HIV Infection in the Elderly

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Introduction

Over the past decade, the percentage of all HIV cases in patients 50 years or older increased to more than 17% [1••]. This increase in the prevalence of HIV in middle-aged and older people is expected to continue over the next decade. Previous data suggested that early in the HIV epidemic, older patients had higher morbidity, mortality, and decreased AIDS-free survival than younger HIV-infected patients [2–4]. This was due to delays in diagnosis and concomitant comorbidities. Since the inception of highly active antiretroviral therapy (HAART), several studies suggested that older patients may not respond as well to HAART as younger patients; particularly, there may be less immune recovery with advancing age [2–4]. HAART has numerous significant toxicities including dyslipidemia, impaired glucose metabolism, pancreatitis, neuropathy, hepatotoxicity, and lactic acidosis. Older patients may be more likely to develop toxicities than younger patients. In addition, older people are more likely to have comorbidities including cardiovascular disease, renal disease, diabetes, bone loss, and obesity that complicate utilization of antiretroviral therapy. Thus, a balance must be found between the need to treat older individuals earlier to sustain immune function and the potentially greater risk of cumulative toxicity from HAART.

Epidemiology

Previously, HIV was thought of as a young person’s disease; however, due to the increasing prevalence of HIV in middle-aged and older people, the epidemiology of the infected population is changing [5,6]. Although few practitioners would use the age of 50 as a threshold to indicate advanced age, the US Centers for Disease Control and Prevention identified patients age 50 years or older as a separate age group, because this age group was so much older compared with the lower mean age of HIV patients early in the HIV epidemic [7]. HIV patients are aging because of the increased survival due to HAART, and an increasing number of new HIV infections in older patients due to high-risk exposures [8]. The number of HIV-infected persons older than 65 years has grown tenfold in the past 10 years [5]. It is estimated that by 2015, 50% of people living with HIV/AIDS will be over 50 years of age [9].

There is often a delay to HIV diagnosis in older patients [10]. This may be because physicians are less likely to ask older patients about high-risk behaviors or even suspect HIV in older patients [5,10]. In addition, even though older patients may be engaging in high-risk sexual activity, they may be less likely to admit to these behaviors [11]. Older Americans appear to be at increased risk for HIV infection, suggesting a need for HIV prevention efforts targeted at older individuals.

Overall, the prevalence of HIV in older patients has increased in the past decade. Consistent with national trends, a demographic shift has occurred such that these patients mirror the national HIV epidemic, with more infected injection drug users, women, and minorities. Older patients are often diagnosed later than younger patients because physicians are reluctant to ask older patients about high-risk behaviors and patients are unwilling to admit to socially unacceptable behaviors. Future trends in HIV during the next decade are likely to include more primary infections in those over 50 years as well as increasing longevity in those infected at younger ages. With greater longevity, we are also likely to see more long-term complications of HIV infection and treatment.
Clinical, Immunologic, and Virologic Response to HAART

HAART is effective at reducing HIV viral load and improving CD4 lymphopenia; however, data regarding the clinical, immunologic, and virologic benefit in older patients treated with HAART have been mixed (Table 1). Some authorities have hypothesized that the degree of immune recovery after treatment with HAART may be dependent on the thymus, which loses function with advanced age [12–16]. Data from the early HAART era suggested that age is inversely proportional to how quickly the immune system recovers and that older patients did not respond as well as younger patients [17–19].

There is controversy about the rates of virologic suppression and CD4 response in older compared with younger patients on HAART. Some studies demonstrated a smaller CD4 boost in older patients compared with younger patients treated with HAART [18,20,21], but others have not noted a significant difference in CD4 response between older and younger patients [22–24]. In addition, some studies demonstrated increased virologic suppression in older compared with younger patients [24–27]; another demonstrated better virologic suppression in younger patients [28]; and several demonstrated no difference in virologic suppression between older and younger patients [17,19,23,29].

The largest study to examine the impact of HIV and aging was performed in nearly 50,000 antiretroviral naïve patients in Europe and compared older with younger patients [30••]. The investigators found the probability of virologic response was higher in individuals older than 50 years (possibly due to greater medication adherence), but the probability of immunologic response was lower in individuals 60 years or older. Of note, individuals older than 55 years had poorer clinical outcomes after adjusting for the latest CD4 cell count. This study did not examine differences in response by HAART treatment class.

Only two studies examined the impact of regimen type on clinical outcomes by age. Greenbaum et al. [31] found a significantly decreased time to virologic suppression in older patients on nonnucleoside reverse transcriptase inhibitors (NNRTIs) compared with younger patients on NNRTIs or protease inhibitors (PIs); however, there was no difference in time to virologic suppression in older patients on NNRTIs compared with PIs. On the other hand, Patterson et al. [32] found immune reconstitution and viral suppression did not vary by treatment regimen when stratified by age. Both studies had relatively small sample sizes. Future studies that are adequately powered to address the impact of specific antiretroviral therapy regimens are needed to further answer the question of most appropriate treatment type for older patients.

Data regarding the impact of age on HIV progression in the HAART era also demonstrated conflicting results (Table 1). A recent study from Johns Hopkins demonstrated fewer opportunistic infections in older patients than in younger HAART-naive patients after starting HAART [31]. Other recent studies, however, found that despite higher rates of virologic suppression, older patients have an increased risk of new opportunistic infections compared with younger patients [20,33].

Not surprisingly, most studies found increasing mortality rates in older patients compared with younger patients [30••,31,34]. Of note, the causes of death in HIV patients treated with HAART have changed from complications of HIV to primarily non–HIV-related causes in American and European cohorts [35].

Overall, these studies have yielded conflicting results regarding clinical outcomes. The previously noted studies are very heterogeneous in study design. Some are cross sectional, others are longitudinal, and many use different outcomes or cutoffs for virologic suppression. In addition, no large trial has evaluated the effect of any one HAART regimen or even class of HAART in regard to outcomes in older compared with younger HIV-infected patients. Therefore, current conclusions regarding HAART therapies in older patients are limited. Larger, controlled trials involving older patients are necessary to evaluate which antiretroviral therapies might be most effective in this population. Until then, current guidelines for HAART regimens should be applied to HIV-infected older patients. Immunologic, virologic, and clinical response should be monitored carefully because recovery may be blunted in older patients.

HAART Metabolism and Toxicity

With prolonged survival, HIV patients are living long enough to develop comorbidities associated with age and chronic substance use as well as HAART therapies [36]. It is probably no longer appropriate to assume that a new condition (eg, diabetes or liver disease) is due to a single etiology such as HIV infection, HIV treatment, or disease processes completely independent of HIV or its treatment. Instead, it is more useful to consider what may be the contributing causes. For example, although hepatitis C infection dramatically increases the risk of liver cirrhosis among those with HIV infection, advancing age and HIV infection both increase the risk of cirrhosis among those with hepatitis C.

Unfortunately, most studies of antiretroviral metabolism have excluded patients of advanced age with comorbid disease; therefore, there are few data on the use of antiretrovirals in elderly HIV patients. One study found reduced elimination of zidovudine in elderly patients that resulted in toxic drug levels [37]. Another European study found that age was a risk factor for changes in serum creatinine level in an expanded access study of tenofovir [38].

Treatment with PIs and NNRTIs has been associated with several metabolic disorders, including dyslipidemia. PI regimens have been associated with increased triglycerides, total cholesterol, and low-density lipoprotein (LDL) levels and these metabolic disturbances vary by specific PI. In addition, NNRTIs may increase total cholesterol and LDL levels and induce a concomitant increase in