Pilot study exploring the association between bone mineral density and lipodystrophy in HIV-positive women taking anti-retroviral therapy

Authors: Rebecca Hicks, Michael Luong, Nisha Andany, Janet Raboud, Desheng Su, Victoria Buckley, Anita Rachlis, Sophie Jamal, Saira Mohammed, Mona Loutfy

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Background

Lipodystrophy:

- Associated with exposure to Protease Inhibitors (PIs), Nucleoside Reverse Transcriptase Inhibitors (NRTIs), and Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)\(^1\)

- Physical symptoms: pathological redistribution of body fat and metabolic disturbances (e.g. insulin resistance and hyperlipidemia)\(^1\)

- Psychological symptoms: self-consciousness, stress, depression, and anxiety\(^2\)


Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Bone Mineral Density (BMD):

- ART (esp. PIs) associated with development of reduced BMD\(^1,2\)
- HIV itself has been implicated in development of reduced BMD\(^1\)
- Women at risk of reduced BMD, especially post-menopause\(^1\)


Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Study Justification

- Lipodystrophy and low BMD
  - Similar biological pathways indicate potential relationship
  - These pathways link both to CVD

- Few studies explore these disease conditions in women
Hypothesis

Lipodystrophy is significantly associated with low BMD in HIV-positive women on ART.
Methodology

Study Design:
Cross-sectional study

Patient Population:
47 HIV+ women recruited
- 35 from Maple Leaf Medical Clinic
- 12 from Sunnybrook Health Centre

Inclusion criteria:
- Patient must be HIV+
- At least 18 years old
- Biologically female
- Stable ART treatment for 2 months
- Have had a DXA BMD test
- Able to give informed consent

Exclusion Criteria:
- Being pregnant

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Methods

Questionnaire collecting information about:

- Demographic data
- Presence and degree of lipodystrophy
- Effect of lipodystrophy on quality of life
- Desire and/or previous requests for treatment, and interest in research studies
- Degree of concern of different components of lipodystrophy
Lipodystrophy Criteria

- Lipodystrophy diagnosed as stated in HIV Outpatient Study\(^1\)

- Validated numerical scale of 0-4 (0=absent, 1=very mild, 2=mild, 3=moderate, 4=severe) was utilized for each location of fat redistribution

- Women were categorized as having lipodystrophy if they had\(^1\):
  - at least one severe symptom of fat redistribution OR
  - at least 2 symptoms of fat redistribution, with one being at least moderate in severity

\(^1\) Lichenstein et al. AIDS 2001 15:1389-1398

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Methods

Data collected from patient charts:

- DXA test results (to measure BMD)
- Osteoporosis risk factors
- Fracture history

Figure 1

Figure 2

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Measuring BMD

Dual-Energy X-Ray Absorptiometry (DXA)

For post-menopausal women:
- T-score used
- >= 2.5 classified as osteoporosis

For younger women:
(utilized for this study)
- Z-score used
- >= 2.5 classified as low bone mass
### Results: Demographics

Table 1: Demographics for women with & without lipodystrophy (red=significant)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women with Lipodystrophy (n= 25)</th>
<th>Women without lipodystrophy (n= 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42</td>
<td>39</td>
<td>0.42</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4</td>
<td>4</td>
<td>0.73</td>
</tr>
<tr>
<td>Black</td>
<td>18</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>First Nation</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.0</td>
<td>163.0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>79.0</td>
<td>70.0</td>
<td>0.22</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>96.0</td>
<td>86.5</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>29.0</td>
<td>26.4</td>
<td>0.18</td>
</tr>
</tbody>
</table>
Table 2: HIV History and Co-infections for women with and without lipodystrophy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women with lipodystrophy (n= 25)</th>
<th>Women without lipodystrophy (n= 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of AIDS defining illness</td>
<td>13</td>
<td>7</td>
<td>0.12</td>
</tr>
<tr>
<td>HIV risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endemic country</td>
<td>19</td>
<td>12</td>
<td>0.12</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>23</td>
<td>17</td>
<td>0.16</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>0</td>
<td>1</td>
<td>0.28</td>
</tr>
<tr>
<td>Not known</td>
<td>1</td>
<td>4</td>
<td>0.12</td>
</tr>
<tr>
<td>Active Hepatitis C</td>
<td>2</td>
<td>1</td>
<td>0.61</td>
</tr>
<tr>
<td>Active Hepatitis B</td>
<td>2</td>
<td>0</td>
<td>0.16</td>
</tr>
</tbody>
</table>
Table 3: ART exposure and immunological status of women with and without lipodystrophy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women with lipodystrophy (n= 25)</th>
<th>Women without lipodystrophy (n= 22)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of HIV infection (years)</td>
<td>7</td>
<td>8</td>
<td>0.73</td>
</tr>
<tr>
<td>Duration of ART</td>
<td>3</td>
<td>4</td>
<td>0.75</td>
</tr>
<tr>
<td>Previous PI</td>
<td>15</td>
<td>13</td>
<td>0.99</td>
</tr>
<tr>
<td>Previous NNRTI</td>
<td>14</td>
<td>11</td>
<td>0.71</td>
</tr>
<tr>
<td>Current CD4 count (cell/ mm³)</td>
<td>500</td>
<td>540</td>
<td>0.93</td>
</tr>
<tr>
<td>Current viral load (copies/mL of blood)</td>
<td>49</td>
<td>49</td>
<td>0.12</td>
</tr>
</tbody>
</table>
Results: Severity of Lipodystrophy

Figure 1: Severity of Lipodystrophy Symptoms

- Absent: 55%
- Very mild (score 1-8): 13%
- Mild (score 9-15): 15%
- Moderate (score 16-24): 6%
- Severe (score 25-32): 11%

* Minimum possible score of 0, Maximum score of 32

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Results: BMD

Figure 2: Average Z-scores as determined by DXA scan

- L1-L4: p=0.86
- Femoral Neck: p=0.44
- Total Hip: p=0.83

Presentation: Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC
Table 4: Univariable Regression Modelling utilizing DXA BMD scores (red=significant)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipodystrophy</td>
<td>0.013 (-0.077, 0.102)</td>
<td>0.78</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>-0.063 (-0.118, -0.007)</td>
<td>0.03</td>
</tr>
<tr>
<td>Race (Black vs. Other)</td>
<td>0.155 (0.070, 0.240)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight</td>
<td>0.002 (-0.000, 0.005)</td>
<td>0.07</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>0.002 (-0.002, 0.005)</td>
<td>0.35</td>
</tr>
<tr>
<td>Age menarche</td>
<td>-0.006 (-0.036, 0.024)</td>
<td>0.69</td>
</tr>
<tr>
<td>Menopause</td>
<td>-0.163 (-0.301, -0.024)</td>
<td>0.02</td>
</tr>
<tr>
<td>Years on ART</td>
<td>-0.005 (-0.014, 0.003)</td>
<td>0.23</td>
</tr>
<tr>
<td>Previous PI</td>
<td>-0.066 (-0.169, 0.037)</td>
<td>0.21</td>
</tr>
<tr>
<td>Previous NNRTI</td>
<td>0.009 (-0.091, 0.109)</td>
<td>0.86</td>
</tr>
</tbody>
</table>
Table 5: Multivariable regression modeling with femoral neck DXA BMD scores (red=significant)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Estimate (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.924 (0.835, 1.014)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lipodystrophy: with vs. without</td>
<td>0.014 (-0.072, 0.100)</td>
<td>0.744</td>
</tr>
<tr>
<td>Race: Black vs. other</td>
<td>0.133 (0.036, 0.231)</td>
<td>0.009</td>
</tr>
<tr>
<td>Age (per 10 yrs) - centered</td>
<td>-0.036 (-0.094, 0.023)</td>
<td>0.222</td>
</tr>
</tbody>
</table>
Conclusions

- Lipodystrophy and reduced BMD not associated with each other
  - Possibly due to reduced power caused by small sample size (N=47)

- BMD was significantly associated with Black ethnicity

- With 70.2% of sample population identifying as Black, results may have been skewed
Points of discussion on DXA and ethnicity

Different ethnicities have different bone parameters

- Black women: decreased region area, increased bone mineral content
- White women: increased region area, decreased bone mineral content

Bone geometry contributes to bone strength

DXA scan results unable to determine differences in bone geometry

Hip Structure Analysis and pQCT capable of detecting bone geometry

Future Directions

- Incorporate larger and more representative sample population
- Utilize Hip Structure Analysis or pQCT to analyze bone geometry
Acknowledgements

Study Participants

Dr. Mona Loutfy

Dr. Janet Raboud

Shari Margolese

WCRI and other Project Partners

Virology Education

Presented at the 1st Int. Workshop on HIV & Women, 10 - 11 January 2011, Washington DC