Novel radiographic measures HRpQCT and HSA as correlates of HIV-associated fractures

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Background

- Areal bone mineral density (aBMD) as assessed by dual energy x-ray absorptiometry (DXA) is often used to assess fracture risk
- However, limitations of this approach in HIV include
  - Lack of a clear fracture threshold
  - Lack of validation in HIV-infected populations
- Alternative bone imaging modalities might aid in fracture risk stratification
- High resolution peripheral quantitative computed tomography (HR-pQCT)
  - Non-invasive
  - Measures bone microarchitectural/geometric properties
  - Measures volumetric, cortical and trabecular BMD
  - Superior to DXA for discriminating those with and without fractures in general population
- Hip structural assessment (HSA)
  - Performed by analyzing images obtained from routine DXA
  - Estimates geometric and mechanical parameters
  - More readily available than HR-pQCT
- We conducted a pilot case-control study to determine whether HR-pQCT and HSA correlate with fracture in HIV-infected adults

Methods

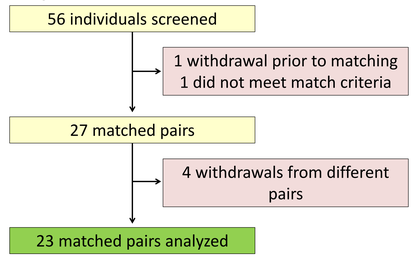
- **Design:** 1:1 matched case-control study
- **Setting:** 2 academic hospital-based HIV clinics in Toronto
- **Key eligibility criteria:**
  - HIV-infected adult aged ≥18 years
  - Not anticipated to change ART regimen during study
  - CASES: fracture after HIV diagnosis, not from major trauma
  - CONTROLS: no fracture, matched 1:1 with cases based on
    - Age (within 5 years)
    - Sex
    - Race (Caucasian, Black or Other)
    - Smoking status at time of fracture (or equivalent)
- **Study visits:**
  - 2 clinic visits (Spring & Fall)
  - 1 DXA (Hologic QDR 4500/Delphi A) at lumbar spine & hip
  - 1 HR-pQCT (X-treme CT, Scanco, Switzerland) at distal radius & tibia
- **Primary outcome measure:**
  - total volumetric BMD (tvBMD) at distal radius on HR-pQCT

Methods continued

- **Analysis:**
  - Differences in DXA, HR-pQCT and HSA parameters expressed as percentages of control group values
  - Conditional logistic regression first used to model relationship between DXA-derived T-scores & fracture, adjusting for duration of HIV
  - Individual HR-pQCT or HSA parameters added to model and nested models compared using likelihood ratio test
- **Ethical approval**: from Research Ethics Boards of the University Health Network and St. Michael's Hospital

Results

Figure 1. Participant enrollment flowchart



Results continued

Table 1. Participant Characteristics [a]

	Fracture (n=23)	No Fracture (n=23)	p
Age (years)	50 (45-57)	49 (46-56)	0.30
Male	18 (78%)	18 (78%)	--
Race			
Black	3 (13%)	3 (13%)	
Caucasian	18 (78%)	18 (78%)	
Other	2 (9%)	2 (9%)	
Smoking status	13 (57%)	13 (57%)	--
Born in Canada	18 (78%)	14 (61%)	0.10
Years from HIV Dx to fracture	11 (4-18)		
HIV risk factor			
MSM	13 (61%)	16 (70%)	
IDU	1 (4%)	2 (9%)	
Heterosexual	6 (26%)	5 (22%)	
Other	2 (9%)	0 (0%)	
Baseline CD4 (cells/mm^3)	496 (369-651)	465 (327-697)	0.52
Nadir CD4 count (cells/mm^3)	234 (123-370)	166 (36-410)	0.54
HIV RNA<40 copies/mL	19 (83%)	20 (87%)	0.71
Body mass index (kg/m^2)	24 (20-28)	25 (22-26)	0.98
Osteoporosis treatment ever[b]	4 (17%)	0 (0%)	--
Osteoporosis risk factors			0.32
Hypogonadism	0 (0%)	1 (4%)	n/a
Chronic Kidney Disease	1 (4%)	0 (0%)	n/a
Rheumatoid arthritis	1 (4%)	0 (0%)	n/a
Post menopausal[c]	3 (60%)	2 (40%)	0.32
Physical Activity (IPAQ)			
MET-minutes/week	3546 (1782-5245)	4314 (2772-7359)	0.95
Categorical Score			
Low	1 (6%)	0 (0%)	
Moderate	17 (94%)	18 (100%)	
High	0 (0%)	0 (0%)	
Missing	5	5	
Bone loading history			
Overall bone loading, hip	31 (20-67)	21 (12-37)	0.30
Overall bone loading, spine	30 (16-57)	18 (10-32)	0.18
Regular weight-bearing exercise (yes/no)	6 (26%)	12 (52%)	0.08
Laboratory values			
25-hydroxy vitamin D (nmol/L)	35 (21-44)	37 (22-45)	0.34
Ionized Calcium (mmol/L)	1.21 (1.18-1.26)	1.26 (1.24-1.28)	<.01

[a] Values shown are median (interquartile range) and frequency (percentage)
[b] Two participants on risedronate, two on alendronate
[c] Proportion among female participants only

Figure 2. Percentages differences in DXA and HR-pQCT parameters in fracture participants relative to matched controls

Figure 3. Percentages differences in HSA parameters in fracture participants relative to matched controls

Results continued

Table 2. Relationships between hip T-score, duration of HIV & radius tvBMD with fracture [a]

Variable	Univariate		Model 1		Model 2[a]	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Hip T-score	0.43 (0.17,1.10)	0.08	0.45 (0.17,1.14)	0.09	0.11 (0.01,1.08)	0.06
Years of HIV at Fracture	1.07 (0.98,1.17)	0.14	1.07 (0.97,1.18)	0.20	1.10 (0.96,1.25)	0.17
Total volumetric BMD (mg/cm3) (per 10)	0.99 (0.88,1.11)	0.81			1.29 (0.93,1.81)	0.13

[a] P=0.06 for likelihood ratio test comparing fit for Model 1 and Model 2

Table 3. Relationships between hip T-score, duration of HIV & buckling ratio at the narrow neck with fracture [a]

Variable	Univariate		Model 1		Model 2[a]	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Hip T-score	0.43 (0.17,1.10)	0.08	0.45 (0.17,1.14)	0.09	0.20 (0.03,1.12)	0.07
Years of HIV at Fracture	1.07 (0.98,1.17)	0.14	1.07 (0.97,1.18)	0.16	1.07 (0.94,1.21)	0.31
Buckling Ratio	1.01 (0.75,1.35)	0.96			0.69 (0.40,1.18)	0.17

[a] P=0.14 for likelihood ratio test comparing fit for Model 1 and Model 2

- Additional of other individual HR-pQCT and HSA parameters did not result in improved model fit compared to models containing T-score and duration of HIV alone (data not shown)
- Use of femoral neck or lumbar T-score instead of hip T-score did not qualitatively change results (data not shown)

Limitations

- Modest sample size due to challenges in recruiting
- Four patients in fracture group were on bisphosphonates
- Some fractures may not meet traditional definition of fragility fracture

Conclusions

- Low-trauma fracture is associated with numerical differences in cortical and trabecular bone architecture as assessed by HR-pQCT, and with estimates of bone strength as assessed by HSA, in HIV-infected adults
- We did not observe an improved ability to discriminate fracture and non-fracture patients using HR-pQCT or HSA beyond what was possible using DXA
- HR-pQCT and HSA warrant further study as supplementary markers of fracture risk in HIV

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