Osteoporosis Screening in HIV

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Osteoporosis Screening in HIV

- Some definitions
- Epidemiology
- Bone loss and HIV: Pathogenesis
  - From HIV
  - From Antiretroviral Therapy
  - Traditional Risk Factors
- Screening recommendations
Bone Health: Some Definitions
Bone Health: Some Definitions

- **T-score**: BMD measurement: the number of standard deviations from the BMD of a healthy 30 yo same sex person.
- **Z-score**: BMD measurement: the number of standard deviations from the BMD of a healthy same aged person. Z-scores are not used to determine osteoporosis or the need for treatment.
- **Osteoporosis**: a T-score < - 2.5
- **Osteopenia**: a T-score between -1 and -2.5
- **Osteomalacia**: loss of mineral content of bone
Bone Health: Some Definitions

• FRAX: WHO Fracture Risk Assessment Tool that incorporates clinical factors in addition to BMD to predict fracture risk
• Fragility fracture: a fracture resulting from a fall from a standing position
• Bone mineral density (BMD): bone mass/bone volume (or area)
• Dual X-ray Absorptiometry (DXA): uses 2 low energy X-ray beams to determine absorption by soft tissue and bone. Then calculates bone absorption by correcting for soft tissue absorption; absorption correlates with bone mass. Bone mass is divided by a calculated bone area to yield (areal, not volume) bone mineral density (BMD: bone mass/bone area or volume)
Bone Health: Epidemiology
Bone Health: Epidemiology

- Brown et al AIDS 2006: meta-analysis of 11 cross-sectional studies
  - 30-40 yo HIV+ males
  - 67% osteopenia, 15% osteoporosis
  - OR (HIV+/HIV-): 6.4 for osteopenia; 3.7 for osteoporosis
Bone Health: Epidemiology

- Triant et al; J Clin Endocrinol Metab 2008
  - 8525 HIV+ pts and 2.2+ million HIV – pts

Fracture Prevalence

Women

Men
Bone Health: Epidemiology

- **Cutter AIDS 2014 (HIV UPBEAT Study)**
  - Prospective study of 474 patients, 210 HIV +
  - Results:
    - HIV associated with lower BMD at the femoral neck, total hip and lumbar spine after adjustment for demographic, lifestyle and BMI.
    - HIV+ patients had higher markers of bone turnover
    - Exposure to ART was not associated with BMD

- **Kooij JID 2014 (The AGEhIV Cohort)**
  - Used DEXA to compare BMD in 581 HIV+ and 520 HIV- patients > 45 years
  - Results
    - Osteoporosis more common in HIV+ (13.3% Vs 6.7%)
    - After adjustment for weight and smoking the difference was no longer significant
Bone Health: Epidemiology

  - Veterans Aging Cohort Study (VACS): 1997 – 2009
  - N = 119,318, 33% were HIV+

- Results:
  - Fragility fracture rate: 2.5/1000 py (HIV+), 1.9/1000 py (HIV-)
  - Adjusted HR (for traditional RF): 1.24 (1.11-1.39)
  - Adjusted for BMI: 1.10 (0.97-1.25)
  - Protease inhibitor use: HR: 1.41 (1.16-1.70)
Bone Health: Pathogenesis
Bone Health: Pathogenesis: HIV

- Effects of HIV (mostly from in vitro studies)
  - \(vpr\) and \(gp120\) increase osteoclast activity
  - \(gag\) proteins suppress osteoblast activity
  - Activated T-cells express increased Receptor-Activator NFκB (RANKL) – potent osteoclast activator
  - HIV is associated with decreased production of osteoprotegerin (counteracts action of RANKL)
  - Enhanced expression of other cytokines (TNF-\(\alpha\), IL-1 and IL-6) increase osteoclast activity

(McComsey, CID, 2010)
Bone Health: Pathogenesis: ART

- Effects of Antiretroviral Therapy: SMART: Decreased BMD in those on continuous ART

(Grund, AIDS, 2009)
Bone Health: Pathogenesis: ART

• Effects of Antiretroviral Therapy
  - Most studies show a 2-6% loss of bone in the first 1-2 years after ART (thought due to rise is CD4 count and increased expression of RANKL and TNF-α…increases osteoclast activity)
  - This is then followed by stabilization of BMD

• Individual agents:
  - Protease inhibitors are associated with lower BMD and increased fracture risk (PIs may inhibit osteoclast/blast differentiation and do inhibit 1-α–hydroxylase activity leading to decreased vitamin D synthesis)
  - Efavirenz is associated with lower BMD, perhaps through increased metabolism of vitamin D
  - Tenofovir: most studies show a decreased in BMD of 0.5 to 2% and TDF is associated with increased fracture risk (mediated through PO4 wasting)

Traditional risk factors (some are over-represented in HIV+):
- Smoking, low body weight, alcohol, opiates, low physical activity, hypogonadism, older age, low vitamin D levels

Veterans Aging Cohort Study: N = 40,115; 588 fractures

Fracture and Age

(Womack JA, CID, 2013)
Bone Health: Screening Recommendations
## Bone Health: Screening Recommendations

<table>
<thead>
<tr>
<th>Agency</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>USPSTF</td>
<td>Women &gt; 65 or &lt;= 65 if risk for fx is &gt;= that of a 65 yo (9.3% 10 yr fx risk)</td>
</tr>
<tr>
<td></td>
<td>No screening for men</td>
</tr>
<tr>
<td>NOF</td>
<td>Anyone &gt; 50 with a fragility fx</td>
</tr>
<tr>
<td></td>
<td>Women &gt; 65 and men &gt; 70</td>
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<tr>
<td></td>
<td>Post-menopausal women and men &gt; 50 with other risk factors for osteoporosis</td>
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<tr>
<td>Some HIV experts</td>
<td>See next</td>
</tr>
</tbody>
</table>
**HIV Bone Health: Screening Recommendations**

**HIV+ adults**

- **Age < 40**
  - No screening needed

- **Age 40-50**
  - Calculate FRAX

  - **FRAX <10%**
    - Ensure adequate Ca intake
    - Ensure adequate Vit D levels
    - Lifestyle advice

  - **FRAX >10%, <20%**
    - Calculate FRAX
    - BMD by DEXA (or FRAX if DEXA not available)

  - **FRAX >20%**
    - FRAX >20% or ≥3% at the hip
    - Or Hip or vertebral fracture
    - Exclude secondary causes of osteoporosis
    - Consider Bisphosphonate therapy

- **H/o fragility fx**
  - Steroid (≥5mg X 3mos)
  - High risk of fall
  - Post-menopausal women
  - Men ≥50

**FRAX <10%**

**FRAX >10%, <20%**

**FRAX >20%**

**T score < -2.5**

HIV Bone Health: Screening Recommendation

• Follow-up testing and treatment
  - 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 and reassess need for bisphosphonates in 3-5 years
### Bone Health: Screening Recommendations

#### Investigation for Fragility Fracture

<table>
<thead>
<tr>
<th>Condition</th>
<th>Evaluation</th>
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<tbody>
<tr>
<td><strong>Endocrine</strong></td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficient</td>
<td>25-OH vitamin D</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>iPTH, Ca, PO4, albumin, Cr</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>TSH, FT4</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Males: Free testosterone, Females: estradiol, FSH, prolactin</td>
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<tr>
<td><strong>Renal</strong></td>
<td></td>
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<tr>
<td>Phosphate wasting</td>
<td>FePO4</td>
</tr>
<tr>
<td>Idiopathic hypercalciuria</td>
<td>24 hr urinary Ca</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
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<tr>
<td>Sprue</td>
<td>IgG and IgA anti-tissue transglutaminase</td>
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<tr>
<td><strong>Hematologic</strong></td>
<td></td>
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<tr>
<td>Multiple myeloma</td>
<td>CBC, SPEP</td>
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<tr>
<td>Mastocytosis</td>
<td>Serum tryptase</td>
</tr>
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*(Harris, JID, 2012)*
Bone Health: Screening Recommendations

- Fracture Risk Assessment Tool (FRAX)
  - Developed to incorporate non-BMD clinical factors into a risk analysis to predict the likelihood of fracture in the next 10 years of untreated patients aged 40 to 90
  - http://www.shef.ac.uk/FRAX/tool.jsp?locationValue=9
Bone Health: Screening Recommendations

- Fracture Risk Assessment Tool (FRAX)
  - 65 yo 60 kg, 5’10” man. HIV+, smoker, parent hip fx +, T score -1.8
  - 10 year risk of major osteoporotic fx 11%, hip fx 2.5%
Questions