



Bone Densitometry in Children and Adolescents

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Concerns about bone health and potential fragility in children and adolescents have led to a high interest in bone densitometry. Pediatric patients with genetic and acquired chronic diseases, immobility, and inadequate nutrition may fail to achieve expected gains in bone size, mass, and strength, leaving 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 clear. This clinical report summarizes current knowledge about bone densitometry in the pediatric population, including indications for its use, interpretation of results, and risks and costs. The report emphasizes updated consensus statements generated at the 2013 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, whereas others reflect expert opinion, because data are sparse on many topics. The statements from this and other expert panels provide general guidance to the pediatrician, but decisions about ordering and interpreting bone densitometry still require clinical judgment. The interpretation of bone densitometry results in children differs from that in older adults. The terms “osteopenia” and “osteoporosis” based on bone densitometry findings alone should not be used in younger patients; instead, bone mineral content or density that falls >2 SDs below expected is labeled “low for age.” Pediatric osteoporosis is defined by the Pediatric Position Development Conference by using 1 of the following criteria: ≥ 1 vertebral fractures occurring in the absence of local disease or high-energy trauma (without or with densitometry measurements) or low bone density for age and a significant fracture history (defined as ≥ 2 long bone fractures before 10 years of age or ≥ 3 long bone fractures before 19 years of age). Ongoing research will help define the indications and best methods for assessing bone strength in children and the clinical factors that contribute to fracture risk. The Pediatric Endocrine Society affirms the educational value of this publication.

abstract

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INTRODUCTION

Threats to bone health are increasingly a pediatric concern. Genetic or acquired disorders can compromise gains in bone quantity and quality, leading to skeletal fragility early in life.¹ Recurrent fractures in otherwise healthy children may also indicate underlying bone fragility.²⁻⁵ 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.^{3,4} The documented increase of 35% to 65% in childhood fractures over the past 4 decades has raised concern that current lifestyles are compromising early bone health.⁵ Vitamin D insufficiency and deficiency are widespread, calcium intake often falls below recommended levels, and physical inactivity is common among American youth, all of which may increase a child's fracture risk.^{6,7} These observations have led to greater demands for diagnostic and therapeutic tools to address bone fragility in children and adolescents. The efficacy, cost-effectiveness, and safety of pharmacologic agents used to treat osteoporosis in older patients have not been fully established in pediatric patients. The limited treatment options make it all the more important to predict accurately who will have fractures and who might recover without drug therapy. Bone densitometry is a valuable part of a comprehensive bone health assessment. Guidelines for densitometry were updated in 2013 by a group of pediatric bone experts at the Pediatric Position Development Conference (PDC) of the International Society of Clinical Densitometry.⁸ The report by the PDC reviewed current bone densitometry methods, indications for ordering densitometry, and the role for densitometry in choosing and monitoring therapy. The Pediatric

Endocrine Society affirms the educational value of this publication.

BONE DENSITOMETRY METHODS

The pediatric skeleton can be assessed by using dual-energy radiograph absorptiometry (DXA), quantitative computed tomography (QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), quantitative ultrasonography, MRI, or plain films (radiogrammetry). Each modality offers distinct advantages and disadvantages, as previously reviewed.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 Three-dimensional densitometry methods (QCT, pQCT, HR-pQCT, and MRI) offer valuable insights into volumetric bone mineral density (BMD) as well as micro- and macroarchitecture. These tools may provide more information about bone strength and fracture risk than traditional DXA measures, but their use in clinical practice is limited in large part by the lack of standardized scanning protocols and pediatric normative data.⁸

FOR WHOM SHOULD BONE DENSITOMETRY BE CONSIDERED?

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" (a term describing the appearance of "washed out" bones) on standard radiographs or to monitor therapy.^{8,11,12} Details about the number of fractures and impacts causing them should guide the decision of whether bone

densitometry is indicated. Most concerning are low-impact fractures occurring from a standing height or less. Specific recommendations have been proposed for monitoring bone health in 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. Another clinical scenario in which a DXA assessment is warranted is in female adolescents with nutritional concerns (eg, related to an eating disorder and/or excessive exercise), with scans recommended after 6 or more months of amenorrhea.

The most rigorous and comprehensive recommendations related to bone densitometry were developed by the PDC after extensive analysis of all relevant literature.⁸ The PDC guidelines identify a list of the primary and secondary disorders that have been associated with low bone mass and increased fracture risk (Table 1). PDC guidelines recommend that the initial densitometry examination be performed when the patient may benefit from intervention and when the results of densitometry would influence management.⁸ These parameters provide general guidance for the pediatrician and may help to secure payment for densitometry from insurance providers.

Beyond these guidelines, the decision to order bone densitometry in an individual patient requires clinical judgment. The risk of bone fragility is influenced by the age of onset and severity of any underlying disorder, associated risk factors such as poor nutrition or inactivity, and exposure to irradiation or to potentially bone-toxic drugs (eg, glucocorticoids, methotrexate, or anticonvulsants). A family history

TABLE 1 Diseases or Therapies That May Affect the Skeleton

Primary bone disorders
o Idiopathic juvenile osteoporosis
o Osteogenesis imperfecta
Potential secondary bone diseases
o Chronic inflammatory disorders
- Inflammatory bowel disease
- Juvenile idiopathic arthritis
- Celiac disease
- Cystic fibrosis
o Chronic immobilization
- Cerebral palsy
- Myopathic disease
- Epidermolysis bullosa
o Endocrine disturbance
- Turner syndrome
- Anorexia nervosa
- Type 1 diabetes
o Cancer and therapies with adverse effects on bone health
- Acute lymphoblastic leukemia
- Chemotherapy for childhood cancer
- Transplantation (nonrenal)
o Hematologic disorders
- Thalassemia
- Sickle cell disease
o Genetic disorders
- Ehlers Danlos syndrome
- Galactosemia
- Marfan syndrome

Adapted from Bishop et al.¹⁵ These are among conditions for which consideration of DXA screening and other diagnostic testing for bone health is warranted.

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 recurrent fractures or hip fractures in family members. 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 causing the injury. Low-trauma fractures are defined as those occurring from a standing height or less. 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 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 Finally, it is important to consider whether the patient can

remain still for the DXA without sedation.

ORDERING DXA FOR CHILDREN AND ADOLESCENTS

The preferred skeletal sites for DXA measurements in children are lumbar spine (L1–4) and total body, not including the head.¹⁰ 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.¹⁶ For children younger than 5 years old, the spine bone mineral content (BMC) and BMD can be measured; whole-body measurements are feasible only for those aged 3 years or older. DXA measurements of the hip region (total hip or femoral neck) are not as reliable in younger patients (<13 years) because of difficulties in

identifying the bony landmarks for this region of interest.

Scans of alternative regions of interest are recommended in special cases. DXA assessments of the lateral distal femur can be valuable in children with immobilization disorders and in those with contractures who cannot be positioned properly for spine or whole-body studies.¹⁷ The distal radius can be measured in patients who exceed the weight limit for the DXA table or those who cannot transfer onto the table because of a mobilization disorder. Scanning of these alternate skeletal sites also may be necessary in patients with metal hardware (eg, rodding for scoliosis) in the standard regions of interest.

A vertebral fracture that occurs without major trauma is an important indication of abnormal bone fragility.⁸ Because these fractures can be asymptomatic, some type of imaging is needed to rule out vertebral fractures in patients at high risk, such as those receiving long-term glucocorticoid therapy. In the past, a lateral thoracolumbar radiograph has been used to assess for loss of vertebral height.¹⁸ Alternatively, vertebral fracture analysis (VFA) by DXA has been used with far less radiation than conventional radiography. Studies using older software found that DXA VFA had lower diagnostic accuracy compared with lateral spine radiography in children.¹⁹ Newer VFA software may provide sufficient image quality to screen for spine fractures with the use of DXA.²⁰

INTERPRETATION OF DXA RESULTS

Bone mass, as measured by DXA, is reported as BMC (g) or areal BMD (g/cm²). These values are compared with reference values from healthy youth of similar age, sex, and 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 Peak bone mass is achieved in the second or third decade, depending on the skeletal site.²¹ Therefore, T-scores (which compare the patient's BMD with that of a healthy young adult) should not be used before 20 years of age. Unfortunately, some older software packages from DXA manufacturers automatically generate a T-score, even in younger subjects. The ordering physician must be careful to not use T-scores when interpreting DXA results.

The 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, factors that contribute to a low bone mass for age or sex. 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 individuals with identical "true" volumetric bone density are compared, the shorter person will have a lower BMD than the taller one.^{9,22} 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 to adjust for variations in bone size, body composition, and maturity as well as the criteria by which the "best method" is defined; ideally, the adjustment method would prove to be a stronger predictor of fracture.²²

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-, sex-, and height-specific z scores.¹⁰ DXA

reference data corrected for all these variables have been published.²³

The terms "osteopenia" and "osteoporosis" are used in older adults to describe lesser or greater deficits in bone mass. These terms should not be used to describe densitometry findings in pediatric patients. Instead, a BMC or BMD z score that is >2 SDs below expected (< -2.0) is referred to as "low for age."¹⁰ The following criteria for osteoporosis in a pediatric patient were agreed on in the 2013 PDC guidelines⁸:

- one or more vertebral fractures occurring in the absence of local disease or high-energy trauma (measuring BMD can add to the assessment of these patients but is not required as a diagnostic criterion); or
- low bone density (BMC or areal BMD z scores < -2.0) and a significant fracture history (2 or more long bone fractures before 10 years of age or 3 or more long bone fractures before 19 years of age).

Last, it is important to recognize that there are certain diseases in pediatrics (eg, end-stage renal disease and spinal vertebral fractures) in which DXA measures do not accurately reflect fracture risk or bone health.¹⁰

INTERPRETING LONGITUDINAL DATA

Repeat DXA studies are performed to monitor the skeletal response to ongoing illness, to recovery from illness, or to bone-active therapies. Repeat measurements must be made on densitometry equipment from the same manufacturer with the use of the same software to avoid variability attributable to software programs alone. For a change in BMD to be technically meaningful, it must exceed the variability that is observed when DXA measurements are repeated in the same individual. The "least significant change" refers

to the smallest percentage difference in measurements that exceeds the variability or "noise" from repeated measurements.²⁴ In densitometry centers that are able to perform a precision study, a least significant change of 3% or less usually can be achieved.²⁴ However, some hospital radiation safety committees prohibit DXA centers from carrying out these protocols. It should also be recognized that interval growth changes and accompanying increases in bone size make it more difficult to differentiate true increases in density from changes in areal BMD that are related to growth. Therefore, careful interpretation by an expert in pediatric densitometry is needed.

Longitudinal changes in bone densitometry must also take into account interval changes in growth and maturity. To assess whether observed gains in bone mass and size are appropriate for age and pubertal stage requires thoughtful assessment of z scores, as described previously. 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 generally is 6 months,¹⁰ but a year often is more appropriate in clinical practice to allow for the detection of meaningful changes.

ABILITY OF BONE DENSITOMETRY TO PREDICT FRACTURES

Low BMD is a sufficiently powerful predictor of fracture in older adults that it has been used as a diagnostic criterion for "osteoporosis" in older individuals.²⁵ Reduced BMD also is associated with increased fracture risk in children and teenagers, but the data are not sufficient to establish the diagnosis of osteoporosis on the basis of bone densitometry criteria alone.^{10,26} In studies in otherwise healthy youth, children with a history of fracture have been shown to have reduced spine or whole-body

bone mass or smaller bone area for height.^{4,26} One study showed diminished bone density (by DXA) and bone strength (by HR-pQCT) in women and men who sustained a mild trauma distal forearm fracture during childhood.²⁷

Less is known about the relationship between low bone mass and fracture risk in children with chronic illness, because studies in these patient 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,^{28,29} and spine fractures are more common in young patients with childhood leukemia, osteogenesis imperfecta, or exposure to glucocorticoids.^{30,31}

Clinical variables have been shown to influence the risk of fractures in older adults independent of their bone mass by densitometry. Age, weight, alcohol or smoking history, glucocorticoid use, and a history of previous fracture are used to calculate the absolute fracture risk.²⁵ The contribution of these or other clinical variables to fracture risk in children has not been established. However, 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 would likely benefit from evaluation by a provider with expertise in bone (eg, a pediatric endocrinologist, nephrologist, geneticist, neurologist, or rheumatologist).^{1,6,26,32}

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 μ Sv of radiation exposure from a spine and whole-body DXA scan is far less than the 80 μ Sv accumulated during a round-trip transatlantic flight.³³ More concerning is the potential risk of misdiagnosis if DXA data are not interpreted by skilled professionals at pediatric densitometry centers. An important 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 on the basis of inappropriate use of a T-score.³⁴ 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

Treatment options for children with low bone mass and fractures are more limited than in adults, underscoring the importance of accurate skeletal assessments.³⁵ General measures to address skeletal risk factors are safe and appropriate first steps for all patients. All strategies to optimize bone health should be considered.³⁶ Calcium intake should meet 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.^{7,36,37} Routine screening of vitamin D levels is not indicated in healthy youth. However, the adequacy of total body vitamin D stores should be assessed in youth at risk of bone fragility by measuring by measuring serum concentrations of 25-hydroxyvitamin D. Concentrations of at least 20 ng/mL (50 nmol/L) have been recommended for healthy children, but some experts aim for a serum 25-hydroxyvitamin D concentration >30 ng/mL in populations at increased risk of fracture.^{7,36} Weight-bearing activity should be encouraged, and even short periods of high-intensity

exercise (eg, jumping 10 minutes/day, 3 times/week) have produced measurable gains in bone mass.³⁸ The childhood and teenage years appear to be of particular importance for bone accretion. The Iowa Bone Development Study (a prospective cohort study) showed 10% to 16% greater hip BMC and 8% greater hip areal BMD in participants who accumulated the greatest amount of activity from childhood through adolescence (12-year follow-up).³⁹ For patients with limited mobility, reducing immobility through physical therapy⁴⁰ or the use of vibrating platforms can be helpful.^{29,41} Reducing inflammation, undernutrition, or hormone imbalances also is necessary. In children with inflammatory bowel disease, 1 study showed that a reduction in inflammation through the use of anti-tumor necrosis factor α therapy led to appreciable differences in bone structure and density.⁴²

If 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 Food and Drug Administration for pediatric use.^{35,43} Nevertheless, therapy with bisphosphonates is considered reasonable for children with moderate to severe osteogenesis imperfecta (2 or more fractures in a year or vertebral compression fractures).⁴⁴ 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.⁴⁵ When pharmacologic therapy is considered, referral to a specialist with expertise in pediatric bone disorders is advised.

SUMMARY

DXA has been established as a valuable tool as part of a comprehensive skeletal assessment in children and teenagers. Normative

data are accumulating for the use of this tool in infants, but they have not yet been fully integrated into clinical practice.⁴⁶ Acquiring and interpreting densitometry data in younger patients remain challenging and should be performed in consultation with experts. Panels of pediatric experts have set standards for when and how to perform DXAs on the basis of the best-available data; experts can be located through the International Society for Clinical Densitometry (www.iscd.org).^{8,10} Ongoing research will serve to refine the best modalities for assessing bone strength in children and to determine the key clinical variables that influence fracture risk independent of bone.

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ABBREVIATIONS

BMC: bone mineral content
BMD: bone mineral density
DXA: dual-energy radiograph absorptiometry
HR-pQCT: high-resolution peripheral quantitative computed tomography
PDC: Pediatric Position Development Conference
pQCT: peripheral quantitative computed tomography
QCT: quantitative computed tomography
VFA: vertebral fracture analysis

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Laura K. Bachrach, Catherine M. Gordon and SECTION ON ENDOCRINOLOGY

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