Serum Creatinine, Height, and Weight Do Not Predict Glomerular Filtration Rate in Children with IDDM

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OBJECTIVE — To assess the validity of two equations: $K \times$ height/serum creatinine (KL/Cr; K = 0.55 for females 1–18 yr of age and 0.7 for males 12–18 yr of age) and (140 − age) × weight/72 × creatinine (×0.85 for women; Cockroft-Gault) in estimating glomerular filtration rate in children and adolescents with IDDM.

RESEARCH DESIGN AND METHODS — From the records of the Children's Hospital Diabetes Clinic, we selected 70 patients with GFR determined by ^{99m}Tc-labeled DTPA plasma clearance, stable renal function, and simultaneous measurements of height, weight, blood pressure, HbA_{1c}, and plasma creatinine. We compared DTPA-GFR with estimated GFR from KL/Cr and Cockroft-Gault equations for three groups: all patients, patients with DTPA-GFR ≤ 140 ml · min^{-1} · 1.73 m^{-2}, and patients with DTPA-GFR >140 ml · min^{-1} · 1.73 m^{-2}.

RESULTS — For all patients, mean values for DTPA-GFR = 147 (95% confidence interval, 139–155), for KL/Cr = 118 (110–125), and for Cockroft-Gault = 84 ml · min^{-1} · 1.73 m^{-2} (78–90). For patients with DTPA-GFR ≤ 140, DTPA-GFR = 123 (117–128), KL/Cr = 110 (100–119), and Cockroft-Gault = 92 (82–102). For patients with DTPA-GFR >140, DTPA-GFR = 167 (158–177), KL/Cr = 125 (114–136), and Cockroft-Gault = 77 (71–84). Linear regression analysis showed significant ($P < 0.05$) relationships for KL/Cr only in patients with DTPA-GFR ≤ 140 ($r = 0.29$), for Cockroft-Gault in all patients ($r = -0.46$), and for patients with DTPA-GFR ≤ 140 ($r = -0.31$). Determination of a revised K for use in KL/Cr from individual calculations of K (DTPA-GFR × Cr/L) yielded an average value of 0.70 (SD = 0.11). With the use of $K = 0.7$, the mean KL/Cr value for patients with DTPA-GFR ≤ 140 ml · min^{-1} · 1.73 m^{-2} was 125 ± 27 (95% confidence interval, 115–135), compared with a DTPA-GFR value of 123 ± 14 (95% confidence interval, 117–128).

CONCLUSIONS — KL/Cr and Cockroft-Gault do not accurately estimate DTPA plasma clearance. We recommend the use of K equal to 0.70 when estimating GFR in children and adolescents with IDDM and DTPA-GFR ≤ 140 using KL/Cr and do not recommend the use of the KL/Cr (for patients with DTPA-GFR >140) or the Cockroft-Gault equation in this population.

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IDDM, INSULIN-DEPENDENT DIABETES MELLITUS; NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; GFR, GLOMERULAR FILTRATION RATE; K, CONSTANT BASED ON AGE AND SEX; L, HEIGHT; Cr, CREATININE; DTPA-GFR, GFR DETERMINED BY DTPA CLEARANCE; BP, BLOOD PRESSURE; sBP, SYSTOLIC BLOOD PRESSURE; dBP, DIASTOLIC BLOOD PRESSURE; CI, CONFIDENCE INTERVAL.

Accurate determination of GFR is necessary in patients with altered renal function. Children and adolescents with IDDM have renal function ranging from normal to severe renal insufficiency. A significant number of patients have elevated GFRs early in disease development and poor metabolic control (1–4). Knowledge of a patient's GFR permits adjustment of medications with renal metabolism or toxicities (such as aminoglycosides), assessment of medication-related alteration of renal function (e.g., angiotensin-converting enzyme inhibitors), and monitoring of renal function with progression of diabetic nephropathy.

Several direct measurements of GFR are currently in use, including DTPA-GFR, ^{51}Cr-EDTA, iothalamate, and Cr or inulin clearance.

Although direct determination of GFR provides the best method for assessment of renal function, practical considerations preclude more widespread use. The methods are expensive. Patients are required to devote 6–24 h to complete testing. Evaluation requires radiation exposure, repeated blood sampling, and/or timed urine collections. Because of inconvenience and discomfort, patients may be unwilling to comply with testing requirements, and the results are therefore inaccurate. Incomplete injection or extravasation of marker substance or other technical limitations may complicate interpretation of results.

Therefore, several investigators have derived methods to estimate GFR from a single determination of serum Cr and various combinations of height, weight, and age (5–9). The association $K \times$ L (in cm)/Cr (in mg/dl) is widely accepted as a valid estimate of GFR in children and adolescents, correlating well with Cr, inulin, and DTPA clearances (5,10). The validity of this association has not been tested in children or adolescents with IDDM. The relationship (140 − age) × wt/72 × Cr for men (×0.85 for women; where age in years,

Table 1—*Description of study population*

	Mean ± SD	Median	Range
Age (yr)	15.7 ± 3.4	17.0	7–21
Duration of IDDM (yr)	8.5 ± 3.7	8.0	2–19
Height (cm)	159.3 ± 12.8	161.7	121.6–179.3
Weight (kg)	58.7 ± 16.8	59.5	29–120
Body surface area (M^2)	1.59 ± 0.27	1.62	0.98–2.31
sBP (mmHg)	127 ± 13	127	97–159
dBP (mmHg)	69 ± 14	68	34–105
Cr (μM)	76 ± 17	71	44–124
HA_{1c} (%)	11.1 ± 0.2	10.9	8.2–15.4

n = 70 (32 males and 38 females).

weight in kilograms, and plasma Cr in milligram per deciliter are used; 6) estimates GFR in adults with IDDM in some studies (11,12) but not in others (14), when corrected for body surface area, but has not been assessed in children or adolescents. In this study, we assessed the validity of these two equations in a population of children and adolescents with IDDM.

RESEARCH DESIGN AND METHODS

— At ≥5 yr duration of diabetes, patients of the Children's Hospital of Buffalo Diabetes Clinic routinely have GFR determined by DTPA plasma clearance, using an established plasma clearance technique (13), with intravenous injection of ^{99m}Tc-labeled DTPA, 103.6 MBq/m^2 of body surface area. DTPA-GFR is calculated from single exponential analysis of the plasma disappearance curve of samples drawn at 2, 3, and 4 h after injection and corrected for body surface area. The normal range in this institution is 80–140 ml · min^{-1} · 1.73 m^{-2}. We selected 70 patients with stable renal function (no significant change in serum Cr or urinalysis over 1 yr) and simultaneous measurements of serum Cr, height (measured by Diabetes Center nurse practitioners using a platform stadiometer), weight, sBP, and dBP. Patients with nondiabetic renal diseases were excluded. Serum Cr was measured by the Jaffe rate method on an automated system (Synchron CX, Beckman Instruments, Brea, CA). Glycemic control was determined by averaging all HbA_{1c} determinations (2–4/patient) during the year in which GFR determination was done.

We analyzed the study population in three groups: all patients, patients with DTPA-GFR ≤140, and patients with DTPA-GFR >140. Calculations of KL/Cr are based on previously published recommendations for use of K, with K = 0.55 for all females and boys ≤12 yr of age, and 0.70 for males >12 yr of age (5). For each group, we compared GFR as determined by DTPA plasma clearance, K times length divided by serum Cr, using the recommended K for each group (5), and the formula of Cockroft and Gault corrected to 1.73 m^2 of body surface area (6). To estimate K for our study population, we calculated K = GFR (ml · min^{-1} · 1.73 m^{-2}) × Cr/L.

We compared mean estimated GFR using the two equations with GFR measured from DTPA clearance using 95% CI and simple linear regression using Minitab Statistical Software (State College, PA).

RESULTS — Table 1 summarizes the study population. The mean values of DTPA-GFR and the calculated values of GFR from the KL/Cr and Cockroft-Gault equations are compared in Table 2. Because both equations have not previously been shown to estimate GFR in patients with elevated GFR, we analyzed data by dividing patients with DTPA-GFR ≤140 ml · min^{-1} · 1.73 m^{-2} (n = 32) and those with GFR >140 ml · min · 1.73 m^{-2} (n = 38). For all groups, both formulas significantly underestimate DTPA-GFR. To examine the relationship between measured GFR and estimates based on plasma Cr, we performed sim-

Table 2—*Comparison of measured GFR (^{99m}Tc-labeled DTPA clearance) with calculated estimates of GFR using KL/Cr and Cockroft-Gault equations*

GFR (ml · min^{-1} · 1.73 m^{-2})	Means ± SD	95% CI
DTPA-GFR		
All patients	147 ± 32	139–155
GFR ≤ 140	123 ± 14	117–128
GFR > 140	167 ± 29	158–177
KL/Cr		
All patients	118 ± 31	110–125
GFR ≤ 140	110 ± 25	100–119
GFR > 140	125 ± 33	114–136
Cockroft-Gault		
All patients	84 ± 25	78–90
GFR ≤ 140	92 ± 28	82–102
GFR >140	77 ± 20	71–84

Table 3—*Results of linear regression analysis of association between measured GFR (^{99m}Tc-labeled DTPA clearance) and calculated GFR from KL/Cr and Cockroft-Gault formulas*

	SE	Regression coefficient	F test	P value
KL/Cr				
All patients	31.8	0.25	3.96	0.051
GFR > 140	29.7	−0.04	0.07	0.789
GFR ≤ 140	12.6	0.29	10.58	0.003
Cockroft-Gault				
All patients	30.7	−0.46	9.53	0.003
GFR > 140	29.7	−0.04	0.03	0.871
GFR ≤ 140	11.7	−0.31	16.92	0.001

ple linear regression, with results shown in Table 3; curves for the KL/Cr estimate are shown in Fig. 1 and for the Cockroft-Gault estimate in Fig. 2.

Although the KL/Cr significantly underestimated DTPA-GFR, a significant positive relationship existed for those patients with DTPA-GFR values ≤140 ml · min · 1.73 m^{-2}, suggesting that a revision of *K* might result in improved predictability of the equation. To determine if a different *K* is more predictive of GFR in our patients with GFRs ≤140 ml · min · 1.73 m^{-2}, we determined the value for each patient by multiplying DTPA plasma clearance times serum Cr divided by height (*K* = GFR × Cr/L). The means ± SD value for this group of patients was 0.70 ± 0.11 (the published value for adult and adolescent males). The mean KL/Cr value for patients with DTPA-GFR ≤140 ml · min^{-1} · 1.73 m^{-2} was 125 ± 27 (95% CI 115–135), compared with a DTPA-GFR value of 123 ± 14 (95% CI 117–128). Linear regression comparing KL/Cr (using *K* = 0.70) with DTPA-GFR resulted in the relationship: DTPA-GFR = 81.1 + 0.334 KL/Cr (*F* test = 18.97, *P* < 0.001), suggesting that a *K* of 0.70 in patients with IDDM, in the absence of hyperfiltration, may provide a better estimate of GFR than previously published values.

The Cockroft-Gault equation did not predict DTPA-GFR in our patient population. For all patients combined, as well as for patients with DTPA-GFR ≤140 ml · min · 1.73 m^{-2}, a significant negative relationship was seen between measured and calculated GFRs.

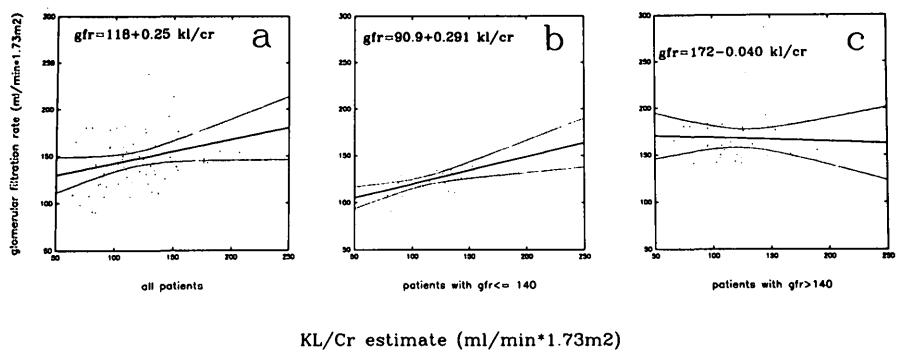

Figure 1—*Regression curves with 95% CI for KL/Cr prediction of DTPA-GFR for all patients (A), patients with DTPA-GFR ≤140 ml · min^{-1} · 1.73 m^{-2} (B), and patients with DTPA-GFR >140 ml · min^{-1} · 1.73 m^{-2} (C).*

CONCLUSIONS— Both formulas that are currently used to estimate GFR from height, weight, and serum Cr (KL/Cr and Cockroft-Gault) underestimate DTPA plasma clearance in this study population. This finding is seen in both patients with low-to-normal GFRs (≤140 ml · min · 1.73 m^{-2}) and those with hyperfiltration (GFR >140 ml · min · 1.73 m^{-2}).

The following are possible reasons for the observed underestimate. *1*) Laboratory error: the method of Cr determination in many laboratories gives a falsely elevated value in the presence of plasma ketones. Our patients were in stable health at the time of DTPA-GFR measurement, and urinary ketones, when measured, were not present; however, plasma ketones were not measured at the time of DTPA-GFR determination. 2) The equations used were based on GFR determined from either inulin or Cr clearance. Although we used DTPA rather than Cr or inulin clearance or both, a recent study (10) shows good correlation between DTPA-GFR and estimates of GFR from KL/Cr in patients with a wide range of renal function. 3) Patients with diabetes may differ from the general population with respect to body composition. Higher values of *K* represent an increased ratio of muscle mass to total body mass (5). The previously published value of 0.7 in adolescent males without diabetes applies, in our population, to younger boys and to all females as well. No studies exist that describe body composition of children with diabetes.

Recently published data for adults (14) show that the Cockroft-Gault equation significantly underestimates measured (^{51}Cr-labeled EDTA) GFR in normoalbuminuric, normotensive pa-

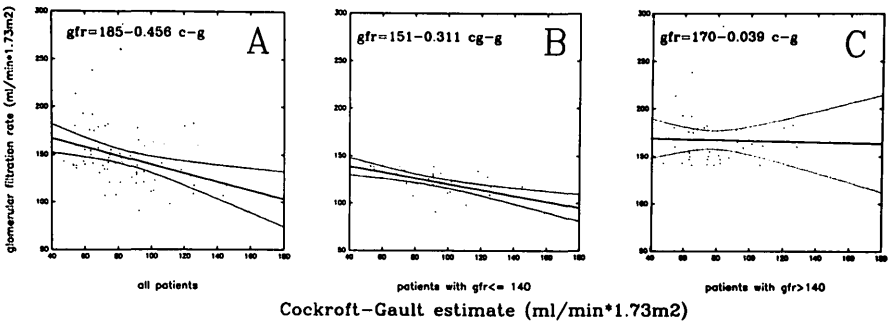

Figure 2—*Regression curves with 95% CI for Cockroft-Gault prediction of DTPA-GFR for all patients (A), patients with DTPA-GFR ≤140 ml · min^{-1} · 1.73 m^{-2} (B), and patients with DTPA-GFR >140 ml · min^{-1} · 1.73 m^{-2} (C).*

tients with both IDDM and NIDDM. Our data from a pediatric population are consistent with these findings. The negative correlation between Cockroft-Gault and DTPA-GFR is difficult to explain, and we have insufficient data to perform multiple regression analysis to help clarify which factors (age, weight, BP, glycemic control) contribute to the relationship.

In summary, *K*L/Cr and Cockroft-Gault are of limited value in estimating GFR determined by DTPA plasma clearance in young patients with IDDM. Additional characterization of body composition in children and adolescents with diabetes may clarify the relationship among age, height, weight, and CR. For children and adolescents with diminished or normal GFR (≤140 ml · min^{-1} · 1.73 m^{-2}), we recommend the use of $K = 0.70$ when estimating GFR with *K*L/Cr in children and adolescents with IDDM whose DTPA-GFR is ≤140 and do not recommend use of *K*L/Cr in those whose DTPA-GFR is >140. We do not recommend use of the Cockroft-Gault equation in this population.

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