

Delayed Diagnosis of HIV Infection and Late Initiation of Antiretroviral Therapy in the Swiss HIV Cohort Study (SHCS)

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Background

Late HIV diagnosis and presentation to HIV care is a common problem leading to significant HIV-related morbidity and mortality, even when ART is started promptly. The goal of the present analysis, within the Swiss HIV Cohort Study (SHCS), was to investigate delayed diagnosis of HIV infection, the extent of late initiation of ART despite cohort follow-up and time to ART uptake after dropping to CD4<200 cells/μL.

Methods

Two subpopulations of the SHCS were included:

Group A (n=1915):

All patients with HIV diagnosis from 1998-2007 and within 3 months before cohort registration.

Purpose: To study delayed diagnosis of HIV infection and subsequent time to ART uptake.

Analyses:

- Predictors for low initial CD4 cell count (using a median regression)

- Clinical outcomes and time to ART uptake

Group B (n=1730):

All treatment-naïve patients with CD4≥200 cells/μL before their second cohort visit after 1998.

Purpose: To study late ART initiation, defined as a CD4 cell count <200 cells/μL prior to initiation of therapy, for patients who were already followed-up in the SHCS.

Analyses:

- Predictors for late ART initiation (using a multinomial logit regression)

- Time to ART uptake for patients dropping to CD4<200 cells/μL without prior ART

Results

Table 1. Characteristics of the two populations

Characteristic	Patients registered within 90 days of HIV diagnosis (group A, n=1915)	Patients who were naïve with CD4 cell counts ≥200 cells/μL until their second cohort visit (group B, n=1730)
Gender: Female	561 (29%)	550 (32%)
Age (years) – median (quartiles)	36 (30 to 43)	35 (30 to 41)
First recorded CD4 count (cells/μL) – median (quartiles)	331 (156 to 535)	540 (400 to 720)
- <50 cells/μL	201 (10%)	-
- 50-199 cells/μL	395 (21%)	-
Status		
- Reached CD4<50 cells/μL while ART-naïve	219 (11%)	26 (2%)
- Reached CD4 50-199 cells/μL while ART-naïve	505 (26%)	279 (16%)
- Initiated ART with CD4≥200 cells/μL	716 (37%)	514 (30%)
- No ART initiation and CD4≥200 cells/μL	475 (25%)	911 (53%)
Number of patients initiating ART (at any time)	1413 (74%)	774 (45%)
CD4 count (cells/μL) at ART initiation – median (quartiles)	207 (101 to 337)	253 (192 to 336)

Table 2. Clinical outcomes in 1915 patients registered within 90 days of HIV diagnosis (group A)

	Patients with first CD4<50 cells/μL (n=201)	Patients with first CD4 50-199 cells/μL (n=395)	Patients with first CD4≥200 cells/μL (n=1319)
CDC B&C events before or within 90 days after diagnosis of HIV infection			
- CDC B&C events €	177 (88%)	196 (50%)	156 (12%)
- CDC C events €	132 (66%)	101 (36%)	50 (4%)
CDC B&C events before or within 90 days after diagnosis of HIV infection with an overall incidence>5%			
- <i>Candida stomatitis</i> €	106 (53%)	74 (19%)	35 (3%)
- <i>Pneumocystis jirovecii</i> pneumonia €	69 (34%)	30 (8%)	5 (0.4%)
Deaths during follow-up			
- Number of deaths	19 (9%)	30 (8%)	42 (3%)
- Total follow-up duration (patient-years)	823	1654	5026
- Death rate per 100 patient-years of follow-up (95% confidence interval) §	2.31 (1.27-3.35)	1.81 (1.16-2.46)	0.84 (0.58-1.09)

€ Chi-square test for comparisons between the three groups: p<0.001

§ Log-rank test for comparison between the three groups: p<0.001

Table 3. Prognostic factors for initial CD4 cell count (cells/μL) in 1915 patients registered within 90 days of HIV diagnosis (group A). Results based on multiple median regression.

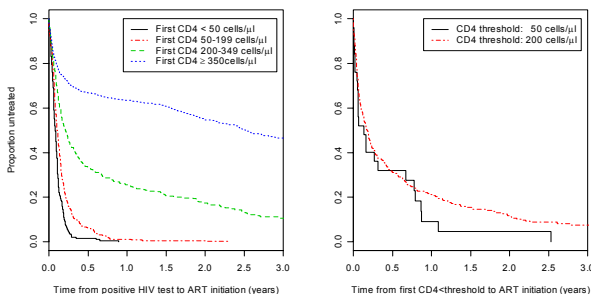
	Coefficient	CI	p
Intercept §	282.60	(249.77, 315.44)	<0.001
Age (by +10 years)	-63.15	(-75.80, -50.50)	<0.001
Female gender	23.39	(-11.25, 58.02)	0.19
Non-Caucasian race (but not sub-Saharan origin)	-111.42	(-153.78, -69.07)	<0.001
Sub-Saharan origin	-89.04	(-127.94, -50.14)	<0.001
Homosexual transmission	54.73	(19.13, 90.32)	0.003
In i.v. drug substitution program or active i.v. drug use	122.73	(57.22, 188.23)	<0.001
Basic education	-12.13	(-45.25, 20.98)	0.47
Receiving psychiatric treatment	47.51	(-25.33, 120.35)	0.20
Living alone	28.93	(0.89, 56.97)	0.04
Calendar year of registration in the SHCS (+1 year)	3.67	(-0.92, 8.26)	0.12

CI= 95% confidence interval

§ Intercept (i.e. 282.60 cells/μL) corresponds to the estimated initial median CD4 cell count for a 40 year old male patients registered in 2000 with none of the characteristics described by the categorical covariates.

Figure 1. Left plot: Time from HIV diagnosis to ART initiation in group A.

Right plot: Time from CD4<threshold to ART initiation in group B.



In group B, patients with a higher CD4 cell count at baseline (OR=0.78 by 100 cells/μL higher, CI 0.71-0.85) and those from sub-Saharan origin (OR=0.34, CI 0.18-0.65) had a lower risk of dropping to CD4<200 cells/μL while ART naïve than others; indeed, only 15 (8%) of the 178 patients from sub-Saharan origin included in group B dropped to CD4<200 cells/μL while naïve and none to CD4<50 cells/μL.

Summary

a) A considerable number of individuals, i.e. 10% and 31% of the study population had a CD4 cell count <50 and <200 cells/μL at HIV diagnosis, respectively.

b) Death rates differed significantly according to initial CD4 cell counts.

c) Low CD4 cell counts at ART initiation and, particularly, very low CD4 cell counts (<50 cells/μL) without prior ART are predominantly associated to late presentation or missed cohort visits.

d) In patients diagnosed late, time to ART uptake was fast; the value of the first CD4 cell count below 200 cells/μL independently predicted the time to ART initiation in both groups A and B.

Conclusions

In Switzerland, late presentation of HIV is the main reason for the substantial number of patients initiating ART at low CD4 cell counts and not delaying ART after patients have attended clinics. As efficacy, convenience and tolerability of ART has made substantial progress in recent years, earlier diagnosis of HIV infection and a stringent follow-up of late presenters is paramount.