Incident Human Immunodeficiency Virus-Associated Wasting (HIVAW)/Low Weight is Associated with Nearly Doubled Mortality Risk in the Modern ART Era

Objective

To evaluate the association between incident HIVAW and all-cause mortality

Background

- HIVAW remains a challenge for some PWH despite HIV viral control
- This study evaluates the association between HIVAW/low weight and all-cause mortality in recent years using EHR data
- Real world evidence studies have strengths and limitations, please see page 2 to learn more

Methods

- Data source: Observational Pharmaco-Epidemiology Research & Analysis (OPERA®) data from EHR
- HIVAW/low weight included a wasting or low BMI/underweight diagnosis (via ICD codes or diagnosis title search), or BMI vitals measurement <20kg/m²

PWH in OPERA [®] (N = 140,817)	Patients Included
PWH with no prior HIVAW eligible for the study (full study population) [‡]	N = 67,119
PWH in care without missing covariate data (model study population) [‡]	N = 62,314

- Incident HIVAW/low weight was a time-dependent exposure
 - For example, someone diagnosed with HIVAW/low weight 8 months after baseline was switched from unexposed to exposed at that time
- The relationship between HIVAW/low weight and all-cause mortality was evaluated based on a model that included a time-updated VACS Mortality Index to aid in the prediction of all-cause mortality risk
- The VACS index¹⁻⁴ is composed of measures of HIV mortality risk and indicators of comorbidity and organ system dysfunction associated with a higher risk of mortality among PWH and is a measure of physiologic frailty

Study Population

Baseline demographic and clinical characteristics of people with HIV and no prior HIVAW/low weight in the OPERA® cohort			
Baseline demographic or clinical characteristic	Full Study Population N = 67,119	Model Study Population ⁺ N = 62,314	
Median age (IQR), yrs	41 (31, 52)	41 (30, 52)	
Female, n (%)	12,315 (18)	11,491 (18)	
Black, n (%)	31,211 (47)	29,898 (48)	
Hispanic, n (%)	14,513 (22)	13,620 (22)	
Median time since HIV diagnosis (IQR), mos	57 (2 <i>,</i> 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)	

AIDS: acquired immunodeficiency syndrome; ART: antiretroviral therapy; BMI: body mass index; EHR: electronic health record; PWH: people with HIV; IQR: interquartile range; mL: milliliter; μ L: microliter; VACS: Veterans Aging Cohort Study

⁺Inclusion Criteria: ≥18 years of age, ≥1 OPERA® visit from 01JAN2016 through 31DEC2020, no malignancy within 3 years prior to baseline, no AIDS-defining opportunistic infection within 12 months prior to baseline, and no HIVAW/low weight prior to baseline

⁺4,805 (7%) of the full study population were not included in the models due to missing data in the included covariates (age, race, ethnicity, viral load, and VACS Mortality Index score) **1.** Tate JP, Justice AC, Hughes MD, et al. An internationally generalizable risk index for mortality after one year of antiretroviral therapy. *AIDS* 2013;27:563–72; **2.** Justice AC, Modur SP, Tate JP, et al. Predictive accuracy of the Veterans Aging Cohort Study index for mortality with HIV infection: a North American cross cohort analysis. *J Acquir Immune Defic Syndr* 2013;62(2):149-63, doi:10.1097/QAI.0b013e31827df36c; **3.** Kuller LH, Tracy R, Belloso W, et al. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. *PLoS Med* 2008;5:e203; **4.** Womack JA, Goulet JL, Gibert C, et al. Physiologic frailty and fragility fracture in HIV infected male veterans. *Clin Infect Dis* 2013;56(10):1498-504, doi:10.1093/cid/cit056

Reference: Wohlfeiler MB, Weber RP, Brunet L, et al. Incident HIV-Associated Wasting/Low Weight is Associated with Nearly Doubled Mortality Risk in the Modern ART Era [published online ahead of print, 2024 Mar 14]. AIDS Res Hum Retroviruses. 2024; doi.org/10.1089/AID.2023.0113

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Results

Virologic Outcomes

- In the full study population, 5,052 (8%) experienced incident HIVAW/low weight
 - This was consistent in the model population
- The predominant core agent class for ART was INSTI (62%)
- 32% were viremic (VL ≥200 copies/mL), of whom 70% achieved suppression (VL <200 copies/mL) and 60% achieved undetectability (VL <50 copies/mL) over follow up

All-cause Mortality

HIVAW/low weight and all-cause mortality in the OPERA® cohort, January 2016 through October 2021*			
	Full Study Population N = 67,119	Model Study Population[†] N = 62,314	
Median follow-up (IQR), mos	44 (26, 65)	45 (27, 65)	
Time-dependent exposure			
Incident HIVAW/low weight, n (%)	5,052 (8)	4,755 (8)	
Censoring events			
Death due to any cause, n (%)	1,421 (2)	1,354 (2)	
Loss to follow-up, n (%)	18,482 (28)	16,358 (26)	
End of study (31OCT2021), n (%)	47,216 (70)	44,602 (72)	
Unadjusted HR (95% CI)	3.14 (2.73, 3.63)	3.10 (2.68, 3.59)	
Adjusted HR (95% CI)	N/A	1.96 (1.68, 2.27)	

Of PWH who experienced incident HIVAW/low weight, 5% (228 of 5,052) died over follow-up vs 2% (1,193 of 62,067) of PWH who had not experienced incident HIVAW/low weight

- The proportion of PWH with complete covariate data who died over follow-up were the same as in the full study population
- Conclusions
- Incident HIVAW/low weight was associated with nearly <u>twice the risk</u> for all-cause mortality compared to remaining free of HIVAW/low weight, when adjusted for time-dependent covariates including viral load measurements and VACS Index scores over follow-up
- Of the 68% of PWH who were virally suppressed, only 7% experienced virologic failure after a median of 16 months (IQR: 8, 26) of follow-up

Strengths of the study

 The OPERA® cohort's database contained prospectively captured, routine clinical data from the electronic health records (EHR) of 140,817 PWH from over 100 clinic locations across 22 US states and territories at the time of this study, representing approximately 13% of people living with diagnosed infection in the US

ART: antiretroviral therapy; CI: confidence interval; HR: hazard ratio; INSTI: integrase strand transfer inhibitor; IQR: interquartile range; OPERA®: Observational Pharmaco-Epidemiology Research & Analysis; PWH: people with HIV; VACS: The Veterans Aging Cohort Study; VL: viral load [†]4,805 (7%) of the full study population were not included in the models due to missing data in the included covariates (age, race, ethnicity, viral load, and VACS Mortality Index score)

Limitations of the study

- The model did not consider other comorbidities (e.g., cardiovascular disease) or their treatments (including HIVAW/low weight treatment)
- The model did not include behaviors that may contribute to the risk of comorbidities and mortality, because these data are not consistently available in the EHR

*Hazard ratios and 95% CI for the association between incident HIVAW/low weight (time-dependent exposure) and all-cause mortality (outcome) were estimated with extended Cox regression models; Incidence rate and 95% CI of the virologic outcomes of interest were estimated using univariate Poisson regression; In a separate analysis of the same eligible PWH at baseline, the authors identified a subset who were on ART at the time they experienced incident HIVAW/low weight over follow-up and they were characterized as viremic or suppressed based on viral load.

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