Vascular Disease and HIV infection

Surrogate markers of vascular disease:

- early development > non-infected age matched controls
- Carotid-intima thickness: non-invasive of detecting early dz
  
  Early in onset / some studies: equal to control pts. 10 yrs older!

Co-hort studies show ↑ incidence of clinical CAD

- HAART likely influences such earlier incidence

Paradox: current NCEP guidelines: HIV ≠ CAD RF

- HIV not “input” into Framingham 10 yr CDV risk calculator
- Potential “under-estimation” of actual CVD risk?
What is Carotid Intima–Media Thickness (CIMT)?

Mean CIMT 1.174 mm
Pathophysiologic basis of early Vascular dz: HIV Infection

Individual factors play a role
- ↑ smoking rates / sedentary lifestyles
- Baseline higher rates of Htn / IR / CKD (micro-albuminuria)

Biologic effect of chronic untreated infection
- CRP levels and chronic inflammatory state
- Inhibition of lipolysis: TNF and FFAs in the serum
- Body morphometric changes over time
  - Loss of peripheral fat
  - Increase in marked VAT (highly vascularized to the blood)
- Pro-thrombotic state / dys-immune vascular monocytes
Actions of Insulin

- Gluconeogenesis: Stop
- Glucose uptake in muscle and adipose tissue: Go
- Glucogenolysis: Stop
- Glycolysis: Go
- Lipolysis: Stop
- Glycogen synthesis: Go
- Ketogenesis: Stop
- Protein synthesis: Go
- Proteolysis: Stop
- Uptake of ions (especially K⁺ and PO₄⁻³): Go

Both HIV Infection and HAART Impact Lipid Parameters

- Seroconversion associated with: 
  ↓ in TC, LDL-C, and HDL-C

- HAART associated with: 
  – ↑ TC above normal
  – ↑ LDL-C to normal
  – HDL-C remained subnormal
Relative risk of cardiovascular disease among people living with HIV: a systematic review and meta-analysis

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Objectives
The aim of this study was to estimate the relative risk of cardiovascular disease (CVD) among people living with HIV (PLHIV) compared with the HIV-uninfected population.

Methods
We conducted a systematic review and meta-analysis of studies from the peer-reviewed literature. We searched the Medline database for relevant journal articles published before August 2010. Eligible studies were observational and randomized controlled trials, reporting CVD, defined as myocardial infarction (MI), ischaemic heart disease, cardiovascular and cerebrovascular events or coronary heart disease among HIV-positive adults. Pooled relative risks were calculated for various groupings, including different classes of antiretroviral therapy (ART).

Results
The relative risk of CVD was 1.61 [95% confidence interval (CI) 1.43–1.81] among PLHIV without ART compared with HIV-uninfected people. The relative risk of CVD was 2.00 [95% CI 1.70–2.37] among PLHIV on ART compared with HIV-uninfected people and 1.52 [95% CI 1.35–1.70] compared with treatment-naive PLHIV. We estimate the relative risk of CVD associated with protease inhibitor (PI)-, nucleoside reverse transcriptase inhibitor- and nonnucleoside reverse transcriptase inhibitor-based ART to be 1.11 [95% CI 1.05–1.17], 1.05 [95% CI 1.01–1.10] and 1.04 [95% CI 0.99–1.09] per year of exposure, respectively. Not all ART was associated with increased risk; specifically, lopinavir/ritonavir and abacavir were associated with the greater risk and the relative risk of MI for PI-based versus non-PI-based ART was 1.41 [95% CI 1.20–1.65].

Conclusion
PLHIV are at increased risk of cardiovascular disease. Although effective in prolonging survival, ART (in particular PI-based regimens) is related to further increased risk of CVD events among people at highest initial absolute risk of cardiovascular disease.
NCEP ATP-III Guidelines

Where is HIV as a Risk Factor?

<table>
<thead>
<tr>
<th>Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals</th>
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<tbody>
<tr>
<td>Cigarette smoking</td>
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<tr>
<td>Hypertension (BP $\geq$140/90 mmHg or on antihypertensive medication)</td>
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<tr>
<td>Low HDL cholesterol ($&lt;40$ mg/dL)*</td>
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<tr>
<td>Family history of premature CHD (CHD in male first degree relative $&lt;55$ years; CHD in female first degree relative $&lt;65$ years)</td>
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<tr>
<td>Age (men $\geq$45 years; women $\geq$55 years)</td>
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* HDL cholesterol $\geq$60 mg/dL counts as a “negative” risk factor; its presence removes one risk factor from the total count.

If 2 or more are present perform a 10 year cardiovascular risk assessment
IDSA Recommendations for Dyslipidemia Management in HIV-infected Patients

Obtain fasting lipid profile, prior to starting ARVS and within 3 to 6 months of starting new regimen.

Count number of CVD risk factors profile, and determine level of risk. If ≥2 risk factors, perform a 10-year risk calculation.

Intervene for modifiable nonlipid risk factors such as diet and smoking.

If above the lipid threshold based on risk group, despite vigorous lifestyle interventions, consider altering ARV therapy / lipid-lowering Tx.

LIPID-LOWERING DRUG THERAPY

- Serum LDL cholesterol above threshold, or TG 200 mg-500 mg/dL with elevated non-HDL cholesterol: STATIN
- Serum TG >500 mg/dL: FIBRATE

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