CD4+ cell decline and time to reaching ART eligibility in HIV patients from Rwanda

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Background

Immunologic status as measured by CD4+ cell count (CD4+) is a key marker of HIV disease progression and is the primary measure for determining eligibility for antiretroviral therapy (ART). Identifying trends in CD4+ cell decline in patients with HIV is critical to understanding the natural history of disease progression and for predicting when patients will reach ART eligibility. Few studies have described the rate of CD4+ decline in HIV-infected patients in resource limited settings (RLS). We analyzed the rate of CD4+ decline in a large cohort of ART-naïve adults in Rwanda and assessed time to reaching ART eligibility as per 2010 and 2013 WHO guidelines.

Methods

We examined CD4+ decline in HIV-infected patients ≥15 years with CD4+ ≥600 cells at enrollment in HIV care and at least one follow-up CD4+ prior to ART initiation. Patients included in the analysis enrolled in HIV care from 2005-2010 at 41 Rwandan health facilities supported by ICAP-Columbia University. The analysis was conducted using de-identified routinely collected patient-level data from health facilities participating in the **Identifying Optimal Models for HIV Care in Africa Study**.

Pre-ART CD4+ decline in the 24 months after enrollment was estimated using mixed linear regression modeling with random intercept. The impact of patient characteristics at enrollment on the slope of CD4+ decline was examined in models fitted with interaction terms for the patient factors and follow-up time. Survival analysis using competing risk estimators was used to assess time to ART eligibility at CD4+ ≤350 or CD4+ ≤500, accounting for death and ART initiation as competing risks. All statistical analyses were preformed in SAS 9.3 and Stata 12.1.

Results

We analyzed data for 4,643 patients:

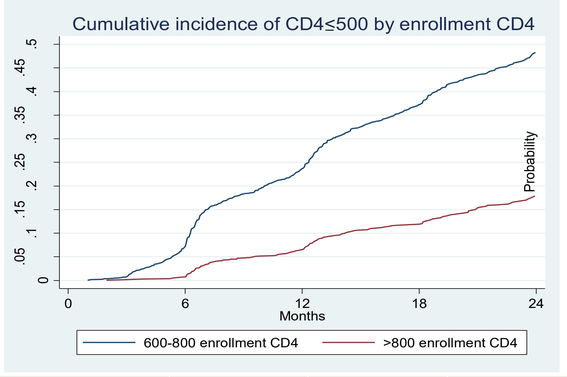
- Median pre-ART follow-up time: 21.4 months
- 20.2% of patients had only one pre-ART follow-up CD4+ measure after enrollment; 34.2% of patients had 4 pre-ART follow-up CD4+ measures (6, 12, 18, 24months)
- Median age at enrollment was 32.1 years [interquartile range (IQR) 25.9-40.1]
- 73% of subjects were female
- CD4+ at enrollment
  - Median: 773.0 [IQR: 676-923]
  - Mean: 830.1 [IQR: 676-923]
  - CD4+ 600-800: 55.4%; CD4+ >800: 44.6%
- Mean CD4+ counts were significantly lower in men (-38.6, 95%CI 25.1-52.1, p<0.0001) and patients >40 years of age (-20.9, 95%CI 7.1-34.7, p<0.01)

Table 1. Patient characteristics at enrollment in adult Rwandan patients with CD4+ ≥600 at enrollment (N=4,643)

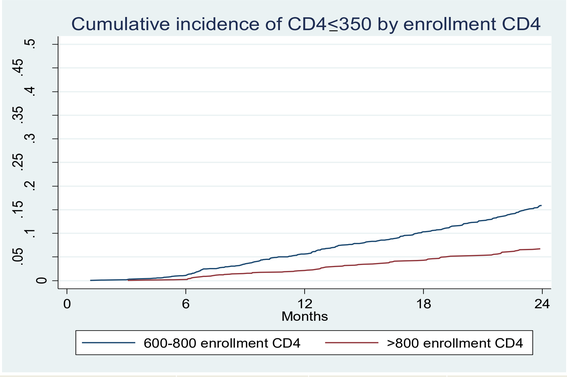
	N (%)
Age (years) median (IQR)	32.1 (25.9-40.1)
15-20	328 (7.1)
21-30	1,825 (39.3)
31-40	1,413 (30.4)
41-50	747 (16.1)
>50	330 (7.1)
Female	3,384 (72.8)
WHO stage enrollment	
I	2,444 (65.4)
II	953 (25.5)
III	332 (8.9)
IV	10 (0.3)
CD4+ enrollment median (IQR)	773.0 [IQR: 676-923]
600-800	2,572 (55.4)
>800	2,071 (44.6)

Pre-ART CD4 Decline

Average CD4+ decline prior to ART initiation was **5.3 cells/month** (95%CI 5.0-5.6) and **63.6 cells by 12 months** (95%CI 60.2-67.0) in unadjusted models.
No significant difference was observed in the slope of CD4+ decline for men compared to women, however age >40 years was associated with more rapid CD4+ decline; compared to those ≤40, patients >40 had a decline of 10.8 more cells per year (95%CI 6.8-14.8, p<0.01).



ART eligibility: CD4+≤500	6 months	12 months	24 months
All patients	4.1 % (3.5-4.7)	16.0% (14.9-17.1)	35.0% (33.4-36.7)
CD4 600-800 enrollment	6.8% (5.8-7.8)	23.6% (21.9-25.3)	48.2% (46.0-50.5)
CD4 >800 enrollment	0.7% (0.4-1.1)	6.4% (5.4-7.6)	17.9% (15.9-19.9)



ART eligibility: CD4+≤350	6 months	12 months	24 months
All patients	0.7% (0.5-1.0)	4.1% (3.5-4.7)	11.9% (10.8-13.1)
CD4 600-800 enrollment	1.0% (0.7-1.5)	5.6% (4.8-6.6)	15.9% (14.3-17.7)
CD4 >800 enrollment	0.2% (0.1-0.5)	2.0% (1.5-2.8)	6.8% (5.5-8.2)

Results (continued)

Time to ART Eligibility

At 12 months after enrollment, 16.0% (95%CI 14.9-17.1%) of patients reached CD4+ ≤500 and 4.1% (95%CI 3.5-4.7%) reached CD4+ ≤350. By 24 months, 35.0% (95%CI 33.4-36.7%) of patients reached CD4+ ≤500 and 11.9% (95%CI 10.8-13.1%) reached CD4+ ≤350. Among patients with CD4+ 600-800 cells at enrollment, almost half (48.2%, 95%CI 46.0-50.5) reached CD4+ ≤500 and only 15.9% (95%CI 14.3-17.7) reached CD4+ ≤350 in 24 months after enrollment into care. Median time to reaching CD4+ ≤500 for those who reached eligibility was 364 days from enrollment; for CD4+ ≤350 the median time to eligibility was 443 days.

Conclusion

In this large cohort of ART-naïve HIV patients from Rwanda with CD4+ ≥600 cells , average CD4+ decline was estimated to be 63.6 cells/year, a similar rate to that found in resource-rich settings. One third of patients reached ART eligibility within 24 months using current WHO guidelines of CD4+ ≤500 and only 12% reached CD4+ ≤350 cells as per 2010 WHO guidelines. Change in ART eligibility to higher CD4+ threshold will result in substantial increase in number of patients requiring ART for more years of treatment.

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