

Routine reporting of estimated glomerular filtration rate: not ready for prime time

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A worldwide movement is underway to oblige laboratories to provide an estimated glomerular filtration rate (eGFR) whenever serum creatinine concentration is measured at the request of a physician. We regard this development with concern. Such reporting constitutes *de facto* screening for chronic kidney disease (CKD), and the validity of eGFR for this purpose has not been appropriately tested.^{1,2} eGFR reporting is already mandatory in the UK and has been endorsed by several organizations in the US and Australasia.^{3,4} UK nephrologists and primary care physicians have experienced the negative effects of mandatory eGFR reporting. Nephrologists in other countries could well have similar experiences if this policy is universally adopted by hospital and commercial clinical laboratories.

In patients already diagnosed with CKD, eGFR (as calculated by the abbreviated Modification of Diet in Renal Disease [MDRD] equation⁵) might provide a less crude description of the degree of impairment in renal function than does a serum creatinine measurement alone, but this view is debatable.^{1,6} Knowledge of eGFR could also aid the selection of safe and effective dosing regimens for potentially toxic drugs that are eliminated largely by glomerular filtration, although the superiority of the MDRD-estimated eGFR over other estimates for this purpose is not well established.⁷ Undoubtedly, the concept of eGFR has raised the profile of CKD in the community at large. However, it was not anticipated that the MDRD equation, which was derived from patients with unequivocal kidney disease, would be used as a means for the diagnosis of kidney disease in patients with no *a priori* evidence of such disease. Herein lies the crux of our concern.

A laboratory-reported eGFR value is usually provided without any confidence intervals, but it might be accompanied by caveats about its interpretation in conditions in which serum creatinine is not in a steady state—such as acute kidney injury—or in conditions wherein the relationship of serum creatinine concentration to eGFR is not accounted for by the variables

used in the MDRD equation.⁵ Laboratory reports also frequently include the statement “eGFR <60 ml/min/1.73 m² indicates stage 3 CKD”, which is in line with the CKD classification system developed by the Kidney Disease Outcomes Quality Initiative (KDOQI).⁸ This statement, however, bypasses the traditional clinical evaluation of an individual patient with suspected CKD.

Laboratories often report a specific value for eGFR only if it is less than 60 ml/min/1.73 m². The unreliability of eGFR values above 60 ml/min/1.73 m² makes the reporting of exact values above this threshold pointless. However, the reporting of values as simply ‘>60 ml/min/1.73 m²’ reinforces the erroneous belief that renal function is in fact normal in all such situations. This convention leads non-nephrologists to the same error of interpretation of renal function as does reliance on a serum creatinine measurement. Individuals aged 40–45 years or below who have eGFR greater than 60 ml/min/1.73 m² do not necessarily have normal renal function.⁹

Conversely, the assumption that any eGFR less than 60 ml/min/1.73 m² is abnormal is based on the false premise that GFR is diet-independent and conserved throughout life in healthy individuals. eGFR values characteristically decline steadily with age, even in people who are not overtly ill,⁹ and the values can be further reduced by a habitually low protein intake in otherwise healthy persons.¹⁰ We have argued elsewhere¹¹ that many individuals aged over 65 years who have an eGFR below 60 ml/min/1.73 m²—particularly females—do not actually have CKD. A large population-based study⁹ showed that a substantial proportion of probably healthy older individuals will fall into the stage 3 CKD category as defined by KDOQI. Only a small fraction of these individuals will have some other manifestation of kidney injury (e.g. proteinuria). A majority of any population will, simply as a result of aging, have eGFR values of less than 90 ml/min/1.73 m². In our view, these observations

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are indicative of a serious calibration problem in the KDOQI classification. This calibration error probably explains the perception of an 'epidemic' of CKD, which we also question.¹¹ The 2007 Australasian guidelines for eGFR reporting acknowledge that in people aged 70 years or over, an eGFR of 45–59 ml/min/1.73 m², if stable and unaccompanied by other evidence of kidney damage, is unlikely to be associated with CKD-related complications.⁴

After the introduction of mandatory eGFR reporting in the UK, a huge increase in referrals to specialty renal clinics of patients with eGFR values of less than 60 ml/min/1.73 m² was noted. Anecdotes abound of similar experiences in the US. Some of these referrals are justified, but many—usually those of women older than 65 years who have no other evidence of kidney disease—are not. The consequences of referral can be considerable in terms of anxiety, loss of insurability and cost. Specialty referrals instigated on the basis of eGFR alone often disregard critical clinical information including previous serum creatinine concentration measurements.

A consensus conference was held in the UK in 2007 to air the above concerns and to formulate recommendations on how to make the KDOQI classification more accurate and useful.¹² Suggestions included taking into account abnormal proteinuria when diagnosing clinically relevant kidney disease and using caution in diagnosing CKD in the elderly solely on the basis of eGFR. Regrettably, these suggestions have not been adopted. Recently developed questionnaire-based instruments for detecting CKD have been based on the flawed notion that anyone with an eGFR of less than 60 ml/min/1.73 m² automatically has *bona fide* CKD.¹³

Until eGFR reporting becomes more suitable for widespread use, we propose that percentile charts of eGFR by age and sex be constructed and made available to all practicing physicians. Patients without any collateral evidence of kidney disease (e.g. proteinuria or urinary sediment) would be referred to a nephrologist only if their eGFR is lower than the fifth percentile by age and sex, or if the value declines considerably over time. This approach would be quite familiar to doctors who track the development of children on growth charts or who monitor bone mineral density. Initially, this approach could be prospectively tested in an unselected population of apparently healthy individuals of diverse age, sex, habitual dietary protein intake

and ethnicity. An additional strategy would be the provision of well-structured referral criteria for suspected CKD and the use of 'e-consultations' to prevent unnecessary specialty referrals and investigations.

In our opinion, the KDOQI guidelines for the diagnosis and classification of CKD need improvement before eGFR is routinely reported. We urge medical societies to endorse the more cautious and scientifically defensible approach. Finally, the correctable shortcomings of eGFR reporting should not be permitted to undermine the benefits of using this parameter in the context of unequivocal CKD.

Supplementary information in the form of a list of UK and US nephrologists who co-endorse this Viewpoint is available on the *Nature Clinical Practice Nephrology* website.

References

- Giles PD *et al.* (2008) New results from the Modification of Diet in Renal Disease Study: the importance of clinical outcomes in test strategies for early chronic kidney disease. *QJM* **101**: 155–158
- Clase CM (2006) Glomerular filtration rate: screening cannot be recommended on the basis of current knowledge. *BMJ* **333**: 1030–1031
- The American Society of Nephrology (online February 2008) ASN's renal express: February 2008 [http://www.asn-online.org/newsletter/renal_express/2008/08-2-Rxpress.aspx] (accessed 2 May 2008)
- Mathew TH *et al.* (2007) Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations. *Med J Aust* **187**: 459–463
- Levey AS *et al.* (2006) Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* **145**: 247–254
- Kallner A *et al.* (2008) Does eGFR improve the diagnostic capability of s-creatinine concentration results? A retrospective population based study. *Int J Med Sci* **5**: 9–17
- Gill J *et al.* (2007) Use of GFR equations to adjust drug doses in an elderly multi-ethnic group—a cautionary tale. *Nephrol Dial Transplant* **22**: 2894–2899
- National Kidney Foundation (2002) K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis* **39** (Suppl 1): S1–S266
- Wetzels JF *et al.* (2007) Age- and gender-specific reference values of estimated GFR in Caucasians: the Nijmegen Biomedical Study. *Kidney Int* **72**: 632–637
- Barai S *et al.* (2008) Levels of GFR and protein-induced hyperfiltration in kidney donors: a single-center experience in India. *Am J Kidney Dis* **51**: 407–414
- Glasscock RJ and Winearls C (2008) An epidemic of chronic kidney disease: fact or fiction? *Nephrol Dial Transplant* **23**: 1117–1121
- Williams B and Rodger RSC (Eds; 2007) Consensus conference on early chronic kidney disease. In *Nephrol Dial Transplant* **22** (Suppl 9): Six1–Six63
- Bang H *et al.* (2007) SCreening for Occult RENal Disease (SCORED): a simple prediction model for chronic kidney disease. *Arch Intern Med* **167**: 374–381

Competing interests

RJ Glasscock has declared associations with the following organizations: the American Society of Nephrology and the National Kidney Foundation. See the article online for full details of the relationships. CG Winearls declared no competing interests.