Letters and Replies

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Need of standardization for creatinine and cystatin C-based GFR equations in renal transplantation

Sir,

We read with interest the detailed comparison of various creatinine- and cystatin C (Cys C)-based equations to determine GFR in patients after kidney transplantation [1]. This publication provides a comprehensive overview of the most commonly used equations and importantly, applies inulin clearance as gold standard GFR measurement. The authors conclude that creatinine-based formulae are not inferior to Cys C-based estimations of GFR.

However, we do have some concerns and would like to draw attention to the fact that neither the creatinine determination calibrated method (e.g. IDMS method) nor the accepted methods for Cys C determination (Dade Behring or DAKO) were used. Although the lack of calibration is discussed as a potential drawback, the consequences of the presented results are not outlined.

As demonstrated in a recent publication, even a very small bias from the IDMS-creatinine (+1.15 µmol/l) results in a considerable modification of bias, precision and accuracy [2]. To provide a mathematical example for the MDRD equation, an overestimation of 5 µmol/l, at a creatinine level of 100 µmol/l, leads to an increase in one of the multipliers of the MDRD equation: \[\left(\frac{[105/88.4]}{1.154}\right) = 0.82 \text{ instead of } \left(\frac{[100/88.4]}{1.154}\right) = 0.867\]. This means, for a 50-year-old Caucasian male, the MDRD equation will yield 64.8 ml/min/1.73m² instead of 68.6 ml/min/1.73m². Surely this is of limited clinical impact; however, it will affect the statistical results of the above-mentioned publication considerably.

In regard to the Cys C-based equations, it should be noted that virtually all of the applied equations are based on Dade Behring or DAKO assays which were not applied in this study. Application of a different Cys C determination technique introduces a bias affecting the performance of the Cys C-based estimation. Naturally, even a high correlation of the applied Cys C method with both assays does not exclude a systematic over- or underestimation.

Thus, a valid conclusion is hampered if non-IDMS-calibrated creatinine-based equations are compared with formulae based on non-standardized Cys C.

In conclusion, this work is only interesting for transplantation centres that determine creatinine by a SYNCHRON LX 20 system and Cys C by ELx808TM absorbance microplates. Outside of these laboratory settings, the presented data are of limited usefulness.

Conflict of interest statement. None declared

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Reply

Sir,

In the above-mentioned letter, concerns regarding the calibration of creatinine and the ELISA method used to measure cystatin C were raised as a potential drawback of the manuscript.

We thank the authors for their constructive criticism. Several points should be raised, however, in support of our conclusion. First, we tested the modified MDRD2-IDMS method, which is suggested as an additional equation for centres that use the Synchron LX20 system to measure serum creatinine. Secondly, many of the above-tested equations were developed with methods closer to ours than the most recently modified assays. Thirdly, as we have identified in the manuscript, Hallan et al. have demonstrated elegantly that the bias between the creatinine-based methods is lower in patients with higher serum creatinine.

Stevens et al. have studied the impact of creatinine calibration on the performance of GFR estimating equations in a pooled individual patient database. They concluded that the effect of calibration was greater at higher levels of GFR. For the C–G equation, calibration worsened the median percentage of difference from −2% to −11.4%. Calibration improved median percentage of difference between measured and estimated GFR by the MDRD2 equation from 9% to 5.8%. A striking finding, however, was their conclusion...