HIV Reservoir Size Predicts Incident Carotid Plaque and Carotid IMT Progression in People With HIV

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BACKGROUND

With expanded ART coverage, non–AIDS comorbidities, especially cardiovascular disease, are a major concern in people with HIV (PWH). Subclinical carotid atherosclerosis is a validated cardiovascular surrogate, yet systematic evaluation in PWH remains limited. HIV reservoirs have been linked to non–AIDS comorbidities. We tested whether reservoir measures associate with incident carotid plaque and intima–media thickness (IMT) progression.

Methods

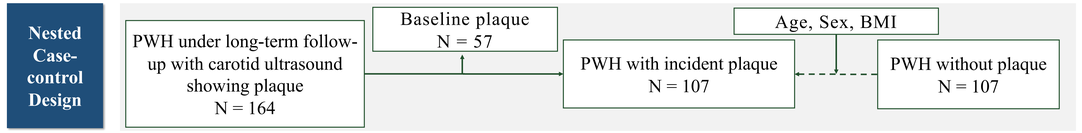
We conducted a case–control study within a longitudinal cohort at our center. Eligible PWH had serial carotid ultrasounds between 2010 and 2025; those with plaque at treatment baseline were excluded. We identified 107 incident plaque cases and 1:1 controls matched on baseline age and sex, comparing their demographics, treatment, HIV reservoir, and lymphocyte subsets at baseline, 1 year, 3 years, and last visit. In a random subset (n=20 per group), inflammatory proteins were measured by Olink Target 96 inflammation panel. Linear regression related baseline reservoir to annual IMT progression; two-sided p<0.05 was significant.

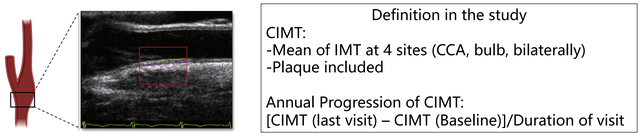
Results

Among 214 PWH (107 incident plaque; 107 controls), mean age was 44.2 years and 87.3% male. Median baseline CD4+ T cell count was 204 cells/μL, and median baseline HIV RNA was 4.81 (lg) copies/mL. Baseline mean carotid IMT was higher in plaque vs controls (0.93 vs 0.79 mm; p<0.0001) and remained higher after 5.9 years' follow-up (1.30 vs 0.82 mm; p<0.0001). 62.6% of carotid plaques were non-calcified. CD4+ T cell counts did not differ across visits, whereas HIV reservoir levels were consistently higher in the plaque group at all time points. Baseline reservoir was positively associated with annual IMT progression (R2=0.2185, p<0.0001). The proportion of HLA-DR+ CD8+ T cells was higher in the plaque group at 1 and 3 years and at last visit. Inflammatory profiling (n=20 per group) showed higher IL-8 (p<0.001), IL-18R1 (p<0.01), IL-6 (p<0.01), TGF-α (p<0.05), and VEGFA (p<0.05).

Higher HIV reservoir predicted incident carotid plaque and faster annual progression of CIMT.

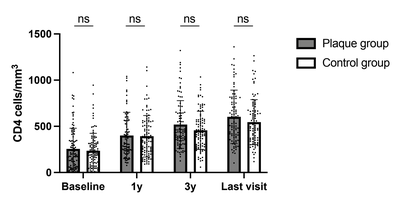
RESULTS

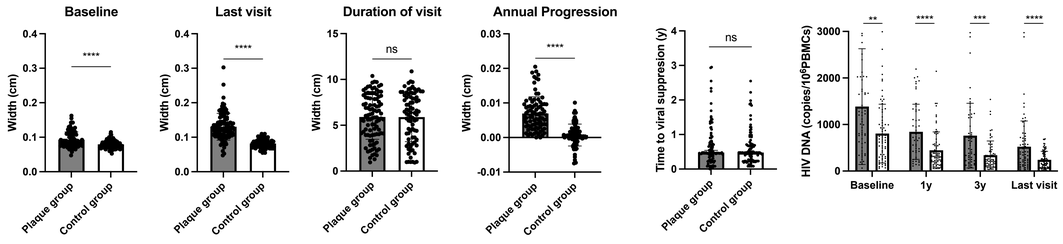




Definition in the study
CIMT:
-Mean of IMT at 4 sites (CCA, bulb, bilaterally)
-Plaque included

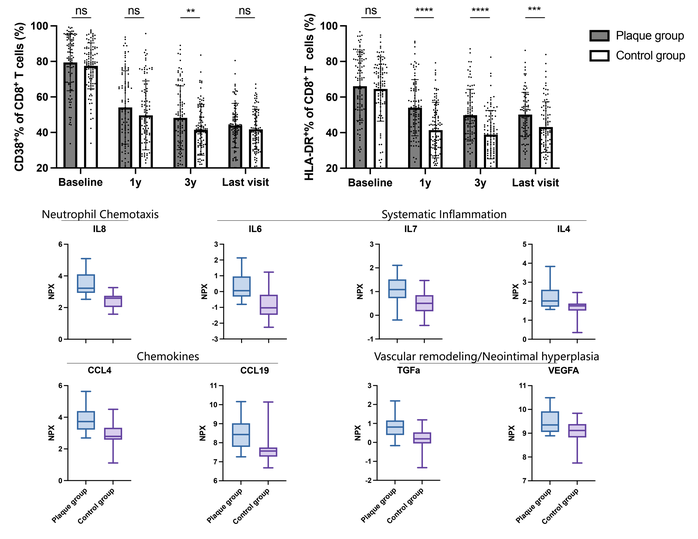
Annual Progression of CIMT:
[CIMT (last visit) – CIMT (Baseline)]/Duration of visit





	Annual Progression of CIMT (95% CI), mm	P value
HIV RNA (per IQR)		
Unadjusted	0.003 (-0.004 to 0.01)	0.361
Demographic adjusted[a]	0.003 (-0.006 to 0.008)	0.449
Demographic + Traditional cardiovascular risk factors adjusted[b]	0.001 (-0.006 to 0.008)	0.764
Multivariable adjusted[c]	0.001 (-0.005 to 0.008)	0.696
HIV DNA (per IQR)		
Unadjusted	0.017 (0.008 to 0.027)	<0.001
Demographic adjusted[a]	0.016 (0.006 to 0.025)	0.002
Demographic + Traditional cardiovascular risk factors adjusted[b]	0.015 (0.005 to 0.025)	0.004
Multivariable adjusted[c]	0.014 (0.003 to 0.024)	0.01
CD4 (per IQR)		
Unadjusted	-0.004 (-0.014 to 0.007)	0.489
Demographic adjusted[a]	-0.003 (-0.013 to 0.007)	0.55
Demographic + Traditional cardiovascular risk factors adjusted[b]	0 (-0.01 to 0.01)	0.948
Multivariable adjusted[c]	0 (-0.012 to 0.011)	0.947

[a]Controlled for Demographic (age, sex and race)
[b]Controlled for Demographic and Traditional cardiovascular risk factors (BMI, Diabetes, Hypertension, LDL-C, Creatine, Usage of statins)
[c]Controlled for Demographic, Traditional cardiovascular risk factors and HIV-related risk factors (ART duration, Treatment Failure, INR, HCV co-infection)



CONCLUSIONS

In this cohort, a larger HIV reservoir was associated with incident carotid plaque. Greater CD8+ T-cell activation, a proinflammatory profile, and faster IMT progression were found in plaque group. Viral persistence may contribute to atherosclerotic risk beyond immune recovery and supports reservoir monitoring for cardiovascular risk stratification and prevention in PWH.

ADDITIONAL KEY INFORMATION

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PLAIN LANGUAGE SUMMARY

- Close monitoring of the HIV reservoir is needed in PWH, especially those with high or slowly declining reservoir levels.
- Such patients may benefit from early cardiovascular screening and long-term follow-up to prevent cardiovascular events.