Interest of Cystatin C in Screening Diabetic Patients for Early Impairment of Renal Function

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We compared cystatin C, creatinine, and the Cockroft formula for assessment of early renal failure, defined as a ^{51}Cr-EDTA clearance < 80 mL/min, in 89 diabetic patients with various degrees of renal impairment (glomerular filtration rate [GFR], 11.4 to 196.5 mL/min). The relationships between cystatin C, creatinine, and ^{51}Cr-EDTA clearance were linearized by plotting the reciprocals of the values, and correlation coefficients were determined. Sensitivity and specificity for the diagnosis of early renal failure were calculated from receiver operating characteristic (ROC) curves. Over the whole population, cystatin C was as well correlated with GFR (r = .74) as was creatinine (r = .67) or the Cockroft formula (r = .88). Moreover, its diagnostic accuracy was comparable to that of the 2 other parameters. Its sensitivity (86.8%) was better than that of creatinine (77.4%) for screening GFR < 80 mL/min, although the Cockroft formula was more sensitive (96.2%). The study of albuminuric diabetics (n = 63) led to similar conclusions, except for a poor sensitivity of cystatin C. In the 36 patients whose plasma creatinine was < 1 mg/dL, 10 (27.7%) had GFR < 80 mL/min. The correlation of creatinine with GFR, its diagnostic accuracy, and sensitivity were significantly lower than those of cystatin C. In this population of patients with normal creatinine levels, the correlation coefficient of cystatin C, its sensitivity, and its diagnostic accuracy were comparable to those of the Cockroft formula. A moderate reduction in GFR may be present in diabetic patients with low creatinine levels. Although Cockroft formula remains the most reliable and the less expensive tool for the evaluation of renal function, cystatin C is a more reliable criterion for screening and assessment than creatinine and represents a useful alternative to the Cockcroft-Gault formula.

DIABETIC NEPHROPATHY is the single most common cause of end-stage renal disease (ESRD) in the western world. Nearly 50% of all new cases of ESRD in the US are diagnosed in diabetic patients,[1] and epidemiologic studies have shown a dramatic increase in incidence and prevalence of ESRD in patients with type 2 diabetes in France.[2] Accurate evaluation of glomerular filtration rate (GFR) is thus of crucial importance in diabetic patients to detect early renal impairment. Indeed, the onset and course of diabetic nephropathy can be favorably influenced by appropriate therapy, such as tight glycemic control, effective antihypertensive treatment, lipid-lowering strategies, and protein restriction.[3] Such treatment can delay the appearance of microalbuminuria, proteinuria, and ESRD, which constitute cardiovascular and mortality risk factors in diabetic patients.[4-6] Therapy must be instigated at an early stage, when renal function is only moderately impaired[7] to avoid a self-perpetuating nephropathic process, which is little influenced by therapeutic intervention.[3] Early markers of diabetic nephropathy thus need to be identified. Although microalbuminuria is considered to be a risk factor for diabetic nephropathy and progressive renal insufficiency,[8,9] recent investigations have raised questions about its predictive value,[10] owing to its variability and low predictivity for the underlying renal pathology. For instance, some patients with microalbuminuria have normal renal structure,[11] while some normoalbuminuric diabetics have well-established diabetic nephropathic lesions.[12,13] Although creatinine concentration is widely used as an indirect estimation of GFR, it is not an ideal marker,[14,15] as it is influenced by muscle mass and diet. The Cockroft-Gault formula estimates glomerular function as a function of age, body weight, and plasma creatinine[16] and is recommended by the American Diabetes Association.[7] However, it is not routinely calculated, and most investigators prefer exogenous markers. Inulin has been supplanted by more conveniently measured labeled compounds, such as chromium ethylenediamine tetracetic acid (^{51}Cr-EDTA).[17] As an alternative to such costly methods, cystatin C has been proposed over the past decade as a marker of GFR. It appears to be as efficient as plasma creatinine and the Cockroft formula for detecting reduced GFR in adults with various types of kidney diseases with normal to moderately impaired kidney function.[18] It is considered to be an endogenous marker of GFR, because its serum concentration is almost totally dependant on GFR.[19-22] Moreover, cystatin C seems to be particularly valuable in patients with normal or slightly reduced GFR.[23] Nevertheless, there still remain discrepancies between studies comparing cystatin C with plasma creatinine, Cockroft formula, and isotopic measurements of GFR in diabetic patients.[23-25]

In this study, we compared cystatin C with conventional markers of renal function (creatinine, Cockroft formula) for predicting GFR, by reference to ^{51}Cr-EDTA clearance. In a population of diabetic patients with various degrees of renal impairment, we singled out microalbuminuric patients and patients in whom plasma creatinine was in the normal range. To our knowledge, we report for the first time the ability of cystatin C to replace creatinine or the Cockroft formula as a marker of early renal impairment in these 2 categories of patients.

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Table 1. Clinical and Biochemical Details of the Total Population, Albuminuric Patients, and Patients With Plasma Creatinine <1 mg/dL

	Total Population (n = 89)	Albuminuric Patients (n = 63)	Patients With Serum Creatinine < 1 mg/dL (n = 36)
Sex (M/F, no.)	53/36	40/23	21/15
Mean age (yr)	61 ± 13.9 (19-93)	59.8 ± 13.8 (19-93)	58.7 ± 15 (19-82)
Type of diabetes (type 1/type 2)	30/59	22/41	11/25
Mean body mass index (kg/m^2)	28.2 ± 4.7 (16.2-40.8)	28.3 ± 4.8 (16.2-40.8)	28.9 ± 4.8 (20-38.7)
HbA_1c (%)	9 ± 1.7 (6.1-15.1)	8.9 ± 1.7 (6.1-15.1)	9.4 ± 1.6 (6.1-13.1)
^{51}Cr-EDTA (mL/min)	73 ± 40.7 (11.4-196.5)	71.6 ± 42.8 (11.4-196.5)	104 ± 35.9 (34.2-196.5)
Plasma creatinine (mg/dL)	1.33 ± 0.67 (0.72-4.19)	1.42 ± 0.75 (0.72-4.19)	0.89 ± 0.08 (0.72-1)
Cockroft formula (mL/min)	70.7 ± 31.5 (20-160)	69.9 ± 33.2 (20-160)	95.2 ± 28.1 (46-160)
Cystatin C (mg/L)	1.23 ± 0.61 (0.53-3.99)	1.3 ± 0.66 (0.63-3.99)	0.87 ± 0.2 (0.63-1.75)
Albuminuria (mg/24 h)	432.8 ± 738.8 (4.6-4,330)	603 ± 820.9 (31.5-4,330)	179.5 ± 407 (11.4-2,358)

NOTE. Values are mean ± SD (min to max).

PATIENTS AND METHODS

Patients

Eighty-nine adult patients with diabetes admitted for assessment of renal function in the diabetes clinic of Haut-Levêque hospital (Pessac, France) were studied. This population comprised 53 men and 36 women, with a mean age of 61 years. Thirty patients had type 1 and 59 type 2 diabetes. The clinical and biochemical details of the patients are listed in Table 1.

Treatment With Diet, Oral Antidiabetics, or Insulin

Renal function was assessed by measuring urinary albumin excretion rate (AER), plasma creatinine, and cystatin C and by determining ^{51}Cr-EDTA plasma clearance. We also calculated the Cockroft-Gault formula. Sixty-three patients had nephropathy defined by AER > 30 mg/24 h. Renal failure was defined as ^{51}Cr-EDTA clearance < 80 mL/min. We studied patients with a wide range of GFR (11.4 to 196.5 mL/min). After correlations were evaluated in the total population of 89 patients, we singled out albuminuric patients (63 patients with AER > 30 mg/24 h) and patients with plasma creatinine in the normal range (36 patients with serum creatinine < 1 mg/dL). All 89 patients gave their informed consent to participate in the study.

Collection of Specimens

Blood plasma was collected on lithium heparinate Vacutainers (Plymouth, UK) for creatinine and cystatin C determinations and on EDTA Vacutainers for measurement of total glycosylated hemoglobin (HbA_{1c}). Three 24-hour urine samples were collected for determination of AER.

Analytical Methods

Plasma creatinine was determined on a multiparameter analyzer (Olympus AU 640; Olympus Optical, Tokyo, Japan) using the Jaffe method with bichromatic measurements according to the manufacturer's specifications. The estimated creatinine clearance was calculated with the formula described by Cockroft and Gault in which estimated creatinine clearance (mL/min) is: (140 − age [yr] × body weight [kg] × K/serum creatinine [μmol/L]) where K is a constant: 1.23 for men and 1.04 for women.[15] Cystatin C was determined on a nephelometric analyzer (Behring Nephelometer 2, Paris La Defense Cedex, France) by means of particle-enhanced immunonephelometry (N latex cystatin C, Dade Behring, Marburg, Germany). AER was determined on an immunonephelometric analyzer (Behring Nephelometer 2) using an appropriate kit (Nantiserum VO human albumin, Dade Behring). Urine cultures were checked for sterility. HbA_{1c} was measured by affinity chromatography using a Hi-AUTOA1c analyzer (A Menarini Diagnostics, Antony Cedex, France). Clearance of the radionucleide marker was measured after intravenous injection of ^{51}Cr-EDTA (Cis Industries, Gif/Yvette, France). After a single bolus of 100 μCi (3.7 MBq) of ^{51}Cr-EDTA, 4 venous blood samples were drawn at 75, 105, 135, and 165 minutes, and urinary samples were collected at 90, 120, 150, and 180 minutes. The ^{51}Cr-EDTA radioactivity was measured on a gamma counter (COBRA 2, model 05003, Packard Instruments, Meriden, CT).

Statistical Analysis

All statistical analyses were performed using Medcalc software on a PC computer (Zenith Data System, Puteaux, France). Correlations between ^{51}Cr-EDTA clearance and the Cockroft formula and reciprocal values of cystatin C and creatinine were calculated and compared. The sensitivity and specificity of plasma creatinine, Cockroft formula, and cystatin C were assessed from receiver operating characteristic (ROC) curves. To evaluate the sensitivity of the serum markers for assessment of renal impairment, a GFR < 80 mL/min was considered as a definition of renal failure. Nonparametric ROC curves were generated by plotting sensitivity versus 1 − specificity, giving the ideal test a sensitivity equal to 1 and a specificity equal to 1. Area under the curve (AUC) was calculated and compared according to the procedure of Hanley and McNeil.[31] The AUC is commonly > 0.5 with values ranging from 1 (ideal perfect separation of the tested values) to 0.5 (no apparent distribution difference between the tested groups). A value of $P < .05$ was considered significant.

RESULTS

Whole Population (n = 89)

Our population had varying degrees of renal impairment with a plasma creatinine ranging from 0.72 to 4.19 mg/dL, ^{51}Cr-EDTA clearance ranged from 11.4 to 196.5 mL/min, and 53 patients (59.5%) had a GFR < 80 mL/min. As shown in Fig 1, the comparison between ^{51}Cr-EDTA and the other parameters produced correlation coefficients of 0.88, 0.74, and 0.67 for the Cockroft formula, cystatin C, and plasma creatinine, respectively. All correlation coefficients with GFR were highly significant ($P < .0001$). Correlation coefficients with the Cockroft formula were significantly higher than those with creatinine ($P = .0004$) or cystatin C ($P = .0076$), which did not differ significantly ($P = .37$).

With a cut-off value of 80 mL/min, areas under the ROC curves were 0.942 for the Cockroft formula, 0.863 for cystatin C, and 0.812 for plasma creatinine. AUC did not differ significantly between serum cystatin C and creatinine (Fig 2). Cys-

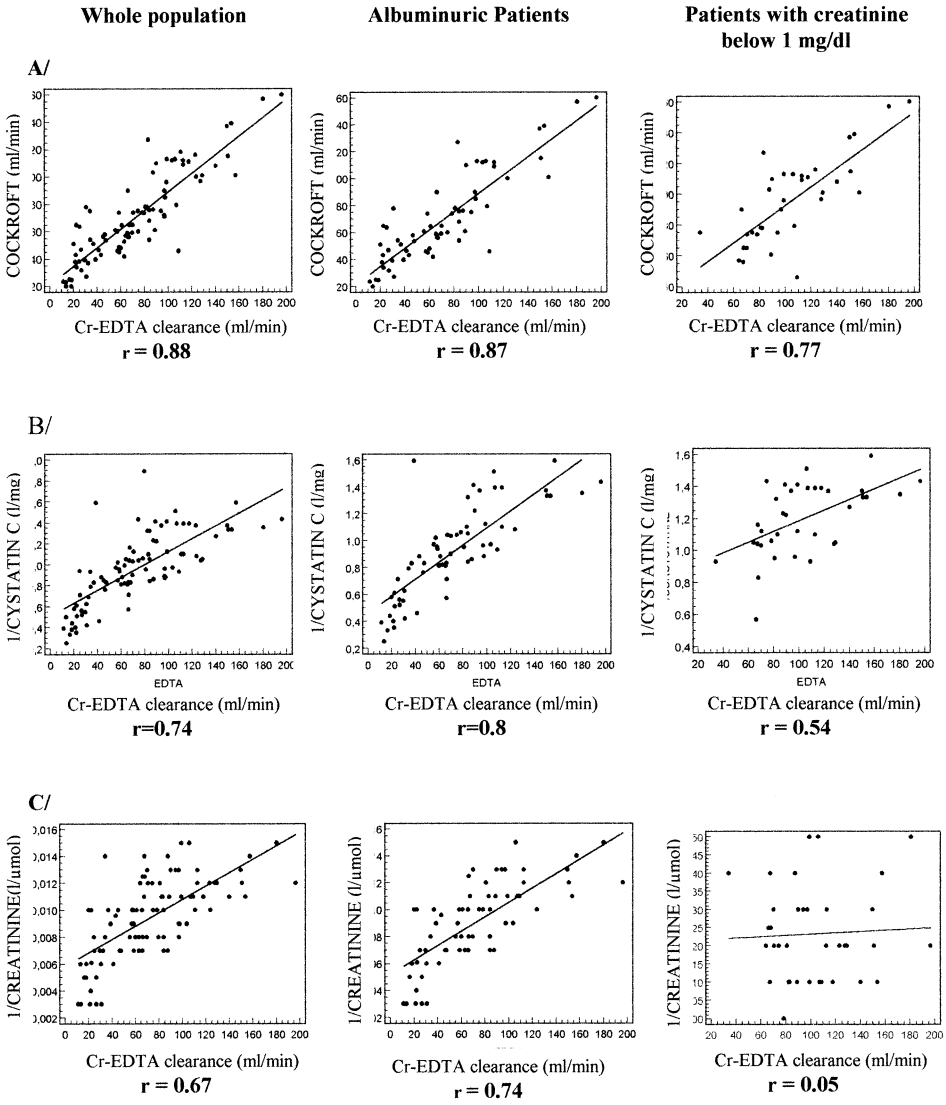

Fig 1. Comparison between (A) ^{51}Cr-EDTA clearance and Cockroft formula, (B) cystatin C, and (C) plasma creatinine in the whole population *v* albuminuric patients *v* patients with creatinine < 1 mg/dL. *r* = correlation coefficient.

tatin C had a higher sensitivity than did creatinine (86.8 *v* 77.4%). Nevertheless, the diagnostic efficiency of the Cockroft formula, with an optimal cut-off of 75 mL/min, was significantly superior to that of cystatin ($P < .05$) and was the better screening test with a sensitivity of 96.2%. Analysis of the results in subpopulations of patients based on other criteria (gender, type of diabetes, HbA_{1c}, body mass index [BMI]) showed no significant differences. Moreover, the indexation of

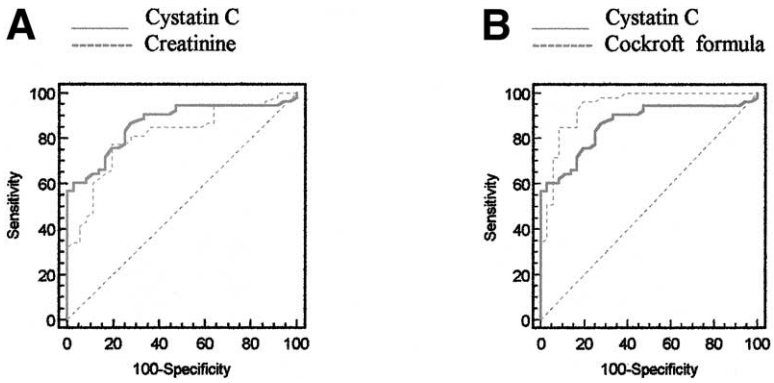

Fig 2. Comparison of AUC between (A) cystatin C and plasma creatinine and (B) Cockroft formula in the whole population (n = 89). AUC: creatinine, 0.812; cystatin C, 0.863; Cockroft formula, 0.942. Comparison of diagnostic accuracy: cystatin C *v* creatinine, *P* = .138; cystatin C *v* Cockroft, *P* = .033.

Table 2. Isotopic GFR Indexed to BMI (mL/min/kg/m^2), Body Surface Area (mL/min/1.73m^2), and Height (mL/min/m)

	GFR (mL/min)	GFR (mL/min/1.73 m^2)	GFR (mL/min/kg/m^2)	GFR (mL/min/m)
1/Cystatin C (1/mg)	$r = .74$	$r = .76$	$r = .71$	$r = .76$
	$P = .0076$	$P = .39$	$P = .38$	$P = .05$
1/Creatinine (1/μmol)	$r = .67$	$r = .72$	$r = .64$	$r = .7$
	$P = .0004$	$P = .15$	$P = .08$	$P = .0077$
Cockroft (mL/min)	$r = .88$	$r = .81$	$r = .77$	$r = .86$

renal measures does not influence these measures. Indeed, when isotopic GFR is indexed to BMI, body surface area, or height, Cockroft formula remains the parameter with the best correlation with isotopic GFR (Table 2). In our population of diabetic patients, the Cockroft formula was the most discriminant and the best marker of an altered GFR.

Albuminuric Patients (n = 63)

In the whole population, the correlation between GFR and albuminuria was poor ($r = -0.25$; $P = .01$). The diagnostic value of albuminuria for screening GFR < 80 mL/min was also poor (sensitivity, 30%; specificity, 88.9%; cut-off, 500 mg/24 h). Thirty-four patients had incipient nephropathy (AER 30 to 300 mg/24 h of albumin) and 29 had overt nephropathy, defined as the presence of macroproteinuria (Table 1).

In these albuminuric patients, the comparison between ^{51}Cr-EDTA and the other parameters gave correlation coefficients of 0.87, 0.8, and 0.74 for Cockroft formula, cystatin C, and plasma creatinine, respectively. All correlation coefficients with GFR were highly significant ($P < .0001$). The correlation coefficient with the Cockroft formula was significantly better than that with creatinine ($P = .036$), but not significantly different from that with cystatin C ($P = .2$). The correlation coefficients with creatinine and cystatin C did not differ ($P = .41$). These results are illustrated in Fig 1.

Analysis of the ROC curves gave an AUC of 0.934 for the Cockroft formula, 0.913 for cystatin C, and 0.872 for creatinine. The Cockroft formula offered the best sensitivity for screening GFR < 80 mL/min (94.7%; cut-off, 75 mL/min). As shown in Fig 3, its diagnostic efficiency was not significantly better than that of cystatin C ($P = .6$). Nevertheless, the sensitivity of cystatin C, at the optimal cut-off of 1.19 mg/L, was lower (68.4%). Thus, the Cockroft formula appeared to be the best parameter for screening GFR < 80 mL/min in this population with a high risk of renal involvement.

Patients With Normal Range Creatinine (n = 36)

In our population, 36 patients had creatinine < 1 mg/dL. Except for involvement of renal function, their characteristics were comparable to those of the whole population (Table 1). Among them 16 had microalbuminuria, and 6 had macroalbuminuria. Albuminuria was not significantly correlated with GFR ($r = -0.14$; $P = .41$). Despite a normal plasma creatinine, 10 (27.7%) of these patients had GFR < 80 mL/min. As shown in Fig 1, the comparison between ^{51}Cr-EDTA clearance and the other parameters gave correlation coefficients of 0.77, 0.54 for the Cockroft formula ($P < .0001$) and cystatin C ($P = .0006$), respectively. These 2 correlations were not significantly different ($P = .09$). Plasma creatinine was not correlated with GFR ($r = .05$; $P = .78$). The correlation of cystatin C was significantly higher than that of creatinine (0.54 *v* 0.05; $P = .02$).

ROC curves were analyzed in these 36 patients (creatinine < 1 mg/dL). With the same cut-off value as above, AUCs were 0.910 for the Cockroft formula, 0.785 for cystatin C, and 0.517 for creatinine. Diagnostic accuracy was not significantly different between the Cockroft formula and cystatin C ($P = .21$). By contrast, cystatin C was a significantly superior screen for GFR < 80 mL/min than was creatinine ($P = .03$) (Fig 4).

Moreover, in this population of patients with moderately impaired renal function, cystatin C was more sensitive than creatinine to screen a GFR < 80 mL/min (90% with a cut-off of 0.82 mg/L *v* 80% with a cut-off of 0.94 mg/dL). The sensitivity of the Cockroft formula was as good as cystatin C, although it underestimated GFR. Indeed, the best diagnostic accuracy was obtained with a cut-off of 75 mL/min, although

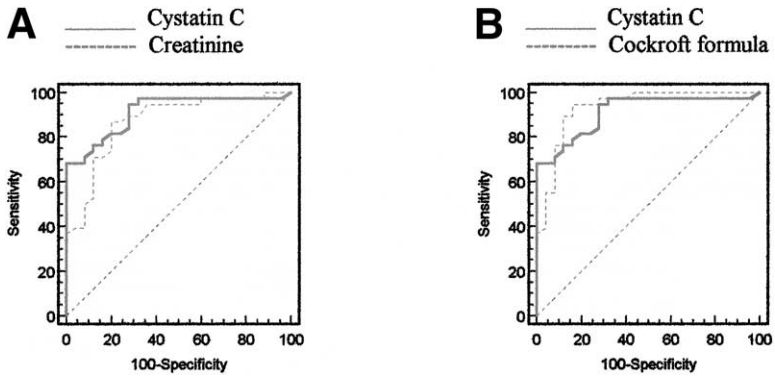

Fig 3. Comparison of AUC between (A) cystatin C and plasma creatinine and (B) Cockroft formula in albuminuric patients (n = 63). AUC: creatinine, 0.872; cystatin C, 0.913; Cockroft formula, 0.934. Comparison of diagnostic accuracy: cystatin C *v* creatinine, $P = .233$; cystatin C *v* Cockroft, $P = .6$.

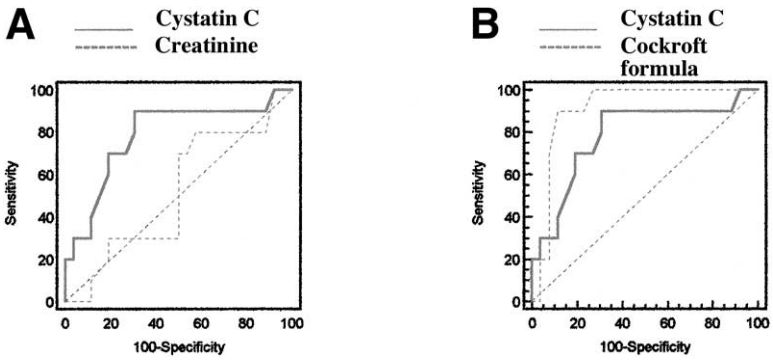

Fig 4. Comparison of AUC between (A) cystatin C and plasma creatinine and (B) Cockroft formula in the patients with creatinine < 1 mg/dL (n = 36). AUC: creatinine, 0.517; cystatin C, 0.785; Cockroft formula, 0.910. Comparison of diagnostic accuracy: cystatin C *v* creatinine, *P* = .03; Cystatin C *v* Cockroft, *P* = .27.

our objective was to detect a GFR < 80 mL/min. Thus, when creatinine is in the normal range, the Cockroft formula and cystatin C were equally efficient markers of GFR, but cystatin C was superior for screening an alteration in renal function, whatever the other characteristics of the patients (gender, age, HbA_{1c}, type of diabetes, BMI, albuminuria). The analyses of the ROC curves for the 3 parameters in the 3 populations are summarized in Table 3.

DISCUSSION

In this study, we compared the diagnostic value of creatinine, cystatin C, and the Cockroft formula for assessment of renal failure, defined as a ^{51}Cr-EDTA clearance < 80 mL/min. In diabetic patients with various degrees of renal impairment (GFR, 11.4 to 196.5 mL/min), the correlation of cystatin C with GFR was comparable to that of creatinine or the Cockroft formula. Furthermore, its diagnostic accuracy was similar to that of the 2 other parameters, while it had a higher sensitivity than creatinine for screening GFR < 80 mL/min. Nevertheless, the Cockroft formula remained the best marker of renal function. No significant correlation was found between GFR and albuminuria. The presence or absence of albuminuria did not predict impairment of renal function.

In albuminuric patients (AER > 30 mg/24 h), the correlation of the Cockroft formula with GFR was significantly better than that of creatinine, but not that of cystatin C, which had a comparable diagnostic efficiency to the Cockroft formula. Nevertheless, the sensitivity of cystatin C, at the optimal cut-off of 1.19 mg/L, was lower (68.4%). The Cockroft formula was thus the best parameter for screening GFR < 80 mL/min in this population with a high risk of renal involvement.

In patients with creatinine values < 1 mg/dL, the reciprocal value of creatinine was not correlated with GFR (r = .05; P = .78). Even though 10 of these 36 patients had GFR < 80 mL/min, creatinine was not a good screening marker, and its diagnostic accuracy and sensitivity were poor. Diabetic patients with plasma creatinine levels < 1 mg/dL may have a moderate reduction in GFR (< 80 mL/min) (10 of our 36 patients). We found cystatin C to be a more reliable parameter than creatinine for screening and evaluation of the GFR in these patients. Because the diagnostic accuracy of the Cockroft formula did not differ significantly from that and it had comparable sensitivity to cystatin C, we concluded that cystatin C represented a valuable screening marker for altered GFR in diabetic patients with creatinine < 1 mg/dL. In this population with creatinine in the normal range, early detection of renal impairment is important, because it enables early treatment. The normality of creatinine levels may be a distortion, as the absolute value does not take account of muscle mass or age of the patient.

Indeed, the Cockroft formula takes account of age, body weight, and gender, which are well-known predictors of muscle mass, and it remains well correlated to GFR in these patients. However, some disabled patients with denutrition and weak fat-free mass cannot stand up, so the measurement of their body

Table 3. Comparison of Sensitivity, Specificity, and AUC for Plasma Creatinine, Cystatin C, and Cockroft Formula in the Three Populations

	AUC	Correlation Coefficient With GFR	Sensitivity (%)	Specificity (%)
Whole population				
Plasma creatinine (>1.05 mg/dL)	0.812	0.67	77.4	80.6
Cystatin C (>0.95 mg/L)	0.863	0.74	86.8	72.2
Cockroft (<75 mL/min)	0.942	0.88	96.2	80.6
Albuminuric patients				
Plasma creatinine (>1.05 mg/dL)	0.872	0.74	86.8	80
Cystatin C (>1.19 mg/L)	0.913	0.8	68.4	100
Cockroft (<75 mL/min)	0.934	0.87	94.7	84
Patients with creatinine < 1 mg/dL				
Plasma creatinine (>0.94 mg/dL)	0.517	0.05	80.0	42.3
Cystatin C (>0.82 mg/L)	0.785	0.54	90.0	69.2
Cockroft (<75 mL/min)	0.910	0.77	90.0	88.5

Abbreviation: AUC, area under the curve.

weight is quite difficult. In these patients with falsely normal creatinine levels, cystatin C can be a valuable alternative to the calculation of Cockroft formula to assess renal function.

Previous studies on the screening value of cystatin C in diabetic patients have led to rather contradictory conclusions. Harmoinen et al[23] found that it was more sensitive than creatinine, while Oddoze et al[24] claimed it was not. More recently, Mussap et al[25] demonstrated that cystatin C was a more accurate serum marker than creatinine or the Cockroft-estimated GFR in discriminating type 2 diabetic patients with reduced GFR (< 80 mL/min) from those with normal GFR. The discrepancies may be accounted for by differences in the populations and/or the experimental conditions.

Oddoze et al studied 49 diabetic patients with an isotopically determined GFR (80 mL/min), which was slightly higher than the mean of our population (n = 89, GFR = 73 mL/min). Although like us, they found no difference in the correlation coefficient with GFR and diagnostic performance of plasma creatinine, cystatin C, and Cockcroft formula, creatinine appeared to be superior to that reported by other investigators,[18,19,21-23,25,31] including Cockroft and Gault.[16] This unusual accuracy of creatinine values was probably due to the inclusion of a high proportion of patients on a protein-restricted diet (50% of the population), as these patients would almost certainly have had a low creatinine intake. Finally, the small number of patients with early renal impairment (n = 12) would have precluded a better diagnostic performance of cystatin C. Thus, the performance of creatinine is better when levels are already increased. Harmoinen et al[23] studied 47 non–insulin-dependent diabetic patients with renal parameters similar to our 36 patients with plasma creatinine < 1 mg/dL. Although they did not report results for the Cockcroft formula, they found a better correlation for cystatin C than for creatinine, and as we did here, a better diagnostic performance. Mussap et al studied 52 type 2 diabetic patients with a mean isotopically GFR of 77 mL/min and a lower mean creatinine than in our population of 89 diabetic patients (1.0 *v* 1.33 mg/dL), and 53.8% of the patients had GFR < 80 mL/min. Surprisingly, they found a poor correlation with the Cockroft formula, especially in patients with GFR < 80 mL/min. Creatinine and Cockroft formula were much less sensitive for screening GFR < 80 mL/min than in our population (62% *v* 77.4% for creatinine; 82% *v* 96.2% for Cockroft formula). In contrast, cystatin C was particularly sensitive (97% *v* 86.8%) and accurate (AUC, 0.954 *v* 0.863) for screening GFR < 80 mL/min at the optimal cut-off of 0.93 mg/L. Although we did not find such good performance in our type 2 diabetic patients (n = 59), results were identical in the whole population. This may reflect the fact that Mussap et al studied patients with less renal impairment than we did, which, as we found, increases the diagnostic accuracy of cystatin C. They also found that cystatin C levels increase earlier and more rapidly than those of plasma creatinine with the reduction in GFR. This is consistent with the superior sensitivity of cystatin C in our population of patients with creatinine values < 1 mg/dL.

These results suggest that cystatin C is a good maker of renal function in patients with incipient renal impairment, as has been reported in nondiabetic patients,[18,21,22,26,27] patients with renal transplants,[28] and healthy patients.[29] Below 1 mg/dL, we found that plasma creatinine was not correlated with GFR, despite the presence of mild renal impairment (GFR < 80 mL/min in 10 of 36 patients). As reported in healthy patients,[29] we found a correlation between cystatin C and GFR. The higher diagnostic performance at low creatinine values led to a better sensitivity for detection of renal insufficiency, which has been reported in nondiabetic patients.[26,30] Indeed, we found that a cut-off of 0.82 mg/L enabled the detection of 90% of patients with early renal impairment with creatinine < 1 mg/dL.

Conclusion

In summary, we evaluated cystatin C as a marker of renal impairment in a large population of diabetic patients (n = 89). Cystatin C was well correlated with GFR, and its diagnostic accuracy was comparable to that of creatinine. However, the Cockcroft formula remained the best marker of renal function in the whole population. The study of albuminuric diabetics (n = 63) led to similar conclusions. The interest of cystatin C is in patients with low creatinine (<1 mg/dL), whose GFR is not predicted by the plasma creatinine level. A significant proportion of these patients (27%) have incipient renal impairment, which is detected by a high cystatin C (> 0.82 mg/L) or by the Cockcroft formula with similar diagnostic accuracy. Although the Cockcroft formula remains the most reliable and the less expensive tool for evaluation of renal function, the high sensitivity of cystatin C and its diagnostic accuracy at low creatinine levels makes it a good predictor of later renal impairment in diabetic patients, especially as the value of microalbuminuria in these patients has been questioned by recent work.

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