Bone quality determination by ultrasonometry in young South African HIV-infected children

Stephen M. Arpadi[1], Stephanie Shiau[1], Louise Kuhn[1], Jonathan J. Kaufman[2], Ashraf Coovadia[3], Renate Strehlau[3], Francoise Pinillos[3], Michael T. Yin[1], CHANGES Study Team

[1]Columbia University, New York, NY, USA, [2]Mount Sinai School of Medicine, New York, NY, USA , [3]University of the Witwatersrand, Johannesburg, South Africa

Stephen Arpadi, MD, MS
Columbia University
G.H. Sergievsky Center
622 W 168th Street PH 19-114
New York, NY 10032
212-305-2384
sma2@columbia.edu

Abstract

Background: Skeletal abnormalities, including decreased bone mineral content and density (BMC; BMD) by dual-energy X-ray absorptiometry (DXA) have been described in children and adolescents with HIV-infection. Although DXA is the most common method for characterizing bone, it is not widely available in resource-constrained settings (RCS) where the majority of HIV-infected children reside. Quantitative ultrasonography (QUS) assesses bone quality by measuring the attenuation and speed of an ultrasound wave through bone. It does not require radiation exposure or high-level training, is portable, costs less than DXA to perform, and has a short scan time, making it potentially well-suited for assessing and tracking bone acquisition in RCS. Here, we evaluate the relationship between QUS and DXA in young South African HIV-infected children.

Methodology: Data for this analysis was obtained at outpatient study visits from CHANGES (Childhood HAART Alterations in Normal Growth, Genes, and aGing Evaluation Study), a longitudinal cohort study of perinatally HIV-infected children in Johannesburg, South Africa. BMC and BMD of the whole body and lumbar spine were measured by DXA (Hologic Discovery Wi bone densitometer) and analyzed using Apex Version 3.4 software. Speed of sound (SOS) and the broadband ultrasound attenuation (BUA) at the heel/calcaneus were obtained by QUS (Lunar Achilles Insight). Calcaneus stiffness index (SI) was calculated as per manufacturer: SI = (0.67 x BUA + 0.28 x SOS) – 420.

Results: Forty seven children with a mean age of 7.7 ± 1.2 years (age range 6.0 to 9.8 years), including 26 (55.3%) boys and 21 (44.7%) girls were evaluated. The mean weight-for-age z-score (WAZ) was -0.62 ± 1.0 and mean height-for-age z-score (HAZ) was -1.33 ± 1.0. Twenty one (44.7%) of the children were on a LPV/r-based regimen and 26 (55.3%) were on an EFV-based regimen. All children were also on two NRTIs, including 3TC and ABC or d4T, but not TDF. BUA was moderately correlated with whole body BMC (0.50, p<0.01) and BMD (0.49, p<0.01) as well as lumbar spine BMC (0.50, p<0.01) and BMD (0.48, p<0.01). SI was also moderately correlated with whole body BMC (0.40, p<0.01) and BMD (0.39, p<0.01) as well as lumbar spine BMC (0.37, p<0.01) and BMD (0.43, p<0.01). Independently, SOS did not have significant correlations with whole body or lumbar spine BMC and BMD.

Conclusions: In this sample of young children with HIV receiving ART, QUS BUA and SI correlate significantly with whole body and lumbar spine BMC and BMD. Although additional research is necessary, QUS may prove to be a valuable method to assess bone quality and acquisition in HIV-infected children in RCS.

Introduction

- Skeletal abnormalities, including decreased bone mineral content and density (BMC; BMD) by dual-energy X-ray absorptiometry (DXA) have been described in children and adolescents with HIV-infection.
- Although DXA is the most common method for characterizing bone, it is not widely available in resource-constrained settings (RCS) where the majority of HIV-infected children reside.
- Quantitative ultrasonography (QUS) is a non-invasive method that assesses bone quality by measuring the acoustic properties of bone.
- It does not require radiation exposure or high-level training, is portable, costs less than DXA to perform, and has a short scan time, making it potentially well-suited for assessing and tracking bone acquisition in RCS.
- Here, we evaluate the inter-rater reliability of QUS and the relationship between QUS and DXA in a cohort of young South African HIV-infected children.

Acknowledgements

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Methods

Study Design

- Data was obtained at outpatient study visits from **CHANGES** (Childhood HAART Alterations in Normal Growth, Genes, and aGing Evaluation Study), a longitudinal cohort study of perinatally HIV-infected children conducted at the Empilweni Service and Research Unit at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa

Dual-energy X-ray absorptiometry (DXA)

- BMC (g) and BMD (g/cm^2) of the whole body, lumbar spine, and forearm were measured by DXA (Hologic Discovery Wi bone densitometer) and analyzed using Apex Version 3.4 software.
- DXA uses 2 X-ray beams at different photon energies to differentiate bone from soft tissue. DXA calculates BMD using areal BMD (aBMD).

Figure 1. DXA of the whole body, lumbar spine, and forearm (A), DXA scan at Rahima Moosa Mother and Child Hospital (B)

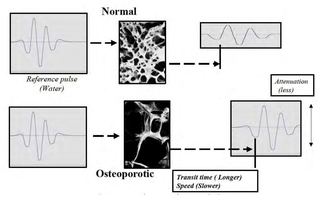
(A) (B)

Quantitative Ultrasound (QUS)

- Two operators performed QUS measurements.
- Speed of sound (SoS) (m/s) and broadband ultrasound attenuation (BUA) (dB/MHz) through the heel/calcaneus were measured with the Lunar Achilles Insight Bone Sonometer (GE Healthcare, United Kingdom).

Figure 2. Ultrasound transmission

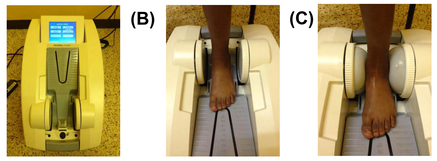
SoS (m/s) is both mass and architecture dependent, whereas BUA (dB/MHz) is sensitive to orientation of trabeculae and may be more reflective of architecture than density.



- While seated with foot in the foot positioner, the heel is surrounded by warm water encapsulated between inflated membranes.
- An electrical signal is converted to a sound wave which passes through the water and the individual's heel. A transducer on the opposite side of the heel receives the sound wave and converts it to an electrical signal that is analyzed.

Figure 3. Achilles Insight quantitative ultrasonometer (A) with membranes deflated (B) and membranes inflated (C)

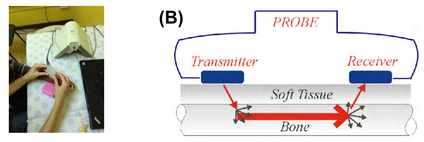
(A) (B) (C)



- The Achilles Insight combines SoS and BUA to form the stiffness index (SI) = (0.67 x BUA + 0.28 x SOS) – 420.
- Transaxial SoS (m/s) along the distal 1/3 radius was obtained by the Sunlight Mini-Omnisense Bone Sonometer (BeamMed, Petah Tikva, Israel).
- MiniOmni uses a hand-held probe to generate and detect ultrasound waves. The probe is applied directly to the skin at the radius and a layer of ultrasound gel is applied between the probe surface and the probe cap. Ultrasound is emitted by the generating transducers and transmitted along the bone.

Figure 4. MiniOmni measurement (A) and ultrasound wave transmission with the MiniOmni probe signal path (B)

(A) (B)



Results

Characteristics

- 130 children with a mean age of 6.5 ± 1.3 years (age range 5.0 to 9.6 years), including 70 (53.8%) boys and 60 girls (46.2%) were evaluated.
- 67 (51.5%) of the children were on a LPV/r-based regimen and 63 (48.5%) were on an EFV-based regimen. All children were also on two NRTIs, including 3TC and ABC or d4T, but not TDF.

Table 1. Characteristics of 130 HIV-infected children age 5-9

Characteristic	N=130
Sex, N (%) Male Female	 70 (53.8) 60 (46.2)
Age (years), Mean ± SD	6.5 ± 1.3
Age (years), Median (IQR)	6.2 (5.5, 7.2)
Weight-for-age Z-score, Mean ± SD	-0.88 ± 0.9
Height-for-age Z-score, Mean ± SD	-1.53 ± 1.0
BMI-for-age Z-score, Mean ± SD	0.14 ± 0.9
Antiretroviral treatment regimen, N (%) EFV-based LPV/r-based	 67 (51.5) 63 (48.5)
CD4%, Mean ± SD	36.2 ± 6.4
Viral Load, N (%) 40-1000 <40	 7 (5.8) 114 (94.2)

Inter-rater Reliability of QUS

Measurement	Intra-class correlation coefficient (ICC)	P-value
Mini Omni SoS	0.956	p<0.05
Insight SoS	0.432	p=0.123
Insight BUA	0.914	p<0.05

DXA and QUS Measurements

Table 2. DXA and QUS Measurements

DXA	Mean ± SD
WB BMC (g)	646 ± 111
WB BMD (g/cm^2)	0.64 ± 0.06
LS BMC (g)	14.7 ± 3.11
LS BMD (g/cm^2)	0.46 ± 0.06
1/3 R BMC (g)	0.71 ± 0.10
1/3 R BMD (g/cm^2)	0.39 ± 0.04

QUS	Mean ± SD
Mini Omni SoS (m/s)	3641 ± 130
Insight SoS (m/s)	1609 ± 62.1
Insight BUA (dB/MHz)	72.5 ± 18.4
Insight SI	78.6 ± 13.6

Correlations between DXA AND QUS

- QUS BUA was moderately correlated with whole body BMC (0.64) and BMD (0.56) as well as lumbar spine BMC (0.61) and BMD (0.46) obtained by DXA.

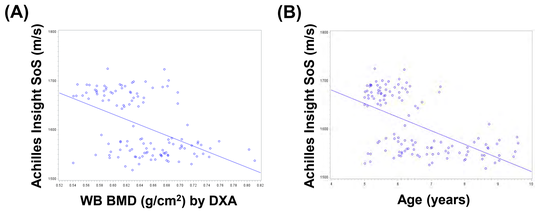
Table 3. Correlations between QUS and DXA Measurements

QUS vs. DXA	WB BMD	WB BMC	LS BMD	LS BMD	1/3 R BMD	1/3 R BMC
MiniOmni SOS	0.432 p<0.001	0.436 p<0.001	0.287 p=0.002	0.257 p=0.005	0.322 p<0.001	0.385 p<0.001
Insight SOS	-0.522 p<0.001	-0.478 p<0.001	-0.479 p<0.001	-0.308 p<0.001	-0.479 p<0.001	-0.393 p<0.001
Insight BUA	0.638 p<0.001	0.556 p<0.001	0.605 p<0.001	0.457 p<0.001	0.587 p<0.001	0.455 p<0.001
Insight SI	-0.08 p=0.395	-0.09 p=0.303	-0.05 p=0.604	0.04 p=0.673	-0.074 p=0.415	-0.09 p=0.319

- Surprisingly, Insight SoS was negatively correlated with all DXA measures, leading to no correlation between Insight SI and DXA.
- A closer look at Insight SoS indicated a bimodal distribution, with a group of younger children (also shorter and lighter in size) having a cluster of higher Insight SoS values.

Figure 5. Plots of Achilles Insight SoS (m/s) vs. WB BMD (g/cm^2) (A) and Achilles Insight SoS (m/s) vs. Age (years) (B)

(A) (B)



- Correlations of a trans-axial SoS as measured by the MiniOmni were correlated better with DXA measurements.

Conclusions

- In this sample of young children with HIV receiving ART, QUS BUA of the calcaneus and transaxial SoS measurements of the 1/3 radius were highly reliable by 2 operators and correlated significantly with DXA measurements.
- Calcaneal SoS measurements varied between operators, was bimodally distributed, and did not correlate well with DXA measurements of bone mass.
- The reason for the bimodal distribution of the Achilles Insight SoS is unknown at this time.
- Although additional research is necessary, QUS may prove to be a valuable method to assess bone quality and acquisition in HIV-infected children in resource-constrained settings.