Controversies Regarding the Value of Estimated Glomerular Filtration Rate (eGFR) To Identify and Monitor Chronic Kidney Disease

(Link to chapters 44 and 46)

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Most clinicians have been trained to estimate renal function by simple equations (e.g., Cockcroft-Gault, Jelliffe), which incorporate patient parameters such as body weight, age, gender, and serum creatinine. Although these equations are somewhat useful for estimating drug doses in renal impairment, they are inaccurate measures of renal function in certain circumstances and do not provide reliable estimates of the true glomerular filtration rate (GFR). Consequently, more accurate and reliable estimates of GFR are needed.

In early 2002 the National Kidney Foundation published the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines in which a classification system for the severity of chronic kidney disease (CKD) was proposed.[4] This classification system was primarily based on a recently proposed methodology (MDRD 4-variable equation) for estimating glomerular filtration rate (eGFR), which was derived from measured GFR values in 1642 patients who participated in the National Institutes of Health-sponsored modification of diet in renal disease (MDRD) study.[5] The National Kidney Foundation has aggressively championed to clinical laboratories the value of routinely calculating the eGFR and reporting it to clinicians every time

they order a serum creatinine, as a means of screening patients for the presence of CKD and to monitor the progression of pre-existing CKD. Although clinicians have long appreciated the strong relationship between measured serum creatinine values and "renal function," up until recently they had to calculate an estimated creatinine clearance (eCLcr) by hand to use a continuous measure to gauge a patient's renal function status. The routine reporting of eGFR with serum creatinine has thus been well accepted by clinicians because it frees them from this calculation.

However, eGFR values do not provide an accurate estimate of renal function for all patients or all purposes (e.g., drug dosage adjustment).[1] The reported value must be interpreted in light of the patient's condition, age, gender, renal function stability, nutritional status (e.g., obesity or cachexia), and the fact that values greater than 60 mL/min per 1.73 m^2 are not reliable. The validity and utility of the eGFR values as a tool to identify the presence as well as stage the severity and monitor the response of chronic kidney disease (CKD) to pharmacotherapeutic interventions has been questioned by two recent reports.[2,3]

A multi-ethnic study of atherosclerosis baseline renal function data from 6747 men and women between the ages of 45 and 85 who self-reported their race/ethnicity as Chinese (n=798), Hispanic (n=1485), Black (n=1870) and Caucasian (n=2594), was used to compare the prevalence of CKD when the creatinine-based MDRD equation was used versus two eGFR estimates derived from serum cystatin C measurements.[2] For each individual, the classification was: *Yes, has CKD*, if the eGFR was less than 60 mL/min per 1.73 m^2, or *No, does not have CKD*, if the eGFR exceeded this value. At the time of study enrollment and CKD classification, none of the participants had any evidence of clinical cardiovascular disease. The CKD prevalence

estimates with the three eGFR equations varied by as much as three-fold among Caucasian women and Chinese men and two-fold in the Chinese and Hispanic women populations. The degree of variability was lower but still marked in the other ethnic and gender groups: 22% to 44%. Because this study did not use a "gold standard" methodology to determine GFR, it is not possible to determine which of the evaluated eGFR methods is the most accurate or reliable. The authors concluded that the substantial differences in CKD prevalence across these racial/ethnic groups, coupled with the high degree of variability based on the method utilized to determine eGFR, strongly suggests the need for further research to determine the accuracy and precision of eGFR equations in racially diverse populations. This variability in single eGFR values further weakens support for the application of any one of these methods as a screening tool to characterize the prevalence of CKD.

Although some authorities have expressed confidence in the accuracy of the MDRD eGFR equation as a clinical tool to monitor the progression of CKD in individual patients, the recent report of Xie et al.[3] casts serious doubt on this foundational utility. Their retrospective study evaluated 542 MDRD study participants who had measured Glomerular Filtration Rate (mGFR) values ranging from 25 to 55 mL/min per 1.73 m^2 at study entry and two or more mGFR determinations during the subsequent 1.5- to 4-year chronic phase of the study. Urinary iothalamate clearance was the basis for the mGFR, and changes in mGFR and eGFR over time were assessed by within-subject linear regression. The slope of the eGFR-over-time relationship underestimated by 28% the actual decrements in GFR, characterized by the mGFR relationship. The absolute mean values of the slopes were: eGFR –2.8 mL/min per 1.73 m^2 per year, mGFR –3.9 mL/min per 1.73 m^2 per year. Although in almost 60% of the patients the differences

between eGFR relative to mGFR were within +/- 2 mL/min per 1.73 m^2 per year, the difference exceeded 4 mL/min per 1.73 m^2 per year in almost 20% of the patients. The degree of inaccuracy associated with the eGFR slope assessment is large compared with the previously published range of slope values. This is particularly distressing since the eGFR equation was developed in this population. Thus, this limited degree of accuracy is likely the best performance that one can anticipate when utilizing this approach to monitor the progression of CKD. These investigators concluded that clinicians should use caution when interpreting eGFR slope as a market of CKD progression. These two reports of emerging evidence suggest clearly that clinicians should recognize that eGFR is not the ultimate way to identify and stage the severity of renal disease nor monitor its progression or response to therapeutic interventions.

References

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