HIV & Aging Co-Morbidities: An update on bone and cardiovascular disease

Jeffrey Kwong, DNP, MPH, ANP-BC, ACRN, AAHIVS
President, ANAC Board of Directors
Professor, Rutgers University

Co-Morbidities:
Elderly vs Geriatric (n=16,436; n=572)

Fast Facts: Falls

- Falls result in more than 2.8 million injuries annually,
- 800,000 hospitalizations
- 27,000 deaths

Source: CDC, 2019
Bone Mass Over Time

![Bone Mass Graph]

Bone Loss

- Osteopenia vs Osteoporosis

![Bone Images]

Healthy/NORMAL  OSTEOPENIA  OSTEOPOROSIS
Bone Health: Epidemiology

- Age-adjusted fracture rates were **1.98 to 3.69 times higher** in PLWH vs general population
- 48 - 67% osteopenia
- 5 - 34% osteoporosis


Risk Factors for Bone Loss

- Female gender
- Advanced age
- Lower BMI
- Physical inactivity
- Corticosteroids
- Menopause
- Smoking
- Weight loss
- Malnutrition
- Hypogonadism
- Vitamin D deficiency
- HIV ART
- Medications
- HCV infection
ART and Bone Loss

• Studies indicate increased rate of bone loss with ART.

• Further studies needed to clarify clinical significance of these BMD declines

• Protease Inhibitors > NNRTI


ART and Bone Loss

• Tenofovir DF > Tenofovir AF

Study 109: Change in lumbar spine and hip BMD at Weeks 24 and 48\(^1,2\)

Results of BMD analysis

Source: Descovy Prescribing Information, 2019
DXA Scan

T and Z Scores

T-score shows bone density vs a healthy 30-year old adult.
Z-score shows bone density vs age-matched adult.
FRAX®

- Fracture risk prediction tool developed by WHO
- Combines BMD + clinical risk factors to predict fracture risk better than either alone
- Predicts the 10-year probability of major osteoporotic fracture

https://www.sheffield.ac.uk/FRAX/
Benefits of FRAX®

- Treatment decisions in osteopenic patients clearer
  - Decision is based on the risk of fracture, not T-score alone
- Identifies patients at high-risk for fractures to ensure that they are offered treatment to lower their risk
- Helps avoid giving medication to those who are at low risk and have little to gain from treatment

“Specific treatment decisions must be individualized”

Bone Health: Screening Recommendations for PLWH

- Age < 40
  - No screening needed

Bone Health: Follow Up Screening

- **FRAX**: recalculate every 2-3 years
- **DXA**
  - If T score was -1 to -1.99, repeat in 5 years
  - If T score was -2 to -2.49, repeat in 1-2 years

- **If started on bisphosphonates**:
  - repeat DXA in 2 years
  - reassess need for bisphosphonates in 3-5 years

---

Calcium Intake Recommendations From the IOM

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Estimated Requirement (mg/day)</th>
<th>Recommended Dietary Allowance (mg/day)</th>
<th>Upper Level Intake (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31–50 y.o.</td>
<td>800</td>
<td>1,000</td>
<td>2,500</td>
</tr>
<tr>
<td>51–70 y.o. male</td>
<td>800</td>
<td>1,000</td>
<td>2,000</td>
</tr>
<tr>
<td>51–70 y.o. female</td>
<td>1,000</td>
<td>1,200</td>
<td>2,000</td>
</tr>
<tr>
<td>&gt;70 years old</td>
<td>1,000</td>
<td>1,200</td>
<td>2,000</td>
</tr>
</tbody>
</table>
Vitamin D Intake Recommendations From the IOM

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Estimated Avg Requirement (IU/day)</th>
<th>Recommended Dietary Allowance (IU/day)</th>
<th>Upper Level Intake (IU/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31–50 years old</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>51–70-year-old male</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>51–70-year-old female</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
<tr>
<td>&gt;70 years old</td>
<td>400</td>
<td>600</td>
<td>4,000</td>
</tr>
</tbody>
</table>


Exercise for Osteoporosis

- Weight bearing Exercise: 30 min most days
- Muscle-strengthening: 20 min 2-3 days/week
- Flexibility/Balance/Posture: Daily Rotate
Pharmacologic Treatment for Osteoporosis/Osteopenia in PLWH

• Data with alendronate (Fosomax)

• Limited data with:
  • Zoledronic acid (Reclast)
  • Teriparatide (Forteo)
  • Denosumab (Prolia)
  • Calcitonin (Fortical)
  • Raloxefine (Evista)

Bisphosphonates

• **Alendronate (Fosomax):** 10 mg daily (tablet) or 70 mg weekly (tablet or liquid) for treatment, 5 mg daily or 35 mg weekly for prevention

• **Risedronate (Actonel):** 5 mg daily or 35 mg weekly (tablet); 150 mg monthly (tablet)

• **Ibandronate (Boniva):** 150 mg monthly by tablet; 3 mg intravenously over 15 to 30 seconds every 3 months

• **Zoledronic acid (Reclast):** 5 mg by intravenous infusion over a minimum of 15 minutes once every year for treatment—and every other year for prevention

Bisphosphonates

Contraindications/Warnings/Precautions
- Creatinine clearance <30 cc/min (<35 cc/min for zoledronic acid)
- For oral dosing: Esophageal stricture or impaired esophageal motility (alendronate); inability to stand or sit for at least 30 minutes (alendronate/risedronate) or 60 minutes (ibandronate)

Oral dosing requirements
- Tablets (with exception of delayed release risedronate) taken on an empty stomach after overnight fast with 6 to 8 oz of plain water while in an upright position
- Patients should not eat or lie down for at least 30 minutes (alendronate and risedronate) or 60 minutes (ibandronate)

“Osteonecrosis” of the Jaw (ONJ)
- 95% of cases have been reported with high-dose, chronic IV bisphosphonate treatment of myeloma and cancer metastatic to bone\(^1\)
- Can occur with denosumab\(^2\)
- Known risk factors: invasive dental procedures, oral trauma, periodontitis, poor oral hygiene, radiotherapy to the jaw, chemotherapy, corticosteroids, infection
- Pathogenesis is not known\(^3\)

FDA Safety Warning

• Be aware of the possibility of atypical fractures in patients taking bisphosphonates

• Evaluate any patient who presents with new groin or thigh pain to rule out fracture of the femoral shaft

• Discontinue potent antiresorptive medication in patients with atypical fractures

• Periodic reevaluation of need to continue bisphosphonate therapy, particularly in patients treated > 5 years

osteoporosis-drugs-bisphosphonates-and-atypical

Bisphosphonate Holidays

• In patients at high risk for fractures, continued treatment seems reasonable. Consider a drug holiday of 1 to 2 years after 10 years of treatment

• For lower risk patients, consider a “drug holiday” after 4 to 5 years of stability

• Follow BMD and bone turnover markers during a drug holiday period, and reinitiate therapy if bone density declines or markers increase

Switching ART

• There is no evidence that switching ART will reduce fracture risk in those with established osteoporosis
• Consider avoiding TDF and boosted-protease inhibitors in patients at high risk for fragility fracture
• Switch TDF -> TAF


Fall Prevention Strategies

• Wear Sensible Shoes
• Check Vision
• Avoid Sedating Meds
• Declutter Environment
• Watch Pet
• Lighten up your Space
• Use Assistive Devices
• Exercise
Summary of Optimal Osteoporosis Management

• Utilize tools to identify high-risk patients
• Target any patient with a fracture for evaluation
• Ensure adequate calcium and vitamin D
• Promote physical activity
• Discuss pharmacologic options with high-risk patients
HIV and CVD

- PLWH are at higher risk of atherosclerotic disease – including MI and Stroke, heart failure, and PAD
- Lower CD4 and HIV viremia are risk factors
- Even in setting of virologic control, MI risk is > than non-PLWH

Rate of mortality if VL > 400copies/mL: 7.7/1000pt yr
Rate of mortality if VL suppressed: 3.9/1000pt yr
General population: 3.2/1000pt yr

Increased CVD Risk is Multifactorial

HIV
Pro-coagulation
Pro-atherogenic lipid profile
Immune activation and inflammation
CD4+ T cell depletion
Immune senescence

Individual
Family history
Smoking
Alcohol/illicit drug use
Obesity
Latent virus co-infection
Natural aging process

Non AIDS-defining comorbidities

Antiretroviral
Direct toxicity
Insulin resistance
Pro-atherogenic lipid profile
Mitochondrial toxicity
Body fat changes

ASCVD Management in PLWH

• Initial step is to get all PLWH on ART and virologically suppressed.

• If on ART and virologically controlled, then consider other risk factors, including modifiable and non-modifiable risk factors.

Prevention and Treatment of HIV-associated ASCVD and HF

• Lifestyle optimization
  • Smoking cessation
  • Limiting alcohol consumption
  • Regular physical activity
  • Diet (healthy protein, whole grains, limiting sugar and red meats)

• Managing Co-Morbid Conditions
  • Diabetes
  • Hypertension
ASCVD Risk Assessment Algorithm

**HIGH RISK APPROACH**
Consider referral to cardiologist; patient-clinician discussion re: benefit vs. risk, patient preference

**LIFESTYLE OPTIMIZATION**
(Particularly Smoking Cessation)

+ **LIPID LOWERING DRUG THERAPY**
  - Atorvastatin 10-80 mg*
  - Rosuvastatin 5-40 mg*
  - Pitavastatin 2-4 mg

Statin Dosing: START LOW, GO SLOW
Decrease dose or discontinue if severe myalgia or unexplained muscle weakness, LFTs >3x the upper limit of normal, or CK >10x the upper limit of normal

Add-On Therapy or Intolerant of Statin

• Ezetimibe (Zetia) 10mg once daily

• Proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9)
  - Evolocumab (Repatha) 140 mg q 2 weeks or 240mg monthly
  - Alirocumab (Praluent) 75mg q 2 weeks or 300mg q 4 weeks
ASCVD Risk Assessment Algorithm

HIV-Related CVD Risk-Enhancing Factors?
Any of the following:
- History of prolonged HIV viremia and/or delay in ART initiation
- Low current or nadir CD4 count (<350 cells/mm³)
- HIV treatment failure or non-adherence
- Metabolic syndrome, lipodystrophy/lipoatrophy, fatty liver disease
- Hepatitis C Virus Co-infection

Risk may not be greater than calculated ASCVD risk
Contemporary studies suggest that people with promptly treated HIV without sustained viremia or immunosuppression may not have significantly elevated ASCVD risk.

Risk may be greater than calculated ASCVD risk
Consider adjusting risk upward. Studies generally demonstrate 1.5-2-fold greater risk for ASCVD in persons with HIV, particularly if there is a history of prolonged viremia, delayed ART initiation, and/or low CD4 count.
http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#/calculate/estimate/
Aspirin 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</td>
</tr>
<tr>
<td></td>
<td>(Unless bleeding risks prohibit)</td>
</tr>
<tr>
<td>Age ≥70 yrs</td>
<td>Insufficient Evidence to Recommend</td>
</tr>
</tbody>
</table>

Suggested Statins in the Setting of ART

Dubé MP. Lipid Management, DOI 10.1007/978-3-319-11161-2_14
What about other forms of screening?

• “Insufficient data to recommend routine measurement of subclinical atherosclerosis on imaging or inflammatory biomarkers because the additive value in risk stratification in HIV is unclear.”

Disparities in CVD and HIV

• PLWH less likely to receive ASA therapy (5.1% vs 13.8%), or use statins (23.6% vs 35.8%).

• Women LWH less likely to receive lipid-lowering, anti-HTN, ACE/ARB, an invasive cardiovascular procedures post-MI

• Persons with SUD less statin use (23% vs 40%)

• Disparities in the South 4x higher vs other regions
How to address this?

- More research
- Healthcare reimbursement
- Care coordination and IPCP

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

Herradorff HH. Endocrine. 2009 Dec;36(3):445-51
Lifestyle Modification: Exercise

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

HIV and CVD Summary

• CVD is a **growing concern** as population ages.

• **ART** remains an **important** aspect of managing risk.

• **Lifestyle modification** can reduce risk.

• Important to **assess** patients for **CVD risk** and educate on ways to decrease risk.

• **Primary** and **secondary risk reduction** is an important aspect of caring for PLWH as they age.
References & Resources

• HIV-Age.org
  www.hiv-age.org

• HIV and Aging: HIV –NYS Guidelines
  http://www.hivguidelines.org/clinical-guidelines/hiv-and-aging

• Adults 50 and Over
  http://www.cdc.gov/hiv/group/age/olderamericans/index.html

• American Heart Association
  www.heart.org