

Baseline CD4 Percentage is Predictive of Survival in Patients Starting Antiretroviral Therapy, Including Those with Absolute CD4 Cell Counts Between 200 and 350 cells/ μL

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Background

CD4 percentage has been used anecdotally as means of determining when to begin HAART, but its prognostic value in terms of patient survival has not been established.

Objectives

- To determine whether HIV disease progression is predicted by the initial CD4 percentage.
- To determine the utility of CD4 percentage as a prognostic factor in a sub-group of AIDS-free individuals with baseline CD4 cell counts between 200 and 350 cells/ μL .

Methods

Participants who initiated triple combination therapy between August 1, 1996 and June 30, 2002 were enrolled in a population-based cohort of antiretroviral therapy-naïve HIV-positive individuals 18 years or older in British Columbia, Canada.

Subjects were followed until death or June 30, 2003. The primary endpoint was non-accidental mortality, which was determined through a data linkage with the provincial vital statistics registry.

Cox-proportional hazard regression was used to model the simultaneous effect of prognostic variables on survival.

Results

Main Analysis

A total of 1,623 participants aged 18 years were included in the main analysis. When combined in a multivariate model including age, adherence to therapy, initial HIV RNA level, and a previous diagnosis of AIDS, a low CD4 percentage remained a highly significant predictor of eventual death (CD4% < 5, RR = 4.46, 95% confidence interval 2.92 – 6.79; CD4% 5 - 14, RR = 2.43; 95% CI 1.75 – 3.38) when compared to those subjects with initial CD4 fraction of 15% or greater.

However, absolute CD4 count strata had higher relative risks associated with mortality (absolute CD4 < 50/ μL , RR = 6.07, 95% CI 4.11 – 8.97; 50 - 199/ μL , RR = 2.95, 95% CI 2.08 – 4.18, relative to counts \geq 200/ μL).

Sub-group Analysis

Sub-group analysis of 417 participants without AIDS at baseline and CD4 cell counts between 200 and 350 cells/ μL , found that baseline CD4 fraction below 15% (RR = 2.71, 95% CI 1.20 – 6.10) and low adherence to therapy (RR = 1.18, 95% CI 1.05 – 1.33) were associated with an increased risk of death.

HIV RNA levels \geq 100 000 copies/ mL were also marginally associated with mortality (RR = 2.57, 95% CI 1.00 – 6.58).

Conclusion

These data demonstrate that CD4 percentages below 15% are independent predictors of mortality in AIDS-free patients starting HAART with CD4 cell counts between 200 and 350 cells/ μL .

Suggest that CD4 percentage should be considered for inclusion in therapeutic guidelines used to determine when to start therapy.

Table 1 Cox proportional hazards analysis of risk of death among 1,623 antiretroviral therapy naïve subjects initiating highly active antiretroviral therapy

Baseline variables	Risk Ratios (95% confidence interval)		
	Univariate	Multivariate*	Multivariate*
Age			
per year	1.04 (1.02 - 1.05)	1.04(1.03 – 1.06)	1.04(1.03 – 1.06)
Sex			
Male versus female	0.76 (0.53 - 1.08)		
AIDS diagnosis			
yes versus no	1.59 (1.12 - 2.25)	5.15 (1.87 – 14.14)	3.45 (1.23 – 9.67)
History of IDU			
yes versus no	0.78 (0.57 - 1.11)		
HIV RNA			
\geq 100 000 copies/ mL	2.09 (1.53 - 2.84)	3.46 (1.54 – 7.79)	3.38 (1.49 – 7.68)
Adherence to therapy			
10% decrements	1.15 (1.10 – 1.20)	1.14(1.04-1.24)	1.14(1.04-1.24)
CD4 %			
\geq 15	1	1	
5 - 14	2.48 (1.81 - 3.41)	2.43(1.75 – 3.38)	
< 5	3.66 (2.51 - 5.36)	4.46(2.92 – 6.79)	
CD4 cell count/ μL			
> 200	1		1
50 - 199	2.86 (2.04 - 4.00)		2.95 (2.08 – 4.18)
< 50	4.97 (3.51 - 7.05)		6.07(4.11 – 8.97)

* both multivariate models adjusted for interactions between adherence and viral load, and adherence and AIDS diagnosis at baseline.

Table 2 Cox proportional hazards analysis of risk of death in 417 naïve, AIDS-free subjects initiating HAART with initial CD4 counts between 200 and 350 cells/ μL

Baseline variables	Risk Ratio (95% confidence intervals)	
	Univariate	Multivariate
Age		
Per year	1.03 (0.98 - 1.07)	
History of injection drug use		
yes versus no	0.90 (0.35 - 2.27)	
Sex		
male versus female	1.80 (0.42 – 7.69)	
HIV RNA		
\geq 100 000 copies/ mL	2.80 (1.10 – 7.10)	2.57 (1.00 – 6.58)
Adherence to therapy		
10% decrements	1.17(1.04 – 1.32)	1.18 (1.05 - 1.33)
CD4 %		
\geq 15%	1	1
< 15%	2.89 (1.29 – 6.46)	2.71 (1.20 – 6.10)

Figure 1 Probability of Survival Stratified by CD4 and CD4% at Baseline

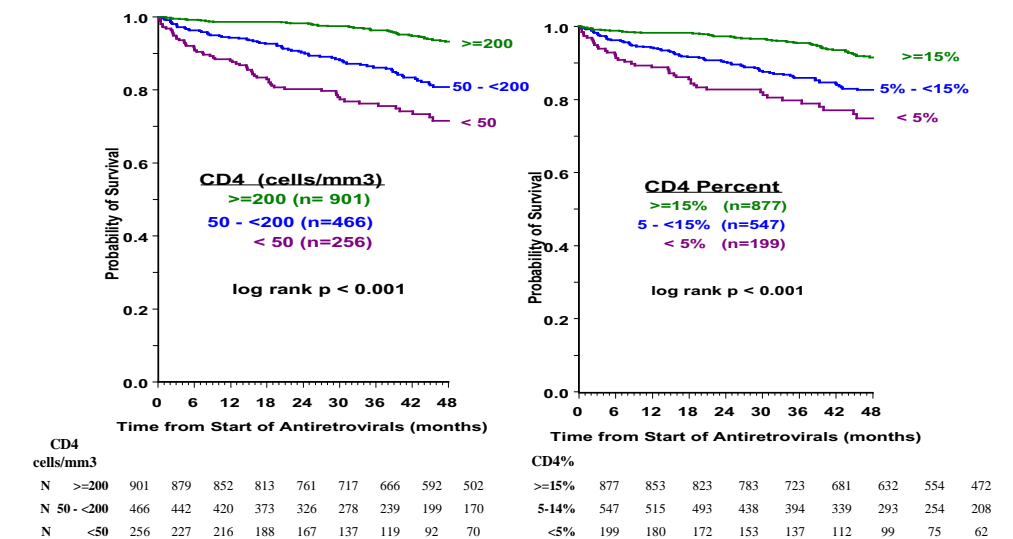
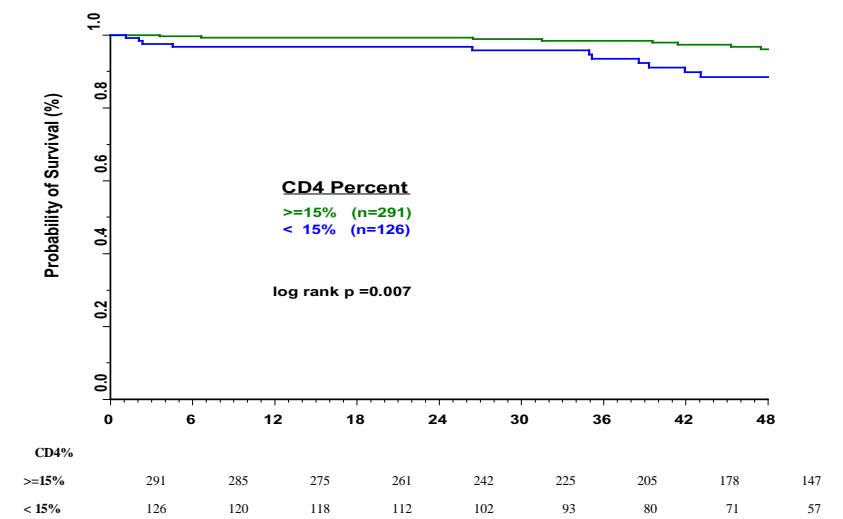


Figure 2 Probability of Survival for AIDS-Free Participants with Baseline CD4 of 200 to 350 cells/ μL



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