[A **technical** review]

Estimated Glomerular Filtration Rate (eGFR)
in the Detection and Assessment of Chronic Kidney Disease in Adults

Introduction

In February 2007, the National Kidney Disease Education Program (NKDEP) published the revised Suggestions for Laboratories as a guideline for all parties interested in accurately reporting eGFR. This document is updated with the most recent recommendations on creatinine methods calibration to be traceable to an isotope dilution mass spectrometry (IDMS) reference method.[10] The NKDEP in collaboration with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Communities Confederation of Clinical Chemistry (EC4), has launched the Creatinine Standardization Program to reduce interlaboratory variation in creatinine assay calibration and provide more accurate estimates of eGFR by employing prediction equations that incorporate serum creatinine measurements.[3-6,12]

To assist in earlier recognition of CKD, it is strongly recommended that clinical laboratories automatically report eGFR, along with values for serum creatinine, when serum creatinine is measured.[10] The eGFR is based on the abbreviated Modification of Diet in Renal Disease (MDRD) study equation[4,5] that adjusts for body surface area without requiring measurement of height, weight, or 24-hour urine collection. This method of determining eGFR was judged preferable to using serum creatinine alone or measuring creatinine clearance.[1] The guidelines also emphasize the estimation of GFR for early detection of CKD, classification of CKD severity, estimation of disease progression, management of complications, and initiation of referral to nephrologists.[11]

Interpretation of GFR Estimates

Normal GFR in young adults is approximately 120 to 130 mL/min/1.73 m[2] and declines with age. A GFR of <60 mL/min/1.73 m[2] for three or more months is defined as CKD, irrespective of age and cause, because of its association with increased risk of adverse outcomes (Table 1). Other criteria for CKD is kidney damage for at least three months, as defined by structural or functional abnormalities of kidney, with or without decreased GFR (pathological abnormalities or abnormalities of kidney damage markers, including blood, urine, or imaging tests).[2] Proteinuria is the most common marker of kidney damage. Other markers may include the findings of RBCs and/or WBCs in urine sediment.

GFR may be reduced due to conditions other than CKD. This includes pregnancy, kidney perfusion alterations (heart failure, cirrhosis), extracellular fluid volume alterations, level of arterial blood pressure, acute protein load and habitual protein intake, blood glucose control in diabetics, nonsteroidal anti-inflammatory and antihypertensive drugs.[13]

The serum creatinine concentration can be falsely elevated due to drug-induced inhibition of creatinine secretion (trimethoprim, cimetidine), interference with the alkaline picrate assay for creatinine (ketones, ketoacids, some cephalosporins) or creatinine supplementation.[2,10] In these circumstances, GFR estimates will be falsely low. More accurate GFR estimates can be obtained by repeating the measurement of serum creatinine after discontinuation of the drug or resolution of the clinical condition.

The guidelines recognize limitations to estimating GFR from prediction equations and identify clinical conditions in which it may be necessary to measure GFR using clearance methods. This includes severe malnutrition or obesity, skeletal muscle disease, paraplegia or quadriplegia, vegetarian diet, rapidly changing kidney function, and prior to dosing toxic drugs that are excreted by the kidneys.[14]

Table 1. Association of Glomerular Filtration Rate (GFR) and Staging of Kidney Disease*		
GFR (mL/min/1.73 m²)	With Kidney Damage	Without Kidney Damage
≥ 90	Stage One	Normal
60-89	Stage Two	"Decreased GFR"
30-59	Stage Three	Stage Three
15-29	Stage Four	Stage Four
<15 (or dialysis)	Stage Five	Stage Five

*Each stage assumes the associated GFR level has been in effect for at least three months. Shaded areas above indicate kidney disease.[2]

Limitations

The MDRD study equation has not been validated in diabetic kidney disease, in patients with serious comorbid conditions, or in individuals who are younger than 18 and older than 70 and will underestimate eGFR in normal healthy adults.[7] The equation also may not be accurate in patients at the extremes of body size or composition. Validation studies are in progress to evaluate the MDRD study equation for additional ethnic groups, the elderly, various disease conditions, and people with normal kidney function.[10]

GFR estimate can be interpreted only during a "steady state" of creatinine balance. The GFR estimate will overestimate true GFR if serum creatinine is rising (such as in acute kidney failure) and will underestimate true GFR if serum creatinine is declining (as in resolution of acute kidney failure).

Since the validation of the MDRD equation occurred in patients with CKD, eGFR results that approach 60 mL/min/1.73 m^2 or below, are accurate and do reflect diminished renal function.

Estimated Glomerular Filtration Rate (eGFR) 100768

Synonyms eGFR; GFR, Estimated;

Test Includes Creatinine, serum; eGFR calculation

Specimen Serum

Volume 1 mL

Minimum Volume 0.5 mL

Container Gel-barrier tube or transport tube

Collection Separate serum from cells within 45 minutes of collection.

Storage Instructions Maintain specimen at room temperature.

Causes for Rejection Hemolysis; improperly labeled specimen

Reference Interval >59 mL/minute/1.73 m^2

Note: The estimated GFR is multiplied by 1.212 in the cases of patients who are African-American.

Limitations The MDRD equation provides a good estimation of the true GFR and reflects diminished renal function. It has been validated for optimal performance in adult patients between 18 and 70 years of age with chronic kidney disease and eGFR results that approach 60 mL/minute/1.73 m2 or below. The following conditions may alter the eGFR result: extremes in body size, severe malnutrition, skeletal muscle disease, paraplegia or quadriplegia, vegetarian diet, pregnancy, and rapidly-changing kidney function.

Methodology Kinetic

For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.

References

1. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: New insights into old concepts. *Clin Chem*. 1992; 38(10):1933-1953.

2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. *Am J Kidney Dis*. 2002; 39(Suppl 1):S1-S266.

3. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976; 16:31-41.

4. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D for the Modification of Diet in Renal Disease Study Group. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. *Ann Intern Med*. 1999; 130(6):461-470.

5. Levey AS, Greene T, Kusek JW, Beck GJ, Group MS. A simplified equation to predict glomerular filtration rate from serum creatinine. [abstract] *J Am Soc Nephrol*. 2000; 11:A0828.

6. National Kidney Foundation. Chronic kidney disease: Developing a clinical action plan. New York, NY: National Kidney Foundation. Available at www.kidney.org/professionals/doqi/action_plan_web.html. Accessed: January 2003.

7. Rule AD, Larson TS, Bergstralh EJ. Using serum creatinine to estimate glomerular filtration rate: Accuracy in good health and in chronic kidney disease. *Ann Intern Med*. 2004; 141(12):929-937.

8. Levey AS, Beto JA, Coronado BE, et al. Controlling the epidemic of cardiovascular disease in chronic renal disease: What do we know? What do we need to learn? Where do we go from here? *Am J Kidney Dis*. 1998; 32(5):853-906.

9. United States Renal Data System. Excerpts from the 2000 US Renal Data System Annual Data Report: Atlas of end stage renal disease in the United States. *Am J Kidney Dis*. 2000; 36:S1-S279.

10. NKDEP - Resources. Suggestions for Laboratories. (Revised February 2007) http://nkdep.nih.gov/resoruves/laboratory_reporting.htm.

11. NKDEP Launches Creatinine Standardization Program. *Clinical Laboratory News*. 2006 Apr; 32(4).

12. NKDEP - Laboratory Professionals. Creatinine Standardization Program. Recommendations for Clinical Laboratory. Available at http://nkdep.nih.gov/labprofessionals/Clinical_Laboratories.htm.

13. Levey AS. Clinical evaluation of renal function. In: Greenberg A, Cheung AK, Coffman TM, Falk RJ, Jennette JC. *Primer on Kidney Diseases*. 2nd ed. San Diego, Calif: Academic Press; 1998:21.

14. Levey AS. Clinical evaluation of renal function. In: Greenberg A, ed. *Primer of Kidney Diseases*. San Diego, Calif: Academic Press; 1994:20-26.

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