Bone Microarchitecture Parameter for Early Diagnosis of Osteopenia in Thalassemia.

Regine Grosse[1], Isolde Frieling[2], Ellen B. Fung[4], Achim Wüsthof[3], H.P. Kruse[2], Roland Fischer[1,4], Gritta E. Janka[1]. *[1]University Medical Center Hamburg-Eppendorf, [2]Osteoporosis Center Hamburg-Neuer Wall, [3]Endocrinology Center, Hamburg, Germany; [4]Children's Hospital & Research Center Oakland, USA.*

In recent decades, survival in thalassemia patients has been prolonged; as a result, complications such as osteoporosis not previously observed will need earlier attention and better diagnostic tools. The diagnosis of osteoporosis is typically made by endocrine assessment and 2-dimensional bone mineral density (BMD) measurements like dual energy x-ray absorptiometry (DXA). However, DXA may be insufficient to assess fracture risk in patients with thalassemia. We compared the microarchitecture and volumetric density of bone using high-resolution peripheral quantitative computed tomography (HR-pQCT) with planar BMD (DXA). In 18 transfused patients (age: 13 - 43 y, 9/18 female) with beta-thalassemia, BMD of the lumbar spine (LS) and total hip was measured by DXA resulting in 7/18 patients with calculated Z-scores < -2.0. In addition, we assessed the volumetric BMD and the bone microarchitecture of the non-dominant distal radius and tibia by HR-pQCT (XtremeCT®, SCANCO Medical AG). Planar BMD values by DXA, correlated with cortical thickness (Spearman rank correlation $R_S = 0.78$, $p = 0.0001$), cortical density ($R_S = 0.67$, $p = 0.003$), while LS Z-scores correlated best with total volumetric density ($R_S = 0.60$, $p = 0.009$) measured by HR-pQCT at the distal radius. Thus, a porous inner bone structure may appear masked by DXA measurements with ostensible normal planar BMD results due to a massive corticalis. From the many different HR-pQCT parameters measured, those with the highest variability (COV) might be of greatest promise to predict defective bone architecture in thalassemia. These parameters were compared with reference data from Boutroy et al (J Clin Endocrinol Metab 2005;90:6508-15) of normal and osteopenic women. Despite relative uniformity in DXA Z-scores, TbSp and TbSp SD parameters of the radius covered a broad range (COV, F-test) of high values in thalassemia compared to osteopenic women (Table I).

Table I. Comparison of Z-scores and radial trabecular density (D_{trab}), separation (TbSp), inhomogeneity (TbSp SD) with reference parameters from Boutroy et al (2005) of normal and osteopenic women ($F_{critical} > 3.0$ for $p < 0.001$).

	Thalassemia (n=18)		*Normal (n=108)*		*Osteopenic (n=113)*	
Parameter	Mean ± SD	COV	Mean ± SD	F-test	Mean ± SD	F-test
LS-Zscore (DXA)	-1.7 ± 1.3	80%	0	Na	-1.4 ± 0.6	4.9
Hip-Zscore (DXA)	-1.3 ± 1.0	78%	0	Na	-1.6 ± 0.5	3.9
D_{trab} [mg/cm^3]	138 ± 71	51%	160 ± 33	4.6	123 ± 36	3.9
TbSp [µm]	959 ± 1265	132%	517 ± 88	207	656 ± 187	45.8
TbSp SD [µm]	600 ± 890	148%	212 ± 58	236	342 ± 201	19.6

The SD of the trabecular separation (TbSp SD) of radius and tibia, characterizing the porosity of the spongiosa, may become the most interesting parameter in thalassemia as it was significantly correlated with age ($R_S = 0.79$, $p = 0.0001$), hip Z-score ($R_S = -0.49$, $p = 0.044$), osteocalcin ($R_S = -0.70$, $p = 0.001$), FSH ($R_S = -0.65$, $p = 0.005$) and with liver iron concentration (tibia: $R_S = 0.55$, $p = 0.017$), respectively. Patients with hypogonadism (n = 9/18, FSH: 0.1 – 1.7 U/l) were significantly different (U-test) from normals (FSH: 2.1 – 6.8 U/l) with respect to TbSp ($p = 0.024$) and TbSp SD ($p = 0.019$), but not DXA Z-scores. Many patients with thalassemia are affected by hypogonadism. For these adolescent patients, the measurement of bone microarchitecture by HR-pQCT of low radiation burden (3 µSv) may help to identify risk early and avoid or minimize future morbidity, especially, in the presence of still normal results from DXA measurements.

3826 characters with spaces (max. 3872)