ULTRASCAN™650: A Low Burden Portable Method for Measuring Bone Mineral Density in Women With HIV

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BACKGROUND

- People with HIV (PWH) have approximately a two-fold greater risk of low bone mineral density (BMD) and osteoporotic fractures compared with people without HIV (PWoH) [1,2].
- Osteoporosis risk accelerates with aging and during the menopausal transition.
- Due to treatment successes, PWH are living longer and more women with HIV (WWH) are reaching menopause.
- The rates of osteoporosis and osteoporotic fractures are consistently reported to be higher in WWH when compared to socio-demographically similar women living without HIV (WWoH) [3,4].
- Due to the increased risk for osteoporosis, the Infectious Disease Society of America (IDSA) advises that all PWH over the age of 50 year undergo screening for osteoporosis via dual energy X-ray absorptiometry (DXA) [5] and yet estimates are that only ~7% of eligible PWH receive DXA [6].
- Barriers to osteoporosis screening in PWH are varied and include limited healthcare access and insurance coverage.
- Rapid and inexpensive point-of-care screening tools could improve osteoporosis diagnoses and allow for early intervention to prevent osteoporotic fractures.

Study Aim

To evaluate (1) the use of a portable quantitative ultrasound device (Ultrascan™650) for outpatient BMD screening, (2) osteoporosis prevalence in WWH and demographically similar women without HIV, and (3) factors associated with low BMD in both groups

METHODS

- 269 women, including 184 WWH and 85 women without HIV (WWoH), enrolled in the MACS/WIHS Combined Cohort Study (MWCCS) were assessed at the Cook County Clinical Research Site.
- Bone mineral density (BMD) was measured at the non-dominant distal radius using the FDA-cleared Ultrascan650 (CyberLogic) quantitative ultrasound (QUS) instrument (*evaluation cohort*).
- 99 participants underwent paired QUS and dual energy X-ray absorptiometry (DXA) BMD assessments (*validation cohort*).
- Clinical, socio-demographic and lifestyle factors were collected concurrently
- Menopause status was dichotomized as pre vs. postmenopausal based on participant self-report of menstrual bleeding and final menstrual period ≥12 months.
- BMD (continuous and categorical), demographic, and lifestyle factors were compared by HIV-serostatus.
- Unadjusted bivariate linear regression models were used for associations with continuous BMD.
- Factors that were significantly associated with continuous BMD were used in multivariate models.
- HIV-serostatus was forced into models evaluating the overall cohort (WWH and WWoH together).
- Separate multivariate models were run with WWH only.

RESULTS

- A total of 99 participants in the *validation cohort* underwent paired QUS-BMD and DXA based BMD assessments (Table 1).
- There were significant positive correlations between QUS-BMD and DXA-measured BMD at all skeletal sites (all $p \leq 0.0003$). Correlations were strongest at the radius (r = 0.761), followed by the total hip (r = 0.575), femoral neck (r = 0.489) and the lumbar spine (r = 0.360)

Table 1. Correlations between paired QUS-BMD measurements.

	Ultrascan BMD (g/cm²)	
	N	R (p-value)
Lumbar Spine BMD (g/cm²)	99	0.360 **(0.0003)**
Hip BMD (g/cm²)	96	0.575 **(<0.0001)**
Femoral Neck BMD (g/cm²)	96	0.489 **(<0.0001)**
Radius BMD (g/cm²)	36	0.761 **(<0.0001)**

- 269 (68% WWH; 32% WWoH) participants underwent QUS-BMD assessments *(evaluation cohort).*
- The mean participant age was 55 ± 8 years, ~80% were either late perimenopause or post-menopausal, 70% were Black, 42% were current former cigarette smokers, 16% were former injection drug users and 7.1% of women had a prior fracture of the hip, wrist or spine.
- WWoH were more likely to be current crack, cocaine or heroin users than WWH (29% vs. 16%), but no other participant characteristic was different by HIV-serostatus.
- A total of 23% of the overall cohort was identified as osteoporotic, 33% as osteopenic and 43% as having normal BMD by QUS-BMD.
- 27% of WWH were identified as osteporotic vs. 15% of WWoH but the results were not significant (Table 2).

Table 2. QUS-BMD T-score by HIV-serostatus.

	Overall (n = 269)	WWH (n= 184)	WWoH (n = 85)	p-value
BMD Categorized T-scores				0.086
Normal	117 (43%)	78 (42%)	39 (46%)	
Osteopenia	89 (33%)	56 (30%)	33 (39%)	
Osteoporosis	63 (23%)	50 (27%)	13 (15%)	

- Women identified as osteoporotic by QUS-BMD were slightly more likely to be HIV-seropositive, but the results were not significant (p=0.086, Table 3).
- Women identified as osteoporotic by QUS-BMD were more likely to be late perimenopausal/post-menopausal (p<0.001) and in WWH, those identified as osteoporotic were more likely to have been exposed to TDF based antiretroviral therapy (ART) and currently taking ART.
- In bivariate (unadjusted) analysis, age was negatively associated with BMD (β=-0.364, p<0.001, Table 4).
- Postmenopausal women had significantly lower BMD than premenopausal women (0.602 vs. 0.652g/cm², p<0.001).
- HIV status did not affect BMD, however, higher nadir CD4 was associated with higher BMD, and exposure to TDF based ART was associated with lower BMD.

Table 3. Characteristics of participants with a baseline Ultrascan by BMD Categorized T-scores.

	BMD Categorized T-Scores			
	Normal (n = 117)	Osteopenia (n = 89)	Osteoporosis (n = 63)	p-value
HIV Serostatus, WWH	78 (67%)	56 (63%)	50 (79%)	0.086
Age (years), mean (SD)	53 (8)	55 (8)	60 (8)	**<0.001**
Race/Ethnicity				0.064
Black	86 (74%)	61 (69%)	41 (65%)	
Hispanic	8 (6.8%)	11 (12%)	5 (7.9%)	
Other	20 (17%)	14 (16%)	8 (13%)	
White	3 (2.6%)	3 (3.4%)	9 (14%)	
Menopausal status				**<0.001**
Pre-menopausal/ early peri	36 (31%)	15 (17%)	4 (6.3%)	
Late peri/post-menopausal	81 (69%)	73 (83%)	59 (94%)	
BMI (kg/m²), mean (SD)	32.7 (9.3)	32.4 (9.3)	31.3 (8.1)	0.754
Nadir CD4, median (IQR)	271 (108, 460)	203 (112, 409)	204 (115, 320)	0.271
Detectable Viral Load	23 (31%)	13 (24%)	21 (43%)	0.108
Years Since ART Initiation, median (IQR)	15.4 (10.4, 21.5)	17.7 (11.6, 23.2)	19.5 (12.6, 23.9)	0.225
Current ART Use	72 (92%)	56 (100%)	50 (100%)	**0.015**
TDF Use				**0.002**
Current	5 (6.4%)	1 (1.8%)	2 (4.0%)	
Former	34 (44%)	38 (68%)	38 (76%)	
Never	39 (50%)	17 (30%)	10 (20%)	

Due to missing data, n's may not add up to total n=269. Data presented as counts (frequencies), unless otherwise noted.
[a]p-value from chi-square tests for categorical variables (Fisher's exact when cells are <5) or Anova/Kruskal-Wallis tests for continuous variables

Table 4. Multivariate (Unadjusted Analysis) of BMD (g/cm²).

		Unadjusted Model		
	BMD (g/cm²)	Beta	SE	p-value
Age (years)	-0.364	-0.004	0.001	**<0.001**
HIV Serostatus				
WWH	0.607 (0.086)	-0.017	0.011	0.13
WWoH	0.624 (0.082)	Ref.		
Ever Crack, Cocaine, Heroin Use				
Yes	0.609 (0.087)	-0.012	0.011	0.3
No	0.620 (0.082)	Ref.		
Menopausal Status				
Pre-menopausal/ early peri	0.652 (0.059)	Ref.		
Late peri/post-menopausal	0.602 (0.088)	-0.050	0.013	**<0.001**
Nadir CD4	0.188	0.0001	0.00003	**0.010**
Viral Load Detection				
Detected	0.598 (0.098)	-0.013	0.014	0.4
Undetected	0.610 (0.079)	Ref.		
Years since ART initiation	-0.093	-0.0004	0.0003	0.2
Ever TDF Use				
Yes	0.591 (0.085)	-0.045	0.013	**<0.001**
No	0.636 (0.080)	Ref.		

[a]Data presented as correlations (r) or means (SD)
[b]SE=Standard Error

Table 5. Multivariate (Adjusted Analysis) of BMD (g/cm²).

	Post-Menopausal[a] (n = 213)					
	Overall Cohort			WWH Only		
	Beta	SE	p-value	Beta	SE	p-value
Age	-0.004	0.001	**<0.001**	-0.004	0.001	**<0.001**
HIV Serostatus						
WWH	-0.026	0.013	**0.043**			
WWoH	Ref.					
Years since ART Initiation				-0.0004	0.0004	0.3
Ever TDF Use						
Yes				-0.043	0.014	**0.004**
No				Ref.		

[a]includes late perimenopausal and post-menopausal women

RESULTS (continued)

- Multivariate models were run separately in pre-menopausal and post-menopausal women.
- There were not significant associations identified in models limited to pre-menopausal women (data not shown), likely due to the relative limited sample size (n=56).
- In multivariate models including post-menopausal women, older age and HIV-serostatus were independently associated with lower BMD (Table 5). Specifically, WWH were more likely to have lower BMD than WWoH.
- In models limited to WWH, both older age and previous exposure to TDF were independently associated with lower BMD (Table 5).

DISCUSSION/CONCLUSIONS

- Significant gaps in osteoporosis diagnosis persist despite the high burden of disease in aging and postmenopausal women, particularly those living with HIV.
- We investigated the feasibility of using an FDA cleared portable, rapid, quantitative ultrasound (QUS)-based instrument in a cohort of women at high risk.
- Consistent with DXA based BMD, QUS-BMD was lower in postmenopausal and older women.
- In post menopausal women, HIV serostatus remained an independent predictor of low BMD, as did exposure to TDF despite the low number of WWH currently taking TDF-based ART (4%).

The Ultrascan650 is an effective, rapid point-of-care screening method for identifying women at risk for low bone mass with little participant burden or cost, which may help to narrow the diagnosis and treatment gap in this vulnerable population.

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