Re: Estimation of Glomerular Filtration Rate With Creatinine-Based Versus Cystatin C-Based Equations in Kidney Transplant Recipients

SIR,

The interesting paper by Savaj and colleagues[1] in a recent issue of the *Iranian Journal of Kidney Diseases* prompted me to make two comments that might be of interest to your readers. First, the variety of equations for the glomerular filtration rate (GFR) based on cystatin C is apparent rather than statistically significant. Second, it is almost inevitable that the modification of diet in renal disease (MDRD) equation is a better measure than the simpler expressions.

At least 4 of the 5 cystatin C-based equations are almost indistinguishable. All the 5 equations can be written in the form below:

$$GFR = GFR_0 + \alpha \times \text{cystatin } C^{-\beta}$$

where $GFR_0 = 0$ for the Filler, Larsson, and Rule equations, but it takes small non-zero values for the Le Bricon and Hoek equations.[1] The values of α and β are 76.6 to 91.1 and 1 to 1.1263, respectively. The theoretical correlation coefficients (r^2) relating these equations are greater than 0.99, as reported by Savaj and coworkers,[1] indicating just how similar the expressions are. Estimates of the within-assay and between-day imprecision (coefficient of variation) of cystatin C determinations are 2% to 3.7% and 5.4% to 6.1%, respectively, depending on the concentration of cystatin C.[2] Using these coefficients of variation (and ignoring any other source of error), the Hoek, Larsson, Rule, and Le Bricon equations lie within a fraction of a standard deviation of one another, from which I infer that it would be very difficult to distinguish them experimentally (Figure). While the Filler expression gives a larger estimate of GFR for any concentration of cystatin C than the other four expressions, at high GFR levels, the estimated error bands overlap
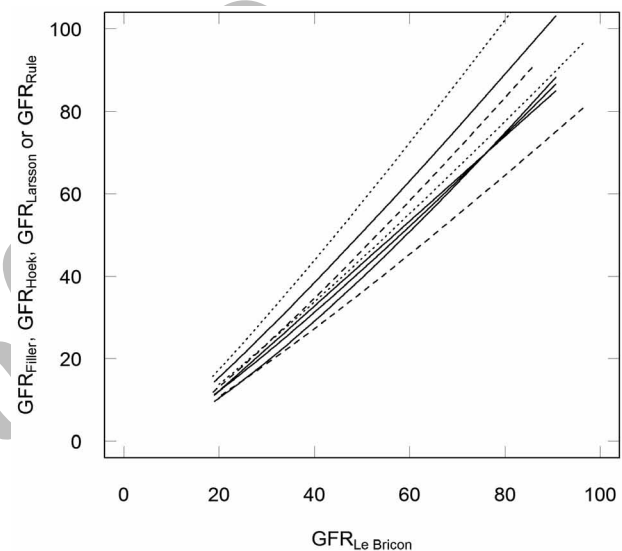
Relationships between the five cystatin C-based equations for GFR. Values of GFR were calculated according to the five equations (denoted by GFR_x, where x denotes the equation) over the range of cystatin C concentration reported by Savaj and colleagues[1] (0.9 mg/L to 5.2 mg/L). The lower 3 solid curves are $GFR_{Larsson}$, GFR_{Hoek}, and GFR_{Rule}, and the upper solid curve is GFR_{Filler}, plotted against $GFR_{Le Bicon}$. The error bands (± 1 standard deviation) were estimated using a straight line fitted to the between-day imprecision coefficient variations reported by Stowe and coworkers[2] (dotted lines relate to GFR_{Filler}, dashed lines relate to the other estimates). The GFR on both axes are in mL/min/1.73 m².

those of the other expressions (Figure). Savaj and colleagues[1] are far from alone in implicitly treating these cystatin C-based equations as though they are distinguishable, as is evident from several of the papers they cite.

The second point is that it is almost inevitable that the MDRD equation is a better measure than the simpler creatinine-based expressions. The MDRD equation not only shares parameters with the abbreviated MDRD and the Cockcroft-Gault equations (both depend on creatinine, age, and

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gender), but also has other parameters (serum urea nitrogen and albumin). It is, therefore, almost inevitable that the MDRD equation is a better measure than the simpler creatinine-based expressions unless either (1) the expressions have not been obtained in some objective manner or (2) the extra parameters have no relation to the GFR.

Of course, as Saraj and colleagues[1] quite rightly suggest, a rigorous statistical analysis of the expressions for GFR, in an appropriate setting, is warranted.

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