

Clinical and Immunological Outcomes of Patients over 55 Years Receiving ART in South Africa

Contact: Dr Mhairi Maskew
 Right to Care
 Postnet Suite 212, Private bag X2600, Houghton, 2041
 Email: mhairi.maskew@righttocare.org
 Tel: +27 11 276 8896
 Fax: +27 11 276 8885



Mhairi Maskew^{1,2} Matthew Fox^{3,4} Patrick MacPhail² Ian Sanne^{1,2}

¹ Right to Care, South Africa, ² Clinical HIV Research Unit, University of the Witwatersrand, ³ Center for International Health and Development, Boston, USA, ⁴ Health Economics Research Office, South Africa



ABSTRACT

Background

Age is an important risk factor for mortality for many diseases, but evidence is limited as to whether initiating HIV treatment later in life increases the risk of early mortality after initiating highly active antiretroviral therapy (HAART) compared to those initiating HAART earlier. Older patients may have poorer immunological and virological responses to HAART.

Methods

This study was a retrospective cohort study among 8,713 HIV-infected adults initiated on HAART at the Thembu Lethu Clinic between April 2004 - March 2008. We used proportional hazards and logistic regression models to assess age-specific differences in 1) early mortality, 2) CD4 cell count response, 3) failure to achieve virologic suppression and 4) risk of viral rebound after suppression post HAART initiation. Models were adjusted for gender, baseline CD4 count, hemoglobin level and BMI.

Results

At baseline, patients aged 55 or older (n= 278, 3.2%) were similar to the 8435 (96.8%) patients under 55 in terms of presenting CD4 count, hemoglobin level and BMI. Older patients were less likely to be receiving TB treatment (15.4% vs. 6.5%, p<0.001) and fewer presented with WHO clinical stage III or IV (44.9% vs. 33.9%, p=0.002). The risk of death for older patients was twice that of younger patients (HR 2.07, 95% CI 0.91 - 4.74) within six months of starting treatment and also after one year on treatment (HR = 2.01, 95% CI 1.02 - 3.96). Failure to increase CD4 count by 50 cells/mm³ appeared more likely among older subjects in the first six months after initiating treatment (OR=1.43, 95%CI 0.95 - 2.16) as well after one year on treatment (OR=1.74, 95%CI 0.92 - 3.28). There was no difference in odds of achieving virologic suppression between age groups at four (OR = 1.07, 95% CI -0.53-2.16) or ten months (OR = 1.04 (95% CI =0.47-2.31)) post ART initiation. We did not find evidence of age group as a risk factor for rebound of HIV viral load after achieving suppression [OR = 1.19 (95% CI =0.27-5.16)] in adjusted models.

Conclusions

The risk of early mortality after initiation of HAART among those aged 55 or older was double the risk of those under 55. Decline in CD4 count numbers with advancing age may impair the increase in CD4 cells after initiation of HAART in subjects over 55 years of age. We found no evidence that failure to achieve viral suppression and viral rebound were more likely in older age groups.

BACKGROUND

- Expanded access to highly active antiretroviral treatment (HAART) means more people aged over 55 years receiving HAART
- Increasing age results in decreased immune function and is important risk factor for mortality for many diseases
- Limited evidence as to whether initiating HIV treatment later in life increases risk of early mortality and poorer immunological and virological responses compared to those initiating treatment earlier

OBJECTIVE

To determine if clinical, immunological and virological outcomes of HIV infected persons aged over 55 years differ from those of younger patients after initiation of HAART

METHODS

- A retrospective analysis of prospectively collected cohort data among 8713 HIV infected adults initiated on HAART at the Thembu Lethu Clinic (TLC) between April 2004 and March 2008
- TLC is an urban public sector HIV Comprehensive Care Management and Treatment site in Johannesburg, South Africa.
- Data is collected and stored on an electronic patient management system TherapyEdge-HIV™

Study Population

- Consisted of HIV infected individuals enrolled at TLC:
 - treatment naive at the time of HAART initiation at TLC
 - ≥18 years old
 - Initiated on treatment at TLC after 1 April 2004

Outcomes definitions

- Early mortality: confirmed death within six months of starting HAART
- CD4 count response: increase in CD4 count of at least 50 cells/mm³
- Undetectable viral load: <400 copies/mL
- Viral rebound: increase in viral load to above 400 copies/mL after achieving undetectable viral load

Statistical Methods

- Proportional hazards regression and logistic regression used to assess age-specific differences in
 - early mortality
 - CD4 cell count response
 - failure to achieve virologic suppression and
 - risk of viral rebound after suppression post ART initiation.
- Models adjusted for sex, baseline CD4 count, haemoglobin level and TB status.

RESULTS

Baseline Characteristics by Age Group

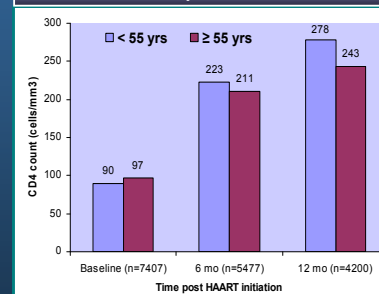
Characteristic	Age group		p
	< 55 yrs n = 8435	≥ 55 yrs n = 278	
Sex (n,%)	male 3065 (64%)	139 (50%)	<0.0001
	female 5369 (36%)	139 (50%)	
Baseline CD4 count cells/mm ³	(mean, std) 89.9 (72.6)	97.0 (65.3)	0.094
Baseline Hb g/dl	(mean, std) 11.4 (3.8)	11.8 (2.0)	0.111
Baseline BMI kg/m ²	(mean, std) 22.0 (6.1)	22.4 (4.8)	0.169
On TB treatment at baseline? (n, %)	Yes 1300 (15%)	18 (6%)	<0.0001
	No 7128 (85%)	260 (94%)	
WHO stage at baseline (n, %)	I/II 4830 (59%)	177 (67%)	
	III/IV 3292 (41%)	88 (33%)	0.017
Initiating HAART regimen (n, %)	d4T-3TC-EFV 7154 (85%)	253 (91%)	
	d4T-3TC-NVP 676 (8%)	5 (2%)	
	AZT-3TC-EFV 258 (3%)	7 (3%)	
	Other 346 (4%)	13 (5%)	0.002

Outcomes by Age Group

Outcome	N (%) Achieving outcome	Crude estimate (95% CI)	Adjusted estimate* (95% CI)
Death within 6 months of initiating treatment			
<55 yrs	273 (3%)	1	1
≥55 yrs	18 (6%)	2.08 (1.29 - 3.35)	2.07 (0.91 - 4.74) †
Death within 12 months of initiating HAART			
<55 yrs	359 (4%)	1	1
≥55 yrs	21 (8%)	1.84 (1.19 - 2.86)	2.01 (1.02 - 3.96) †
Failure to increase CD4 count 50 cells/mm³ within 6 months of initiating HAART			
<55 yrs	1006 (21%)	1	1
≥55 yrs	45 (29%)	1.50 (1.05 - 2.14)	1.43 (0.95 - 2.16) †
Achieve undetectable viral load within 6 months of initiating HAART			
<55 yrs	3848 (89%)	1	1
≥55 yrs	129 (92%)	1.43 (0.77 - 2.67)	1.07 (0.53 - 2.16) †
Viral rebound after achieving viral suppression			
<55 yrs	147 (6%)	1	1
≥55 yrs	5 (7%)	1.18 (0.47 - 3.00)	1.19 (0.27 - 5.16) †

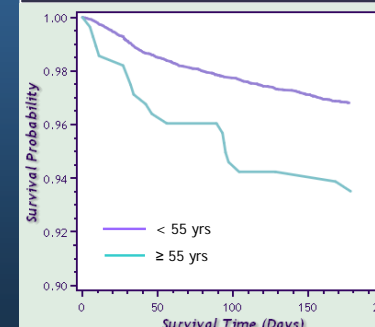
* Adjusted for sex, Hb, TB status, baseline CD4 count † Hazard Ratio ‡ Odds ratio

Mean CD4 count post HAART initiation



Time post HAART initiation	<55yrs	≥55yrs
6 mo:	127 (95% CI: 120-134)	107 (95% CI: 93-122)
12 mo:	183 (95% CI: 176-191)	137 (95% CI: 116-158)

Crude Kaplan-Meier estimate of early mortality



Log-Rank test p = 0.002

CONCLUSIONS

- Risk of early mortality after HAART initiation was double for over 55y age group
- Decline in CD4 count numbers with advancing age may impair the increase in CD4 cells after initiation of HAART in subjects over 55 years of age
- No evidence that failure to achieve viral suppression and viral rebound were more likely in older age groups