

Immunodeficiency and viral load and the risk of non-AIDS events among untreated HIV-infected patients

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Background

Immunodeficiency and higher HIV RNA levels are associated with an increased risk of non-AIDS diseases in patients treated with cART.

- But therapy could confound this association by increasing the risk of non-AIDS events through adverse effects and simultaneously reverse the harm by restoring immunity.
- In addition, the range in RNA levels is limited in treated patients.

Objective: to investigate the association between CD4 counts, RNA levels and non-AIDS diseases in untreated patients.

Methods

Study population

- 9356 patients, diagnosed with HIV in or after 1998, were selected from the Athena Cohort.
- Follow-up started at the first available CD4 measurement, and censored at the earlier of start of antiretroviral therapy, or events of interest, or end of follow-up.

Outcome

- four newly diagnosed non-AIDS endpoints (fatal and non-fatal) were considered.
- cardiovascular disease (21 events): myocardial infarction, stroke, invasive coronary procedures
- renal disease (38 events): acute and chronic renal failure
- liver disease (31 events): fibrosis, cirrhosis
- overall (88 events): combination of non-AIDS events abovementioned

Statistical analyses

- time-discrete proportional hazards model.
- CD4 and RNA level included as time-updated variables.
- Both univariate and multivariate analyses were conducted, and multivariate analyses were adjusted for age, gender, diabetes, HBV/HCV co-infection, CDC stage, transmission group, smoking, alcohol abuse.

Results

Table 1. Characteristics of the study population

N=9356	N (%) / median (IQR)	
Age (years)	36.9	30.1-44.0
Gender, male	7256	77.6
Transmission group		
homosexual contact	5117	54.7
heterosexual contact	3383	36.2
injection drug use	141	1.5
other/unknown	715	7.6
Region of origin		
Netherlands	5130	54.8
Sub-Saharan Africa	1881	20.1
Disease stage at baseline		
CDC-B	611	6.5
CDC-C	993	10.6
Hepatitis B co-infection	410	4.4
Hepatitis C co-infection	287	3.1
Diabetes mellitus	151	1.6
History of alcohol abuse	530	5.7
Smoking status		
never	2411	25.8
current or former	3270	35.0
unknown	3675	39.3
CD4 counts (cells/mm ³)	340	150-540
Log ₁₀ HIV RNA plasma level	4.8	4.1-5.2
Follow-up time (years)	0.35	0.08-1.90

Non-AIDS incidence rates

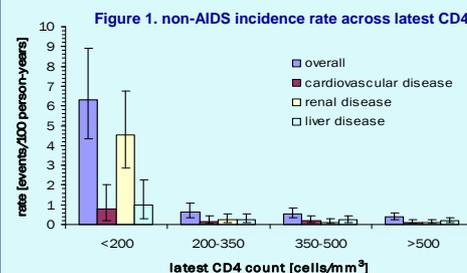


Figure 1. showed the overall incidence decreased from 6.32 (95% CI, 4.32-8.92) per 100 person-years for CD4 <200 cells/mm³ to 0.40 (0.26-0.61) for CD4 >500.

Non-AIDS events with latest CD4 counts

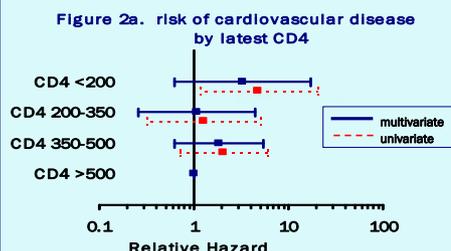


Figure 2a. showed in univariate analysis, CD4 counts <200 cells/mm³ were associated with cardiovascular disease (vs. CD4 >500), but this association disappeared in multivariate analysis.

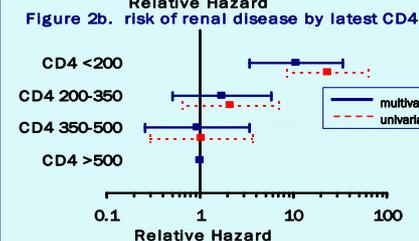


Figure 2b. showed CD4 counts <200 cells/mm³ had a 10.7 (3.37-33.7) times higher risk of renal disease compared to CD4 counts >500 in multivariate analysis.

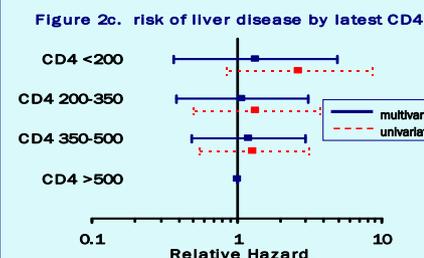


Figure 2c. showed there was no association found between latest CD4 counts and liver disease.

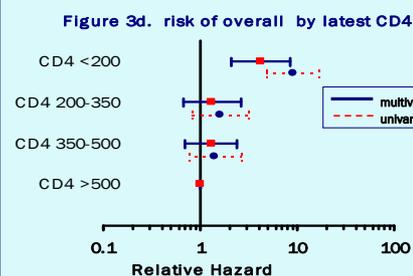


Figure 2d. showed CD4 counts <200 cells/mm³ were in higher risk of getting combined non-AIDS events (RH 4.21; 2.09-8.48) compared to CD4 counts >500 in adjusted analysis.

Non-AIDS events with latest RNA levels

In univariate analysis, log₁₀RNA was associated with renal disease (RH 1.64; 1.11-2.41, per log increase), but this association disappeared in multivariate analysis.

Sensitivity analyses

By extending follow-up till 3 months of therapy, the results stayed the similar trend.

Conclusions & discussion

- Lower CD4 counts in untreated patients were associated with an increased risk of renal disease, but not CVD and liver disease.
- The power to detect an association of CD4 and RNA with non-AIDS events may have been small given the limited amount of follow-up and number of events.