Creatinine based equations and glomerular filtration rate: interpretation and clinical relevance

Ghana Med J 2016; 50(3): 119-121 DOI: http://dx.doi.org/10.4314/gmj.v50i3.1

Introduction

Chronic Kidney Disease (CKD) is now a major public health problem globally, more so in developing countries with Sub-Saharan Africa (SSA) being the most affected sub-region.[1] A systematic review and meta-analysis estimated CKD prevalence in SSA to be 13.9%.[2] In Ghana the true prevalence still remains unknown. The growing burden of CKD in Africa can be largely attributed to the rising prevalence of hypertension, diabetes and chronic glomerulonephritis.[1,3] CKD affects people who are economically productive in the African continent[1]. Aside the heightened cardiovascular morbidity and mortality, CKD imposes huge economic burden on affected individuals and their care takers.[1,3] Additionally patients with CKD suffer from various psychological problems such as depression, anxiety, cognitive dysfunction amongst others.[4,5] Thus the disease, cost of treatment and these psychological problems may lead to poor quality of life. It is therefore imperative to make accurate diagnosis. The diagnosis of CKD is usually made by estimating Glomerular Filtration Rate (GFR). Measuring GFR is relatively cumbersome therefore more simple endogenous variables have been used to estimate renal function. The most commonly used variable is serum creatinine.[6]

Serum Creatinine and Estimated GFR equations

Creatinine based estimated equations used currently for diagnosing CKD include MDRD and CKD-EPI. The use of serum creatinine in estimating GFR is not without limitations. The most important limitation is the dependence of this biological marker on muscle mass. In view of this relationship to muscular mass, serum creatinine concentration and creatinine excretion vary with age, gender and ethnicity independent of changes in GFR.[7,8] Thus several creatinine based equations have been developed taking into account age, gender and ethnicity amongst other variables to estimate GFR.[9,10] As a result serum creatinine level will differ for different ethnicities for the same level of GFR especially among Africans who typically have larger muscular mass than Caucasians and Asians.[11,12] For the same GFR, serum creatinine levels are higher among Africans not because of high muscle mass per se but also because creatinine tubular secretion could be a variable according to ethnicity.[7,13]

Laboratory measurements of serum creatinine levels are subject to calibration bias. This is in reference to the differences in serum creatinine concentrations across various laboratories due to variations in the assay calibration.

This is a very important matter in clinical application of estimated equations especially among people with normal serum creatinine levels.[14,15] A bias of up to 0.37mg/dl (32.7µmol/L) of serum creatinine measurement among laboratories in the United States has been reported.[16] The clinical importance of this difference is shown by the fact that a serum creatinine level of 88µmol/L in one laboratory may represent a value of 112µmol/L in a different one. Applying this value to a 65-year-old African woman using CKD-EPI equation may give GFR ranging from 68.8 to 51.4 mL/min/1.73m^2, which obviously shows a possible decrease in kidney function. This may represent lack of standardization or calibration error among the laboratories. In order to generalize clinical applicability of creatinine based equations to all laboratories, reference materials must be standardized and traceable to a gold standard recognized institutions such as Ghana Standards Board, National Institute of Standards and Technology (NIST) amongst others.

Additionally estimated GFR equations cannot be uniform across the various clinical situations encountered by the physician globally.[16] Evidence shows that the overall performance of MDRD estimated equation is superior to that of Cockcroft-Gault formula in estimating GFR, because the later estimates creatinine clearance and not GFR.[9] More so, Cockcroft-Gault equation was developed among Caucasians and is thus inaccurate for estimating GFR among other ethnic groups.[7,9,17]

When the MDRD equation was introduced in 1999 a correction factor for African Americans was proposed.[18] In recent times Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was published with other ethnic factors.[18,19] While MDRD equation was developed in people with GFR < 60ml/min/1.73m^2, the CKD-EPI was developed taking into consideration those with GFR of > 60ml/min/1.73m^2.[18,19] Recognition of the limitations of these equations is necessary when using the information obtained from them. More so the estimated equation will be clinically relevant in the settings that resemble the population and methods used to develop the equation.

CKD is defined as a progressive loss of kidney function that last for more than three months to years and its classification depends largely on the degree of kidney damage; thus decline in GFR or presence of proteinuria.[20]

Most patients usually visit our consulting rooms already psychologically disturbed because of laboratory results showing their estimated GFRs; it is therefore very important for clinicians to interpret laboratory results with estimated GFR in the context of the patient's clinical situation and not in isolation. Additionally a study by Eastwood et al, assessing GFR among Ghanaians in the Ashanti region using four methods, showed that CKD-EPI appeared to be the most useful.[12]

Conclusion

Estimation of GFR to assess kidney function is appropriate for detection, evaluation and management of Kidney disease, nevertheless these equations should be interpreted in the context of the clinical setting in which it is applied. In addition, acknowledgement and recognition of the limitations of these estimated equations is important. Finally these equations may be more accurately applied in the settings that resemble the original population and methods used to develop the model such as patients with established chronic kidney disease for instance.

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Conflict of interest: None declared

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