Lean and Fat Mass are Stronger Predictors of Impaired Functional Status than Bone

Erlandson KM. Allshouse AA. Jankowski CM. MaWhinney SM. Kohrt WM. Campbell TC.
Background

• Nearly one-half of HIV-infected persons in the US are ≥ 50 years of age
• Those aging with HIV appear to manifest impairments in physical function & frailty at earlier than expected ages

• Impaired physical function & frailty may result in:
  – decreased quality of life
  – difficulty obtaining or maintaining employment
  – social isolation
  – hospitalization
  – higher morbidity & mortality
Research Goal

• To identify factors associated with increased risk of frailty & physical function decline.
Body Composition in Functional Impairment

Body Composition in Functional Impairment

• Hypothesis: Increased fat, low lean body mass, and low bone mineral density are significant predictors of frailty & physical function impairment
Methods

• Participants:
  – 45-65 year old subjects with HIV-1 infection
  – Combination antiretroviral therapy for ≥ 6 months
  – ≥ 1 undetectable HIV-1 RNA (<48 copies/mL)
  – No HIV-1 RNA >200 copies/mL
  – Body weight < 300 lbs (limit of dual-energy X-ray absorptiometry [DXA] machine)
Methods

• **Study visit #1:**
  - Questionnaires
  - Medical history
  - 400-m walk
  - Frailty
    • Gait speed
    • Grip strength
    • Weight loss
    • Subjective fatigue
    • Subjective activity limitation
    • 0 = fit, 1-2 = prefrail, 3-5 = frail

• Short Physical Performance Battery (SPPB)
  - Gait speed
  - Time to rise from chair 5x
  - Tandem stand
  - 12 = no deficits, <9 = highly predictive of disability
# Methods: Matching Low & High Function

<table>
<thead>
<tr>
<th>Tool</th>
<th>SPPB &lt;9</th>
<th>SPPB 9-11</th>
<th>SPPB 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frailty 3-5 (frail)</td>
<td>LOW</td>
<td>LOW</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Frailty 1-2 (pre-frail)</td>
<td>LOW</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Frailty 0 (fit)</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

SPPB= Short Physical Performance Battery
Methods

• **Matching for Nested Case-Control:**
  – Matched low function (LF) cases to 1-2 high function (HF) controls by age, gender and time of HIV diagnosis.

• **Study Visit #2:**
  – LF and HF persons return for DXA scan
DXA Scan Analyses

• **Fat**
  – % fat
  – Fat index (kg fat/height)
  – % Trunk fat/% leg fat

• **Lean Body Mass**
  – Total body lean mass (non-fat/non-bone mass)
  – Appendicular skeletal muscle index (arm & leg lean mass/height)

• **Bone**
  – Bone mineral density at total hip and lumbar (L1-L4) spine
Methods

- Conditional logistic regression was utilized for primary case-control analysis.
- The best predictors from fat, lean mass, and bone were chosen using Akaike information criterion (AIC).
- 1 criteria from each component was considered for the final model, which included covariates significant at $p<0.05$. 
Results

• 359 subjects completed Study Visit #1
  – 33 (9%) identified as low function
    • 2 not interested in returning
    • 1 exceeded limits of the DXA machine
  – 140 (39%) identified as high function
  – 30 LF persons were matched to 48 HF controls
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low function N=30 (%)</th>
<th>High function N=48 (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.1 ± 0.8</td>
<td>52.8 ± 0.8</td>
<td>0.42*</td>
</tr>
<tr>
<td>Women</td>
<td>7 (23)</td>
<td>9 (19)</td>
<td>--*</td>
</tr>
<tr>
<td>White</td>
<td>23 (77)</td>
<td>37 (77)</td>
<td>1</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>7 (23)</td>
<td>6 (13)</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td><strong>15 (50)</strong></td>
<td><strong>10 (21)</strong></td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>7 (23)</td>
<td>8 (17)</td>
<td>0.48</td>
</tr>
<tr>
<td>Current CD4+ T-cell count</td>
<td>551 ± 50</td>
<td>628 ± 40</td>
<td>0.27</td>
</tr>
<tr>
<td>Time since HIV diagnosis (years)</td>
<td>15.3 ± 1.4</td>
<td>15.6 ± 1.4</td>
<td>0.60*</td>
</tr>
</tbody>
</table>

* Matched on age (within 5 years), gender, and HIV diagnosis before or after 1996.
## Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low function N=30 (%)</th>
<th>High function N=48 (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B or C</td>
<td>14 (47)</td>
<td>12 (26)</td>
<td>0.10</td>
</tr>
<tr>
<td>Lipoatrophy</td>
<td>7 (23)</td>
<td>8 (17)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hx stress fracture</td>
<td>4 (13)</td>
<td>2 (4)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Activity Level &lt;500 Kcal/week</strong></td>
<td><strong>19 (63)</strong></td>
<td><strong>7 (15)</strong></td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir (any)</td>
<td>24 (80)</td>
<td>41 (85)</td>
<td>0.59</td>
</tr>
<tr>
<td>Protease inhibitor (any)</td>
<td>24 (80)</td>
<td>32 (67)</td>
<td>0.08</td>
</tr>
<tr>
<td>Testosterone</td>
<td>3 (10)</td>
<td>6 (13)</td>
<td>0.79</td>
</tr>
<tr>
<td>Estrogen</td>
<td>1 (3)</td>
<td>4 (8)</td>
<td>0.31</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>9 (30)</td>
<td>10 (21)</td>
<td>0.41</td>
</tr>
<tr>
<td>Bisphosphonate</td>
<td>2 (7)</td>
<td>1 (2)</td>
<td>0.34</td>
</tr>
</tbody>
</table>
No Differences in Fat Mass Between Functional Groups

OR* 0.91 (0.80, 1.02)  
*Adjusted for CD4+ < 350 cells/µL, current protease inhibitor, any use of ZDV, DDI, D4T.

OR* 1.0 (0.94, 1.03)

p=0.18

p=0.54

*Bars represent mean ± SE. P value from conditional logistic regression.
No Differences in Fat Distribution Between Functional Groups

OR* 1.0 (0.9, 1.1)  
*p=0.68

*Adjusted for CD4+ < 350 cells/µL, current protease inhibitor, any use of ZDV, DDI, D4T.
- Bars represent mean ± SE. P value from conditional logistic regression.
Total Body Lean Mass Differed between Functional Groups

OR* 1.1 (1.01, 1.2)

\[ p=0.03 \]

*Adjusted for CD4+ < 350 cells/µL, any use of didanosine, stavudine or zidovudine
- Bars represent mean ± SE. P value from conditional logistic regression.
Appendicular skeletal muscle index (kg/m²) differed between functional groups.

OR* 1.8 (1.1, 2.9)  
\( p=0.01 \)

*Adjusted for CD4+ < 350 cells/µL, any use of didanosine, stavudine, or zidovudine
- Bars represent mean ± SE. P value from conditional logistic regression.
Differences in Bone Mineral Density Between Functional Groups

Hip (per 0.1 g/m$^2$):  
OR* 2.4 (1.1, 5.6)  p=0.03

L-spine (per 0.1 g/m$^2$):  
OR* 2.1 (1.1, 4.0)  p=0.02

*Adjusted for nadir CD4+, body mass index, tobacco use, and current tenofovir use
- Bars represent mean ± SE.  P value from conditional logistic regression.
Proposed Interaction of Body Composition in Functional Impairment
Select the Best Parameter

- **Fat**
  - % Fat
  - Fat Index
  - % Leg: % Trunk

- **BMD**
  - Hip BMD
  - L spine BMD

- **Lean Body Mass**
  - Total lean body mass
  - ASMI (appendicular skeletal muscle index)

Model selected to minimize Akaike Information Criteria (AIC), a goodness of fit measure for comparing non-nested models
Select the Best Parameter

- **Fat**
  - % Fat
  - Fat Index
  - % Leg: % Trunk

- **Lean Body Mass**
  - Total lean body mass
  - ASMI (appendicular skeletal muscle index)

- **BMD**
  - Hip BMD
  - L spine BMD

Model selected to minimize Akaike Information Criteria (AIC), a goodness of fit measure for comparing non-nested models.
Select the Best Parameter

- **Fat**
  - % Fat
  - Fat Index
  - % Leg: % Trunk

- **BMD**
  - Hip BMD
  - L spine BMD

- **Lean Body Mass**
  - Total lean body mass
  - ASMI (appendicular skeletal muscle index)

Model selected to minimize Akaike Information Criteria (AIC), a goodness of fit measure for comparing non-nested models.
Select the Best Parameter

• **Fat**
  – % Fat
  – Fat Index
  – % Leg: % Trunk

• **BMD**
  – Hip BMD
  – L spine BMD

• **Lean Body Mass**
  – Total lean body mass
  – ASMI (appendicular skeletal muscle index)

Model selected to minimize Akaike Information Criteria (AIC), a goodness of fit measure for comparing non-nested models
Fat & lean mass but not bone are associated with greater odds of functional impairment.

- **Fat mass (% body fat)**: OR 1.1 (1.0, 1.2), p=0.01
- **Lean Mass (ASMI)**: OR 2.6 (1.4, 4.8), p=0.003
- **BMD (hip BMD)**: OR 1.7 (0.8, 3.5), p=0.16

Functional impairment

Model selected to minimize Akaike Information Criteria (AIC), a goodness of fit measure for comparing non-nested models.
Summary

• Nearly 50% of our cohort met commonly used criteria for sarcopenia

• In the case-control comparison, low lean mass and low bone mineral density were associated with greater odds of impaired function
Summary

• In a model including all three components, lower lean mass and higher fat mass were stronger predictors of functional status than bone mineral density.
Limitations

• Did not include a measure of visceral fat
• Cohort limited to persons well-controlled on antiretroviral therapy
• Cross-sectional analysis precludes conclusions regarding direction and causality
Future investigations:

• Understanding whether maintained/increased muscularity will preserve function among persons aging with HIV infection

• Establishing the longitudinal role of muscularity in clinical outcomes (hospitalizations, falls, morbidity, mortality)
Thank you

• Study subjects
• Funding sources:
  – National Institutes of Health [5UL1 TR000154, P30 DK048520, and T32 AI007447-1]
  – Hartford Foundation Center of Excellence in Geriatric Medicine
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References