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Cystatin C versus creatinine-based GFR formula in CKD patients

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Abstract

Introduction. Glomerular Filtration Rate (GFR) is the main tool to assess kidney function. Some experts suggest cystatin C as a more precise and accurate indicator than creatinine to calculate GFR. This study is designed to assess if cystatin C is more helpful in early diagnosis and better follow-up of Chronic Kidney Disease (CKD) patients who may benefit more from appropriate and timely management.
Methods. We studied 312 patients in different stages of CKD and normal kidney function as control. GFR based on creatinine (Jaffe and enzymatic) and cystatin C were calculated and compared.
Results. A total of 146(46.8%) patients were male with a mean age of 53±17.5 years. The patients were divided into 3 groups based on GFR (>60 cc/min/1.73m^2, 30< GFR<60cc/min/1.73m^2, 15<GFR<30cc/min/1.73m^2). No significant differences in GFR estimation based on creatinine and cystatin C were found.
Conclusions. There were no significant differences between serum cystatin C-based formula and creatinine-based formula for GFR calculation. Therefore, they can be used interchangeably.

Key words: chronic kidney disease, estimated glomerular filtration rate, cystatin C, creatinine

Introduction

Chronic Kidney Disease (CKD) can occur due to different acute or chronic disease conditions. It can occur due to hypotensive attacks in patients undergoing chronic processes such as hypertension and diabetes mellitus [1]. The huge cost of renal replacement therapy (RRT) for health community system is the main reason that health care providers are keen on early detection programs of CKD [2]. Therefore, any more reliable tool than creatinine to assess kidney function, estimated glomerular filtration rate (GFR), to find CKD at an earlier stage to postpone end-stage renal disease and RRT is welcomed [3,4].

GFR is estimated routinely by different creatinine-based formulas like Cockroft-gault (CG) and modification of diet in renal disease (MDRD). Furthermore, other molecules like uthalamate and inulin have been introduced for GFR calculation. However, they have limited popularity because of the expensive and time-consuming process. Recently, serum cystatin C (s-CysC) has been suggested as a more reliable marker than serum creatinine to evaluate GFR [5-7].
Cystatin C is a cystein proteinase inhibitor that is constantly synthesized by all nucleated cells. It can be freely filtrated through glomerulus and then be absorbed without secretion [6,8,9]. There are some unrelated conditions to renal function that may cause serum cystatin C to rise, such as malignancy, thyroid disease, pregnancy and chronic infection [10]. Hejes, *et al.* found that-CysC-based GFR to be more accurate than creatinine-based GFR in patients with GFR <60cc/min/1.73m2 [11]. It is well-known that serum creatinine level is affected by muscle mass, catabolic state, age, gender, diet and medications. Some researchers believe that cystatin C is a better parameter than creatinine for GFR estimation [5,6].
This study was designed to assess the correlation of creatinine-based formula and s-CysC-based formula of GFR calculation in different stages of kidney function and to see if it has a significant impact on timely CKD diagnosis.

Material and methods

The study included patients who were admitted in the Nephrology Ward or the Clinic for CKD management and to other wards or clinics in Imam Khomeini Hospital Complex. They had normal creatinine in 2013 and were consecutively visited and enrolled in the study if they did not have thyroid disease, current infection and malignancy. Blood samples were collected in order to determine creatinine (Jaffe), creatinine (enzymatic), cystatin C (enzymatic), cholesterol (CHOD Manner with autoanalyzer), triglyceride (PAP manner with auto analyzer), albumin (BCG manner with autoanalyzer), hemoglobin and blood glucose.

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GFR was calculated based on Cys C (CKD-EPI equation) if cys ≤0.8:133× (Scys/0.8)-0.499×0.996-age [0.932 if female] and if cys>0.8: 133× (Scys/0.8)-1.328×0.996-age [0.932 if female]. MDRD formula was used for calculating creatinine:

$$GFR = {}^{cc}/_{min/1.73m^2} \text{ "} = 186 \times [serumCr(^{mg}/_{dl})^{-1.154}] \times [age(year)]^{-0.203} \times$$

$[1.212 \text{ if Black}] \times [0.742 \text{ if female}]$ and CKD-EPI equation: $144 \times$ (S Cr/0.7) $^{-1.209} \times (0.993)^{age}$ in females and $141 \times$ (S Cr/0.9) $^{-1.209} \times (0.993)^{age}$

Patients were divided into three groups based on their GFR: >60 cc/min/1.73m^2, between 30-60cc/min/1.73m^2, between 15-30cc/min/1.73m^2 and correlation between s-CysC-based formula GFR with creatinine-based formula (Jaffe and enzymatic) GFR were assessed. All statistical analyses were conducted with the software package SPSS, version 15. Student's t-test and ANOVA were used to analyze correlations between variables. P<0.05 was regarded as statistically significant.

Results

A total of 312 patients were enrolled into the study. The mean age of patients was 53±17.5 (14-94) years. Of these, 146 patients were male (46.8%). One hundred and four patients (33.3%) suffered from hypertension and 95 patients (30.4%) had diabetes mellitus. The laboratory data are presented in Table 1.

Table 1. Laboratory data of patients

Laboratory findings	Mean± SD
Cystatin C	1.76±0.53
Jaffe creatinine (mg/dl)	1.37±0.58
Creatinine (mg/dl) enzymatic	0.79±0.32
Triglyceride (mg/dl)	145±84
Cholesterol(mg/dl)	182±44
Albumin (g/dl)	6.7±2.4
TSH	1.2±3.2
Hemoglobin (g/dl)	8.6±5.13
FBS (mg/dl)	60±6.12

Table 2. Mean eGFR calculated by different equations in different stages (Cys-C versus creatinine-based formula)

CKD stages	Cystatin-based eGFR calculation	Creatinine-based eGFR calculation	
	CKD-EPI equation	MDRD standard	CKD-EPI
Normal	96.4±13.7	103.6±15.2	103.90±10.7
60<GFR<90	78.4±16.6	77.4±12.3	75.2±8.7
30<GFR<60	39.9±16.2	44.8±10.3	42.4±8.3
15<GFR<30	26.5±14.7	25.5±4.6	24.1±2.9

The findings showed there were no significant differences in GFR estimation based on each of the mentioned markers (Table 2).

Cystatin C showed positive correlation with age (r=0.420 P<0.001), creatinine (Jaffe method, r=0.694, P<0.001), enzymatic creatinine measurement (r=0.591, P<0.001), triglyceride (r=0.188, P<0.001), and it had negative correlation with cholesterol (r=-0.122, P=0.04). Correlation of GFR calculation based on creatinine and cystatin C was 0.816, p<0.001. The GFR calculated by the two methods of CKD-EPI and MDRD based formula correlated significantly (r=0.995, P<0.001).

Discussion

In this study, accuracy of GFR estimation based on cystatin C or creatinine-based formulas was assessed. The results obtained showed that cystatin C can be used similarly to creatinine for estimating GFR in different stages of kidney function. Kumaresan, *et al.* also investigated this issue. They analyzed CKD patients and measured GFR by [99m]TC-DTPA (diethylene triamine penta acetic acid) as the gold standard. They found a significant correlation with cystatin C based-formula GFR calculation (r=0.8, P<0.001). Furthermore, they showed a significant correlation between serum creatinine and serum cystatin C (r=0.6, p>0.001) [12]. Sakaguchi, *et al.* showed correlation of cystatin C with MDRD GFR estimation in CKD patients (r=0.85, P<0.001) [13]. Khorgami, *et al.* found no significant differences between cystatin C-based GFR and creatinine-based GFR in hemodialysis patients. Their study included only hemodialysis patients with mean GFR of about 4-8 cc/min/1.73 m^2. They also showed the importance between the two formulas for GFR estimation: cystatin C (CKD-EPI) and creatinine-based GFR estimation (MDRD), (r=0.51, p<0.001). We studied a larger number of patients and compared GFR in normal and different stages of CKD. Our study also confirmed the previous studies with more solid data in wider range of kidney function [14]. However, Hejes, *et al.* insisted that cystatin C-based GFR formula was more accurate than creatinine-based GFR formula in patients with GFR<60cc/min/m^2 [11]. Soleimani, *et al.* found that creatinine and cystatin C was correlated on the third, seventh and 14th day after kidney transplantation and they showed higher accuracy

of serum cystatin C in renal function assessment the first week after kidney transplantation [15]. It seems that the situation of kidney transplantation looks like an acute process, which is not comparable with stable situation in CKD patients. Shlipak, *et al.* showed serum cystatin C to be more accurate than creatinine to predict cardiovascular accidents, especially when GFR was higher than 60cc/min/m^2 [16]. We did not include children in our study, but Filler, *et al.* found that cystatin C was as much useful for children under dialysis as was for adults [17].

Conclusions

There were no significant differences between serum cystatin C-based formula and creatinine-based formula for GFR calculation. Therefore, they can be used interchangeably.

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