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A High Risk of Hospitalization Immediately Follows HAART Initiation

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Abstract

Background: HAART decreases long-term morbidity and mortality; however its short term effect on hospitalization rates is unknown.

Methods: Hospitalizations among 1329 HAART-naïve subjects in an urban HIV clinic 1997 – 06 were examined for one year after HAART initiation. Rates were stratified by virologic responders (≥1 Log_{10} decrease in HIV-1 RNA within 6 months) and non-responders. Multiple negative binomial regression was used to assess factors associated with hospitalization.

Results: Responders (n = 965) were less likely than non-responders (n = 362) to be African American (75 vs. 87%, p < 0.001). Through 45 days after HAART, responders' mean hospitalization rate was similar to non-responders' (75.4 vs. 79.4 per 100 person years (PY)) and to pre-HAART rates (figure). Between 45 and 90 days, responders' rate decreased (p < 0.05 vs. baseline). After 90 days it settled near 45 per 100 PY (p < 0.01 both for decrease from baseline and vs. non-responders after 90 days). Findings were unchanged in multiple regression which included calendar time and in which women (IRR 1.39 [1.12, 1.72]), injection drug users (1.46 [1.19, 1.80]) and persons with baseline CD4 <100 cells/ml (2.20 [1.70, 2.84]) had higher rates.

Conclusions: For 90 days after HAART initiation, virologic responders remain at comparable hospitalization risk to non-responders and therefore warrant close clinical surveillance. Further studies will need to evaluate causes of hospitalization in this high risk time period.

Background

In the short term after starting HAART, HIV-infected patients are at risk of immune reconstitution inflammatory syndromes, traditional opportunistic infections, and adverse drug reactions. While HAART decreases morbidity over the long-term, hospitalization risk immediately following initiation is unknown.

Our main objective was to measure the rates of all-cause hospitalizations stratified by virologic response over time in the year after HAART initiation.

Methods

All HAART naïve patients in the Johns Hopkins HIV Clinical Cohort who initiated HAART 1997 – 2005 were considered for inclusion. Virologic response was defined as a decrease in HIV-1 RNA of 1 Log_{10} or more or suppression below the detectable limit at 6 months after the HAART initiation date.

Hospitalization rates were calculated per 100 person years (PY) for the periods: 180 days prior to HAART initiation and days 1 – 45, 46 – 90, 91 – 180, and 181 – 365 after HAART. Analysis was performed with Chi^2 and Wilcoxon rank-sum tests and multivariate negative binomial regression using generalized estimating equations to estimate relative rates and standard errors.

TABLE 1. Baseline Characteristics

	Responders N = 965 (%)*	Non-Responders N = 362 (%)*	*P*
Age at HAART Initiation (years)			
18 – 29	109 (11.3)	48 (13.3)	**0.04**
30 – 39	387 (40.1)	169 (46.7)	
40 – 49	353 (36.6)	113 (31.2)	
≥50	116 (12.0)	32 (8.8)	
Median (IQR)	39.5 (34, 44.5)	38 (33, 43)	**<0.01†**
Gender			
Women	328 (34.0)	141 (39.0)	0.09
Men	637 (66.0)	221 (61.1)	
Racial / Ethnic Category			
African American	722 (74.8)	314 (86.7)	**<0.001**
White	221 (22.9)	42 (11.6)	
Hispanic	7 (0.7)	5 (1.4)	
Asian	4 (0.4)	0	
Other	11 (1.1)	1 (0.3)	
HIV risk factors			
IDU alone	196 (20.3)	89 (24.6)	0.21
IDU-Heterosexual	173 (17.9)	76 (21.0)	
IDU-MSM	41 (4.3)	12 (3.3)	
Heterosexual alone	284 (29.4)	102 (28.2)	
MSM alone	210 (21.8)	62 (17.1)	
Unknown/other	61 (6.3)	21 (5.8)	
IDU (alone or in combination)	410 (42)	177 (49)	**0.04**
CD4 Count at HAART (cells/mm^3)			
<50	249 (25.8)	114 (31.5)	0.20
50 – 199	312 (32.3)	104 (28.7)	
200 – 349	235 (24.4)	87 (24.0)	
≥350	169 (17.5)	57 (15.8)	
Median (IQR)	156 (46, 297)	148 (29, 282)	0.09 †
HIV-1 RNA at HAART (Log_{10} copies/mL)			
<4	174 (18.0)	75 (20.7)	0.32
4 – 5	372 (38.6)	145 (40.1)	
≥5	419 (43.4)	142 (39.2)	
Median (IQR)	4.9 (4.3, 5.4)	4.8 (4.1, 5.3)	0.08 †
HAART Type			
NNRTI (plus >2 NRTI's)	355 (36.8)	91 (25.1)	**<0.001**
PI (plus ≥2 NRTI's)	497 (51.5)	230 (63.5)	
PI and NNRTI (plus ≥1 NRTI)	113 (11.7)	41 (11.3)	
Calendar Era of HAART Initiation			
1997 – 1998	383 (39.7)	217 (59.9)	**<0.001**
1999 – 2002	384 (39.8)	105 (29.0)	
2003 – 2005	198 (20.5)	40 (11.1)	

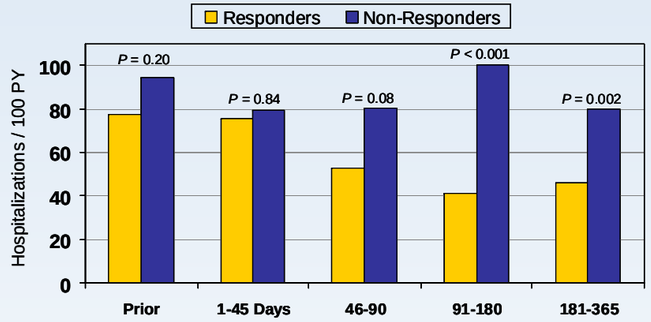
* Values are Num (%) unless otherwise specified. Statistical comparisons made using Chi^2-test except † indicates Wilcoxon rank-sum test. IDU, injection drug use; MSM, men who have sex with men; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

TABLE 2. Bivariate and Multivariate Relative Hospitalization Rates

	Bivariate Incidence Rate Ratio (95% CI)	*P*	Multivariate Incidence Rate Ratio (95% CI)	*P*
Response Status by Time Periods				
Prior 6 mon				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.22 (0.90, 1.65)	0.20	1.07 (0.80, 1.43)	0.67
Days 1 – 45 After HAART				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.05 (0.64, 1.72)	0.84	0.96 (0.59, 1.55)	0.86
Days 46 – 90				
Responders	1.00	Ref	1.00	Ref
Non-Responder	1.52 (0.95, 2.43)	0.08	1.42 (0.89, 2.28)	0.14
Days 91 – 180				
Responders	1.00	Ref	1.00	Ref
Non-Responder	**2.44 (1.59, 3.76)**	<0.001	**2.25 (1.48, 3.43)**	<0.001
Days 181 – 365				
Responders	1.00	Ref	1.00	Ref
Non-Responder	**1.74 (1.22, 2.48)**	0.002	**1.58 (1.11, 2.24)**	0.01
Age at HAART Initiation (years)			---	---
18 – 29	1.00	Ref		
30 – 39	0.98 (0.65, 1.48)	0.92		
40 – 49	1.18 (0.77, 1.80)	0.45		
>50	1.09 (0.68, 1.75)	0.71		
Women	**1.41 (1.14, 1.75)**	0.002	**1.39 (1.12, 1.72)**	0.002
African American	**1.86 (1.36, 2.54)**	<0.001	1.36 (1.00, 1.86)	0.05
IDU	**1.56 (1.25, 1.93)**	<0.001	**1.46 (1.19, 1.80)**	<0.001
CD4 Count at HAART (cells/mm^3)				
<50	**2.80 (2.19, 3.59)**	<0.001	**2.49 (1.81, 3.42)**	<0.001
50 – 199	**1.56 (1.18, 2.06)**	0.002	**1.44 (1.07, 1.93)**	0.02
≥200	1.00	Ref	1.00	Ref
HIV-1 RNA at HAART (Log_{10} copies/mL)				
<4	1.00	Ref	1.00	Ref
4 – 5	1.03 (0.74, 1.44)	0.87	0.88 (0.64, 1.22)	0.45
≥5	**1.75 (1.28, 2.40)**	<0.001	1.21 (0.85, 1.71)	0.29
HAART Type			---	---
NNRTI (plus ≥2 NRTI's)	1.00	Ref		
PI (plus >2 NRTI's)	1.05 (0.84, 1.32)	0.67		
PI and NNRTI (plus ≥1 NRTI)	1.12 (0.80, 1.56)	0.51		
Calendar Era of HAART Initiation			---	---
1997 – 1998	1.00	Ref		
1999 – 2002	1.11 (0.88, 1.40)	0.38		
2003 – 2005	1.05 (0.76, 1.45)	0.76		

--- Indicates not included in multivariate model because bivariate *P* > 0.20. PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

Hospitalization Rates by Virologic Response over Time After HAART



	Prior	1-45 Days	46-90	91-180	181-365
N (%), Resp.	909 (94)	965	949 (98)	934 (97)	874 (91)
N (%), Non-Resp.	347 (96)	362	324 (90)	304 (84)	264 (73)

Conclusions

- Hospitalization rate remains high (comparable to the pre-HAART rate) for the first 45 days after HAART initiation for virologic responders and non-responders
- Responders' hospitalization risk falls significantly between 45 and 90 days after initiation until reaching a plateau of 45/100 PY
- In multivariate analysis, non-responders had no statistically significant change in hospitalization rate and had higher rates than responders after 90 days
- The rate of 45/100 PY for responders after 90 days is comparable to the overall hospitalization rate in our clinic population (44/100 PY) over the years in study
- Lower CD4, female sex, and IDU were associated with increased hospitalization risk but age, HAART type and calendar era were not

Implications

- Providers should maintain close clinical monitoring through at least the first 90 days after HAART initiation
- Future studies should assess changes in diagnoses across time by responder status