Toplamda MDRD ve KBH-EPI eGFR sonuçlarında güçlü bir korelasyon ($r=0.949$) saptandı. Evreler dikkate alındığında Evre 1 ve Evre 2 için korelasyon katsayısının daha düşük olduğu belirlendi. (sırasıyla $r=0.711$ ve $r=0.924$). Tıbbi karar limiti olarak sınıflandırması geçiş limitleri alındığında en yüksek farkın Evre 1-2 geçiş seviyesinde (90 ml/dk) %9.8 olduğu saptandı.

Sonuç: İki yöntem arasındaki %fark <%9.8 olmakla birlikte, %15.6'lık kategorik uyumsuzluk hasta izleminde takip sorunu yaratacaktır. MDRD'nin düşük serum kreatinininde daha yüksek sonuçlar verdiği göz önüne alındığında, sağlıklı bir popülasyonda kullanımının uygun olmayacağını göstermektedir.

AnahtarKelimeler: eGFR, KBH-EPI, MDRD, Yöntem Karşılaştırma

INTRODUCTION

Chronic Kidney Disease (CKD) is one of the most important public health problems worldwide (1). Glomerular filtration rate (GFR) is one of the most essential tests used to estimate renal function (2,3). Correct measurement of GFR is important in the diagnosis and CKD classification, risk grading, and adjustment of drug dose (4). GFR can be measured from the clearance of exogenous substances such as inulin, iothexol, and iohalamate (5–7). However, the determination of GFR with these methods is not practical due to the difficulty of urine collection, allergic reactions and invasive intervention, cost, and radiation risk(8).

National Kidney Disease Education Program-Laboratory Working Group (NKDEP-LWG) recommends the use of eGFR equations defined by Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) study groups. These eGFR equations contain the parameters of serum creatinine, age, gender, and race (9–13). The difference between MDRD and CKD-EPI eGFRs may be due to the population in which the formula was developed. The MDRD equation was obtained from a study conducted on people with CKD (14). CKD-EPI was obtained from a population with relatively different clinical conditions, both with and without CKD. Both

formulas have been derived from studies conducted in North America and Europe; it consists mainly of white and black. Therefore, it is suggested that these formulas will be less accurate in other racial and ethnic groups(15). Another reason for the differences between formulas is the reference methods used in the comparison. Iothalamate was used in MDRD and CKD-EPI eGFR. It is known that there are small differences between these and other reference methods (7).

Due to the development of computer and software technologies today, eGFR calculations are made by Laboratory Information Systems (LIS). When the serum creatinine is requested from the patient and the result comes out, the eGFR results are calculated automatically. To quickly determine the GFR values of patients with CKD and in general medicine; it will provide convenience and effectiveness in diagnosis and treatment. It is seen that comparisons of both methods with reference methods are frequently made in the literature. However, the two different eGFR methods were not compared with each other in high sample numbers and in the "method comparison" format made in medical laboratories. This study aimed to investigate the agreement between the two methods in high case numbers and different creatinine concentrations.

MATERIAL and METHODS

This study carried out on a large population data, is a retrospective study in methodological design that compares the MDRD and CKD-EPI eGFR results and compares the compatibility of CKD classification defined by both two methods. This study was conducted with the approval of the "Dokuz Eylul University Non-Invasive Ethics Committee" (Date: October 26, 2017, and Decision Number: 2017/25-27). The demographic information and eGFRs were obtained from data generated between March 2016 and December 2016 of Dokuz Eylul University Hospital Central Laboratory having

ISO 15189 accreditation. The imported database has been turned into a data warehouse. Serum creatinine levels, the main parameter in eGFR calculation, were determined in the Beckman Coulter AU5800 (USA) auto-analyzer using a method with isotope-dilution mass spectrometry (ID-MS) traceability.

Exclusion criteria: 1) patients with creatinine levels below the reference range (female<0.51 mg/dL; male <0.67 mg/dL), which may have resulted from preanalytical errors; 2) samples with hemolysis, lipemic, empty samples, and sample types other than serum; 3) patients younger than 18 years of age; 4) emergency and intensive care patients; 5) patients with suspected acute kidney injury; and 6) recurrent results of the same patients (Figure 1).

There was a total of 265980 eGFR results. The 56228 results remaining after exclusion were included in the study. The study does not have dependent-independent variables in terms of cause-and-effect relationships. The Outcome variables in methodological design are the CKD stages. The variables to evaluate compliance in these stages are eGFR levels calculated by different methods (MDRD and CKD-EPI eGFR).

eGFR Equations Used:

MDRD equation (mL/min/1.73 m²) = 175 × (S_{cr})^{-1.154} × (age)^{-0.203} × (0.742, if female) × (1.212, if black)

S_{cr}: Serum creatinine (mg/dL)

CKD-EPI equation (mL/min/1.73 m²) = 141 × min (S_{cr}/K, 1)^α × max (S_{cr}/K, 1)^{-1.209} × 0.993^{age} × (1.018, If female) × (1.159, If black)

S_{cr}: Serum creatinine (mg/dL)

K: 0.7 (if female), 0.9 (if male)

α= -0.329 (if female), -0.411 (if male)

In females, if creatinine is ≤0.7 mg/dL, "min" is used, if >0.7 mg/dL, "max" is used; in male, if creatinine is ≤0.9 mg/dL, "min" is used, if >0.9 mg/dL, "max" is used.

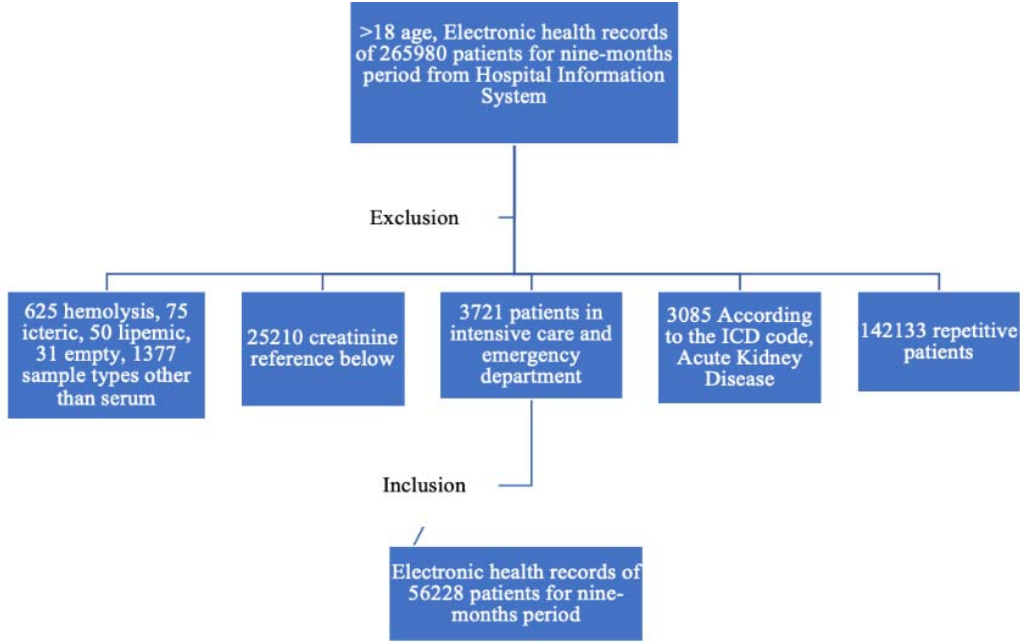


Figure 1. Flowchart of the patients
Şekil 1. Hastaların akış şeması

The agreements between the two eGFR results in the different CKD categories were tested by Kappa analysis. In addition, the agreement and correlation between the two methods were determined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, as conventionally applied in clinical laboratory tests; first, the differences across the whole range were examined with the Bland-Altman plot, then the difference% between the two methods was tested at the medical decision limits with regression analysis. As the medical decision limit, eGFR levels of 90, 60, 30, and 15 ml/min/1.73 m², which are the transition boundaries between CKD categories, were used(16).

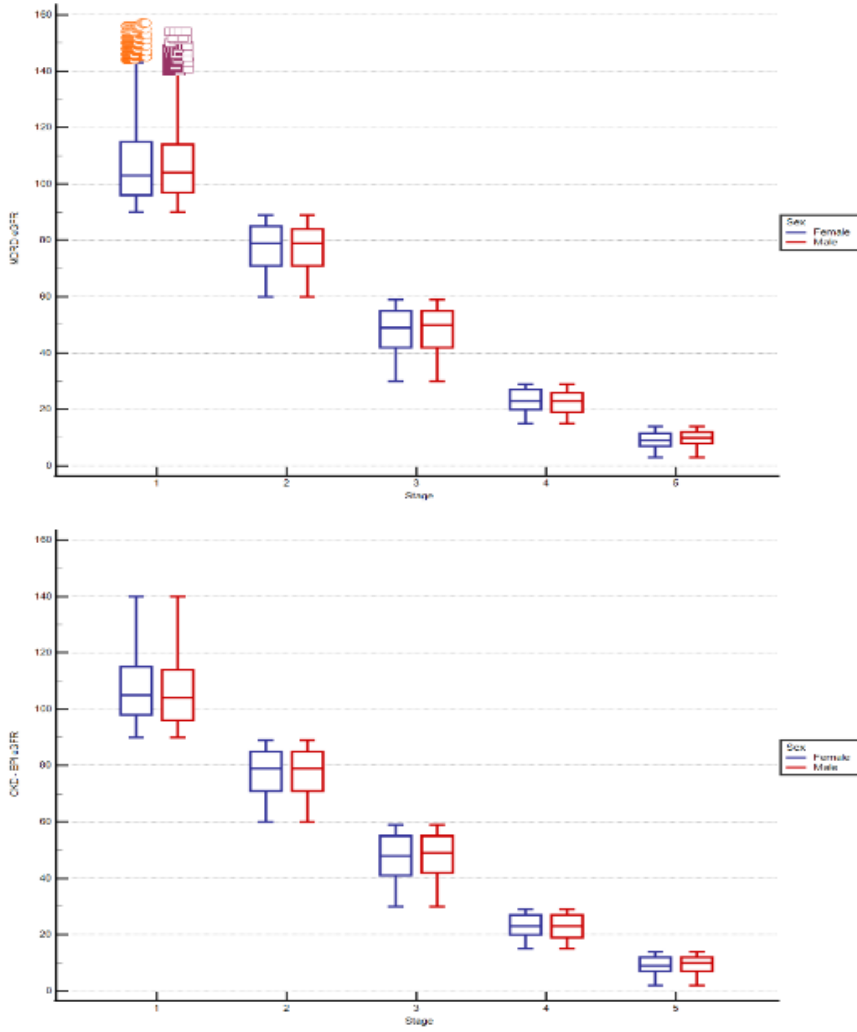
Statistical analyzes were performed using MedCalc v 19.2.3 (MedCalc Software, Ostend, Belgium) and IBM SPSS Statistics for Windows, Version 24.0 (Armonk, NY: IBM Corp) package programs.

RESULTS

Age, serum creatinine, and eGFR results in total and gender subgroups are shown in

Table 1. The distribution of eGFR results is given in the Box-Plot graph in Figures 2a and 2b. Of the 56228 patients, 32029 (57%) were female and 24199 (43%) were male. eGFR results were not normally distributed in total and both genders, MDRD eGFR and CKD-EPI eGFR levels were higher in women compared to men, serum creatinine values were lower, but only the difference of CKD-EPI and serum creatinine values between women and men was significant (p<0.001).

When all CKD categories were evaluated together, the Kappa coefficient of agreement between both eGFRs was 0.729 (p<0.001). The compliance rate between the categories was 84.4%, and the non-compliance rate was 15.6% (Table 2). GFR categories (from G1 to G5), non-compliance rates were found to be 3.0%, 33.2%, 13.0%, 7.2%, and 1.1%, respectively (Table 2). When both genders are considered separately; for women, the compliance rate is 83.0%, the non-compliance rate is 17.0%, and the Kappa coefficient is 0.702; for males, the compliance rate was 86.3%, the non-compliance rate was 13.7% and the Kappa coefficient was 0.764 (Table 3 and Table 4).



Figures 2a and 2b. The distribution of MDRD (a) and CKD EPI (b) eGFR results in CKD classification
Şekil 2a ve 2b. KBH sınıflandırmasında MDRD (a) ve KBH EPI (b) eGFR sonuçlarının dağılımı

Table 1. Demographics, serum creatinine, and eGFR result from
Tablo 1. Demografik özellikler, serum kreatinin ve eGFR sonuçları

Feature		Mean ± SD	Median	Minimum-Maximum
Age		53±17	54	18-104
Serum Creatinine (mg/dL)	Total	0.88±0.53	0.79	0.51-17.73
	Female	0.77±0.43 ^{&}	0.69	0.51-13.94
	Male	1.01±0.61 ^{&}	0.89	0.67-17.73
MDRD eGFR (mL/min/1.73 m²)	Total	88.3±24.1	90	3-157
	Female	88.4±24.1	89	3-157
	Male	88.1±24.0	90	3-154
CKD-EPI eGFR (mL/min/1.73 m²)	Total	91.8±23.8	95	2-140
	Female	98.9±23.6 [*]	96	2-140
	Male	90.4±23.9 [*]	94	2-140

[&]P<0.001; * p<0.001

Table 2. The numerical and proportional compliance of stages according to MDRD and CKD-EPI eGFR in total

Table 2. Totalde MDRD ve KBH-EPI eGFR'ye göre aşamaların sayısal ve oransal uyumu

		CKD-EPI Category, n (%)					Total
		1	2	3	4	5	
MDRD Category, n (%)	1	27533 (97.0)	886 (3.0) ↓	-	-	-	28419
	2	7024 (32.8) ↑	14298 (66.8)	88 (0.4) ↓	-	-	21410
	3	-	650 (12.0) ↑	4678 (87.0)	56 (1.0) ↓	-	5384
	4	-	-	31 (4.7) ↑	618 (92.8)	17 (2.5) ↓	666
	5	-	-	-	4 (1.1) ↑	345 (98.9)	349
Total		34557	15834	4797	678	362	*56228

*Kappa=0.729; p<0.001; Up arrow and yellow color indicate CKD-EPI shows individuals in better eGFR category than MDRD, down arrow and red color shows worse eGFR category, green shows no change in category.

Table 3. Numerical and proportional compliance of MDRD and CKD-EPI eGFR results according to CKD stages in female

Table 3. Kadınlarda KBH evrelerine göre MDRD ve KBH-EPI eGFR sonuçlarının sayısal ve orantılı uyumu

		CKD-EPI Category, n(%)					Total
		1	2	3	4	5	
MDRD Category, n (%)	1	15663 (97.8)	343 (2.2) ↓	-	-	-	16006
	2	4586 (36.7) ↑	7876 (63.0)	25 (0.3) ↓	-	-	12487
	3	-	445 (14.8) ↑	2548 (84.5)	23 (0.7) ↓	-	3016
	4	-	-	16 (4.5) ↑	326 (93.8)	6 (1.7) ↓	348
	5	-	-	-	3 (1.7) ↑	169 (98.3)	172
Total		20249	8664	2589	352	175	*32029

*Kappa =0,702; p<0,001; Up arrow and yellow color indicate CKD-EPI shows individuals in better eGFR category than MDRD, down arrow and red color show worse eGFR category, green shows no change in category.

Table 4. Numerical and proportional compliance of MDRD and CKD-EPI eGFR results according to CKD stages in male

Table 4. Erkeklerde KBH evrelerine göre MDRD ve KBH-EPI eGFR sonuçlarının sayısal ve orantılı uyumu

		CKD-EPI Category, n(%)					Total
		1	2	3	4	5	
MDRD Category, n (%)	1	11870 (95.6)	543 (4.3) ↓	-	-	-	12413
	2	2438 (27.3) ↑	6422 (71.9)	63 (0.7) ↓	-	-	8923
	3	-	205 (8.7) ↑	2130 (90)	33 (1.3) ↓	-	2368
	4	-	-	15 (4.7) ↑	292 (91.8)	11 (3.5) ↓	318
	5	-	-	0 (0.0)	1 (0.5) ↑	176 (99.5)	177
Total		14308	7170	2208	326	187	*24199

*Kappa=0,764; p<0,001; Up arrow and yellow color indicate CKD-EPI shows individuals in better eGFR category than MDRD, down arrow and red color show worse eGFR category, green shows no change in category.

When the differences between MDRD and CKD-EPI eGFR results were examined in the Bland-Altman graph, it was determined that CKD-EPI eGFR results were an average of 4.4% higher than MDRD in total (Figure 3). This was 5.6% for women and 2.9% for men (Figures 4a and 4b). When the Bland-Altman graph was examined according to the stages, it was found that although the CKD-EPI median in G1 was higher than MDRD, CKD-EPI gave low results exceeding 10.9% in some individuals. Moreover, it is seen that discordant results are more in this stage than in another stage (Figure 3).

The results of the regression analysis of the CKD categories are given in Table 5. A strong correlation ($r=0.949$) was found in the MDRD and CKD-EPI eGFR results in total

(Figure 5). Considering the CKD categories, it was determined that the lowest correlation coefficient was in G1 and G2 ($r=0.711$ and $r=0.924$, respectively) (Table 5). When the CKD classification transition limits are taken as the "medical decision limit", the highest difference% calculated from the regression equation was determined to be 9.8% at the G1-G2 transition level of 90 ml/min. The differences% in the G2-G3 limit (60 mL/min), G3-G4 limit (30 mL/min), and G4-G5 limit (15 mL/min) were -2.2%, 3.9%, -2.6%, respectively.

Disease classification and kappa compliance are demonstrated in Table 6. While kappa compliance was highest in kidney diseases ($\text{kappa}=0.883$), it was lowest in obstetric diseases ($\text{kappa}=0.434$).

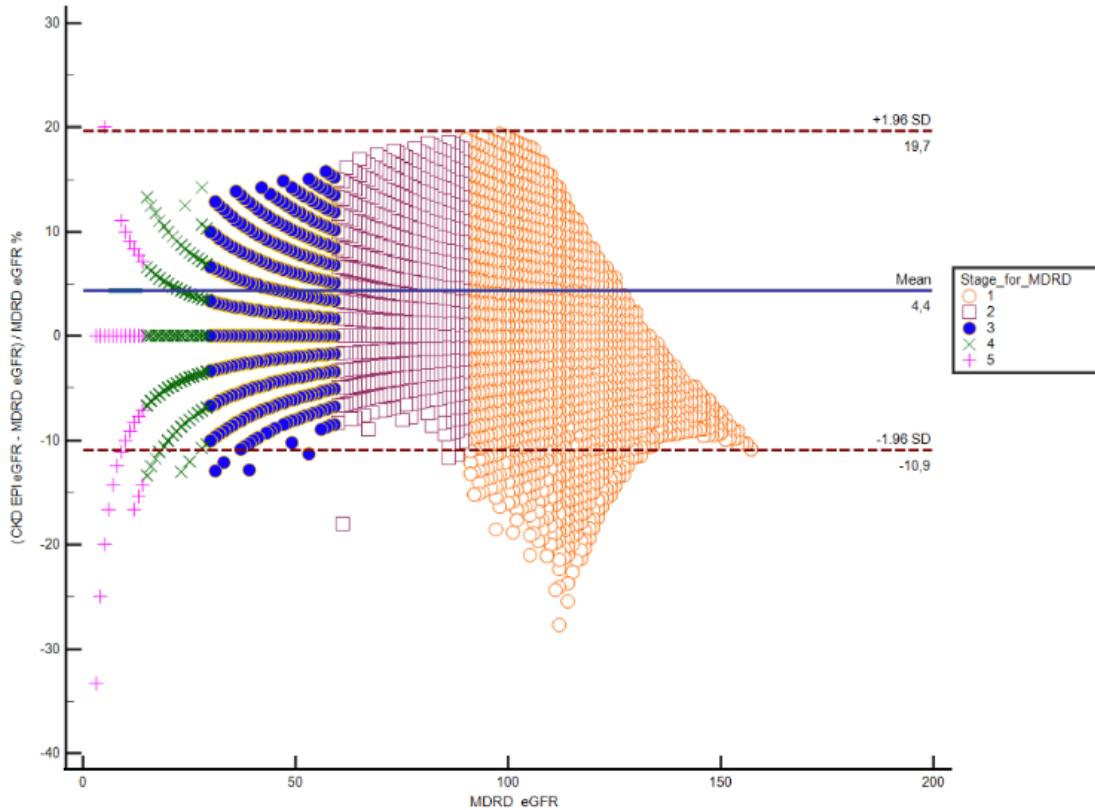
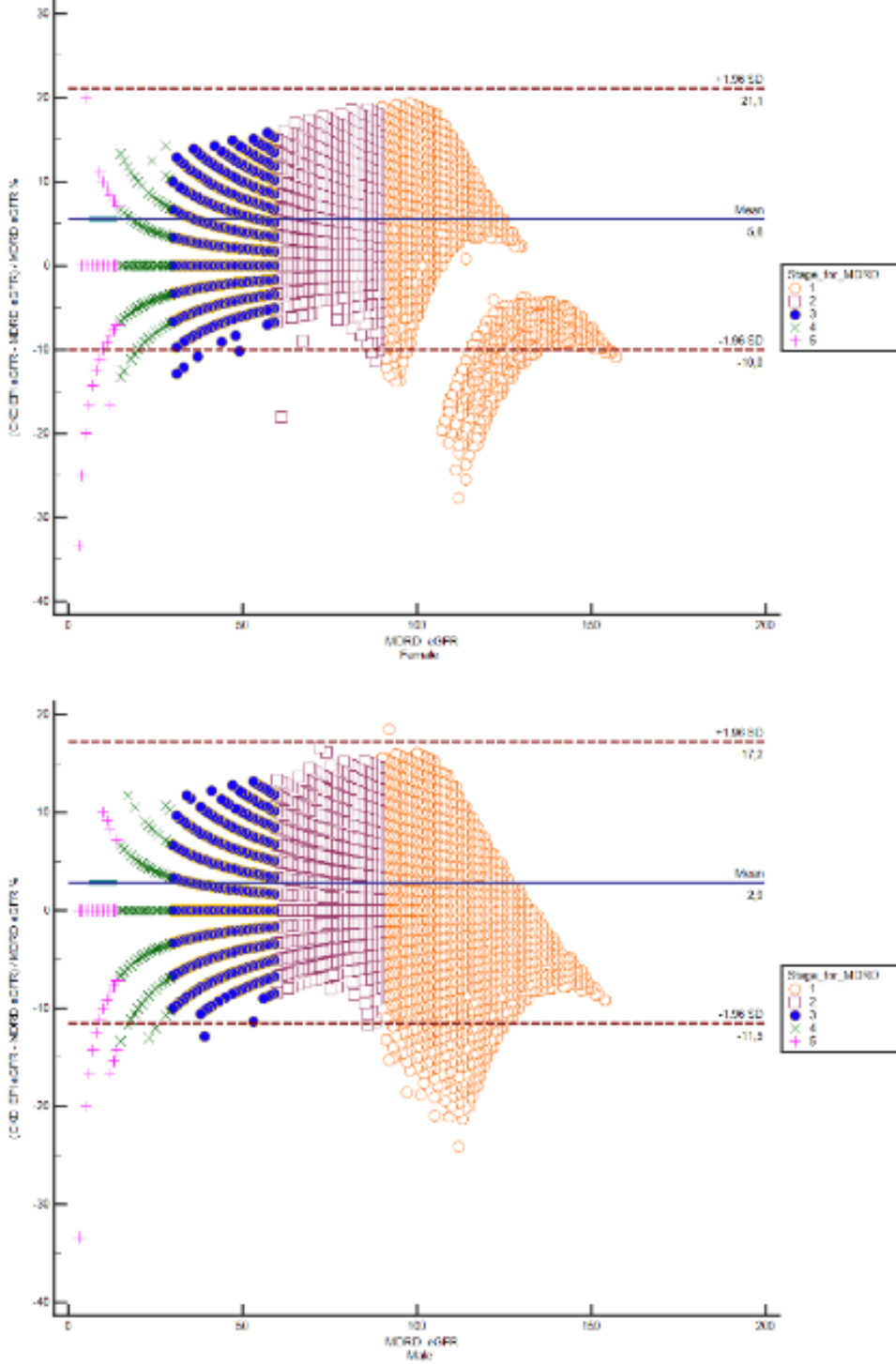


Figure 3. Bland-Altman differences plot between MDRD and CKD-EPI eGFR results in total
Şekil 3. Totalde MDRD ve KBH-EPI eGFR sonuçları arasındaki Bland-Altman farklılıkları grafiği



Figures 4a and 4b. Bland-Altman differences plot between MDRD and CKD-EPI eGFR results in female and male

Şekil 4a ve 4b. Kadın ve erkekte MDRD ve KBH-EPI eGFR sonuçları arasındaki Bland-Altman farklılıkları grafiği

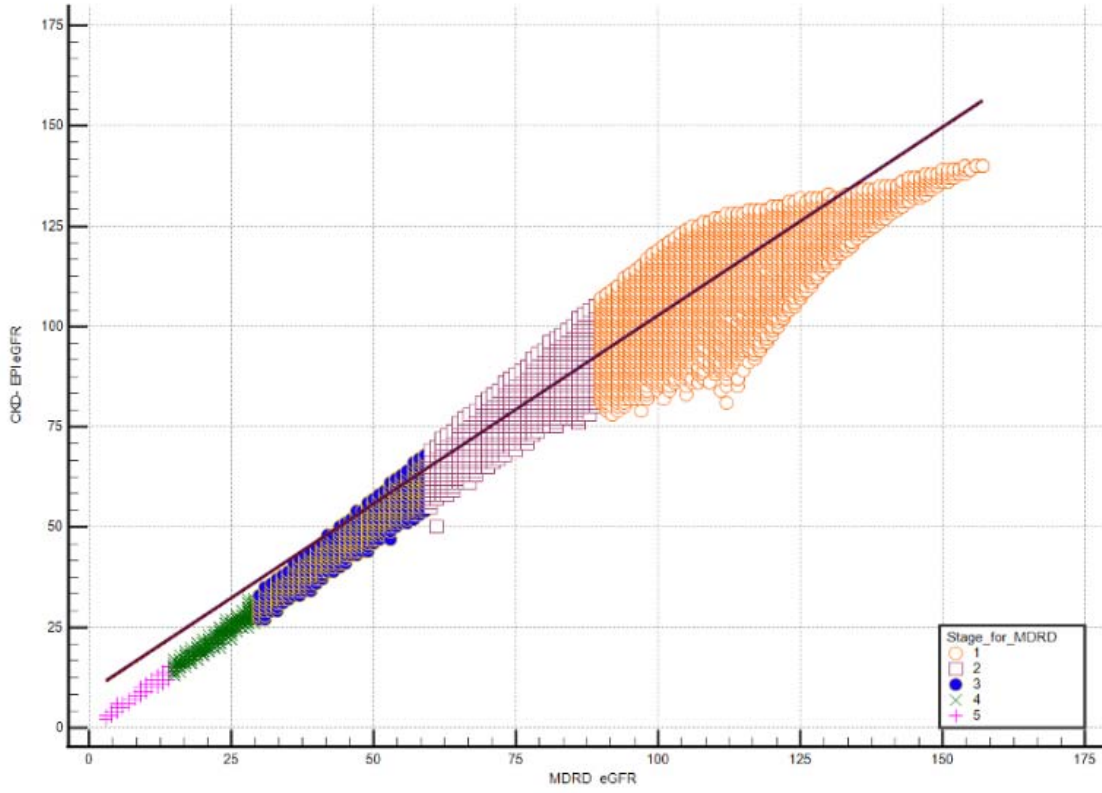


Figure 5. The correlations between MDRD and CKD-EPI GFRs
 Şekil 5. MDRD ve KBH-EPI GFR'leri arasındaki korelasyonlar

Table 5. The regression analysis results between MDRD and CKD-EPI eGFR in total and CKD classification

Tablo 5. Totalde MDRD ile KBH-EPI eGFR ve KBH sınıflandırması arasındaki regresyon analizi sonuçları

Category	n	Equation	Slope (CI 95%)	Intercept (CI 95%)	RSD	SEM	R
1	28419	$y=43.10+0.62x$	0.62 (0.61-0.62)	43.09 (42.33-43.85)	8.05	0.05	0.711
2	21410	$y=-10.22+1.210x$	1.210 (1.204-1.21)	-10.22 (-10.74-9.70)	5.78	0.03	0.924
3	5384	$y=-3.15+1.085x$	1.085 (1.078-1.092)	-3.15 (-3.52-2.78)	3.93	0.05	0.968
4	666	$y=-0.53+1.011x$	1.011 (0.990- 1.033)	-0.5292 (-1.06-0.01)	2.42	0.09	0.962
5	349	$y=-0.19+0.992x$	0.992 (0.97-1.013)	-0.1871 (-0.43-0.06)	1.30	0.07	0.980
Total	56228	$y=3.74+0.999 x$	0.999 (0.997-1.001)	3.74 (3.56-3.92)	8.06	0.03	0.949

Dependent (y)=CKD-EPI eGFR, independent (x)=MDRD eGFR

RSD: Residual standard deviation, SEM: Standard error of mean, R: Correlation coefficient

Table 6. The agreement and correlation between CKD-EPI and MDRD eGFR

Tablo 6. KBH-EPI ve MDRD eGFR arasındaki uyum ve korelasyon

Diagnosis	n (%)	Measurement of agreement	Spearman Rank Correlations
		Kappa	R
Kidney Disease	953 (1.7)	0.883	0.973
Multiple Myeloma	170 (0.3)	0.799	0.918
Organ and Tissue Transplants	373 (0.7)	0.782	0.892
Hypertension	1362 (2.4)	0.776	0.865
Ophthalmological Disease	227 (0.4)	0.774	0.850
Urological Diseases and Malignancies	1355 (2.4)	0.770	0.847
Empty Diagnosis Code	9075 (16.1)	0.757	0.843
Gastroenteritis	26 (0.1)	0.751	0.819
Diabetes Mellitus	2601 (4.6)	0.750	0.822
Cardiovascular Diseases	4233 (7.5)	0.747	0.819
Respiratory Diseases and Malignancies	1493 (2.6)	0.740	0.789
Psychiatric Diseases	936 (1.7)	0.738	0.789
Renal System Stone Diseases	807 (1.4)	0.735	0.819
Haematological Diseases and Malignancies	3548 (6.3)	0.732	0.799
Total	56228 (100)	0.729	0.803
Otorhinolaryngological Diseases	85 (0.1)	0.711	0.767
Infectious Diseases	1797 (3.2)	0.710	0.783
Neurological Diseases	2218 (3.9)	0.708	0.763
Rheumatological Diseases	6216 (11)	0.705	0.769
Neoplasms	5305 (9.4)	0.702	0.769
Orthopedic Diseases	306 (0.5)	0.693	0.743
Gastrointestinal Disease	3282 (5.8)	0.675	0.751
General Symptoms	1962 (3.5)	0.652	0.731
Endocrine and Metabolic Diseases	5117 (9.1)	0.647	0.724
Traumas	36 (0.1)	0.624	0.666
Dermatological Diseases	1022 (1.8)	0.618	0.690
Gynaecological Diseases and Malignancies	1547 (2.7)	0.579	0.684
Obstetric Diseases	176 (0.3)	0.434	0.527

R: Correlation coefficient

DISCUSSION

The use of eGFR in the medical routine is increasing day by day. eGFR is one of the most essential tests used to estimate renal

function (2,3). The fact that eGFR can be easily calculated from the serum creatinine level without the need for 24 h urine collection for GFR provides convenience for clinicians and patients. Easy and fast

reporting of eGFR makes it easy to diagnose kidney disease (17).

When all stages were evaluated together, it was determined that CKD-EPI eGFR tended to show GFR higher than MDRD eGFR (Figures 3, 4a, and 4b). Since it has been reported in the literature that MDRD eGFR gives lower results at > 60 ml/min/1.73 m² GFR levels (18), NKDEP recommends reporting MDRD eGFR results as >60 mL/min/1.73 m²(19). The MDRD eGFR formula has historically been derived from studies conducted on patients with CKD. CKD-EPI eGFR was obtained from general population studies, and it is reported that it is more suitable for use in general medicine except for renal failure, i.e. in nephrology clinics (20). The data of our study support the literature knowledge that the MDRD formula tends to show patients at lower eGFR levels than they are (4).

In our study, it was determined that the CKD-EPI eGFR values were higher on average by 4.4%, and the difference% exceeded the limits of -10.9%-19.7%, which was 95% CI, in some categories, especially in G1 and G5 (Figure 3). These findings show that apart from the systematic difference between the two eGFR results, there are also differences due to random scattering. Except for the extreme eGFR values in G 1, where serum creatinine values are low, our findings that MDRD results are lower than CKD-EPI, support the literature (13,20).

When the Bland-Altman difference graph is examined carefully; unlike the general trace, it is seen that differences% decrease partially before eGFR ~ 80 ml/min/m², increase between ~ 80 -115 ml/min/m² and decrease trend again after ~ 115 ml/min/m² (Figures 3, 4a and 4b). So, what is the meaning of this geometric image that first opens and then contracts like a rhombus? In the CKD-EPI formula, serum creatinine values of 0.7 mg/dL in women and 0.9 mg/dL in men are the cut-off points for the use of two different formulas. That is, two different equations are used for serum creatinine results below and above these limits to calculate CKD-EPI eGFR. For example, different CKD-EPI

formulas are used for creatinine levels of 0.70 and 0.71 in women, and 0.90 and 0.91 mg/dL in men. As obviously seen in females (Fig 4a), this mismatch, which corresponds to the G1-G2 transition boundaries, suggests that the difference between the two eGFRs is in a sense due to normalization at these cut points in the CKD-EPI. This indicates that the difference between the two eGFRs may arise not only from the derivation of formulas from the kidney failure or general population for which they were determined but also from the mathematical modeling of the equations.

Although there is a strong correlation between the two eGFRs throughout the whole range ($r=0.949$), it was found lower than the value of $r=0.975$, which indicates the strong fit suggested by CLSI (Table 5). When the regression analysis is evaluated separately for each phase, it is seen that the deviation from the line of identity, that is, the deviation from slope 1, is mostly in G1 and G2. Likewise, it is also seen from the higher residual standard deviations, which is the indicator of scattering around the regression line, where the discordance is most in G1 and G2 (Table 3). When the category transition limits are taken as medical decision limits and the differences% between the two methods are calculated at these levels, the highest difference% was determined at the G1-G2 transition border and was 9.8%. This difference% is slightly higher than the total allowable error (TEa) of 8.87% for serum creatinine (21).

When we look at the distributions in all stages for both GFRs, and Box-Plot plots; it is seen that in eGFR >145 values, MDRD has more extreme values and gives higher results (Figure 2). These findings suggest that MDRD produces extreme values and higher results in high GFR or conversely at low serum creatinine levels. These findings are consistent with studies in the literature reporting that the MDRD eGFR should not be used because of its extreme values, scattering, and higher results in adults with a low serum creatinine value, in children with a low reference range of serum creatinine, and

in individuals with low muscle mass, such as in individuals amputees (19).

The main difference between the MDRD and CKD-EPI eGFR equations is that both equations are calculated from regressions from different populations. The MDRD equation is the regressions obtained from patients with CKD, and the CKD EPI equation is obtained from the general populations (11,14,20). Therefore, it is not surprising that both formulas yield different results in different clinical diagnosis groups. In our study, it was determined that the lowest agreement and correlation between the two equations were in gynecological and obstetric diseases (Table 6). It is known that GFR increases and serum creatinine values decrease during pregnancy. As can be seen in Figures 2a and 2b, at low creatinine (high e-GFR) concentrations, inconsistency between the two methods is evident, especially due to scattering and extreme values in MDRD e-GFR. Therefore, it is thought that the reason for the lowest agreement between both equations in gynecological and obstetric diseases may be due to these scattering in MDRD eGFR results.

CONCLUSION

- There was a total of 15.6% categorical discordance between both eGFR grades, the most being G2 and G3,

REFERENCES

1. Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitations of creatinine as a filtration marker in glomerulopathic patients. *Kidney Int.* 1985;28(5): 830–8.
2. Cystatin C: an improved estimator of glomerular filtration rate? - Document - Gale OneFile: Health and Medicine.
3. Vassalotti JA, Stevens LA, Levey AS. Testing for chronic kidney disease: a position statement from the National Kidney Foundation. *Am J Kidney Dis.* 2007 Aug;50(2):169–80.
4. Stevens LA, Coresh J, Greene T, Levey AS. Assessing Kidney Function — Measured and Estimated Glomerular Filtration Rate. 2006 Jun 8;354(23):2473–83.
5. Perrone RD, Steinman TI, Beck GJ, Skibinski CI, Royal HD, Lawlor M, et al. Utility of radioisotopic filtration markers in chronic renal insufficiency: simultaneous comparison of 125I-iothalamate, 169Yb-DTPA, 99mTc-DTPA, and inulin. The Modification of Diet in Renal Disease Study. *Am J Kidney Dis.* 1990;16(3):224–35.

- MDRD shows patients in a lower CKD stage than CKD-EPI,
- The difference% between formulas is higher in G1 and G2,
- Although the systematic difference between the two methods is 9.8%, a total of 15.6% categorical discordance may cause problems in patient follow-up. In addition, considering the extremely high and scattered results of MDRD at eGFR> 140 ml/min/1.73 m², it indicates that the use of MDRD eGFR is not appropriate in individuals with low creatinine levels and in the healthy population.

Conflict of interest

All authors declare that: (i) no support, no financial or otherwise, has been received from any organization that may have an interest in the submitted work; and (ii) there are no other relationships or activities that could appear to have influenced the submitted work.

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6. Levey AS, Greene T, Schluchter MD, Cleary PA, Teschan PE, Lorenz RA, et al. Glomerular Filtration Rate Measurements in Clinical Trials. *J Am Soc Nephrol*. 1993 Nov;4(5):1159.
7. Stevens LA, Levey AS. Measured GFR as a confirmatory test for estimated GFR. *J Am Soc Nephrol*. 2009 Nov;20(11):2305–13.
8. Goldberg TH, Finkelstein MS. Difficulties in Estimating Glomerular Filtration Rate in the Elderly. *Arch Intern Med*. 1987 Aug 1;147(8):1430–3.
9. Myers GL, Miller WG, Coresh J, Fleming J, Greenberg N, Greene T, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem*. 2006 Jan;52(1):5–18.
10. Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem*. 2007 Apr;53(4):766–72.
11. 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. *Am J Kidney Dis*. 2010 Apr;55(4):622.
12. Becker BN, Vassalotti JA. A software upgrade: CKD testing in 2010. *Am J Kidney Dis*. 2010 Jan;55(1):8–10.
13. Levey AS, Coresh J, Bolton K, Culleton B, Harvey KS, Ikin TA, et al. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39.
14. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999 Mar 16;130(6):461–70.
15. Rule AD, Teo BW. GFR Estimation in Japan and China: What Accounts for the Difference? *Am J Kidney Dis*. 2009;53(6):932–5.
16. Eknoyan G, Lameire N, Kasiske BL, et al. Hryniewicz E. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. KDIGO. 2012.
17. Kagoma YK, Weir MA, Iansavichus A V., Hemmelgarn BR, Akbari A, Patel UD, et al. Impact of estimated GFR reporting on patients, clinicians, and health-care systems: a systematic review. *Am J Kidney Dis*. 2011 Apr;57(4):592–601.
18. Xie P, Huang JM, Lin HY, Wu WJ, Pan LP. CDK-EPI equation may be the most proper formula based on creatinine in determining glomerular filtration rate in Chinese patients with chronic kidney disease. *Int Urol Nephrol*. 2013 Aug;45(4):1057–64.
19. Madero M, Sarnak MJ. Creatinine-based formulae for estimating glomerular filtration rate: Is it time to change to chronic kidney disease epidemiology collaboration equation? *Curr Opin Nephrol Hypertens*. 2011 Nov;20(6):622–30.
20. Levey AS, Inker LA, Coresh J. GFR estimation: from physiology to public health. *Am J Kidney Dis*. 2014;63(5):820–34.
21. Desirable Biological Variation Database specifications - Westgard. [cited 2022 Jul 24]. Available from: <https://www.westgard.com/biodatabase1.htm>