

Prognosis of HIV Patients Receiving Antiretroviral Therapy According to CD4 Counts: A Long-term Follow-up study in Yunnan, China

Li Ren^{1,2,3#}, Juan Li^{4#}, Shiyi Zhou⁵, Xueshan Xia⁶, Zhenrong Xie⁵, Pan Liu⁷, Yu Xu⁵, Yuan Qian⁸, Huifeng Zhang², , Litang Ma⁸, Qiuwei Pan⁴, Kunhua Wang^{1,5*}

¹Faculty of Environmental Science and Engineering, Kunming University of Science and Technology, Kunming, 650093, Yunnan Province, China;

²The First People's Hospital of Yunnan Province, Kunming, 650031, Yunnan Province, China;

³Medical faculty of Kunming University of Science and Technology, Kunming, 650093, Yunnan Province, China;

⁴Department of Gastroenterology and Hepatology, Erasmus University Medical Center Rotterdam, The Netherlands;

⁵Yunnan Institute of Digestive Disease, the First Affiliated Hospital of Kunming Medical University, Kunming, 650032, Yunnan Province, China;

⁶Faculty of Life Science and Technology, Center for Molecular Medicine in Yunnan province, Kunming University of Science and Technology, Kunming, 650093, Yunnan Province, China;

⁷Yan'an Hospital of Kunming Chenggong hospital, Kunming, 650501, Yunnan Province, China;

⁸The First People's Hospital of Zhaotong City, Zhaotong, 657000, Yunnan Province, China.

#These authors contributed equally.

***Correspondence:**

Kunhua Wang, Yunnan Institute of Digestive Disease, the First Affiliated Hospital of Kunming Medical University, Kunming, 650032, Xichang Road 295, Yunnan Province, China.

Tel: (+86)871-6532 4888 Email: kunhuawangProf@163.com

Running title: Survival of antiretroviral treated HIV Patients

Supplementary materials

Table S1. Baseline Characteristics of the Patients who Died at First 6 Months of Follow-Up Period

Characteristics	Descriptive statistics
Total	
no.	82
Gender, no. (%)	
Male	58 (70.7)
Female	24 (29.3)
Marital status, no. (%)	
Unmarried	11 (13.4)
Married	61 (74.4)
Divorced	3 (3.7)
Widowed	7 (8.5)
Age at ART initiation, year	
Mean (SD)	47.6 (15.8)
Median (IQR)	42.0 (34.3-60.0)
WHO HIV Clinical Stage, no. (%)	
Stage I/II	35 (42.7)
Stage III/IV	47 (57.3)
CD4, cells/μl	
Mean (SD)	152.7 (128.9)
Median (IQR)	129.0 (44.5-215.0)
<50	21 (25.6)
50-199	32 (39.0)
\geq 200	22 (26.8)
Transmission category, no. (%)	
Injecting drug users (IDU)	12 (14.6)
Homosexual	0 (0)
Heterosexual	53 (64.6)
Others/unknown	17 (20.7)

ART indicates antiretroviral treatment

Table S2. Testing the Proportional Hazards Assumption of a Cox Regression Model Fit^a

	rho	chisq	p
Gender			
Female	-	-	(Reference)
Male	-0.014	0.040	.841
Marital status			
Married	-	-	(Reference)
Unmarried	-0.071	1.073	.300
Divorced	0.107	2.25	.134
Widowed	0.066	0.991	.320
Age at ART initiation, year			
WHO HIV Clinical Stage			
Stage I/II	-	-	(Reference)
Stage III/IV	-0.081	1.536	.215
CD4, cells/ μ l			
\geq 200	-	-	(Reference)
50-199	-0.104	2.425	.119
<50	-0.150	5.029	.025
Transmission category			
Blood transfusion	-	-	(Reference)
Injecting drug users (IDU)	-0.031	0.192	.661
Homosexual	0.003	0.002	.957
Heterosexual	-0.039	0.296	.586
Mother-to-Child	-0.013	0.036	.850
Others/unknown	-0.022	0.093	.760
GLOBAL ^b	NA	19.958	.096

^aComputed by `cox.zph()` function in package of "survival" from R

^bIndicates the global test

rho = Spearman's rank correlation coefficient

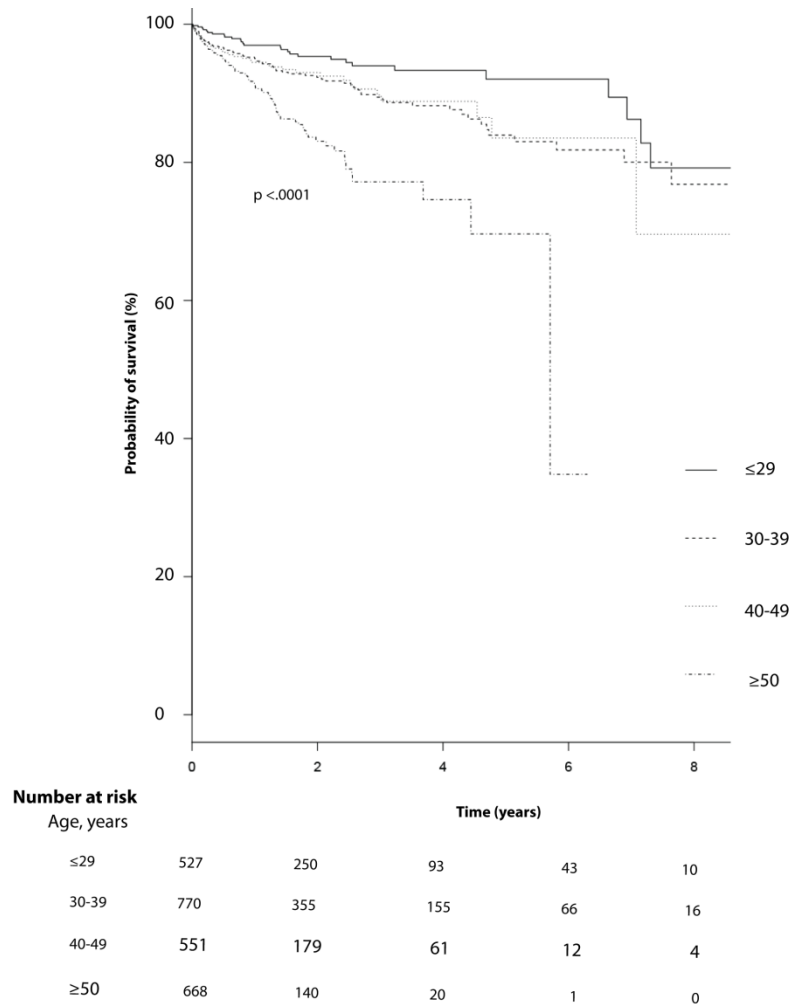


Figure S1. Cumulative mortality from all-cause mortality for study population infected by human immunodeficiency virus (HIV) receiving antiretroviral therapy (ART) according to age ($p < .0001$). Corresponding numbers at risk at different time-points split by age categories have been indicated below the graph.

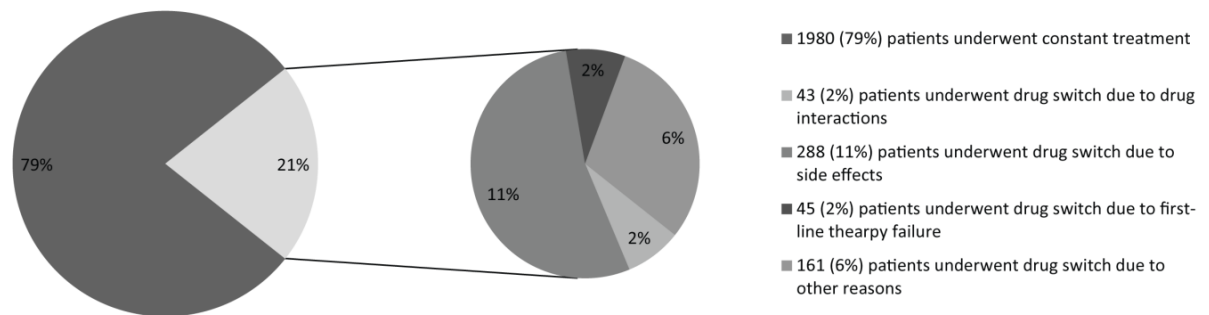
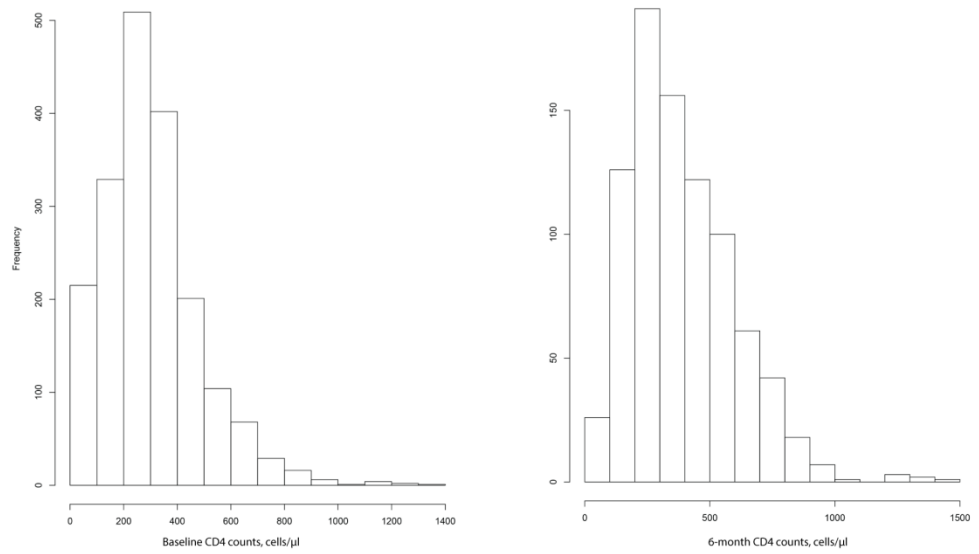


Figure S2. The Pie Chart showing the percentage of patients who switched drugs during Antiretroviral Therapy.

A. Histograms



B. Stacked bar chart

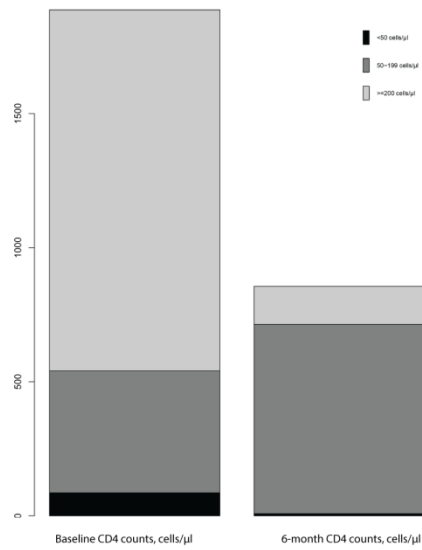


Figure S3: Plots presenting the values of baseline CD4 counts and 6-month CD4 counts for the patients who had survived 6 months after antiretroviral therapy. (A): histograms for continuous data of CD4 counts; (B): stacked bar chart for categorical data of CD4 counts: <50, 50-199, and \geq 200 (unit: cells/ μ l).

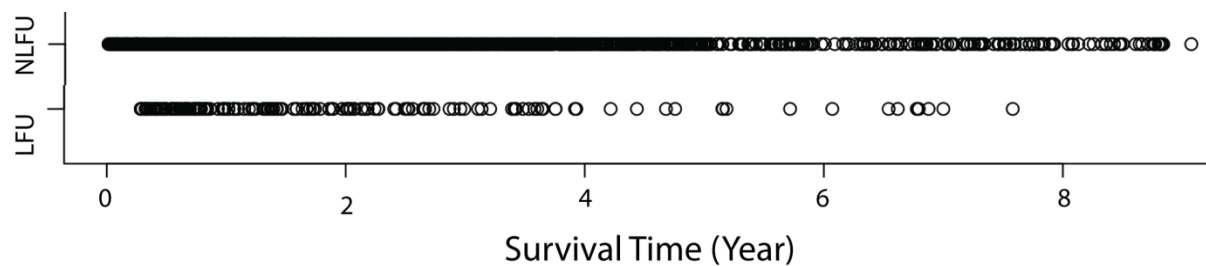


Figure S4: Plot of loss to follow up or not loss to follow up against survival time. LFU = loss to follow up; NLFU = not loss to follow up.

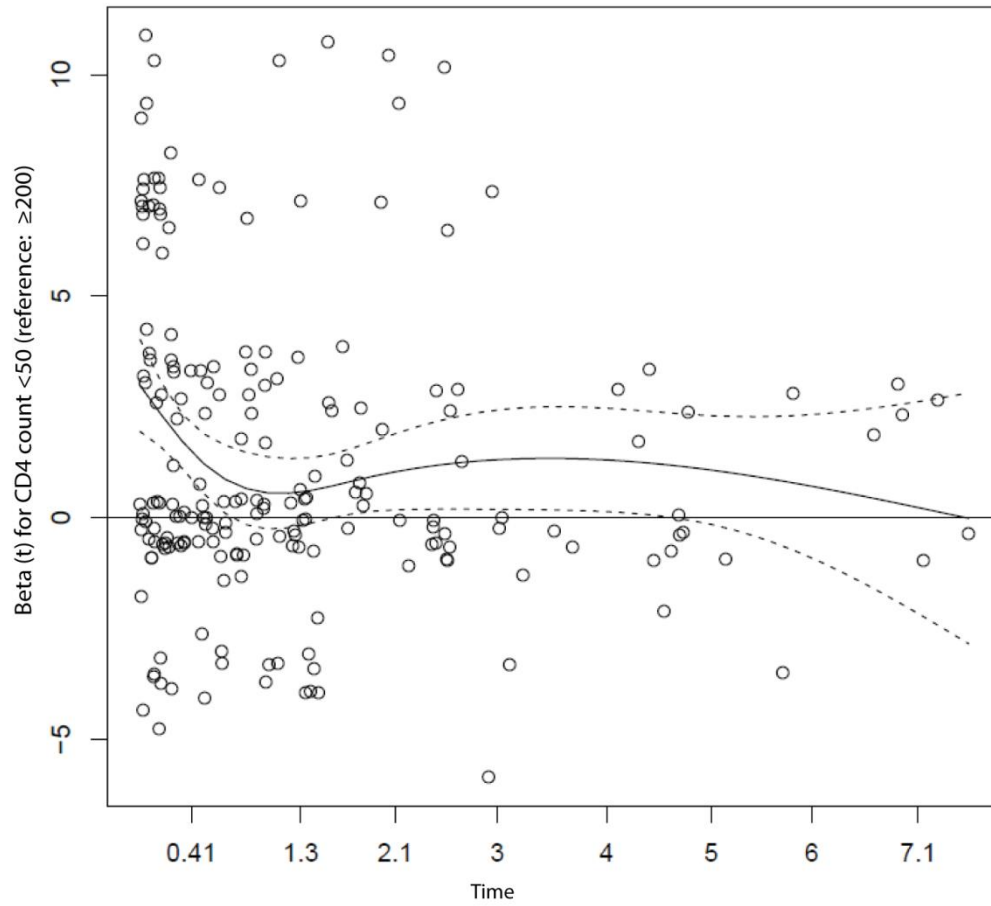


Figure S5: Plot of scaled Schoenfeld residuals against transformed time for covariate CD4 count in Cox model fit. The upper solid line is a smoothing spline fit to the plot, with the broken lines representing a ± 2 -standard-error band around the fit; and the bottom solid line is a horizontal line.


```

# Import data.....
data1 <- read.csv ('HIV_data.csv')

# Split dataset into two time intervals: <=0.5 year; >0.5 year.....
data2<-survival::survSplit(Surv(time,event)~.,data1,cut=c(0.5),
      episode = "tgroup",
      id="id")

# Cox model.....

# 1.Univariate analysis
## CD4 for two time intervals
summary(coxph(Surv(tstart,time,event)~CD4:strata(tgroup),data=data2))
## Other factors
variables<-c('sex','marriage','transmission','WHO_stage','age')
lapply (variables, function(x)summary(coxph(Surv(time,event)~data2[,x],data=data2)))

# 2.Multivariate analysis
summary(coxph(Surv(tstart,Time_m,Event)~CD4:strata(tgroup)+sex+marriage+transmission+WHO_s
tage+age, data=data2))

```

Figure S6. R code for performing Cox proportional regression analyses