

Understanding HIV-associated wasting (HIVAW) in the modern ART era

Unintentional weight loss with or without an identifiable cause could signal HIVAW, even in people with undetectable HIV^{1,2}

- In contrast to the pre-ART era, HIVAW may also occur among PWH who are virologically suppressed¹
- Prevalence of HIVAW is 3.1% annually, even among those taking ART²

People with HIVAW experience

5X more annual
hospitalizations

2X more emergency
department visits

vs people without HIVAW³

Correlates of HIVAW in the age of modern ART²



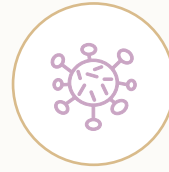
Hospitalization/
ED visit after
HIV diagnosis



Being male



Comorbidities



Opportunistic
infection (OI) or
HIV/AIDS-related
conditions



Older age

Both acute and chronic inflammation in PWH can trigger unintended weight loss and HIVAW, regardless of viral control^{2,4,5}

Acute inflammation caused by OI or other acute illness may lead to unintended weight loss³

- Catabolism and anabolism may become unbalanced, in part due to GH/IGF-1 axis disruption, leading to loss of LBM, unintended weight loss, and reduced physical endurance^{6,7}
- If weight and energy do not improve, HIVAW should be suspected⁸

HIV can lead to a chronic inflammatory state that may contribute to unintended weight loss over time⁵

- As PWH are living longer, they are at higher risk of age-associated comorbidities, including HIVAW^{2,9,10}
- Certain comorbidities, including metabolic and mental health disorders, are more frequent in those with HIVAW²

HIVAW is multifactorial: metabolic changes, endocrine dysfunction, immune dysregulation, and gastrointestinal changes are all contributing factors²

HIV+ patients experiencing unintentional weight loss may be in a catabolic state¹¹

- Lean body mass is broken down for use as energy¹¹
- Dysfunction within multiple body systems contributes to this catabolic state and HIVAW
- **Metabolic changes**
 - PWH have an increased resting energy expenditure (REE), the amount of energy needed to maintain normal body function at rest^{6,12}
 - The impacts of HIV infection on immune and endocrine system dysregulation lead to activation of multiple catabolic pathways, ultimately resulting in LBM loss^{6,13}
- **Endocrine dysfunction**, characterized by disruption of hormone regulation and abnormal hormone levels^{13,14}
 - Endocrine disorders in PWH are associated with chronic inflammation
 - As PWH live longer in the modern ART era, it is important to remember that hormone imbalances may contribute to HIVAW
 - Increased levels of catabolic hormones such as cortisol, and decreased levels of anabolic hormones such as testosterone and IGF-1, may contribute to protein degradation and muscle atrophy in PWH
 - PWH may exhibit resistance to GH, IGF-1, or both. This disruption of the GH/IGF-1 axis is thought to contribute to muscle wasting in PWH
- **Immune dysfunction**
 - Both the innate and adaptive immune systems can become dysfunctional in response to HIV infection. Even with ART-induced viral suppression, latently infected cells remain^{15,16}
 - Dysregulation of cytokine production is a key immunological abnormality associated with HIVAW. Chronic overproduction of pro-inflammatory cytokines such as TNF-alpha can suppress expression and function of the anabolic hormone IGF-1, and can alter muscle protein metabolism¹³
- **GI disorders**
 - The HIV virus, and subsequent inflammatory conditions, can disrupt GI function and structure, and affect the system's ability to absorb nutrients^{17,18}
 - Even while on ART, patients may have persistent HIV-related GI tract dysfunction¹⁷

Timely identification and treatment of HIV-associated wasting (HIVAW) is important to help restore health and potentially reduce mortality risk¹⁹

HIVAW was associated with nearly twice the risk for all-cause mortality compared to those without HIVAW^{19*}

Over nearly 6 years of follow up¹⁹:

5% of PWH who experienced HIVAW died **vs** **2%** who had not experienced HIVAW

Continuous assessment and timely diagnosis of HIVAW can^{3,19}:



Prevent further weight loss



Prevent functional decline



Reduce morbidity and mortality

HIVAW should be top of mind and treatment considered if unintentional weight loss persists and comorbid conditions or other causes of unintentional weight loss have been addressed

*When adjusted for time-dependent covariates, including viral load measurements and VACS Index scores over follow-up (n=1193 of 62,067).

ART=antiretroviral therapy; GH/IGF-1=growth hormone/insulin growth factor-1; LBM=lean body mass; PWH=people with HIV; TNF=tumor necrosis factor; VACS=Veterans Agent Cohort Study.

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