

Bone Mineral Density at the Hip Declines Twice as Quickly Among HIV-Infected Women than Men

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BACKGROUND

- Nearly all ART initiation trials demonstrate a decline in bone mineral density (BMD) that is most pronounced in the first 48-96 weeks after starting ART.
- Data on long-term changes and risks for BMD decline, particularly among women, are limited.
- Aim: compare long-term changes in BMD in a large cohort of HIV-infected men and women and to determine sex-specific risk factors for BMD.

METHODS

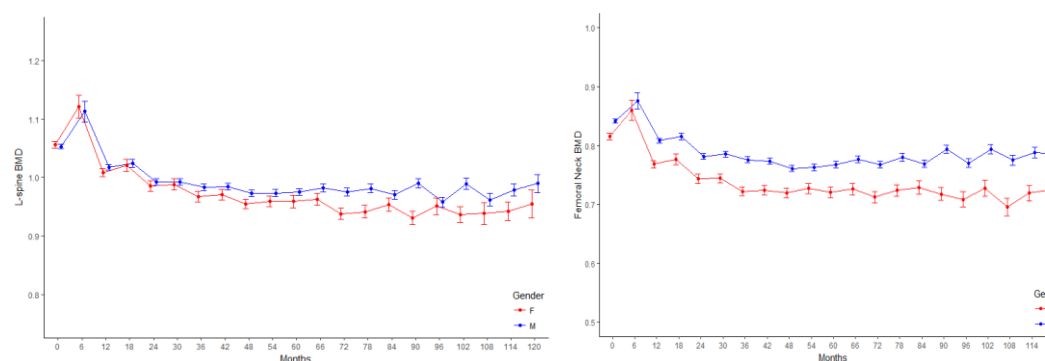
- HIV-infected men and women in the Modena Metabolic Clinic underwent dual-energy X-ray absorptiometry (DXA) scans every 6-12 months for up to 10 years (median 4.6 years).
- Mixed methods regression models were created for women and men in combined and stratified models to determine factors associated with BMD.
- Models included variables described below; CD4 nadir, CD4 total and %, smoking, diabetes, and duration of protease inhibitor use were considered in univariate models but were not significant.

RESULTS

| Baseline Characteristics | Women (N=839) N (%) or Median (IQR) | Men (N=1759) N (%) or Median (IQR) |
|---------------------------------------|----------------------------------------|---------------------------------------|
| Age >55 years | 37 (4) | 166 (9) |
| 51-55 years | 71 (9) | 197 (11) |
| 46-50 years | 183 (22) | 450 (26) |
| 41-45 years | 303 (36) | 536 (31) |
| 35-40 years | 182 (22) | 265 (15) |
| <35 years | 63 (8) | 145 (8) |
| Body mass index (median, IQR) | 21.6 (20.0, 24.1) | 23.5 (21.6, 25.5) |
| Smoking (pack yrs median, IQR) | 10.0 (1.1, 20.0) | 12.5 (0, 25.0) |
| Physical activity | | |
| None | 577 (69) | 1020 (58) |
| Moderate | 184 (22) | 438 (25) |
| Vigorous | 44 (5) | 224 (13) |
| Post-Menopausal | 124 (15) | -- |
| Hypogonadism | -- | 124 (7) |
| Metabolic Syndrome | 84 (10) | 144 (8) |
| Hepatitis C Virus | 250 (30) | 468 (27) |
| Vitamin D < 30 ng/dL | 414 (49) | 831 (47) |
| History of AIDS Wasting | 113 (13) | 81 (5) |
| CD4 Nadir <200 cells/ μ L | 448 (53) | 856 (49) |
| HIV-1 VL \leq 50 | 646 (77) | 1319 (75) |
| ART duration (years) | 9.6 (5.6, 13.1) | 8.3 (3.4, 12.0) |
| TDF use | 538 (64) | 1144 (65) |
| INSTI use | 70 (8) | 129 (7) |
| Total BMD (g/cm ²) | 1.009 (0.116) | 1.162 (0.115) |
| Femoral Neck BMD (g/cm ²) | 0.816 (0.154) | 0.842 (0.152) |
| Lumbar Spine BMD (g/cm ²) | 1.057 (0.170) | 1.054 (0.167) |

RESULTS

Unadjusted Changes in Femoral Neck (top) and Lumbar Spine (bottom) BMD between Males (blue) and Females (red)



Adjusted Annual Rates of Change SE)

| | | |
|----------------------------------------|------------------------|-------|
| Female L-Spine (g/cm ²) | -0.01223 (0.000702) | <.001 |
| Male Lumbar Spine (g/cm ²) | -.000725 (0.000788) | <.001 |
| Female Fem Neck (g/cm ²) | -0.00845 (0.000871) | <.001 |
| Male Fem Neck (g/cm ²) | -0.00430 (0.000832) | <.001 |

Characteristics Associated with BMD (g/cm²) in Adjusted Analyses (M/F Combined)

| Baseline Characteristics | Femoral Neck | | | Lumbar Spine | | |
|-----------------------------------------|--------------|----------------------|---------|--------------|------------------------|---------|
| | Estimate | SD | P value | Estimate | SD | P value |
| Women (vs Men) | -0.0353 | 0.0052 | <.001 | NS | NS | NS |
| Body mass index | 0.00487 | 0.00047 | <.001 | 0.00257 | 0.00048 | <.001 |
| INSTI exposure (years) | 0.00003 | 5.4x10 ⁻⁶ | <.001 | 0.000027 | 5.3 x 10 ⁻⁶ | <.001 |
| TDF exposure (years) | -0.00284 | 0.00047 | <.001 | -0.00295 | 0.00048 | <.001 |
| Age > 55 years (vs <35) | -0.0522 | 0.012 | <.001 | -0.0187 | 0.015 | 0.21 |
| 51-55 years (vs <35) | -0.0481 | 0.012 | <.001 | -0.0354 | 0.014 | 0.012 |
| 46-50 year (vs <35) | -0.0330 | 0.010 | .001 | -0.0175 | 0.012 | 0.15 |
| 41-45 year (vs <35) | -0.0078 | 0.0098 | 0.42 | 0.00664 | 0.012 | 0.57 |
| 35-40 year (vs <35) | -0.00336 | 0.0103 | 0.75 | 0.0165 | 0.013 | 0.19 |
| No PA (vs intense) | -0.00632 | 0.0029 | 0.031 | -0.00893 | 0.0029 | 0.002 |
| Moderate PA (vs intense) | -0.00071 | 0.0028 | 0.80 | -0.00556 | 0.0028 | 0.046 |
| Hypogonadism (M) or Post-Menopausal (F) | -0.0322 | 0.0036 | <.001 | -0.0460 | 0.0036 | <.001 |
| Hx of AIDS Wasting | -0.0285 | 0.0047 | <.001 | -0.0189 | 0.0048 | <.001 |
| HIV-1 VL \geq 50 copies | 0.0579 | 0.0020 | <.001 | 0.0581 | 0.0019 | <.001 |
| Vitamin D Insufficiency | -0.0152 | 0.0025 | <.001 | -0.0119 | 0.0025 | <.001 |
| Hepatitis C | -0.0130 | 0.0052 | 0.012 | -0.0174 | 0.0063 | 0.0055 |

Adjusting for other covariates, female sex is associated with a 0.0353 g/cm² greater femoral neck BMD

- Sex-stratified models yielded similar results with a few exceptions:
- Among women: metabolic syndrome was associated with lower lumbar spine BMD (estimate -0.0193, SD 0.0061, p=0.0025); physical activity was not associated with lumbar spine or femoral neck BMD.
- Among men, neither lumbar spine nor femoral neck BMD was associated with HCV.

SUMMARY AND CONCLUSIONS

- In a large cohort of HIV-infected men and women on long-term ART, bone density at the hip (femoral neck), a significant predictor of fracture risk, declined nearly twice as quickly among HIV-infected women compared to HIV-infected men.
- Female sex was independently associated with lower femoral neck BMD in adjusted models.
- Age-associated changes in BMD were most pronounced after age 45; INSTI therapy was protective, and the effect of HCV on BMD was similar to that of 5 additional years of aging, and was most significant among women.
- Traditional bone risk factors (BMI, physical activity, vitamin D insufficiency) were also identified.
- The majority of our study population were less than 50 years old, and only 15% of female participants were menopausal at baseline. Thus, with aging, the rate of BMD decline among HIV-infected women is expected to be even more pronounced.