Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–8, 2017

1094-6950/■:1–8/$36.00
http://dx.doi.org/10.1016/j.jocd.2017.06.007

Bone Mineralization and Fracture Risk Assessment in the Pediatric Population

Halley Wasserman,[1] and Catherine M. Gordon*[,2]

[1]Division of Endocrinology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; and [2]Divisions of Adolescent Medicine and Endocrinology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

Abstract

Identifying children most susceptible to clinically significant fragility fractures (low trauma fractures or vertebral compression fractures) or recurrent fractures is an important issue facing general pediatricians and subspecialists alike. Over the last decade, several imaging technologies, including dual-energy X-ray absorptiometry and peripheral quantitative computed tomography, have become useful to identify abnormal bone mineralization in children and in adolescents. This review aimed to summarize the latest literature on the utility of these modalities as they pertain to use in pediatrics. In addition, we review several disease states associated with poor bone health and increased fracture risk in children, and discuss the implications of low bone mineral density in these patients. Finally, we will highlight the gaps in knowledge with regard to pediatric bone health and make recommendations for future areas of research.

Key Words: Bone mineral density; child; fracture; pediatrics.

Introduction

Fractures are a common morbidity in pediatrics with nearly 50% of children sustaining at least 1 fracture by their 18th birthday *(1)*. Fracture incidence peaks during early adolescence, shortly after the pubertal growth spurt, with most fractures occurring in the upper extremity following moderate or high trauma. Identifying which children are most susceptible to clinically significant fragility fractures (low trauma or vertebral compression fractures) or recurrent fractures is an important issue facing general pediatricians and subspecialists alike.

Over the last decade, advances in imaging technologies, each originally designed to detect osteoporosis and to predict subsequent fracture risk in adults, have become clinically useful to identify abnormal bone mineralization in children and in adolescents. Dual-energy X-ray absorptiometry (DXA), generating measurements of areal bone mineral density (aBMD), bone mineral content (BMC), and bone mineral apparent density (BMAD), have been the primary tools used to assess bone health in pediatric patients. In 2013, updated guidelines were released by the International Society for Clinical Densitometry (ISCD) to provide recommendations for evaluating children at risk of fragility fractures and redefined criteria for osteoporosis in the pediatric population. These guidelines have been formulated by international experts, following a careful review of the best available evidence and expert consensus when evidence was lacking. Clinical criteria deemed necessary to diagnose osteoporosis in this age group include the presence of 1 or more vertebral compression fractures in the absence of local disease or high-energy trauma, or both a bone mineral density (BMD) *Z*-score less than or equal to –2 standard deviations (SDs) with 2 or more long bone fractures by age 10 yr, or 3 or more long bone fractures by 19 yr of age *(2)*. This definition aims to identify children with poor bone health who may benefit from further interventions to decrease their subsequent risk of fracture. It is important to understand that children are growing and continuing to acquire bone; thus, using diagnostic criteria applicable for adult osteoporosis, such as those defined by the World Health Organization, is not appropriate.

*Address correspondence to: Catherine M. Gordon, MD, MSc, Divisions of Adolescent Medicine and Endocrinology, 3333 Burnet Ave., MLC 4000, Cincinnati, OH 45229. E-mail: catherine.gordon@cchmc.org

Additional measures derived from new DXA software, such as vertebral fracture assessment (VFA) and trabecular bone score (TBS), as well as other imaging techniques such as peripheral quantitative computed tomography (pQCT) and high-resolution peripheral quantitative computed tomography (HR-pQCT), are being explored. This review aimed to highlight the advantages and limitations of the various clinical and research tools available to assess bone health in pediatric patients, to discuss the identification of unique populations of children at high risk of osteoporosis, and to review the critical gaps in knowledge in understanding the process of bone mineralization during the pediatric years and the impact on adult manifestations of osteoporosis.

Bone Health Assessment Tools in Children and Adolescents

The pediatric years are characterized by rapid linear growth during early childhood and again at puberty. As bones grow in length and width, mineralization of new bone must occur *(3,4)*. During periods of rapid growth, there is a lag in mineral apposition, as well as an increase in cortical porosity, that may partly explain the increased fracture risk observed during early adolescence *(4,5)*. Bone mass continues to accrue throughout the second decade and into the third decade of life, at which time a plateau is reached until BMD declines during late adulthood *(6,7)*. Achieving optimal bone health during the pediatric years is critically important to decrease the future risk of osteoporosis and fragility fractures *(8)*. However, it is less clear which bone health parameters are most useful to predict incident fractures in children. The following sections review commonly utilized tools to assess bone health as they pertain to children and adolescents.

Dual-Energy X-Ray Absorptiometry (DXA)

DXA imaging is the most widely available and preferred tool to assess aBMD and BMC in children. Over the past several years through the work of the Bone Mineral Density in Childhood Study (BMDCS) and other groups, age-appropriate reference ranges for children have been developed *(9,10)*. These reference ranges allow for the computation of a *Z*-score where values are compared to age-, sex-, and race-matched controls. Further adjustment for height is also recommended as BMD obtained via DXA is actually an areal measure and does not capture the true volumetric density *(11)*. Therefore, aBMD may be falsely low in short children with small bones and falsely elevated in tall children with larger bones. In addition, some advocate for adjusting for pubertal status, as well as pubertal timing, as the associated changes in the hormonal milieu impact bone accretion *(12)*.

The recommended sites for aBMD and BMC measurement via DXA in children include the posterior-anterior lumbar spine (LS) and the total body less head (TBLH). The LS assesses primarily trabecular bone and reference ranges are available starting in infancy. The TBLH represents a predominantly cortical outcome as 80% of the skeleton is composed of cortical bone. The density of the head (i.e., skull) is excluded because it comprises a relatively large proportion of the pediatric skeleton without being affected by weight-bearing activity or nutritional or environmental factors that influence bone mineralization. In addition, skull fractures do not represent osteoporotic fractures; thus, it is not helpful to include this region in the measurement. Reference ranges for the TBLH are available for children and adolescents, ages 5–20 yr, whereas aBMD and BMC for children ages 3 and up may be compared to reference ranges for the whole body. Additional adjustments for stature are recommended with the use of a height *Z*-score for either TBLH or LS, or the use of BMAD for the LS. Although the total hip and femoral neck are frequently assessed in adult patients to evaluate for osteoporosis, these sites are not recommended in pediatrics because of the great variability in landmarks among growing children and the limited reproducibility. Finally, in select populations where scanning of the preferred sites is not feasible because of contractures, significant scoliosis, or spinal instrumentation, the lateral distal femur (LDF) has been a useful site for the assessment of cortical and trabecular BMDs and BMCs. Clinically, DXA measures are useful to monitor bone health in pediatrics as results are highly reproducible. However, it is important to ensure that scans are of high quality and that scans are reviewed for motion artifact and proper positioning of the patient before the interpretation of the results *(13)*. Additionally, accurate interpretation of DXA results requires knowledge of the least significant change for all sites measured and for all technologists at the DXA facility. Repeat assessments for monitoring change in aBMD should be obtained no more frequently than every 6 mo *(14)*. Clinicians should know the least significant change value for their DXA machine and interpret serial aBMD measurements in light of this value to determine if differences represent true bone loss, gain, or inadequate accrual *(13)*. DXA scans are of low risk for the child as radiation exposure is minimal (<13 μSv). Therefore, pediatric clinicians should not be hesitant to obtain this measure if it will be helpful in treating the child.

DXA measures may be useful to predict fracture risk during childhood. Clark et al found an 89% increased risk of fracture in the subsequent 2 yr for each SD decrease in the TBLH BMC *(15)*. In another prospective study of 183 children followed up for 8 yr, BMC and aBMD at the LS and total body exhibited an increased risk of fracture when adjusted for age, sex, height, and weight (hazard ratio [HR] ranging from 1.53 to 2.47) *(16)*. Neither obesity status nor histories of prior fracture were significantly associated with increased risk of incident fracture in this study.

Calculations estimate that 50% of the variability in BMD in elderly adults can be explained by differences in peak bone mass during childhood *(17)*. Data from BMDCS demonstrate that bone measures correlate well throughout the