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Short communication

Validation of estimated renal function measurements compared with the isotopic glomerular filtration rate in an HIV-infected cohort

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ABSTRACT

We performed a cross-sectional study to determine the best method for estimating the glomerular filtration rate (GFR) in HIV-infected subjects. Isotopic GFR was correlated with 24-h urine creatinine clearance, cystatin C levels, and 3 creatinine-based equations—the Modification of Diet in Renal Disease (MDRD), Cockcroft–Gault (CG), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)—in 15 patients. Cystatin C showed the strongest correlation with isotopic GFR ($r = -0.760$, $p = 0.001$). When cystatin C was used as the reference variable for all 106 patients, CKD-EPI proved to be superior to the other equations ($r = -0.671$, $p < 0.001$). Time with HIV infection, unsuppressed viral load, low CD4 T-cell counts, and use of protease inhibitors are related to an increased risk of renal impairment, leading us to recommend early initiation of antiretroviral therapy accompanied by a regular renal study.

Renal dysfunction has become increasingly relevant in HIV-infected patients, reaching an estimated prevalence of up to 30% (Campbell et al., 2009; Choi et al., 2009; Gupta et al., 2005; Mocroft et al., 2007; Wyatt et al., 2007). In addition to traditional risk factors, this disorder has been associated with specific HIV conditions, such as CD4+ T-cell count, HIV-1 RNA viral replication, and importantly, antiretroviral therapy (Campbell et al., 2009; Mocroft et al., 2007; Wyatt et al., 2007; Hawkins, 2010).

The importance of recognizing renal damage is emphasized by the strong relationship between chronic kidney disease and increased morbidity and mortality (Choi et al., 2009; Gardner et al., 2003; Szczech et al., 2002). Kidney disease tends to be silent during the initial stages; therefore, early detection and management are essential. Isotopic determination of the glomerular filtration rate (GFR) is the reference method for determining renal function (Stevens et al., 2006). However, procedures using exogenous substances are invasive, time-consuming, and not without risk for the patient and technical personnel; consequently, they are not routinely used. Renal function can be estimated using creatinine-based equations: the Cockcroft–Gault equation (CG) (Cockcroft and Gault, 1976), the Modification of Diet in Renal Disease equation (MDRD) (Levey et al., 1999), and more recently, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey et al., 2009). Serum cystatin C level is an alternative measurement of kidney function and, since it is not related to age or muscle mass, has proven superior to creatinine-based measurements in the general population for detection of kidney disease.

Studies assessing the usefulness of different estimations of renal function in the HIV-infected population are scarce and have controversial results (Barraclough et al., 2009; Odden et al., 2007).

We performed a cross-sectional observational study of patients attended at our HIV Unit over a 6-month period to validate CG, MDRD, CKD-EPI, and cystatin C as methods for estimating renal function using isotopic GFR as the reference technique. The first 106 patients who agreed to participate were included. The exclusion criteria were malnutrition (defined as a body mass index [BMI] < 18.5 kg/m^2), decompensated liver disease, and myopathy. Isotopic GFR was measured in the first 15 patients who agreed

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to participate. The Independent Ethics Committee of our centre approved the study (EO-08-020), and all patients gave their signed informed consent before inclusion.

All participants were interviewed to obtain demographic, lifestyle, and clinical data, as well as data on concomitant treatment and HIV infection. BMI was calculated, blood pressure was recorded, and a blood sample was extracted for biochemistry determinations. Cystatin C levels were measured using nephelometric immunoassay (Nephelometer BN ProSpec, Siemens). Creatinine clearance and quantitative urine protein were determined using 24-hour urine collection (24 h CrCl). Isotopic GFR was measured as described elsewhere (Gault and Dossetor, 1968).

The Pearson correlation coefficient was calculated to assess the correlation between the reference method (isotopic GFR) and the estimated methods in the bivariate analysis. Multivariate linear regression models were used to evaluate this association by adjusting for HIV-related conditions and demographic and clinical covariates. The analyses were performed using SPSS, version 15 (SPSS Inc., Chicago, IL, USA).

The baseline characteristics of the 106 patients are summarized in Table 1. The proportion of patients with altered glomerular filtration (<60 ml/min/1.73 m^2) was 5.7% (6 patients) by the MDRD equation and 3.8% (4 patients) by the CG equation. Of the total number of patients included, 19 [18%] presented proteinuria and 20 [19%] had haematuria.

Table 1
Baseline characteristics.

	Total (n = 106)	Isotopic glomerular filtration substudy (n = 15)
Gender (male, %)	92 [86.8%]	14 (93%)
Caucasian, n [%]	105 [99%]	15 [100%]
Age, years	45.5 (41.75; 50)	45 (42; 50)
>50 years old, n [%]	21 [19.8%]	4 [26.6%]
>60 years old, n [%]	8 [7.5%]	2 [13%]
BMI (kg/m^2)	23.9 (21.76; 26.16)	23.15 (21.31; 26.35)
Diabetes, n [%]	6 [5.7%]	1 [6.7%]
Hypertension, n [%]	25 [23.6%]	6 [40%]
Hepatitis B/C co-infection, n [%][a]	29 [47.2%]	5 [33%]
Potentially nephrotoxic concomitant therapy, n [%]	32 [30%]	5 [33%]
Time since HIV+ diagnosis, years	14 (8; 20)	11 (3; 17)
Current CD4+ T (cells/μl)	544 (351; 719)	553 (430; 902)
Nadir CD4+ T (cells/μl)	210 (91; 296)	207 (23; 306)
Suppressed viral load, n [%]	90 [84.9%]	12 [80%]
Time with suppressed viral load, months	59 (27.73; 106.53)	90 (7.23; 114.13)
Proportion of time with suppressed viral load[b]	43.8% (19; 65.7)	44% (22.6; 66.4)
Time on ARV therapy, months	139 (83; 179)	137 (29; 167)
Proportion time of infection on ARV therapy[c]	84% (63; 95.7)	86% (63.3; 93.3)
Current use of ARV therapy, n [%]	104 [98%]	15 [100%]
Current use of PI, n [%]	63 [59%]	7 [46.7%]
Current use of TDF, n [%]	65 [61%]	7 [46.7%]
Time on PI, months	76 (18.77; 127.73)	66.7 (15; 97.9)
Time on TDF, months	29 (4.6; 62)	26.7 (4.4; 55.5)

Data are expressed as the median (IQR) unless otherwise indicated.
BMI, body mass index; IQR, interquartile range; ARV, antiretroviral; PI, protease inhibitors; TDF, tenofovir; n, number of patients.

[a] No patients were receiving interferon/ribavirin for at least 6 months before the study.

[b] Proportion of time with suppressed viral load: time on suppressed viral load/time with HIV infection × 100.

[c] Proportion time of infection on ARV therapy: time on antiretroviral therapy/time with HIV infection × 100.

First, we compared isotopic GFR with cystatin C, CG, CKD-EPI, MDRD, and 24 h CrCl in the 15 patients for whom isotopic GFR was determined. Cystatin C showed the strongest correlation with isotopic GFR (r = −0.760, p = 0.001), followed by CG (r = 0.728, p = 0.02), CKD-EPI (r = 0.660, p = 0.007), MDRD (r = 0.655, p = 0.008), and 24 h CrCl (r = 0.583, p = 0.023) (Fig. 1).

In a subsequent analysis including all 106 patients, cystatin C was used as the reference estimation, as it showed the highest correlation with isotopic GFR. It was compared with the creatinine-based equations and 24 h CrCl. The strongest correlation was with CKD-EPI (r = −0.671, p < 0.001), followed by MDRD (r = −0.598, p < 0.001), CG (r = −0.572, p < 0.001), and 24 h CrCl (r = −0.372, p = 0.001) (Fig. 2).

Evaluation of comorbid conditions (Table 2) revealed that patients with hypertension had statistically significant worse levels in all the variables analysed. In the subgroup of patients included in the isotopic GFR analysis, 40% fulfilled the criteria for hypertension. Patients with hepatitis co-infection showed a low level of estimated GFR, but the results did not achieve statistical significance, except in the case of cystatin C, where the results were significantly worse in co-infected patients (p = 0.029).

The median values of the creatinine-based equations, cystatin C, and isotopic GFR were worse in patients with more years since diagnosis of HIV infection. The differences achieved statistical significance in the case of CG (p = 0.040) and 24 h CrCl (p = 0.032). However, no differences were observed with respect to time on antiretroviral treatment (p = 0.097 and p = 0.207, respectively) (Table 2). These parameters were also worse in patients with a detectable viral load, and the difference was statistically significant in the case of cystatin C (p = 0.002, Table 2). In the case of CD4+ cell counts, only cystatin C exhibited a statistically significant difference between the groups (p = 0.002).

Regarding antiretroviral treatment, no differences were observed for GFR between patients who received NRTIs, NNRTIs, integrase inhibitors, fusion inhibitors, or CCR5 inhibitors (data not shown), except in patients taking a PI-containing regimen who had a low estimated GFR and for whom statistical significance was achieved with the CG equation (p = 0.036). As for patients on regimens containing TDF, the percentages of patients with haematuria and proteinuria were similar to those of patients who did not receive this antiretroviral, as were the median values for estimated filtration rates, even when only those patients with prolonged exposure to TDF (more than 5 years) were taken into account.

In the subgroup of 15 patients, the comparison of isotopic GFR with cystatin C, 24 h CrCl, and the estimated GFR equations revealed that the results of the multivariate model were not significantly different when adjusted for clinical and demographic covariates. When cystatin C was used as a reference, hypertension was the only variable that modified the relationship between cystatin C and isotopic GFR, 24 h CrCl, and the GFR equations. The highest response was obtained with isotopic GFR (R^2 = 71.7%, p = 0.032), followed by 24 h CrCl (R^2 = 63.4%, p = 0.006), MDRD (R^2 = 63.3%, p = 0.029), and CG (R^2 = 62.8%, p = 0.013). The other variables did not achieve statistical significance.

Although 24 h CrCl is one of the most frequently used methods for evaluating renal function in the general population, it is cumbersome and susceptible to error. In our study, 24 h CrCl showed the worst correlation (inferior to estimated GFR equations and cystatin C) when compared with isotopic GFR. Therefore, other parameters have been assessed to better estimate renal filtration (Delanaye et al., 2008; Delanaye and Cohen, 2008; Levey et al., 2006; Levey et al., 2009; Stevens et al., 2007, 2010).

Studies in the general population show that cystatin C level is a more linear predictor of renal function, especially in older patients or those with mild or moderate renal abnormalities (Shlipak et al.,

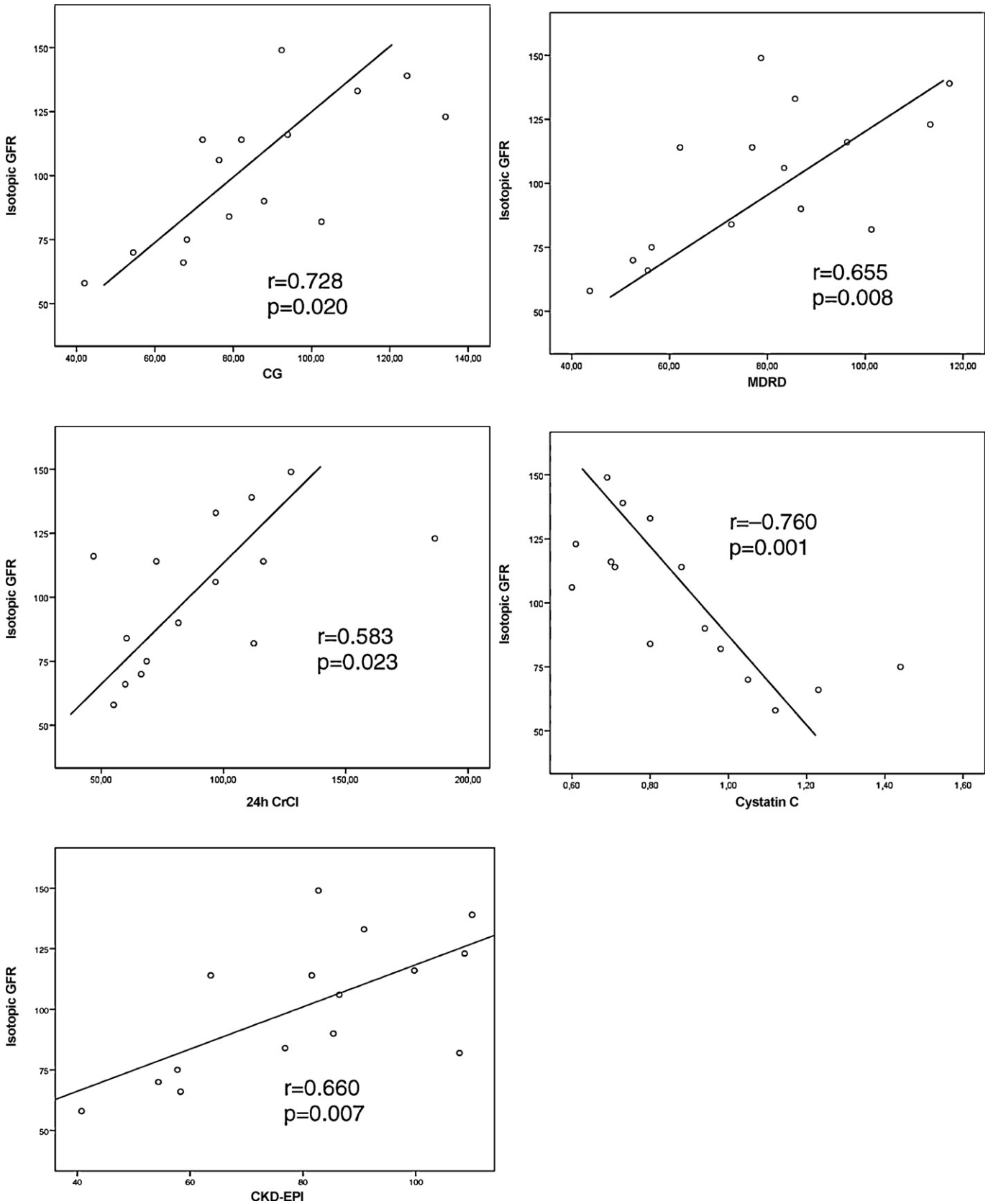

Fig. 1. Results of Pearson correlation. Comparisons of patients included in the isotopic glomerular filtration substudy ($n = 15$). CG, Cockcroft–Gault; MDRD, Modification of Diet in Renal Disease; 24 h CrCl, 24-hour creatinine clearance; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate.

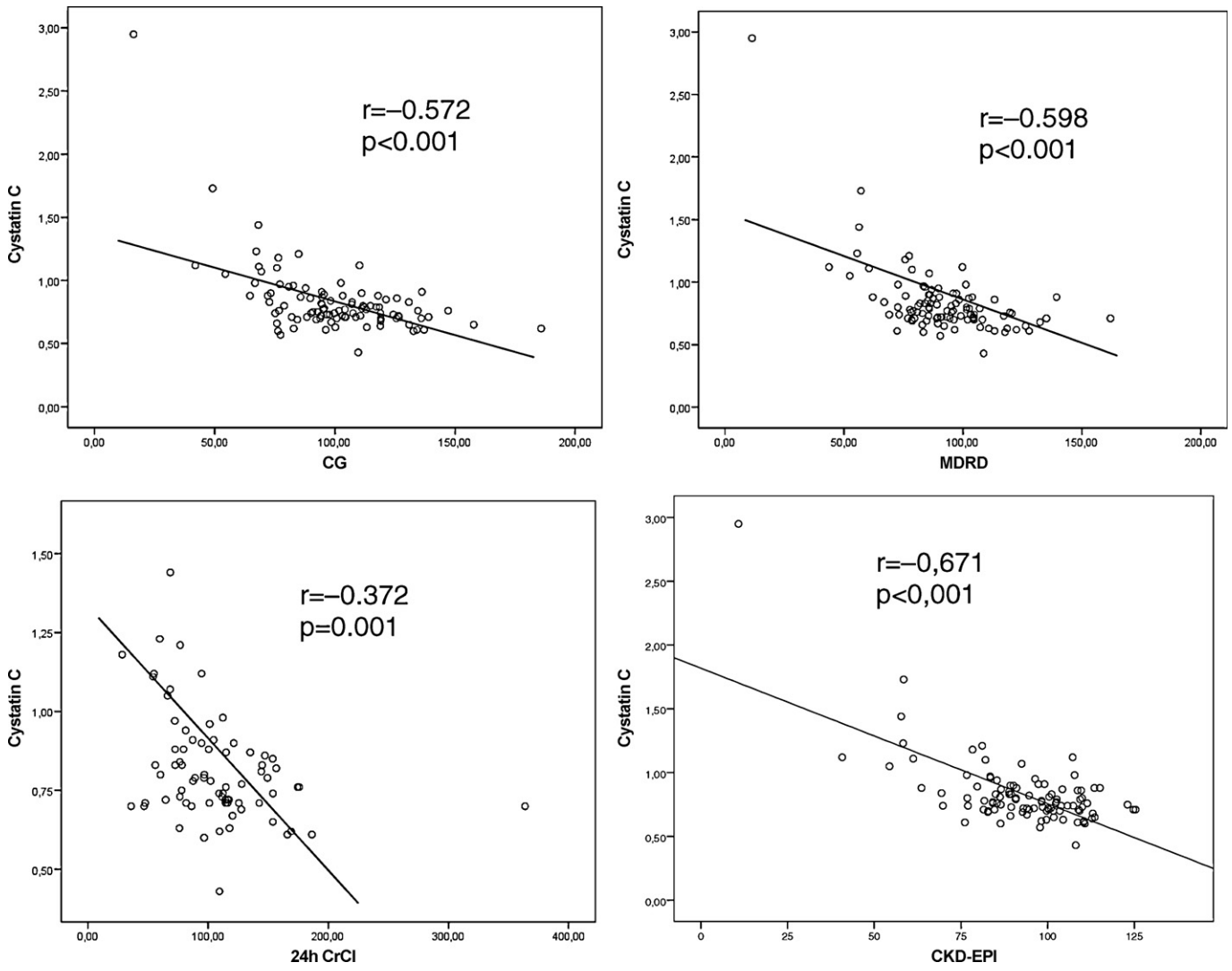

Fig. 2. Results of Pearson correlation. Comparisons in all the patients included (n = 106). CG, Cockcroft–Gault; MDRD, Modification of Diet in Renal Disease; 24 h CrCl, 24-hour creatinine clearance; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate.

2005). In fact, unlike creatinine-based measurements, cystatin C is very accurate and responds more quickly to changes in GFR than creatinine (Filler et al., 2005; Gourishankar et al., 2008; Le Bricon et al., 2000; White et al., 2005). However, the results of recent studies assessing cystatin C in the HIV-infected population are controversial, probably due to differences in patient characteristics, mainly in terms of age and BMI. Our data confirm the greater sensitivity for cystatin C in HIV-infected patients with normal renal function, followed by the CG equation. CKD-EPI, on the other hand, is a new formula that seems to be more precise than MDRD in the non-HIV-infected population, especially in subjects with normal GFR (>60 ml/min/1.73 m^2); however, no data are available for the HIV-infected population. Our analysis evaluated HIV-infected patients with normal GFR and demonstrated a correlation between CKD-EPI and isotopic GFR that is similar to that of the CG and MDRD equations, but superior to them when these equations were correlated with cystatin C.

As for comorbid conditions, both hypertension and liver disease led to poorer renal filtration in our patients. These results are consistent with those of other studies (Mocroft et al., 2007; Overton et al., 2009; Winston et al., 2008). Evaluating the impact of HIV itself and antiretroviral therapy on renal function, GFR values were inferior in all the measurements in patients with detectable viral load, and reached statistical significance for cystatin C. In addition, time with HIV infection also negatively influenced GFR. More prolonged viral suppression, however, did not mean better renal function, possibly because of the negative effect of some antiretroviral agents (Choi et al., 2009; Overton et al., 2009; Winston et al., 2008), comorbid conditions and the progressive increase in age. All the estimations of GFR tended to deteriorate in immunosupressed patients, but only cystatin C level was statistically different when the CD4+ T-cell count was categorized.

These results support previously reported data (Choi et al., 2009; Odden et al., 2007; Szczech et al., 2002; Winston et al., 2008; Wyatt et al., 2007) and show the effect of virological and immunological parameters on renal function.

No differences in GFR values were observed between patients with and without TDF-containing regimens in our group, indicating that TDF is safe in patients with normal renal function and no other nephrotoxic conditions. A lower estimated GFR, however, was detected in patients exposed to PIs, with a statistically significant difference in the case of the CG equation. In addition, patients on regimens containing TDF or PIs exhibited higher proportions of proteinuria and haematuria. The proportions of these alterations were similar to those reported in other series for TDF (Gallant and Moore, 2009; Gallant et al., 2005; Goicoechea et al., 2008; Izzedine et al., 2005; Labarga et al., 2009; Overton et al., 2009; Pozniak et al., 2006; Rodriguez-Novoa et al., 2009) and PIs (Bochet et al.,

Table 2
Renal function in patients according to different clinical and HIV-related conditions.

	Proteinuria, *n* [%]	Haematuria, *n* [%]	MDRD Median (IQR) (ml/min/1.73 m^2)	CG Median (IQR) (ml/min)	Cystatin C Median (IQR) (mg/l)	24 h CrCl Median (IQR) (ml/min)	CKD-EPI Median (IQR) (ml/min/1.73 m^2)	Isotopic GFR *n* (ml/min/1.73 m^2)
No hypertension, *n* = 81	14 [19%]	14 [19%]	93 (83; 104)	101.7 (89.9; 118.5)	0.75 (0.70; 0.85)	110.5 (86.5; 143.9)	98.26 (86.32; 107.56)	116 (95; 136)
Hypertension, *n* = 25	5 [21%]	6 [26%]	84.15 (59.6; 93.8)	84.3 (67.5; 109.4)	0.85 (0.72; 1.1)	79 (65.5; 112)	86.59 (61; 96)	72.5 (64; 96)
p-Value	0.773	0.560	**0.010**	**0.006**	**0.014**	**0.004**	**0.003**	**0.008**
No hepatitis B or C co-infection, *n* = 53	12 [22.6%]	11 [20.8%]	91.5 (79; 104.7)	101.7 (90; 119.12)	0.735 (0.697; 0.847)	112.4 (77.6; 126.60)	97.10 (83.62; 106.92)	102 (73.75; 127)
Hepatitis B or C co-infection, *n* = 42	7 [16.7%]	9 [21.4%]	88 (81.8; 100.2)	95.1 (76.3; 112)	0.800 (0.730; 0.910)	95.6 (73.52; 124.6)	92.65 (84.81; 195.48)	106 (75; 124.5)
p-Value	0.470	0.913	5.541	0.097	**0.029**	0.181	0.749	0.953
Current TDF use, *n* = 41	9 [15.5%]	12 [18%]	93 (83; 104.5)	95.5 (75.6; 119)	0.78 (0.70; 0.87)	96.75 (76.5; 137)	97.32 (86.32;105.56)	116 (84; 133)
No current use of TDF, *n* = 65	10 [27%]	8 [19%]	89.9 (77; 100)	100.46 (88.8; 113)	0.75 (0.71; 0.90)	111.5 (79.6; 120.4)	94 (81.63; 104.93)	86 (71.25; 114)
p-Value	0.171	0.913	0.168	0.212	0.906	0.659	0.236	0.203
Time on TDF (*n*)								
<6 months (5)	1 [20%]	1 [20%]	85.65 (58; 113)	104 (60; 113)	0.80 (0.75; 0.96)	78.6 (56; 100)	90.81 (58.80; 102.30)	84 (58; 133)
6–1 year (5)	1 [20%]	1 [20%]	83.6 (75; 107.6)	83.6 (73.6; 103)	0.87 (0.67; 1)	82 (82; 82)	89.92 (78.94; 113.58)	–
>1 <5 years (36)	5 [14%]	5 [14%]	92 (79.5; 104.4)	100 (84; 119)	0.77 (0.71; 0.93)	92 (69.4; 126)	97.33 (83.98; 104.29)	90 (70; 114)
>5 years (26)	6 [23%]	6 [23%]	86 (81.4; 100.5)	97.4 (84.5; 108.4)	0.75 (0.68; 0.85)	102 (80.6; 134)	91 (84.68; 100.42)	116 (106; 123)
p-Value	0.853	0.455	0.351	0.406	0.865	0.543	0.666	0.732

	Proteinuria, *n* [%]	Haematuria, *n* [%]	MDRD Median (IQR) (ml/min/1.73 m^2)	CG Median (IQR) (ml/min)	Cystatin C Median (IQR) (mg/l)	24 h CrCl Median (IQR) (ml/min)	CKD-EPI Median (IQR)	Isotopic GFR Median (IQR) (ml/min/1.73 m^2)
No current PI use (*n* = 55)	7 [17.5%]	8 [20%]	93 (82; 103)	100.7 (94; 124)	0.74 (0.68; 0.86)	109 (78; 121)	92.80 (83.44; 104.24)	115 (73; 130)
Current PI use (*n* = 40)	12 [22%]	12 [22%]	89 (79; 103)	94.6 (76.7; 111.4)	0.79 (0.71; 0.89)	100.5 (74.6; 127.8)	98.26 (86.59; 107.74)	90 (75; 114)
p-Value	0.603	0.830	0.319	**0.036**	0.135	0.881	0.348	0.602
Time on PI (*n*)								
<6 months (2)	1 [50%]	0	87 (72; 101.5)	96.8 (79; 115)	0.80 (0.80; 0.80)	60.4	93.39 (76.83; 109.94)	84
6–1 year (2)	1 [50%]	0	86 (82; 132)	105.75 (73; 119)	0.79 (0.86; 0.90)	89.5 (84.4; 94.6)	89.23 (87.43;113)	–
>1 <5 years (22)	4 [19%]	3 [14%]	89.6 (77.5; 105.4)	98 (91; 122)	0.75 (0.68; 0.85)	109 (87; 124)	95.53 (81.67; 103.24)	118.5 (96; 142.5)
>5 years (60)	11 [20.8%]	16 [30%]	88 (79; 102.6)	94.7 (76; 110.6)	0.77 (0.71; 0.88)	98.6 (72.4; 126)	92.65 (83.61; 103.29)	90.5 (67; 115.5)
p-Value	0.460	0.136	0.878	0.822	0.734	0.135	0.265	0.157
Time with HIV infection (*n*)								
<10 years (33)	4 [13%]	4 [13%]	93 (84.6; 110.7)	104.6 (91; 126)	0.72 (0.67; 0.85)	117.5 (94.6; 153.8)	101.63 (87.12; 109.80)	114 (84; 133)
10–20 years (51)	11 [24%]	8 [17%]	89.5 (78; 98)	96.8 (82.5; 112)	0.79 (0.72; 0.89)	98.6 (76.7; 116.8)	94.03 (84.17; 102.34)	90.5 (67; 121.7)
>20 years (22)	4 [18%]	8 [40%]	88.7 (76.3; 104.5)	95.4 (71.4; 110)	0.77 (0.71; 0.92)	78 (69.3; 113.4)	91.77 (79.73; 103.62)	90 (66; 114)
p-Value	0.477	0.075	0.184	**0.040**	0.145	**0.032**	0.097	0.394

Table 2 (*Continued*).

	Proteinuria, *n* [%]	Haematuria, *n* [%]	MDRD Median (IQR) (ml/min/1.73 m^2)	CG Median (IQR) (ml/min)	Cystatin C Median (IQR) (mg/l)	24 h CrCl Median (IQR) (ml/min)	CKD-EPI Median (IQR)	Isotopic GFR Median (IQR) (ml/min/1.73 m^2)
Suppressed viral load (*n* = 90)	17 [20.5%]	18 [21.7%]	90.9 (80.60; 104)	100 (84.6; 118.24)	0.74 (0.70; 0.86)	102 (76.6; 127.6)	98.26 (69.80; 108.64)	110 (71.25; 121.25)
Unsuppressed viral load (*n* = 16)	2 [16.7%]	2 [16.7%]	86.8 (80; 100.8)	89 (77.6; 111.4)	0.87 (0.80; 0.98)	95.7 (79.5; 120)	94.66 (84.64; 105.41)	84 (82; 133)
p-Value	1	1	0.698	0.187	**0.002**	0.808	0.629	1
Time with suppressed viral load (*n*)								
<1 year (13)	5 [38.5%]	2 [15.4%]	84 (74; 100.5)	92.6 (77.6; 112.7)	0.83 (0.77; 0.97)	104.6 (74.6; 140)	87.5 (78.31; 109.17)	108.5 (82.5; 145)
1–2 years (7)	1 [14%]	0	94 (86; 103.5)	110.7 (91.6; 128)	0.86 (0.70; 1.07)	86 (78.4; 121.4)	98.59 (86.57; 105.79)	90 (90; 90)
2–3 years (9)	0	3 [33%]	95 (83; 103)	111 (99.8; 125.7)	0.77 (0.71; 0.80)	99.3 (44.75; 131)	98.26 (87.7; 105.5)	
3–4 years (10)	2 [20%]	3 [30%]	92.1 (83; 96)	94 (73; 109.7)	0.75 (0.65; 0.90)	109.5 (78; 142.6)	100.14 (86.46; 102.49)	75 (75; 75)
4–5 years (10)	2 [20%]	3 [30%]	96 (86; 107)	94.5 (85.7; 119)	0.74 (0.69; 0.95)	101 (66.5; 150.5)	99 (86.59; 110.34)	66 (66; 66)
>5 years (46)	9 [19.6%]	9 [19.6%]	89.5 (78.6; 104)	98 (80.35; 114.4)	0.74 (0.68; 0.84)	106.8 (76.5; 117.5)	94 (83.44; 104.45)	114 (79; 121)
p-Value	0.256	0.386	0.301	0.067	0.121	0.845	0.894	1
CD4+ cell counts (*n*)								
<200 cells/μl (4)	2 [50%]	1 [25%]	85.8 (27; 100)	85.6 (31; 109.7)	1.04 (0.82; 2.5)	57.9 (28.6; 87)	88.69 (27.74; 107.22)	–
200–500 cells/μl (42)	9 [23.7%]	5 [13%]	89.9 (77.65; 103)	97.8 (79.9; 118.5)	0.8 (0.72; 0.96)	93 (73.3; 115)	94.41 (81.67; 107.97)	84 (74; 123.5)
>500 cells/μl (60)	8 [15%]	14 [26.4%]	90 (83; 104)	100.46 (88; 116)	0.73 (0.67; 0.83)	111.5 (78.4; 142.6)	95 (86.45; 104.32)	110 (73.5; 127)
p-Value	0.229	0.287	0.598	0.442	**0.002**	0.067	0.741	0.581

n, number of patients; IQR, Interquartile range; MDRD, modification of diet in renal disease; CG, Cockcroft–Gault; 24 h CrCl, 24-hour creatinine clearance; GFR, glomerular filtration rate; –, no patients in this subgroup. Bold numbers expressed statistically significant *p* values.
Data are expressed as the median (IQR) unless otherwise indicated.

1998; Dieleman et al., 2002; Tashima et al., 1997), although our cross-sectional study design made it impossible to determine the development of renal function over time. Patients with prolonged exposure to drugs tolerated their regimen, whereas those who had already discontinued the culprit antiretroviral drug experienced toxicity and were therefore not evaluated in this analysis.

In conclusion, our results show that cystatin C level was the parameter that best correlated with isotopic GFR, with the limitation that only 15 patients were included in the isotopic substudy, because of the complexity of the process and the elevated cost. In the overall sample of 106 HIV-infected patients with normal GFR, the newly developed equation CKD EPI showed the highest correlation with cystatin C levels, followed by MDRD, and CG. The worst correlation was with 24 h CrCl. We provide sufficient evidence to enable early detection and optimum clinical management of renal dysfunction in HIV-infected patients with normal GFR. The additional cost of cystatin C determination or the effort involved in incorporating the CKD-EPI equation into clinical routine could be compensated by an early diagnosis of renal impairment.

Finally, our findings extend knowledge on the role of virological and immunological conditions and antiretroviral therapy in renal dysfunction. Time on HIV infection, unsuppressed viral load or low CD4 T-cell counts are related to increased risk of renal impairment, thus urging us to recommend early initiation of antiretroviral therapy accompanied by a regular renal study, especially in patients taking PIs.

Further studies are necessary to determine the usefulness of these measurements in specific subpopulations, such as women and patients with more deteriorated renal function and other comorbid conditions.

Contributors

A. Bonjoch, C. Estany, B. Bayés, E. Negredo, and B. Clotet participated in the design of the study. A. Bonjoch, E. Negredo, J. Puig and B. Clotet participated in the recruitment of patients and reporting of data for those patients. J. Riba recorded the isotopic glomerular filtration rate of the patients included. N. Perez-Alvarez performed the statistical analyses. All authors approved the final version of the manuscript.

Conflict of interest statement

A.B. has received lecture fees from Bristol Myers Squibb and Merck. B.B. has received lecture fees from Novartis and Roche and has received reimbursement for a research project from Abbott. J.P. has received lecture fees from Abbott and Roche. B.C. has received reimbursement, fees, and/or funding for attending symposiums, speaking, advisory board membership, organising educational activities, consulting and/or research from Gilead, Roche, Bristol Myers Squibb, GlaxoSmithKline, Tibotec, Boehringer Ingelheim, Pfizer, and Abbott. E.N. has received fees from Gilead, Roche, Bristol Myers Squibb, GlaxoSmithKline, Tibotec, Boehringer Ingelheim, Merck and Abbott. J.R., C.E., N.P.: no conflicts.

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