Title: Changes in Bone and Fat derived hormones are correlated with BMD and Body Fat at 12 months after initiation of antiretroviral therapy in men with HIV.

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Objective/Aim/Hypothesis:

Low bone mineral density (BMD) is commonly observed in people living with HIV (PLWH), especially after initiation of combination antiretroviral therapy (cART). cART initiation is also associated with lipodystrophy, which is characterized by body fat redistribution. Although previous studies have reported an association between cART initiation and change in bone and fat mass the mechanisms remain unclear. There is growing evidence that bone and fat cells produce hormones that influence the function of one another. Therefore, in the current study, we tested the hypothesis that cART initiation induces changes in the circulating levels of the bone-derived hormones, undercarboxylated osteocalcin (ucOCN) and sclerostin, and the fat-derived hormones, leptin, adiponectin, and lipocalin-2, and that these changes are associated with BMD and fat mass.

Design/Approach/Methods:

Serum samples were collected from a small cohort of men with HIV (n=15) initiating fixed dose tenofovir disoproxil fumarate/emtricitabine/efavirenz at baseline, prior to cART initiation, and at 12-months after initiation. BMD at the lumbar spine (LS) and femoral neck (FN), as well as, trunk fat was evaluated using dual energy x-ray absorptiometry (DXA) 12 months after initiation. Serum ucOCN, sclerostin, leptin, adiponectin and lipocalcin-2 were measured using enzyme-linked immunosorbent assays (ELISAs). Baseline and 12-month hormones levels were compared using paired t-test or a Wilcoxon rank test. The correlation between change in hormone levels and BMD and body fat was evaluated using Spearman's rank order correlation analysis.

Results:

There was a significant reduction in LS BMD ($p<0.05$) and FN ($p=0.003$). There was a significant increase in lipocalin-2 ($p=0.012$), and no significant changes in ucOCN, leptin, adiponectin, and sclerostin at baseline and 12-months. Change in sclerostin between baseline and 12-months was positively associated with LS ($r=0.649$, $p=0.012$) and FN BMD ($r=0.548$, $p=0.043$). Change in ucOCN was negatively associated with trunk fat ($r=0.538$, $p=0.047$) and change in adiponectin was negatively associated with LS BMD ($r=-0.600$, $r=0.023$).

Conclusion:

Our findings support previously published work suggesting circulating sclerostin is a biomarker of BMD. The associations noted between the bone-derived hormone, ucOCN, and trunk fat and the fat-derived hormone, adiponectin, and lumbar spine BMD are supportive of bone-fat hormonal cross-talk in PWH treated with ART

Variables	Mean Baseline (Stdev)	Mean 12 Months (Stdev)	Mean Delta (Stdev)	P-value
Sclerostin	0.41 (0.010)	0.37 (0.137)	-0.03 (0.105)	NS
ucOCN pg/mL	499.70 (465.859)	589.34 (594.481)	89.63 (564.548)	NS
Leptin ng/mL	24.16 (24.262)	27.46 (27.568)	6.29 (16.344)	NS
Lipocalcin2 ng/mL	58.12 (17.982)	91.20 (48.016)	33.08 (50.326)	**0.012**
Adiponectin ng/mL	5547.07 (2995.726)	6002.98 (2941.353)	455.90 (1800.179)	NS
Trunk Fat	31.709 (14.291)	33.931 (13.727)	2.222 (10.930)	NS
Trunk Lean	68.290 (14.291)	66.068 (13.727)	-2.222 (10.930)	NS
Lumbar Spine BMD	1.065 (0.111)	1.038 (0.114)	-0.027 (0.020)	**P<0.001**

Femoral Neck BMD	0.943 (0.126)	0.908 (0.124)	-0.034 (0.035)	**0.003**