Frailty and Cause-Specific Hospitalization among Aging HIV-Infected and Uninfected Persons

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ABSTRACT

Background: Hospitalization events exact a substantial economic and clinical burden for aging HIV-infected populations. Frailty is a key aging-related syndrome, predictive of major adverse clinical outcomes, including all-cause hospitalization among older HIV-uninfected adults. We have previously reported the association of frailty with advanced HIV and mortality; however, limited data exist on the relationship of frailty to hospitalizations due to infectious or non-infectious causes among HIV-infected persons or their uninfected counterparts.

Methods: Frailty was ascertained in the ALIVE cohort of persons with prior or current injection drug use based on the 5 Fried phenotype criteria. Hospitalization events were ascertained from 2005-2012 and categorized using Agency for Healthcare Research and Quality clinical classification software into: chronic disease, infectious disease, and non-chronic non-infectious conditions. Cox proportional hazards models were used to estimate the risk (hazard ratios [HR] with 95% confidence intervals [CI]) for time to first hospitalization for each category.

Results: Among 1303 participants with a median age of 48 years, 32% were HIV infected, and 12% were frail. In multivariable models adjusting for age, sociodemographics, comorbidity, substance use, and HIV/AIDS status, frailty was significantly associated with chronic disease (aHR 2.03; 95% CI, 1.40, 2.96), and infectious disease (aHR 2.41; 95% CI, 1.54, 3.76) hospitalization; but not with non-chronic non-infectious hospitalization (aHR 1.07; 95% CI, 0.72, 1.59). A prior AIDS diagnosis was associated with increased hospitalization risk in all 3 categories. Among HIV-infected persons, independent of CD4 count, HIV viral load, or prior AIDS, frailty was significantly associated with increased AIDS hospitalization risk (aHR 6.30; 95% CI, 1.20, 33.1). Frailty was also independently associated with non-AIDS infectious disease hospitalization risk (aHR 2.21; 95% CI, 1.40, 3.50).

Conclusion: The frailty phenotype selectively predicts vulnerability to chronic disease and infectious disease related hospitalization, independent of comorbidity, degree of HIV immunosuppression and virologic control. Frail persons are susceptible to increased hospitalization for both AIDS and Non-AIDS infection. Further elucidation of frailty pathways may facilitate targeted interventions to reduce health care utilization and improve clinical management for aging HIV-infected persons and their high risk counterparts.

INTRODUCTION

Persons with a history of injection drug use (PWID) comprise a significant subset of the U.S. population and continue to be at heightened risk for HIV acquisition. Both the HIV and PWID populations have been aging over the last 2 decades. The synergistic interaction between HIV, injection drug use, and age can result in increased mortality, morbidity, and health care utilization.

Early identification of those HIV+ and at risk PWID most vulnerable to adverse clinical outcomes may facilitate interventions to improve health outcomes for this high risk group. Frailty is a key aging-related syndrome of vulnerability found to be associated with increased morbidity and mortality among older HIV-uninfected adults.

We have previously identified a significant relationship of frailty with both HIV and increased mortality risk among PWID. In this study, we sought to determine the relationship of frailty to risk for specific classes of hospitalization events in this population.

METHODS

FRAILTY PHENOTYPE	
Physical shrinking (Weight loss)	≥ 5% body weight loss since prior visit by direct measurement of weight
Low physical activity	"Does your health now limit the kinds or amounts of vigorous activities you can do, like lifting heavy objects, running, or participating in strenuous sports?" Positive : limited a lot
Poor endurance (Exhaustion)	"During the past week, I felt that everything I did was an effort" OR "During the past week, I could not get going" Positive : moderate or most of time
↓ Strength & Power (Weakness)	Grip strength (Jamar dynamometer) Positive : weakest 20% stratified by gender and BMI quartiles
Slow gait	Time to walk 4m at usual pace Positive : slowest 20% by gender and median height
FRAIL	Positive for 3 or more criteria

Comorbid Disease Conditions

- Diabetes
- Hypertension
- Cerebrovascular accident
- Cardiovascular disease
- Renal disease
- Obstructive lung disease
- Obesity
- Malignancy
- Liver disease

AIDS Linked to the Intravenous Experience (ALIVE)

- Prospective observational cohort
- Baltimore, MD
- Community-recruited, followed 'out-of-clinical-care'
- HIV+ and HIV- adults (≥18 yrs) with history of past or current injection drug use
- Semiannual visits

- Study period : 2005 - 2012
- 1303 participants
- Cox proportional hazards models

CHARACTERISTICS OF PWID IN ALIVE

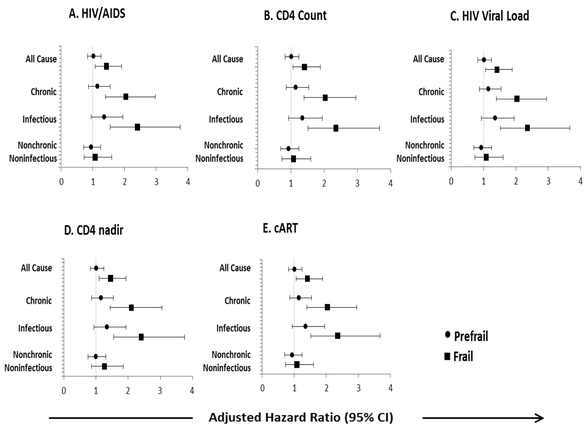
	HIV-	HIV+
n	888	415
Median age (IQR)	48 (42.8, 52.9)	47.9 (43.7, 52.3)
Female	32.9%	35.4%
African American	87.3%	93%
<High school education	55.9%	62.9%
Homeless	15%	13.3%
Alcohol use		
None	43%	53.1%
<Daily	48.9%	39.6%
Daily	8.1%	7.3%
Recent injection drug use	47.9%	33.3%
Prescription drug abuse	13.2%	6.3%
# Comorbid conditions		
0	41.3%	40.4%
1-2	49%	50.8%
≥ 3	9.7%	8.9%
Prior AIDS diagnosis		21%
CD4 cell count, median (IQR)		304 (180, 463)
HIV RNA, median (IQR), $\log_{10}$ copies/ml		2.6 (1.6, 4.4)

FRAILTY AND ALL-CAUSE HOSPITALIZATION

	Adjusted HR (95% CI)†
Alcohol use	
None	Ref
<Daily	1.19 (0.98, 1.45)
Daily	**1.56 (1.13, 2.15)**
Recent injection drug use	**1.29 (1.07, 1.56)**
Prescription drug abuse	**1.59 (1.22, 2.08)**
Marijuana use	**0.62 (0.44, 0.89)**
Homeless	**1.50 (1.18, 1.89)**
# Comorbid conditions	
0	Ref
1-2	**1.33 (1.10, 1.61)**
≥ 3	**2.39 (1.79, 3.21)**
HIV Status	
Negative	Ref
HIV+, no AIDS	**1.34 (1.08, 1.65)**
HIV+, AIDS	**2.77 (2.08, 3.69)**
Frailty Status	
Robust	Ref
Prefrail	1.02 (0.83, 1.26)
Frail	**1.43 (1.07, 1.91)**

†Adjusted for age, gender, race, education

FRAILTY AND CAUSE-SPECIFIC HOSPITALIZATION



†Adjusted for age, gender, race, education, substance use, # comorbid conditions and HIV clinical factors

FRAILTY AND HOSPITALIZATION FOR AIDS AND NON-AIDS INFECTION

	Non-AIDS aHR (95% CI) †	AIDS aHR (95% CI) ¥
HIV Status		
Negative	Ref	
HIV+, no AIDS	**2.82 (2.05, 3.88)**	Ref
HIV+, AIDS	**6.59 (4.42, 9.81)**	**14.2 (5.52, 36.4)**
Frailty Status		
Robust	Ref	Ref
Prefrail	1.34 (0.92, 1.94)	3.85 (0.89, 16.7)
Frail	**2.21 (1.40, 3.50)**	**6.30 (1.20, 33.1)**

†Adjusted for age, gender, race, education, substance use, # comorbid conditions and HIV status
¥ Adjusted for age, gender, race, education and prior AIDS status

SUMMARY

- Frailty is significantly associated with all-cause, chronic disease and infectious disease hospitalization risk
- Frailty is significantly associated with both AIDS and Non-AIDS infectious disease hospitalization risk
- Frailty targeted interventions may mitigate infectious disease and chronic disease related morbidity and healthcare utilization among aging HIV-infected persons

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