Risk of peripheral artery disease in human immunodeficiency virus infected individuals

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According to the report from the World Health Organization (WHO), 1.8 million individuals become HIV infected every year (1). Several studies have demonstrated higher incidence, prevalence and progression of subclinical atherosclerosis in HIV infected individuals as compared to general population despite optimal control of traditional risk factors (2,3).

In a recently published article "*Association of human immunodeficiency virus infection and risk of peripheral artery disease*" Beckman *et al.* (4) studied participants of Veterans Aging Cohort Study. The study consisted of 91,953 Veterans with no cardiovascular disease at baseline. Their primary outcome was incident peripheral artery disease (PAD) in HIV infected versus HIV uninfected participants, while secondary endpoints were to evaluate mortality and amputation in subjects with incident PAD. They further performed sub-analysis of events by CD4 count and viral load among HIV infected individuals. Interestingly HIV infected Veterans had a lower prevalence of traditional risk factors such as obesity, diabetes, hypertension and low-density lipoprotein cholesterol. The authors concluded that "*infection with HIV is associated with a 19% increased risk of PAD beyond that explained by traditional atherosclerotic risk factors. However, for those with sustained CD4 cell counts <200 cells/mm^3, the risk of incident PAD events is nearly 2-fold higher whereas for those with sustained CD4 cell counts ≥500 cells/mm^3 there is no excess risk of incident PAD events compared with uninfected people*". This study enriches the limited literature available on association of HIV infected and PAD. Several studies have demonstrated higher cardiovascular morbidity and mortality, including coronary heart disease (5), stroke (6) and PAD (7) in HIV infected population. Prevalence of PAD is estimated to be 1% at age 50 and 3% at 60 years in large epidemiological studies (8,9). Previously, Periard *el al.* (7) showed the prevalence of PAD was 9.8% in HIV infected individuals <50 years, considerably higher than general HIV uninfected population. Although, exact mechanism for HIV-associated premature atherosclerosis has yet to be unraveled, it seems to be multifactorial, including traditional cardiovascular risk factors, combination antiretroviral therapy related side effects and increased inflammation due to direct effect of HIV infection leading to endothelial dysfunction (5,10,11).

In study by Beckman *et al.* (4), there was a 19% increased risk of incident PAD in HIV infected individuals beyond what could be explained by traditional risk factors, suggest HIV infection as an independent risk factor for PAD. This idea is further supported by a number of studies, which demonstrated increased prevalence of non-calcified plaque in HIV infected individuals as compared to HIV uninfected after adjusting for traditional cardiovascular risk factors (2,12).

Cardiologist and HIV specialists lack the tools to identify HIV individuals at high cardiovascular risk. Framingham risk score and American College of Cardiology/American Heart Association pooled cohort risk equation both seem

to underestimate risk for cardiovascular events in HIV infected population (13,14). Arterial Imaging such as ^{18}Floruodeoxyglucose (^{18}FDG), brachial artery ultrasound and Cardiac computed tomography (CT) could be useful tools to identify HIV infected individuals at risk for developing PAD (2,15,16). In another study there was an inverse relationship of HIV RNA load and brachial flow mediated dilation (16). ^{18}FDG uptake by arterial macrophages can be used to identify arterial inflammation. The Strategies for Management of Antiretroviral Therapy study found that HIV infected patients with interrupted ART had increased inflammatory markers such as IL-6 and D-dimers (17,18), these biomarkers were in turn associated with increased mortality and cardiovascular events (18).

The current study by Beckman *et al.* support these observations, with a low CD count (<200 cells/mm^3), incident risk of PAD was doubled, while those with CD4 count >500 cells/mm^3 risk was similar as compared to HIV uninfected individuals. Furthermore, 50% of HIV infected individuals with higher viral load were deceased after diagnosis of PAD within 5 years.

Lastly, non-contrast and contrast cardiac CT scans can be used to identify high risk patients. Coronary artery calcium (CAC) is strong predictor of cardiovascular events. Several studies have demonstrated prognostic value of CAC in general population and in some studies of HIV infected population (3,19,20). The Multicenter AIDS Cohort Study demonstrated that HIV positivity was significantly associated with higher burden of non-calcified plaque (2). PAD significantly affects quality of life and increases mortality. With 36.7 million (1) currently living with HIV and estimated higher prevalence and incident risk of PAD, we need better methods to identify and treat those individuals at high risk for developing PAD and other cardiovascular diseases.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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