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A Comparison of Estimated Glomerular Filtration Rates (eGFRs) Using Cockcroft-Gault (CG) and the CKD-EPI Estimating Equations in HIV Infection

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BACKGROUND

The CG and CKD-EPI formula are widely used for estimating GFR and creatinine clearance. A key question is which performs better in HIV-infection in diagnosing moderate and advanced chronic kidney disease (CKD), or predicting end stage renal disease (ESRD) or all-cause mortality

AIMS

- To investigate the correlation and differences between the 2 most commonly used formulae, CG and CKD-EPI
- to explore which is best correlated with different levels of chronic kidney disease (CKD), ESRD or death from renal disease and all-cause mortality.

METHODS

eGFRs were calculated using CG, standardised for body surface area, and CKD-EPI formula. Discordance was defined as >15% difference between the 2 formulae (CKD-EPI-CG); the odds of discordance was modelled using binary regression and generalised linear models, with robust standard errors.

Moderate CKD was defined as confirmed (>3 months apart) eGFR < 60mL/min/1.73m^2 and advanced CKD as confirmed eGFR <30mL/min/1.73m^2.

Incidence rates and proportion progressing to moderate and advanced CKD were calculated for both CG and CKD-EPI. Poisson regression was used to investigate the relationship between eGFR and ESRD or death from renal disease or all cause mortality.

The fit of the models were compared using the log-likelihood, the Akaike Information Criteria.

RESULTS

Characteristics of the 9059 included persons are shown in ***Table 1***. There were 123,724 eGFRs at the same date with both CG and CKD-EPI, a median of 13 (IQR 8–18) measurements per person and a median time of 3.6 months (IQR 2.8–5.5) apart. CG estimates were generally lower than the CKD-EPI eGFR; the median difference between CKD-EPI and CG (CKD-EPI minus CG) was 0.5 (IQR -5.8 to 5.9 ml/min/1.73m^2).

Table 1

Baseline Characteristics of 9059 persons with >3 eGFRs using CG and CKD-EPI

		N	%
Gender	Male	6676	73.7
Race	White	7933	87.6
Exposure group	Homosexual	3728	41.2
	IDU	1806	19.9
	Heterosexual	2800	30.9
Prior AIDS	Yes	2661	29.4
Prior non-AIDS*	Yes	547	6.0
Prior CV event	Yes	250	2.8
Diabetes	Yes	428	4.7
Hypertension	Yes	2692	29.7
On cART	Yes	7462	82.4
		Median	IQR
CD4	/mm^3	438	294 – 421
Viral load	log_{10}copies/ml	1.69	1.69 – 3.24
Age	years	41.9	35.7 – 49.0
Serum creatinine	mg/dL	0.89	0.77 – 1.00

Figure 1

Agreement between eGFRs calculated using CG and CKD-EPI

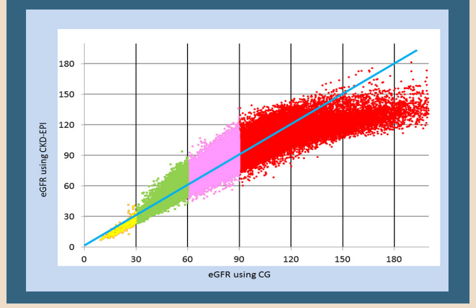


Table 2

Odds of discordance (>15% difference) between CG and CKD-EPI: median CG and CKD-EPI <90

		Univariate			Multivariate⁺		
		OR	95% CI	P	OR	95% CI	P
Race	Other vs White	1.52	1.23 – 1.87	<0.0001	1.86	1.46 – 2.37	<0.0001
Prior AIDS	Yes vs no	1.12	0.97 – 1.30	0.13	1.05	0.89 – 1.23	0.56
Prior non-AIDS	Yes vs no	1.80	1.50 – 2.17	<0.0001	1.22	0.94 – 1.58	0.14
Prior CV event	Yes vs no	1.85	1.44 – 2.38	<0.0001	0.90	0.63 – 1.29	0.57
Diabetes	Yes vs no	1.69	1.34 – 2.12	<0.0001	1.07	0.83 – 1.39	0.60
Hypertension	Yes vs no	1.26	1.09 – 1.46	0.0015	0.75	0.64 – 0.87	0.0003
Smoking	Current vs never	0.92	0.79 – 1.07	0.28	1.31	1.11 – 1.54	0.0011
cART	Yes vs no	1.94	1.48 – 2.54	<0.0001	0.96	0.88 – 1.05	0.37
CD4 nadir	100/mm^3 higher	0.92	0.88 – 0.97	0.0013	1.02	0.96 – 1.09	0.48
CD4	100/mm^3 higher	0.94	0.91 – 0.97	<0.0001	0.97	0.94 – 1.00	0.024
Viral load	Per log_{10} lower	0.97	0.92 – 1.03	0.35	1.12	1.06 – 1.20	<0.0001
Age	Per 10 yr older	1.95	1.82 – 2.10	<0.0001	2.23	2.03 – 2.44	<0.0001
eGFR* (mL/min/1.73m^2)	60-90	0.69	0.58 – 0.82	<0.0001	1.33	1.10 – 1.60	0.0031
	30-60	1.00	-	-	1.00	-	-
	<30 mg	3.75	2.31 – 6.10	<0.0001	3.90	1.80 – 8.45	0.0006

⁺Also adjusted for gender, exposure group, region, hepatitis B and C status, anaemia, and year of eGFR measurement; *median of CG and CKD-EPI measurement

Figure 1 shows a scatter plot of the overlap between the 2 eGFR estimates, the difference between the 2 values gets greater as the median of the 2 eGFR values increases. Comparing the eGFR groups (high [>90], average [60-90], low [30-60] and very low [<30]) gave a kappa of 0.75 (95% CI 0.75–0.76). The overall correlation coefficient between CG and CKD-EPI was 0.886. Corrrelations and kappas were similar for those on and off antiretroviral therapy.

Of 123,724 eGFR values, 102,944 (83.2%) were concordant, ie the CG and CKD-EPI eGFR were within 15% of each other. The univariate and multivariate odds ratios of discordance between CG and CKD-EPI (ie >15% difference) among those with a median CG and CKD-EPI eGFR value <90/ml/min/1.73m^2 are shown in ***Table 2***.

The highest incidence and progression to moderate CKD was seen with the CG formulae, with an incidence of 8.7 per 1000 PYFU, and 5.1% estimated to have developed moderate CKD by 6 years after baseline, using Kaplan-Meier estimation. Differences in the incidence or Kaplan-Meier progression rates of advanced CKD between the 2 formulae were much smaller; ***Table 3***

27 persons developed ESRD or died from renal disease (incidence rate 0.6/1000 PYFU; 95% CI 0.4-0.8) and 469 deaths (incidence 9.7/1000 PYFU; 95% CI 8.8–10.6) occurred during prospective follow-up. CG derived eGFRs were equal to CKD-EPI at predicting both ESRD and death, as measured by a lower Akaike Information Criteria and log-likelihood. CG moderate and advanced CKD were associated with ESRD as was CKD-EPI moderate and advanced CKD. CG moderate and advanced CKD were also both associated with all-cause mortality, while CKD-EPI moderate CKD was not significantly associated with all-cause mortality, but advanced CKD was ***(Figure 2).***

CONCLUSIONS

There were modest differences in eGFRs In HIV-positive persons when comparing CG and CKD-EPI eGFR formulae. It would be reasonable to use either formulae in HIV-positive populations similar to those in EuroSIDA. Although there were no gold-standard GFR available (.e., measurements of Inulin clearance), predictors of CG or CKD-EPI defined moderate CKD were similar and CG eGFRs performed as well as CKD-EPI in predicting two key clinical outcomes. In the absence of a large study comparing eGFRs to a gold standard, HIV cohort studies can use either formulae, although sensitivity analyses should investigate the robustness of the findings with both formulae, wherever possible.

Table 3

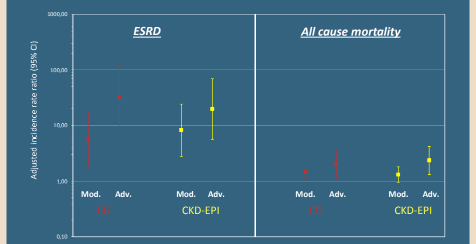
Incidence and Kaplan-Meier (KM) estimates of moderate and advanced CKD

	CG	CKD-EPI
Moderate CKD (N=8630)		
Baseline median eGFR (IQR)	98.7 (85.4 – 113.6)	101.1 (88.1 – 111.3)
N (%) eGFR > 90	5737 (66.5)	6189 (71.7)
Events (%)	360 (4.2)	306 (3.6)
PYFU	41177	45146
Incidence/1000 PYFU (95% CI)	8.7 (7.8 – 9.7)	6.8 (6.0 – 7.5)
KM 24 months (95% CI)	1.2 (1.0 – 1.4)	0.8 (0.6 – 1.0)
KM 48 months (95% CI)	3.0 (2.6 – 3.4)	2.2 (1.9 – 2.6)
KM 72 months (95% CI)	5.1 (4.5 – 5.7)	3.9 (3.4 – 4.4)
Advanced CKD (N=9038)		
Baseline median eGFR (IQR)	97.4 (93.6 – 112.7)	100.1 (86.0 – 110.8)
N (%) eGFR > 90	5740 (63.5)	6195 (68.5)
Events	36	40
PYFU	43903	47938
Incidence/1000 PYFU (95% CI)	0.8 (0.6 – 1.1)	1.1 (0.7 – 1.4)
KM 24 months (95% CI)	0.1 (0.0 – 0.2)	0.1 (0.0 – 0.1)
KM 48 months (95% CI)	0.2 (0.1 – 0.3)	0.3 (0.2 – 0.4)
KM 72 months (95% CI)	0.6 (0.4 – 0.8)	0.6 (0.4 – 0.7)

Moderate CKD; confirmed (>3 months apart) eGFR <60; advanced CKD; confirmed eGFR <30

Figure 2

Incidence rate ratios of ESRD and all-cause mortality using CG or CKD-EPI eGFR equations



Moderate CKD (confirmed [>3 months apart] eGFR <60) and advanced CKD (confirmed eGFR <30) included as time-updated. *Multivariate models adjusted for gender, race, ethnic origin, region, CD4 nadir and baseline date as fixed baseline covariates and hepatitis B, C, prior AIDS, non-AIDS, CV event, diabetes, hypertension, smoking status, anaemia, starting cART , CD4, viral load and age as time-updated.

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