Impact of Low CD4 Count and HIV Persistence on Endothelial Function in Patients with Low Plasma RNA

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Background
HIV-positive individuals are at high risk for myocardial infarction and sudden cardiac death. Chronic inflammation, increased cardiovascular risk in HIV-infected individuals, even among those with low plasma viral RNA levels, suggests that low-level virus production is proatherogenic and not fully defined the role of low-level virus production and/or replication have on microvascular function. Therapies targeted at further reduction of HIV persistence may provide additional benefit on reduction of cardiovascular risk.

Methodology
Patient selection - We performed a cross-sectional study of 70 HIV-infected adults from the SCOPE cohort at San Francisco General Hospital. Criteria: Treated HIV patients with viral suppression defined as stable ART for ≥12 months and HIV RNA levels <75 copies/mL, for ≥12 months

Patient characteristics (Table 1). After adjustments for age and gender, worsened hyperemic velocity and lower CD4+ T-cell count (RR 1.04, p=0.045) but not measures of HIV persistence (plasma HIV RNA, cell-associated RNA, cell-associated DNA). When analyzed in treated suppressed only the association between worsened hyperemic velocity and lower CD4+ T-cell count remained (RR 1.04, p=0.045) and also remained when analysis was performed in elite controllers only (RR 1.10, p=0.011) (Figure 3). After adjusting for age and gender, impaired MDW was associated with lower eGFR (RR 1.72, p=0.003), smoking (RR 1.26, p=0.035) and higher cell-associated RNA (RR 0.85, p=0.049). Inflammatory and coagulation markers were not significantly associated with HIV or FMD. Among treated and suppressed individuals only, lower eGFR and smoking remained significantly associated with impaired FMD while the association with cell-associated RNA was weaker.

Conclusions
Among HIV-infected individuals with undetectable plasma RNA levels using a long-term ART regimen, a lower current CD4+ T-cell count but not measures of viral persistence, was independently associated with impaired microvascular function, as defined by hyperemic velocity. In contrast, suppressed HIV RNA levels was associated with impaired macrovascular function, as measured by FMD, suggesting that HIV may preferentially affect the microvasculature, leading to worsened endothelial function. Further studies using other markers of HIV progression, including in vitro studies using vascular tissue samples, will be necessary to more fully define the role of low-level virus production and/or replication have on cardiovascular risk.

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Results
We studied two “atricentric” groups: those doing well on long-term ART and elite controllers. Subject demographics and clinical characteristics are displayed in Table 1. After adjustments for age and gender, worsened hyperemic velocity was independently associated with lower CD4+ T-cell count (p=0.045) and all eligible controllers (n=51, p=0.011).

Table 1. After adjustments for age and gender, worsened hyperemic velocity and lower CD4+ T-cell count (RR 1.04, p=0.045) but not measures of HIV persistence (plasma HIV RNA, cell-associated RNA, cell-associated DNA). When analyzed in treated suppressed only the association between worsened hyperemic velocity and lower CD4+ T-cell count remained (RR 1.04, p=0.045) and also remained when analysis was performed in elite controllers only (RR 1.10, p=0.011) (Figure 3). After adjusting for age and gender, impaired MDW was associated with lower eGFR (RR 1.72, p=0.003), smoking (RR 1.26, p=0.035) and higher cell-associated RNA (RR 0.85, p=0.049). Inflammatory and coagulation markers were not significantly associated with HIV or FMD. Among treated and suppressed individuals only, lower eGFR and smoking remained significantly associated with impaired FMD while the association with cell-associated RNA was weaker.

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