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Perspective Article

Hylonome

The bone behind a low areal bone mineral density: Peripheral quantitative computed tomographic analysis in a woman with osteogenesis imperfecta

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Abstract

Areal bone mineral density (BMD) is the most widely used densitometric parameter. However, this approach makes it difficult to understand the structural basis of bone diseases, because a large number of bone properties are integrated into a single number. This is exemplified in the present case of a 27-year-old woman with osteogenesis imperfecta type I. Peripheral quantitative computed tomographic analysis at the radial metaphysis and at the radial diaphysis revealed a decreased areal BMD at both sites (z score -3.9 and -3.4, respectively). Yet, the structural basis for this decrease was different for the two locations: At the distal radius areal BMD was decreased because volumetric BMD was very low, whereas bone size was above the mean of the reference range. At the proximal radius areal BMD was decreased, because bone size was very low but volumetric BMD was above average. Bone mineral content of the radial diaphysis was very low for forearm muscle size, a finding which is compatible with Frost's hypothesis that the mechanostat setpoint is increased in osteogenesis imperfecta.

Keywords: Bone Mineral Density, Radius, Muscle, Osteogenesis Imperfecta, Peripheral Quantitative Computed Tomography

Introduction

Areal bone mineral density (BMD) is the most widely used densitometric parameter[1]. When a low value is found, osteopenia or osteoporosis are said to be present[2]. However, as Parfitt noted in a recent editorial, reducing the complex anatomy of a bone to a single number comes at the cost of losing touch with the underlying structural reality[3]. Peripheral quantitative computed tomography (pQCT) offers the opportunity to regain a handle on bone structure and to bring bone pathophysiology back into the focus of the clinician. This is exemplified in the present case of a woman with osteogenesis imperfecta (OI).

Subject and methods

The study subject was a 27-year-old woman with OI type I. Sclerae were clearly blue. The family history was positive for OI, as the subject's father and her son were also affected. She had sustained multiple fractures during childhood, but only one fracture had occurred after puberty (in a high velocity car accident). Mobility was unrestricted. Body height was 162 cm, body weight was 55 kg. pQCT measurements (scanner XCT-2000; Stratec Inc., Pforzheim, Germany) were performed at two sites of the non-dominant forearm, as described in detail before[4-7]. Briefly, the distal radial metaphysis was analyzed at the site whose distance to the distal radial articular surface corresponded to 4% of forearm length[4]. Measurements of the radial diaphysis and muscle cross-sectional area (CSA) were performed at a location whose distance to the ulnar styloid process corresponded to 65% of forearm length[5,6]. Total CSA of the radius, bone mineral content (BMC), total volumetric BMD (vBMD), trabecular and cortical vBMD, cortical thickness, cortical CSA and muscle CSA were determined as described[4-7]. Areal BMD was calculated as BMC/bone width. z scores were calculated using reference data established in our unit[4-7].

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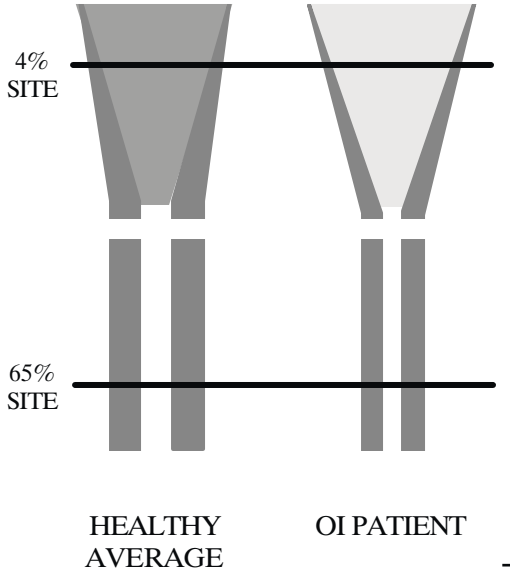
Results

Results of pQCT analyses and the corresponding age-dependent z scores are shown in Figure 1. The total CSA of



	ABSOLUTE VALUES	Z SCORES
DISTAL RADIUS		
TOTAL CSA (mm^2)	318	1.0
BMC (mg/mm)	73	-3.0
TOTAL vBMD (mg/cm^3)	230	-3.6
AREAL BMD (mg/cm^2)	365	-3.9
TRABECULAR vBMD (mg/cm^3)	74	-3.2
CORTICAL THICKNESS (mm)	0.8	-2.2
PROXIMAL RADIUS		
TOTAL CSA (mm^2)	50	-3.3
CORTICAL CSA (mm^2)	34	-4.6
RELATIVE CORTICAL CSA (%)	67	0.2
TOTAL vBMD (mg/cm^3)	808	0.5
CORTICAL vBMD (mg/cm^3)	1176	0.8
BMC (mg/mm)	41	-5.3
AREAL BMD (mg/cm^2)	508	-3.4
MUSCLE CSA (mm^2)	2618	-1.3
CORT. CSA/MUSCLE CSA (%)	1.30	-3.5

Figure 1. Schematic representation of the radial metaphysis and diaphysis to visually demonstrate the findings in a 27-year-old woman with OI type I.

the distal radius was above average, whereas BMC, total vBMD, areal BMD, trabecular vBMD and cortical thickness were very low. At the radial diaphysis, total CSA and cortical CSA were decreased, but the ratio between these two measures (relative cortical CSA) was normal. Total vBMD and cortical vBMD were slightly above average, while BMC and areal BMD were low. Muscle CSA was below the age-specific mean value. The ratio between cortical CSA of the radial diaphysis and muscle CSA was clearly below the reference range.

Discussion

Although bone densitometry is not essential for establishing the diagnosis of OI, such a procedure is commonly performed in OI patients. This is often done with the intent to assess fracture risk. As exemplified in this report, densitometry can not only be used to estimate the probability of events in the patient's future, but may also provide some information whether the skeleton is adapted to its current functional requirements. This OI patient had an areal BMD z score below -2.5 both at the radial metaphysis and at the diaphysis. This is expected in OI, and one might be content to diagnose 'osteoporosis' or 'high fracture risk' and leave it at that. Yet, there is quite a complex reality behind the low areal BMD.

The decrease in total vBMD was 'site-specific', with a low value at the metaphysis but a normal result at the diaphysis. Total vBMD at the metaphysis was low, because trabecular vBMD was decreased to about 40% of the mean value in healthy young women[4], cortical thickness was decreased, and total CSA was relatively large. Total vBMD at the diaphysis was normal, because total CSA and cortical CSA were decreased to the same extent and therefore relative cortical CSA was normal. Relative cortical CSA is the main determinant of total vBMD at diaphyseal sites[8]. The second determinant of total vBMD, cortical vBMD, was slightly above average. This may even be an underestimation, because pQCT yields falsely low values for cortical vBMD when cortical thickness is decreased, due to the partial volume effect[9]. A relatively high vBMD in the cortical compartment does not come as a surprise, because the material density of mineralized bone tissue is increased in OI[10].

These observations show that the low values for areal BMD had a different basis at the metaphyseal and diaphyseal sites. Areal BMD depends both on total vBMD and on the path length of the radiation beam through the bone[8]. At the metaphysis, areal BMD was low despite large bone size, because total vBMD was very low. At the diaphyseal site, areal BMD was low despite normal total vBMD, because bone size was decreased. As to the underlying pathophysiology, why was the bone's cross-section relatively large at the metaphysis and decreased at the diaphysis, a finding which in many OI patients is also obvious from standard X-rays[11]? During longitudinal growth, the increase in the external size of the metaphysis depends on the balance between lateral expansion of the growth plate

and resorption at the periosteal surface of the metaphysis[7]. In contrast, the external size of the diaphysis increases by periosteal apposition. These two tissue mechanisms appear to react differently to the molecular abnormalities that cause OI.

The ratio between cortical CSA and muscle CSA was well below the reference range. This matches the predictions of Frost's hypothesis that the mechanostat setpoint is too high in OI[12]. According to this theory there should be a decreased amount of bone relative to the level of mechanical stimulation. Since the largest physiological loads on bones result from muscle contraction and muscle force depends on muscle size, a decreased ratio between bone mass and muscle size is therefore expected from mechanostat theory.

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