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CASE REPORT

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The Importance of Height-Adjusted Bone Z-Score in 3 Cases of Densitometry in Low Height Children

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Abstract

Introduction: Bone health assessment in pediatric patients, through total body less head and lumbar spine DXA scans, is important to identify children who may be at risk of poor mineral accretion or future risk of osteoporosis due to low bone mineral density. Because of its two-dimensional nature, DXA is vulnerable to size-related artifacts. Consequently, because childhood bone density is closely linked to height, low (or high) bone density relative to that of same-age peers may be attributed to short stature. Case Reports: Case 1: 16-year-old female, diagnosed with Smith-McCort syndrome. Case 2: 17-year-old male, diagnosed with spondyloepiphyseal dysplasia congenital. Case 3: 7-year-old male, diagnosed with Duchenne muscular dystrophy. Discussion: The Pediatric Positions of the ISCD state: "In children with short stature or growth delay, spine and total body less head BMC and areal BMD results should be adjusted, using the height Z-score". The height-adjustment for bone Z-score was the only approach for which the effects of short stature were not significant and the age effect was most modest. Conclusion: DXA bone Z scores adjusted for HAZ yielded the least biased approach for estimating the effect of short stature on measures of BMD. Comparison of the age-based bone Z-score and the height-adjusted bone Z-score provides the clinician with a frame of reference for the degree to which the bone Z-score may be attributable to short stature, which may be useful in determining when a child with decreased BMD requires treatment. Keywords: Densitometry, Osteoporosis, Metabolic Bone Diseases, Bone Density, Disabled Children.

Introduction

Bone tissue is responsive to metabolic, genetic, and behavioral factors. It is widely accepted that bone mineral accrual during childhood and adolescence is a critical determinant of bone health in adulthood. Inadequate bone accretion during childhood can be related to lifestyle factors, such as diet and physical activity, chronic medical conditions with primary or secondary effects on bone, and concomitant medications.1 Assessment of bone health in pediatric patients is important to identify children who may be at risk of poor mineral accretion or future risk of osteoporosis due to low bone mineral density (BMD) [2].

The bone mass achieved by young adulthood is a critically important determinant of lifelong bone health. About 40% of adult total body bone mineral content (BMC) is acquired during the 2 year around peak height velocity in adolescence [3]. Peak bone mass (PBM), the maximum amount of bone mineral an individual accrues, is considered the best predictor of osteoporotic fracture. Optimizing PBM in early adulthood is one of the most important factors in preventing osteoporosis and fracture later in life [4]. The relative risk of fracture increases as much as 2.6-fold for each 1 standard deviation decrease in bone mass, and a 10% increase in PBM in the population is estimated to decrease risk of fracture in the elderly by 50%. Furthermore, bone mass predicts fractures in children [5].

Dual-energy X-ray absorptiometry (DXA) is a cornerstone of bone health assessment. DXA is low in cost, accessible, easy to use, provides precise quantification, and is the most accurate measure of BMC and BMD clinically available [6]. Total body and lumbar spine scans are recommended for clinical assessment of bone health in children. Total body less head (TBLH) BMC or BMD is preferred due to the changes in relative contribution of the head to total BMC and BMD during growth and the importance of the postcranial skeleton in fracture risk assessment [7] However, there are several challenges in accurately interpreting DXA scans in pediatric patients with chronic conditions that threaten bone health.

Because of its two-dimensional nature, DXA is vulnerable to size-related artifacts. Consequently, because childhood bone density is closely linked to height, low (or high) bone density relative to that of same-age peers may be attributed to short (or taller) stature. In addition, DXA-acquired measures of BMC and BMD are dependent on age, sex, and population ancestry and become increasingly variable and nonlinear with age. Collectively, these points support the need for appropriately constructed age-, sex-, and population ancestry-specific reference ranges for bone density indices that adequately account for variations in height. For clinicians, such resources are essential for understanding the extent to which low bone density is attributed to short stature [8]

The International Society for Clinical Densitometry (ISCD) has endorsed height-adjustment approaches for lumbar spine DXA scans in children with short stature or growth delay [7]. Height-for-age Z-score (HAZ) is calculated using the Centers for Disease Control and Prevention growth charts, [9] and spine BMD-for-age Z-score is then adjusted for HAZ (BMDHAZ) [10].

Case Reports

Postero-anterior lumbar spine (L1-L4) and whole body scans were acquired using a Hologic DXA scanner (Discovery W, QDR Series; Hologic Inc., Bedford, MA, USA). The high-definition mode was used for spine scans. The precision error for BMD and BMC were less than 1% for the spine phantom and less than 2.5% for the whole-body phantom. Measurements following the manufacturer's guidelines for patient positioning were performed using a standard protocol and all scans were acquired and analyzed by the same trained physician, using Hologic Inc. software Apex (version 3.0). Sex specific HAZ, weight-for-age Z-scores, and body mass index-for-age Z-scores were calculated using the revised reference curves for BMC and BMD according to age and sex for black and non-black children.2 Spine BMDHAZ were calculated as described2 because this method accounts for the effects of short or tallerstature on spine BMD Z-scores. BMD/BMC Z-scores were adjusted for height-for-age Z-scores as described to minimize potential confounding by skeletal size on DXA outcomes [2]. None of the patients had previous history of fractures. Informed consent was received from the families.

Case 1

DMO, 16-year-old, female, with history of hypogonadotrophic hypogonadism, presented with short stature and chest deformity. Her height was 78 cm and her weight was 15.6 kg. Her phenotype included short neck and trunk, kyphoscoliosis and genu varum. Brachydactyly with plump interphalangeal joints and varying toe anomalies and pes planus were noticed. She had an abnormal gait, with limited elbows extension and hip abduction, and was not able to squat. Her diagnosis was Smith-McCort syndrome (SM-C).

SMC was first described as an osteochondrodystrophy by Smith and McCort11 in 1958. It is a rare progressive autosomal recessive disorder, with skeletal phenotypes characterized by spondylo-epiphyseal-metaphyseal dysplasias. It is one of the rare syndromes that can present with skeletal dysplasia and mimic some of the common bone diseases.

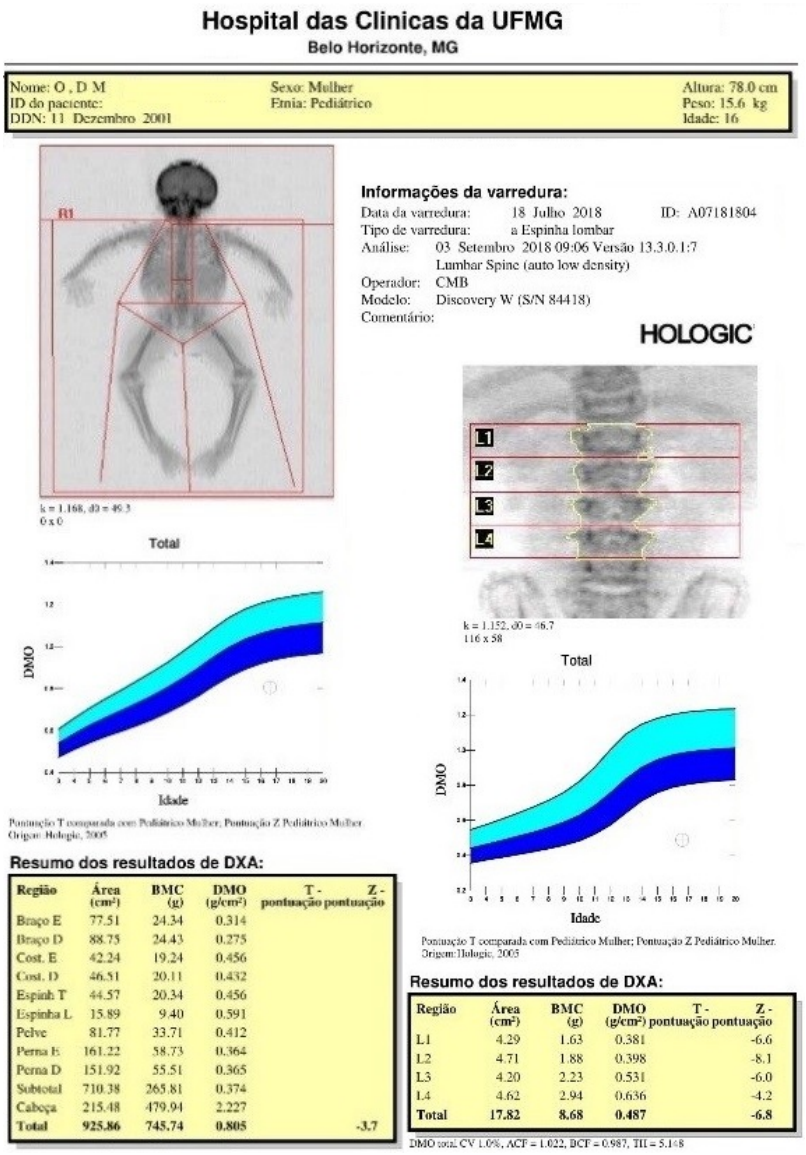

Figure 1: Postero-anterior lumbar spine (L1-L4) and whole body scan

Case 2

GNO, 17-year-old, male, diagnosed with spondyloepiphyseal dysplasia congenita (SEDC), in addition to thoraco-lumbar scoliosis with inoperability criteria and rib cage restriction deformity, associated with respiratory failure due to the rib cage characteristics, bronchial hyperreactivity, mild pulmonary hypertension and pyramidalism secondary to chronic hypoxia. His height was 90 cm

and his weight was 22.9 kg. His phenotype included globally diminished tonus, accentuated dwarfism, macrocrania, wide front, shallow supraorbital ridges, ears with low and round implantation, wider nasal root, low and wider nasal bridge, malar hypoplasia, thick lips, short neck, infundibuliform chest, thoracic scoliosis, lumbar hyperlordosis, short arched limbs, limited elbow extension, enlarged wrists, small trident hands, enlarged knees and ankles and prominent heels. Radiological exams showed: atlanto-axial instability, "S" deformity in spine with 72º curvature in right thoracic convexity and 72º arching of thoraco-lumbar segment to the left, deformity and reduced height of the vertebral bodies, dysplastic metaphyses, costal arches fusion defects in the dorsal spine middle segment, spinal canal widening in the laterolateral direction of the cervical-dorsal transition, spinal cord atrophy and compression at the cranio-spinal junction as well as in the area of thoraco-lumbar kyphosis caused by anterior hypoplasia, dorsal displacement of T12-L1, gross bone trabeculation in humeral heads, absence of ossification of femoral heads. Genetic investigation of DNA extracted from peripheral blood revealed skeletal dysplasia associated with heterozygosity in the COL2A1 gene, variant c.1969g>A. In 1966 Spranger and Wiedemann [12] suggested the designation of spondyloepiphyseal dysplasia congenita (SEDC) for a short-trunk dwarfing condition affecting primarily the vertebrae and the proximal epiphyses of the long bones. SEDC is an autosomal dominantly inherited chondrodysplasia characterized by disproportionate short stature (short trunk), abnormal epiphyses, and flattened vertebral bodies [13]. Most cases result from new sporadic mutations in the COL2A1 gene on chromosome [12, 14].

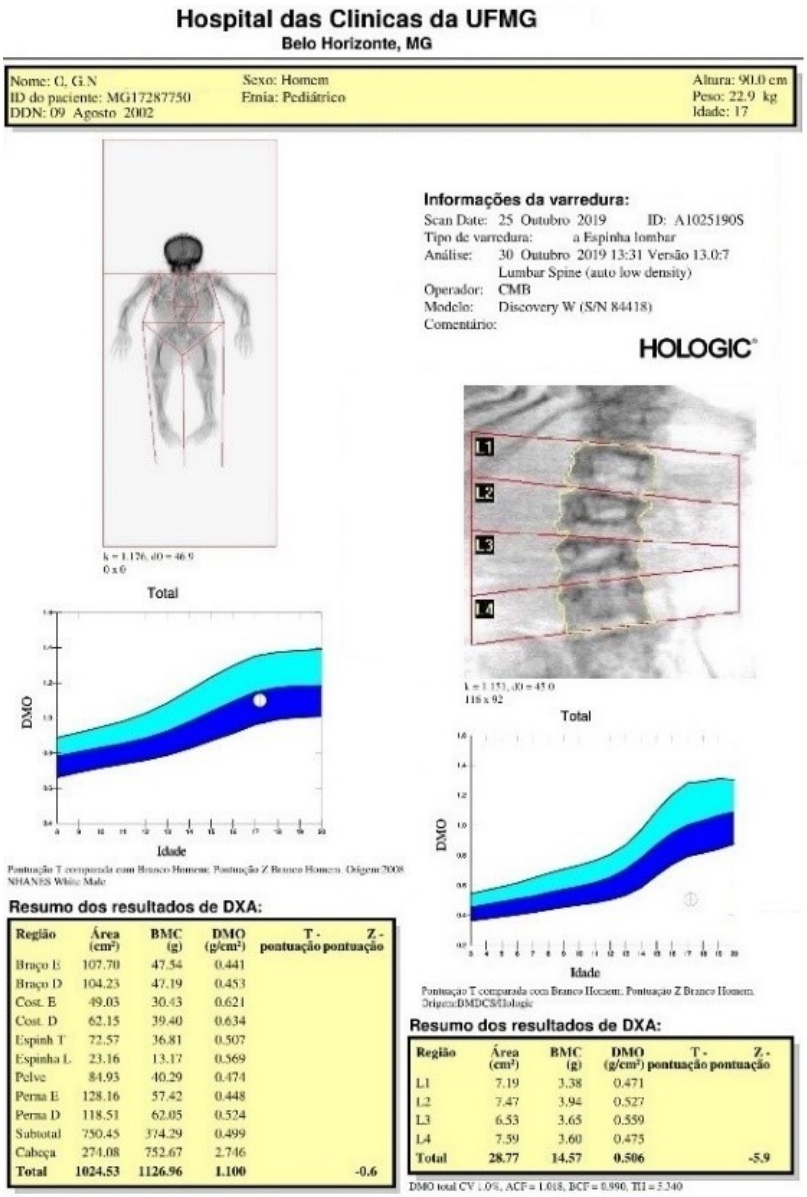

Figure 2: Postero-anterior lumbar spine (L1-L4) and whole body scan

Case 3

JBAS, 7-year-old, male, diagnosed with Duchenne muscular dystrophy (DMD). His height was 118 cm and his weight was 20.2 kg. DMD is caused by mutations in the gene encoding the dystrophin protein, located on the short arm of the X chromosome. Affected males experience delayed motor development, typically leading to diagnosis by age 5 years. Progressive muscle weakness leads to independent ambulation loss in second life decade and premature death often in third decade [15] Glucocorticoids have been and remain the therapy mainstay to slow cardiopulmonary function and muscle strength declines, thus delaying ambulation loss and lengthening life expectancy. As a result of glucocorticoid therapy, DMD patients often exhibit low height-for-age and delayed puberty, resulting in delayed skeletal maturity and increased bone fragility. This translates into increased risk of spine compression fractures and long-bone fractures, often heralding mobility loss. Thus, timely diagnosis and treatment of osteoporosis in these patients is one of the main goals of disease management [16].

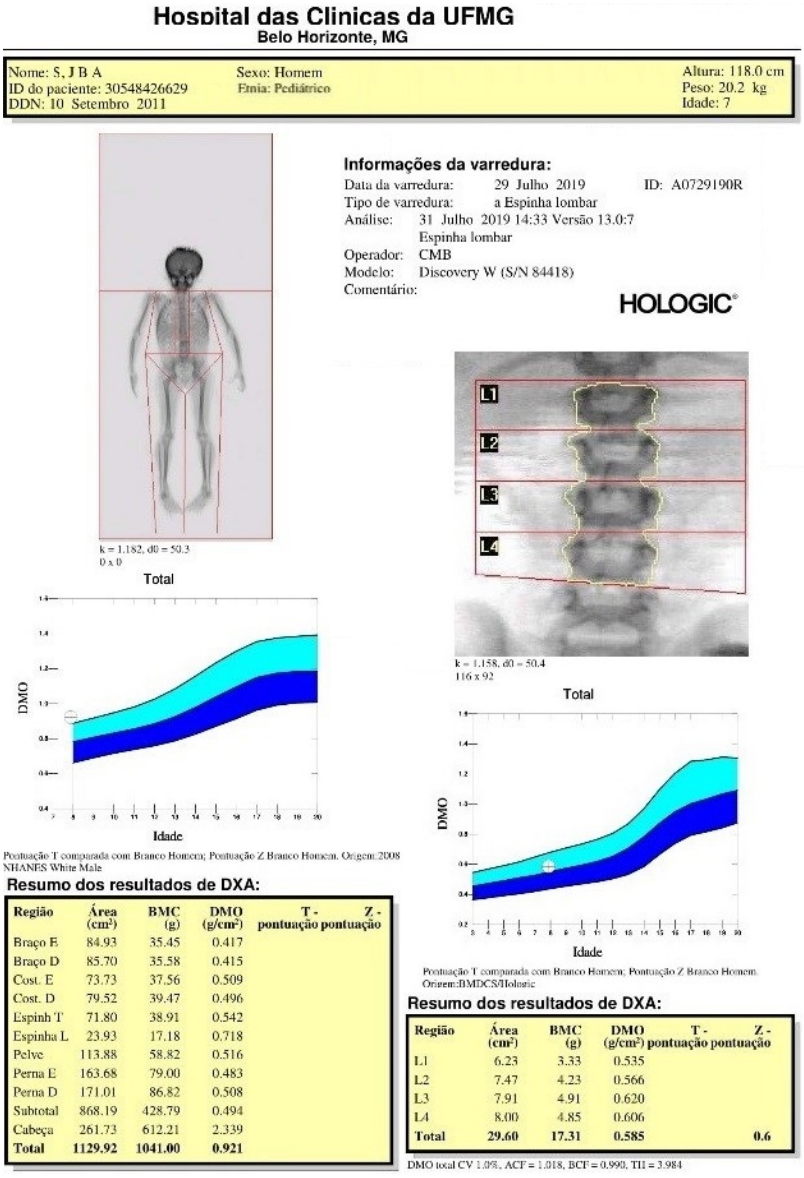

Figure 3: Postero-anterior lumbar spine (L1-L4) and whole body scan

	Patient 1				Patient 2				Patient 3			
Body Part	Total Body Less Head (BMC)	Lumbar Spine (BMC)	Total Body Less Head (BMD)	Lumbar Spine (BMD)	Total Body Less Head (BMC)	Lumbar Spine (BMC)	Total Body Less Head (BMD)	Lumbar Spine (BMD)	Total Body Less Head (BMC)	Lumbar Spine (BMC)	Total Body Less Head (BMD)	Lumbar Spine (BMD)
Body Part Value	265.81	8.68	0.374	0.487	374.29	14.57	0.499	0.506	428.79	17.31	0.494	0.585
Height Z-Score	-13.21	-13.21	-13.21	-13.21	-9.79	-9.79	-9.79	-9.79	-1.64	-1.64	-1.64	-1.64
…for Age Z-Score	-10.22	-9.23	-11.48	-5.95	-12.47	-8.13	-11.71	-5.31	-3.46	-1.27	-3.54	0.13
…for Age Z-Score adjusted for HAZ	1.80	1.99	-2.98	1.84	-4.38	-0.24	-6.49	-0.24	-1.88	0.09	-2.36	0.81

Table I: Results of Postero-anterior Lumbar Spine (L1-L4) and Whole Body Scan Less Head After Height-Adjustment

Discussion

BMC and BMD increase substantially during childhood and adolescence. Differences in body size and composition and maturational timing promote sex differences during this period. Consequently, BMC and BMD must be evaluated as age- and sex-specific Z-scores to account for expected developmental changes in bone. Therefore, a large healthy reference sample is essential to characterize the normal range of age-related changes in BMC and BMD [2].

Like height and weight, the age-related increases in BMC and BMD are nonlinear, and variability also increases with age. Consequently, pediatric BMC and BMD results are expressed as Z-scores, so that an individual child's test results can be appropriately compared with those of his/her same-age peers. However, many children with health conditions that affect bone acquisition, at-risk for inadequate bone accrual, such as those with disorders involving inflammation, malabsorption, or immobilization, also have faltering linear growth and delayed sexual maturation. Consequently, low BMD or BMC Z-score in the context of short stature or delayed maturation is difficult to interpret, raising the question of the degree to which the low bone status can be attributed to smaller bone size relative to age [10].

A commonly used technique in clinical practice is to substitute bone age or "height age" (the age at which a child's height is the median height-for-age on the growth chart) for chronological age as a means of adjusting for short stature. Of particular concern with the use of the height age approach is that children who are short-for-age will be compared with children of similar height who are younger and at an earlier stage of sexual maturation. A similar problem may occur using height-specific Z-scores because they do not take age into account. An alternative approach that would simultaneously consider both height and age involves adjusting for height-for-age Z-score (HAZ) [10].

To identify bone deficits, appropriate reference data are needed that adequately characterize the normal patterns of bone mineral accretion. Important characteristics of pediatric reference database include 1) most current measurement technology with standardized data acquisition and 2) well characterized, healthy, and ethnically diverse sample that is large enough to capture the normal variability in BMD. Additionally, data should be analyzed using statistical methodology that adequately characterizes age-related trends and distribution of values at different ages [17].

The Pediatric Positions of the International Society for Clinical Densitometry state: "In children with short stature or growth delay, spine and total body less head BMC and areal BMD results should be adjusted, using the height Z-score" and "An appropriate reference data set must include a sample of healthy representatives of the general population sufficiently large to capture variability in bone measures that takes into consideration gender, age, and race/ethnicity" [18, 19]

The HAZ adjustment method was the only approach for which the effects of short (or tall) stature were not significant and the age effect was most modest. HAZ can easily be calculated using the EpiInfo software provided to the public at no cost from the Centers for Disease Control and Prevention [20] and the HAZ adjustment involves simple calculations using the equations provided. Therefore, this technique can be readily applied in clinical practice, overcoming one of the major obstacles to applying the ISCD pediatric guidelines [10].

Conclusion

The most important thing about the densitometries realized in the 3 cases above, is to give substrates and enable the tracking of bone mineral status of these patients in the future and, perhaps, to direct interventions, if necessary, to prevent osteoporosis later in life.

DXA bone Z scores adjusted for HAZ yielded the least biased approach for estimating the effect of short stature on measures of BMD, especially among children who are within the age range when normal timing of puberty occurs. Comparison of the age-based bone Z-score and the height-adjusted bone Z-score provides the clinician with a frame of reference for the degree to which the bone Z-score may be attributable to short stature, which may be useful in determining when a child with decreased BMD requires treatment. Future studies are needed to evaluate the accuracy of the height Z-score adjustment method in identifying individual children at-risk for fracture.

Accurate assessment of bone health in children depends on robust reference data to determine whether an individual child's BMC or aBMD is comparable with same-age and -sex peers. To meet criteria for robust reference ranges, a larger, multicenter sample of data including other population ancestry groups is needed.

Contributor's Statement

Author's contribution

The authors declare no conflict of interest

Conception and Design of Study

Barral CM, Sanches SMD

Acquisition of Data

Barral CM

Analysis and/or Interpretation of Data

Barral CM

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