Glomerular filtration rate measurement: from equations to report consensus

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In the clinical assessment of kidney function a simple measure of solute concentration or solute excretion or urine output does not describe the real "function" of the organ, since urinary flow, body size and solute concentration in blood could be very different between individuals. The Glomerular Filtration Rate (GFR), i.e. flow rate of filtered fluid through the kidney, is considered the best overall index of kidney function both in health and disease. The GFR cannot be measured easily in clinical practice. It takes an integration of many parameters, in a balance between capillary and interstitial hydrostatic and oncotic pressure. In practice, it is not possible to directly identify the needed values for this equation. The "clearance" of an ideal molecule, fully filtered by the glomerular membrane, without reabsorpion or secretion by renal tubuli, could be a way to compare renal function among different individuals. But the "ideal" marker does not exist and many exogenous molecules currently used are expensive, complex or lead to error of 5-20% in different measurements. Since seventies, a number of formulas have been devised to estimate GFR values on the basis of serum creatinine levels. The Cockcroft-Gault equation is one of the most widely recommended and used. In 1999 a new prediction equation, derived from 1628 subjects with renal insufficiency enrolled in the Modification of Diet in Renal Disease study (MDRD), was published and a simplified equation, that used serum creatinine as the only serum assay, was published in 2000. One of the main advantages of this equation is to avoid the anthropometric measurement.

The formula has been widely applied in both clinical care and research since its publication. Later studies demonstrated the MDRD equation to be accurate at least as much as the other formulas. Moreover, this formula was the only studied and reformulated in regard to the standardization of creatinine measurement and it is the only corrected for the isotope dilution mass spectrometry (IDMS) calibrated creatinine. All creatinine-based equations, other than the IDMS-traceable MDRD Study equation will give values that, in most cases, are higher than the values obtained using traditionally calibrated creatinine methods.

However, MDRD formula not solves every problem and cannot be applied in all subjects.

First of all, it is expected that the in vitro diagnostics (IVD) industry will complete the recalibration of routine blood, serum, or plasma creatinine methods during 2009. During this interim phase, clinical laboratories need to choose between IDMS-original MDRD or IDMS-traceable MDRD, according to the used method to measure creatinine.

Secondly, this formula was derived by adult individuals. Subjects under 18 or over 75 years cannot be evaluated in their renal function. For children, other formulas could be applied, and the Schwartz formula, known since 1970, was recently improved. This new equation is based on an enzymatic creatinine method, IDMS traceable.

Thirdly, the MDRD was derived by subjects with chronic kidney disease. It is known that the MDRD formula systematically underestimates the renal function. Especially for this reason, the National Kidney Disease Education program and many other guidelines recommend reporting eGFR values greater than or equal to 60 mL/min/1.73 m^2 simply as ≥60 mL/min/1.73 m^2, and not as an exact number. It could reinforce the erroneous belief that renal function is normal in all such situation.

Given these limitations, Levey and colleagues few months ago published their new formula on behalf of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI):

$$\text{GFR} = a \times (\text{serum creatinine}/b)^{c} \times (0.993)^{\text{age}}$$

where a takes on race and sex, b sex and c sex and creatinine measurement. Obtained from a dataset of 5504 subjects, the new equation seems to be more accurate than the MDRD study equation, yielding a lower estimated prevalence of kidney disease, and could replace it for routine clinical use.

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