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Obesity among HIV-Infected Persons: Impact of Weight on CD4 Cell Count

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Summary

To assess the effect of obesity on CD4 counts, we estimated the association of time-updated BMI categories with CD4 changes among 1,001 documented HIV seroconverters. During the pre-HAART era, a higher BMI was associated with less reduction in CD4 counts over time. However during the HAART era, obese versus normal weight patients had smaller increases in CD4 counts (+69 v. +116 cells, $p=0.01$). Lower CD4 counts may now be another adverse consequence of obesity.

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Keywords

HIV; immunology; obesity; CD4 counts; antiretroviral therapy

The prevalence of obesity among HIV-infected persons is increasing [1-3]. While excess weight is associated with several medical conditions [4,5], its impact on immune status remains largely unknown. In the pre-HAART era, studies showed that being underweight was associated with lower CD4 counts and shorter survival, while higher weights were associated with slower HIV progression [6-10]. However, since HAART has become available and wasting less frequent [2,3,11,12], the impact of weight may differ.

We investigated the relationship between longitudinal weight measurements and CD4 counts among 1,001 documented HIV seroconverters using the U.S. Military HIV Natural History Study (1986-2008). Participants had a seroconversion window of ≤ 3 years (mean 15.8 months) and biannual weight measurements and CD4 counts. Weight was categorized using body mass index (BMI, kg/m^2) as previously described [13,14].

Using longitudinal linear mixed models with a random intercept for each participant, regressions for change from HIV diagnosis in CD4 count were fitted. All models were adjusted for age, gender, race, length of seroconversion window, baseline CD4 and HIV RNA level, time-updated cumulative time on ART and HAART, BMI category, and follow-up visit. Since several characteristics varied by era, analyses were performed separately for those diagnosed in the pre- and HAART eras (cutpoint 1/1/1996). Among participants diagnosed in the HAART era, additional analyses on change in CD4 count before and then after HAART initiation were performed (SAS version 9.1, Cary, NC).

Of 1,001 HIV seroconverters, 400 (40%, mean follow-up 5.1 years) were overweight, 84 (8%, mean follow-up 4.5 years) obese, and 12 (1%, mean follow-up 4.1 years) were underweight at HIV diagnosis. Mean age was 29 years; 96% were male; 45% were Caucasian and 40% African American; 61% were diagnosed in the HAART era.

Among HIV-infected seroconverters diagnosed in the pre-HAART era ($n=394$, mean follow-up 6.5 years), the estimated mean post-diagnosis decreases in CD4 cell counts were less as BMI category increased: -158, -125, -95, and -50 cells/ mm^3 , respectively ($p<0.001$) (Table 1). Compared to normal weight patients, overweight ($p=0.005$) and obese ($p<0.001$) patients had smaller reductions in the CD4 count.

Among HIV-infected patients diagnosed in the HAART era ($n=607$, mean follow-up 4.2 years), the estimated mean post-diagnosis change in CD4 count was -1, +103, +116, and +69 cells/ mm^3 , respectively ($p<0.001$) (Table 1). Obese HIV patients compared to those with normal weight had significantly smaller increases in CD4 count ($p=0.01$). Those who were underweight had a mean decline in the CD4 count, whereas those with normal weight averaged an increase (-1 vs. 103 cells/ mm^3 , $p=0.004$).

Among patients diagnosed in the HAART era, the impact of weight on CD4 responses was also evaluated before and after HAART initiation. Prior to initiation, CD4 counts declined in each BMI category (-153, -55, -57, -76 cells/ mm^3 across increasing BMI categories, $p=0.33$), although no comparisons between normal weight and the other weight categories were statistically different. After HAART initiation, CD4 counts increased in each weight category (+127, +210, +230, and +188, respectively, $p=0.01$). Obese compared to overweight HIV patients gained significantly fewer CD4 cells after HAART initiation (42 cells less, $p=0.008$).

Analyses were also performed for change in the CD4 percentage with similar findings for both the pre- and HAART eras (Table 1).

Our study demonstrates that weight appears to affect CD4 counts over the course of HIV infection. While higher BMI categories were associated with less reduction in CD4 counts during the pre-HAART era, excess weight was not similarly beneficial during the HAART era, with obese patients achieving smaller CD4 count and percentage increases over time. These data suggest that obesity may be associated with poorer immunologic recovery among HIV in the setting of HAART availability.

Concurrent with our findings, prior studies during the pre-HAART era found that higher weights were associated with more robust CD4 counts as well as slower HIV progression and improved survival [6,8,9]. It has been hypothesized that nutritional reserves, in the form of fat stores, may prevent severe wasting and lean body loss at the time of AIDS-related crises and may help preserve immune counts [7].

As the incidence of wasting and end-stage AIDS has significantly declined due to HAART use [2,3,11,12], the potential benefits of maintaining higher weights may have changed. Our study was unique in that it also evaluated the impact of weight on CD4 counts after the advent of HAART. To our knowledge there has only been one similar study in the late HAART era, which showed no effect of obesity on CD4 counts; however, this study was limited by its cross-sectional design and lack of data on HIV seroconversion dates [15]. In our longitudinal study, we found that among HIV seroconverters diagnosed in the HAART era, obese patients had smaller increases in CD4 counts and percentages than normal weight patients. Our data suggest that the advantages of excessive weight may no longer be present among HIV patients who have access to HAART and robust CD4 counts, and that obesity may adversely affect CD4 recovery; further studies are needed to confirm our findings.

Possible mechanisms for the association between obesity and less robust CD4 counts include that obesity is associated with elevated levels of inflammatory markers (e.g., C-reactive protein and interleukin-6 (IL-6)) and adipokines which may have negative immune effects [16-20]. It is also plausible that excess weight may negatively affect antiretroviral drug levels since lipophilic drugs have a greater volume of distribution among obese patients. Further studies examining functional immune parameters, biomarkers and drug levels are needed.

In summary, although higher weight categories were associated with less reduction in CD4 counts in the pre-HAART era, excessive weight ($\text{BMI} > 30 \text{ kg/m}^2$) was not beneficial in the HAART era and was associated with smaller CD4 count increases. These data suggest that HIV providers should be cognizant of the potential negative effects of obesity among their patients, including potential adverse effects on CD4 counts. Weight monitoring and maintenance programs may be useful components of HIV clinical care visits.

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Adjusted Models¹ for the Association between Time-Updated BMI Category and Change from HIV diagnosis in CD4 Cell Counts and Percentages: HIV Seroconverters Diagnosed in the Pre- and HAART Eras.

Table 1

Factors	Pre-HAART Era			HAART Era		
	Est. Mean Change	Est. Diff. (SE)	p-value	Est. Mean Change	Est. Diff. (SE)	p-value
CD4 Count						
BMI Category (time-updated)						
Underweight ²	-158.0	-33.4 (38.9)	0.39	-1.3	-104.1 (36.5)	0.004
Normal	-124.6	Referent	--	102.8	Referent	--
Overweight	-95.0	29.7 (10.7)	0.005	116.3	13.5 (9.1)	0.14
Obese	-50.1	74.6 (18.9)	<0.001	69.2	-33.6 (13.7)	0.01
CD4 Percentage						
BMI Category (time-updated)						
Underweight ²	-10.4	-6.3 (1.3)	<0.001	1.1	-2.9 (1.1)	0.009
Normal	-4.2	Referent	--	4.0	Referent	--
Overweight	-3.0	1.2 (0.4)	<0.001	3.7	-0.3 (0.3)	0.27
Obese	-2.2	2.0 (0.7)	0.002	2.4	-1.6 (0.4)	<0.001

¹ Models additionally adjusted for visit, age, gender, race/ethnicity, length of seroconversion window, baseline CD4 and HIV-RNA, time-updated years on non-HAART ART, and time-updated years on HAART.

² Results presented for each BMI category represent averaging CD4 changes across those visits at which participants were in that BMI category.