Estimating glomerular filtration rate (GFR): Information for laboratories

The National Service Framework (NSF) for Renal Services recommended that "Local health organisations can work with pathology services and networks to develop protocols for measuring kidney function by serum creatinine concentration together with a formula-based estimation of GFR, calculated and reported automatically by all clinical biochemistry laboratories". The aim of this information sheet is to co-ordinate implementation and harmonise reporting of GFR nationally.

Why?

Glomerular filtration rate (GFR) is an important test of kidney function and knowledge of GFR is essential for the diagnosis and management of chronic kidney disease (CKD). Gold standard methods of assessing GFR are technically demanding, expensive, time consuming and unsuitable for widespread identification of CKD in the 'at risk' population. Serum creatinine measurement, a widespread test of kidney function, is insufficiently sensitive to detect moderate CKD and is affected by a range of non-renal influences. Creatinine clearance has significant practical problems and is known to be inaccurate. An alternative is to measure serum creatinine and estimate GFR using an equation which corrects for some of the more significant non-renal influences. This approach is known to be more sensitive for the detection of CKD than serum creatinine and more accurate than creatinine clearance.

How?

In adults (≥18 years) estimated GFR (eGFR) should be calculated using the 4-variable (i.e. serum creatinine concentration, age, gender and ethnic origin) isotope dilution mass spectrometry (ID-MS) traceable version of the Modification of Diet in Renal Disease (MDRD) equation:

GFR (mL/min/1.73 m^2) = 175 x [serum creatinine (umol/L) x 0.011312]$^{-1.154}$ x [age]$^{-0.203}$ x [1.212 if black] x [0.742 if female]

If the ethnic origin of the patient is unknown, or the patient is not Caucasian or African-Caribbean, an assumption of Caucasian ethnicity can be made (but see below).

Laboratories should communicate to their users (possibly using the laboratory report) the following information:

1. that GFR estimates between 60 and 89 mL/min/1.73 m^2 do not indicate CKD unless there is other existing laboratory/clinical evidence of disease
2. that eGFR should be multiplied by 1.212 for African-Caribbean patients, unless ethnic origin was available to the laboratory and this correction has already been applied
3. that eGFR has not been validated for use in acute renal failure, pregnancy, oedematous states, muscle wasting disorders, amputees and malnourished people.

The MDRD equation should not be used in children. When required, eGFR can be calculated using the Schwartz equation which requires knowledge of height (length) of the child. Whilst these estimates may be used in specialist settings, routine reporting of eGFR in children by all laboratories is not recommended.

The precision and accuracy of eGFR decreases as GFR increases. When eGFR exceeds 89 mL/min/1.73 m^2, it should be reported as '≥90 mL/min/1.73 m^2' rather than as an exact number.

Inter-laboratory variation in bias of creatinine estimation causes significant differences in estimates of GFR. However, irrespective of this, reporting eGFR still enables identification of CKD in patients who would be missed using serum creatinine alone. Pilot external quality assessment schemes including the UK National External Quality Assessment Scheme (UKNEQAS) have been established to monitor relative performance of eGFR and facilitate improved inter-laboratory comparison. Laboratories reporting eGFR should subscribe to such schemes.

UKNEQAS are undertaking a programme of work aimed at improving inter-laboratory agreement in creatinine measurement, and hence reported eGFR. This will include providing recommended correction factors for the MDRD equation to adjust for method-related differences compared to the ID-MS reference method. These correction factors will only work if laboratories use their creatinine methods strictly according to the manufacturer's instructions. Failure to adhere to this process will invalidate the approach and may result in diagnostic misclassification. It seems likely that there will also be increasing alignment to ID-MS reference methods by reagent manufacturers in the future.

Estimation of GFR using the MDRD equation has not been well validated in certain populations, for example Chinese and other Asian groups. However, at present there is no evidence to suggest that they are invalid in such groups.

When?

The Department of Health is recommending implementation of routine eGFR reporting by all NHS clinical biochemistry laboratories by 1 April 2006 to fit in with the Quality and Outcomes Framework coming into effect.

In whom?

The NSF and the UK CKD Guidelines have made specific recommendations concerning which groups should be screened for CKD, and how often. In particular, people with diabetes, vascular disease, heart failure, hypertension, urinary tract obstruction, neurogenic bladder or surgical urinary diversion, people taking diuretics, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers and people with a family history or genetic risk of kidney disease should undergo regular surveillance. eGFR should be reported on all adult samples carrying a request received by laboratories for serum creatinine measurement, bearing the above caveats in mind. Local laboratory service providers, primary care trusts and renal networks should develop systems to manage these groups in which a conservative approach to clinical application of eGFR should be exercised.

What does it mean?

eGFR is the pillar of CKD diagnosis, staging and management but is only one component of clinical assessment. The UK CKD Guidelines provide extensive guidance on the further investigation and management of patients with CKD.

Further information may be obtained from:

Burden R, Tomson C. *Identification, management and referral of adults with chronic kidney disease: concise guidelines*. Clin Med 2005; 5: 635–42

Department of Health. National Service Framework for Renal Services. Part Two: Chronic Kidney Disease, Acute Renal Failure and End of Life Care. 2005. Available at: www.dh.gov.uk/renal, accessed 3 March 2006

Joint Specialty Committee for Renal Disease Royal College of Physicians of London and the Renal Association. *Chronic Kidney Disease in Adults: UK Guidelines for Identification, Management and Referral*. Royal College of Physicians of London, 2006, in press. Available at: www.renal.org/CKDguide/full/UKCKDfull.pdf, accessed 3 March 2006

National Kidney Disease Education Program. *Suggestions for Laboratories*. Available at www.nkdep.nih.gov/resources/ laboratory_ reporting.htm, accessed 3 March 2006

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