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Mini Review

Contemporary HIV Patients and the Frailty Syndrome: A Short Review

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Abstract

Frailty is a well-known syndrome found in elderly, community dwelling people over the age of 65 years and is associated with morbidity. Frailty is also described in HIV-infected people, a patient group whose mean age is rising due to effective treatment and longer survival. Researchers are questioning whether frailty in the elderly is the same as frailty in HIV-infected people. We address this question in light of our recent findings in HIV-infected patients attending an ambulatory clinic. We found that frail HIV patients were exhausted and expended little energy; 100% were also depressed. On the other hand symptoms of sarcopenia, a hallmark of frailty in the elderly, were much less frequent.

Keywords: Frailty; Frailty phenotype; Aging; HIV; Chronic infection

Abbreviations

HIV: Human Immunodeficiency Virus; ART: Anti-Retroviral Therapy; FP: Frail Phenotype

Introduction

Humanity is into the fourth decade of pandemic HIV. The use of combination Anti-Retroviral Therapy (ART) since 1995 has led to viral control in HIV-infected patients thus, decreasing mortality and increasing survival. Consequently HIV is now a manageable chronic illness and AIDS is theoretically preventable [1]. For the past several years, clinicians have encountered aging-related issues in the care of their HIV patients, often on a daily basis. Many urban HIV clinics, like our own, have HIV-infected patients who have survived infection since the 1980s and are in their sixth, seventh and eighth decade of life. The mean age of HIV patients continues to increase [2]. Many patients experience early occurrence of common geriatric comorbidities [3].

Older non-infected adults accumulate the effects of the aging process and some become frail. Frailty was initially described as a geriatric syndrome resulting from age-related cumulative declines across multiple physiologic systems, impaired homeostatic reserve, and reduced capacity to resist stress [4]. Frailty increases vulnerability towards adverse health outcomes including falls, hospitalization, institutionalization and mortality [4]. Based on recent estimates, 7-11% of community-dwelling older persons are frail and another 40% are pre-frail [5]. In this review we discuss features of frailty as seen in elderly, community-dwelling individuals and compare it to "frailty" observed in young and old HIV-infected individuals (Table 1). Although the term, frailty, is used for both populations of individuals, elderly and HIV-infected alike, we believe frail HIV-infected individuals are different clinically than un-infected frail elderly individuals.

Measuring Frailty

Currently there are two popular models used to measure frailty in the elderly. One is measurement of the Frailty Phenotype (FP) as described by Fried et al. and involves 5 clinical characteristics [4]. The other is the cumulative deficit model [6] which is a compilation of historical clinical characteristics. The latter model forms the basis of the frailty index derived from a baseline list of 92 symptoms, signs, laboratory tests and disabilities. Both models have considerable overlap in the identification of frailty and statistical convergence [5]. In our HIV clinics we have worked extensively with the FP model and will confine our discussion to this methodology when comparing frailty in uninfected elderly and HIV-infected individuals. It should be noted that there is no consensus as to the best method to measure the FP in the elderly and HIV-infected persons and many surrogate markers are often used [7]. The landmark paper by Fried et al. measured five clinical factors [4] which include: unintended weight loss of >10 pounds in a year; self-reported exhaustion (measured by responses to the Center for Epidemiological Studies depression scale [8]); low energy expenditure (established by recall of activities expressed as kcal/week and stratified to sex); slow gait speed, measured by a timed walk (stratified to height and sex) and weak grip strength as measured by a dynamometer (stratified to BMI and sex). A patient with abnormal results on three or more of the five factors is said to be frail and if the individual demonstrates one or two abnormal factors they qualify as pre-frail. These 5 clinical factors can be separated into two major components, factors indicating the

Table 1: Comparison of characteristics of frail elderly patients living in the community and frail HIV-infected patients attending an ambulatory clinic.

Characteristics	Frail Elderly	Frail, HIV-infected
Population measured	community dwelling persons >65 years of age	community dwelling HIV-infected persons
Age-related	yes	no
Prevalence	7%	~20%
Reversibility	limited	yes
Sarcopenia	a defining feature	least important factor in measuring FP
Depression		most common factor present in measuring FP

Abbreviation: FP: Frailty Phenotype.

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presence of sarcopenia (a hallmark of FP in the elderly) and factors denoting low energy and exhaustion which may represent abnormal mood or depression. It is an assumption that the pathogenesis of frailty in HIV-infected individuals is similar to or identical to frailty occurring in older patients. We believe the two frail populations are not equivalent for the following reasons.

Prevalence of frailty is high in HIV-infected individuals

An unusual feature of frailty in HIV-infected patients is that FP is very common; about 1 in 5 patients at any one time presents with FP (using the standard 5 Fried criteria).We studied 100 HIV-infected individuals attending an ambulatory care clinic and discovered a frailty prevalence of 19%. Men were 81% of the sample and women, 19% and ages ranged from 21 to 78 years. Over 90% of patients in the clinic are on ART [9]. In a follow-up study of 122 individuals attending the same clinic and utilizing standard FP criteria, frailty was present in 19% as well [10]. In a study of 5210 adults (un-infected) over the age of 65 years of age living in the community, the prevalence of frailty was 7% [4]. Thus, using identical measurements of FP, frailty was found to be two to three times more common in HIV-infected persons than the 7-11% found in community dwelling elders.

Frailty is transient in HIV-infected individuals

The FP is a predictor of future adverse health outcomes [4]. The time course of frailty can be schematically represented by a descending staircase, each step down representing a morbid event contributing to frailty. At some point the stepwise decline becomes very steep, one morbid event rapidly following another. Following an adverse incident there is little time for homeostatic resolution and inevitably an inability to return to the prior functional status. Scientifically the underlying "lesion" of frailty is believed to be sarcopenia or loss of functional muscle mass that accompanies aging but is hastened in those with frailty. However, our studies of ambulatory HIV-infected, community dwelling patients demonstrated something we did not expect. For example, in the first study of 100 individuals [9], 7 frail individuals returned for a follow up visit within 6 months and were re-measured for frailty. Of those 7 individuals, 2 died refusing to take ART, 4 were no longer frail and only 1 remained frail. In the second study of 122 patients, 6 frail patients returned for a second visit and re-measurement for frailty. Four of those returning were no longer frail and only 2 remained frail. We concluded that frailty in HIV-infected patients, particularly in the younger individuals was transient and reverted to a pre-frail state. This is opposite of the outcome for frail elderly patients where stepwise-decline would be expected.

Frailty is not primarily age-related in HIV-infected individuals

Frailty in the elderly is a function of aging of the patient and is physiologically linked to aging-related decline in organ systems where homeostatic reserves are depleted. It is estimated that perhaps 50% of individuals over the age of 85 years are frail [5]. If one looks at large populations of community dwelling individuals over the age of 65 years, estimates of FP prevalence are 7% [4]. In our studies we have not found a relationship of frailty and age in HIV-infected individuals. There was no significant difference between HIV-infected patients below or over the age of 50 years the age at which HIV patients are considered "older" [2]. Neither was there an increased incidence of frailty with each increasing decade of life. We actually found the opposite, i.e., individuals who took ART for the longest had the lowest incidence of frailty [9]. In other words anti-retroviral therapy protected against frailty. A recent presentation at the 14th Annual CROI meeting reported similar results, i.e., an incidence of FP of 9% in 142 HIV-infected individuals on ART with undetectable viral loads over the age of 50 years [11].

Factors associated with sarcopenia are not the most common characteristics in frail HIV-infected individuals, depression is

We found in our second study of 122 HIV-infected individuals that factors associated with sarcopenia such as decreased grip strength, slow walking and shrinkage were seen less frequently than exhaustion and low physical activity. For example, in the frail individuals shrinkage or weight loss occurred in 65%, decreased grip strength occurred in 43%, and decreased gait speed in 39 % whereas, low physical activity occurred in 83% and exhaustion occurred in 100% of the frail individuals. Documented psychiatric illness occurred in 31% of the patients irrespective of frailty status [9]. Exhaustion, one of the 5 FP criteria, is actually synonymous with depression. It is obtained by administering the Center for Epidemiologic Studies Depression scale. As noted, 100% of the frail HIV-infected individuals were depressed, 30% with scores indicating mild to moderate depression and 70% with scores indicating a major depressive disorder.

Conclusion

We believe that "frailty" in HIV is bi-modal, indicating a hyperinflammatory sarcopenic milieu in some, and depression, in others. We recommend that future research take into account this hypothesis, by carefully considering frailty sub-components, clinical depression screening, and measures of sarcopenia, to enable better discrimination of these findings.

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