Accurate Estimation of Glomerular Filtration Rate in Diabetic Nephropathy From Age, Body Weight, and Serum Creatinine

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OBJECTIVE — To assess, in diabetic nephropathy, the accuracy of a method that estimates glomerular function with age, body weight, and serum creatinine as parameters.

RESEARCH DESIGN AND METHODS — Glomerular filtration rate (GFR) was measured 57 times in 20 subjects with insulin-dependent diabetes mellitus and nephropathy with a single injection of ^{51}Cr-EDTA. At the same time, the estimated creatinine clearance (ml/min) was calculated with the Cockroft-Gault formula

$$(140 - \text{age [yr]}) \times \text{body wt [kg]} \times K/\text{serum creatinine [}\mu\text{mol/L]})$$
$$K = 1.23 \text{ for men, } 1.05 \text{ for women}$$

These values were then corrected for body surface area (1.73 m^2).

RESULTS — For GFR measurements <100 ml $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2} (n = 41), there was a strong positive correlation with the estimated creatinine clearance corrected for body surface area (r = 0.94, $P < 0.0001$). The slope of this regression line did not differ significantly from identity or the y-intercept from zero. On average, the Cockroft-Gault formula (corrected for body surface area) underestimated the GFR by only 3.1 ml $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2} (9.7 SD).

CONCLUSIONS — This formula, corrected for body surface area, gives accurate estimates of GFR when GFR <100 ml $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2}. This formula could be used with an acceptable degree of confidence when repeated isotope assessments of renal function in diabetic nephropathy are impracticable.

The accurate measurement of renal function in diabetic nephropathy is essential, because most patients show a progressive decline in glomerular filtration rate (GFR; 1). The most commonly used isotopic method of measuring renal function is by a single injection of ^{51}Cr-EDTA, which is accurate but time consuming and expensive, and repeated measurements are needed.

Other markers of renal glomerular function, e.g., the serum creatinine (or its inverse) or serum β_2-microglobulin are either inaccurate or not widely available (2,3). Cockroft and Gault (4) described a formula that allows the rapid estimation of creatinine clearance from age, body weight, and serum creatinine measurements; we assessed the accuracy of this method in measuring renal function in patients with diabetic nephropathy.

RESEARCH DESIGN AND METHODS

— As part of a prospective study on the progression of diabetic nephropathy, 20 insulin-dependent diabetic subjects with nephropathy and serum creatinine <250 μM were studied. All had been diagnosed with diabetes before the age of 30 yr and had required insulin from diagnosis. All patients had persistent proteinuria of at least 300 mg/24 h on at least two occasions, had sterile urine with a normal urinary sediment, a normal renal ultrasound, and no immunological evidence of renal disease other than diabetic nephropathy (Table 1). All patients gave informed consent to these procedures, which were approved by the hospital ethical committee.

Measurement of renal function

GFR was measured with a method based on that described by Brochner-Morten-

Table 1—*Clinical features in the patients at the time of the initial glomerular filtration rate measurement*

N (M/F)	10/10
AGE (YR)	43 ± 10.2
DIABETES DURATION (YR)	26.1 ± 7.2
DURATION OF PROTEINURIA (YR)	5.9 ± 4.1
SYSTOLIC BLOOD PRESSURE (MMHG)	154 ± 21
DIASTOLIC BLOOD PRESSURE (MMHG)	89 ± 15
SERUM CREATININE (μM)	115 ± 43

Values are means ± SD.

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Table 2—*Mean true glomerular filtration rate (GFR) and the equivalent values obtained with the Cockroft-Gault formula*

	ALL MEASUREMENTS	MEASUREMENTS <100 ML · MIN^{-1} · 1.73 M^{-2}
N	57	41
TRUE GFR (ML · MIN^{-1} · 1.73 M^{-2})	77.3 ± 38.0	58.4 ± 25.3
ESTIMATED CREATININE CLEARANCE (CORRECTED FOR BODY SURFACE AREA)	73.9 ± 34.5*	55.3 ± 22.5*
ESTIMATED CREATININE CLEARANCE (UNCORRECTED FOR BODY SURFACE AREA)	69.6 ± 31.0*	58.8 ± 25.8*

Values are means ± SD.
*Not significant vs. true GFR.

sen and Rodbro (2). A single injection of 75 μCi i.v. ^{51}Cr-EDTA was given at 0930, after a normal breakfast and morning insulin. After 2 h, four consecutive blood samples were taken at precisely 45-min intervals. Fifty-seven measurements of GFR were made in these patients over a mean period of 13 mo (3 times in 18 patients, twice in 1 patient, and once in another). The GFR was corrected to 1.73 m^2 body surface area. All measurements were made by the same observer.

Serum creatinine (modified Jaffé reaction; normal range <106 μM) was measured in the blood sample taken 2 h after isotope injection and body weight was measured to the nearest 0.1 kg. The estimated creatinine clearance was measured with the formula described by Cockroft and Gault (4) in which estimated creatinine clearance (ml/min) is

(140 − age [yr]) × body wt [kg] × *K*/serum creatinine [μM]) where
K is a constant factor that is
1.23 for men,
1.05 for women

The relationship between the estimated creatinine clearance and the isotopically measured or "true" GFR was assessed in four groups:

1) between all true measurements and all estimated measurements (both corrected for body surface area; $n = 57$);
2) between all true measurements and all estimated measurements, the latter uncorrected for body surface area ($n = 57$);
3) between true measurements <100 ml · min^{-1} · 1.73 m^{-2} and the equivalent estimated measurements (both corrected for body surface area; $n = 41$); and
4) between true measurements <100 ml · min^{-1} · 1.73 m^{-2} and the equivalent estimated clearances, the latter uncorrected for body surface area ($n = 41$).

Statistical methods

Mean estimated creatinine clearance in each group was compared with the equivalent mean true GFR for each group with a paired *t* test. Agreement between the two methods was then examined with simple linear regression in each group, with estimation of the slope and *y*-intercept of the regression line and their 95% confidence intervals. The difference between the true GFR and the estimated GFR for each observation was then plotted against the true GFR to give a further estimate of the agreement between methods. Data are means ± SD, and $P < 0.05$ was significant.

RESULTS — The mean true GFR for all measurements was 77.3 ± 38.0 ml · min^{-1} · 1.73 m^{-2} ($n = 57$) and 58.4 ± 25.3 ml · min^{-1} · 1.73 m^{-2} for measurements <100 ml · min^{-1} · 1.73 m^{-2} ($n = 41$). The equivalent mean values obtained with the Cockroft-Gault formula are shown in Table 2 and did not differ significantly from the true GFR. In all four groups, there was a strong positive correlation between the estimated creatinine clearance and the true GFR ($r = 0.90–0.94$, $P < 0.0001$).

The regression equations for the relationships between the true GFR and the equivalent estimated clearance in the four groups are shown in Table 3. The slope of this line was closest to identity for groups B and C (Fig. 1), and in the latter group the *y*-intercept was close to 0.

However, when the difference between the true GFR and the estimated creatinine clearance for paired observations in groups B and C were plotted against the true GFR (Fig. 2), it was clear that the degree of scatter in group 2 was less acceptable and increased markedly with the GFR (Fig. 2). The scatter was much less in group 3 (Fig. 2) in which

Table 3—*Slope and y-intercepts for simple linear regression between the estimated creatinine clearance and true glomerular filtration rate (GFR) in each group*

GROUP	SLOPE	Y-INTERCEPT
A	1.16 (1.04–1.28)	−3.3 (−11.8–5.2)
B	1.02 (0.91–1.13)	1.73 (−7.7–11.2)
C	1.04 (0.90–1.17)	0.97 (−7.2–9.1)
D	0.883 (0.75–1.02)	6.4 (−2.3–15.0)

Values in parentheses are 95% confidence intervals. Regression equations are: isotope GFR = (estimated creatinine clearance × slope) + *y*. Groups are defined in METHODS.

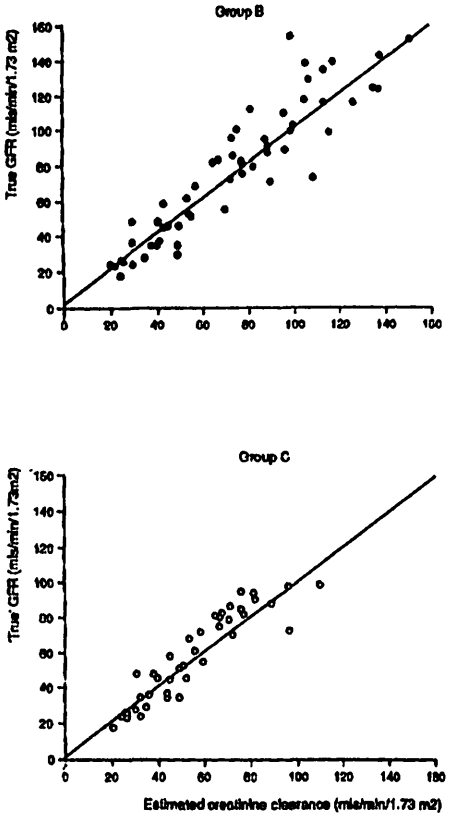

Figure 1—*Relationships between the true glomerular filtration rate and the estimated creatinine clearance in group B (all measurements uncorrected for body surface area; r = 0.92, P < 0.0001, n = 57) and group C (measurements <100 ml · min^{-1} · 1.73 m^{-2} corrected for body surface area; r = 0.94, P < 0.0001, n = 41).*

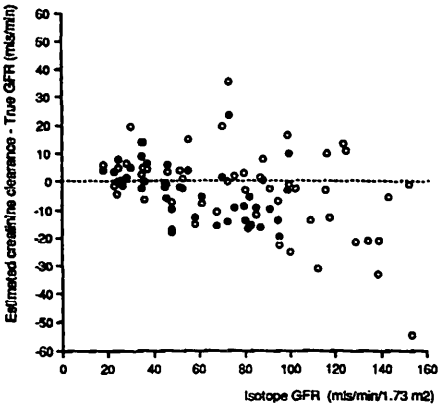

Figure 2—*Relationship between true glomerular filtration rate (GFR) and the residual difference between paired measurements (estimated creatinine clearance–true GFR). ●, Group B; ○, group C.*

the estimated creatinine clearance (corrected to body surface area) underestimated the true GFR by a mean of only 3.1 ± 9.7 ml · min^{-1} · 1.73 m^{-2}.

CONCLUSIONS— We have shown that it is possible to estimate GFR in insulin-dependent diabetic patients with nephropathy from their age, body weight, and serum creatinine with a reasonable degree of accuracy. The agreement between the true GFR and the estimated creatinine clearance is closest when the former is <100 ml · min^{-1} · 1.73 m^{-2} and when the estimated clearance is corrected for body surface area. If these criteria are fulfilled, then the regression line between the methods does not differ significantly from identity, and the estimated clearance underestimates the true GFR by a mean of 3.1 ml · min^{-1} · 1.73 m^{-2} up to a GFR of 100 ml · min^{-1} · 1.73 m^{-2}. The stronger relationship for GFR values <100 ml · min^{-1} · 1.73 m^{-2} is to be expected. Any imprecision in the measurements of serum creatinine would lead to the greatest inaccuracies in the Cockroft-Gault equation when the serum creatinine is low and the GFR normal or high.

The agreement between these two methods is better than that described in diabetic subjects without nephropathy and nondiabetic subjects with acute illnesses (5,6). This may reflect the fact that all GFR measurements were made at the same time of day, by the same observer, and that the serum creatinine and body weight were measured at the same time as the true GFR.

Correction of the estimated creatinine clearance for body surface area improved the agreement between the two methods and also reduced the scatter in the difference between estimations. Although body weight is already included in the Cockroft-Gault formula, it would seem reasonable to further correct the results to a standard body surface area to allow comparison with the true GFR.

A single measurement of GFR with ^{51}Cr-EDTA takes several hours and it may not be feasible to perform repeated observations in large numbers of diabetic subjects with nephropathy. One possible application of the Cockroft-Gault formula would be to measure the GFR isotopically until it fell below 100 ml · min^{-1} · 1.73 m^{-2} and then to continue the assessment of declining renal function with the formula when it is most reliable (<100 ml · min^{-1} · 1.73 m^{-2}). It could also be used to predict the mean GFR of groups with diabetic nephropathy, providing values were corrected for body surface area and the GFR was <~100 ml · min^{-1} · 1.73 m^{-2}.

We suggest that this method may therefore be of clinical use in assessing renal function in subjects with diabetic nephropathy.

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