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Equations to Calculate Estimated Glomerular Filtration Rate (eGFR)

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Abstract: ***Chronic kidney disease (CKD) is defined by the presence of kidney damage or decreased kidney function for at least three months, irrespective of the cause. The majority of patients with CKD are at risk of accelerated cardiovascular disease and death. The major challenge in preventing kidney disease relates to the early identification of high risk patients. The role of the clinical laboratory to screen, detect, manage and follow CKD is very important. Two variables are of particular interest in this context: glomerular filtration rate (GFR) and albuminuria or proteinuria. According to these two parameters, a diagnosis of CKD will be made and important decisions will be taken regarding therapy. The GFR is generally estimated from serum concentrations of endogenous filtration markers such as creatinine or cystatin C. During the past two decades, automated clinical laboratory reporting of GFR estimated using creatinine (eGFRcr) has become widespread, coincident with increased awareness of CKD. This paper focuses on various equations to calculate estimated GFR (eGFR) in clinical practice based on the serum concentration of endogenous biomarkers and demographic data.***

Keywords: CKD, eGFR, Creatinine, Cockcroft and Gault, MDRD, CKD - EPI

1. Introduction

Chronic kidney disease (CKD) is characterized by the presence of kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m², persisting for 3 months or more, irrespective of the cause [1]. CKD is a state of progressive loss of kidney function, ultimately resulting in the need for renal replacement therapy, such as dialysis or transplantation. The role of clinical laboratory to screen, detect, manage and follow CKD is very important. In the diagnosis of CKD, the estimation of eGFR and albumin (for albuminuria) are very important. Based on these two parameters, a diagnosis of CKD will be made and/or confirmed and also the important decisions will be taken regarding therapy, inscription on the waiting list for kidney transplantation or, at least in part, starting renal replacement therapy [2]. In clinical practice, GFR is most of the time estimated from equations using biological biomarkers and demographic variables like sex, age and for some, weight, height and/or ethnicity. For more than a century, the biomarker used to estimate GFR has been serum creatinine, which is available worldwide and for which assays are standardized and inexpensive [3]. Accurate ascertainment of GFR is crucial for the diagnosis of early kidney disease, which may manifest as hyperfiltration (GFR greater than 2 standard deviations above the mean GFR in normal, healthy individuals [4] or rapid GFR decline (annual GFR loss greater of >3 mL/min/1.73m^2 [5]. An accurate GFR is critical for the diagnosis of CKD (GFR < 60 mL/min/1.73m^2) [6]. The GFR is generally estimated from serum concentrations of endogenous filtration markers such as creatinine or cystatin C. During the past two decades, automated clinical laboratory reporting of GFR estimated with the use of creatinine (eGFRcr) has become widespread, coincident with increased awareness of CKD.

Creatinine - based Equations for Estimating Creatinine Clearance

(1) Cockcroft and Gault equation

The first equation that has been widely used for calculation eGFR is the Cockcroft and Gault equation [7]. This equation was published in 1976 and included serum creatinine, age, gender and weight. The equation was relatively easy to use and to calculate and before the computer era, this simplicity probably explains part of its popularity. The Cockcroft and Gault equation had, however, many limitations: the development cohort included very few women, the equation is supposed to estimate creatinine clearance expressed in mL/min (not measured GFR, expressed in mL/min/1.73 m²) and serum creatinine was measured with an old assay. Even though the Cockcroft–Gault equation is still considered in pharmacology [8], several studies have clearly shown that the Cockcroft and Gault equation was less accurate than modern equations to estimate GFR [9, 10, 11]. Moreover, clinical decisions are based on more recent equations in clinical practice [12]. The Cockcroft – Gault Equation is,

$$CrCl\ (mL/min) = \frac{(140 - \text{Age}) \text{ x Lean Body Weight (Kg)}}{Serum\ Creatinine\ (mg/dl) X72}$$ (X 0.85if female)

(2) Modification of Diet in Renal Disease study (MDRD) equation

In the year 1999 Levey et al., who would later lead the Chronic Kidney Disease Epidemiology (CKD - EPI) consortium, proposed a new equation, the Modification of Diet in Renal Disease study (MDRD) equation. The novelty was that this equation, which is mathematically much more complex than the Cockcroft–Gault equation, did not include the weight variable, but only serum creatinine, age, sex and race [9]. This is of importance because age and sex variables were available in clinical laboratory allowing automatic and systematic reporting of an estimating GFR result along with serum creatinine [13]. This equation has rapidly replaced the Cockcroft and Gault equation in Nephrology. The MDRD equation has been developed from the MDRD cohort in which

GFR was measured by iothalamate urinary clearances. Serum creatinine was measured by a Jaffe assay that was not standardized to the gold standard in the seminal publication [19], but the equation was later recalibrated to be used with standardized, isotope dilution mass spectrometry (IDMS) traceable assays [14]. The MDRD Equation is,

GFR = 186 x Scr - $^{1.154}$ x Age - $^{0.203}$ (x0.742, if female)

After Modification

GFR = 186 x Scr - $^{0.830}$ x Age - $^{0.230}$ (x 0.742, if female)

(3) Chronic Kidney Disease Epidemiology (CKD - EPI) equation

The original CKD - EPI (Chronic Kidney Disease Epidemiology Collaboration) equation was developed in 2009 in an effort to create a more precise formula to estimate glomerular filtrate rate (eGFR) from serum creatinine and other readily available clinical parameters, especially at when actual GFR is > 60 mL/min per 1.73m ^{2}. A subsequent revision of this equation was published in 2021. The 2021 version, which is used by this tool, revised the equation based on more data and removed the racial component from the equation, which was found to overestimate GFR, especially in Black patients [15]. The CKD - EPI equations performed better than the MDRD (Modification of Diet in Renal Disease Study) equation, especially at higher GFR, with less bias and greater accuracy [16]. The CKD - EPI Equation 2021 is, eGFR = 142 x min (standardized Scr/K, 1) $^{\alpha}$ x max (standardized Scr/K, 1) - $^{1.200}$ x 0.9938 $^{\text{age in years}}$ x 1.012 [if female]

where,

- Scr = serum creatinine in mg/dL
- K = 0.7 (females) or 0.9 (males)
- α = - 0.241 (females) or - 0.302 (males)
- min (standardized Scr/K, 1) = the minimum of Scr/K or 1
- max (standardized Scr/K, 1) = the maximum of Scr/K or 1

2. Conclusion

Assessment of GFR is essential to accurately diagnose kidney disease. GFR is difficult and impractical to measure directly with current methodologies and estimates of GFR by serum creatinine is most accurate. The approach of screening for any underling kidney damage has been facilitated and become routinely available with the advent of calculating the eGFR from serum creatinine based equation that to be taken into consideration of a number of patient's characteristics. By this approach, the result of serum creatinine is converted into physiological units of GFR. The creatinine - based calculated eGFR has improved the validity of serum creatinine which is considered alone an insensitive index of glomerular function whereby at least approximately 50% of glomerular function has to be lost before creatinine is raised in the blood.

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