Association Between Incident HIV-Associated Wasting/Low Weight and All-Cause Mortality in the OPERA® Cohort

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OPERA® The Longitudinal Cohort

Background

- HIV-associated wasting (HIVAW) is defined as progressive, involuntary weight loss with both fat and lean muscle tissue loss
- HIVAW remains an under-appreciated AIDS-defining illness in the modern era, despite highly effective antiretroviral therapy (ART)[1]
- The 2012-2018 period prevalence of HIVAW was reported as 18% in a recent claims study in the United States (US)[2]
- HIVAW and substantial weight loss have been associated with an increased risk of mortality in the past, regardless of ART use[3, 4]

Objective

To assess the association between incident HIV-associated wasting/low weight and all-cause mortality in the era of modern combination antiretroviral therapy

Methods

Study Population

- OPERA® observational cohort
  - Prospectively captured, routine clinical data from electronic health records
  - > 140,000 PWH as of November 2021, representing ~13% of people living with diagnosed HIV infection in the US[5]
- Inclusion criteria
  - People living with HIV (PWH)
  - 18 years of age or older
  - In care: ≥ 1 visit in OPERA® from 2016-2020
  - No malignancy within 3 years or AIDS-defining opportunistic infection (OI) within 12 months of eligibility date
  - No prior HIVAW/low weight
- Baseline: First date between 01JAN2016 and 31DEC2020 when eligibility criteria were met
- Follow-up through 31OCT2021

Incident HIVAW/Low Weight

- New wasting or low BMI/underweight diagnosis (ICD codes, title search) or first BMI < 20 kg/m^2 over follow-up

Statistical Analyses

- Extended Cox regression models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between incident HIVAW/low weight and all-cause mortality
- Time-dependent variables: HIVAW/low weight (exposure), $\log_{10}$ viral load (surrogate for ART use), Veterans Aging Cohort Study (VACS) Mortality Index score (surrogate for comorbidities)
- Fixed covariates: Age at baseline, race, ethnicity
- Linear and quadratic terms of continuous variables were included in the adjusted model

Results

Table 1. Characteristics of people with HIV with no prior HIVAW/low weight in the OPERA® cohort

	Full Study Population (N = 67,119)	Model Study Population[a] (N = 62,314)
Baseline demographic or clinical characteristic		
Median age (IQR), years	41 (31, 52)	41 (30, 52)
Female, n (%)	12,315 (18)	11,491 (18)
Black race, n (%)	31,211 (47)	29,898 (48)
Hispanic ethnicity, n (%)	14,513 (22)	13,620 (22)
Median time since HIV diagnosis (IQR), months	57 (2, 156)	58 (2, 157)
Ever on ART, n (%)	52,087 (78)	48,488 (78)
Median CD4 cell count (cells/μL) (IQR)	568 (371, 789)	567 (370, 789)
Median $\log_{10}$ viral load (copies/mL) (IQR)	3.00 (2.94, 8.65)	3.00 (2.94, 8.68)
Median VACS Mortality Index score (IQR)	13 (6, 25)	13 (6, 25)
Follow-up characteristic		
Median follow-up (IQR), months	44 (26,65)	45 (27, 65)
Incident HIVAW/low weight, n (%)	5,052 (8)	4,755 (8)

ART, antiretroviral therapy; HIV, human immunodeficiency virus; HIVAW, HIV-associated wasting; IQR, interquartile range; mL, milliliter; n, number; μL, microliter; VACS, Veterans Aging Cohort Study

[a] 4,805 (7%) of the full study population were not included in the models due to missing data in one or more included covariates

Figure 1. Censoring events of people with HIV and no prior HIVAW/low weight in the OPERA® cohort

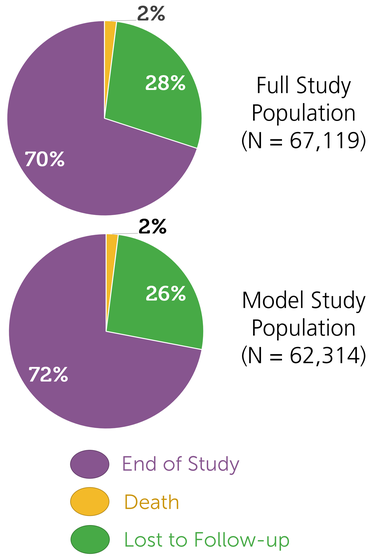
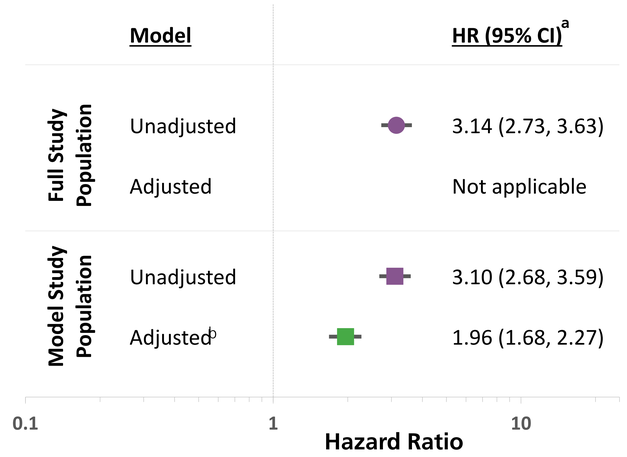


Figure 2. Association between incident HIVAW/low weight and all-cause mortality over follow-up



[a] Hazard ratios (HR) and 95% confidence intervals (CI) for the association between mortality and HIV-associated wasting (HIVAW)/low weight were estimated with extended Cox regression models

[b] Adjusted for baseline (age, race, ethnicity), and time-dependent covariates ($\log_{10}$ viral load and Veterans Aging Cohort Study [VACS] Mortality Index score); age, $\log_{10}$ viral load, and VACS score were modeled as continuous variables with linear and quadratic terms

Discussion

- Of 67,119 PWH without prior HIVAW/low weight in OPERA®, 93% of PWH had non-missing covariate data over follow-up
  - Baseline characteristics did not differ between the full and model study populations (**Table 1**)
- The study population was young (i.e., median age at baseline: 41 years) and relatively healthy (i.e., low viral load and VACS Mortality Index scores at baseline) (**Table 1**)
- Death due to any cause was very uncommon; most PWH were followed through the end of the study (31OCT2021) (**Figure 1**)
- In unadjusted analyses, PWH with incident HIVAW/low weight were more than 3 times as likely to experience death over follow-up than PWH without incident HIVAW/low weight (**Figure 2**)
- After adjusting for covariates, including viral load and VACS Mortality Index scores over follow-up, PWH with incident HIVAW/low weight remained twice as likely to experience death (**Figure 2**)
- Particular attention needs to be paid to incident HIVAW/low weight among PWH, regardless of ART use and presence of other comorbidities, to restore health and potentially reduce the risk of death

Key Finding

Incident HIVAW/low weight was associated with twice the risk of all-cause mortality, despite adjustment for changes in viral load (surrogate marker for ART use) and VACS Mortality Index scores (surrogate marker for comorbidities) over follow-up.

References

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