Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2022;47(4):1523-1530
DOI: 10.17826/cumj.1122223

ARAŞTIRMA / RESEARCH

New analysis of the comparative diagnostic performances of five different eGFR equations: The revised 2021 CKD-EPI eGFR, and the four older equations

Beş farklı eGFR denkleminin karşılaştırmalı teşhis performanslarının yeni analizi: Gözden geçirilmiş 2021 CKD-EPI ve dört eski denklem

Süheyl Uçucu[1], Erdinç Serin[2]

[1]Department of Medical Biochemistry, Mugla Public Health Laboratory, Muğla, Turkey
[2]Department of Medical Biochemistry, Şişli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey

Cukurova Medical Journal 2022;47(4):1523-1530

Abstract

Purpose: In 2021, the CKD-EPI-creatinine and CKD-EPI-creatinine-cystatin-C combined equations were revised again by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and the National Institute of Diabetes & Digestive and Kidney Diseases (NIDDK) and it was reported that its accuracy was increased. The main object of this study is to compare the diagnostic accuracy and performance of 2009 CKD-EPI eGFRcr, 2012 CKD-EPI eGFRCysC, 2012 CKD-EPI eGFRcr-CysC, MDRD, and revised 2021 CKD-EPI to provide a better estimation.

Materials and Methods: The study design was prospective. The sample consisted of 111 CKD patients and 35 healthy individuals who applied to the nephrology clinic. All participants were evaluated by a nephrologist. The participants were divided into study groups according to their KDIGO classification. Five variables were used: age, race, gender, serum creatinine, and serum cystatin-C.

Results: 2012 CKD-EPI eGFR cystatin-C out performed existing equations in terms of accuracy, specificity, and sensitivity (AUC:0.988). Furthermore, when both creatinine and cystatin-C are included in an equation, it consistently improves diagnostic values over formulas containing only creatinine (2009CKD-EPI eGFRcr AUC:0.953, 2012CKD-EPI eGFRcr-CysC AUC: 0.985, 2021CKD-EPI eGFRcr AUC:0.954, MDRD AUC: 0.953, 2021CKD-EPI eGFRcr-CysC AUC: 0.985).

Conclusion: The new formula has not been confirmed to be superior to other equations in its ability to estimate eGFR values, particularly at higher levels of chronic kidney disease. When compared with existing equations, 2012 CKD-EPI eGFRCysC had higher specificity and

Öz

Amaç: 2021 yılında Kronik Böbrek Hastalığı Epidemiyoloji İşbirliği (CKD-EPI) ve Ulusal Diyabet&Sindirim ve Böbrek Hastalıkları Enstitüsü (NIDDK) tarafından CKD-EPI-kreatinin ve CKD-EPI-kreatinin-sistatin-C kombine formülü yeniden revize edilmiş ve doğruluğunun arttırıldığı bildirilmiştir. Bu çalışmanın temel amacı daha iyi bir öngörü sağlamak için 2009 CKD-EPI eGFRcr, 2012 CKD-EPI eGFRCysC, 2012 CKD-EPI eGFRcr-CysC, MDRD ve revize edilmiş 2021 CKD-EPI'nin tanısal doğruluk ve performansını karşılaştırmaktır.

Gereç ve Yöntem: Çalışma tasarımı prospektifti. Örneklem, nefroloji kliniğine başvuran 111 KBH hastası ve 35 sağlıklı bireyden oluşmaktaydı. Tüm katılımcılar bir nefrolog tarafından değerlendirildi. Katılımcılar KDIGO sınıflandırmalarına göre çalışma gruplarına ayrılmıştır. Yaş, ırk, cinsiyet, serum kreatinin ve serum sistatin-C olmak üzere beş değişken kullanılmıştır.

Bulgular: 2012 CKD-EPI eGFR sistatin-C, doğruluk, özgüllük ve duyarlılık açısından mevcut denklemlerden daha iyi performans gösterdi (AUC:0.988). Revize edilmiş 2021 CKD-EPI denklemleriyle karşılaştırıldığında, eGFR sistatin-c, üç performans metriğinin hepsinde sürekli olarak daha iyi performans gösterdi. Ayrıca, bir denkleme hem kreatinin hem de sistatin-C dahil edildiğinde, yalnızca kreatinin içeren formüllere göre tanısal değerleri tutarlı bir şekilde iyileştirir (2009CKD-EPI eGFRcr AUC:0.953, 2012CKD-EPI eGFRcr-CysC AUC: 0.985, 2021CKD-EPI eGFRcr AUC:0.954, MDRD AUC: 0.953, 2021CKD-EPI eGFRcr-CysC AUC: 0.985).

Sonuç: Yeni formülün, özellikle daha yüksek kronik böbrek hastalığı seviyelerinde eGFR değerlerini öngörme

Yazışma Adresi/Address for Correspondence: Dr. Süheyl Uçucu, Department of Medical Biochemistry, Mugla Public Health Laboratory, Muğla, Turkey E-mail: suheyllucucu@gmail.com
Geliş tarihi/Received: 27.05.2022 Kabul tarihi/Accepted: 29.09.2022

sensitivity. Combined formulas containing both blood tests had higher diagnostic values than equations containing only creatinine. Our results can help inform which equations to use for better estimation in renal function screening.

Keywords:. eGFR, Ckd-Epi, renal disease, cystatin C, creatinine

yeteneği bakımından diğer denklemlerden üstün olduğu doğrulanmamıştır. Mevcut denklemler karşılaştırıldığında 2012 CKD-EPI eGFRCysC daha yüksek özgüllüğe ve duyarlılığa sahipti. Her iki kan testini içeren birleşik formüller, sadece kreatinin içeren denklemlerden daha yüksek tanısal değerlerine sahipti. Sonuçlarımız, böbrek fonksiyon taramasında daha iyi tahmin için hangi denklemlerin kullanılacağı konusunda bilgi vermede yardımcı olabilir.

Anahtar kelimeler: Glomerular filtrasyon hızı, Ckd-Epi, kronik böbrek hastalığı, sistatin C, kreatinin

INTRODUCTION

It is estimated that the number of people suffering from kidney disease will increase enormously and it will become one of the leading causes of death by 2040. Global chronic kidney disease (CKD) is a major cause of death. Despite many studies in this field, the prevalence of CKD continues to increase in many developed countries, and one of the important problems is early diagnosis and preventing the progression of kidney disease[1, 3]. Although it requires a multifaceted approach, one of the most important factors is the accurate measurement of kidney function[4]. One of the most important factors in diagnosing, staging, and managing CKD is eGFR, which means estimated glomerular filtration rate. eGFR is an expression explaining how quickly our kidneys filter the blood. eGFR estimates the functional capacity of our kidneys and is used to test kidney damage[4,5]. However, there is not always a consensus on this calculation method.

Currently, creatinine is the most widely used indicator to determine eGFR. It is practical and cost-effective. This method has become common for measuring kidney health worldwide, however it has some drawbacks[5, 6]. Since creatinine is produced by muscle activity, it should not be used as the sole basis for estimating eGFR. It should be taken into account that the relationship and interaction between variables such as muscle mass, diet, age, race, gender, and creatinine may affect the clinical decision and lead to errors[4,5,7]. Alternatively, it has been well documented in studies that the diagnostic accuracy of cystatin-c is highly correlated with inulin and iothalamate and is higher than that of creatinine[5,7]. However, if cystatin-c testing cannot be performed due to cost or other factors, eGFR calculation should be made with the most accurate and precise equation. In this way, the bias of pathophysiological factors such as muscle, race, gender, and diet, which affect creatinine, is reduced[5].

The most common method for measuring eGFR worldwide is to calculate eGFR by the CKD-EPI [Chronic Kidney Disease Epidemiology Collaboration] and MDRD [Modification of Diet in Renal Disease] equations, which are based on the serum creatinine measurement (Table 4)[8-11]. In 2021, the CKD-EPI-Creatinine-Cystatin-C equation was revised again and it was reported that its accuracy increased by the Chronic Kidney Disease Epidemiology Collaboration and the National Institute of Diabetes & Digestive and Kidney Diseases (NIDDK)[11]. In the study published by the researchers, the data of 13.000 white and black patients at different stages were used and this data set was used during the development of the CKD-EPI equation in a population of patients with varying degrees of renal impairment. In the new equation, racial difference is especially emphasized[12].

The main object of this study is to compare the diagnostic accuracy and performance of the current 2009 CKD-EPI eGFRcr, 2012 CKD-EPI eGFRcr-CysC, 2012 CKD-EPI eGFRCysC, 2021 CKD-EPI eGFRcr, MDRD and revised 2021 CKD-EPI eGFRcr-CysC equations to provide guidance on their better utilization.

MATERIALS AND METHODS

The study design was prospective and the study duration was one year. 111 chronic kidney patients and 35 healthy controls were included in this study, and it was conducted under the supervision of Şişli Hamidiye Etfal Training and Research Hospital Nephrology Clinic. Of the 146 participants examined in this study, 72 (49.3%) were female and 74 (50.7%) were male.

Initially, 138 patients were examined, then 27 patients were excluded due to reasons such as dialysis, hyperthyroidism, drug use, and age. The study was conducted in accordance with the guidelines of the Helsinki Declaration. The study protocol was approved by the Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (Ethics code 774). Written informed consent was obtained from all participants.

In the Nephrology Clinic of Şişli Hamidiye Etfal Training and Research Hospital, the participants were evaluated for chronic kidney disease according to the KDIGO criteria. All participants were evaluated by a nephrologist. The participants were divided into study groups according to KDIGO classification. The study included patients over 18 years of age who did not have a kidney transplant, heart disease, thyroid dysfunction, chemotherapy, were not on dialysis (two types of renal replacement therapy), and had a creatinine level above 97 μmol/L (a marker of renal failure).

Sample

Patients with liver disease, heart failure, hypothyroidism, or hyperthyroidism, cardiac causes, inflammation, immunosuppressive therapy, organ transplantation, and peritoneal dialysis patients were excluded from the study. The control group was selected from healthy volunteers who do not have personal or family history of the disease.

Cystatin C levels were measured using a commercial kit (Siemens Systems) following the manufacturer's instructions. The intra- and inter-assay coefficients of variation were at least 4.3% and 7.1%, and at most 5.3% and 7.9%, respectively. The lower detection limit was 0.65 mg/L.

A power analysis has been performed. The sample size was calculated to be 111, predicting that the medium effect size would be statistically significant in the correlation between the calculated values.

Procedure

The blood samples were taken from both control and patient groups in BD Vacutainer tubes. The blood samples of the patient group were centrifuged at 4000 g for 10 minutes, and creatinine levels were analyzed on the same day. The samples were stored at -80 °C for subsequent Cystatin C analysis. The sera were thawed before analysis by being stored at -80°C, -20°C, 2-8°C, and room temperature, respectively.

Laboratory analysis

Cystatin C levels were measured by particle amplified immunonephelometry (Dade Behring, Germany) using the BNProSpec plasma protein analyzer with N-latex Cystatin C (ERM-DA471/IFCC-standardized) reagents. Serum creatinine levels were measured by the colorimetric-Jaffe method using original Roche reagents on the Cobas c 501 instruments (Roche Diagnostic, Germany).

Statistical analysis

Data were analyzed using the open-source statistical software Jamovi 1.6.23 (Sydney, Australia) and MedCalc 20.112 (Belgium). Descriptive statistics were given as numbers and percentages for categorical variables, and median and interquartile range (IQR) for numerical variables. The Shapiro-Wilk test was used to determine the data's conformity to the normal distribution. An independent T-test was used to evaluate the normally distributed variables. Categorical variables showed normal distribution. Since the numerical variables did not meet the normal distribution condition, two independent groups were compared by using the Mann-Whitney U test. The relationship between the numerical variables was examined by Spearman correlation analysis as they did not meet the parametric test conditions. The difference between the means of the equations was analyzed with One-Way ANOVA. For non-parametric tests, the Kruskal-Wallis H test and then Post-Hoc test were performed. To determine the difference between the groups, the multiple comparison Post-Hoc test (Dwass-Steel-Critchlow-Fligner pairwise comparisons) was used. MedCalc program was used to produce the ROC curves and the box plots. The specificity, sensitivity, and accuracy were investigated by ROC curve analysis. Differences between the two groups were considered significant at a p-value $\leq$ 0.05.

RESULTS

Table 1 shows the main demographic findings of 111 patients and 35 controls. The patients and the control group were similar in terms of gender.

Table 1. Demographic characteristics of the patient group and control group.

		Patient Group		Control Group		
		Mean±SD	**Min-Max**	**Mean±SD**	**Min-Max**	**P***
Age		62±14.4	18-88	57±14.9	20±83	0.001
		n	%	n	%	
Gender	Female	49	54.4	23	65.5	
	Male	62	55.6	12	34.5	

Min: minumum, Max: maximum, SD: standart sapma, Significant p < 0.05*

A comparison of the serum creatinine, cystatin-C, and estimated glomerular filtration rate (eGFR) levels between the patient group with diabetes and the control group revealed statistically significant differences (Table 2).

All eGFR estimates obtained by different equations were determined to be significantly different in the patient group and the control group (Figure 1, Table 2).

Table 2. Comparison of 2021 CKD-EPI eEGFRcr-cys, 2021 CKD-EPI eEGFRcr, 2009 CKD-EPI eEGFRcr, 2012 CKD-EPI eEGFRcr-cys, 2012 CKD-EPI eEGFRcys and MDRD in patient and control groups

	Patient Group		**Control Group**		***P****
	Median	IQR	Median	IQR	
Creatinine	1.45	1.29	0.72	0.12	<0.001
Cystatin C	1.91	1.45	0.90	0.14	<0.001
2009 CKD-EPI Creatinine e-GFR	45.70	37.30	93.80	19.40	0.003
2012 CKD-EPI Cystatin C e-GFR	29.90	28.40	85.69	21.10	<0.001
2012 CKD-EPI Creatinine-Cystatin C GFR	35.98	32.40	91.30	22.16	0.002
2021 CKD-EPI Creatinine e-GFR	49.00	39.20	99.00	18.70	0.004
2021 CKD-EPI Creatinin-Cystatin C eGFR	37.20	33.50	95.10	23.30	0.002
MDRD e-GFR	43.90	32.90	92.40	33.00	0.015

e-GFR: Estimated glomerular filtration rate, IQR: Interquartile range, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, MDRD: Modification of Diet in Renal Disease, P: alpha significance p< 0.05*

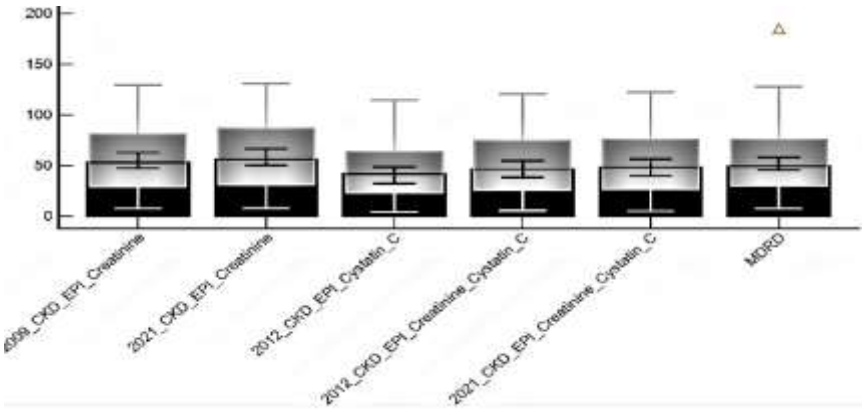

Figure 1. Intensity distribution plot in patient and control groups.

CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, MDRD: Modification of Diet in Renal Disease, Grey:Control group, Black:Patient group.

Table 3. Comparison of the difference between the One-Way ANOVA (Non-parametric) test and the mean of GFR equations in the patient and control group

Kruskal-Wallis	χ^2	df	p
2009 CKD-EPI Creatinine			
2021 CKD-EPI Creatinine			
2012 CKD-EPI Cystatin C	15.5	5	0 .008
2012 CKD-EPI Creatinine-Cystatin C			
2021 CKD-EPI Creatinine-Cystatin C MDRD			
Post-Hoc Test (Dwass-Steel-Critchlow-Fligner pairwise comparisons)			
		W	*p*
2009 CKD-EPI Creatinine 2012 CKD-EPI Creatinine-Cystatin C		-2.127	0.662
2009 CKD-EPI Creatinine 2012 CKD-EPI Cystatin C		-3.982	0.055
2009 CKD-EPI Creatinine 2021 CKD-EPI Creatinine		1.225	0.955
2009 CKD-EPI Creatinine 2021 CKD-EPI Creatinine-Cystatin C		-1.584	0.873
2009 CKD-EPI Creatinine MDRD		-0.791	0.994
2012 CKD-EPI Creatinine-Cystatin C 2012 CKD-EPI Cystatin C		-1.836	0.786
2012 CKD-EPI Creatinine-Cystatin C 2021 CKD-EPI Creatinine		3.123	0.234
2012 CKD-EPI Creatinine-Cystatin C 2021 CKD-EPI Creatinine-Cystatin C		0.651	0.997
2012 CKD-EPI Creatinine-Cystatin C MDRD		1.479	0.902
2012 CKD-EPI Cystatin C 2021 CKD-EPI Creatinine		4.996	0.006
2012 CKD-EPI Cystatin C 2021 CKD-EPI Creatinine-Cystatin C		2.312	0.576
2012 CKD-EPI Cystatin C MDRD		3.277	0.187
2021 CKD-EPI Creatinine 2021 CKD-EPI Creatinine-Cystatin C		-2.601	0.441
2021 CKD-EPI Creatinine MDRD		-1.866	0.775
2021 CKD-EPI Creatinine-Cystatin C MDRD		0.926	0.987

Note. X2: Asymptotic significance, df: Degrees of freedom, w: P: Alpha significance p < 0.05*

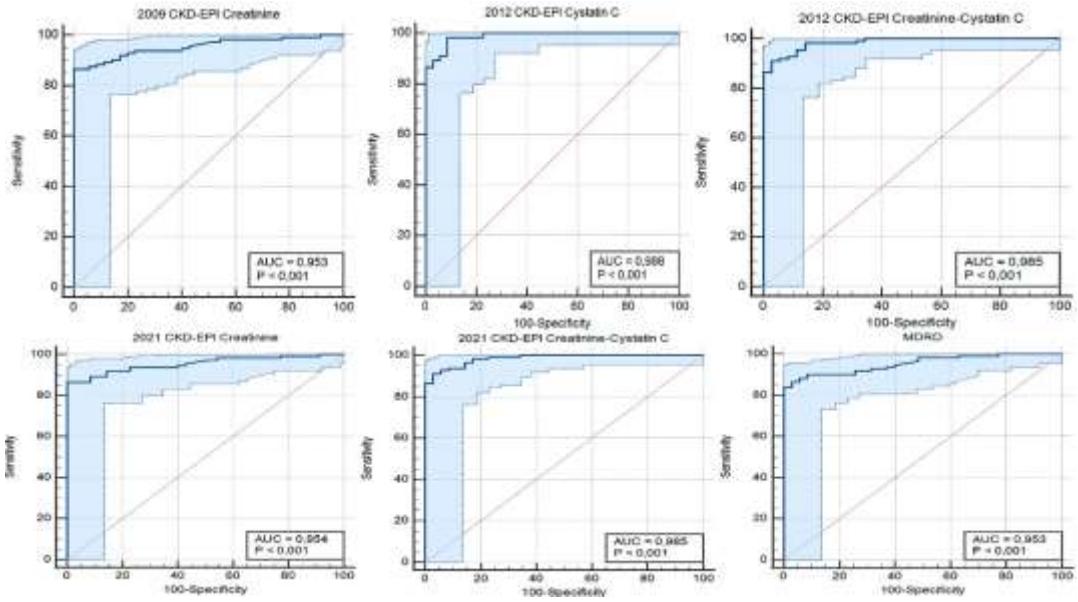

Figure 2. Sensitivity, specificity, and area under ROC curves for equation diagnostic value estimation.

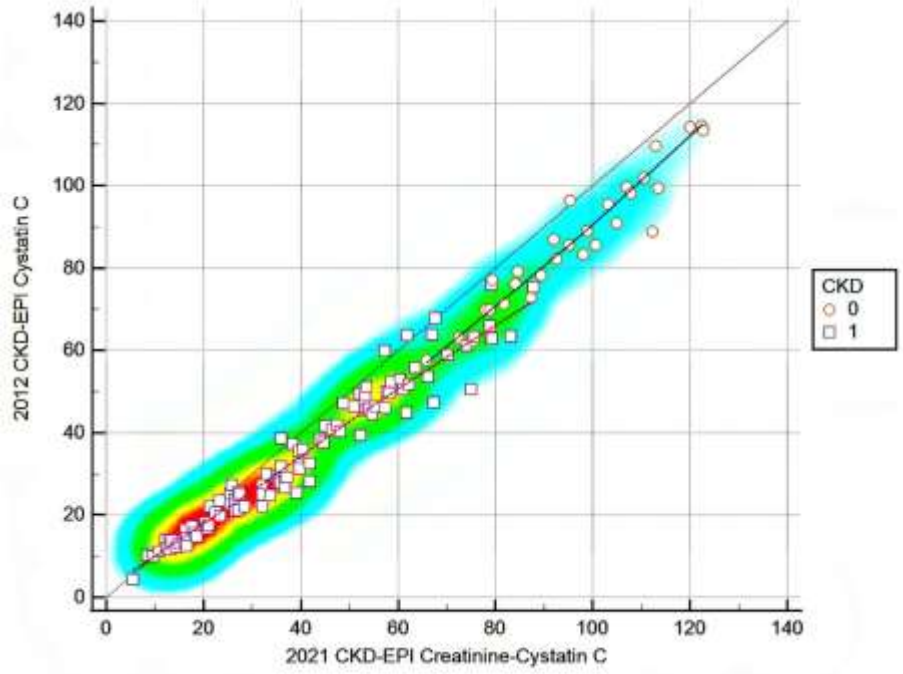

Figure 3. Heatmap of spearman correlation coefficients between 2021 CKD-EPI eEGFR Creatinine-Cystatin C and 2012 CKD-EPI eEGFR Cystatin C Levels.

Table 4. Comparison of the different CKD-EPI and MDRD GFR equations

Equations
CKD-EPI Creatinine Equation (2009)
GFR = 141 × min(Scr/ϰ, 1)α × max(Scr/ϰ, 1)-1.209 × 0.993Age × 1.018 [if female] _ 1.159 [if black]
CKD-EPI Cystatin C Equation (2012)
eGFR =133 x min(Scys/0.8, 1)-0.499 x max (Scys/0.8, 1)-1.328 x 0.996Age x 0.932 [if female]
CKD-EPI Creatinine-Cystatin Equation (2012)
eGFR =135 × min(Scr/ϰ, 1)α × max(Scr/ϰ, 1)−0.601 × min(Scys/0.8, 1)−0.375 × max(Scys/0.8, 1)−0.711 × 0.995Age [× 0.969 if female] [× 1.08 if black]
CKD-EPI Creatinine Equation (2021)
eGFRcr = 142 x min(Scr/ϰ, 1)α x max(Scr/ϰ, 1)-1.200 x 0.9938Age x 1.012 [if female]
CKD-EPI Creatinine-Cystatin Equation (2021)
eGFRcr-cys = 135 x min(Scr/ϰ, 1)α x max(Scr/ϰ, 1)-0.544 x min(Scys/0.8, 1)-0.323 x max(Scys/0.8, 1)-0.778 x 0.9961Age x 0.963 [if female]
MDRD Study Equation
eGFR = 175 x (SCr)-1.154 x (age)-0.203 x 0.742 [if female] x 1.212 [if Black]

Note. e-GFR: Estimated glomerular filtration rate, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, MDRD: Modification of Diet in Renal Disease , Scr:Serum creatinine, Min: minimum, Max: maximum, Scys: Serum cystatin C, ϰ: kappa factor, α: alfa factor.

In the Post-Hoc (Pairwise comparisons) analysis, a statistically significant difference was found between the 2012 CKD-EPI cystatin C and 2021 CKD-EPI creatinine equations (w: 4.996, p: 0.006) (Table 3).

2012 CKD-EPI eGFR cystatin-C outperformed existing equations in terms of accuracy, specificity, and sensitivity (Figure 2). Compared to the revised 2021 CKD-EPI equations, the performance of eGFR cystatin-C was consistently better on all three performance metrics. Furthermore, when both creatinine and cystatin-C are included in an equation, it consistently improves diagnostic values over formulas containing only creatinine (Figure 2-3).

DISCUSSION

In 2021, the CKD-EPI estimation equation was revised again by KDIGO and NIDDK for estimating the estimated glomerular filtration rate (eGFR), and it was reported that its diagnostic accuracy was increased [12]. In the study published by the researchers, the data of 13.000 white and black patients at different stages were used and this data set was used during the development of the CKD-EPI equation in a population of patients with varying degrees of renal impairment. As a result, it was stated that the new 2021 CKD-EPI eGFRcr-CysC equation outperforms the existing single-parameter equation. They suggested that the new algorithm reduces the margin of error in the black race when compared to the previous equations and that the new combined formula should be used in the general population[12]. There are different opinions in recent studies[13-16]. In the study of Eneanya et al., it was reported that race is a social structure, not a biological one, as in the 2021 CKD-EPI equation, and this variable should not be used in the estimation of renal function[14]. In the study of Hsu et al., creatinine and cystatin values were used without using the race feature in the MDRD equation, and this has a similar approach to the 2021 CKD-EPI. While it was stated that some deviations in creatinine can be related to race and genotype, it was stated that cystatin-c was not affected by race and it should be used. Different results were obtained between creatinine and cystatin depending on the renal staging, race, and age group in the population used. However, the diagnostic accuracy rates in the current eGFR estimation equations vary depending on the stage and especially the age group[15].

Our results in the study did not confirm that the new formula is superior to other equations in terms of its ability to estimate eGFR values, especially at higher levels of chronic kidney disease. However, the 2012 CKD-EPI eGFR cystatin-c was found to have higher accuracy, specificity, and sensitivity compared to the existing equations (Figure 2). When compared to the revised 2021 CKD-EPI equations, it is consistently better on all three performance indicators (Figure 2). We found that combined formulas containing both blood tests had higher diagnostic values than equations containing only creatinine. Therefore, the combined formulas of 2012 CKD-EPI-creatinine-cystatin-C and 2021 CKD-EPI-creatinine-cystatin-c can be considered as an improvement over existing creatinine equations. This also indirectly sheds light on the role of cystatin-c in improving eGFR estimation. The possible reason for the higher diagnostic value of cystatin-c may be that it is less affected by factors such as muscle mass, age, and diet. This is especially important in the accurate determination of renal function in the elderly[12-13]. In our previous studies and the literature, it has been shown that the decrease in renal function can be detected earlier and faster using cystatin-c-based eGFR estimates in the elderly than using creatinine-based estimates[15-18].

Although methods containing creatinine have become common for measuring kidney health worldwide, they have several shortcomings. Since creatinine is produced by muscle activity, it can be misleading to use it as the sole basis for estimating eGFR. It should be taken into account that the relationship and interaction between variables such as muscle mass, diet, age, gender, and creatinine may affect the clinical decision and lead to errors[5, 6]. In addition, various drugs used (trimethoprim, cimetidine, etc.) cause an increase in creatinine in the blood by blocking creatinine secretion in distal tubules, although it indirectly causes a low eGFR, the renal function does not change[19].

The search for a better equation continues around the world and consensus is sought. The results are in line with what we have seen in practice over the past few years. Our results can help provide information on which equations can be used for better estimation of eGFR for renal function screening[20].

This study has some limitations. The sample size in this study is small. The average age of patients is around 60 years and most of them are in the advanced stage. Due to the small number of patients, features such as age, stage, and gender could not be evaluated by distinguishing them.

In conclusion, the new formula has not been confirmed to be superior to other equations in terms of its ability to estimate eGFR values, particularly at higher levels of chronic kidney disease. 2012 CKD-EPI eGFR cystatin-c had higher accuracy, specificity, and sensitivity compared to the existing equations. Combined formulas containing both blood tests had higher diagnostic values than equations containing only creatinine. Our results can help provide information on which equations can be used for better estimation in renal function screening. Future studies need to evaluate the performance of the equations in larger populations by adding more features and comparing them with exogenous standards such as inulin and iothalamate.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SU, ES; Veri toplama: SU; Veri analizi ve yorumlama: SU; Yazı taslağı: SU; İçeriğin eleştirel incelenmesi: SU; Son onay ve sorumluluk: SU, ES; Teknik ve malzeme desteği: SU, ES; Süpervizyon: SU; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Istanbul Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan 18.04.2017 tarih ve 774 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : SU, ES; Data acquisition: SU; Data analysis and interpretation: SU; Drafting manuscript: SU; Critical revision of manuscript: SU; Final approval and accountability: SU, ES; Technical or material support: SU, ES; Supervision: SU; Securing funding (if available): n/a.
Ethical Approval: For this study, ethical approval was obtained from the Clinical Research Ethics Committee of Istanbul Şişli Hamidiye Etfal Training and Research Hospital with the decision dated 18.04.2017 and numbered 774.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M et al. Bikbov B, Purcell CA, Levey AS, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of disease study 2017. Lancet. 2020;395:709-33.
2. Kovesdy, Csaba P. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl. 2022;12:7-11.
3. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. et al. A single number for advocacy and communication worldwide more than 850 million individuals have kidney diseases. Nephrol Dial Transplant. 2019;34:1803-5.
4. Lamb EJ, Tomson CR, Roderick PJ. Estimating kidney function in adults using formulae. Ann Clin Biochem. 2005;42:321-45.
5. Lopes MB, Araújo LQ, Passos MT, Nishida SK, Kirsztajn GM, Cendoroglo MS et al. Estimation of glomerular filtration rate from serum creatinine and cystatin C in octogenarians and nonagenarians. BMC Nephrol. 2013;14:1-9.
6. Güner İ. Biochemistry of Acute and Chronic Renal Failure. Sisli Etfal Hastan Tip Bul.12:279-88.
7. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function—measured and estimated glomerular filtration rate. N Engl J Med. 2006;354:2473-83.
8. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis. 2002;40:221-6.
9. Wasén E, Isoaho R, Mattila K, Vahlberg T, Kivelä SL, Irjala K. Serum cystatin C in the aged: relationships with health status. Am J Kidney Dis. 2003;42:36-43.
10. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro III AF, Feldman HI et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-12.
11. Stevens LA, Coresh J, Schmid CH, Feldman HI, Froissart M, Kusek J et al. Estimating EGFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. Am J Kidney Dis. 2008;51:395-406.
12. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y et al. New creatinine-and cystatin C–based equations to estimate eGFR without race. N Engl J Med. 2021;385:1737-49.
13. Diao JA, Wu GJ, Taylor HA, Tucker JK, Powe NR, Kohane IS et al. Clinical implications of removing race from estimates of kidney function. JAMA. 2021;325:184-6.
14. Eneanya ND, Yang W, Reese PP. Reconsidering the consequences of using race to estimate kidney function. JAMA. 2019;322:113-4.
15. Hsu CY, Yang W, Parikh RV, Anderson AH, Chen TK, Cohen DL et al. Race, genetic ancestry, and estimating kidney function in CKD. N Engl J Med. 2021;385:1750-60.
16. Amutah C, Greenidge K, Mante A, Munyikwa M, Surya SL, Higginbotham E et al. Misrepresenting race the role of medical schools in propagating physician bias. N Engl J Med. 2021;384:872-8.
17. Shlipak MG, Katz R, Kestenbaum B, Fried LF, Newman AB, Siscovick DS et al. Rate of kidney function decline in older adults: a comparison using creatinine and cystatin C. Am J Nephrol. 2009;30:171-8.
18. Uçucu S, Ayan D, Serin E. Comparison of the diagnostic accuracy of CKD-EPI cystatin-C, CKD-EPI creatinine and 24-hour creatinine clearance for estimating EGFR: a preliminary study. Cukurova Med J. 2020;46:1-10.
19. Mouton R, Holder K. Laboratory tests of renal function. Intensive Care Med. 2006;7:240-3.
20. Diao JA, Inker LA, Levey AS, Tighiouart H, Powe NR, Manrai AK. In search of a better equation performance and equity in estimates of kidney function. N Engl J Med. 2021;384:396-9.

Çukurova Üniversitesi Tıp Fakültesi Dergisi
Cukurova Medical Journal