Bone mineral density measurement in children and adolescents

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Summary

Interpretation of densitometric measurements in children is more complicated than in adults because of steady growth of children over expressed by heterogeneity of skeletal development. Obtained results are additionally affected by age, sex, body mass, height, bone age, environmental factors and illnesses. The aim of this review is to provide overview of present status concerning measurements in children and potential technical possibilities and limitations.

KEY WORDS: bone mass measurements, possibilities, limitations, children, results interpretation.

Introduction

The clinical assessment of bone strength and fracture risk as well in children as in adults has always been a difficult challenge for its practical solution. The reason for that seems to be matter of both – focus and target. The problem concerns not only how or how well to measure, but essentially what to measure, and mostly how to interpret the data. The additional special challenge is interpretation of children's data, what is related to the fact that bone mineral accrual throughout childhood and adolescence involves changes in bone size, geometry, and mineral content (1). The processes evolve at varying rates in different regions of the skeleton, with appendicular growth preceding spinal mineral acquisition. Trabecular and cortical compartments respond variably to sex steroids, calcium intake, and mechanical loading. The tempo of mineral accrual is more closely linked to pubertal and skeletal maturation than to chronological age, and these processes vary with gender and ethnicity. Additional problem is related to limited access to pediatric reference data (2).

Dual-Energy X-Ray Absorptiometry (DXA)

The most commonly used technique for the assessment of bone mineral content has became densitometric measurement with the use of DXA. DXA measurements are performed in the lumbar spine, femurs, forearms, and the whole body. Principle of operation of DXA measurement relies on the fact that when X-ray beam scans across the region of interest, bone attenuates the passing energy (3, 4). The differences in relative attenuation are calculated and expressed as bone mineral content (BMC) in grams. Later on BMC values became divided by the projected area of the bones analyzed, referred conventionally as BMD and expressed as grams per square centimeter. Limitation is that referred as areal density DXA does not represent a volumetric density measurement. Additionally DXA cannot eliminate cancellous from cortical bone, and the resulting values reflect as the sum of both components (2). Beside substantial differences, a remarkable increase in BMD is observed in both sexes after the onset of puberty reaching a peak at approximately the time of cessation of longitudinal growth and epiphyseal closure (5, 6).

Quantitative Computed Tomography (QCT)

QCT is an established technique for measuring BMD in the axial and appendicular skeleton (7, 8). CT image is formed by three dimensional voxels, which are small squares of different optical density depending on the tissue they represent. Unfortunately, beside significant irradiation, in small or sick children the size of cancellous and cortical bone is frequently smaller than the voxel size, therefore, not only bone but also marrow can be represented (9). The recent application of QCT to assess the appendicular skeleton as pQCT has significantly dropped potential irradiation and improved the ability to measure cortical bone in this area. By this means it can be measured: the cross-sectional area (cm^2), bone geometry, and the cortical bone density. Results expressed as grams per cubic centimeter (vBMD) beside being true volumetric measurements (9) are providing with information about bone geometry what allow to calculate noninvasively (using special algorithm) so called Strength-Strain Index (SSI). The SSI has been shown to provide a good estimate of bone mechanical strength at least of the human radius and tibia (1).

Quantitative Ultrasound measurement (QUS)

The first generation of QUS systems characterized the bone tissue with the use of two relevant parameters: the speed of sound (SOS) and the attenuation of the signal [broadband ultrasound attenuation (BUA)] (2). The amount of attenuation depends on the structure, the specific acoustic properties of the medium, and the wavelength the ultrasound signal used (10). In performed in vivo ultrasound measurements, it is not possible to separate absorption from scattering what is resulting measurement of total attenuation (11). Generally, QUS devices provide a combined measurement nominated "stiffness" or "quantitative ultrasound index". These parameters are calculated from both SOS and BUA values indirectly reflected information of strength as bone quality (2). Amplitude of the ultrasound signal decreases with the increase in bone porosity and lead to the identification of an amplitude-related measurement of SOS (AD-SOS).

Expressed in meters per seconds parameter is able to magnify the differences in SOS as measured in diverse bone status (12). SOS measured along cortical bone with little interference of soft tissue could also provide some relevant information about the biomechanical behavior of that kind of tissue as a whole, regarding all the matrix mineralization and the microstructural factors of bone material quality together. Even when this approach is used it still needs to be validated. In sum up, QUS can be regarded as promising technique for improving noninvasively the resources of bone strength (1).

Limitations of bone mass measurements

Bone mass measurements obtained with DXA in children have the advantages of low cost, accuracy, and low radiation exposure (2). However, DXA is a projection technique, and its measurements are based on the two dimensional assessment of a three dimensional structure without taking to consideration potential changes in three skeletal functions: the size of the bone, the volume of the bone examined and its mineral density. In trial of solving these issues mathematical models were developed that account for the dimensions of the bone; as examples cross-sectional area of the vertebrae is shaped in them like a cube and long bones – like cylinder with a circular base. Similar formulas were proposed for the femur and the midradius (13). The potential inaccuracies of DXA measurements are related to lack of homogeneous distribution of soft tissues. Inhomogeneous fat distribution may influence DXA measurements by as much as 10% (14). The next source of error for DXA bone mineral analysis can be the use of inappropriate software for both the acquisition and the subsequent analysis of the data. It became obvious that only appropriate use of reference data necessitates comparison of the results of DXA examinations with different normative data sets (15). Another considerable error of DXA measurements is head density involvement in total body program (16).
Some resolution of DXA limitations are over passed by the use of CT but the cost and inaccessibility of CT scanners have markedly limited its use in bone measurements. It should be noted that when assessing the metaphyseal regions of the long bones by QCT trabecular bone measurements are influenced by cortical bone thickness due to beam-hardening effects or photon scattering. This error is especially prominent in pQCT evaluations of the radius (17).
On the last, coming to QUS, despite extensive research, the question what it really measure when using this technique, still remains unanswered. SOS signals are greatly influenced by the material density of bone whereas BUA depends on many structural parameters that contribute to scattering and attenuation of sound waves. Also QUS measurements are limited to skeletal locations where the interference of soft tissue is minimal such as the calcis, the patella, and the phalanxes (2).
In addition, no matter which techniques are used for measurement of bone mass, the development of proper reference data for its evaluation is crucial matter. Chronological age- and sex-matched normal values are not sufficient to correctly interpret the data. Important for evaluation are anthropometrical variables like: weight and height, but also skeletal age, and pubertal stage (2). Moreover, the functional association between muscle and bone through a regulatory mechanism (mechanostat) should be considered. Mechanostat theory suggests that the statistical association between LBM and BMC reflects a direct cause-and-effect relationship. If muscle forces drive bone development, then analyses of muscle function should also be added to the armamentarium of clinicians diagnosing bone disorders. Many bone disorders may at least partly be due to muscle disuse or dysfunction, opening a new field of potential targets for therapeutic interventions (18).

Novelties in measurement programs

Speed of measurement by densitometric techniques in children is of great importance, because it is hard to keep children motionless during the performance. However, utilization of speeding up measurement as fan beam technique has still some disadvantages enforcing the needs of its further evaluation and cross-calibration. For accurate determination of bone mineral accrual in growing subjects with the use of DXA correction of all magnification errors is needed. Children with growth abnormalities often show deficient BMD for chronological age. That might be a reflection of growth irregularities rather than poor bone mineralization. Taking on account body size deficit, improves significantly the assessment of bone status in children. In the newest software for DXA appeared the possibility of adjusting body size using three-step assessment: height for age, BMC for height and bone area for height (19). Moreover, incorporation of the variable standard deviations in DXA pediatric reference data results in more accurate assessment of pediatric skeletal health; what is especially ortant during pubertal growth spurt. The other prospective technical improvements are related to incorporation of reference ranges for subcranial BMD and normalization of skeletal status with the use of muscle mass adjustment (20).

Summary

Summing up the following points should be specially underlined. In children data evaluation exclusively Z-scores should be used. The diagnosis of osteoporosis in children should be not only limited to densitometric criteria. In diagnostic, helpful are the factors like bone geometry, bone size, pubertal stage, skeletal maturity, and body composition. Terminology such as "low bone density for chronological age" may be used when the Z-score is below -2.0, with spine and total body usage as preferred skeletal sites for measurement. Serial BMD studies should be done on the same machine using the same scanning mode and software. Such a way of thinking is steadily executed in general practice. It is also supported by International Society for Clinical Densitometry (ISCD) published in November 2003 in their position statement (21).

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