

Automatic Reporting of the Estimated Glomerular Filtration Rate (eGFR)

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Chronic Kidney Disease as a Public Health Threat

Although the prevalence of end-stage kidney disease (ESKD) in the United States has stabilized over the last 2-3 years at 400 000 patients, it has been estimated that as many as 13% (26.3 million) of the population of the United States has chronic kidney disease (CKD).¹ While approximately 15.5 million Americans have stage 3 and approximately 10.1 million have stage 1 or 2 CKD, recent evidence suggests that as many as 80% of patients with stage 3 CKD are not aware of having this diagnosis.¹⁻³ It is widely acknowledged that CKD progresses to ESKD, yet the risk for progression is about 4 times higher in African Americans, and overall, the percentage of patients with CKD progressing to ESKD is 3 times greater in the US than in Norway.^{2,3} While precise data are not available for the state of North Carolina, one can safely assume that at least 450 000 individuals in our state have stage 3 CKD, an equal number have stage 2 CKD, and approximately 35 000 have either stage 4 or 5 CKD.¹ This population of CKD patients in North Carolina is at risk for progression to ESKD or dying from cardiovascular disease before reaching dialysis.

Chronic kidney disease represents a public health threat due to (1) the high burden of the disease; (2) the evidence that the problem is distributed unfairly with regard to ethnicity; (3) the undisputed evidence that upstream preventive strategies could reduce the burden of the condition; and (4) the fact that preventive strategies are not yet in place.^{3,4}

Two Simple Diagnostic Tests to Diagnose CKD Earlier

Because CKD is a progressive disease, it must be diagnosed earlier in the course of the disease to facilitate the initiation of appropriate therapy in order to slow progression to ESKD. The

National Kidney Disease Education Program (NKDEP) has emphasized the importance of 2 simple tests to identify those patients with CKD:⁵

1. The urine albumin to creatinine ratio on a voided, untimed urine specimen
2. An estimated glomerular filtration rate (eGFR) from the serum creatinine using the MDRD (Modification of Diet in Renal Disease) study equation⁶⁻⁹

“...a wider availability of eGFR will be a necessary first step in the accurate diagnosis and treatment of this devastating illness.”

Although the serum creatinine is the usual means of assessing kidney function, the creatinine concentration in isolation has a complex relationship to the GFR. Failure to recognize CKD at an early stage may result in the failure to prescribe medication proven to slow the progression of CKD.^{5,9,10-13}

The Estimated Glomerular Filtration Rate (eGFR)

The eGFR calculation from the MDRD equation requires the following variables: the serum creatinine, age and sex of the individual, and designation of whether the patient is African American or not.⁶ Moreover, the MDRD formula for eGFR is simple, straightforward, and does not necessitate a 24-hour urine collection. This equation is available through a number of electronic resources,⁷ can be easily downloaded and incorporated

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into laboratory computer-based reporting systems, and can be calculated instantaneously by supplying the 4 variables whenever the serum creatinine is measured. The MDRD eGFR is the most thoroughly evaluated and validated equation available to date.¹⁴ While the method is less accurate with higher values for eGFR (>60), it is currently being evaluated additionally in individuals with a normal GFR.

What Subspecialty Societies Recommend

A number of subspecialty societies and organizations including the American Society of Nephrology, the American Diabetes Association, the American Association of Clinical Chemistry, the College of American Pathologists, and the National Kidney Disease Education Program, have emphasized that automatic eGFR reporting is the most desirable method of identification of patients with CKD. The National Kidney Disease Education Program has recommended the routine use of the eGFR instead of the serum creatinine alone in order to more accurately assess kidney function and thus the presence of CKD in adults over the age of 18.¹⁵

Given concerns about the precision of the MDRD formula for eGFR values greater than 60 mL/min/1.73m², it has been recommended specifically that laboratories should report the calculated eGFR (when calculated as above 60 mL/min) as ">60" rather than denoting the actual calculated value.^{7,8,16}

Why Should We Screen for CKD?

Since chronic kidney disease generally progresses in the absence of symptoms, early detection of CKD is critically important for both surveillance and for the implementation of specific strategies to slow progression. That this silent disease is both underdiagnosed and undertreated can be attributed in part to the fact that kidney function is not intuitively evident from measurement and reporting of the serum creatinine alone. A case study approach to test the physician's ability to assess the patient's kidney function from interpretation of a serum creatinine was recently shown to be associated with systematic overestimation of kidney function.¹⁷ Routine reporting of the eGFR for all serum creatinine determinations by hospital, commercial, and physician office clinical laboratories has been recommended.^{5,18} When this practice has been adopted voluntarily, physician appreciation of the diagnosis of CKD has improved significantly.^{11,19}

How Prevalent is eGFR Reporting?

Despite such effort, it is likely that only 35% of clinical laboratories calculate and report the eGFR routinely, while adoption of this practice by physician office laboratories is even lower. One can conclude, therefore, that the majority of laboratories in the United States are not reporting eGFR. Such data are of concern because a low acceptance of automatic reporting of eGFR creates the potential for significant underrecognition of chronic kidney disease and missed opportunities to both

diagnose this condition, and to provide appropriate and proven therapy to slow the progression of CKD.

Risk Factors for CKD

The risks for chronic kidney disease include diabetes mellitus, hypertension, cardiovascular disease, obesity, older age, proteinuria, the presence of peripheral vascular disease, cigarette smoking, hypercholesterolemia, sedentary lifestyle, dietary salt intake, and a history of receiving nephrotoxic drugs or contrast agents.^{12,13,20} Of the 100 000 new end-stage kidney disease patients in the United States annually, 42% have diabetes mellitus, and 90% of the diabetics have type 2 diabetes mellitus.^{20,21} Since the prevalence of type 2 diabetes mellitus is growing at a significant rate, progressively larger numbers of patients are at risk for developing CKD. Therefore surveillance for the presence of CKD is extremely important in the diabetic population. It would be prudent to measure the urine albumin to creatinine ratio and the eGFR annually in this at-risk population, especially in those with type 2 diabetes or a family history of ESKD.^{22,23}

When There Is No Surveillance, There Is No Recognition or Treatment

Given the low level of automatic eGFR reporting, it should not be surprising that, based on Medicare enrollment and claims data, it appears that some primary care practices screen no more than 20% of Medicare patients with diabetes for the presence of CKD through application of the eGFR or microalbumin excretion.²⁴ In addition, less than one-third of those patients diagnosed with CKD receive an Angiotensin-Converting Enzyme (ACE) inhibitor or an Angiotensin Receptor Blocker (ARB).²⁴

CKD and CVD: Dual Risk Factors

Chronic Kidney Disease should be recognized and treated as early as possible because of the increasing prevalence of both CKD and ESKD and because CKD is a major and independent risk factor for the presence and progression of cardiovascular disease (CVD).^{25,26} The majority of patients with stages 2 and 3 CKD die from CVD before progressing to ESKD. A mortality rate of approximately 24% has been observed for stage 2 and stage 3 chronic kidney disease, but the mortality rate reaches 45% for stage 4 CKD. The reverse relationship has also been proven recently: CVD is associated with a higher prevalence of CKD.²⁷ As many as 23% of patients with coronary artery disease, 33% of patients with acute myocardial infarction, and 46% of patients with congestive heart failure have an eGFR of less than 60 mL/min.²⁸⁻³⁰

Who Should Care For CKD Patients?

Based on the growing population of patients in the United States with stage 3 or higher CKD (15.5 million) and with only

5000 full-time practicing nephrologists, there is an inadequate nephrology workforce to provide care for these patients without the involvement of primary care physicians.¹⁹ It is important, therefore, that primary care physicians develop an increasing awareness of the diagnosis of chronic kidney disease. The North Carolina Institute of Medicine has recommended that all physicians encourage clinical laboratories to provide and report an estimated GFR every time a serum creatinine is ordered.³¹ These same providers are encouraged to work with nephrologists in partnership to provide testing and treatment for CKD. A practical disease management paradigm for the coordinated care of chronic kidney disease involving both primary care and nephrology physicians is badly needed.

Voluntary Versus Mandatory Reporting

Statutory language has been adopted in a few states requiring calculation of the eGFR for all determinations of serum creatinine by clinical laboratories.³² The College of American Pathologists and the National Kidney Foundation issued a joint statement, and the American Medical Association adopted a resolution, opposing mandating automatic reporting through state statutes.^{33,34} Concern was voiced regarding automatic reporting of eGFR as an example of legislative mandate of clinical practice. It should be emphasized that neither group opposes the voluntary adoption of eGFR reporting.

A recent workgroup on automatic GFR reporting was

convened as a component of the North Carolina Institute of Medicine Task Force on Chronic Kidney Disease. This workgroup recommended that clinical laboratories in North Carolina be encouraged to report eGFR values on all creatinine determinations voluntarily rather than through a legislative mandate. However, because the diagnosis and staging of chronic kidney disease requires knowledge of a value for GFR, the full task force strongly supported that laboratories automatically calculate eGFR whenever the provider orders a creatinine measurement. Furthermore, the task force recommended that if North Carolina laboratories do not voluntarily begin computing the eGFR on all creatinine determinations, the General Assembly should mandate automatic reporting.

Conclusion

With wider adaptation of automatic reporting of eGFR, a more evidence-based and coordinated method of care can be adopted more widely. Several professional societies are planning to develop a paradigm for the coordinated management of CKD by primary care physicians and nephrologists. While such an approach will be necessary because of the need for primary care coordination of chronic disease management, it is clear that a wider availability of eGFR will be a necessary first step in the accurate diagnosis and treatment of this devastating illness. **NCMJ**

REFERENCES

- Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298(17):2038-2047.
- Coresh J, Byrd-Holt D, Astor BC, et al. Chronic kidney disease awareness, prevalence, and trends among US adults, 1999 to 2000. *J Am Soc Nephrol*. 2005;16(1):180-188.
- Schoolwerth AC, Engelgau MM, Hostetter TH. A public health action plan is needed for chronic kidney disease. *Adv Chronic Kidney Dis*. 2005;12(4):418-423.
- Schoolwerth AC, Engelgau MM, Hostetter TH, et al. Chronic kidney disease: a public health problem that needs a public health action plan. *Prev Chronic Dis*. 2006;3(2):A57.
- Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Ann Intern Med*. 2003;139(2):137-147.
- Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130(6):461-470.
- GFR MDRD calculators for adults (conventional units). National Kidney Disease Education Program Web site. http://nkdep.nih.gov/professionals/gfr_calculators/orig_con.htm. Updated December 19, 2007. Accessed March 10, 2008.
- Verhave JC, Baljé-Volkers CP, Hillege HL, de Zeeuw D, de Jong PE. The reliability of different formulae to predict creatinine clearance. *J Intern Med*. 2003;253(5):563-573.
- Myers GL, Miller WG, Coresh J, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem*. 2006;52(1):5-18.
- Akbari A, Swedko PJ, Clark HD, et al. Detection of chronic kidney disease with laboratory reporting of estimated glomerular filtration rate and an educational program. *Arch Intern Med*. 2004;164(16):1788-1792.
- Quartarolo JM, Thoeke M, Schafers SJ. Reporting of estimated glomerular filtration rate: effect on physician recognition of chronic kidney disease and prescribing practices for elderly hospitalized patients. *J Hosp Med*. 2007;2(2):74-78.
- Owen WF Jr. Patterns of care for patients with chronic kidney disease in the United States: dying for improvement. *J Am Soc Nephrol*. 2003;14(7 suppl 2):S76-80.
- Powe NR. Early referral in chronic kidney disease: an enormous opportunity for prevention. *Am J Kidney Dis*. 2003;41(2):505-507.
- Rationale for use and reporting of estimated GFR. National Kidney Disease Education Program Web site. http://www.nkdep.nih.gov/professionals/estimated_gfr_508.pdf. Accessed May 21, 2008.
- Creatinine standardization program. Recommendations for pharmacies and authorized drug prescribers. National Kidney Disease Education Program Web site. http://www.nkdep.nih.gov/labprofessionals/Pharmacists_and_Authorized_Drug_Prescribers.htm. Updated November 12, 2007. Accessed March 10, 2008.

- 16 Miller G. Current status of reporting eGFR. College of American Pathologists Web site. http://www.cap.org/apps/docs/disciplines/chemistry/current_status_reporting_egfr.pdf. Accessed September 14, 2007.
- 17 Survey of primary care providers' knowledge and practices related to kidney disease: a follow-up survey report. National Kidney Disease Education Program Web site. <http://www.nkdep.nih.gov/about/reports/literaturereview.pdf>. Accessed May 21, 2008.
- 18 American Diabetes Association. Standards of medical care in diabetes—2007. *Diabetes Care*. 2007;30(suppl 10):S4-S41.
- 19 Levin A. The need for optimal and coordinated management of CKD. *Kidney Int Suppl*. 2005;68(99):S7-S10.
- 20 DuBose TD. American Society of Nephrology Presidential Address 2006: chronic kidney disease as a public health threat – new strategy for a growing problem. *J Am Soc Nephrol*. 2007;18(4):1038-1045.
- 21 US Renal Data System. *USRDS 2007 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health; 2007.
- 22 Schelling JR, Abboud HE, Nicholas SB, et al. Genome-wide scan for estimated glomerular filtration rate in multi-ethnic diabetic populations: the Family Investigation of Nephropathy and Diabetes (FIND). *Diabet Med*. 2008;25(1):235-243.
- 23 Freedman BI, Bowden DW, Rich SS, et al. Genome-wide linkage scans for renal function and albuminuria in type 2 diabetes mellitus: the Diabetes Heart Study. *Diabetes*. 2008;25(3):268-276.
- 24 Lea JP, McClellan WM, Melcher C, Gladstone E, Hostetter T. CKD risk factors reported by primary care physicians: do guidelines make a difference? *Am J Kidney Dis*. 2006;47(1):72-77.
- 25 Berl T, Henrich W. Kidney-heart interactions: epidemiology, pathogenesis, and treatment. *Clin J Am Soc Nephrol*. 2006;1(1):8-18.
- 26 Go AS, Chertow GM, Fan D, McCulloch CE, Shu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351(13):1296-1305.
- 27 Elsayed EF, Tighiouart H, Griffith J, et al. Cardiovascular disease and subsequent kidney disease. *Arch Intern Med*. 2007;167(11):1130-1136.
- 28 Ix JH, Shlipak MG, Liu HH, Schiller NB, Whooley MA. Association between renal insufficiency and inducible ischemia in patients with coronary artery disease: the heart and soul study. *J Am Soc Nephrol*. 2004;14(12):3233-3238.
- 29 Anavekar NS, Pfeffer MA. Cardiovascular risk in chronic kidney disease. *Kidney Int Suppl*. 2004;(92):S11-S15.
- 30 Shlipak MG, Smith GL, Rathore SS, Massie BM, Krumholz HM. Renal function, digoxin therapy, and heart failure outcomes: evidence from the digoxin intervention group trial. *J Am Soc Nephrol*. 2004;15(8):2195-2203.
- 31 North Carolina Institute of Medicine, Task Force on Chronic Kidney Disease. *Task Force on Chronic Kidney Disease: Addressing Chronic Kidney Disease in North Carolina*. Morrisville, NC: North Carolina Institute of Medicine; 2008.
- 32 Andrews A, El Reda DK, Radford G, Burrows NR, Ernst K. Kidney disease mortality—Michigan, 1989—2005. *MMWR*. 2007;56(10):225-227.
- 33 Joint statement of the College of American Pathologists and the National Kidney Foundation. National Kidney Foundation Web site. <http://www.kidney.org/news/pdf/JointStatement.pdf>. Published January 24, 2007. Accessed September 17, 2007.
- 34 American Medical Association House of Delegates. Inappropriate legislative mandates of eGFR calculations. American Medical Association Web site. <http://www.ama-assn.org/ama1/pub/upload/mm/471/525a06.doc>. Published May 3, 2006. Accessed September 17, 2007.