Research Article

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Journal of Nephrology and Urology

2017
Vol. 1 No. 1: 4

Assessment of Glomerular Filtration Rate in Older Adults in Brazil

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Citation: Duque GC, Passos MT, Nishida SK, Sabino ARP, Kirsztajn GM (2017) Assessment of Glomerular Filtration Rate in Older Adults in Brazil. J Nephrol urol. Vol. 1 No. 1: 4

Abstract

Objective: To evaluate the performance of renal function markers in the elderly.

Methods: 105 individuals over 60 years old were divided in group A (60 to 79) and group B (≥ 80 years old) to determine the estimated glomerular filtration rate (eGFR) using creatinine and cystatin C equations.

Results: In group A, the best correlations were observed between the serum creatinine levels and the eGFR calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine, and the cystatin C levels with CKD-EPI cystatin and Larsson equations, and in group B, between creatinine and CKD-EPI creatinine-cystatin and CKD-EPI cystatin and cystatin with CKD-EPI cystatin equation.

Conclusions: The CKD-EPI equations (especially CKD-EPI cystatin) presented the best performance in our study, and CKD-EPI creatinine seems to be appropriate for daily practice. The elderly population requires a different renal function assessment or possibly a different definition of CKD according to age ranges.

Keywords: Creatinine; Cystatin; Age; Glomerular filtration rate

Received: November 07, 2016; **Accepted:** December 29, 2016; **Published:** January 09, 2017

Introduction

The global life expectancy increase has paralleled with an increase in the number of CKD cases [1-4]. Serum creatinine has been widely used to assess renal function. However, the creatinine production rate is low in elderly people due to the muscle mass decrease related to age [5]. Therefore, the serum creatinine might not be a satisfactory parameter for the renal function assessment in the elderly [2, 4].

Equations to estimate glomerular filtration rate (GFR) are a more reliable and accurate method to assess the renal function [6]. The most widely used in clinical practice are the Modification of Diet in Renal Disease (MDRD) and the Cockcroft-Gault (CG) equations [5-7]. However, the CG equation may underestimate the actual GFR, especially in individuals older than 79 years [5] and the MDRD equation underestimates the GFR in patients with a GFR>60 mL/min/1.73 m^2 [7].

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation that is based on creatinine (CKD-EPI creatinine) has been suggested recently as a more accurate alternative to the MDRD equation, especially when the GFR is >60 mL/min/1.73 m^2 [6, 8]. Furthermore, two equations were subsequently developed: the CDK-EPI cystatin equation, which is based on the cystatin C and the CDK-EPI creatinine-cystatin equation, which uses both parameters [7].

Cystatin C is a well-known marker of the renal function and recently it has been considered to be an alternative marker for the renal function in elderly adults since it does not seem to be influenced by age, muscle mass or nutritional status [5, 6, 9, 10]. Our previous studies with iohexol clearance used as gold standard have indicated that cystatin C might be useful for the renal function assessment in elderly adults [8].

Methods

The present population consisted of 105 participants, 66 individuals were 60 to 79 years old (A) and 39 individuals over 79 years old (B). The participants were recruited from a population that is regularly assessed at the Geriatric and Chronic Outpatient Clinic of the Hospital for Civil Servants of the State of São Paulo (São Paulo, Brazil) and agreed to participate. Individuals with diabetes

or severe dementia and/or those who were bedridden were excluded from this study as well as individuals with other severe diseases (malignancies and severe chronic obstructive pulmonary disease, among others) or who were frequent nephrotoxic drugs users. An informed consent was obtained from all the participants. The serum creatinine was measured using the modified kinetic Jaffé colorimetric method on an auto analyzer (Beckman Coulter AU 400, CA, USA), which was calibrated to isotope dilution mass spectrometry (IDMS) using a standard reference material (914a) traceable to the National Institutes of Standards and Technology (NIST). The total colorimetric method analytical variation (CV%) was 1.4-3.0%. The intra-assay coefficient variation (CV) for the creatinine was 1.9%.

The serum cystatin C levels were determined by an automated particle-enhanced immunoturbidimetric method [5] using a Beckman AU 400 analyzer (Beckman Coulter, Inc. CA, USA), reagents (code Nos. LX002, s2361, X0973, X0974) obtained from DakoCytomation (Glostrup, Denmark) and followed the recommended procedures by the reagent producer. The estimated GFR (eGFR) was determined using the CG [11], the simplified MDRD [12, 13], the CKD-EPI creatinine [14], the CKD-EPI creatinine-cystatin, the CKD-EPI cystatin [15] and Larsson [16] equations.

Statistical analysis were performed with the statistical program "Statistical Package for the Social Sciences" (SPSS) version 19.0 for Windows and R version 2.11.1.

Results

The ranges of serum creatinine and cystatin C levels were: 0.58 to 1.39 mg/dL (mean 0.88) and 0.48 to 1.84 mg/dL (mean 1.08) in group A, and 0.61 to 1.72 mg/dL (mean 1.01) and 0.58 to 1.89 mg/dL (mean 1.23) in group B, respectively. The two-dimensional dispersion analyses of the serum creatinine level versus the eGFR and the serum cystatin C level versus the eGFR using various equations are presented in **Figures 1 and 2**, respectively.

A positive and statistically significant correlation was found between the serum creatinine and the serum cystatin C levels. A negative and statistically significant correlation was found between the serum creatinine or serum cystatin C level and the eGFR determined using the six assessed equations. A linear regression analysis (multivariate approach) showed that in group A, the serum creatinine levels could be explained only by the eGFR that was calculated using the CKD-EPI creatinine equation ($p<0.001$). In contrast, in group B, the serum creatinine levels were explained by the results of the CKD-EPI creatinine-cystatin ($p<0.001$) and CKD-EPI cystatin equations ($p<0.001$). The serum cystatin C levels could be explained by the eGFR calculated using the CKD-EPI cystatin ($p<0.001$) and Larsson equations ($p=0.031$) in group A, whereas in group B, the serum cystatin C levels could be explained only by the CKD-EPI cystatin equation ($p<0.001$).

Discussion

Aging is considered to be one of the most relevant independent risk factors for CKD [17, 18].

In the present study, we performed a cross-sectional renal function assessment using equations to estimate the GFR in elderly people randomly selected and they were divided in group A (aging from 60 to 79 years old) and group B (≥ 80 years old).

To assess the GFR, we used CG equations, simplified MDRD, CKD-EPI creatinine, CKD-EPI cystatin, CKD-EPI creatinine-cystatin and Larsson equations.

Overall, the eGFR yielded by the CKD-EPI equations using the different variables exhibited a better correlation with the creatinine and cystatin C markers in both groups. In our study, it was evident that the CDK-EPI cystatin equation allowed the most precise assessment of elderly people. Several studies have shown that the CG equation consistently underestimates the actual GFR [18], particularly in elderly adults [5]. The correlation of the CG equation results with the serum creatinine and cystatin C levels

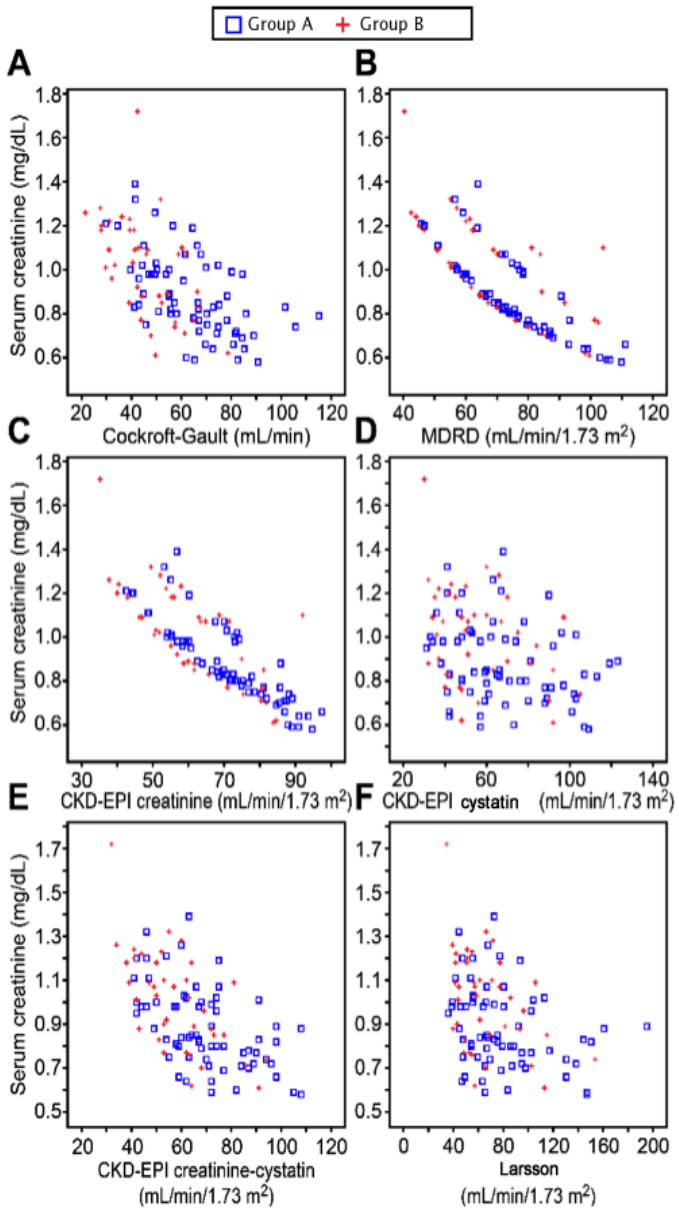

Figure 1 **(a-f)** Two-dimensional dispersion of serum creatinine (mg/dL) versus eGFR, according to various equations in the group A and group B participants.

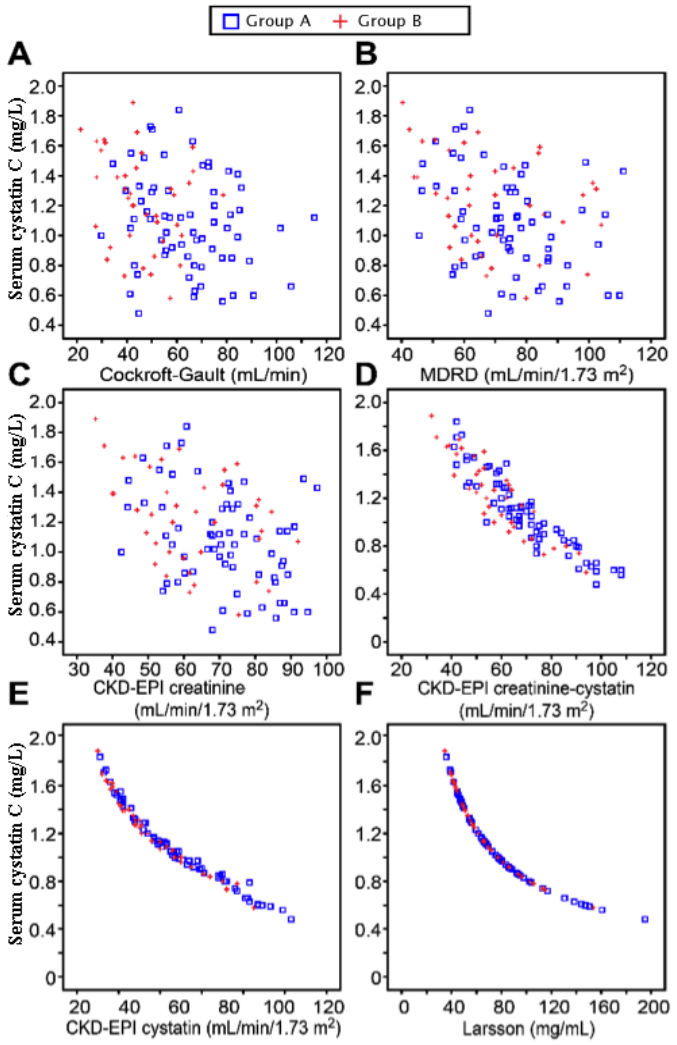

Figure 2 **(a-f)** Two-dimensional dispersion of serum cystatin C (mg/L) versus eGFR, according to various equations in the group A and group B participants.

in this present study was quite poor, which is consistent with previous reports.

The MDRD equation performance in elderly adults is better than that of the CG formula [5], although the study in which the MDRD equation was formulated did not include participants older than 70 years of age [6]. Pei et al. [18] assessed an elderly Chinese population (average age of 66 years old) and found that the MDRD equation overestimated the actual GFR, as measured using ^{99m}Tc-diethylenetriamine pent acetic acid (DTPA). In a study of elderly adults (older than 60 years of age) with CKD (stages 3-5), Wasén et al. [6] performed a cross-sectional study on elderly adults who were living in the community or institutionalized and found that the cystatin C equation performance was closer to that of the MDRD equation than to that of the CG equation when used to determine the serum creatinine level. Our study found a weak correlation between the MDRD equation results and the serum creatinine and cystatin C concentrations, which also occurred using the CG equation.

The CKD-EPI equation exhibited less bias than the MDRD equation did, especially among individuals with a GFR>60 mL/min/1.73 m^2 [14]. Upon analyzing the pooled data of 16 studies, Stevens et al. [9] found this equation performance to be better among younger individuals (less than 65 years old). In our study, the eGFR yielded by the CDK-EPI creatinine equation only exhibited a satisfactory correlation with the serum creatinine level (which is a variable used in the equation) in group A. The performance of the Larsson equation, which uses the cystatin C level, was found to be better in certain studies [16] but not in all studies [19].

In 2012, Inker et al. [15] found that the CKD-EPI creatinine-cystatin equation precision and accuracy were better than those of the CKD-EPI creatinine and CKD-EPI cystatin equations, although the bias was similar among all the three equations. Kilbride et al. [7] showed that the MDRD, CKD-EPI creatinine, and CKD-EPI creatinine-cystatin equations overestimated the measured GFR, with the CKD-EPI creatinine-cystatin equation exhibiting less bias. The MDRD and CKD-EPI creatinine equations overestimated the GFR when the value was <60 mL/min/1.73 m^2, whereas the CKD-EPI cystatin equation underestimated it. All of the equations overestimated the GFR when it was >60 mL/min/1.73 m^2. However, the performance of all three CKD-EPI equations was better. The CKD-EPI cystatin and CKD-EPI creatinine-cystatin equations exhibited less bias in individuals older than 80 years of age.

Conclusion

In this study, the CKD-EPI equations results, and particularly the CKD-EPI cystatin formula, exhibited better correlations with the serum creatinine and cystatin C concentrations. This finding might have been due to the lower interference of the muscle mass with the serum cystatin C level. Our findings suggest that the CDK-EPI cystatin equation is the most appropriate equation for assessing the renal function in individuals who are 60 or older and particularly those over 80 years old. However, a correlation analysis with the selected standard for this study, i.e., the serum cystatin C level, also showed that the CKD-EPI creatinine equation performance was satisfactory, which has clinical implications, as the serum creatinine concentration measurement is much more accessible and significantly less expensive. We conclude that decreased GFR is a common occurrence among elderly adults, and this population requires a different approach for renal function assessment, as different equations or even different thresholds for altered GFR according to age groups. More studies specifically targeting the elderly population should be performed.

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