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ARAŞTIRMA / RESEARCH

Comparison of the diagnostic accuracy of CKD-EPI cystatin-C, CKD-EPI creatinine and 24-hour creatinine clearance for estimating GFR: a preliminary study

GFR tahmininde CKD-EPI sistatin-C, CKD-EPI kreatinin ve 24 saatlik kreatinin klirensinin tanısal doğruluğunun karşılaştırılması: bir ön çalışma

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Abstract

Purpose: Serum cystatin C level is a specific marker to estimate the glomerular filtration rate (GFR). Due to this specificity, we assume that GFR estimations based on cystatin C have higher diagnostic performances than GFR estimations using other biomarkers. In this study, we aimed to compared the diagnostic performances of CKD-EPI cystatin C equation, CKD-EPI creatinine equation and 24-hour creatinine clearance to estimate GFR.

Materials and Methods: A total of 130 participants who consisting of 101 acute and chronic renal disease patients and 29 healthy volunteers, who applied to the Nephrology Clinic, have been included in our study. Their urine creatinine levels and serum creatinine levels were measured by the colorimetric-Jaffe method, and cystatin C was by the nephelometric method.

Results: There was a statistically significant relationship between CKD-EPI cystatin C, between CKD-EPI creatinine and standard creatinine clearance. The Area Under the Receiver Operating Characteristics curve (AUROC) was found to be 1, 0.995, and 0.954 respectively.

Conclusion: According to the results, we think that serum cystatin C levels will present earlier findings in GFR decrease and may be a more effective marker than serum creatinine and standard creatinine clearance in the early period.

Keywords: Cystatin C, CKD-EPI, Glomerular Filtration Rate, creatinine, kidney failure

Öz

Amaç: Serum sistatin C düzeyi, glomerüler filtrasyon hızını (GFH) tahmin etmek için spesifik bir belirteçtir. Bu özgüllük nedeniyle, sistatin C'ye dayalı GFH tahminlerinin, diğer biyobelirteçleri kullanan GFH tahminlerinden daha yüksek tanısal performanslara sahip olduğunu varsayıyoruz. Bu çalışmada, GFH'yi tahmin etmek için CKD-EPI sistatin C denklemi, CKD-EPI kreatinin denklemi ve 24 saatlik kreatinin klirensinin tanısal performanslarını karşılaştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamıza Nefroloji Kliniğine başvuran akut ve kronik böbrek hastalarından oluşan 101 hasta ve 29 sağlıklı gönüllüden oluşan toplam 130 katılımcıdâhil edildi. İdrar kreatinin düzeyleri ve serum kreatinin düzeyleri kolorimetrik-Jaffe yöntemi ile ölçülürken, sistatin C nefelometrik yöntemle ölçüldü.

Bulgular: CKD-EPI sistatin C, CKD-EPI kreatinin ve standart kreatinin klirensi arasında istatistiksel olarak anlamlı bir ilişki vardı. Alıcı Çalışma Karakteristikleri eğrisinin (AUROC) Altındaki Alan sırasıyla 1, 0.995 ve 0.954 olarak bulundu.

Sonuç: Elde edilen sonuçlara göre, serum sistatin C düzeylerinin GFH azalmasında daha erken bulgular sunacağı ve erken dönemde serum kreatinin ve standart kreatinin klirensinden daha etkili bir belirteç olabileceği kanısındayız.

Anahtar kelimeler: Sistatin C, CKD-EPI, Glomerüler Filtrasyon Hızı, kreatinin, böbrek yetmezliği

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INTRODUCTION

Today, there are more than 850 million kidney patients worldwide. Also, kidney disease is predicted to be the fifth most common cause of death worldwide in the future[1]. The frequency of kidney failure (15.7%) is increasing dramatically day by day in Turkey[2]. Due to the asymptomatic nature of kidney failure, the accurate determination of glomerular filtration rate (GFR) has a vital role that may shape detecting the disease at an early stage, course of progression, and management of specific complications[3,4]. GFR is considered to be the most specific and most sensitive indicator for measuring kidney functional level and determining the stage of kidney disease. GFR is also a good marker for the diagnosis, evaluation, staging, and monitoring of chronic kidney disease (CKD)[2,5]. Calculation of GFR in a classical way is difficult due to challenges in 24-hour urine collection. Apart from being impossible to apply to infants and children, it is also not a suitable method for diseases and emergencies which often require GFR monitoring. Therefore, it was calculated by equations consisting of serum creatinine concentration and some demographic information that could be easily accessed[4,6]. The equation frequently used today, also recommended by Kidney Disease Improving Global Outcome (KDIGO) and adopted worldwide, is the Chronic Kidney Disease Epidemiology Collaboration, i.e. CKD-EPI[4,7].

The GFR value calculated with this formula is recommended to be given by each laboratory along with serum creatinine levels in addition to the patient outcome report[8]. However, the accuracy of this GFR estimate is limited as the serum creatinine concentration is affected by some pathophysiological factors as well as by creatinine filtration[7,9,10]. Thus, some alternative biochemical parameters were searched for GFR. One of them is cystatin C, which is low molecular weight (13 kDa) basic protein that is produced at a constant rate in almost all nucleated cells in the body. Therefore, cystatin C is not affected by variables such as serum level, muscle mass, age, race, and gender[4,11].

Cystatin C has been reported superior to creatinine as a GFR marker in many studies. However, there are contradictory results among some previous studies on this subject. Although Yong et al., Jacobs et al., Yang SK et al., Kwon et al. suggest that cystatin C is a marker of kidney function superior to creatinine, Bevc et al., Eriksen et al., Royakkers et al. concluded that cystatin C is not superior[12-17].

In the light of all this information, our study aims to investigate the relationship compared the diagnostic accuracies, in-between correlations as well as performances of standard 24-hour creatinine clearance calculation and KDIGO 2012 guideline-recommended CKD-EPI cystatin C and CKD-EPI creatinine equations to estimate GFR[4,8].

MATERIALS AND METHODS

Within the scope of this prospective study, a study group consisting of 101 individuals who have applied to the nephrology clinic of our hospital and have been diagnosed with acute or chronic renal disease according to KDIGO criteria (57 male (56.4%), 44 female (43.6%) and 29 healthy volunteers (6 male (20%), 23 female (80%)) who applied to Şişli Hamidiye Etfal Training and Research Hospital Nephrology Clinic between dates 01.01.2017 - 31.03.2017, were included in the study. Blood samples taken from the patients were studied at Şişli Hamidiye Etfal Training and Research Hospital Medical Biochemistry Laboratory. Ethical approval was obtained from Şişli Hamidiye Etfal Training and Research Hospital Local Ethics Committee on 18.04.2017 with the document numbered 774 for the study. The study was carried out under the Helsinki Declaration principles.

Sample

Acute or chronic renal disease patients who havecreatinine values above 97 μmol/L are over 18 years old, have not undergone kidney transplantation and don't received replacement (hemodialysis or peritonealdialysis), were informed about the 24-hour urine collection and collected 24-hour urinewere selected.Patients who have organ failure (liver, heart failure),have thyroid dysfunction, such as hyperthyroidism and hypothyroidism are under 18 years old, have undergone kidney transplantation and received hemodialysis or peritoneal dialysis treatment, have undergone cardiac surgery were excluded from the study.The control group was selected from completely healthy volunteers who did not have any personal and familial disease history.

Procedure

Blood samples were collected in Vacutainer tubes (

Becton Dickinson) with gel seperator tubes, following a 10-12 hours fasting process in both contol and patients groups. Blood samples were centrifugated at 4000 g for 10 minutes. Creatinine levels were analyzed on same day and stored at -80 °C for analyzing cystatine C. Blood samples were stored for a while at -20°C and 2-8 °C before day of analysis, respectively.

Laboratory analysis

Serum creatinine levels were measured spectrophotometrically using original Roche reagents on Cobas c 501 device (Roche Diagnostic, Germany). Creatinine level in 24-hour urine was measured by using the colorimetric method on Cobas c 501 device (Roche Diagnostic, Germany). Serum cystatin C levels were measured by the Particle – Enhanced Immunonefelometry method on BN ProSpec plasma protein analyzer (Dade Behring, Germany) using N latex Cystatin C Reagents, and original Siemens Reagents were used. The N latex Cystatin C assay has low impression (total CV < 5%). Therefore, the N latex Cystatin C has been standardized by IFCC (ERM-DA471/IFCC).

The CKD-Epidemiology Collaborative group (CKD-EPI) is a new equation designed in 2009 to match and provide greater accuracy of MDRD accuracy. The new CKD-EPI equation was developed from 8254 data points from four clinical populations. Includes sex, race and age markers. Thus, there are four different equations that are effective for whites (male, female, above knot value, below knot value) and four factors using a different factor for African-Americans. The CKD-EPI equation was shown to be as accurate as MDRD in the subgroup with HGFH <60 ml / min / 1.73 m2, and more accurate in the subgroup with HGFH> 60 ml / min / 1.73 m2.

Statistical analysis

"SPSS 15.0 for Windows" program was used in statistical analysis. Descriptive statistics were given as the number and percentage for categorical variables and the mean and standard deviation for numerical variables. Since numerical variables did not satisfy the normal distribution condition, the comparison of two independent groups was made using the Mann Whitney U test. A comparison of rates in independent groups was made using Chi-Square Analysis. Relationships between numerical variables were examined by Spearman Correlation analysis as they did not meet the parametric test condition. Relationship levels were examined by Linear Regression Analysis. Cut-off values were analyzed by ROC Curve Analysis using the MEDCALC program. The statistical alpha significance level was accepted as $p<0.05$.

RESULTS

As a result of the statistical analysis the 'p' values of the average, standard deviation, minimum, maximum, and statistical significance level of the measurements and demographic information made in the healthy control group and patient group are shown in Table 1.

Table 1. Demographic features of patients and controls

		Patient Group (N=101)		**Control Group (N=29)**		
		Mean.±SD	Min-Max	Mean.±SD	Min-Max	*p*
Age		60.0±14,3	18-88	53.7±15,4	20±83	0.039
		n	%	n	%	
Gender	Female	44	43.6	23	79.3	0.001
	Male	57	56.4	6	20.7	

Min: minumum, Max: maximum, SD: standard deviation

A statistically significant relationship was found between CKD-EPI cystatin C clearance level and standard creatinine clearance level, between CKD-EPI creatinine clearance level and standard creatinine clearance level, and between CKD-EPI creatinine and CKD-EPI cystatin C level ($p <0.001$). (Table 2).

When the data in patient and control groups were revised by age and gender and compared again, a statistically significant relationship was found in the patient group ($p <0.001$). In the control group, there was no statistical difference between CKD-EPI creatinine and CKD-EPI cystatin C level ($p = 0.010$) (Table 3).

When the cut-off value was taken as 63 mL/min /1.73m²; the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the standard creatinine clearance test which defines renal dysfunction were identified as 73.27%, 96.55%, 98.7%, and 50.9% respectively.

Table 2. Comparison of standard creatinine, CKD-EPI creatinine and CKD-EPI cystatin c in the patient and control groups

		Standard Creatinine Clearance		GFR (CKD-EPI)-Creatinine Clearance	
	GFR (CKD-EPI)	*rho*	*p*	*rho*	*p*
Patient Group	Creatinine Clearance	0.835	<0.001		
	Cystatin C Clearance	0.865	<0.001	0.867	<0.001
Control Group	Creatinine Clearance	0.467	0.011		
	Cystatin C Clearance	0.566	0.001	0.727	<0.001

GFR: glomerular filitration rate, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration,

Table 3. Comparison of standard creatinine, CKD-EPI creatinine and CKD-EPI Cystatin C adjusted for age and gender in patient and control groups

Patient Group		**B**	**Beta**	**p**	***R²***
StandardCreatinine Clearance	Constant	0.630			0.652
	e-GFR(CKD-EPI)- Creatinine	1.377	0.808	<0.001	
StandartdCreatinine Clearance*	Constant	-2.376			0.654
	e-GFR(CKD-EPI)- Creatinine	1.384	0.811	<0.001	
StandardCreatinine Clearance	Constant	2.477			0.703
	e-GFR(CKD-EPI)- Cystatin C	1.651	0.838	<0.001	
StandardCreatinine Clearance*	Constant	9.016			0.707
	e-GFR(CKD-EPİ)- Cystatin C	1.668	0.847	<0.001	
e-GFR (CKD-EPI)- Creatinine Clearance	Constant	7.621			0.705
	e-GFR(CKD-EPİ)- Cystatin C	0.969	0.840	<0.001	
e-GFR (CKD-EPI)- Creatinine Clearance*	Constant	13.516			0.711
	e-GFR(CKD-EPI)- Cystatin C	0.975	0.844	<0.001	
Control Group		B	Beta	p	*R Squared*
StandardCreatinine Clearance	Constant	27.892			0.243
	e-GFR(CKD-EPI)- Creatinine	0,840	0.493	0.007	
StandardCreatinine Clearance*	Constant	43.393			0.248
	e-GFR(CKD-EPI)- Creatinine	0.794	0.466	0.044	
StandardCreatinine Clearance	Constant	18.296			0.299
	e-GFR(CKD-EPI)- Cystatin C	1.053	0.547	0.002	
StandardCreatinine Clearance*	Constant	35.566			0.325
	e-GFR(CKD-EPI)- Cystatin C	1.074	0.557	0.010	
e-GFR (CKD-EPI)- Creatinine	Constant	34.312			0.416
	e-GFR(CKD-EPI)- Cystatin C	0.730	0.645	<0.001	
e-GFR (CKD-EPI)- Creatinine*	Constant	79.550			0.522
	e-GFR(CKD-EPI)- Cystatin C	0.525	0.464	0.010	

*Adjusted by age and gender;
e-GFR: estimated glomerular filitration rate, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration,

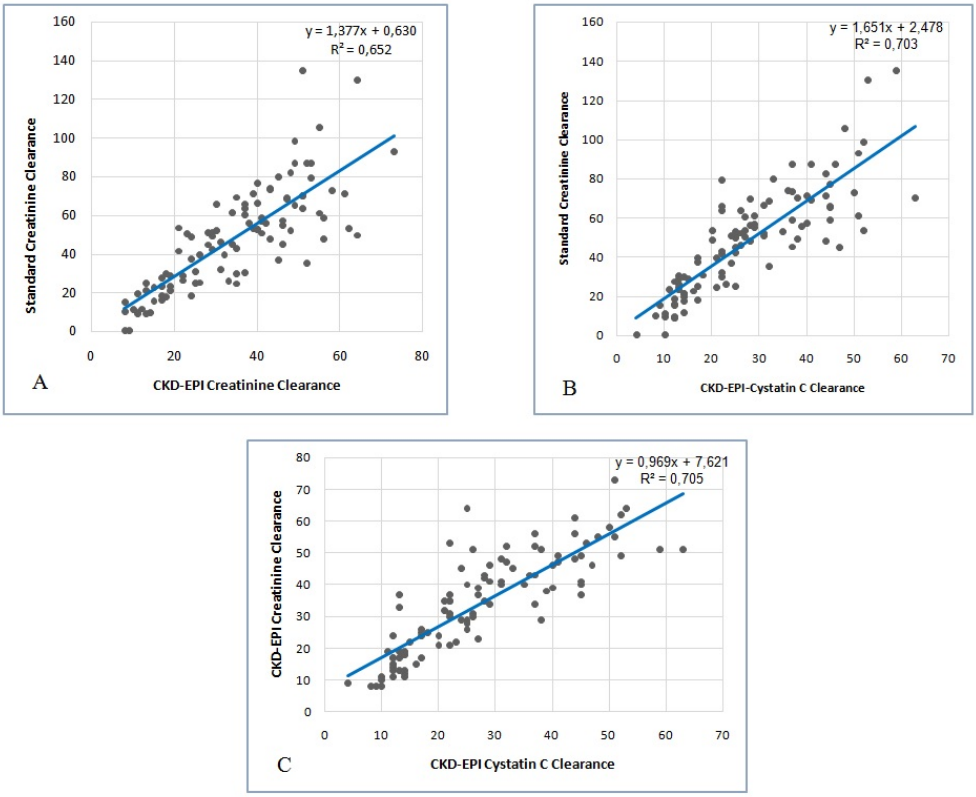

Figure 1. Linear regression graph of the levels of CDK-EPI Cystatin C, Creatinine and Standard Creatinine Clearance A) Standard Creatinine, CKD-EPI Creatinine Linear Regression Graph B)Standard Creatinine, Cystatin C Linear Regression Graph C)CKD-EPI Creatinine, Cystatin C Linear Regression Graph (CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration).

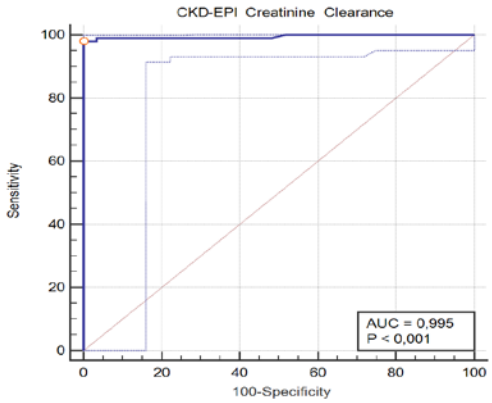

Figure 2. CKD-EPI Creatinine ROC Curve

CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, ROC: Receiver Operating Characteristic, AUC: area under the curve

Table 4. CKD-EPI- Creatinine ClearanceROCCurve Results

Positive if Greater Than or Equal To(a)	Sensitivity	Specifiity
≤61	98.02	96.55
≤63	**99.01**	**96.55**
≤65	99.01	93.10
≤69	99.01	86.21
≤72	99.01	82.76
≤75	99.01	79.31
≤77	99.01	75.86
≤78	99.01	72.41
≤79	99.01	68.97
≤81	99.01	65.52

ROC: Receiver Operating Characteristic, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

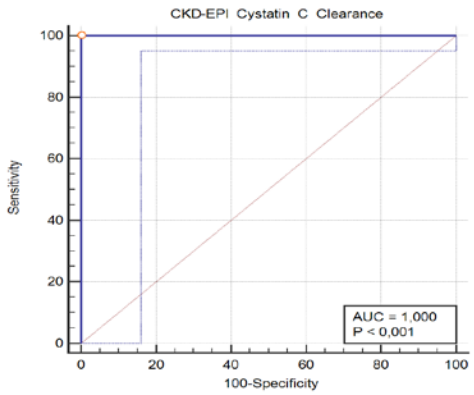

Figure 3. CKD-EPI Cystatin C ROC Curve

CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration, ROC: Receiver Operating Characteristic, AUC: area under the curve

Table 5. CKD-EPI- Cystatin C Clearance ROC Curve results

Positive if Greater Than or Equal To(a)	Sensitivity	Specifiity
≤62	97.03	100.00
≤64	99.01	100.00
≤73	100.00	100.00
≤78	100.00	96.55
≤79	100.00	93.10
≤84	100.00	82.76
≤85	100.00	79.31
≤87	100.00	75.86
≤88	100.00	72.41
≤89	100.00	65.52

ROC: Receiver Operating Characteristic, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

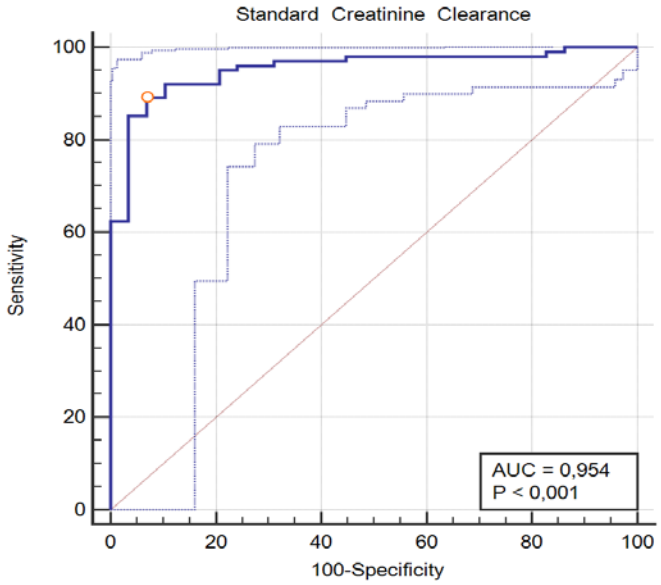

Figure 4. Standard Creatinine Clearance ROC Curve

ROC: Receiver Operating Characteristic, AUC: area under the curve

Table 6. Standard Creatinine Clearance ROC Curve Results

Positive if Greater Than or Equal To(a)	Sensitivity	Specifiity
≤58.79	69.31	96.55
≤63.7	73.27	96.55
≤68.8	80.20	96.55
≤69.29	81.19	96.55
≤70.06	82.18	96.55
≤73.16	87.13	93.10
≤79.05	89.11	89.66
≤79.33	**90.10**	**89.66**
≤84.65	92.08	86.21
≤85	92.08	82.76

AUROC: Area under the ROC curve (AUC: area under the curve)
CKD-EPI Cystatin C AUC=1.00 p<0.001, CKD-EPI Creatinine AUC=0.995 p <0.001, Standard Creatinine clearance AUC=0.954 p<0.001

When the cut-off value was taken at 63 mL/min /1.73m²; the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the CKD-EPI creatinine clearance test which defines renal dysfunction were identified as 99.01%, 96.55%, 99% and 96.6% respectively. When the cut-off value was taken as 64 mL/min /1.73m²; the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the CKD-EPI cystatin C clearance test which defines renal dysfunction were identified as 99.9%, 100%, 100%, and 99.9% respectively.

When the cut-off value was taken as 73mL/min /1.73m², the sensitivity and specificity of the standard creatinine clearance test which defines the renal dysfunction were identified as 97.80% and 67.50% respectively. When the cut-off value was taken as 75 mL/min /1.73m², the sensitivity and specificity of the CKD-EPI creatinine clearance test which defines

renal dysfunction were identified as 99.01% and 79.31% respectively. When the cut-off value was taken as 73 mL/min /1.73m2, the sensitivity and specificity of the CKD-EPI cystatin C clearance test which defines renal dysfunction were both identified as 100%. Again; its positive predictive value (PPV), negative predictive value (NPV), and accuracy rate were 100% for all. When the cut-off value was taken below 60 mL /min /1.73m² and above 90 mL / min /1.73m²; there was no statistically significant difference between the susceptibility and specificity of CKD-EPI creatinine and CKD-EPI cystatin C, which defines renal dysfunction.

DISCUSSION

In this study that includes adult population with kidney disease, we compared the diagnostic accuracies, in-between correlations and performances of standard 24-hour creatinine clearance calculation and KDIGO 2012 guideline-recommended CKD-EPI cystatin C and CKD-EPI creatinine equations, which have increased number of use in recent years to estimate GFR[4-8].

Strengths of the study include performing the study of serum cystatin C levels with the internationally standardized N-Latex cystatin C kit and the PENIA nephelometric method accepted as the reference method; calibration of serum cystatin C levels to international values with internationally standardized ERM-DA471 / IFCC in each study; measuring all tests in one laboratory, and using a separate verification dataset for the three filtration markers.

In our study, the main findings showed that cystatin C had a stronger relationship with the results in the our study group and its diagnostic value and performance were better in the adult population. All three markers individually showed high specificity and sensitivity for the prediction of GFR. However, cystatin C sensitivity and specificity is almost 100% in cut off values that will enable acute kidney damage to be diagnosed at an early stage. Since the half-life of cystatin C is three times shorter than creatinine, it may be more affected by acute changes[9,10]. According to various findings in our study, the low specificity of CKD-EPI creatinine in cut off values that will enable the diagnosis of chronic kidney disease at an early stage suggests that creatinine levels are affected by some pathophysiological factors other than GFR[3,18].

In the study, we tried to provide the most accurate prediction with the values of both markers related to age, gender, and race with the CKD-EPI equation developed by nephrology associations to provide more accurate GFR estimates. However, although rigorous inclusion and exclusion criteria were determined, the pathophysiological factors affecting the above-mentioned serum creatinine could not be calculated. In the calculation of standard creatinine clearance, the patient's muscle mass, gender, and age are not taken into account in the formula[19]. Therefore, the normality of creatinine levels may not reflect the real situation. This is one of the few limitations of the analysis. To understand the relationship between serum creatinine, cystatin C and GFR and their interactions, all pathophysiological variables must be known and all their possibilities must be tested.

In our study, linear regression models were used to define explanatory variables for GFR differences between parameters. According to the linear regression graphs shown, it was observed that the standard creatinine clearance was high and more insensitive compared to CKD-EPI cystatin C and CKD-EPI creatinine in early stages. Besides, false negativity was detected in 26 patients by standard creatinine clearance. Improper classification of these differences due to normal evaluation of GFR in decreased kidney function may result in early diagnosis errors in potentially renal patients.

Some of the previous studies reported that serum cystatin C increased before serum creatinine increased in kidney dysfunction due to acute kidney damage, and that it was more sensitive and early biomarker than creatinine in the early diagnosis[12,14-16]. In the study of Yong et al. in 2017, the GFR estimation value of serum cystatin C for acute kidney injury (AKI) in adults was investigated. Assessment parameters such as sensitivity, specificity, positive probability rate, negative probability rate, and relative risk ratio for cystatin C were determined as 0.82, 0.82, 4.6, 0.22 and 21% respectively. As a result, cystatin C has been reported to show a high predictive power for AKI screening and that it might be a useful marker[12].

In the meta-analysis reports published by Yang SK et al. in 2016, it was aimed to evaluate the diagnostic value of serum cystatin C in the evaluation of renal dysfunction in diabetic patients. The study consisted of 17 different studies, including 2173 patients. As a result of the analysis of the study, it was stated that serum cystatin C was more sensitive in the evaluation of kidney functions in diabetic patients[15].

In the study of Kwon et al. comparing serum cystatin C and serum creatinine levels in 2016, the best predictive GFR equation that could be used to determine osteopenia in 780 CKD patients aged 50 years and older was investigated, and the correlation of CKD-EPI creatinine and CKD-EPI cystatin C was examined. As a result, they reported that the decreased kidney function evaluated by CKD-EPI cystatin C showed a better correlation than the essential creatinine-based methods[14].

In our study, similar results were obtained as in the studies of Yong et al., Jacobs et al., Yang SK et al., Kwon et al., which have been made recently. The area under the comparative recipient study characteristic curve of cystatin C, creatinine, and standard creatinine clearance (AUROC) was 1, 0.995, and 0.954 respectively (Figure 1). When the cut-off value was taken as 73 ml/min / 1.73m² the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rate of CKD-EPI Cystatin C clearance test was detected as 100% for all parameters. At the same cut-off value, the sensitivity and specificity of standard creatinine clearance and CKD-EPI creatinine clearance were found as 97.8%, 67.5%, and 99.01%, 79.31%, respectively. While the standard creatinine clearance did not reach these values at all cut off limits, we were able to detect the sensitivity of the CKD-EPI creatinine clearance as 99% and the specificity as 96.6% only after the cut-off value was taken as 63 mL/dak /1.73m². Accordingly, in our evaluation with ROC curve analysis; we determined that cystatin C was a more effective marker in terms of sensitivity and specificity than creatinine and standard creatinine clearance at the cut-off limits which are possible in the early diagnosis of kidney failure and glomerular structural change.

While some of the previous studies found cystatin C as a reliable marker, several studies related to the superiority of serum cystatin C over serum creatinine have suggested no significant difference[16,17,20]. When we examine these studies, it is observed that they were made on different groups consisting of heterogeneous patients such as geriatric, hypothyroidism, CKD, cardiopulmonary bypass surgery, neurosurgery, septic shock, hemorrhagic shock. It is known that cystatin C has different performance among populations of patients with organ failure (liver, heart failure), patients with thyroid dysfunction such as hyperthyroidism and hypothyroidism, under 18 years of age, had kidney transplantation and hemodialysis or peritoneal dialysis treatment, undergone cardiac surgery[21-25]. In addition, Rule et al. demonstrated in their studies that cystatin C had different performances among kidney transplant recipients in the presence of thyroid disease[20]. Therefore, we cannot conclude the performance of serum cystatin C or creatinine in other populations. Besides, all of these diseases were used as exclusion criteria in our study.

In the current study, CKD-EPI cystatin C is a better predictor in terms of sensitivity and specificity for slight fluctuations in renal functions. Performance of serum creatinine and standard serum creatinine clearance and cystatin C were found close at decreased GFR levels. It suggests that the stronger association of creatinine with results at decreased GFR levels is due to factors other than GFR that affect the serum levels.

Main limitation of this study; Firstly, as discussed above; our study population has an average age of 60 years andit consisted of mostly CKD patients, including weak and elderly patients. Therefore it may not adequately reflect the general population and the relationship between serum creatinine and cystatin C and GFR. However, it gives an idea of the population in Turkey. In order to clarify this situation, the number of patients can be increased and gender differences can be examined.

After evaluating all the cases, a statistically significant correlation was found between GFR values and standard creatinine clearance calculated using the CKD-EPI equation. In the early diagnosis of glomerular structural change, the highest diagnostic accuracy and performance were obtained with serum cystatin C. To make the relationship between creatinine, cystatin C and GFR as well as the differences in the accuracy of equations more sensitive, multicentre, and randomized controlled studies should be conducted in large populations. We believe that cystatin C (CKD-EPI) can be a useful biomarker in early diagnosis and staging of kidney failure, and can detect patients at high risk for CKD.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SU, ES; Veri toplama: SU, DA, ES; Veri analizi ve yorumlama: SU, DA, ES; Yazı taslağı: SU, DA, ES; İçeriğin eleştirel incelenmesi: SU, DA, ES; Son onay ve sorumluluk: SU, DA, ES; Teknik ve malzeme desteği:SU, ES; Süpervizyon: SU, DA, ES; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için 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.
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Author Contributions: Concept/Design : SU, ES; Data acquisition: SU, DA, ES; Data analysis and interpretation: SU, DA, ES; Drafting manuscript: SU, DA, ES; Critical revision of manuscript: SU, DA, ES; Final approval and accountability: SU, DA, ES; Technical or material support: SU, ES; Supervision: SU, DA, ES; Securing funding (if available): n/a.
Ethical Approval: For this study, ethics approval was obtained from the Clinical Research Ethics Committee of Şişli Hamidiye Etfal education and Research Hospital with the decision dated 18.04.2017 and numbered 774.
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