



Geriatric Syndromes in Older Adults Living with HIV and Cognitive Impairment

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OBJECTIVES: Nearly half of the population living with human immunodeficiency virus (HIV) in the United States is now older than 50 years with at least 6% over age 65. Between 35% and 50% live with mild to moderate cognitive impairment. Older persons living with HIV (PLWH) also have a substantial burden of HIV-associated non-acquired immunodeficiency syndrome medical conditions and are at risk for frailty, geriatric syndromes, and early mortality compared with HIV-uninfected peers. We sought to define the magnitude of geriatric conditions and multimorbidity in PLWH older than 60 years who are living with symptomatic cognitive impairment. In a subset of participants, we examined associations between these geriatric conditions.

DESIGN: Retrospective cohort study.

SETTING: HIV Elders Study at the University of California, San Francisco, Memory and Aging Center.

PARTICIPANTS: Participants were HIV infected, virally suppressed, 60 years or older, and clinically diagnosed with mild neurocognitive disorder (MND).

MEASUREMENTS: We conducted standardized assessment of geriatric conditions and everyday function and investigated multimorbidity burden using the Veterans Aging Cohort Study (VACS) index.

RESULTS: Among 141 older PLWH with MND, 58% report incontinence, 55% meet criteria for pre-frailty, and a substantial proportion report dependence with instrumental activities of daily living (52%) or activities of daily living (41%). The mean VACS index score is 33 (standard deviation = 14), suggesting a 13.8% 5-year all-cause mortality risk.

CONCLUSIONS: Older PLWH with symptomatic cognitive impairment carry a substantial burden of other geriatric conditions. Our work supports the need for comprehensive geriatric systems of care for cognitively impaired individuals aging with HIV. *J Am Geriatr Soc* 67:1913-1916, 2019.

Key words: HIV; aging; frailty; cognition

Nearly half of the population living with human immunodeficiency virus (HIV) in the United States is now older than 50 years with at least 6% over age 65.^{1,2} People with HIV are living longer due to effective antiretroviral therapy (ART), a trend also seen in resource-limited settings.³ Particularly concerning for older adults with HIV is their increased risk for cognitive impairment. HIV-associated neurocognitive disorder persists in older adults with HIV despite combination ART and is associated with overall morbidity.⁴ It is estimated that between 35% and 50% of older adults living with HIV experience mild to moderate cognitive impairment.⁴

Frailty and geriatric syndromes may occur at a younger age in individuals with HIV than they do in those who are not infected with HIV.⁵ Older persons living with HIV (PLWH) also have a greater burden of comorbidities, termed HIV-associated non-acquired immunodeficiency syndrome medical conditions,⁶ and multimorbidity as measured by the Veterans Aging Cohort Study (VACS) index.⁷ Past work indicates that the VACS index better predicts hospitalization and all-cause mortality than typical severity measures like CD4 T-lymphocyte counts, HIV RNA levels, and age.⁷ One group identified direct correlations between the VACS index and cognitive impairment.⁸

In PLWH or without ART, geriatric conditions, such as decreased instrumental activities of daily living (IADLs) and poor medication adherence, are associated with a higher VACS score.⁹ It is thought that inflammation, particularly monocyte activation, is a key predictor of increased morbidity and all-cause mortality even in the context of viral suppression.^{1,10,11}

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In this study, we sought to define the frequency of geriatric conditions and burden of multimorbidity in adults older than age 60 with virally suppressed HIV and diagnosed with mild neurocognitive disorder (MND). We also investigated multimorbidity burden using the VACS index.

METHODS

Participants

We recruited participants from the HIV Elders Study at the University of California, San Francisco. To meet inclusion into the parent study, participants were HIV infected, virally suppressed (<50 HIV copies/mL), 60 years or older, and clinically diagnosed with MND based on 2007 criteria, as previously described.¹² Similar to a mild cognitive impairment diagnosis in people without HIV infection, people with MND have mild symptoms and remain functionally independent despite performances on cognitive measures that are impaired in two cognitive domains. All were screening for enrollment into an intervention trial testing mindfulness-based stress reduction (MBSR) and thus were also required not to be a current practitioner of MBSR. For this study, individuals with conditions other than HIV potentially contributing to cognitive change were allowed to enroll provided they otherwise were symptomatic and had documented poor neuropsychological testing performance in at least two cognitive domains, and, in the opinion of the investigators, HIV was a likely contributor to the cognitive change. We examined standardized assessment of geriatric conditions and everyday function conducted during the screening visit. All participants were enrolled between March 2013 and August 2017. Using a regional clinical laboratory, we measured current CD4 T-lymphocyte counts, plasma HIV RNA levels, hemoglobin, liver function tests including aspartate aminotransferase (AST) and alanine aminotransferase (ALT), platelet count, creatinine, and hepatitis C serostatus. The VACS index was calculated in standard fashion using age, current CD4 T-lymphocyte count, plasma HIV RNA level, hemoglobin, liver function tests including AST and ALT, platelet count, creatinine level, and hepatitis C coinfection.

Geriatric Syndromes

We identified the presence of geriatric syndromes in participants based on both subjective reports and objective measures. These included self-reported responses to structured questionnaires indicative of conditions common in the aging population regarding falls in the past year, any report of urinary incontinence, mobility, and difficulty and dependence with activities of daily living (ADLs) and IADLs.¹³ Hearing difficulty was determined if the participant was unable to identify whispered numbers or letters in either ear. Vision difficulty was determined if Snellen acuity was worse than 20/40. We defined mild to moderate depression as a Center for Epidemiological Studies Depression (CES-D) scale of 16 or greater. Difficulty with mobility was defined as reporting a struggle walking across a room or two blocks.

Frailty assessment was based on Fried's frailty model that included information on self-reported weight loss, exhaustion, and low physical activity as well as objective measure of grip strength and walking speed.¹⁴ Self-report of exhaustion was based on two items from the CES-D questionnaire, and low

physical activity was based on the Minnesota Leisure score. We measured walking speed, standardized by height and sex, and weakness using grip strength, standardized by sex and body mass index. Frailty was defined as three or more of the criteria just described, and pre-frailty was defined as at least one of the criteria met.

Multimorbidity/VACS Index

We calculated the VACS index in standard fashion using age, current CD4 T-lymphocyte count, plasma HIV RNA level, hemoglobin, liver function tests including AST and ALT, platelet count, creatinine level, and active hepatitis C infection.

Statistical Analysis

Descriptive statistics to characterize the frequency of geriatric conditions included the median and range for continuous variables and frequencies and percentages for categorical data. Statistical significance was defined as $P \leq .05$ for two-sided hypotheses. SPSS v. 25.1 (IBM, Inc., Chicago, IL) was used for all statistical analyses.

RESULTS

A total of 141 participants were enrolled in our study (Table 1). The participant group had a median age of 64 years (range = 60–80 y), were mostly white (91%), and more than half had at least 16 years of education (57%). About half of participants reported living alone (56%). The mean CD4 count was 600 (standard deviation [SD] = 273), the median estimated duration of HIV was 26 years (range = 3–40 y), and the percentage of participants with a CD4 nadir lower than 200 cells was 71% ($n = 100$).

Frequency of Geriatric Conditions

Among participants studied, 58% reported incontinence, 55% reported pre-frailty, and 52% reported IADL difficulties (Figure 1). Frailty was noted in 7%. We found that 32% indicated difficulty with mobility, and 41% reported a fall in the last year. Mild to moderate depression was present in 39%. In the overall cohort, the mean VACS score was 33 with an SD of 14 ($n = 138$).

Table 1. Demographic and Clinical Characteristics of Study Participants

Age, y, median (range)	64 (60–80)
Male, n (%)	128 (91)
White, n (%)	110 (78)
Education ≥ 16 y, n (%)	80 (57)
Lives alone, n (%)	79 (56)
Current CD4, cells/ μ L, mean (SD)	600 (273)
EDI, y, median (range)	26 (3–40)
CD4 nadir <200 (%)	100 (71)

Abbreviations: EDI, estimated duration of infection; SD, standard deviation.

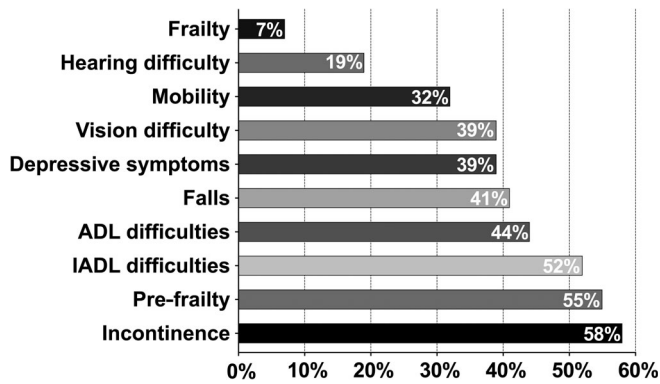


Figure 1. Frequencies of geriatric syndromes among older HIV-infected adults with mild neurocognitive disorder (n = 141). ADL, activity of daily living; IADL, instrumental activity of daily living.

DISCUSSION

Results from this study show that virally suppressed older PLWH with symptomatic cognitive impairment also have a substantial burden of other geriatric conditions, particularly incontinence (58%), pre-frailty (55%), and difficulty with IADLs (52%) and ADLs (41%). The burden of depressive symptoms was also quite high, at 39%, and similar to prior reports.^{15,16} We identified a mean VACS index score of 33, supportive of a higher risk for mortality. Based on prior reports, this score is associated with a 13.8% all-cause 5-year mortality risk.^{17,18} This mortality risk should be considered in the context of our selection with all participants having well-controlled HIV with suppressed HIV RNA in plasma, and most had CD4 counts higher than 200 cells (n = 133/139). The risk in those who are unsuppressed and, particularly those with lower CD4 counts, is expected to be higher.

A little more than half of participants live alone (56%), raising concerns for the availability of social support of older adults with HIV. Older adults with HIV tend to have higher rates of social isolation than younger adults.¹⁹ Social isolation in combination with difficulty with performing ADLs contributes to feelings of social loneliness and was associated with depressive symptoms.²⁰ The combination of cognitive impairment, social isolation, and other geriatric syndromes highlights the substantial vulnerability of this aging group of individuals.

We conducted our study in a convenience sample of individuals with MND enrolling in an MBSR intervention, limiting generalizability of our findings to the broader population living with HIV. Those with MND may already be more vulnerable to adverse clinical outcomes than individuals without cognitive symptoms and those without objective cognitive impairment. A comparison group of HIV-uninfected adults of comparable age and those without cognitive impairment could have provided added clarity to our findings. Because 39% of our participants reported symptoms of depression, we cannot exclude the possibility that depression impacted rates of self-reporting symptoms related to geriatric syndromes.

Geriatric syndromes are useful in assessing the trajectory of patients' physical function and functional status as they age. Assessing geriatric syndromes can predict how patients will respond to environmental stressors and situational challenges.^{13,21} Early and accurate identification of geriatric

syndromes may aid clinicians in focusing resources on assisting the most vulnerable patients.

Our work has important implications for clinicians managing older PLWH who report cognitive symptoms. In the context of well-managed HIV care, these individuals remain vulnerable with a high burden of multimorbidity and geriatric conditions. We add to the literature that geriatric conditions and early functional decline persist in the era of combination ART. In older adults with MND, cognitive symptoms are just a small part of the conditions that would benefit from careful clinical management. Future studies should look more closely at the role that monocyte activation plays in functional decline.

In an era of HIV and aging, multimorbidity, polypharmacy, and functional decline are primary concerns.¹ A geriatrics-focused approach of functional preservation will become increasingly important in caring for older adults with HIV living in the community.⁵ Taken together, an urgent need remains to develop systems of care that better address the holistic needs of older adults living with HIV despite optimal management of HIV itself.

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Conflict of Interest: Victor Valcour has served as a consultant to ViiV Healthcare and Merck on issues related to HIV and aging. Lishomwa C. Ndhlovu has served as an advisory board member to ViiV Healthcare related to ART and HIV.

Author Contributions: Drafted the manuscript: Hosaka and Valcour. Designed the study cohorts and acquisition of participant demographic and clinical data: Valcour and Javandel. Performed data analyses: Hosaka, Premeaux, and Allen. Conceived design of the study and coordinated integration of collaboration between all participating groups: Valcour. Aided in the study design: Javandel, Ndhlovu, and Greene. Critically reviewed and edited final version of the manuscript: All authors.

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