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Bone Densitometry in Children and Adolescents

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Clinical Report—Bone Densitometry in Children and Adolescents

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SECTION ON ENDOCRINOLOGY

KEY WORDS

bone densitometry, DXA, osteoporosis, pediatrics

ABBREVIATIONS

DXA—dual-energy x-ray absorptiometry

PDC—[Pediatric] Position Development Conference

BMD—bone mineral density

BMC—bone mineral content

The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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abstract

FREE

Concern for bone fragility in children and adolescents has led to increased interest in bone densitometry. Pediatric patients with genetic and acquired chronic diseases, immobility, and inadequate nutrition may fail to achieve the expected gains in bone size, mass, and strength, which leaves them vulnerable to fracture. In older adults, bone densitometry has been shown to predict fracture risk and reflect response to therapy. The role of densitometry in the management of children at risk of bone fragility is less certain. This clinical report summarizes the current knowledge about bone densitometry in the pediatric population, including indications for its use, interpretation of results, and its risks and costs. This report emphasizes consensus statements generated at the 2007 Pediatric Position Development Conference of the International Society of Clinical Densitometry by an international panel of bone experts. Some of these recommendations are evidence-based, and others reflect expert opinion, because the available data are inadequate. The statements from this and other expert panels have provided general guidance to the pediatrician, but decisions about ordering and interpreting bone densitometry still require clinical judgment. Ongoing studies will help to better define the indications and best methods for assessing bone strength in children and the clinical factors that contribute to fracture risk. *Pediatrics* 2011;127:189–194

INTRODUCTION

The bone health of children and adolescents has become an increasingly important medical concern. There is growing recognition that low bone mass and fractures may complicate several genetic and acquired chronic disorders of childhood.¹ Fractures are common in otherwise healthy youth as well; peak incidence occurs during the peripubertal growth spurt.² The documented 35% to 65% increase in common childhood fractures over the past 4 decades has raised concerns that current lifestyles are compromising early bone health.³ Children with forearm fractures have been shown to have lower bone mass, a greater percentage of body fat, and less calcium intake than their peers without a history of fracture.^{4,5} Vitamin D insufficiency and deficiency are widespread, calcium intake often falls below recommended levels, and physical inactivity is common among American youth.^{6,7}

These observations have increased the demand for better diagnostic and therapeutic tools to address bone health in children and adolescents. Bone densitometry and pharmacologic therapy for osteoporosis in older adults have been refined in recent years. The efficacy, cost-effectiveness, and safety of these tests and treatments in pediatric

patients have not been adequately determined. This lack of data has left the pediatrician in a quandary about how to best diagnose and manage skeletal fragility in children and teenagers. To address these uncertainties, pediatric bone experts have proposed guidelines for evaluating skeletal health in youth.⁸ This report briefly reviews current bone-densitometry methods, indications for ordering densitometry, and the role for densitometry in choosing and monitoring therapy.

BONE-DENSITOMETRY METHODS

The pediatric skeleton can be assessed by using dual-energy x-ray absorptiometry (DXA), quantitative computed tomography, peripheral quantitative computed tomography, quantitative ultrasonography, magnetic resonance imaging, or plain films (radiogrammetry). Each modality offers distinct advantages and disadvantages, which have been reviewed previously.⁹ DXA remains the preferred method for clinical measurements of bone density in children because of its availability, reproducibility, speed, low exposure to ionizing radiation, and robust pediatric reference data.¹⁰

FOR WHOM SHOULD BONE DENSITOMETRY BE PERFORMED?

The general goals of bone densitometry are to identify patients at greatest risk of skeletal fragility fractures, to guide decisions regarding treatment, and to monitor responses to therapy. Skeletal assessments have been recommended for children with recurrent fractures, bone pain, bone deformities, or osteopenia on standard radiographs or to monitor therapy.^{11,12} Specific recommendations have been proposed for monitoring bone health in patients with cystic fibrosis¹³ and childhood cancer.¹⁴ For example, a baseline DXA is recommended by 18 years of age or 2 years after the end of chemotherapy (for cancer survivors) but earlier in patients with more severe

disease, low body weight, chronic glucocorticoid therapy, delayed puberty, gonadal failure, or a history of fracture. For patients receiving drugs that may adversely affect bone, such as anticonvulsants or depot medroxyprogesterone (Depo-Provera), there is insufficient evidence to support routine bone densitometry.^{15,16}

The most comprehensive recommendations related to bone densitometry have evolved from the Pediatric Position Development Conference (PDC) of the International Society of Clinical Densitometry after rigorous analysis of the literature.⁸ The PDC guidelines identified the primary and secondary disorders that have been associated with evidence of increased fracture risk (Table 1). PDC guidelines recommended that densitometry be performed “at clinical presentation” of these disorders and “before initiation of bone-active treatment,” such as bisphosphonates.¹⁷ The authors of the guidelines acknowledged that the recommendations are controversial and that experts will not agree with all the

TABLE 1 Diseases That May Affect the Skeleton

Primary bone disorders
Idiopathic juvenile osteoporosis
Osteogenesis imperfecta
Potential secondary bone diseases
Chronic inflammatory disorders
Inflammatory bowel disease
Juvenile idiopathic arthritis
Cystic fibrosis
Chronic immobilization
Cerebral palsy
Myopathic disease
Epidermolysis bullosa
Endocrine disturbance
Turner syndrome
Anorexia nervosa
Cancer and therapies with adverse effects on bone health
Acute lymphoblastic leukemia
Status post chemotherapy for childhood cancer
Status post transplantation (nonrenal)
Hematologic disorders
Thalassemia

Data source: Bishop N, Brailion P, Burnham J, et al. *J Clin Densitom.* 2008;11(1):29–42.¹⁷

statements,¹⁸ which reflects the lack of sufficient high-quality evidence to support some of the recommendations. Until such evidence is obtained, however, these parameters provide general guidance for the pediatrician and may help to secure reimbursement from insurance providers.

Beyond these guidelines, the decision to order bone densitometry for an individual patient requires clinical judgment. The risk of bone fragility will depend on age of onset and severity of the underlying disorder, if any; the number of associated risk factors (such as poor nutrition or inactivity); and exposure to potentially bone-toxic drugs (eg, glucocorticoids, anticonvulsants) or irradiation. A family history of bone fragility is relevant, because an estimated 60% to 80% of the variability in bone mass between individuals is determined by genetic factors.⁶ This history is best assessed by asking about a history of hip fractures in older relatives. The decision to evaluate an otherwise healthy child with a history of fractures will depend on the number of broken bones and the intensity of the trauma that caused the injury. Low-trauma fractures are defined as those that occur from standing height or less. The PDC has defined a clinically significant fracture history as “one long bone fracture of the lower extremity, two or more long bone fractures of the upper extremity or a vertebral fracture.”⁸ Children with this history sustained after minimal or no trauma should be considered for evaluation with densitometry, whereas children with fractures of digits and toes do not warrant such investigation. Data are insufficient to recommend routine densitometry for infants in these situations. A final consideration before ordering DXA scans should be how the results will influence patient management. For example, it may not be helpful to document that bone mineral

density (BMD) is low for age in a child with cerebral palsy if the child has not had a fracture, because low BMD alone is not considered an indication for bisphosphonate therapy.⁸

ORDERING DXA IN PEDIATRICS

The preferred skeletal sites for DXA measurements in children are the lumbar spine and total body.¹⁰ If possible, the cranium should be excluded from the total-body-scan analysis, because the head constitutes a large portion of the total body bone mass but changes little with growth, activity, or disease; inclusion of the skull potentially masks gains or losses at other skeletal sites.¹⁹ DXA measurements of the hip region (total hip or femoral neck) are not as reliable in younger patients because of difficulties in identifying the bony landmarks for this region of interest. For children with contractures who cannot be positioned properly for spine or whole-body studies, measurements of the lateral distal femur may be a useful alternative but have been less extensively studied than spine or whole-body measurements.²⁰ Scanning alternative skeletal sites may also be necessary for patients with metal hardware (such as rodding for scoliosis) in the usual regions of interest. Vertebral fractures are best detected by standard lateral radiographs of the thoracolumbar spine,²¹ not by DXA.²²

INTERPRETATION OF DXA RESULTS

Bone mass, as measured by DXA, is reported as bone mineral content (BMC) (g) or areal BMD (g/cm^2). These values are compared with reference values from healthy youth of similar age, gender, and, if possible, race/ethnicity to calculate a z score, the number of SDs from the expected mean. Abundant pediatric reference data are now available for children and teenagers but not for infants.¹⁰ It is essential to select norms collected by using equipment

from the same manufacturer as that used for the patient because of systematic differences in software.¹⁰ T scores (which compare the patient's BMD with that of a healthy young adult) should not be used before 20 years of age, because the person may not have achieved peak bone mass. Unfortunately, some software packages from DXA manufacturers automatically generate a T score, even for younger subjects. The ordering physician must be careful to not use T scores when interpreting DXA results.

Appropriate interpretation of DXA results may require more than the calculation of z scores. Children with chronic illness often have delayed growth and pubertal development, which are factors that contribute to a low bone mass for age or gender. BMD, as measured by DXA, corrects bone mineral for the area (height and width) but not for the volume (height, width, and thickness) of bone. For this reason, if 2 people with identical "true" volumetric bone density are compared, the shorter person will have a lower BMD than the taller one.^{9,23} Similarly, a child with delayed puberty will not have had the gains in bone size, geometry, and density that occur with sex-steroid exposure. Controversy persists about the optimal method for adjusting for variations in bone size, body composition, and maturity as well as the criteria by which "best method" is defined; ideally, the adjustment method would prove to be a stronger predictor of fracture.²³ The PDC guidelines recommend that BMD in children with delayed growth or puberty be adjusted for height or height age or compared with reference data with age-, gender-, and height-specific z scores.¹⁰

A BMC or BMD z score of more than 2 SDs below expected (less than -2) should be labeled "low for age."¹⁰ The terms "osteopenia" and "osteoporosis," which are used to describe milder or greater deficits in bone mass in older adults, should not be used for pediatric patients. Instead, the PDC guidelines suggested that the diagnosis of osteoporosis in children be made only when both low bone mass (BMC or BMD z scores of less than -2) and a clinically significant fracture history (defined previously) are present.²⁴

Repeat DXA studies are performed to monitor the skeletal response to ongoing illness, the regaining of health, or the response to bone-active therapies. For a change in BMD to be technically meaningful, it must exceed the variability that is observed when DXA measurements are repeated for the same patient. The "least-significant change" refers to the smallest percentage difference in measurements that exceeds the variability or "noise" from repeated measurements.²⁵ In densitometry centers that provide rigorous attention to precision, a least-significant change of 3% or less can be achieved.²⁵ Gains or losses of BMD that are less than that cannot be labeled as change with certainty.

INTERPRETING LONGITUDINAL DATA

Longitudinal changes in bone densitometry must also take into account interval changes in growth and maturity. Assessing whether observed gains in bone mass and size are appropriate for age and pubertal stage requires thoughtful assessment of z scores, as described above. The recommended interval between repeat densitometry studies will depend on the progression of disease or the type of intervention being used. The minimal interval between scans should be 6 months,¹⁰ but often 1 year or more may be appropriate to allow for measurable change to occur.

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CAN DXA PREDICT FRACTURES?

Low BMD is such a sufficiently powerful predictor of fracture in older

adults that it has been used as a diagnostic criterion for “osteoporosis” in elderly patients.²⁶ Reduced BMD is associated with increased fracture risk in children and teenagers as well, but data are not sufficient to establish the diagnosis of osteoporosis on the basis of bone-densitometry criteria alone.^{10,24} In studies of otherwise healthy youth, children with a history of fracture have been shown to have lower BMC, BMD, and estimated volumetric BMD than their peers without fractures.^{4,5} In particular, children with reduced spine or whole-body bone mass or smaller bone area for height had an increased risk of fracture.^{5,24}

Less is known about the relationship between low bone mass and fracture risk in children with chronic illness, because the studies in these populations have been limited to smaller cohorts with varying diagnoses and risk factors for poor bone health. The most common site of fractures in these children may not be the forearm; lower-extremity fractures are common in immobilized children,²⁷ and spine fractures are more common in young patients with childhood leukemia, osteogenesis imperfecta, or exposure to glucocorticoids.²⁸ In a study that examined only children with acute lymphoblastic leukemia, the odds for fracture increased by 80% for every 1-SD reduction in spine BMD z score.

Clinical variables other than bone mass influence the risk that a person will have a fracture. For older adults, age, weight, family history of hip fracture, exposure to glucocorticoids, smoking and alcohol use, and history of a fracture are key predictors of absolute fracture risk.²⁶ Clinical factors that influence bone fragility in children have not yet been well established. However, it has been recognized that bone densitometry by DXA is only part of a comprehensive skeletal

health screening that includes review of nutrition, physical activity, pubertal stage, disease severity, patient and family fracture history, and medication exposure. A child with low bone mass for age or one with a significant fracture history warrants evaluation by a pediatric endocrinologist, nephrologist, geneticist, or rheumatologist (depending on clinical presentation) with expertise in bone.¹⁰

RISKS AND COSTS OF DENSITOMETRY

Exposure to the very low doses of ionizing radiation with DXA poses no known health risk. The estimated 5 to 6 microsieverts (μSv) of radiation exposure from a spine and whole-body DXA scan is far less than the 80 μSv accumulated during a round-trip transatlantic flight.²⁹ More concerning is the potential risk of misdiagnosis if DXA data are not interpreted by skilled professionals at pediatric densitometry centers. One study revealed errors in 88% of the scans from children referred for an osteoporosis-intervention study; 62% of the errors involved a misdiagnosis of osteoporosis based on inappropriate use of a T score.³⁰ Errors in interpreting DXA results generate considerable parental concern and can result in costly and unnecessary use of pharmacologic agents and restrictions on physical activity.

THERAPY FOR CHILDHOOD SKELETAL FRAGILITY

It is beyond the scope of this review to discuss therapy in detail. However, treatment options for children with low bone mass and fractures are more limited than those for adults, which underscores the importance of accurate skeletal assessments.³¹ General measures to address skeletal risk factors are safe and appropriate first steps for all patients. Calcium intake should meet the current recommended daily intake of 500 mg for children 1 to 3

years of age, 800 mg for children 4 to 8 years of age, and 1300 mg for children and adolescents 9 to 18 years of age.⁶ Adequacy of total-body vitamin D stores should be assessed by measuring serum concentrations of 25-hydroxyvitamin D; concentrations of at least 20 to 32 ng/mL (50–80 nmol/L) have been recommended for children.⁷ Weight-bearing activity should be encouraged, and even short periods of high-intensity exercise (such as jumping 10 minutes/day, 3 times per week) have produced measurable gains in bone mass.³² For patients with limited mobility, reducing immobility through physical therapy³³ or use of vibrating platforms can be helpful.³⁴ Reducing inflammation, undernutrition, or hormone imbalances is necessary as well.

If these general measures fail to prevent further bone loss and fracture, pharmacologic therapy may be considered. None of the drugs used to treat bone fragility in the elderly have yet been approved by the US Food and Drug Administration for pediatric use.³⁵ Nevertheless, therapy with bisphosphonates is considered reasonable for children with moderate-to-severe osteogenesis imperfecta (≥ 2 fractures in 1 year or vertebral compression fractures).³⁶ For secondary osteoporosis attributable to chronic disease, bisphosphonates may be used on a compassionate basis to treat low-trauma fractures of the spine or extremities.³⁷

SUMMARY

DXA has been established as a valuable tool as part of a comprehensive skeletal assessment of children and teenagers but not yet of infants. Acquiring and interpreting densitometry data from younger patients remains challenging and should be performed in experienced pediatric densitometry centers. Panels of pediatric experts have set standards

for when and how to perform DXA scans on the basis of the best available data.¹⁰ Ongoing research will serve to refine the best modalities for assessing the bone strength of children and to determine the key clinical variables that influence fracture risk independent of bone.

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