eGFR: WHAT THE INTERNIST SHOULD KNOW

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DEFINITION

Glomerular filtration rate (GFR) is the total amount of plasma that is ultrafiltered across all the glomeruli of both the kidneys in unit time. Estimated glomerular filtration rate (eGFR) is a calculated estimate of the glomerular filtration rate and is therefore also referred to as the calculated GFR. eGFR has come into use over the last decade because it is easy to calculate and is a convenient substitute for the measured GFR which is not to easy to determine and requires measurement of clearance of substances such as inulin, creatinine, radioisotope (Tc-DTPA, Cr-EDTA) and radiopaque agents (iothalamate, iohexol) from the plasma. These measurements are not entirely accurate and cumbersome to carry out.

METHOD OF CALCULATION

The commonest method used for calculating the eGFR depends on the abbreviated MDRD (Modification of Diet in Renal Disease) equation. This equation uses four variables viz. serum creatinine, age, sex and race to calculate the eGFR. The calculation is often done by the laboratory carrying out the serum creatinine estimation and reported along with it. Otherwise web based calculators on websites such as nephron.com can be used when the values of the variables are known. The normal eGFR is about 100ml/min/1.73m². eGFR of a well functioning transplanted kidney is only about 60ml/min since it is a single functioning kidney. The routine reporting of eGFR with each measurement of serum creatinine has identified large numbers of patients with hitherto undiagnosed chronic kidney disease (CKD).

An important caveat while using the MDRD formula is that its accuracy is dependent on the accuracy of measurement of serum creatinine. The accuracy of serum creatinine measurement is a problematic area because of significant inter-assay and intra-assay variations. The original MDRD equation used serum creatinine values measured by a kinetic alkaline picrate assay. Isotope dilution mass spectrometry (IDMS) is presently the reference method, and assay methods are being revised to produce results aligned with this method.2 The eGFR is only an estimate and is particularly unreliable in amputees, children, pregnant women and malnourished patients. The confidence intervals are quite wide with 90% of individuals having a measured GFR within 30% of eGFR. The abbreviated MDRD equation underestimates GFR at near normal levels of GFR. Also a stable serum creatinine is a pre-requisite for using the equation which rules out its use in the setting of acute kidney injury.

The other widely used equations for calculating eGFR are the Cockcroft-Gault, CKD-Epi and Rule’s equations.3,4,5 The formulae are given in table 1 with serum creatinine expressed in mg/dl. The Cockcroft-Gault equation in fact gives the creatinine clearance. It is simple to calculate but needs to be corrected for body surface area. There are in fact eight CKD-Epi equations based on race, sex and serum creatinine. The one given in the table is for a black female with serum creatinine less than 0.7 mg/dl. The CKD-Epi equation reportedly performs better than the MDRD equation at normal or near normal GFR. Other equations in use include the Mayo quadratic equation. The Rule’s equation is based on measurement of cystatin C (in mg/l). Some new formulae use both serum creatinine and cystatin C measurements to calculate eGFR.

In children the most widely used equation is the Schwartz formula, originally given in 1976. The equation is as follows:

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12 : 3
eGFR = k x height (in cm)/S. creat (in mg/dl)

k is a constant which equals:

- 0.33 in preterm neonates
- 0.45 in term neonates
- 0.55 in boys 1-12 years of age and girls 1-18 years of age
- 0.70 in boys 13-18 years of age

In 2009 the above equation was simplified. (7) It is as given below:

eGFR = 0.413 x height (in cm)/S. creat (in mg/dl)

or

eGFR = 36.5 x height (in cm)/S. creat (in µmol/l)

**UTILITY:**

The principal utility of eGFR is in staging CKD. CKD is defined by the National Kidney Foundation (NKF) as:

- Kidney damage for three or more months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by pathologic abnormalities or markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests
- GFR < 60 mL per minute per 1.73 m² for three months or more, with or without kidney damage.⁸

Based on levels of eGFR, a proposed staging of CKD is as shown in table 2.⁹ Increasing stages denote increasing severity of decrease in GFR and hence disease severity. The progression of CKD can be ascertained by serial estimations of eGFR. A decreasing eGFR can alert the physician to look for and manage complications of CKD like hypertension, anemia, bone disease, malnutrition which are largely asymptomatic in the early stages. Referral to a nephrologist is recommended once the eGFR falls below 30 mL/min/1.73m². Dose adjustment for drugs is also facilitated by eGFR estimates.

eGFR has been used, frequently with other variables to develop risk scores for both progression of CKD ("renal risk score") and cardiovascular disease ("CV risk score"). For example, a recently published study used serial estimates of eGFR, age, urinary albumin excretion, systolic BP, C-reactive protein, and known hypertension to develop and validate a renal risk score to identify individuals at increased risk of progressive CKD.¹⁰ Another study used data from the Third National Health and Nutrition Examination Survey (NHANES III) of 14,586 US adults followed up for 13 years. The authors concluded that moderately decreased estimated GFR and albuminuria independently predict cardiovascular and all-cause mortality in the general population.¹¹

CKD is highly prevalent in the general population. According to the Third National Health and Nutrition Examination Survey (NHANES III) the prevalence of CKD in the US adult population was 11% (19.2 million). (12) By stage, an estimated 5.9 million individuals (3.3%) had stage 1, 5.3 million (3.0%) had stage 2, 7.6 million (4.3%) had stage 3, 400,000 individuals (0.2%) had stage 4, and 300,000 individuals (0.2%) had stage 5, or kidney failure. A recent Indian study by Verma et al. also found a similar high prevalence of CKD stages 1 to 3 in apparently healthy adults.¹³ The study was conducted in 3,398 adults with 66% of the participants being males and 34% being females. eGFR was calculated using both the MDRD and CKD-Epi equations. The results are summarized in table 3.

It must be borne in mind that though used in individual cases; none of the above equations for calculating eGFR has been validated in Indian subjects. Because of lower muscle mass, Indians are likely to have lower serum creatinine levels. Large scale studies are required to validate the above equations in the Indian population.

**REFERENCES**

1. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A


