

DELIMITATION OF PLASMA CREATININE CONCENTRATION VALUES FOR ASSESSMENT OF RELATIVE RENAL FUNCTION IN ADULT PATIENTS

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Abstract. Plasma creatinine concentrations and glomerular filtration rates (GFR) were determined simultaneously in 200 females and 180 males of various ages (20–79 years) covering all degrees of *relative* renal function: normal (>75%); moderately impaired (75–52%); considerably impaired (51–28%); and severely impaired (<28%). The percentages express GFR relative to corresponding age—and sex-dependent normal means. This relative parameter evaluates whether—and to what extent—the combined function of the two kidneys is affected by nephro-urological disorders. For practical purposes plasma creatinine was found to be independent of age in all function groups for both sexes. The data were used to delimit plasma creatinine concentrations for the assessment of relative renal function. For females the limits of plasma creatinine ($\mu\text{mol per litre}$) were: “normal” (<115); “moderately elevated” (115–150); “considerably elevated” (151–250); and “profoundly elevated” (>250). The corresponding figures for males were: <128; 128–170; 171–270; and >270.

From a prognostic as well as from a therapeutic point of view it would seem valuable to know whether—and to what extent—the combined function of the two kidneys is affected by nephro-urological disorders of any kind.

It is generally accepted that the glomerular filtration rate (GFR) is the best single parameter for assessing renal function. With advancing age there is a physiological decrease in GFR, in the range of 1% per year from the fourth decennium and onwards (Wesson, 1969). In order to evaluate the effect on renal function caused solely by disease, GFR values should consequently be calculated relative to corresponding normal sex- and age-dependent mean values, i.e. the *relative renal function*, expressed as percentages of corresponding normal means.

The endogenous clearance, closely related to GFR, as well as the production of creatinine (and with it the urinary excretion rate) both decline to the same extent with age in normal subjects (Ahlert, Brüscke, Dietze, Franke & Haase, 1967; Kampmann, Siersbæk-Nielsen, Kristensen & Møholm Hansen, 1974). This implies that the plasma creatinine concentration is unchanged throughout life in adult normal subjects (Kuhlback, Eriksson & Forsius, 1964).

If mean plasma creatinine in different degrees of impaired *relative* renal function is likewise independent of age, plasma creatinine would be a suitable parameter for the assessment of relative renal function, since the same plasma creatinine value in various ages would correspond to the same degree of impaired relative renal function.

This problem (previously not studied) can be investigated in a large material of adults in various ages covering all degrees of relative renal function by simultaneous determination of plasma creatinine and GFR, using a precise and accurate GFR measurement. We have performed such a study with the aim of delimitating plasma creatinine values for assessment of relative renal function.

MATERIAL AND METHODS

The plasma creatinine concentration and the GFR were measured simultaneously in 380 patients.

Plasma creatinine

Blood samples were drawn in the morning with the patients supine, irrespective of whether the patients had eaten or not. After centrifugation, plasma creatinine concentrations were determined on a Technicon SMA®

Table I. Delimitation of normal and varying degrees of impaired relative renal function

The limits are given as percentages of the age—and sex-dependent normal mean glomerular filtration rates

Normal renal function	Moderately impaired	Considerably impaired	Severely impaired
>75%	75–52%	51–28%	<28%

12/60 autoanalyser system, using Technicon creatinine standards. The normal range at this hospital is 56–114 $\mu\text{mol/l}$ for females; 63–127 $\mu\text{mol/l}$ for males.

Glomerular filtration rate

With the patient confined to bed but not fasting, GFR was determined during the course of 4–5 hours from the total [^{51}Cr] EDTA plasma clearance (E) determined by a simplified single injection method (Brøchner-Mortensen, 1972; Brøchner-Mortensen & Rødbro, 1976*b*). The reproducibility (total day-to-day variation) is 4% for $E \geq 30$ ml/min, 12% for $E < 30$ ml/min (Brøchner-Mortensen & Rødbro, 1976*a*). The individual relative renal function (%) was calculated as the ratio between the measured GFR value (ml/min/1.73 m^2) and the corresponding sex- and agedependent normal mean GFR (see below), the ratio being multiplied by 100.

Delimitation of relative renal function

In our department the normal mean GFR in men aged 20–39 years ($n=66$) is 111 ml/min per 1.73 m^2 surface area (coefficient of variation=12%). From this mean value and Wesson's collection of available inulin clearance data in normal men of various ages (Wesson, 1969) we calculated the regression of GFR on age in normal men from the age of 40 and onwards to be

$$\text{GFR} = -1.16 \text{ Age (years)} + 157.8 \text{ (ml/min/1.73 m}^2\text{)}$$

According to Smith (1951) the GFR in females is on the average 92.9% of GFR in males, i.e. 103 ml/min/1.73 m^2 for normal females aged 20–39 years. Assuming a similar relative decrease in GFR with age the regression of GFR on age in females from the age of 40 and onwards is

$$\text{GFR} = -1.07 \text{ Age (years)} + 146.0 \text{ (ml/min/1.73 m}^2\text{)}$$

Assuming the same coefficient of variation (12%) in normal subjects of both sexes and different ages, we defined normal ranges and different degrees of impaired relative renal function as stated in Table I; the delimitation of the four groups (normal, moderately, considerably, and severely impaired) corresponds to the successive subtraction of twice the coefficient of variation (24%) from corresponding normal mean.

The aim was to procure data from 480 subjects, 10 subjects in each of 48 (=2 \times 6 \times 4) sex-, age-, and function-dependent sub-groups:

- 2 sex-dependent groups (males and females)
- \times 6 age-dependent groups (20–29 years ... 70–79 years)
- \times 4 function-dependent groups (see above and Table I)

The patients were selected from a consecutive series of 1377 GFR determinations, from January 1974 to June 1976, mainly admitted from the Department of Nephrology. In the overwhelming majority of patients, plasma creatinine was determined simultaneously with GFR, but a difference in time of up to 2 days was accepted. The final material consisted hereafter of 380 determinations in 380 different patients, since it proved impossible in 21 of the 48 subgroups to reach the wanted 10 patients. The distribution of the 380 patients is given in Table II.

RESULTS

Plasma creatinine as a function of age

The coefficients of correlation between plasma creatinine and age for the four groups of relative renal function are given in Table III. In females, the plasma creatinine level increased significantly with age in only one of the four groups of relative renal function (moderately decreased). In males, too, the plasma creatinine level increased significantly with age in patients with moderately impaired relative renal function and in addition in patients with normal renal function.

Table II. 380 subjects investigated. Distribution according to normal and varying degrees of impaired relative renal function

Relative renal function	Age groups (years)											
	20–29		30–39		40–49		50–59		60–69		70–79	
	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂
Normal	10	10	10	10	10	10	10	10	10	10	8	5
Moderately impaired	10	7	10	7	10	10	10	10	10	10	5	2
Considerably impaired	3	2	7	7	9	6	10	10	10	10	3	1
Severely impaired	2	6	5	6	10	9	10	10	10	10	8	2

Table III. Correlation between plasma creatinine and age at normal and varying degrees of impaired relative renal function

Relative renal function	Coefficient of correlation		Significance	
	♀	♂	♀	♂
Normal	0.16	0.35	n.s.	$p < 0.01$
Moderately impaired	0.30	0.57	$p < 0.05$	$p < 0.001$
Considerably impaired	0.08	0.18	n.s.	n.s.
Severely impaired	-0.13	0.03	n.s.	n.s.

Mean values (± 1 standard error of mean) of plasma creatinine in each of the four function groups for each 10-year age group are depicted in Fig. 1. The figure demonstrates that plasma creatinine in each function group tends to be constant with age, the exceptions being the groups mentioned above in which the significant correlations between plasma creatinine and age appear to be due to a slightly higher plasma creatinine level in

one or two of the sub-groups with the eldest patients. Further calculations in these three function groups revealed that the mean relative renal function within each of these groups was slightly lower in the elderly than in the young patients. Since this is so and since the correlation analysis lends considerable weight to a few deviating values at one extreme of the investigated range, it can be assumed that mean plasma creatinine values in each of the function groups are, for practical purposes, independent of age.

Delimitation of plasma creatinine for assessment of relative renal function

The distribution of individual plasma creatinine concentrations in the four function groups is given in Fig. 2 for females and in Fig. 3 for males. In Fig. 2 the three horizontal hatched lines indicate from below: the upper limit of normal; the lower limit of "considerably increased plasma creatinine" (keeping all patients with moderately impaired relative renal function below this line); and the lower limit of "profoundly elevated plasma creatinine" (keeping all patients but one with considerably impaired

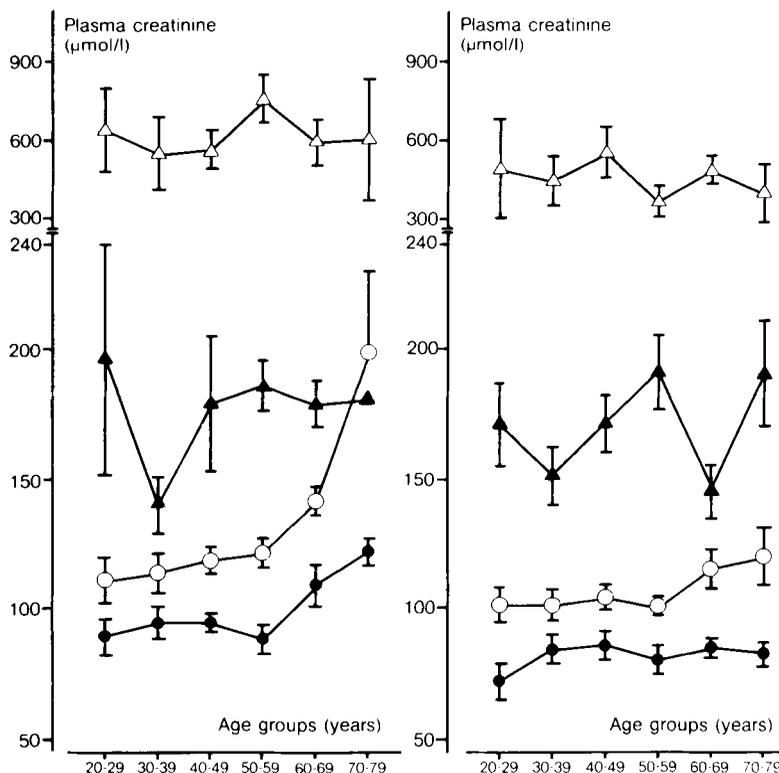


Fig. 1. Mean values ± 1 S.E.M. of plasma creatinine in 10-year age groups in males (left) and females (right) with different degrees of relative renal function: normal (●); moderately impaired (○); considerably impaired (▲); and severely impaired (△).

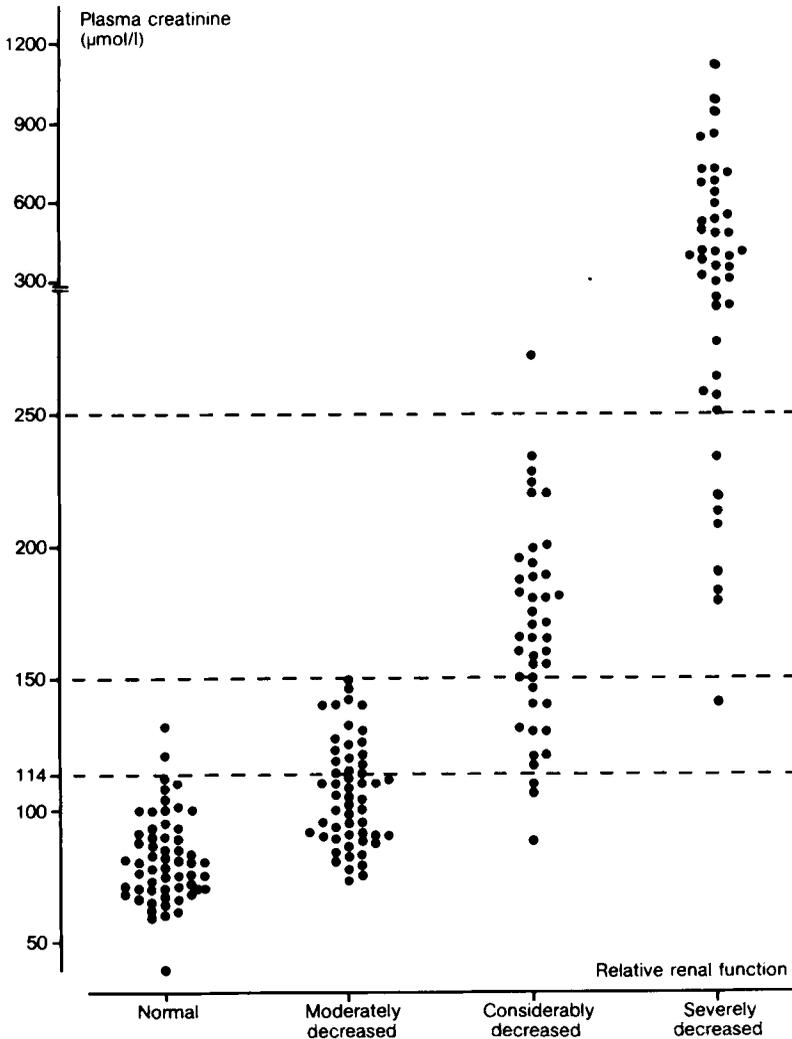


Fig. 2. Individual plasma creatinine concentrations in 200 females (aged 20–79 years) distributed according to normal and varying degrees of decreased relative renal function. The hatched lines indicate the limit for normal, moderately elevated, considerably elevated, and profoundly elevated plasma creatinine concentrations.

relative renal function below the line). In Fig. 3 the three horizontal hatched lines were drawn in analogy with the lines in Fig. 2.

Table IV summarizes the proposed delimitations of plasma creatinine for both sexes. The terms “moderately”, “considerably”, and “profoundly increased” values of plasma creatinine were so chosen (Figs. 2 and 3) in an attempt to reflect the more or less corresponding terms for relative renal function: normal, moderately *impaired*, and so forth.

DISCUSSION

In order to determine whether plasma creatinine can be used to assess relative renal function, it is

essential that GFR is measured with a reliable method. The method used in the present study is accurate and the most precise available (Brøchner-Mortensen & Rødbro, 1976a and 1976b).

The slightly lower than predicted values of relative renal function in a few sub-groups of elderly subjects may be due to chance, the more so since the numbers of subjects investigated in these sub-groups were relatively small (Table II). It may also be due to a less than optimal fit to the regression equations used, when these are applied to the oldest patients. Notwithstanding, the present study has demonstrated that mean plasma creatinine values for each sex in different groups of relative renal function can for practical purposes be considered to

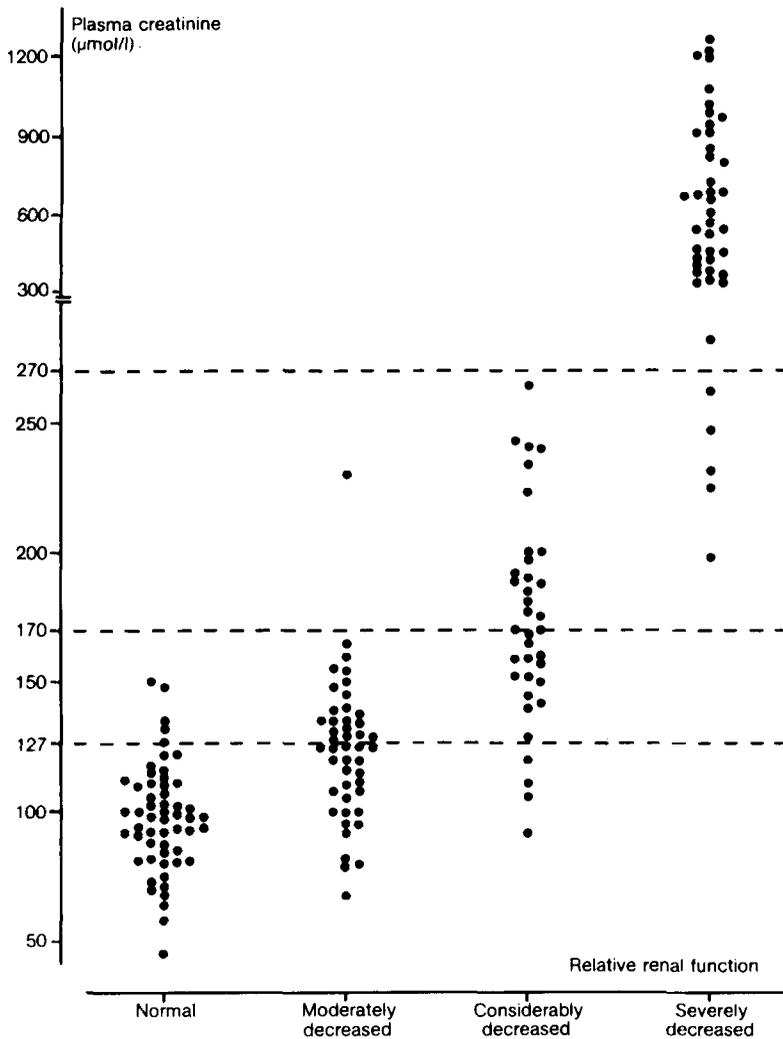


Fig. 3. Individual plasma creatinine concentrations in 180 males (aged 20–79 years) distributed according to normal and varying degrees of decreased *relative* renal function. The hatched lines indicate the limits for normal, moderately elevated, considerably elevated, and profoundly elevated plasma creatinine concentrations.

be independent of age. This indicates that plasma creatinine can in principle be used to assess different degrees of relative renal function without regard to age. The nosographic and diagnostic probabilities of this approach (with the suggested limits of plasma creatinine (Table IV) will be dealt with in a subsequent article. It should be stressed that the present study deals exclusively with *relative* renal function (in per cent of corresponding normal mean), and takes no account of the problem concerning the measurement of GFR in *absolute* terms (ml/min), which is highly relevant for the preoperative evaluation of postoperative renal function and dose calculations for potentially toxic drugs excreted via the kidneys. The *relative* renal function determines if, and to what extent, nephro-urological

disorders have affected the combined function of the two kidneys as a proportion of the normal value for that age and sex. Obviously, the present limits of plasma creatinine for such purposes are not ap-

Table IV. *Proposed limits of plasma creatinine concentrations for assessment of normal, moderately, considerably, and severely impaired relative renal function*

Sex	Plasma creatinine (µmol/l)			
	Normal	Moderately elevated	Considerably elevated	Severely elevated
Females	<115	115–150	151–250	>250
Males	<128	128–170	171–270	>270

plicable in patients who have undergone unilateral nephrectomy. The residual kidney may be quite healthy, with a finding of moderately or considerably impaired relative renal function; and furthermore, it is well known that the residual kidney often hypertrophies after unilateral nephrectomy (Tønnesen, Mogensen, Wolf, Hald & Munck, 1976).

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