Popular Prediction Equation Underestimates Glomerular Filtration Rate

Rule AD, Larson TS, Bergstralh EJ, et al. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and chronic kidney disease. Ann Intern Med 2004;141:929–37.

Study Overview

Objective. To determine the accuracy of using the Modification of Diet in Renal Disease (MDRD) equation to estimate glomerular filtration rate (GFR) in healthy subjects compared with those with chronic kidney disease (CKD).

Design. Retrospective cohort study.

Setting and participants. Single institution involving 580 healthy patients with no kidney disease and 320 patients with clinically diagnosed CKD. All patients received an iothalamate clearance test to verify GFR, either as part of an evaluation for potential kidney donation (healthy patients) or as an evaluation for known or suspected kidney disease (CKD patients).

Main outcome measures. Iothalamate clearance test results were used as the gold standard for measuring GFR. GFR was then estimated using measured serum creatinine and the MDRD equation, which incorporates patient age, gender, and race.

Main results. The mean measured GFR was 101 mL/min/1.73 m^2 among healthy patients and 48 mL/min/1.73 m^2 among CKD patients. Among CKD patients, 53% had native kidney disease alone (including hypertensive kidney disease, glomerulopathy, and diabetes), 31% had a kidney transplant alone, and 16% had a non-kidney solid organ transplant with or without a kidney transplant. The MDRD equation more accurately predicted GFR in patients with CKD (correlation coefficient [R^2] = 0.79) than in healthy patients (R^2 = 0.186). The MDRD equation systematically underestimated GFR in healthy patients by 26%. A new quadratic equation was derived to estimate GFR independent of kidney disease status, which achieved an R^2 of 0.86 (see below).

Conclusion. In this single center series, the commonly used MDRD equation performed well in estimating GFR among patients with CKD; however, it significantly underestimated renal function in healthy patients.

Commentary

CKD represents a fast-growing disease epidemic, with recent reports indicating that 20 million people (over 10% of the U.S. population) have some form of renal dysfunction [1]. The high prevalence of CKD contributes to an increasing burden of dialysis-dependent kidney disease as well as increased cardiovascular disease. This has led to recent guidelines defining evaluation and treatment goals for CKD, including recommendations for automated reporting of estimated GFR based on the MDRD equation [2].

The study by Rule et al highlights an important aspect of the evaluation of CKD by analyzing the accuracy of our main diagnostic tool: estimated GFR using serum creatinine. Although iothalamate clearance tests may represent the gold standard for measuring GFR, they are cumbersome to implement in a busy primary care setting, and an accurate surrogate measure using the more easily obtained serum creatinine would likely increase the routine use of GFR in patient management. Rule et al found that although the MDRD equation is indeed accurate for patients with CKD, it may underestimate kidney function in healthy patients. This has important implications for screening programs for patients with no known kidney disease but significant risk (eg, those with longstanding diabetes or hypertension). This new analysis provides an estimating equation that appears to be more accurate across a broader range of measured GFRs.

There are important limitations to this study noted by both the authors and an accompanying editorial. The data represent a convenience sample from a single institution, and therefore, it is not clear that the results can be general-

$$\text{GFR} = \exp\left(1.911 + \frac{5.249}{\text{Creatinine}} - \frac{2.114}{\text{Creatinine}^2} - 0.00686 \times \text{Age} - 0.205\ [\text{female}]\right)$$

(Note: if creatinine < 0.8 mg/dL, use 0.8).

ized to the U.S. population. Of note, almost no minority individuals were included in this analysis, and these populations often carry a disproportionate CKD burden. In addition, since there are no current screening recommendations that involve all healthy individuals, it would be important to know the accuracy of the more established MDRD equation among healthy patients with significant risk factors for CKD that may prompt screening by clinicians.

Applications for Clinical Practice

CKD is an area of growing concern in the U.S. health care system, and effective programs to evaluate and treat this condition are needed. Although this study sheds light on important limitations to our current methods of estimating renal function, future studies across more diverse clinical practice settings are needed to validate the findings.

–Review by Thomas D. Sequist, MD, MPH

References

1. Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003;41:1–12.
2. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification [published erratum appears in Ann Intern Med 2003;139:605]. Ann Intern Med 2003;139:137–47.