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Frailty and neurocognitive impairment: Impacts on quality of life in HIV

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Abstract

Little is known about the effects of aging-related conditions on health-related quality of life (HRQOL) among people living with HIV (PLWH). The purpose of our study was to examine the independent effects of neurocognitive impairment (NCI) and frailty, and the interactive effects with HIV serostatus on HRQOL. Our sample consisted of 121 adults (63 PLWH and 58 HIV-uninfected), participating in the Multi-Dimensional Successful Aging among HIV-Infected Adults study at the University of California, San Diego. HRQOL was measured via the Medical Outcome Study SF-36 scale. We found that frailty was significantly associated with HRQOL ($p < .001$) in the overall sample and this effect was significantly stronger for PLWH than HIV-uninfected adults. NCI was not significantly associated with HRQOL in our sample. Frailty may be a particularly important factor in HRQOL for PLWH, highlighting the need for prevention and intervention strategies to mitigate the risks for frailty.

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Keywords

co-morbidities; Fried Frailty Index; geriatric syndromes; HIV; neurocognitive disorders; observational study; people living with HIV

The introduction of effective antiretroviral therapy (ART) resulted in a significant reduction in HIV-related deaths and an increase in the longevity of people living with HIV (PLWH). Life expectancy among PLWH is approaching that of demographically comparable HIV-uninfected adults (May et al., 2014). According to projections, approximately 70% of PLWH in the United States will be ages 50 and older by 2020 (Senate Special Committee on Aging, 2013). The status of HIV has thus changed from an almost always fatal disease to a mostly manageable chronic condition (Degroote, Vogelaers, & Vandijck, 2014). Similar to other chronic illnesses, health-related quality of life (HRQOL) has emerged as an important indicator of HIV care and an essential target for HIV-related research (Shrestha et al., 2018; Trepanier et al., 2005).

HRQOL is a multi-dimensional measure of subjective overall health and wellbeing that includes physical, mental, and social aspects of everyday function (Mulasso, Roppolo, & Rabaglietti, 2014; Nguyen, McNeil, Han, & Rhodes, 2018; Trepanier et al., 2005). Research has shown that HRQOL in PLWH can be affected by many psychosocial, sociodemographic, and biomedical factors (Degroote et al., 2014). Studies have consistently found that higher socio-economic status, increased social support, physical activity, and better nutrition and virologic status are associated with improved HRQOL in PLWH (Degroote et al., 2014; Shrestha et al., 2018). Conversely, stigma and discrimination, smoking, drug use, and the presence of co-morbidities, such as depression, and HIV-related symptoms have been found to decrease HRQOL (Degroote et al, 2014; Nguyen et al., 2018).

The presence of co-morbidities is one of the important factors that may affect HRQOL in PLWH. Compared to HIV-uninfected adults, PLWH experience higher prevalence and earlier onset of chronic illnesses and age-related conditions, including neurocognitive impairment (NCI) and frailty (Desquilbet et al., 2007; Sacktor et al., 2007). To date, research has focused on negative associations between an overall co-morbidity burden and HRQOL, but less is known about the independent effects of NCI and frailty (Degroote et al., 2014; Trepanier et al., 2005).

NCI continues to be prevalent even in the era of combination ART (Heaton et al., 2010). The co-occurrence of HIV and aging appears to have additive or synergistic negative effects on the central nervous system, with existing research observing elevated rates of NCI in older cohorts of PLWH compared to cohorts of younger PLWH and older HIV-uninfected persons (Sacktor et al., 2007). Approximately half of PLWH have NCI (Heaton et al., 2010), which has been linked to adverse functional outcomes, such as poor medication management and adherence (Ettenhofer, Foley, Castellon, & Hinkin, 2010). NCI may negatively affect HRQOL by contributing to difficulties in everyday function, such as remembering names, concentrating, or finding solutions to a problem (Degroote et al., 2014). NCI has been associated with poorer HRQOL in PLWH and HIV-uninfected adults (Constantinidou, Prokopiou, Nikou, & Papacostas, 2015; Shrestha, Weikum, Copenhaver, & Altice, 2017).

However, it is unknown whether this association differs by HIV status and whether the effects of NCI on HRQOL are independent of other age-related conditions that commonly co-occur with NCI, including frailty (Erlandson et al., 2019).

Frailty is a state of physiologic vulnerability that, in the presence of internal or external stressors, puts an individual at increased risk of adverse clinical outcomes, such as falls, hospitalizations, institutionalization, disability, and mortality (Gustafson et al., 2016). Following Fried et al. (2001), we further defined frailty as a phenotype marked by multisystem and energy dysregulation, and consisting of a constellation of five possible components: unintentional weight loss, slow walking speed, exhaustion, weakness, and low physical activity. Compared to HIV-uninfected adults, PLWH experience earlier onset and higher prevalence of a frailty-related phenotype (Bloch, 2018; Desquilbet et al., 2007). Both cross-sectional and longitudinal studies conducted among community-dwelling older adults in several European countries have suggested that frailty significantly reduces HRQOL, especially via decreased endurance and energy (Kojima et al., 2016; Mulasso et al., 2014). However, it is unclear whether these finding can be generalized to PLWH and whether the association between frailty and HRQOL differs by HIV status. The relationship between frailty and HRQOL in PLWH has not been well explored, although a recent study found that frailty was associated with a poorer physical dimension of HRQOL (Blanco et al., 2019). It is possible that frailty may reduce HRQOL in PLWH via increased falls, co-morbidity (e.g., cardiovascular disease, kidney disease, osteoporosis) and pain, and poorer function and self-care (Bloch, 2018). Furthermore, we are not aware of any studies that investigated the effects of both frailty and NCI on HRQOL in the same model, although recent research found associations between frailty and NCI in PLWH (Ding et al., 2017; Oppenheim et al., 2018; Zamudio-Rodriguez et al., 2018) and their joint effects on health outcomes (Erlandson et al., 2019).

The aim of our study was to examine the independent effects of NCI and frailty and their interactive effects with HIV serostatus on HRQOL, controlling for biomedical and sociodemographic factors. Similar to other studies (Lin et al., 2011; Mulasso et al., 2014), HRQOL is measured by the Mental Component Summary (MCS) and the Physical Component Summary (PCS) of the Medical Outcome Study 36-item Short Form Health Survey (MOS SF-36; Ware & Sherbourne, 1992). We hypothesized that both NCI and frailty would be independently and negatively associated with HRQOL, and these associations would be stronger for PLWH compared to HIV-uninfected adults.

Methods

Study Sample

Our sample came from baseline data collected in 2013–2016 by the Multi-Dimensional Successful Aging among HIV Infected Adults study at the University of California, San Diego. The study recruited PLWH and HIV-uninfected adults 35 to 65 years of age, fluent in English, and willing and able to provide informed consent. The University of California, San Diego Institutional Review Board approved the study; participants were provided written informed consent and compensated $90 for participation. Participants with unknown HIV status were tested on the day of their visit with Miriad rapid HBc/HIV/Hepatitis C virus

(HCV) antibody test (MedMira Inc, Halifax, Canada). No participants who reported being HIV-uninfected were found to have HIV or HCV. Exclusion criteria for the parent study were: (a) history of a psychotic disorder or a mood disorder with psychotic features; (b) presence of a neurological condition not related to HIV infection and known to affect cognitive functioning, such as Alzheimer's disease, stroke, or traumatic brain injury; and (c) a positive urine toxicology test for drugs of abuse, except for marijuana, at the baseline visit. Details of our study were described by an earlier publication (Moore et al., 2017). Inclusion criteria for our analyses were having baseline data available on the main variables of interest: HRQOL, NCI, and Fried Frailty Index. Our analytic sample included 121 participants, 63 PLWH and 58 HIV-uninfected adults with an average age of 50.4 (SD = 8.3).

Measures

Quality of life.—The primary outcomes for our study were the PCS and MCS components of the MOS SF-36 (Ware & Sherbourne, 1992), which was similar to previous research (Lin et al., 2011; Mulasso et al., 2014). The MOS SF-36 has high levels of reliability and validity as a measure of HRQOL in PLWH (Cooper, Clatworthy, Harding, & Whetham, 2017). It is a short questionnaire comprised of 36 self-report questions, which can be grouped into two composite scales: PCS and MCS (Ware & Sherbourne, 1992). PCS summarizes the physical component of the SF-36 and includes measures of physical function (10 items), physical role limitations (4 items), bodily pain (2 items), and general health perceptions (6 items). MCS summarizes mental components of the SF-36 and includes measures of energy and fatigue (4 items), social function (2 items), emotional role limitations (3 items), and emotional well-being (5 items). For each item, scores were linearly transformed to a scale from 0 to 100, with higher scores indicating better outcomes.

Neuropsychological evaluation.—Neurocognitive performance was assessed through a comprehensive standardized battery of tests with strong psychometric properties that have been widely used in clinical and research settings and measure seven domains of cognition, including motor skills, executive function, attention/working memory, episodic learning, episodic memory, verbal fluency, and information processing speed. Motor skills were assessed by the Grooved Pegboard Dominant and Non-dominant Hand tests (Kløve, 1963). Executive function was assessed by the Trail Making Test Part B (Army Individual Test Battery, 1944) and the Stroop Color and Word Test (Golden, 1974) interference score. Attention/working memory was assessed by the Paced Auditory Serial Addition Task (Gronwall, 1977), and the Wechsler Adult Intelligence Scale – 3rd edition (WAIS-III; Wechsler, 1997) Letter-Number Sequencing. Episodic learning was assessed by the Total Learning scores of the Hopkins Verbal Learning Test-Revised (HVLT-R; Brandt & Benedict, 2001) and the Brief Visuospatial Memory Test-Revised (BVMT-R; Benedict, 1997). Episodic memory was assessed by the Delayed Recall scores of the HVLT-R (Brandt & Benedict, 2001) and the BVMT-R (Benedict, 1997). Verbal Fluency was assessed by the Letter and Category Fluency tests (Borkowski, Benton, & Spreen, 1967). Information processing speed was assessed by the WAIS-III Digit Symbol and Symbol Search, the Trail Making Test Part A (Army Individual Test Battery, 1944), and the Stroop Color and Word Test (Golden, 1974) color score. Raw test scores were transformed into T-scores adjusted for

age, education, gender, and race (Heaton, Miller, Taylor, & Grant, 2004). *T*-scores for each test were then converted to deficit scores, ranging from 0 (*T*-score > 40, no impairment) to 5 (*T*-score < 20, severe impairment). Deficit scores from each test were averaged to obtain a Global Deficit Score (GDS). NCI was defined as a global deficit score of at least 0.5.

Frailty.—Frailty was assessed using the Fried Frailty Index (FFI), a well-validated measure that defined frailty as a phenotype based on the following criteria: unintentional weight loss, low physical activity, exhaustion, weakness, and slow walking speed (Fried et al., 2001). FFI is the most commonly used measure of frailty for PLWH (Greene, Justice, & Covinsky, 2017). According to the FFI, individuals are usually classified as "robust" when none of the above five criteria are present, "prefrail" when one or two of the criteria are present, and "frail" when at least three criteria are present. Similar to other studies, physical exhaustion, unintended weight loss, and physical activity were assessed via self-report, whereas weakness was measured by a grip strength test via a dynamometer and slow walking speed in a 15-foot timed walk (Gustafson et al., 2016). Because our sample was relatively young, with an average age of 50 years, only 8% of participants had three or more FFI criteria; 30% had one criterion and 12% had two criteria. Therefore, for the purposes of our analyses, we combined the frail and prefrail categories, defining frailty as an FFI of at least 1.

Covariates.—As potential biomedical covariates, we considered several co-morbidities found by research to be associated with HRQOL. We included dichotomous measures of HCV (determined by a blood test) and self-reported current smoking. For psychiatric co-morbidity, we considered lifetime history of major depressive disorder and substance use disorders, as well as current substance use diagnoses, measured using the Composite International Diagnostic Interview, which is an interviewer-administered, computer-assisted, fully structured clinical interview based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (Andrews & Peters, 1998). Current clinically depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale (Radloff, 1977). HIV disease characteristics included current CD4+ T cell count and plasma viral load, which were assessed via the blood draw; history of an AIDS diagnosis, estimated duration of HIV infection, nadir CD4+ T cell count, and ART use status were based on medical records abstraction or, when unavailable, self-reports. Last, the following sociodemographic variables were considered as potential covariates: age, gender, race/ethnicity, completed years of formal education, and estimated premorbid function/quality of education, as measured by the Wide Range Achievement Test - 4th Edition Reading score (Wilkinson & Robertson, 2006).

Data Analysis

All statistical analyses were performed using Stata 14 software. Descriptive statistics were computed and the differences between the HIV serostatus groups were assessed using independent *t*-tests for continuous and chi-square tests for the categorical variables. We used unadjusted bivariate linear regression analyses to identify covariates for multivariable models. These analyses were run separately for PCS and MCS outcomes and included as an independent variable of each potential covariate listed in the previous section. Those covariates, significant at the level $p \leq .10$ were subsequently included in the multivariable

models. The $p \leq .10$ was used only in unadjusted bivariate models to identify potentially relevant covariates. In all following multiple linear regression models, the critical alpha was set at $p < .05$.

Multiple linear regression models were fitted to evaluate the main effects of NCI and frailty and their interactive effects with HIV serostatus on continuous measures of HRQOL. For each of the two HRQOL outcomes, we first fitted a model with NCI, frailty, HIV status, and covariates. We secondly assessed a model with two interaction terms, NCI X HIV status and frailty X HIV status, in addition to the variables included in the first model. We performed a likelihood ratio test to assess overall improvement in the model fit by including the interaction terms. Next, we conducted postestimation analyses. Postestimation diagnostics uncovered the presence of heteroscedasticity and an influential outlier. After examination of the influential observation by a senior research team member who was familiar with the details of data collection, it was concluded that the influential observation was due to a data collection error. We therefore reran the analyses without the influential observation and using robust standard errors to correct for heteroscedasticity. As the last step, differences in the effects of frailty and NCI by HIV status were further examined via HIV-stratified analyses.

Results

The demographic and disease characteristics of our sample by HIV status are presented in Table 1. There were no significant differences by HIV status in age or gender. However, PLWH had significantly fewer years of education and a lower proportion of non-Hispanic Whites. Compared to HIV-uninfected participants, a significantly higher proportion of PLWH had NCI, frailty, depressive symptomatology, and met criteria for a lifetime substance abuse or dependence diagnosis. PLWH also had greater rates of current smoking and HCV and lower scores on both PCS and MCS components of HRQOL. Nearly 60% of PLWH reported a history of AIDS diagnosis, and most were on ART and virally suppressed.

Results for PCS Outcome

Linear regression analyses showed a significant negative effect of frailty (B = −17.9, $p < .001$), such that frail participants had poorer PCS outcomes than robust participants, and no effect of NCI on PCS scores (Model 1 in Table 2). In this intercept-only model, there were significant group differences by HIV status so that the predicted value of PCS was approximately 11 scale points lower for PLWH versus HIV-uninfected participants (B = −11.1, $p = .004$). Model 2, which included interactive terms of NCI and frailty with HIV status, was significant (F = 14.6, $p < .0001$) and explained 44.1% of variance in PCS scores. The likelihood ratio test indicated that Model 2 had a better fit than Model 1 ($\chi^2(1) = 7.7$, $p = .01$). While the interactive term for NCI and HIV was not significant ($p = .69$), there was a significant HIV by frailty interaction (B = −23.5, $p = .002$) so that PCS scores were lower in PLWH who were frail as compared to all other groups (Figure 1). In HIV-stratified analyses, NCI had no significant effects while frailty had a negative effect on PCS scores in PLWH (B = −29.8, $p < .001$), but not for HIV-uninfected participants ($p = .20$). All of the models with the PCS outcome were adjusted for participant ages and depressive symptomatology; a

stratified model within the PLWH subsample included nadir CD4+ T cell count as an additional covariate.

Results for MCS Outcome

Similar results were obtained for the MCS outcome. Model 3 (Table 2) showed no effects of NCI but a significant negative effect of frailty. In this model, frail participants had significantly lower MCS scores than robust counterparts ($p < .001$). HIV infection also had a significant negative effect on MCS (B = −7.7, $p = .01$). Model 4, which included interactive terms of NCI and frailty with HIV status, was significant (F = 13.1, $p < .0001$) and explained 50.3% of variance in MCS scores; it also provided a better fit than Model 3 as indicated by the likelihood ratio test ($\chi^2(1) = 5.5$, $p = .02$). The interaction of frailty and HIV was significant (B = −15.1, $p = .01$) but the interaction of HIV and NCI was not ($p = .63$). As displayed in Figure 2, the frailty by HIV interaction was driven by lower MCS scores in PLWH who are frail compared to all other groups. In HIV-stratified analyses, NCI was not associated with MCS, while frailty had a significant negative effect on MCS scores in PLWH (B = −17.8, $p < .001$) but not for HIV-uninfected participants ($p = .3$). All of the models with the MCS outcome were adjusted for participant verbal IQ (WRAT) and depressive symptomatology; a stratified model in the PLWH subsample included nadir CD4+ T cell count as an additional covariate.

Discussion

In the context of aging PLWH, both frailty and NCI become increasing concerns due to higher prevalence and earlier occurrence than in the general population and the link to various adverse health outcomes (Desquilbet et al., 2007; Erlandson et al, 2019; Sacktor et al., 2007). Ours was among the first studies to examine the effects of frailty and NCI on HRQOL in PLWH. Our multivariate analyses showed that, when included in the same model with NCI, frailty significantly reduced both PCS and MCS scores and these results differed by HIV status in such a way that frailty had a negative effect on HRQOL outcomes for PLWH but not for HIV-uninfected persons. In contrast, NCI was not significantly associated with HRQOL for PLWH or HIV-uninfected adults. Given that as many as 50% of PLWH who are 50 or older may suffer from frailty (Bloch, 2018), the link between frailty and reduced HRQOL deserves serious consideration.

We contribute to an understanding of the effect of frailty on HRQOL. Although similar research has existed for those without HIV (Kojima et al., 2016; Mulasso et al., 2014), along with Blanco et al. (2019) ours is among the first attempts to assess the relationships between frailty and HRQOL in PLWH. Our HIV-stratified analyses showed that frailty reduced HRQOL for PLWH but not for HIV-uninfected adults. These findings should be interpreted within the context of the relatively young age of the participants in our sample. Within our 35 to 65 age sample, only 8% of participants met three or more FFI criteria (frail), whereas 42% met one or two criteria (prefrail). This suggested that, especially at its early stages, prefrailty and frailty have more debilitating effects on PLWH compared to HIV-uninfected adults. It is possible that, for PLWH, frailty not only has an earlier onset and higher prevalence compared to those without HIV, but also has symptoms (e.g., slow walking

speed, weakness, exhaustion, low physical activity, unintended weight loss) that may be stronger and more pronounced resulting in poorer daily function, decreased mobility, less access to employment and health care, and, thus, poorer quality of life. Future qualitative research is needed to examine the comparative experiences of prefrailty and frailty in those with and without HIV.

Alternative explanations should also be considered. It is possible that the weaker association between frailty and HRQOL in HIV-uninfected adults can be explained by low prevalence of frailty in our group ($n = 19$). Given this low prevalence, our sample may not have been powered to detect significant effects in HIV-uninfected adults. It will be important to conduct additional research using larger samples of PLWH and HIV-uninfected adults. Another alternate explanation concerns more general associations between frailty and PCS scores. It is possible to argue that these associations could be explained by the fact that these measures are somewhat similar, both assessing physical dimensions of aging. As a counterargument, however, we should note that FFI and PCS tap into different aspects of physical function. Whereas PCS measures the extent to which physical health and pain interfere with performance of work or tasks of daily life (e.g., lifting or carrying groceries), frailty assesses physiologic vulnerability to stressors. Thus, someone who exhibits weak grip strength and unexpected weight loss will have increased risk of adverse health outcomes, such as falls, but may be well capable of carrying groceries and experiencing few limitations in daily activities. Even individuals who meet multiple frailty criteria may still be able to perform most tasks of daily life and have adequate HRQOL due to the development of compensatory strategies. We thus believe that it is meaningful to consider relationships between PCS and FFI as we did in this study. It should also be noted that (a) both MOS SF-36 and FFI are validated measures of HRQOL and frailty widely used by researchers, and (b) published studies about the general population employed precisely these measures (FFI and PCS subscale of MOS-36) to examine the effects of frailty on the physical health dimension of HRQOL (Lin et al., 2011; Mulasso et al., 2014). This being said, it will be a task of future research to use alternate operationalizations of frailty and the physical health dimension of HRQOL.

We did not find significant associations between NCI and HRQOL, either in the combined sample or among PLWH. To date, few studies have examined the relationship between these variables in the presence of HIV infection (Benedict, Mezhir, Walsh, & Hewitt, 2000; Doyle, Weber, Atkinson, Grant, & Woods, 2012; Kaplan et al., 1995; Osowiecki et al., 2000; Shrestha et al., 2017; Tozzi et al., 2003; Trepanier et al., 2005). While four of these studies found negative associations between NCI and HRQOL (Kaplan et al., 1995; Osowiecki et al., 2000; Shrestha et al., 2017; Tozzi et al., 2003), Benedict et al. (2000) found no association, Trepanier et al. (2005) found a negative association of NCI with physical but not with mental health, and Doyle et al. (2012) found significant associations in the younger but not in the older PLWH. Additionally, two of these studies found that the relationship between NCI and HRQOL may have been mediated or moderated by depression (Shrestha et al., 2017; Trepanier et al., 2005). It should also be noted that the studies used widely varying measures for HRQOL as well as NCI. For example, HRQOL was measured by MOS HIV (Tozzi et al., 2003; Trepanier et al., 2005), Sickness Impact Profile (Benedict et al., 2000), Quality of Well-Being (Kaplan et al., 1995), MQOL-HIV (Osowiecki et al., 2000), and MOS

SF-36 (Doyle et al., 2012; Shrestha et al., 2017) scales; NCI was assessed by Memory for Intentions Screening Test (Doyle et al., 2012), Brief Inventory of Neurocognitive Impairment (Shrestha et al., 2017), or various neuropsychological test batteries, which included different numbers and specific types of tests (Osowiecki et al., 2000; Tozzi et al., 2003; Trepanier et al., 2005).

Among the studies of HRQOL uncovered by our search, only two used MOS SF-36 outcomes but they measured neurocognitive performance by the Memory for Intentions Screening Test (Doyle et al., 2012) and the Brief Inventory of Neurocognitive Impairment (Shrestha et al., 2017) and had nuanced findings. Doyle et al. (2012) found that deficits in prospective memory were associated with decreased MCS and PCS scores in the younger (≤ 40 years) but not in the older (≥ 50 years) PLWH. Doyle et al. (2012) hypothesized that these age-related differences could be explained by compensatory strategies used by older adults in their daily lives to overcome the negative effects of NCI. Similarly, Shrestha et al. (2017) found a negative association between the NCI and SF-36 summary score in a relatively young population (mean age 38.9 ± 6.8) of incarcerated, opioid dependent, HIV-infected Malaysian men. Perhaps not incidentally, two other studies that found associations between NCI and HRQOL also had mean participant ages in their samples younger than 40 years: Tozzi et al. (2003; mean age = 36.8, range = 20–58) and Osowiecki et al. (2000; mean age = 37.9 ± 6.7).

Our overview suggests complexity in the relationship between the NCI and HRQOL, which may be mediated by other factors and vary depending on specific age group. Although participants in our sample were relatively young, the mean age of 50.4 was considerably higher than that of participants in other studies (Osowiecki et al., 2000; Shrestha et al., 2017; Tozzi et al., 2003) and was closer to the older age group in the study by Doyle et al. (2012). Thus, the lack of association between the NCI and HRQOL in our study was consistent with the findings of Doyle et al. (2012) as applied to the 50 and older age group.

In the light of our significant findings for frailty, we suggest that the effects of age-related co-morbidities in older PLWH (> 40 years) on HRQOL may overshadow those of NCI. Additionally, younger PLWH who are in the prime of employment may feel the effects of NCI more strongly in effects on work performance, whereas older PLWH may experience fewer work-related effects and be more likely to use compensatory strategies. The lack of a direct relationship between NCI and HRQOL may also be a result of mediation or moderation by other factors, such as depression (Shrestha et al., 2017; Trepanier et al., 2005). Clearly, more studies with standardized measures of NCI and HRQOL and in different age groups and varying PLWH subpopulations are needed to unpack the complex relationships between these variables.

Limitations

While our study had a well-characterized sample and robust standardized assessments of key variables, it had several limitations. Not unlike other research on HRQOL in PLWH (Benedict et al., 2000; Osowiecki et al., 2000; Trepanier et al., 2005), our study had a relatively small sample size, which may have reduced its power to detect significant effects. Additionally, several HIV-disease characteristics (i.e., history of AIDS diagnosis, estimated

duration of HIV infection, nadir CD4+ T cell count, ART use status) were based on self-reports in those cases where medical records were not available. Given the cross-sectional nature of our analyses, we also cannot make conclusions about the temporal relationships between frailty and HRQOL. However, existing longitudinal research in those without HIV (Kojima et al., 2016) suggested that development of frailty precedes the worsening of quality of life. Lastly, the sample for our study was predominantly non-Hispanic White (54.6%), male (78.5%), relatively young (Mean age = 50.4), and consisted of participants residing in the metro San Diego area. Our findings, thus, cannot be generalized to other subpopulations of PLWH, such as women, racial and ethnic minorities, rural populations, or adults greater than 65 years of age. Longitudinal research will be needed to explore the relationships between the NCI, frailty, and HRQOL, using large cohort studies of PLWH.

Conclusion

Our results suggest that frailty may be a particularly important factor in HRQOL in PLWH and highlight the need for early screening for prefrailty and frailty. Prevention strategies and interventions aimed at mitigating or reversing frailty may be key to improving HRQOL. Targeting instrumental activities of daily living, physical health, medication adherence, lifestyle, and co-morbidities may further improve HRQOL in PLWH and should be addressed by health care practitioners. Identifying and treating the synergistic effects of HIV and aging is necessary to help PLWH improve their quality of life.

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Key Considerations

- In the context of aging in PLWH, frailty is an important concern.
- Prefrailty and frailty are common in PLWH and have earlier onset than in HIV-uninfected adults; even middle-age PLWH are at risk of frailty development.
- In PLWH, frailty and prefrailty may have negative effects on health-related quality of life.
- Clinicians should screen PLWH for (pre)frailty as early as middle age; if diagnosed, frailty should be effectively managed.

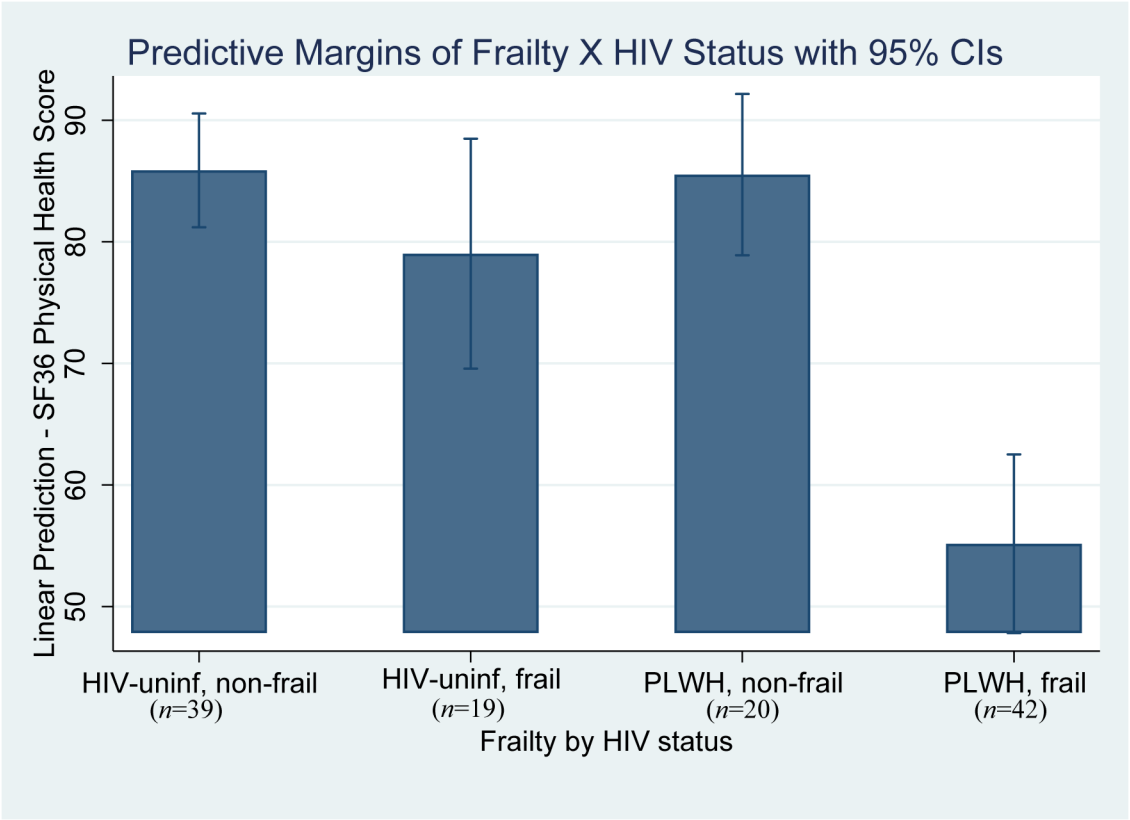

Figure 1.

Significant interaction frailty X HIV status for Physical Component Summary outcome.

Note. CI = confidence interval; SF36 = Medical Outcome Study 36-item Short Form Health Survey; HIV-uninf = HIV-uninfected; PLWH = people living with HIV.

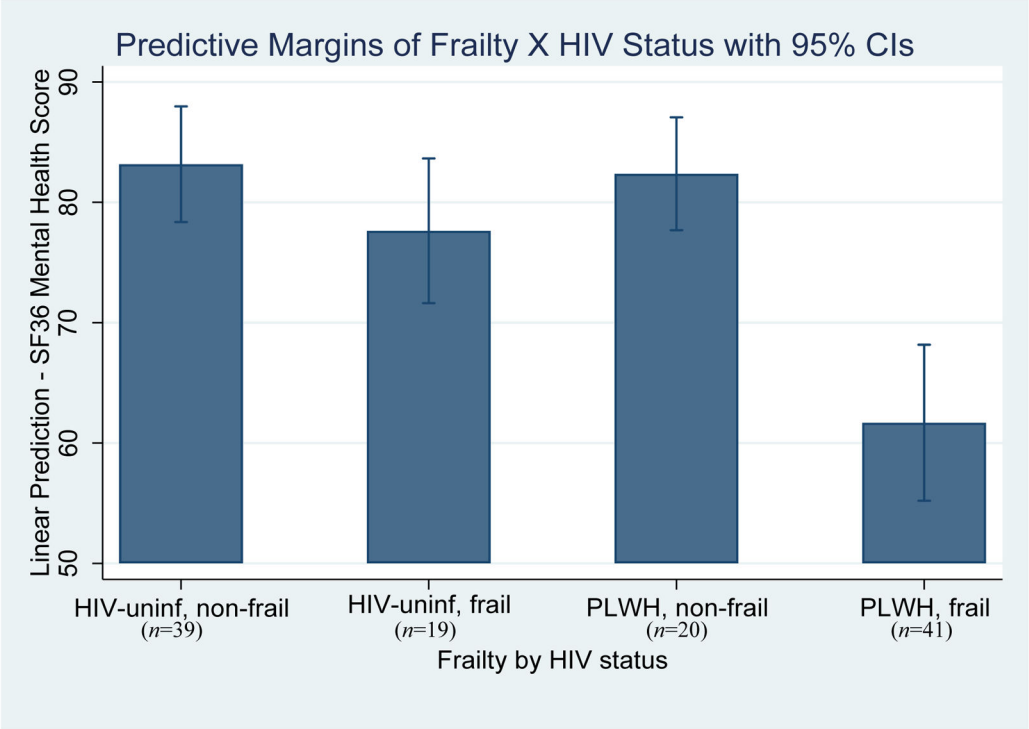

Figure 2.

Significant interaction frailty X HIV status for the Mental Component Summary outcome.

Note. CI = confidence interval; SF36 = Medical Outcome Study 36-item Short Form Health Survey; HIV-uninf = HIV-uninfected; PLWH = people living with HIV.

Table 1

Sample Characteristics by HIV Status

	PLWH (*N* = 63) *N* (%) or *M (SD)*	HIV-uninfected (*N* = 58) *N* (%) or *M (SD)*	*p* value
Demographic & psychosocial characteristics			
Age	50.1 (9.0)	50.7 (7.6)	0.72
Gender, male	47 (74.6%)	48 (82.8%)	0.23
Race, White	27 (42.9%)	39 (67.2%)	0.01
Education, years	13.7 (2.4)	15.2 (2.1)	0.001
Verbal IQ (WRAT) score	101.5 (15.1)	105.0 (11.8)	0.16
Health-related quality of life			
SF-36 Physical Component Summary	62.9 (27.7)	85.0 (17.5)	< 0.001
SF-36 Mental Component Summary	66.1 (24.8)	83.3 (14.4)	< 0.001
Frailty & neurocognitive impairment			
Neurocognitive impairment	26 (41.3%)	14 (24.1%)	0.05
Frail (FFI ≥ 1)	42 (66.7%)	19 (32.8%)	< 0.001
Co-morbidities			
Depressive symptomatology (CES-D ≥ 16)	37 (58.7%)	16 (28.1%)	0.001
Lifetime major depressive disorder	34 (55.7%)	12 (21.4%)	< 0.001
Lifetime any substance use disorder	40 (64.5%)	21 (37.5%)	0.003
Currently smoking	23 (36.5%)	7 (12.1%)	0.002
Hepatitis C infection	11 (17.5%)	0	0.001
HIV disease characteristics			
Nadir CD4+ T cell count, median [IQR]	189.0 [36, 300]		
Current CD4+ T cell count, median [IQR]	640.5 [466.5, 857.5]		
Undetectable plasma viral load	41 (69.5%)		
Estimated duration of HIV disease, years	17.4 (8.2)		
AIDS diagnosis	37 (58.7%)		
ARV status			
ARV Naïve	2 (3.2%)		
ARV use	60 (95.2%)		
No-ARV	1 (1.6%)		

Note. IQ = Intelligence Quotient; WRAT = Wide Range Achievement Test; SF-36 = Medical Outcome Study 36-item Short Form Health Survey; FFI = Fried Frailty Index; CES-D = Center for Epidemiologic Studies Depression Scale; IQR = interquartile range; ARV = antiretroviral medications.

Table 2

Results of Multivariable Linear Regression Analyses Modeling the Independent Effects of NCI and Frailty and Their Interactive Effects With HIV Serostatus on MCS and PCS Scores

	Model *N*	HIV serostatus		Frailty (prefrail and frail vs. robust)		NCI (yes vs. no)		Frailty X HIV serostatus		NCI X HIV serostatus	
		B (SE)	*p* value	*B (SE)*	*p* value	*B (SE)*	*p* value	*B (SE)*	*p* value	*B (SE)*	*p* value
Physical Health[1] Summary Score											
Model 1	120	−11.1 (3.8)	0.004	−17.9 (3.8)	< .001	−6.7 (4.3)	0.12	-	-	-	-
Model 2	120	−1.3 (4.5)	0.77	−6.9 (5.2)	0.19	−7.7 (5.4)	0.16	−23.5 (7.5)	0.002	3.3 (8.3)	0.69
PLWH only[2]	61	-	-	−29.8 (5.8)	< .001	−4.8 (6.2)	0.44	-	-	-	-
HIV-uninfected only	58	-	-	−6.7 (5.2)	0.2	−8.0 (5.5)	0.15	-	-	-	-
Mental Health[3] Summary Score											
Model 3	119	−7.7 (2.8)	0.01	−12.6 (2.9)	< .001	−4.0 (3.6)	0.27	-	-	-	-
Model 4	119	−1.7 (3.9)	0.67	−5.6 (3.9)	0.15	−4.7 (3.9)	0.23	−15.1 (5.8)	0.01	2.9 (6.0)	0.63
PLWH only[2]	60	-	-	−17.8 (4.7)	< .001	−2.9 (5.5)	0.6	-	-	-	-
HIV-uninfected only	58	-	-	−4.5 (4.3)	0.31	−1.9 (4.1)	0.65	-	-	-	-

Note. NCI = neurocognitive impairment; MCS = Mental Component Summary; PCS = Physical Component Summary; B = unstandardized regression coefficient; SE = standard error; PLWH = people living with HIV; WRAT = Wide Range Achievement Test; IQ = intelligence quotient.

[1]The analyses were adjusted for participant ages and depressive symptomatology.

[2]The analyses of the subsample of PLWH included nadir CD4+ T cell count as an additional covariate.

[3]The analyses were adjusted for participant verbal IQs (WRAT) and depressive symptomatology.