

CREATININE CLEARANCE, DIFFERENT METHODS OF DETERMINATION

We read with interest the article by Kampmann & Molholm Hansen (1981) published in the July issue of the journal, and wish to comment on a number of aspects.

The authors state that the different methods for the prediction of creatinine clearance (CCr) suffer by ignoring the large variation in urinary excretion of creatinine. In contrast to the measured CCr, which suffers from these variations, prediction methods by definition are not influenced because in these methods serum creatinine (SCr) is the only variable parameter for a given individual. The diurnal variation of SCr has been reported to be only 10–15% in an individual (Addis et al., 1950; Doolan et al., 1962; Statland et al., 1973; Winkel et al., 1975), while the urinary creatinine excretion can vary between 30 and 400% (Clark et al., 1951; Pasternack & Kuhlback, 1971; Greenblatt et al., 1976; Maruhn et al., 1977). Because of these large variations in urinary creatinine excretion, measured CCr will vary accordingly. These large variations do not seem to correlate with changes in renal function as has been observed by the relatively poor correlation (r = 0.77) of the measured CCr and the elimination rate constant of amikacin (Hallynck et al., 1981a). A significantly better correlation (r = 0.94, P < 0.02, two-sided t-test) was found with the predicted CCr in the same group (n = 62).

It is also our feeling that theologically the inulin and 31Cr EDTA methods are preferable, but in daily clinical routine they are too cumbersome and are invalid when there are rapid changes in renal function. For these reasons we prefer the prediction of CCr as a measure of renal function on condition that the method is useful in all age groups, valid in rapidly changing renal function and simple for use in clinical practice. We have developed such a method which estimates CCr from SCr (Hallynck et al., 1981a). In stable renal function CCr can be estimated from the equation CCr = E/S (CCr is expressed in ml/min per 50 kg lean body mass (LBM)) where E is the urinary creatinine excretion obtainable from a graph according to the age (1 day–100 years) of the subject, and S being a measured SCr. When renal function is unstable (S1 – S2 ≥ 0.5 mg/100 ml) the equation becomes

\[ CCr = \frac{E}{S} + \frac{600 \times (S_1 - S_2)}{T \times S} \]  

(ml min⁻¹ 50 kg⁻¹ LBM)

S1 and S2 are two consecutive SCr values taken with T h intervals and S is the mean of S1 and S2. This method has been compared with a previously published nomogram (Siersback-Nielsen et al., 1971) and three other equations (Mawer et al., 1972; Cockcroft & Gault, 1972; Jelliffe, 1973). As well as in conditions of stable (n = 303) and in rapid changes (n = 38) in renal function, significantly better correlations with the measured 24 h endogenous CCr were obtained (Hallynck et al., 1981b). We were able to make an accurate assessment of acute changes in CCr as soon as 5 h after a sudden decrease or 2 h after an improvement in renal function. The other methods give estimations with a similar accuracy only after several days. Because the method is based on lean body mass instead of total body weight the real advantage of this method is that it represents a uniform formula applicable in all age groups and both sexes.

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We greatly appreciate the comments and suggestions made by Thomis and coworkers (1982) concerning our review on different methods in the evaluation of endogenous creatinine clearance. It is correct to emphasize the large variation in urinary creatinine excretion, but this aspect has been taken into consideration by the developed nomogram as the age-axis expresses the daily urinary excretion of creatinine per kg body weight. This value decreases with advancing age and the figure seems to be related to the E value in their equation. The normalization of creatinine clearance to lean body mass instead of total body weight or body surface seems appropriate but the method introduces a new area of variation originating from the precision of the formulas of James (1976).

We have also been confounded about their references to the paper of Hallynck et al. (1981) comparing their new method with our nomogram and the equations of Mawer et al. (1972), Cockcroft & Gault (1976) and Jelliffe (1973). The cited paper does not contain any documentation on the comparison between measured and various methods of predicting creatinine clearance.

Finally, we find it important to present a uniform formula predicting creatinine clearance applicable to all age groups. We thank the authors for this valuable contribution towards a better drug dosing in renal failure.

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