Cardiovascular Disease Management in HIV Infection

Turner Overton, MD
Professor of Medicine
University of Alabama at Birmingham
Birmingham, Alabama

Learning Objectives

After attending this presentation, learners will be able to:
- Describe changing epidemiology of CVD in HIV
- Identify risk factors for CVD in HIV
- Develop patient-centered strategies to prevent CVD

Expanding 1917 Clinic Population

<table>
<thead>
<tr>
<th>ART Utilization And Viral Suppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
</tr>
<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>All Patients seen in last 12 months</td>
</tr>
<tr>
<td>1970</td>
</tr>
<tr>
<td>Recorded CD4 in last 6 months</td>
</tr>
<tr>
<td>1623 (92%)</td>
</tr>
<tr>
<td># Receiving ART</td>
</tr>
<tr>
<td>1568 (92%)</td>
</tr>
<tr>
<td>HIV VL &lt; 1000 cp/mL</td>
</tr>
<tr>
<td>1668 (92%)</td>
</tr>
<tr>
<td>HIV VL &lt; 200 cp/mL</td>
</tr>
<tr>
<td>1547 (75%)</td>
</tr>
<tr>
<td>HIV VL &lt; 50 cp/mL</td>
</tr>
<tr>
<td>1547 (75%)</td>
</tr>
</tbody>
</table>

QM Metrics: ART
1. > 85% on ART
2. > 85% on ART VL < 1000 cp/mL
3. > 80% on ART VL < 50 cp/mL

134 not receiving ART
79 pts with CD4 > 500
44 pts with CD4 200-500
7 pts with CD4 < 200
CD4 counts at clinic entry are increasing!

Case

- A 45 yo white male presents for care.
  - He smokes and had a BMI of 24.5 kg/m².
  - BP is 145/86. He does not exercise.
  - CD4 count is 325 c/mm³ (16%)
  - Plasma HIV RNA of 42,000 cp/mL.
  - Total cholesterol is 196 mg/dL, LDL 125 mg/dL, HDL 25 mg/dL, TG 175mg/dL.
- What is the most important intervention to reduce cardiovascular disease risk?

ARS Question: What is the most important intervention to reduce cardiovascular disease risk?

1. Smoking cessation
2. Initiate Mediterranean Diet
3. Initiate statin
4. Initiate daily aspirin
5. Initiate ART
CVD Mortality Higher in HIV-positive, even with Suppressed HIV Virus.

- 145,009 HIV+ subjects 2001-2012
  - 71% male, median age 49 yrs
  - CVD mortality 54% ↑increase (7→13%)
  - Decreasing in gen population
  - aHR 1.54 (95% CI: 1.47-1.62)
  - Adjusted for age, sex, race/ethnicity, location, and year
- Rate if VL > 400cp/mL: 7.7/1000pt yr
- Rate if VL suppressed: 3.9/1000pt yr
- General population: 3.2/1000pt yr

Lifespan increased but increased burden of CVD

- 1.5-2 fold increased risk

Impact of HIV on risk comparable to traditional risk factors including HTN, DM and hyperlipidemia.

- Increased risk for
  - Myocardial infarction
  - Ischemic stroke
  - Heart failure
  - Pulmonary Hypertension
  - Venous thrombosis

Risk Factor Contribution to CVD

- Diabetes
- Lipids
- Current Smoking
- HCV
- HTN
- Sex
- Race
- Age
- Year

Increasing Burden of CVD among Adult PWH

Males Aged >25 years

Females Aged >25 years
Increased CVD Risk is Multifactorial

Interplay between
- Traditional Risk Factors
- HIV-specific Risk Factors (Immune activation/Inflammation)
- ART-related toxicities
- Certain behaviors (i.e. smoking)
- Disparities in access/receipt of care

The Inflammation Hypothesis
- Many pathogenic stimuli induce a similar inflammatory response.
  - Interleukins
  - Tumor Necrosis Factor
  - TGF-beta
- With removal of the stimulus, Inflammation decreases
  - Healing occurs
- When the stimulus persists
  - Pathogenic responses occur
    - Fibrosis
    - Tissue destruction
    - Altered function
    - Progressive Disease

HIV INFECTION
END ORGAN DISEASE
Residual CV Disease Risk With Suppressed Viremia

- Vascular inflammation is greater with HIV infection
  - Increased metabolically active macrophages
  - Greater non-calcified, metabolically active, rupture-prone plaque

Potential Interventions Beyond Suppressive ART

- Smoking cessation
- Key lifestyle factors
  - Diet
  - Exercise
- ART Switch
- Lipid lowering therapy, aka statins
- Address other traditional factors
  - HTN
  - DM/Insulin resistance

ARS Question: In a suppressed patient with a history of MI, which statement about statin use is accurate?

1. Persons on ART should avoid statin therapy given overlapping toxicity.
2. Simvastatin is the preferred statin for persons on ART.
3. Statin dosing is the same for persons with HIV as the general population.
4. HIV protease inhibitors interact with some statins and increase the risk of statin-related adverse events.
5. In HIV, statin therapy is used to raise HDL since LDL is not a reliable measure in the setting of HIV infection.
Statins Reverse Atherosclerosis!

- **Atorvastatin**: Reduction in Coronary Artery Plaque Volume by coronary CT angiography (CCTA).
  - Coronary plaque in:
    - 53% of the HIV group (also rupture-prone noncalcified plaque)
    - 35% of the HIV-negative group
  - Regression with Atorvastatin beyond expected with LDL lowering alone

**Baseline** | **Month 12**
---|---
Plaque Regression with Atorvastatin


**KEY RECOMMENDATIONS**

- Clinicians should be aware that HIV-infected patients are at an increased risk for ASCVD.
- Risk is independent of major established risk factors.
- A fasting lipid panel should be obtained in all newly identified HIV-infected patients.
- For primary prevention, HIV infection may be counted as an additional risk factor for risk stratification.
- Statin therapy is first-line therapy for elevated LDL-C and non-HDL-C.
- Drug-drug interactions must be considered.
- Atorvastatin, rosuvastatin, and pitavastatin are preferred agents.

**Randomized Trial to Prevent Vascular Events in HIV: REPRIEVE (A5332)**

Principal Investigators: Steven Grinspoon, MD, Pamela S Douglas, MD, Udo Hoffmann, MD, MPH, Heather Ribaudo, PhD

Funded by NHLBI and NIAID. Supported by Kowa Pharmaceuticals.
ARS Question: Which statement about the metabolic syndrome is accurate?

1. The metabolic syndrome is not applicable to persons with HIV.
2. The metabolic syndrome is correlated with cardiovascular disease risk.
3. The metabolic syndrome predisposes patients to chronic obstructive pulmonary disease.
4. Persons with the metabolic syndrome should be referred to a neurologist for neurocognitive testing.
5. I am currently in a metabolic syndrome because of the delicious desserts that Donna Jacobson provided at lunch.

Don’t Forget:
The “ABCDEs” of Cardiovascular Disease Management

A: Aspirin
B: Blood pressure
C: Cholesterol
D: Diabetes
E: Exercise
S: Smoking

ASPIRIN Use For Primary Prevention

US Preventive Services Task Force

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;50 yrs</td>
<td>Insufficient Evidence to Recommend</td>
</tr>
<tr>
<td>Age 50-59 with 10% CVD risk</td>
<td>Low Dose ASA for primary CVD prevention</td>
</tr>
<tr>
<td>Age 60-69 with 10% CVD risk</td>
<td>Low Dose ASA for primary CVD prevention (Unless bleeding risks prohibit)</td>
</tr>
<tr>
<td>Age ≥70 yrs</td>
<td>Insufficient Evidence to Recommend</td>
</tr>
</tbody>
</table>

Cross sectional study from UAB 1917 HIV Clinic
• Only 17% who qualified were prescribed ASA


Underutilization of ASA for primary CVD prevention.
How to Beat Inflammation and Prevent CVD

- Adherence to HIV medications. Stay undetectable
- Smoking cessation
- Maintain normal weight
- If overweight, lose at least 5-10% of body weight
- Exercise
- Have a healthy diet
- Cut down on alcohol, avoid drugs

We Mind Very Much If You Smoke

- Tobacco use decreased in the US population
  43% in 1964 → 19% in 2010
  Remains leading cause of preventable death → Contributing to >440,000 deaths annually.
- 40-60% of PLWH continue to smoke tobacco
  Independent risk factor for all cause mortality


Lifestyle Modification: Diet

- Cutting 500 calories per day will decrease your weight by 1-2 lbs week
- Watch portion sizes
- Watch liquid calories (soda, juice, fruit drinks)
- Go natural
  Avoid foods in boxes and cans (less salt and preservatives)
  Maximize fresh fruits and vegetables

- Effect of Cutting 500 cal/day for 8 wks in Obese HIV neg Persons
  - Significant declines in inflammation
    CRP
    IL-6
    TNFα
    Homocysteine
**Lifestyle Modification: Exercise**

- 150 minutes/week of exercise (minimum)
  - Do something you like (combination of cardio/strength)
- Set a fitness goal (e.g., 5K race)
- Find a fitness buddy
- Unplug
- Be active during day: If job is sedentary, take breaks to walk
- Take stairs rather than elevator; park further away to walk to work

**Exercise Training Reduced Oxidative Stress and Improves Functional Status in HIV**

- 8 week intervention of 24 sessions (aerobic, resistance, or combined)

  ![Graph](image)

  - Significant improvements in muscular strength and cardiopulmonary function.

**HIV and CVD Summary**

- HIV and its therapy contribute to cardiac risk along with the traditional host factors
- Controlling viral replication partially reduces CVD risk.
- Early ART may significantly mitigate HIV-associated CVD risk.
- No reliable inflammatory markers to predict risk.
- Currently available risk scores fail to accurately estimate CVD risk in the setting of HIV infection.
- Smoking cessation, dietary and exercise interventions are effective.
- Statins may provide benefit in addition to lipid lowering effects.
- HOWEVER, more data are needed to inform use in traditional low risk populations.
Question-and-Answer
Cardiovascular Disease Management in HIV Infection
*Turner Overton, MD*

**SUGGESTED READINGS**


