EVALUATION OF BONE MINERAL DENSITY AND MICROARCHITECTURAL PARAMETERS BY DXA AND HR-pQCT IN X-LINKED HYPOPHOSPHATEMIC RICKETS

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BACKGROUND

The **X-linked hypophosphatemic rickets (XLH)** is caused by inactivating mutations in the *PHEX* gene. It is characterized by a pathological increase in FGF23 levels, hyperphosphaturia and hypophosphatemia, resulting in mineralization defects in the growth plate and bones.

The areal bone mineral density (**aBMD**) is usually evaluated by dual-energy x-ray absorptiometry (**DXA**) but, in XLH patients, anatomical and anthopometric factors can interfere with the results. In contrast, high-resolution peripheral quantitative computed tomography (**HR-pQCT**) determines the volumetric bone mineral density (**vBMD**), which reduces the confounding effect of the anthropometry; in addition, HR-pQCT analyzes the cortical and cancellous compartments separately and characterizes the bone microarchitecture. However, there is scarce information about HR-pQCT analysis in XLH patients.

AIM

To evaluate the BMD and bone microarchitecture in XLH patients with confirmed *PHEX* mutations, followed in a single center, compared to healthy controls.

PATIENTS AND METHODS

- Thirty-six patients (**13 children** and **23 adults**; 26 women and 10 men), with disease-causing *PHEX* mutations determined by Sanger and MLPA methods, were selected.
- **aBMD** at the lumbar spine, the femoral neck, the total hip and the distal radius were analyzed by **DXA** using a Hologic QDR 4500 device (Hologic Inc, Waltham, Massachusetts, USA).
- **HR-pQCT** was performed using the Xtreme CT scanner (SCANCO Medical AG, Brüttisellen, Switzerland) at the distal radius and distal tibia. The parameters calculated by HR-pQCT were: **vBMD**, **Tb vBMD** (trabecular vBMD), **Ct vBMD** (cortical vBMD); **Tb.N** (mean trabecular number), **Tb.Th** (trabecular thickness), **Tb.Sp** (mean space between trabeculae), **SD.1/Tb.N** (trabecular network inhomogeneity) and **Ct.Th** (cortical thickness).
- Results in all patients were compared to 36 healthy age-, gender- and pubertal stage-matched control subjects (age range 12 to 72 years).
- The comparison between the patients and control subjects was performed using the independent unpaired Student's t test or Mann-Whitney U test. All tests were 2-tailed and a *p* value <0.05 was considered statistically significant.

RESULTS

XLH patients, mainly the adults, presented with higher aBMD at the L1-L4 ($p<0.01$) and lower aBMD at the distal third of the radius ($p<0.01$) than healthy controls – **figure 1**. Besides, there was a trend towards lower aBMD at the total radius ($p=0.12$). There were no differences between groups at the femoral neck, the total hip and the ultradistal radius ($p=0.49$, $p=0.90$ and $p=0.57$, respectively).

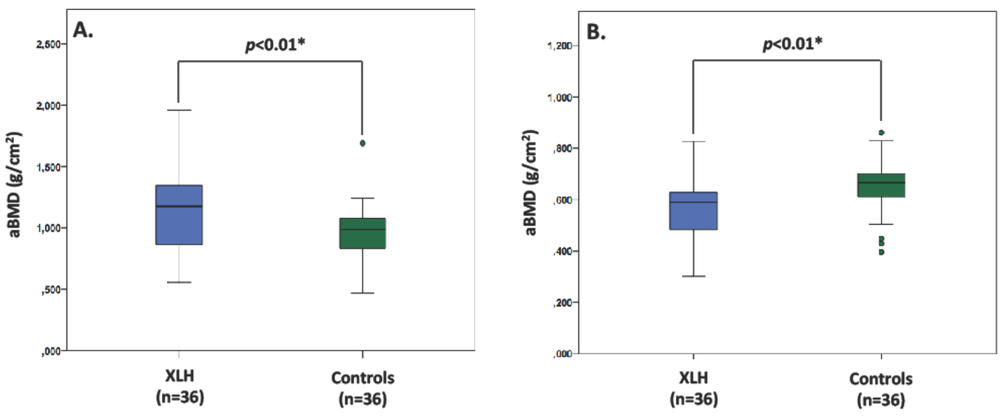

Figure 1. Comparison of the **aBMD** at the **L1-L4 (A)** and at the **distal 1/3 of the radius (B)** measured by DXA between XLH patients and healthy controls.

No differences were observed in vBMD at the distal radius ($p=0.50$), although the XLH patients presented lower total vBMD ($p<0.01$) at the distal tibia compared to the controls, probably resulting from decreased Tb.vBMD ($p<0.01$). Ct.vBMD was similar between groups ($p=0.27$) – **figure 2**.

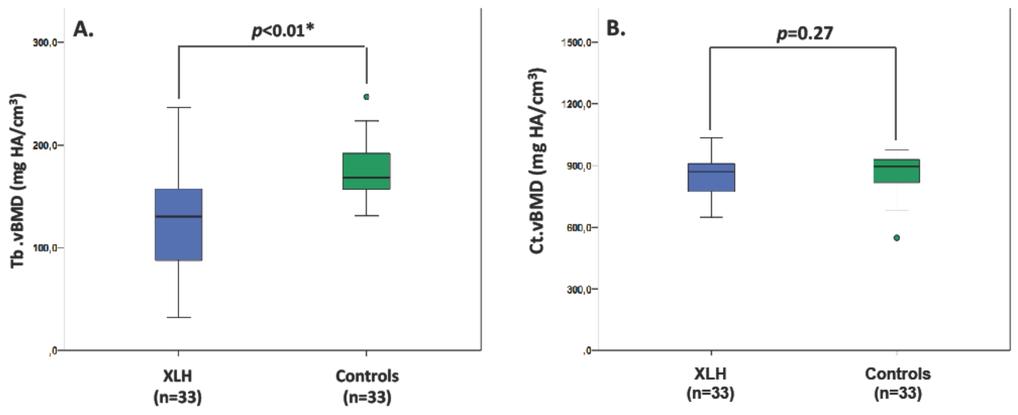

Figure 2. Comparison of the **Tb.vBMD (A)** and the **Ct.vBMD (B)** at the **distal tibia** measured by HR-pQCT between XLH patients and healthy controls.

Regarding to the microarchitectural parameters, XLH patients presented lower Tb.N ($p<0.01$), greater Tb.Sp ($p<0.01$) and more inhomogeneous trabecular network ($p<0.01$) at both sites – **figures 3-5**. No differences were observed in the Tb.Th and the Ct.Th at the distal radius ($p=0.25$ and $p=0.82$, respectively) and at the tibia ($p=0.56$ and $p=0.68$, respectively).

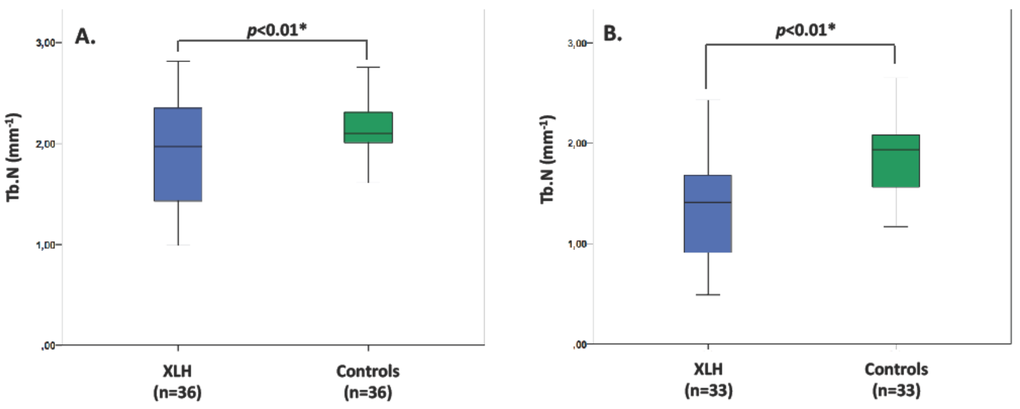

Figure 3. Comparison of the **Tb.N** at the **distal radius (A)** and at the **distal tibia (B)** measured by HR-pQCT between XLH patients and healthy controls.

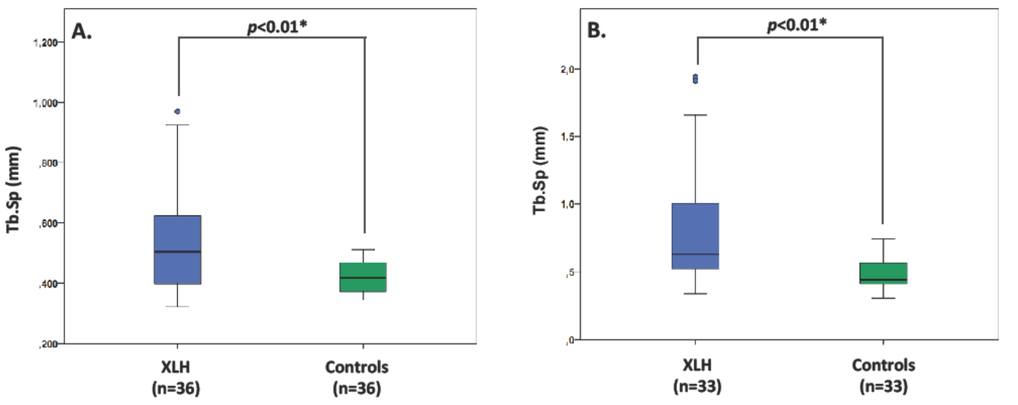

Figure 4. Comparison of the **Tb.Sp** at the **distal radius (A)** and at the **distal tibia (B)** measured by HR-pQCT between XLH patients and healthy controls.

Figure 5. Comparison of **SD.1/Tb.N** at the **distal radius (A)** and at the **distal tibia (B)** measured by HR-pQCT between XLH patients and healthy controls.

CONCLUSIONS

DXA analysis requires caution due the interference of anatomical and anthropometric factors. On the other hand, **HR-pQCT** analysis was more reliable and suggested that the negative effects of the XLH are primarily manifested in the cancellous compartment and that the distal tibia seems to be more affected than the distal radius.

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