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Level Of Creatinine And Cystatatin C In Different Stages Of Kidney Failure

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ABSTRACT

INTRODUCTION:Chronic kidney disease (CKD) is a major public health concern, and for the assessment of patients with CKD, estimation of the glomerular filtration rate (GFR) is vital. Serum biomarkers, such as serum creatinine and serum cystatin C, have been commonly used to test renal function in patients who have chronic kidney disease (CKD). It is necessary to recognise the elevated risk of CKD progression to delay the deterioration of kidney failure and to plan for the evolution to end-stage renal disease. Therefore, the purpose of this study is to compare serum cystatin C and creatinine diagnostic output with measured GFR and estimated GFR in patients with CKD.

METHODS:This study was conducted at SMHRC, Maharashtra India throughout the period of September 2019 to August 2020. We enrolled 100patients (50 males and 50 females) aged 40-60years with CKD stages2–5from Nagpur. In each patient, serum creatinine and serum cystatin C were determined. Serum cystatin C was measured with a particle-enhanced nephelometric immunoassay (PENIA) method. The detection methods for SCr were the enzymatic method and the Jaffe's method. GFR was measured using diethylenetriaminepenta aceticacid (DTPA) renal scan method.

Results: In females, serum cystatin C had significantly greater diagnostic specificity than serum creatinine. In males, no distinction between serum cystatin C and serum creatinine was observed. Serum cystatin C's diagnostic accuracy was significantly greater than that of creatinine.

Conclusion: In young and elderly patients with CKD, serum cystatin C showed a high correlation with measured GFR compared with creatinine. Cystatin C is therefore a good alternative marker for CKD patients compared to creatinine. Our findings show that in patients with mild to moderately impaired kidney function, serum cystatin C is a reliable marker of GFR and has greater diagnostic accuracy than serum creatinine and measured clearance of creatinine.

Keywords: GFR,CKD, Cystatin C, Creatinine and Kidney Failure

INTRODUCTION

CKD poses significant risks to human health, as well as end-stage renal disease (ESRD). Aging significantly raises the incidence and prevalence of CKD worldwide [1, 2]. As a progressive disorder, CKD leads to ESRD in many cases. Accurate and convenient renal function assessment is crucial for both healthy populations and patients with CKD, especially those with mild to moderate decreased renal function. Early treatment initiation in patients with CKD has shown that the occurrence and severity of adverse effects can be delayed or even avoided.

The current guidelines of the Kidney Disease Outcomes Quality Initiative stratify CKD into 5 steps, also based on GFR estimates [3]. Only in the presence of kidney damage (stage 2 of CKD; GFR 89-60 ml / min) was the mild reduction in GFR known as CKD. Moderate (CKD stage 3; GFR 59-30 ml / min) to serious (CKD stage 4; GFR 29-15 ml / min) reduction in GFR and kidney failure (CKD stage 5; GFR < 15 ml / min) have been identified as CKD, regardless of the existence of kidney damage.

Therefore, for early initiation of treatment, early phase prognosis of CKD is required in order to assist patients, in particular those at highest risk of progression. GFR is known to be an effective indicator for renal surgery, and this measurement is known to be the gold standard for renal disease assessment. Furthermore, as an independent risk factor influencing cardiovascular function, GFR is used [4]. An endogenous molecule that, generated at a constant rate, is cleared only by the kidneys through free glomerular filtration should be the ideal marker of GFR, with neither secretion by tubular cells nor reabsorption into peri-tubular circulation. [5]

A tool used to quantify endogenous substances in the blood is to estimate GFR. In several studies, SCr is indicated to be less susceptible to kidney failure, especially in patients with minor kidney dysfunction and in older patients with CKD who are often under-recognized for kidney failure. As GFR decreases, the level of plasma cystatin C increases earlier than plasma creatinine, which may be a valuable marker in detecting early impaired renal function. [6,7]It fulfils a range of GFR endogenous marker criteria: it is freely filtered and catabolized without being secreted in the proximal tubule.[8] The concentration of serum cystatin C was introduced as an endogenous kidney function marker and was used to measure the eGFR. Age , sex, and body mass are stated to be independent [9,10]. In patients with muscle wasting or chronic disease, the value of the cystatin C-based equation is that it is independent of race and obtains a more reliable calculation of GFR. [11]

METHODS

Study design and participants we did a population-based retrospective cohort study in 100 CKD patients contain (50 male and 50 female) admitted in SMHRC, Nagpur from September 2019 to March 2020. This study was approved by the Institutional Review Board of the JNMC & ABVRH. All participants provided written informed consent before enrolment.

Biochemical Investigation: Both clinical approaches have been included for SCr and SCysC detection. Particle-enhanced nephelometric immunoassay (PENIA) and particle-enhanced turbid metric immunoassay (PETIA) [12, 13] were the research processes for SCysC. The enzymatic method and the Jaffé method [14] were the detection methods for SCr.

Study population

For the present study, 100 adults (aged ⁇ 39 years) with CKD who had been exposed to at least three simultaneous measurements of both creatinine and cystatin C levels over a 1-year period at a hospital's SMHRC between September 2019 and March 2020 were retrospectively described. As the first simultaneous measurement, we set the baseline. Based on a baseline eGFR of < 60 mL / min, CKD was specified. A level of kidney function as described by a GFR is expressed by each CKD stage as follows: stage 3, eGFR 30-59 mL / min; stage 4, eGFR 15-29 mL / min; stage 5, eGFR < 15 mL / min. 100 patients were omitted because they were treated with dialysis or a kidney transplant, or were lost from baseline to follow-up within 1 year. Finally, the study analysed 100 patients with non-dialysis CKD stage 3–5.

STATISTICAL ANALYSIS

Meta-analysis was conducted using Rev Man version 5.3 and Meta-Disc version 1.4 software. Using Stata 14.0 (Stata Corp, College Station, TX, USA), publication bias analysis was performed. When a cell with a value of 0 was found in a four-fold table, the measurements were corrected by adding 0.5 to the cell. The study did not involve studies involving two cells with a value of 0. For diagnostic tests, each document was summarised by SPE, SEN, ± PVs, ± LRs, and also evaluated for heterogeneity with the $\chi 2$ test. This was measured using the I2 tool, and when I2 was > 50 percent, substantial study heterogeneity was considered. I2 values were considered to exhibit moderate heterogeneity between 25 and 50 percent and I2 values < 25 percent were thought to suggest low heterogeneity.

(I) Creatinine clearance calculated according to C&G[15]

Formula:

(140 - age years) × body weight kg/0.815×serum creatinine mmol/l_

(II) Creatinine clearance calculated according to MDRD

Formula:

186 - serum creatinine (mg/dl) $^{-1:154}$× age (years) $^{-0:203}$

RESULTS

The study included 100 patients with CKD, including 50 males and 50 females. In enrolled patients, the average Pcr and cysC levels were 1.971.7 mg / dl and 2.171.5 mg / dl respectively. Measured by 99mTc-DTPA plasma clearance, the mean reference GFR (rGFR) was 57.9736.4ml / min.

Causes of CKD and CKD stage classification are shown in Table 1 and 2.

Table 1- Causes of CKD

Table 2 – CKD stage

Causes of CKD	
glomerular disease	5 (%)
HTN	10 (%)
Obstructive kidney disease	50(%)
Renovascular disease	20 (%)
Chronic tubulointerstitial disease	5 (%)
Diabetic nephropathy	2 (%)
Polycystic kidney disease	5 (%)
Unknown or other causes	3 (%)
CKD stages	
Stage I	25(%)
Stage II	30 (%)
Stage III	15 (%)
Stage IV	18 (%)
Stage V	12 (%)

Table 3: Diagnostic accuracy at cut-off value for GFR 60 ml/min of serum cystatin C, serum creatinine calculated

Male patients	
Cystatin C	0.21±0.008
Creatinine	0.15±0.002
Female patients	
Cystatin C	0.19±0.004
Creatinine	0.13• ±0.001

*P-values are given relative to cystatin C results.

Table 3 shows diagnostic specificity for all patients included in the study. Serum cystatin C had substantially greater diagnostic specificity in women than serum creatinine. No difference between serum cystatin C and serum creatinine was observed in males. The diagnostic precision of serum cystatin C was substantially greater than that of creatinine.

DISCUSSION

A stage of variable duration, during which GFR decreases, precedes kidney failure due to CKD. Serum creatinine concentration is still commonly used for GFR estimation, despite all of its drawbacks, as it is easy and inexpensive. As a new endogenous marker of GFR, serum cystatin C has recently been suggested. The findings of our research suggest that serum cystatin C in patients with mild to moderate kidney function impairment is a reliable marker of GFR. [16]

Creatinine has been unambiguously shown to differ with age, gender and body mass. However, there are contrasting opinions, some supporting evidence,[17] and some other opposing evidence,[18,19] in the case of cystatin C, on the effect of age , gender and body mass on the levels of cystatin C. The present research was performed in patients with CKD in order to explore this dispute. In this patient population, the clinical applicability of Pcr-based estimate equations has been increasingly challenged because the underestimation may result in unnecessary investigation and/or referral to nephrologists, excessive surveillance, and treatments.

In the last decade, hundreds of papers have compared the applicability of cysC with Pcr in various stages of CKD in GFR estimation.

Perlemoine et al. ,[20] Christensson et al. ,[21] and Mussap et al.[22] claimed that plasma cysC was more sensitive in the identification of early or moderate diabetic nephropathy patients; similar conclusions were also obtained in non-diabetic patients,[23,24] in renal transplantation patients [25] and in healthy adults. [26]

Perkins et al.[27] found that 100 / cysC could reliably detect changes in GFR patterns in patients with normal or elevated GFR for diabetes.

Macdonald et al.[28], a recently published paper, found that the amount of cysC was not independent of lean body mass.

In 100 children and young adults, the findings showed that the GFR estimate was substantially increased if the equation contained both Pcr and cysC. Bouvet et al.[29] compared equations based on either Pcr, cysC, or a mixture of them. These findings support our hypothesis that the output of GFR-estimating equations based on Pcr or cysC alone could be improved by an equation involving Pcr, cysC, age, and gender.

The output of the equation based on a combination of cysC and Pcr was only marginally superior to the modified MDRD equation in the CKD stages 5, 4, and 3. This may be due to the fact that in humans with moderately / severely impaired kidney function, the non-renal clearance of cysC in humans is significantly higher.[30] Therefore, in advanced kidney failure, plasma cysC may be unsuitable as a GFR marker. Since the calculation of cysC is currently more costly than Pcr and the modified MDRD equation can provide reasonable precision in CKD stages 5, 4, and 3, the modified MDRD equation in advanced kidney failure was recommended.

Serum cystatin C and creatinine clearance calculated from the C&G formula offered better diagnostic accuracy than serum creatinine in a study conducted by Hoek et al.[31], but no substantial difference in diagnostic precision was observed between serum cystatin C and creatinine clearance calculated from the C&G formula. Just 100 patients with various CKD stages were included in this review[32-33].

CONCLUSION

In conclusion, CKD is an important public health concern and patients are classified on the basis of GFR estimates, according to the current guidelines. Our findings suggest that serum cystatin C and creatinine are accurate markers of GFR in patients with mild to moderate impairment of renal function at different levels. Serum cystatin C had better diagnostic accuracy in our well-defined CKD stage 5 patients than serum creatinine and assessed clearance from the C&G formula in identifying patients with mildly to moderately impaired kidney function. Between serum cystatin C and the measured creatinine clearance from the MDRD formula, there was no difference in diagnostic precision. It is no longer theoretically difficult to estimate serum cystatin C, and cystatin C can be used as a GFR marker in patients with mild to moderate kidney function disability. Cystatin C can be used in female patients to reduce diagnostic errors, despite the fact that it is still more costly than estimating the concentration of serum creatinine.

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