HIV ELITE CONTROLLERS HAVE LOWER ASYMMETRIC DIMETHYLARGININE AND IMPROVED ENDOTHELIAL FUNCTION AS COMPARED TO INDIVIDUALS WITH TREATED AND SUPPRESSED HIV

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Background: A small proportion of HIV-infected adults are able maintain an undetectable circulating HIV RNA level in the absence of antiretroviral therapy (ART). Compared to uninfected persons and effectively treated HIV-infected individuals, these “elite” controllers have elevated levels of certain inflammatory markers and more efficient killer CD8+ cells. We investigated endothelial function in elite controllers using flow-mediated dilation (FMD) of the brachial artery, a physiologic measure of vascular reactivity. We also measured levels of asymmetric dimethylarginine (ADMA), an endothelial nitric oxide synthase inhibitor inversely correlated with endothelial function.

Methods: FMD and ADMA were measured in 25 elite controllers, 177 HIV-infected adults on ART with undetectable HIV RNA levels (“ART-suppressed”), and 82 uninfected controls. We adjusted for traditional cardiovascular and HIV-related risk factors.

Results: FMD was comparable in elite controllers and uninfected controls, but lower (more abnormal) among those on ART [median (IQR) of 5.0% (2.2-7.4), 4.6% (2.7-5.6) and 3.9% (2.6-5.3), respectively; p=0.076]. Concordantly, ADMA was also comparable in elite controllers and uninfected controls, but the elite controller group had significantly lower ADMA than that observed in the ART-suppressed group [0.42 µM (0.40-0.48) vs. 0.47µM (0.42-0.53), p=0.008]. This association remained significant even in the fully adjusted analysis [0.041µM (0.008-0.073), p=0.015].

Conclusions: Although our group and others have found evidence supporting accelerated atherosclerosis among HIV elite controllers, we found limited evidence in the present study for substantial vascular dysfunction as assessed by markers of endothelial function. Elite controllers had similar FMD and ADMA compared to uninfected controls; in contrast, in comparison to ART-suppressed individuals, the elite controllers had significantly reduced ADMA and displayed a trend towards improved FMD. Collectively, these findings suggest that while HIV-associated inflammation in elite controllers may contribute to atherosclerosis over time, the immediate impact on vascular function seems less evident.