that calibration could not account for variation in assay performance among individuals. After calibration, larger errors remained for GFR estimates >16 ml/min/1.73 m² [1].

In regard to the limitations of the ELISA method to measure cystatin C, we have presented data to show an excellent correlation to the Dade Behring or DAKO assays. Therefore, we believe that limitations in our creatinine and cystatin C measurements cannot explain the significant limitations of GFR equations.

Conflict of interest statement. None declared.

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doi: 10.1093/ndt/gfn027

Advanced Access publication 19 January 2008

Comment on ‘Comparison between creatinine and cystatin C-based GFR equations in renal transplantation’

Sir,

In their paper ‘Comparison between creatinine and cystatin C-based GFR equations in renal transplantation’, Zahran et al. [1] checked various formulae of GFR determination in stable renal transplant patients using the technique of constant infusion of inulin with urine collection as reference test. They considered this procedure as a ‘historical gold standard’ of GFR determination. Although this view may be valid amidst the plethora of other techniques using e.g. 125I-lothalamate applied in constant infusion, or radio-labelled markers such as 99m Tc-DTPA, assessed as a single sample [2], and although the characterization as ‘historical’ may be right, the widespread and ever-persisting characterization as ‘gold standard’, and thus as obligatory reference test, must be questioned. Not only is the technique extremely impractical from a clinical standpoint, it is also inevitably error-prone since even the approximate attainment of stationary marker concentration levels is generally most insecure and needs much more time than suggested by traditional recipes. Too short experimental horizons result in considerable underestimation of GFR, as we were able to show in a previous study [3]. We used a single-injection technique with sufficiently long inulin concentration contours adapted to a two-compartment kinetic model for the determination of distribution volumes and GFR. Our results were then validated by predicting the concentration contours to be expected in constant-infusion experiments of arbitrary protocol length in the same test subjects and we were able to demonstrate full accordance of theoretical and experimental concentration contours, a validation never done before ‘historically’. The mean GFR obtained by this validated kinetic method in healthy subjects was 146 ± 19 ml/min, whereas the traditional assessment of the concentration values employing the constant-infusion method with urine collection yielded 133 ± 20 ml/min and 132 ± 13 ml/min without urine collection. By such computer-based analyses of the marker elimination process, we were able to show that in most patients with renal insufficiency, even only approximately steady states could not be achieved within 3–4 h and in one subject with decreased renal function not even before 50 h. In virtually all scientific disciplines, kinetic processes such as marker distribution and elimination processes are no longer meaningfully assessed by trying to attain equilibrium states reachable only after an infinite time horizon, but rather are studied by the modern computer-based system identification of kinetic models using marker concentration contours of practicable experimental horizons [4]. In fact, such techniques provide much more detailed information about the relevant processes than the classical method: in nephrology, enabling one to get information about the micro-vascular state additionally to GFR [5].

Conflict of interest statement. None declared.

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doi: 10.1093/ndt/gfn927