Risk of progression to osteoporosis in HIV-infected subjects and role of protease inhibitors

BACKGROUND

- Patterns of morbidity and mortality among HIV–infected individuals are changing
- Comorbidity because of non-AIDS diseases become more important in care
- Low bone mineral density (BMD), osteoporosis and fractures are more common in those living with HIV
  - Low rate of bone fracture attended in our daily clinical practice -> low sensitivity to consider the bone health?
- Osteoporosis in HIV and the epidemiology of fractures differ from the general population
  - VIH-infected people present high risk of osteoporosis due to factors related to the host and to the virus, the chronic inflammation and the antiretroviral treatment
OBJECTIVES

- To estimate the magnitude of the osteopenia and osteoporosis in HIV infected patients

- To assess
  - the evolution of BMD as a function of age
  - the effect of the antiretroviral therapy on BMD
METHODS

- Design
  - Retrospective
  - Longitudinal
  - Observational
  - DXA scans
  - HIV-infected patients with $\geq 2$ DXA
  - attended in our unit between January 1999 and December 2016

- Population
  - 3,726 DXA scans
  - 875 subjects
Bone Mineral Density (BMD)

- Dual-energy x-ray absorptiometry (DXA) test measures BMD (g/cm²) at different parts of the body
  - Lunar Prodigy, GE Healthcare, Belgium

- BMD (g/cm²) is compared it to established norms
  - T-score: comparison to 30-years-old healthy adult (same sex)

<table>
<thead>
<tr>
<th>T-score</th>
<th>Diagnosis*</th>
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</thead>
<tbody>
<tr>
<td>-1 &lt;= T</td>
<td>Normal</td>
</tr>
<tr>
<td>-2.5 &lt;= T &lt; -1</td>
<td>Osteopenia</td>
</tr>
<tr>
<td>T &lt; -2.5</td>
<td>Osteoporosis</td>
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</tbody>
</table>

- T score for the lumbar (L1-L4) spine and hip (femoral neck, trochanter and total femur)

Minimum T-score → outcome variable

*NIH Osteoporosis and Related Bone Diseases National Resource Center
3-progressive bidirectional multistate model

- Multi-state process \( \{X(a) \ a \in A\} \) with finite state space \( S=\{0,1,2\}=\{\text{Normal, Osteopenia, Osteoporosis}\} \)
  - \( a \): patient's age at each DXS scan
  - \( X(a) =s \in S \): patient's state at \( a \)
- Markov property assumed:
  - The future time course does only depend on the present state and not on the previous process history
Factors related to a change in the BMD evolution

- Age is used as time scale
- The effect of time is NOT the same at all “ages”
  - Time-inhomogeneous model
  - PCI for Age (≤ 45, > 45)
- Models for women and men are fitted separately
- The use of antiretroviral drugs during the year prior to a DXA scan was included as a covariate in the model

- The effects of the covariates were studied by transition-specific hazard regression models
  - the hazard ratio is the effect size measure of interest
# RESULTS

<table>
<thead>
<tr>
<th></th>
<th>875 patients</th>
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<tbody>
<tr>
<td><strong>Gender, men, n (%)</strong></td>
<td>659 (75.3%)</td>
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<tr>
<td><strong>Age, years</strong></td>
<td>41.7 (36.1; 47.8)</td>
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<tr>
<td><strong>DXA scans per patient, number</strong></td>
<td>3 (2; 18)</td>
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<tr>
<td><strong>Patients and DXA scans, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Two DXA scans</td>
<td>294 (33.6%)</td>
</tr>
<tr>
<td>Three DXA scans</td>
<td>188 (21.5%)</td>
</tr>
<tr>
<td>Four DXA scans</td>
<td>118 (13.5%)</td>
</tr>
<tr>
<td>Five or more DXA scans</td>
<td>275 (31.4%)</td>
</tr>
<tr>
<td><strong>Time from the first to the last DXA scan, years</strong></td>
<td>5 (2.2; 9.6)</td>
</tr>
<tr>
<td><strong>Time between consecutive DXA scans, years</strong></td>
<td>1.1 (0.6 – 2.2)</td>
</tr>
<tr>
<td><strong>Antiretroviral therapy during the year before DXA, number of DXA scans (%)</strong></td>
<td></td>
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<tr>
<td>PI + TDF</td>
<td>567 (16.1%)</td>
</tr>
<tr>
<td>Only PI</td>
<td>1290 (36.7%)</td>
</tr>
<tr>
<td>Only TDF</td>
<td>734 (20.9%)</td>
</tr>
<tr>
<td>Neither PI, nor TDF</td>
<td>925 (26.3%)</td>
</tr>
<tr>
<td><strong>Among subjects receiving a PI, number of DXA scans (%)</strong></td>
<td></td>
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<tr>
<td>Darunavir</td>
<td>519 (27.9%)</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>616 (33.2%)</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>253 (13.6%)</td>
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<tr>
<td>Other PIs</td>
<td>469 (25.3%)</td>
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</table>

*Values are expressed as median (IQR) or number (%).*
Prevalence and transitions

FIGURE: Transitions from first to last DXA among all HIV-infected patients.
Risk of progression

The risk of progression of bone loss or bone gain as a function of age (<= vs. >45 years)

FIGURE: Estimated hazard ratios for all the transitions associated to age <=45 vs. >45 years.
Probability of progression

Estimated transition probabilities from normal bone mineral density to osteopenia/osteoporosis throughout 10 years for HIV-infected patients of ages 30, 40, and 50 years.

FIGURE: Normal BMD to osteopenia and osteoporosis (Left panel: Women).
Estimated transition probabilities from osteopenia to osteoporosis throughout 10 years for HIV-infected patients of ages 30, 40, and 50 years.

FIGURE: Osteopenia to osteoporosis (Left panel: Women).
Risk of low BMD according to the PI

Men

Women

FIGURE: Estimated hazard ratios associated to PIs.
CONCLUSIONS

- In this large cohort of HIV-infected people, the progression to osteoporosis was high for those subjects aged 45 years over 5 years, mainly for women.
  - NEED OF MONITORING THE BMD

- Osteoporosis can be related to the use of protease inhibitors, in particular with darunavir.
  - CHANGES IN SOME ANTIRETROVIRAL DRUGS
THANK YOU FOR YOUR ATTENTION