Poster P82

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Chronic Kidney Disease in Patients with Normal eGFR at Baseline - Results from EuroSIDA

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BACKGROUND

Chronic kidney disease (CKD) is an emerging co-morbidity among HIV positive patients. EuroSIDA, a prospective multi-centre cohort study of more than 16,500 patients, recently reported an overall CKD incidence of 1.05/100 person-years of follow-up (PYFU), and identified CKD risk factors including hypertension, diabetes, hepatitis C, age›50, low CD4 count, prior AIDS events, and cumulative exposure to certain antiretrovirals (ARVs); tenofovir, indinavir, atazanavir, and, probably, lopinavir/ritonavir.

"eGFR, Chronic kidney disease and antiretroviral drug use in HIV-positive patients", AIDS 2010, 24:1667-1678 Mocroft A., Kirk O., Reiss P. et al. for the EuroSIDA study group &"Chronic renal failure among HIV-1-Infected patients" Aids 2007, 21:1119-1127 Mocroft A., Kirk O., Gatell J. et al for the EuroSIDA study group.

OBJECTIVES

We aimed to extend our previous findings by estimating the incidence of CKD among patients with normal kidney function at baseline (with/without known renal risk factors) to disentangle if cumulative ARV exposure also poses a risk to patients with normal kidney function, and not only to those with pre-existing renal impairment.

METHODS

The Cockcroft-Gault equation standardised for body surface used to calculate estimated glomerular filtration rate (eGFR, ml/min/1.73m²). Patients with baseline eGFR› 90, defined as normal kidney function, were included. Baseline was defined as the first eGFR assessment after 01.01.2004 (date from which creatinine has been routinely collected in EuroSIDA). CKD was defined as 2 consecutive eGFR‹60 with estimates ›3 months apart. Follow-up was from baseline until CKD or last eGFR. Patients were followed to a median date of March 2009. Unadjusted incidence rates (IR) for patients with normal baseline function with and without renal risk factors (hypertension, diabetes, hepatitis C, age›50, low CD4 cell count, prior AIDS events, and certain ARVs) are presented per 100 PYFU and stratified by cumulative ARV exposure (never exposed, ‹1 year, 1-2, 2-3, and ›3).

RESULTS

4,824 of 7,771 patients with available eGFR measurements had baseline eGFR›90. Baseline characteristics are shown in **Table 1**.

During 15,391 PYFU and a median follow-up of 41 (IQR 21-56) months, 34 patients (0.7%) developed CKD with an IR of 0.22/100 PYFU (95% CI 0.15-0.30).

Among patients without any known renal risk factors, 7 patients developed CKD during 8,076 PYFU with an IR of 0.09/ 100 PYFU (95% CI 0.04-1.18).

In unadjusted analyses CKD incidences increased with increasing cumulative ARV exposure for the four ARVs tested. Test for trend was significant for all drugs investigated, **Table 2**.

Table 3 shows the distribution of CKD incidence rates in the EuroSIDA population.

LIMITATIONS

The study is not a randomised clinical trial, but a large, well described and heterogeneous cohort study. There were too few events for detailed adjusted analyses and to account for the influence of potential confounders. No information on proteinuria is routinely collected within the study.

CONCLUSIONS

This study of almost 5,000 HIV positive patients, and a median follow-up longer than 3 years demonstrates that CKD development from normal baseline kidney function was an infrequent event.

The IR was higher in patients with known renal risk factors and those with greater cumulative exposure to the ARVs investigated in univariable analyses.

Our findings suggest that cumulative exposure to certain ARVs might also pose a risk in patients with normal kidney function. This risk, however, seems predominantly to be in patients with known renal risk factors despite their normal function.

Adjusted analyses were not possible due to the low total number of events. Future studies with substantially larger size and longer follow-up are needed to reproduce the findings in adjusted models, determine the role of cumulative exposure to individual ARVs, and investigate the clinical implications.

Table 1

Baseline characteristics of included patients

		N	%	Unknown (N /%)
All		4824	100	-
Gender	Male	3591	74.4	-
Race	White	4169	86.4	-
Risk group	Homosexual	1995	41.4	-
	IDU	977	20.2	-
	Heterosexual	1479	30.7	-
	Other	373	7.7	-
Prior AIDS		1369	28.4	-
Prior Non-AIDS defining malignancy		87	1.8	-
HBV Status (HBsAg)	Positive	314	6.5	453 / 9.4
HCV Status (HCV-ab)	Positive	1162	24.1	510 / 0.6
Diabetes	Yes	176	3.7	436 / 9.0
Hypertension	Yes	851	17.6	1268 / 26.3
Smoking	Never	1407	29.2	1510 / 31.3
	Current	1708	35.4	-
	Past	199	4.1	-
MI	Yes	45	0.9	373 / 7.7
stroke	Yes	29	0.6	375 / 7.8
ARV use at/before baseline	None	569	11.8	-
	ART	117	2.4	-
	cART	4138	85.8	-
Ever used potential toxic drugs*		514	10.7	-
		Median	IQR	
Age , years		40	34.6-45.1	-
CD4 , cells/mm³		446	300-640	-
VL, log¹⁰ copies/ml		1.69	1.69-3.26	-
Nadir CD4, cells/mm³		170	68-280	-
eGFR, ml/min/1.73m²		108	99-120	-
Number eGFR mesurements		9	5.0-13	-

*Pentamidine, Cidoforvir, Aciclovir, Foscarnet or Amphotericin B

Table 2

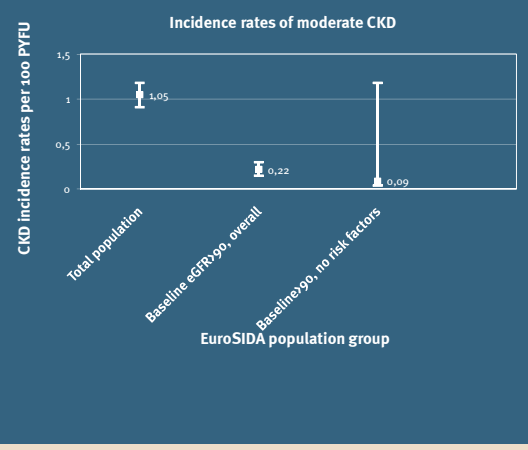
Incidence rates of CKD stratified by cumulative ARV exposure in patients with normal baseline renal function*

	IR (95% CI) per 100 PYFU cumulative exposure to ARVs					Univariate IRR** per year exposure (95% CI)	p-value (test for trend)
ARV	None	0-1 years	1-2 years	2-3 years	›3 years		
Tenofovir	0.11 (0.05 -0.20)	0.28 (0.09-0.67)	0.52 (0.23-1.03)	0.25 (0.05-0.72)	0.48 (0.21-0.94)	1.33 (1.12-1.57)	0.0011
Events/PYFU	10/ 9186	5/ 1784	8/ 1531	3/ 1209	8/ 1681		
Indinavir	0.11 (0.05 -0.20)	0.17 (0.04 -0.50)	0.53 (0.21 -1.09)	0.66 (0.24- 1.43)	0.39 (0.17- 0.78)	1.24 (1.10- 1.39)	0.0005
Events/PYFU	10/ 938	3/ 1742	7/1323	6/ 915	8/ 2027		
Lopinavir/r	0.14 (0.08 -0.23)	0.23 (0.05-0.67)	0.31 (0.06-0.89)	0.14 (0.003-0.59)	0.65 (0.35- 1.11)	1.37 (1.20 -1.57)	‹0.0001
Events/PYFU	14/ 10159	3/ 1304	3/ 984	1/ 950	13/ 1995		
Atazanavir	0.15 (0.09- .24)	0.45 (0.15-1.06)	0.64 (0.21-1.49)	0.39 (0.05-1.34)	0.64 (0.13-1.88)	1.37 (1.11- 1.69)	0.0032
Events/PYFU	19/ 12504	5/ 1100	5/ 782	2/ 538	3/ 467		

* Not stratified by the presence of renal risk factors **IRR, incidence rate ratio from Poisson regression

Table 3

CKD incidence rates



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