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University of Southern Denmark

Bone Geometry, Volumetric Bone Density, Microarchitecture and Estimated Bone Strength Assessed by HR-pQCT in Adult Patients with Hypophosphatemic Rickets

V.V. Shanbhogue[1,2], S. Hansen[1,2], L. Folkestad[1,2], K. Brixen[1,2], S.S. Beck-Nielsen[1,3]

[1]Dept. of Endocrinology, Odense University Hospital, Denmark,[2]Institute of Clinical Research, University of Southern Denmark, Odense, [3]Dept. of Pediatrics, Hospital of Southwest Denmark, Esbjerg

CONCLUSIONS

Adult patients with Hypophosphatemic Rickets have:

- **decreased total vBMD at the radius and tibia, decreased cortical vBMD and cortical thickness at the radius, normal trabecular vBMD, but the trabecular microarchitecture is compromised**
- **preserved estimated bone strength due to geometrical adaptation with larger total and trabecular cross-sectional areas at radius and tibia**
- **increased cortical porosity, when treated long term with calcitriol and phosphate, supporting the opinion that medical treatment should be limited to those being symptomatic and/or to improve fracture healing or surgical recovery**

Introduction

Hypophosphatemic rickets (HR) is characterized by a generalized mineralization defect with osteomalacia. Osteomalacia is most often associated with impaired bone strength, but paradoxically, HR patients show a decreased fracture risk. The explanation for this is unclear; while data from bone biopies describe decreased mineralization, densitometric studies have found HR patients to have an elevated axial bone mineral density (BMD), and a normal to decreased appendicular BMD. Data on the bone geometry and microstructure in HR are scarce. Whether or not to treat adult HR patients with calcitriol and phosphate is unclear.

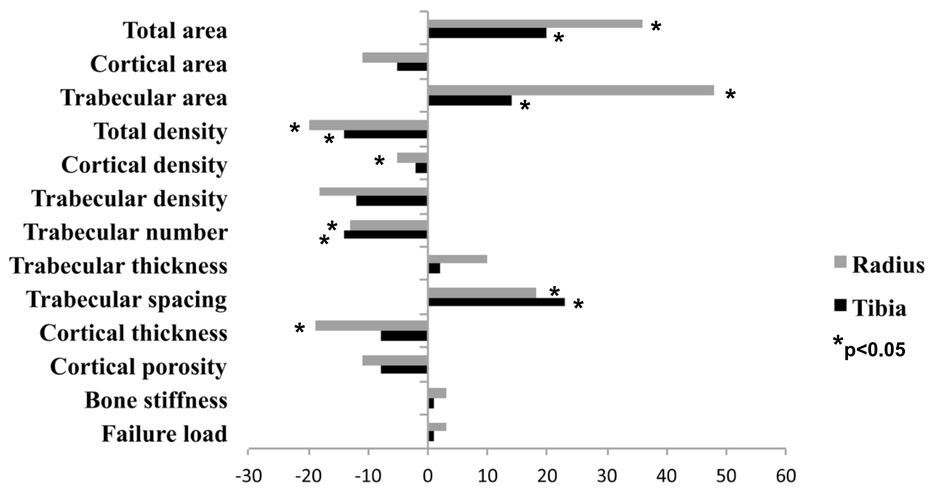
Aim

To assess bone geometry, volumetric BMD (vBMD), microarchitecture and estimated bone strength in adult patients with HR, and to evaluate effects of medical treatment.

Methods

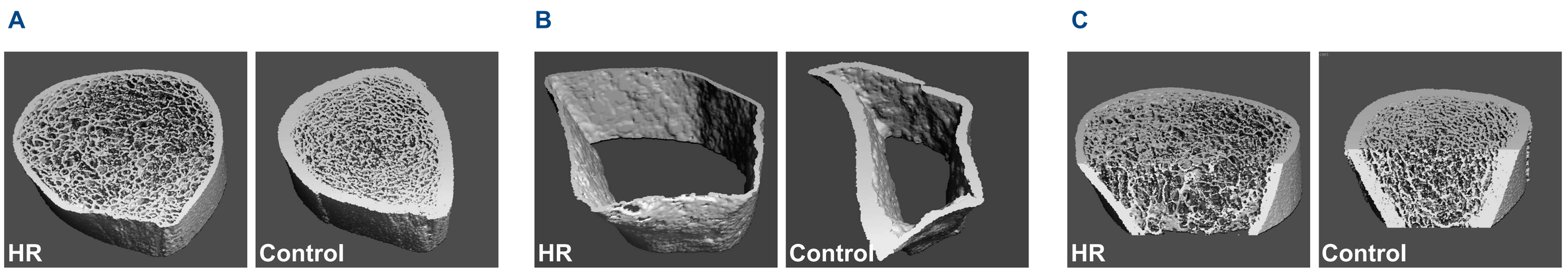
High-resolution peripheral quantitative computed tomography (HR-pQCT) (Scanco Medical AG, Brüttisellen, Switzerland) was used studying 29 patients (aged 19 to 79 years; 21 female, 8 male patients), 26 of whom had genetically proven X-linked HR. Exclusion criteria were non-FGF23 associated or aquired HR. Due to the disproportioned stature in HR, the region of interest in the HR-pQCT images at the distal radius and tibia was placed in a constant proportion to the entire length of the bone. Finite Element Analysis was performed to estimate the mechanical properties of the bone. Eighteen HR patients received medical treatment, defined as current treatment and with a duration of at least 10 years. Each HR patient was matched with respect to age and sex with a healthy subject.

FIGURE 1: Bone Parameters in HR compared to controls



Percentage diference between Hypophosphatemic Rickets patients and control subjects (reference to control)

FIGURE 2: Cross-sectional images from HR and controls



Results

- At both radius and tibia, HR patiets had significantly larger **total and trabecular bone areas** (both p<0.001), compared to controls. There were no differences in **cortical area** (radius: p=0.27, tibia: p=0.70), but the **cortical thickness** was significantly lower in radius (p<0.01), bot not tibia (p=0.23), **figure 1 and 2A+B**
- At radius, both **total vBMD** and **cortical vBMD** were significantly lower (both p<0.001) in HR patients compared to controls, while **trabecular vBMD** was similar between the two groups (p=0.25). In tibia, **total vBMD** was also lower (p<0.01), **cortical vBMD** and **trabecular vBMD** were not different to controls (p=0.13 and p=0.07), **figure 1**
- The **trabecular integrity** was compromised at both radius and tibia, with a lower number of trabeculae (both p<0.01) and a greater trabecular network inhomogenity (both p<0.01), but the trabecular thickness was within the normal range (radius: p=0.15, tibia: p=0.54), **figure 1 and 2C**
- At tibia, **currently treated** HR patients had significantly larger **total** (p<0.05) and **trabecular areas** (p<0.05) compared to those not on current therapy, in addition to a lower **cortical vBMD** of both radius and tibia (radius: p<0.01, tibia: p<0.05) and a higher **cortical porosity** at both sites (both p<0.05)
- **Total bone stiffness** and **estimated failure load** of both radius and tibia, were not significantly different between HR patients and controls, or between currently treated vs. untreated HR patients

Contact: sbeck-nielsen@health.sdu.dk