Influence of Muscle Mass, Physical Activity and Nutritional Status on Serum Creatinine and Serum Cystatin C in Elderly Population

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ABSTRACT

Introduction: Decreased kidney function is common in elderly persons. Measurement of renal function is important in the diagnosis and management of renal diseases. GFR is the standard measure of renal function. It correlates with renal damage in patients with chronic kidney disease. Measurement of GFR is a complex process but easily estimated using serum creatinine and serum cystatin C based formula. Aim of the study was to address the influence of muscle mass, physical activity and nutritional status on serum creatinine and serum cystatin C and assess the merits of cystatin C over creatinine in estimating renal function in elderly population.

Material and methods: 50 individuals aged 60-70 years attending medicine department were selected for the study. Relevant history was obtained. Anthropometric evaluation was done. Muscle mass, Nutritional status and physical activity was evaluated using body composition analyser, Mini Nutritional Assessment questionnaire, Short Physical Performance Battery protocol respectively. Blood samples were collected for estimating serum creatinine and serum cystatin C.

Results: A significant relation is found between serum creatinine and eGFR from creatinine with body weight, muscle mass, fat free mass and physical activity. Serum cystatin C and eGFR from cystatin C did not show a significant correlation with body weight, muscle mass, fat free mass and physical activity.

Conclusion: Study showed that cystatin c is a better reliable marker than serum creatinine in estimating renal function in elderly population.

Keywords: Serum creatinine, Serum Cystatin C, eGFR

Introduction

The proportion of elderly individuals is growing rapidly in all societies and the incidence of chronic kidney disease among elderly people increases constantly.1 The dramatic increase in prevalence of chronic kidney disease (CKD) with ageing makes the recognition of these patients of paramount relevance in order to implement interventions preventing or delaying the development of CKD complications and end-stage renal disease. Nevertheless, several issues make the diagnosis of CKD in the elderly cumbersome. Among these are age related changes in structures and functions of the kidney, which may be difficult to distinguish from CKD and multimorbidity. Thus, symptoms, clinical finding and laboratory abnormalities should be considered as potential clues to suspect CKD and to suggest screening.2

Measurement of renal function is important in the diagnosis and management of renal diseases. GFR is the standard measure of renal function. It correlates with renal damage in the kidneys of patients with chronic kidney disease, and it therefore reflects overall renal functional capacity. Most functions of the kidney, including endocrine ones i.e., 1,25-dihydroxyvitamin D and erythropoietin synthesis, are directly related to GFR.

In addition, appropriate dosing of drugs excreted by the kidney depends on accurate estimation of GFR. For these reasons, GFR is the most widely accepted measurement for assessing the overall function of the kidney.

Traditional methods for the determination of glomerular filtration rate (GFR) are renal or plasma clearance of suitable exogenous substances such as inulin, radiographic contrast media (e.g. iohexol) or EDTA. Although useful when high precision is necessary, clearance measurements are time-consuming and impractical in acute situations or when a decision on drug dosing based on GFR is required at the bedside.3

Plasma (serum) creatinine is a breakdown product of creatine and phosphocreatine found only in muscle. Despite its long tradition as a marker of GFR, does not accurately reflect renal function, especially in elderly people as it is influenced by body weight, muscle mass, nutritional status, gender, ethnicity, physical activity and in early renal impairment (the
creatinine blind window).

Cystatin C is a proteinase inhibitor eliminated mainly via glomerular filtration and tubular reabsorption and degradation. It is an endogenous filtration marker produced by all nucleated cell. It is being considered as a potential replacement for serum creatinine as it is less influenced by age, sex, muscle mass and diet than creatinine. The serum concentration of cystatin C has been shown to be a more reliable marker for estimating renal function than serum creatinine.\(^4\)

Serum cystatin level, eGFR based on serum cystatin C concentration and comparing with serum creatinine and eGFR based on serum creatinine has not been studied extensively, but seems to be a promising method for evaluating the renal function of elderly patients.

Study aimed to address the influence of muscle mass, physical activity and nutritional status on serum creatinine and serum cystatin C in elderly population and to assess the merits of cystatin C over creatinine in estimating renal function in elderly population.

**MATERIAL AND METHODS**

The present study was conducted in the department of medicine, MVJ Medical College and Research Hospital, Bangalore from June 2017 to May 2019. It was a hospital based observational study. Consent was obtained from the patients participated in the study.

A total of fifty healthy elderly between 60 – 70 years of age group were included in this study. 25 were males and 25 were females. All of them had normal urinalysis. Muscle mass was evaluated using body composition analyser. Nutritional status was evaluated using Mini Nutritional Assessment questionnaire and people were classified as being normal, at risk of malnutrition and malnourished based on the score points obtained. Physical activity was evaluated using Short Physical Performance Battery protocol and people were classified as having very low, low, moderate and high physical activity based on the score points obtained.

Blood samples were collected for estimating serum creatinine and serum cystatin C. Serum creatinine was measured by Jaffe’s calorimetric assay. Serum cystatin C was measured using nephelometry.

**RESULTS**

A total of fifty individuals aged between 60 – 70 years and willing to participate in the study was included. Patients with renal disease, active rheumatological problems, taking steroids, thyroxine and creatine supplement and with congestive cardiac failure were excluded from the study.

50 individuals attending medicine department in MVJ MC & RH were selected in the study as per above mentioned inclusion and exclusion criteria. Relevant history was obtained. Anthropometric evaluation was done. Muscle mass was evaluated using body composition analyser. Nutritional status was evaluated using Mini Nutritional Assessment questionnaire and people were classified as being normal, at risk of malnutrition and malnourished based on the score points obtained. Physical activity was evaluated using Short Physical Performance Battery protocol and people were classified as having very low, low, moderate and high physical activity based on the score points obtained.
status was assessed using Mini Nutritional Assessment (MNA). Physical activity was assessed using Short Physical Performance Battery (SPPB) protocol. The correlations between muscle mass, physical activity and nutritional status with serum creatinine and cystatin C values were analysed using Pearson correlation coefficient.

Serum creatinine was high in people with high physical activity (0.9 ± 0.15 mg/dl) than in people with moderate activity (0.82 ± 0.11 mg/dl) and sedentary life (0.72 ± 0.15 mg/dl).

This change in serum creatinine with changes in physical activity was statistically significant (p=0.002). These changes can be explained by the changes in muscle mass, body weight, fat mass and fat free mass according to physical activity.

People with high physical activity had high muscle mass (16.86 ± 4.02 kg) compared to those with moderate activity (12.36 ± 3.6 kg) and sedentary life (11.15 ± 2.89 kg). The fat free mass was high in people with high physical activity (49.82 ± 8.62 kg) than those with moderate activity (39.55 ± 7.27 kg) and sedentary life (37.33 ± 6.9 kg). This change in fat free mass with physical activity is significant (p=0.000).

The fat mass is high in people with sedentary life (15.16 ± 6.37 kg) compared to those with moderate activity (11.63 ± 3.88 kg). BMI is high in people with high physical activity (24.91 ± 3.3 kg/m²).

Similarly, eGFR measured from serum creatinine values using CG formula was high in people with high physical activity (72.84 ± 12.98 ml/min/1.73 m²) than those with moderate activity (5.12 ± 9.18 ml/min/1.73 m²) and sedentary life (69.5 ± 25.93 ml/min/1.73 m²).

Serum creatinine C did not change with changes in physical activity. It was 1.07 ± 0.16 mg/L in people with sedentary life, 1.08 ± 0.09 mg/L in people with moderate activity and 1.08 ± 0.21 mg/L in people with high physical activity. It was statistically insignificant. (p=0.969).

Similarly, eGFR measured from cystatin C values was nearly constant in people with high (77.97 ± 19.06 ml/min/1.73 m²), moderate (75.69 ± 10.17 ml/min/1.73 m²) and sedentary life (75.46 ± 14.51 ml/min/1.73 m²). It was statistically insignificant. (p=0.869).

Serum creatinine was low (0.72 ± 0.15 mg/dl) in people with low muscle mass (11.15 ± 2.89 kg) and was high (0.9 ± 0.15 mg/dl) in people with high muscle mass (16.86 ± 4.02 kg). It was statistically significant. (p=0.000).

Serum cystatin C did not change with changes in muscle mass. It was (1.07 ± 0.16 mg/L) in people with low muscle mass (11.15 ± 2.89 kg) and (1.08 ± 0.21 mg/L) in people with high muscle mass (16.86 ± 4.02 kg).

Serum creatinine was high in individuals (0.88 ± 0.17 mg/dl) with normal nutritional status and low in individuals who were malnourished (0.85 ± 0.13 mg/dl) with P value of 0.210. Similarly, eGFR was high (70.4 ± 15.35 ml/min/1.73 m²) in people with normal nutritional status and was low (45.85 ± 2.86 ml/min/1.73 m²) in people who were malnourished (p=0.090).

A significant relation was found between serum creatinine and body weight (R²=0.253), (p=0.004), muscle mass (R²=0.312), (p=0.001) and fat free mass (R²=0.307), (p=0.001), 25.3% of variations in serum creatinine values is due to changes in body weight. 31.2% of variations in serum creatinine is due to changes in muscle mass, 30.7% of variations in serum creatinine was due to changes in fat free mass.

The estimated GFR from creatinine has significant relation with body weight (R²=0.472), (p=0.000), muscle mass (R²=0.261), (p=0.003) and fat free mass (R²=0.313), (p=0.001). 47.2% of variations in eGFR from creatinine was due to changes in body weight. 26.1% of variations in eGFR from creatinine was due to changes in muscle mass. 31.3% of variations in eGFR from creatinine was due to changes in fat free mass.

**DISCUSSION**

Accurate detection and staging of chronic kidney disease are integral components of clinical medicine, since such evaluations have a major effect on disease labelling, drug dosages, drug interaction and risk stratification for clinical procedures.

Serum creatinine has been used as a surrogate of GFR based on the assumption that it is produced, filtered and secreted in a steady state.

The Cockcroft Gault equation was then developed to estimate creatinine clearance on the presumption that creatinine clearance was a direct measure of GFR, which is not. The reason is many factors can affect the metabolism of creatinine like creatine in the muscle, rate of secretion of creatinine in the tubules, muscle mass, gender and ethnicity, dietary protein intake, malnutrition, prescribed medications, nonlinear relationship between creatinine and GFR. All these leads to overestimation of GFR.

These limitations of creatinine led to the development of eGFR equations based on other serum biomarkers, one such biomarker is cystatin C, a protease inhibitor that is freely filtered through glomeruli, reabsorbed and degraded by the proximal tubules. Cystatin C levels are not affected by age, muscle mass of the individual. The use of cystatin C improves the role of eGFR in risk categorization, as judged by the risk of death from any cause and to a lesser extent the risks of death from cardiovascular causes and end-stage renal disease.

Most notably, reduced values for cystatin C–based eGFR and eGFR based on combined measurements of creatinine and

| Table-3: Multi variate analysis of covariance adjusted for physical activity and nutrition. | R² | P Value |
|---------------------------------------------|-----|---------|
| Serum creatinine                           |     |         |
| Weight                                      | 0.253 | 0.004  |
| Muscle mass                                 | 0.312 | 0.001  |
| Fat free mass                               | 0.307 | 0.001  |
| Serum Cystatin C                           |     |         |
| Weight                                      | 0.071 | 0.329  |
| Muscle mass                                 | 0.003 | 0.984  |
| Fat free mass                               | 0.009 | 0.934  |
| eGFR creatinine                            |     |         |
| Weight                                      | 0.472 | 0.000  |
| Muscle mass                                 | 0.261 | 0.003  |
| Fat free mass                               | 0.313 | 0.001  |
| eGFR Cystatin C                            |     |         |
| Weight                                      | 0.085 | 0.248  |
| Muscle mass                                 | 0.009 | 0.938  |
| Fat free mass                               | 0.017 | 0.851  |
Serum creatinine and Cystatin C in elderly population. The study showed that muscle mass, nutritional status and physical activity affect the serum creatinine values and not serum cystatin values. Thus, cystatin C is a better marker than serum creatinine in estimating renal function in elderly population.

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