



Pulmonary Hypertension in an Elderly HIV-infected Veteran Population

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Abstract:

Pulmonary hypertension may occur as a co-morbid disease in HIV. We examined the characteristics of our HIV infected veterans with pulmonary hypertension and compared them with a control group of HIV infected patients without pulmonary hypertension. Among our cohort, patients were diagnosed with pulmonary hypertension at a mean age of $49.8 \text{ y} \pm 11.0\text{y}$. This diagnosis came about $8.1\text{y} \pm 6.7\text{y}$ after the diagnosis of HIV. Our pulmonary hypertension patients lived for about $3.4 \pm 3.0\text{y}$ after their pulmonary hypertension diagnosis. The presence of pulmonary hypertension in HIV infection confers an increased risk of mortality. Mortality in our pulmonary hypertension cohort was 73%.

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Introduction:

With the advent and continued evolution of highly active antiretroviral therapy HIV has become a chronic disease. HIV patients now face comorbid diseases seen the general population with pulmonary hypertension being among them. HIV-infected individuals are at a much higher risk of developing pulmonary hypertension than the general population with a prevalence in the range of 0.5% to 10% in those with HIV [1-5]. When pulmonary hypertension occurs in the presence of HIV, mortality is increased [6]. As a result it is important for providers in HIV care to understand which patients are more likely to develop pulmonary hypertension. In so doing the disease may be detected and treated early. As patients age with the diagnosis of HIV, providers will be challenged to address health care disorders common to the population of patients represented in their clinics and, additionally, be faced with managing conditions which occur among HIV-infected patients at higher rates than those not infected with HIV. In this study we examined patients with pulmonary hypertension presenting to our urban clinic and describe the characteristics and associated comorbidities among older HIV-infected veterans.

Methods:

Between 1989 and 2009 we identified patients with a pulmonary hypertension diagnosis enrolled in the Washington DC Veterans Affairs Medical Center (DCVAMC) Primary-Care HIV Clinic Registry. The diagnosis of pulmonary hypertension was made either by echocardiography or right heart catheterization. Age, gender and HIV diagnosis-year were used to create a control group without pulmonary hypertension, matched at 3:1 to those with pulmonary hypertension. A retrospective review of our comprehensive electronic medical record (Vista_CPRS) was supplemented with paper-charts where needed. Prior to initiation of work, the study was approved by our Institutional Review Board and the Research and Development Committee.

All analyses were conducted with two-tailed tests, accepting a P value of <0.05 (SPSS v21, Chicago, IL).

Results:

We identified twenty-two HIV-infected subjects as having pulmonary hypertension in the 20-year observation period and matched sixty-seven HIV-infected control patients. All subjects (N=89) were male and the majority were African American (60.6%). Among all subjects, the mean age was 56.5 years(y) \pm 10.1y.

Among those with pulmonary hypertension, the mean age at diagnosis of pulmonary hypertension was 49.8 y \pm 11.0y. On average, our patients lived 3.4y \pm 3.0y with their pulmonary hypertension diagnosis and developed pulmonary hypertension 8.1y \pm 6.7y after their HIV-diagnosis.

At the time of pulmonary hypertension diagnosis, only 25% of patients were on antiretroviral (ARV) therapy. Only 13% of those with pulmonary hypertension had achieved appropriate viral suppression. We found no difference in the mean nadir CD4-T lymphocyte counts in those with or without pulmonary hypertension.

The incidence of underlying disease was generally common in our urban population, with the most common being tobacco use (90.6%), drug abuse (52.9%), hypertension (HTN, 37.8%), hepatitis C virus infection (HCV, 39.3%), coronary artery disease (CAD, 13.3%) and diabetes mellitus (DM, 13.1%).

We failed to identify significant added risk from preexisting diagnoses of COPD, obstructive sleep apnea, sarcoidosis, connective tissue disease or interstitial lung disease when compared to HIV positive controls without pulmonary hypertension. We did find that congestive heart failure (CHF) was significantly more prevalent among pulmonary hypertension patients (56% vs 2%, p <0.001). The presence of pulmonary hypertension was the one significant risk factor among our cohort for CHF

after controlling for the presence of HTN, DM, smoking and CAD (OR 62.0, $P < 0.001$).

During the 20 year study period, the all cause mortality was high among our patients with a diagnosis of pulmonary hypertension (17/22, 73%). This was significantly higher than the all-cause mortality experienced by the age, gender and HIV diagnosis-year matched controls without pulmonary hypertension (28/67, 41.7%, $P = 0.006$). Although the pulmonary hypertension contribution to mortality was also present after controlling for the contribution of HTN, CAD, smoking and DM, it failed to reach the level of significance (OR 2.51, $P = 0.09$). Among those who died in the cohort (45/89, 50.6%), there were significantly more patients with a pulmonary hypertension diagnosis (37.8% vs 11.4%, $p = 0.0032$) and a non-significant trend in the underlying presence of CHF (26.7% vs 6.7%, $P = 0.08$).

Discussion:

In our cohort the median age at the time of pulmonary hypertension diagnosis was 49.8 years. This is older than the average age of 41-42 years reported elsewhere [1]. The interval between the diagnosis of HIV and development of pulmonary hypertension was, on average, 8 years (median 10 years). This interval is considerably longer when compared to a case-series review where the mean time to development of pulmonary hypertension from HIV diagnosis was 33 months [4]. The changes in physiology that herald pulmonary hypertension in subjects infected with HIV can occur as early as 3 months after HIV infection [5]. Despite presenting later in their HIV-disease with the pulmonary hypertension diagnosis, our patients lived a median of 3 years with their pulmonary hypertension diagnosis.

We found our aged and aging patients were particularly vulnerable to a diagnosis of pulmonary hypertension. HIV care providers should be vigilant in

screening for pulmonary hypertension, even in the elderly. A concurrent diagnosis of congestive heart failure or diastolic dysfunction may serve to help identify patients who should be further screened and followed closely for the development of PH. As a disease where HIV-infection conveys a particular risk, the diagnosis of pulmonary hypertension has the potential to offset the positive impact of HIV-care and HIV-care related outcomes.

Conclusion:

Pulmonary hypertension is an important disease process that may occur in those infected with HIV. Although in other studies pulmonary hypertension occurs in younger HIV patients this study of our veterans shows that the disease may also occur in the aging and aged. It is important for providers of HIV care to be cognizant of this disease as its presence confers an increased risk of mortality. Perhaps early detection and treatment can decrease this risk. Further study of this population is needed.

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