Learning Objectives

After attending this presentation, learners will be able to:

▪ Describe the common comorbidities occurring in the aging population of persons with HIV
▪ Educate and counsel persons with HIV on risk factor modification to reduce co-morbidities associated with aging
▪ Detect and manage comorbid conditions among persons with HIV according to evidence-based guidelines

Introduction

▪ HIV infection, even when controlled, is associated with chronic immune activation that is superimposed upon immunologic senescence in the older adult
▪ Older persons may be diagnosed later and have more advanced HIV infection at presentation
▪ There is a less robust immunologic response to antiretroviral therapy in this population
▪ HIV-infected patients accumulate “age-related” diseases at a younger chronological age and these conditions account for majority of deaths
▪ Providers need guidance on how best to manage PWH with comorbidities: manifestations, drug interactions, drug vs disease vs host interplay
New HIV Diagnoses by Age United States, 2016

People Living with HIV by Age United States, 2015

HIV Among People Aged 50 and Older

Since the 1980s, the percentage of PWH > 50 years has gradually increased.

- In 2015, approximately 47% of HIV-infected persons in the US were > 50 years old. 16% were > 65 years old
- In 2016, 17% of newly diagnosed cases of HIV infection were in adults ≥ 50 years old with 35% dx AIDS (down from 40% 2015)
- African Americans accounted for 42% of cases, whites for 37% of cases, and Hispanics/Latinos for 18%
- MSM is the most common mode of transmission in older men, and heterosexual contact is the most common mode in older women

Chicago, Illinois, May 23, 2019
Aging with HIV

- Increased life expectancy on ART. However, life expectancies still shorter than for general population
  - Especially for low CD4 and/or salvage regimens
- What is the impact of increased life expectancy on comorbidity prevalence and types?
- More likely to be treatment experienced with consequences of previous ART toxicities
- The impact of increased comorbidity on
  - Timing of ART initiation
  - Appropriateness of primary care practice guidelines (e.g., colorectal cancer screening). No systematic method to predict whether guidelines developed on general population should apply to individuals with HIV

Health Conditions and Prescriptions

- Cardiovascular: Arrhythmias, ASCVD, CHF, Transplant, Valvular HD
- Endocrine: Bone, Diabetes, HLD, Hormonal
- Kidney: Acute and Chronic; Transplant
- GI/GU: Malignancies
- Liver: HBV, HCV, NAFLD, Transplant
- Lung: COPD, Malignancies; Transplant
- Nervous System: Cognitive, Central vs Peripheral
- Psychosocial: Depression, Substance Use
Tobacco


HIV and Multimorbidity 2000-2009

HLD and HTN remain most common

Hypercholesterolemia

Hypercholesterolemia

Hypertension

Diabetes

CKD
Cardiovascular Disease Mortality Among HIV-Infected

- In HIV+ individuals, CVD deaths increased from 6% to 15% of all deaths (p<0.001)
  - Decreased in the general population: 47% → 39%
- HIV associated with a 56% increased rate of CVD death
- Both viremic and virologically suppressed HIV+ individuals had higher CVD mortality rates than uninfected individuals until age 65.

New York City HIV Surveillance Registry
Evaluation of age-adjusted mortality rates due to CVD in New York City from 2001-2012; N=29,588 deaths

<table>
<thead>
<tr>
<th>Age Group</th>
<th>CVD Mortality Rates</th>
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</thead>
<tbody>
<tr>
<td>25-34 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>35-44 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>45-54 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>55-64 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>75-84 yrs</td>
<td>0.10/1,000</td>
</tr>
<tr>
<td>85+ yrs</td>
<td>0.10/1,000</td>
</tr>
</tbody>
</table>

CVD mortality was lower among HIV-diagnosed individuals with a suppressed HIV RNA level (<40 copies/mL) versus an unsuppressed level (age-standardized rate 3.9 vs. 7.7/1,000, p<0.001).
Defining CVD risk among PWH

- Risk scores fluctuate as we age, change behaviors and treat conditions
- At what time is the risk score accurate?
- When does HIV contribute to risk?
**HIV as Risk Enhancing Factor**

- In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), risk-enhancing factors favor initiation of statin therapy
- Risk-enhancing factors may favor statin therapy in patients at 10-year risk of 5-7.5% (borderline risk).

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**Top 10 Take Home Messages**

6. In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician–patient risk discussion before starting statin therapy.

Risk discussion should include a review of major risk factors (e.g., cigarette smoking, elevated blood pressure, LDL-C, hemoglobin A1C [if indicated], and calculated 10-year risk of ASCVD);
- the presence of risk-enhancing factors (see No. 8);
- the potential benefits of lifestyle and statin therapies;
- the potential for adverse effects and drug–drug interactions;
- the consideration of costs of statin therapy; and
- the patient preferences & values in shared decision-making.

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**Imaging**

- In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dl-89 mg/dl (≥1.8-4.9 mmol/L), at a 10-year ASCVD risk of ≥7.5%-19.9%, if a decision about statin therapy is uncertain, consider measuring CAC.
  - If the CAC score is zero, treatment with statin therapy may be withheld or delayed, except in cigarette smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD.
  - A CAC score of 1-99 favors statin therapy, especially in those >55 years of age.
**Cardiovascular Disease Prevention: Lipid Management**

- Screening: fasting or non-fasting lipids
  - At HIV diagnosis
  - Start of ART
  - Change of ART
  - To assess response to statin
  - Every 12 months

<table>
<thead>
<tr>
<th>Statin</th>
<th>Level of Use</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>Safe (Precaution with DRV/r)</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Safe (Precaution with DRV/r)</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Safe (Precaution with DRV/r)</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Safe (Precaution with DRV/r)</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>

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**INTREPID: Statins Work in PWH with Dyslipidemia**

**REPRIEVE Study Design**

- Study Design:
  - Asymptomatic people with HIV, 10-year ASCVD risk ≥15%
  - Randomization
  - Follow-up: 5 years
  - Outcomes: cardiovascular disease, death, non-AIDS-related death, non-AIDS-related disease, secondary endpoints
Background ASA

- PWH on ART have an increased risk of ischemic cardiovascular events
- Activated platelets have been implicated in thrombotic cardiovascular events because of their proinflammatory and thrombogenic effects
- HIV-infected patients have increased circulating platelet-monocyte complexes and their platelets express high levels of P-selectin
- Aspirin is a low-risk and low-cost platelet inhibitor that has immunomodulatory properties
- Aspirin decreases risk of mortality and cardiovascular events in individuals with known CVD and may play an important role in cardiovascular and cancer prevention in those at risk

Refs:


Aspirin Benefits

- Aspirin has proven benefits in secondary prevention
- Questionable to no benefits as primary prevention except in DM
  - ARRIVE: over 12,000 pts RCT asa 100 mg vs plb over 5 years (Lancet 2018; 392:1036-1046)
    - No significant differences in the rates of deaths, heart attacks, or strokes
    - Significant increase in GIB
  - ASCEND: over 15,000 pts with DM RCT over 7.4 years (N Engl J Med 2018; 379:1529-1539)
    - Serious vascular events 658 participants [8.5%] vs. 743 [9.6%]; rate ratio, 0.88; 95% confidence interval [CI], 0.79 to 0.97; P=0.01
    - Major bleeding events occurred in 314 participants (4.1%) in the aspirin group, as compared with 245 (3.2%) in the placebo group (rate ratio, 1.29; 95% CI, 1.09 to 1.52; P=0.003)

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Diabetes Mellitus 2019 ADA Definitions

- 1. A1C ≥6.5%
- 2. Fasting plasma glucose ≥ 126 mg/dL, confirmed by repeat testing
- 3. Plasma glucose 2 hours after 75 g oral glucose tolerance test ≥ 200 mg/dL
- 4. Random plasma glucose ≥ 200 mg/dL with polyuria and polydipsia

- "In conditions associated with an altered relationship between A1C and glycemia, such as sickle cell disease…HIV….only plasma blood glucose criteria should be used to diagnose diabetes."

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A1C Studies based on prior ART

- Eckhardt BJ, Holzman RS, Kwan CK et al. Glycated Hemoglobin A1c as screening for diabetes mellitus in HIV-infected individuals. AIDS Patient Care STDS. 2012;26:197-201
A1C may under or over estimate depending on ART

- HIV (n=100)
- Control (n=200)

HIV (n=100) - Control (n=200)

http://www.shef.ac.uk/FRAX/

FRAX® WHO Fracture Risk Assessment Tool

Calculation Tool

http://www.shef.ac.uk/FRAX/

Work-up

- 10 year fractures risk in USA
- 20% high fracture score
- 0% low risk

Secondary cause

- 10 year fractures risk
- 20% high fracture score
- 0% low risk

Treatment

- Treat secondary cause
- Life style advice
- Continue ART
- Consider high-fracture therapy or other treatment

Follow-up

- Monitor BMI in 3-5 years
- Monitor BMI in 3-5 years
Take Home Points

- Excess CVD risk in HIV + population (1.5 x)
- Individuals aging with HIV vs. Individuals newly diagnosed with different CVD risk
- Largest modifiable RF for co-morbid conditions is smoking
- **Etiology multifactorial**: chronic inflammation, direct viral effect, ARVs etc.
- Treat HIV and manage co-morbidities aggressively
- Need for improved risk assessments
- AAA screening if male, over 65 and smoke
- Use FBS to diagnose diabetes in PWH (although may be accurate on newer ART)
- Over age 40 PWH and diabetes w/ LDL >70 should be on a statin and aspirin if no contraindications (often overlooked population in HIV clinical practice).