Male Astronauts Have Greater Bone Loss and Risk of Hip Fracture following Long Duration Spaceflights than Females

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Astronauts lose bone rapidly in microgravity

Percent change in aBMD per month of spaceflight vs Rate of bone loss in postmenopausal osteoporosis

-0.04%
-1.06%
-1.35%
-1.56%
-0.34%

-1 to 2%/year

LeBlanc JMNI 2000
In-flight Countermeasures

- Exercise up to 2.5 hours/day (allotted time)
- Vitamin D supplementation

Treadmill (TVIS)  Cycle ergometer (CEVIS)  Resistance (IRED)
Research Questions

1. Is there a sex-specific difference in microgravity induced bone loss?
2. Can factor-of-risk analysis be used to identify individuals at risk for hip fracture?
3. Do BMD and factor-of-risk recover to baseline levels after returning to Earth?
Subjects

- All long duration NASA astronauts who completed missions on the ISS (2000 - May 2009)
  - 20 males (1 repeat)
  - 5 females (1 repeat)

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>67.5 ± 4.2</td>
<td>81.4 ± 8.5</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Height (m)</strong></td>
<td>1.69 ± 0.03</td>
<td>1.75 ± 0.07</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>43 (41 to 47)</td>
<td>46 (37 to 54)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Mission Length (days)</strong></td>
<td>175 (134 to 195)</td>
<td>170 (95 to 215)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Outcome assessments: aBMD

- Bone mineral density by DXA
  - Whole body and L hip
    - Preflight
      - 1 month to 1.5 years before flight
      - 80% within 6 months
    - Postflight
      - 5 to 32 days after landing
  - Follow up
    - Annually until “full” recovery, then triennially
    - 1 to 6 postflight scans per person
Outcome assessments: Factor-of-Risk

$$\text{Factor of Risk} = \frac{\text{Fall Force}}{\text{Bone Strength}}$$

- **Fall Force**: impact force due to sideways fall
  - Estimated from biomechanical model
  - Function of height, weight, soft tissue thickness
- **Bone strength**: failure strength of hip with sideways fall loading
  - Estimated from mechanical testing of cadaver femora
  - Function of aBMD
Weight and soft tissue thickness do not change in flight

**Change in Weight**

<table>
<thead>
<tr>
<th></th>
<th>Preflight</th>
<th>Postflight</th>
</tr>
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<tbody>
<tr>
<td>Women</td>
<td>n=5</td>
<td>n=5</td>
</tr>
<tr>
<td>Men</td>
<td>n=20</td>
<td>n=20</td>
</tr>
</tbody>
</table>

**Change in STT**

<table>
<thead>
<tr>
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<th>Postflight</th>
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<td>n=20</td>
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</tr>
</tbody>
</table>

**Graphs:**
- Change in Weight
- Change in STT

- **Women:**
  - Preflight: 75 kg
  - Postflight: 75 kg

- **Men:**
  - Preflight: 75 kg
  - Postflight: 75 kg

- **Women:**
  - Preflight: 25 mm
  - Postflight: 25 mm

- **Men:**
  - Preflight: 25 mm
  - Postflight: 25 mm
Bone loss is greater in men than women

- Women: -6.7% (p<0.01)
- Men: -3% (p=0.16)

Monthly Rate

<table>
<thead>
<tr>
<th>Gender</th>
<th>Monthly Rate (g/cm^2/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>-1.30%</td>
</tr>
<tr>
<td>Women</td>
<td>-0.55%</td>
</tr>
</tbody>
</table>
Factor-of-risk is markedly higher in men and increases more postflight.

- High risk for hip fracture

![Graph showing increased factor-of-risk in men postflight](image)

- * = p<0.01
- ** = p<0.0001
Many male crewmembers are at high risk for hip fracture postflight.
Recovery of bone is incomplete and variable

- Highly variable rate of bone loss and recovery
- Most recovery occurs within first 1.5 years postflight
  - Average slope = +0.038 g/cm²/year
  - No significant change in aBMD after 1.5 years
- n of people who don’t reach baseline BMD in 1.5 years
Strengths and Limitations

▪ Strengths
  ▪ Large data set of long-duration NASA astronauts
  ▪ Accounts for other biomechanical factors leading to hip fracture

▪ Limitations
  ▪ Femoral strength estimated from DXA aBMD measurement
  ▪ Modeled for sideways fall only
  ▪ Small sample set
Conclusions

- Male astronauts experience a greater decrease in hip BMD than females after exposure to microgravity
- Men have a significantly higher factor-of-risk than women
  - Due to less soft tissue padding and greater height and weight
- Most recovery of BMD occurs within the first 1.5 years after return.
  - 5 male astronauts continue to be at high risk for hip fracture 3 years after return
Why do men lose more than women?

Possible explanations

- Physiological
  - Estrogen is protective for pre-menopausal female crewmembers

- Environmental
  - Men are stronger than women and max out the exercise equipment
    - iRED can only provide 135 kg of resistance
Acknowledgements

- Lisa King (NASA JSC)
- Ben Roberts (BIDMC)

- Funding: NSBRI Bioastronautics Fellowship
Estimation of Fall Force

\[ F_{atten} = \sqrt{2ghmk} - 71 \times ST \text{ thickness} \]

- \( g = 9.81 \text{ m/s}^2 \)
- \( h = \) height of c.g.
- \( m = \) effective mass
- \( k = \) stiffness constant

Soft tissue thickness
Estimation of Femoral Strength

- Mechanical testing of cadaver femora to failure in sideways fall configuration

- Linear regression used to predict subjects’ femoral strength

\[ \text{Estimated Femoral Strength (N)} = 10118 \times \text{TrochaBMD (g/cm}^2\text{)} - 1512.5 \]

Bouxsein, JBMR 2007

Roberts, Bone 2010