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Vascular Disease and Aging in HIV: Time to Extend the Treatment Cascade

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Over the last two decades, much painstaking epidemiologic work has shown that compared to HIV-uninfected controls, people living with HIV (PLWH) appear to have a higher risk of a broad range of cardiovascular diseases (CVD) including acute myocardial infarction (MI)¹, peripheral artery disease², and ischemic stroke³, even after accounting for traditional risk factors. Mechanisms for this residual risk include chronic inflammation and immune activation, direct viral effects, and certain antiretroviral drugs¹. Yet, despite growing awareness, focus on CVD prevention in this population has lagged. It is time for change.

In this issue of *Vascular Medicine*, Lin and colleagues have given us another piece of the puzzle focused on carotid intervention among PLWH and controls from the United States Nationwide Inpatient Sample over the period of 2004–2014⁴. Their principal findings are that the prevalence of HIV among those undergoing carotid intervention is increasing over the period studied and that PLWH who undergo carotid intervention tend to be approximately 9 years younger than those without HIV infection after adjusting for a number of potential confounders.

Does this study provide evidence that HIV is associated with “accelerated aging”, such that PLWH might expect to suffer a stroke or need to undergo carotid endarterectomy 9 years earlier than they otherwise would have if they didn’t have HIV? Or does it simply reflect the younger age structure of the HIV-infected population compared to the general population (only 7% of PLWH are over 65 compared to 15% of the general US population)⁵. The Veterans Aging Cohort Study (VACS)—a well-designed clinical cohort that has produced much of the epidemiologic data in this field—would suggest that while the risk of MI is higher in HIV across all age groups, the mean age at the time of MI does not differ by HIV status⁶. A large longitudinal study from Denmark also showed that risk of MI and stroke does not grow with longer duration of HIV infection, which would be expected if HIV caused “accelerated aging”⁷. On the other hand, the magnitude of HIV-associated ischemic stroke risk does appear to be higher in younger individuals in both the VACS and Danish studies^{3,7}. HIV may also be associated with increased carotid intima-media thickness only at younger ages (< 30 years), but not among middle-aged or older adults⁸. One interpretation of these data is that HIV-specific risk factors may be more important at younger ages, whereas traditional risk factors predominate as PLWH age.

As Lin and colleagues point out, the benefit of carotid endarterectomy or stenting for PLWH is not clear. Ultimately, the best way for us to prevent atherosclerotic CVD events for our

patients with HIV is to promote healthy lifestyles, smoking cessation, and aggressive management of lipids and blood pressure. Although there are barriers to CVD prevention in the HIV specialty clinic (e.g. infectious disease specialists who went into HIV medicine to treat opportunistic infections and manage AIDS may not be interested in managing lipids and blood pressure), there are also unique opportunities. Quality improvement efforts in HIV care have recently focused on the HIV treatment cascade—that PLWH must first be diagnosed, then linked and engaged in care, and finally clinically managed to achieve suppression of detectable HIV virus in the blood with effective antiretroviral therapy (ART). Thanks to campaigns such as UNAIDS 90–90–90, many HIV specialty care clinics in the USA now have over three quarters of their patients with suppressed HIV viral loads on ART⁹. To improve AIDS and non-AIDS outcomes, the focus should absolutely be on getting more PLWH on effective treatment, because we know that uncontrolled viral loads and low CD4+ counts are associated with higher rates of MI and stroke^{1,3}. However, once controlled on ART, the attention should be turned toward extending the treatment cascade for atherosclerotic CVD prevention by appropriately managing traditional risk factors. While we await the results of REPRIEVE—the first placebo-controlled, randomized controlled trial of statins for prevention of atherosclerotic CVD events among PLWH (www.reprievetrial.org)—these patients should be prescribed statins and other preventive therapies according to guidelines used for the general population. Unfortunately, guideline-based statin therapy is underutilized for PLWH¹⁰, a treatment disparity that may be even worse for women¹¹.

Despite the barriers, I am profoundly optimistic about the future of atherosclerotic CVD care for PLWH. Even as absolute rates of CVD rise as this population ages, some studies show that the relative risk of CVD among HIV-positive vs. HIV-negative controls is declining over time^{7,12}. The provider community is engaged, PLWH are demanding more attention be paid to non-AIDS comorbidity, and the National Heart Lung and Blood Institute is investing in implementation science to address treatment disparities. Compared to younger people without chronic disease who do not engage with the health care system, young PLWH with suppressed HIV may have better opportunities to have hypertension and dyslipidemia properly managed. Extending the HIV treatment cascade for CVD prevention will begin with changes in HIV specialty care clinics but will also require collaboration with non-HIV primary care providers and vascular disease specialists who are knowledgeable about HIV. Who knows, maybe increased awareness and high-quality prevention programs will eventually lead to lower rates of atherosclerotic CVD among PLWH than in the general population.

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