EDITORIAL COMMENT

Frailty and cognition in older people with HIV: recognizing the importance of geriatric syndromes

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The widespread use of increasingly effective combination antiretroviral therapy (cART) since 1996 has led to the long-term survival of people with HIV (PWH) [1,2] which now approximates that of unexposed individuals. This, in concert with other factors, has resulted in an aging population of PWH. Most PWH in high-income countries are now over 50 years, and it is not uncommon to see stable older PWH (OPWH) over 70 years. Similar trends have occurred in low to middle income countries [3]. This positive outcome has however been associated with the earlier onset of several age-related comorbidities [4]. Importantly, there has also been an increase in disorders referred to as geriatric syndromes [5]. In contrast to single organ or system-based comorbidities (e.g. cardiometabolic, bone, renal, non-AIDS related malignancies) geriatric syndromes do not easily fit into discrete disease categories, have multifactorial etiologies, involve multiple organ systems, and may occur concurrently. These commonly include frailty, polypharmacy, falls and dysmobility, sarcopenia, and cognitive changes, among others [6]. The association between frailty and cognitive impairment in particular has been studied both in the general population and more recently among people aging with HIV [5,7]. In this population, both conditions are increasingly recognized and contribute to impaired health span and reduced survival [8]. Thus studies assessing these conditions carefully are to be welcomed as they provide important perspectives which may help the management of this vulnerable population.

The study by Makinson *et al*. [9] from the French ANRS EP66 SEPTAVIH Cohort, assessed cognitive impairment and frailty in a large group of effectively treated, mostly male, native French born PWH older than 70 years. Frailty was assessed using the Fried Frailty Phenotype (FP) metric, categorized as frail, prefrail, and nonfrail or robust [10]. Over 75% of this cohort were either frail or prefrail. Although there was no HIV-unexposed control group, this prevalence of being nonrobust among OPWH of this age is similar to that seen in the general population of the same age [11,12], with frailty defined either by the FP metric, or the also commonly used Frailty Index [13]. Being frail, regardless of the metric used to make the diagnosis, is associated with adverse outcomes, including increased overall mortality [14]. The more common state of prefrailty, defined by the FP model, is also associated with negative health effects [15].

Cognitive impairment was diagnosed using the reliable Montreal Cognitive Assessment. The prevalence of cognitive impairment, diagnosed by a MoCA score <26, or <23, was 58.5% and 36%, respectively. Those with a MoCA score <26 had an significant adjusted odds ratio (OR) of 1.80 of being frail or prefrail, suggesting a higher risk compared to OPWH without cognitive impairment. A more stringent MoCA score <23 revealed an adjusted OR of 2.75. Other risk factors that independently associated with a MoCA score <26 included older age, birth outside of France, lower education level, and being diabetic. Less formal education and cardiometabolic conditions are recognized risk factors for cognitive decline [16,17].

This study has several important clinical implications. Firstly, frailty and cognitive impairment often occur

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together in OPWH. The diagnosis of either condition should prompt assessment for the other. However, the ongoing challenge of diagnosing frailty is the lack of consensus on which single, simple, and reliable metric can easily be used in a busy clinical setting. Indeed many different metrics are used to measure frailty in the general population, several of which have been studied in PWH [8,18]. A particularly unique aspect of this analysis is that it addresses the conditions of frailty and cognitive impairment in a truly geriatric population of OPWH over 70 years old. Previous studies have assessed younger 'aging' PWH, usually in their mid-fifties or early sixties [19,20]. While this study confirms the relationship between frailty and cognitive impairment in OPWH, this is not unexpected given that this holds true in the non-HIV exposed older population [21,22]. However, it remains uncertain, and is of major clinical importance, whether this relationship also occurs in younger PWH. Evidence-based recommendations for initial and ongoing longitudinal screening for both frailty and cognitive impairment are necessary, as preventive measures that may mitigate or delay the onset of these geriatric syndromes should be considered [23,24].

Multimorbidity is increasingly recognized in OPWH [4,25]. Indeed, these investigators has recently shown that multimorbidity is associated with frailty in this same cohort [26]. The clinical consequences of aging with HIV are more than just the earlier accumulation of age-related comorbidities The increased risk of developing geriatric syndromes must also be recognized. In HIV unexposed older persons, geriatric syndromes often occur together because of shared risk factors [27], and this study emphasizes their co-occurrence. In addition to assessing OPWH for frailty and cognitive impairment, providers should be aware that other undiagnosed geriatric syndromes, such as polypharmacy, impaired mobility and falls, sarcopenia, impaired cognition and depression may also be present. For example, ageing related decreased gait speed is a risk factor for impaired mobility and falls [10]. Sarcopenia is increasingly recognized in PWH, regardless of age [28], and contributes to frailty, muscle weakness, and impaired bone health, among other health deficits [29]. The prevalence of depression is high in OPWH [30], and may contribute to physical inactivity, social isolation, malnutrition, and impaired ability to perform basic and instrumental activities of daily living. A possible consequence of age-related comorbidities and geriatric syndromes is polypharmacy which increases the risk of important adverse drug reactions, especially neurocognitive toxicity [31], as well as drug-drug interactions, often involving cART drugs [32]. Importantly, geriatric syndromes themselves independently increase mortality [33].

While cART has resulted in the quantitative improvement in the lifespan of PWH, this has not consistently led to an improved quality of life. In fact, many OPWH struggle with aging as a result of developing geriatric syndromes. Healthcare providers are proficient at diagnosing and managing age-related comorbidities, but more attention needs to be paid to the evaluation and management of geriatric syndromes, which remain largely underappreciated. Ultimately, this study serves as a reminder that diagnosing one aging related condition may be only the tip of the iceberg. As clinicians, we need to evaluate more broadly to improve the quality of life and health-span of all PWH.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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