Notable Steps in Obtaining Improved Estimates for Glomerular Filtration Rate

Knowledge of the glomerular filtration rate (GFR) is of crucial importance in the management of patients. In addition to a general evaluation of kidney function, a more precise assessment is valuable on many occasions, e.g., to detect early impairment of renal function, to allow correct dosage of drugs cleared by the kidneys, to monitor renal transplants, and to evaluate patients before use of potentially nephrotoxic radiographic contrast media. Determination of GFR with high accuracy requires the use of invasive techniques based on measuring the plasma clearance rate of injected substances that are excreted exclusively via glomerular filtration, e.g., inulin, $^{125}$I-iothalamate, iohexol, and $^{51}$Cr-EDTA. Such procedures are labor-intensive and not free of risk for the patient.

The plasma or serum concentrations of endogenous substances, particularly creatinine, have been used as indicators of GFR for more than a century (1). The creatinine concentration, however, is far from ideal as a GFR marker because it is strongly influenced not only by GFR, but also by factors such as muscle mass, sex, age, diet, race, and tubular secretion (2, 3). To compensate for the shortcomings, several investigators have made successful attempts at constructing GFR prediction equations that include creatinine and additional variables. The most widely used GFR prediction equations for adults are those proposed by Cockcroft and Gault (4), which produces absolute GFR values in mL/min, and the Modification of Diet in Renal Disease (MDRD) equation, which produces relative GFR values in mL·min$^{-1}$(1.73 m$^2$)$^{-1}$ (3, 5). Although both prediction equations are used frequently, their general implementation in healthcare remains far from realized, mainly because of limitations related to the use of different creatinine measurement procedures among laboratories. For this reason, a prediction equation associated with a specific method and a specific set of calibrators will not have the same diagnostic performance when used in conjunction with other methods and calibrators.

To harmonize the Jaffe procedures, merely introducing a negative offset value is not sufficient, although this reduces the positive bias in the low measuring range; it also is often necessary to compensate for the concomitant negative bias found in the measuring range above the high calibration point (6). The only way to achieve general implementation of creatinine-based prediction equations, with the associated clinical benefits for patients, is therefore to suggest steps that will produce worldwide harmonization of methods to determine creatinine. Although this may seem easy in principle, implementation of a plan to harmonize methods can be complicated because the suggested steps must be recognized as sound by all those involved in measuring creatinine. The special report entitled ‘Recommendations for Improving Serum Creatinine Measurement’ by Myers et al., published last month in Clinical Chemistry (7), represents a document of such quality that the steps recommended should be recognized as worthwhile to undertake. The document not only presents an up-to-date and thorough report on advantages and disadvantages associated with all known methods for creatinine determination, it also suggests clearly feasible ways for the engaged parties to achieve worldwide harmonization and metrologic traceability for the reported creatinine values.

Implementation of the steps suggested by Myers et al. (7) for harmonization of creatinine measurement may also allow further progress in the development of new GFR prediction equations with improved diagnostic performance. It is already known that use of different prediction equations might be necessary for optimal prediction of GFR in different patient cohorts (8, 9), but easy and reliable evaluation of the diagnostic performances of different prediction equations in different patient cohorts requires harmonization of creatinine measurements. In addition, comparison of different mathematic–statistical models for derivation of prediction equations could also be greatly facilitated by harmonization of creatinine measurement.

The recommendations for harmonization of creatinine measurement presented by Myers et al. (7) are also of great extent pertinent for the harmonization of measurements of GFR markers other than creatinine, e.g., cystatin C (10, 11).

Several internet-based tools are available to facilitate the use of GFR prediction equations (12, 13), but the clinical usefulness of these tools is hampered by the lack of harmonization of creatinine and cystatin C measurements. The steps toward harmonization suggested by Myers et al. (7) may very well increase the clinical benefits of using these tools.

References


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Anders Grubb1*
Gunnar Nordin2

1 Department of Clinical Chemistry
University Hospital
Lund, Sweden

2 External Quality Assurance in Laboratory Medicine in Sweden (EQUALIS)
Uppsala, Sweden

* Address correspondence to this author at: Department of Clinical Chemistry, University Hospital, S-22185 Lund, Sweden. E-mail anders.grubb@klinkem.lu.se.

DOI: 10.1373/clinchem.2005.062737