

# ESTIMATION OF CREATININE CLEARANCE IN PATIENTS WITH UNSTABLE RENAL FUNCTION.

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Measurement of creatinine clearance (CCr) has long been a problem in sick patients, largely because of the need to collect a carefully timed urine specimen to determine it. However, a number of years ago, several methods were developed to estimate CCr without a urine specimen [1-4]. However, all these approaches only considered the situation where serum creatinine was stable. Because of this, a dynamic approach to the problem was developed.

## A Model of Creatinine Kinetics

This dynamic model [5] used the relationship that the daily change in the total amount of creatinine in the patient's body is the difference between production (P) and excretion (E) during that day. This was described by

$$V(C_2 - C_1) = P - E \quad (1)$$

where V is the apparent volume of distribution of serum creatinine (in hundreds of ml), C<sub>1</sub> and C<sub>2</sub> are the first and second serum creatinine values taken typically one day apart (in mg/dL), and P and E are in mg. Since V is less than total body water, it was approximated as 40 % of the patient's body weight (in hundreds of grams).

## Calculation of Daily Creatinine Production

### Adjustment for Age.

The data of Siersbaek-Nielsen et al. [2] of the effect of age upon the carefully measured urinary creatinine excretion was shown to be described by

$$E = 29.305 - 0.203A \quad (2)$$

where E is the measured urinary creatinine excretion (in mg/kg/day) and A is the age (in years). That data was obtained in hospitalized patients who were clinically free of any renal disease. Since the patients were all quite stable,

$$E = P. \quad (3)$$

In this way, one can use this carefully measured data of excretion to make a reasonable estimate of daily creatinine production. This can be further refined as described below. It should also be noted that in these patients, the average serum creatinine their patients was 1.1 mg/dL. This will be useful below.

### Adjustment for Degree of Uremia.

It was shown by Goldman [6] that uremic patients also have a decreased excretion (and therefore production) of creatinine. Using data from that report, creatinine production (CP, in mg/kg/day) is related to serum creatinine (C, in mg/dL) by

$$CP = 1344.4 - 43.76C \quad (4)$$

One can thus adjust the first estimate of creatinine production for age to the average value ( $C_{avg}$ ) of  $C_1$  and  $C_2$  by the ratio R, where

$$P_1 = 1344.4 - 43.76 \times C_{avg}, \quad (5)$$

and

$$P_2 = 1344.4 - 43.76 \times 1.1, \quad (6)$$

where 1.1 = the average serum creatinine in Siersbaek-Nielsen's patients, in each age group. Then,

$$R = P_1 / P_2, \text{ and} \quad (7)$$

$$\text{the adjusted } P = P \times R \quad (8)$$

In this way, daily creatinine production can be estimated for men, based on many careful measurements of 24 hour urinary creatinine excretion, and adjusted to the patient's age, weight, and degree of uremia. In further adjustments, 90% of this value was then taken if the patient was female, and 85% of that for either men or women if the patient was a dialysis patient. Further, if a patient's muscle mass is clearly below normal, as may be the case with cirrhotic patients or those with AIDS, for example, one can simply make a rough clinical estimate of the patient's body (muscle) mass as a percent of normal, if desired, to make a further final adjustment of P. This last adjustment for body mass was not done in the original study [5].

### Calculation of Daily Creatinine Excretion

In the traditional calculation of creatinine clearance,

$$C = UV/P, \quad (9)$$

where U is the urinary creatinine concentration, V is the 24 hour urine volume, P is the plasma or serum creatinine concentration, and C is creatinine clearance. This can be rearranged to show that what comes out of the body is equal to what was cleared from the body. Thus

$$CP = UV. \quad (10)$$

Because they are numerically equal, PC can therefore be substituted for UV, the measured 24 hour excretion. Thus

$$E = UV = PC, \text{ and}$$

$$E = PC = C_{\text{avg}} \times (\text{CCr}/100) \times 1440, \quad (11)$$

where E is expressed in mg/day,  $C_{\text{avg}}$  is in mg/dL, CCr is in ml/min, and 1440 represents the minutes in 1 day.

The final relationship to calculate creatinine clearance from unstable serum creatinine values, and without requiring a urine specimen may now be written as

$$0.4W(C_2 - C_1) = P - C_{\text{avg}} \times \text{CCr}/100 \times 1440 \quad (12)$$

After this, the raw creatinine clearance (CCr) above can be corrected for body surface area to that of an average patient having a body surface area of 1.73 square meters. The above equation thus represents a dynamic model of creatinine kinetics, and permits estimation of CCr from routine clinical data of age, sex, height, weight, and either a pair of unstable and changing serum creatinine levels or a single stable serum creatinine, all without having to collect a urine specimen, which is an extremely unreliable procedure in all but research situations.

### **Comparison of Estimated with Measured Creatinine Clearance**

In a first set of 128 observations on 15 patients [5], the algorithm was shown to have an accuracy essentially equal to that of Jadorny [1]. In an additional set of 250 observations on a group of 14 patients who had just undergone renal transplantation, the standard error of the estimate ( $\pm 14.9$  ml/min) was slightly more precise than the equations of Jadorny ( $\pm 16.6$  ml/min), with an overall scatter of about  $\pm 25\%$  between the estimated and the measured values, as shown in Figure 1.

It is also interesting to consider the errors present in the traditional determination of CCr. If one can measure a serum creatinine level with a coefficient of variation of 5%, as is the case with common autoanalyzer methods, and if one measures urinary creatinine concentrations with a coefficient of variation of 8%, as is also common, then if one can collect a 24 hour urine specimen with a coefficient of variation of 5%, the resulting value of measured creatinine clearance will have a coefficient of variation of 11%, and a 95% confidence limit of  $\pm 22\%$ . This closely corresponds to the scatter found between the estimated and the measured CCr values shown in Figure 1. Because of this, it is likely that this method of estimating CCr has a precision about equal to the classical measurement of it. In addition, it is practical in clinical situations. It is also probably better at sensing changes in renal function in response to sudden changes in serum creatinine than are the more simple formulas of Jadorny [1], Jelliffe [3], or Cockcroft and Gault [4], which were designed only for use when serum creatinine is stable. Serum creatinine usually requires about one week to stabilize following a change in renal function.

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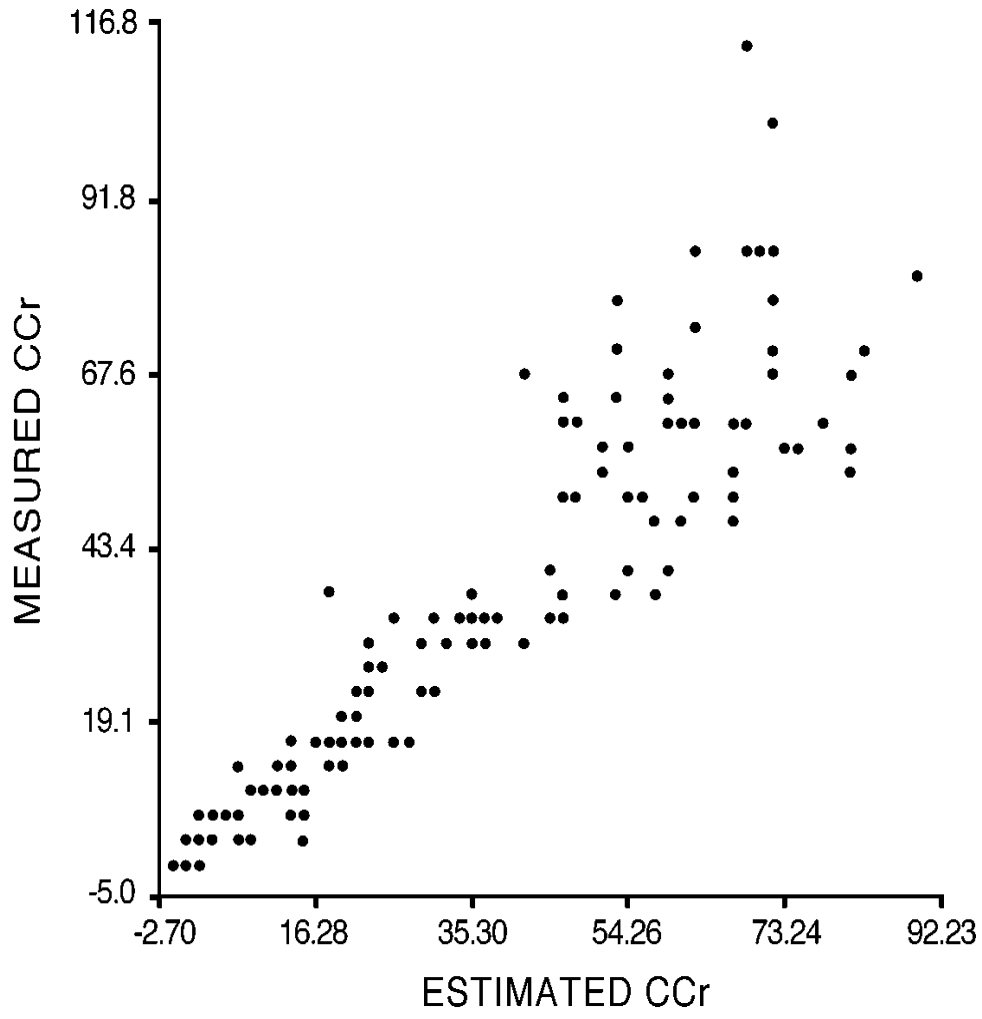


Figure 1. Comparison of Estimated CCr as described herein, with measured CCr [5].