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Children with Spina Bifida are at Risk for Low Bone Density

Elizabeth A. Szalay MD, CCD, Asad Cheema

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Abstract

Background Patients with spina bifida frequently sustain lower extremity fractures which may be difficult to diagnose because they feel little or no pain, although the relative contributions of low bone density to pain insensitivity are unclear. Routine dual-energy xray absorptiometry (DXA) scanning is unreliable because these patients lack bony elements in the spine, and many have joint contractures and/or implanted hardware.

Questions/purposes We asked (1) if the lateral distal femoral scan is useful in spina bifida; (2) whether nonambulatory children with spina bifida exhibit differences in bone mineral density (BMD) compared with an age-and-sex-matched population; and (3) whether Z-scores were related to extremity fracture incidence.

Methods We retrospectively reviewed 37 patients with spina bifida who had DXA scans and sufficient data. Z-scores were correlated with functional level, ambulatory status, body mass index, and fracture history.

Results The distal femoral scan could be performed in subjects for whom total body and/or lumbar scans could not be performed accurately. Twenty-four of 37 had Z-scores below −2 SD, defined as "low bone density for age." Ten of 35 patients (29%) with fracture information had experienced one or more fractures. Our sample size was too small to correlate Z-score with fracture.

Conclusion We believe BMD should be monitored in patients with spina bifida; nonambulatory patients with spina bifida and those with other risk factors are more likely to have low bone density for age than unaffected individuals. The LDF scan was useful in this population in whom lumbar and total body scans are often invalidated by contracture or artifact. Although lower extremity fractures occur regardless of ambulation or bone density, knowing an individual's bone health status may lead to interventions to improve bone health.

Introduction

Patients with spina bifida (myelomeningocele) sustain fractures of the lower extremities with an incidence estimated to be from 11% to 30% [6]. Fractures may go unrecognized or the diagnosis may be delayed because the patients do not perceive the fracture pain. The importance of this insensitivity, relative to low bone density as factors contributing to fracture incidence, is unclear.

The current standard for measurement of bone density is dual photon xray absorptiometry (DXA scanning) as a result of its availability, accuracy, reproducibility, and low radiation exposure. Applying DXA scanning to any pediatric population is challenging as a result of changing bone density with growth and maturation; unlike adult DXA studies in which an individual is compared with one standard, the "ideal" mature adult, children have not yet achieved peak bone density, so each must be compared

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Each author certifies that his or her institution approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.
This study was performed at the University of New Mexico, Carrie Tingley Hospital, Albuquerque, NM, USA.

E. A. Szalay (✉), A. Cheema
University of New Mexico, Carrie Tingley Hospital,
1127 University Boulevard NE, Albuquerque,
NM 87102, USA
e-mail: ESzalay@salud.unm.edu

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with a population mean that changes with age progression [7]. Children of the same chronologic age may differ in skeletal maturity, making the "best" mean to use for each patient complicated to choose [13]. If children have myelomeningocele, DXA studies are more challenging yet; the International Society for Clinical Densitometry (ISCD) recommends that, in children, regions studied should include the spine and the total body less head [7] and these regions often cannot be scanned in these children. In this population, deficient bone elements of the spine, contractures of hips, and orthopaedic hardware defy application of these recommendations [1, 14]. Awareness of the pitfalls of DXA as applied to the spina bifida population is imperative to prevent inappropriate diagnosis and to adequately monitor treatment.

Rosenstein et al. [11] and Quan et al. [10] examined bone density in children with myelomeningocele using ^{125}I single photon absorptiometry. Rosenstein et al. found bone density of both upper and lower extremities in patients with spina bifida related to neurologic level and ambulatory status [11]. Quan et al. found bone mineral density in the distal radius averaged 1 to 2 standard deviation units below the expected norm in patients with spina bifida who were 6 to19 years of age [10]. Apkon et al. [1] performed DXA of the whole body and femoral neck in 21 children with spina bifida, suggesting limitations of the technique resulting from contractures and other physical differences. Valtonen et al., evaluating DXA scans on adult rehabilitation patients with spina bifida, noted low bone density was a likely and "unrecognized" entity in this population [16]. There are, however, insufficient data to recommend the methods for DXA scanning in children and adolescents with spina bifida to avoid errors in diagnosis and insufficient data to determine whether fractures in spina bifida relate to low bone density or other factors such as neurosegmental level.

We asked whether (1) difficulties in scanning children with spina bifida might be obviated by using the lateral distal femoral scan, which was designed for children with cerebral palsy [3]; (2) children with spina bifida who are nonambulatory or who have other bone health risk factors exhibit differences in bone mineral density (BMD) compared with an age-and-sex-matched population; and (3) Z-scores in these children relate to extremity fracture occurrence?

Patients and Materials

We retrospectively identified 40 patients with spina bifida who had DXA scans from 2003 to 2009. Indications for scanning in this population were nonambulatory status, fracture, or comorbidities that would affect bone health such as seizures, use of DepoProvera, steroid use, and so on. Exclusion criteria were other neurogenic paraparesis and spinal cord injury. Also excluded were scans in which BMD and Z-scores were deemed to be inaccurate as a result of orthopaedic hardware or prior fracture with deformity or callus formation or where data were incomplete.

The 40 patients (Table 1) had undergone 60 clinically indicated DXA scans, of which only the first was used for this analysis. One patient had a lumbar spine scan performed (L1–L4 Z-score −1.1), but the lateral distal femur scans showed abundant fracture callus from bilateral distal femur fractures, which would have skewed results. This and one other patient with DXA dictations had incomplete documentation, although it was noted that "all distal femur DXA sites were above the mean." Data from these three patients were not included in the statistical evaluations, leaving 37 patients with sufficient data for analysis (Table 1). No patients were recalled specifically for this study; all data were obtained from medical records. Approval was gained from the Human Research Review Committee of the University of New Mexico Health Sciences Center to conduct this study.

The scans all were performed by the same technician using a Hologic Delphi W densitometer (Hologic, Inc, Bedford, MA). The standard regions of interest scanned included the lumbar spine, right and left hips in patients 8 years old or older, and right and left lateral distal femur scans [3]. Techniques used were in accordance with recommendations of ISCD and the Hologic company; the LDF technique was as described by Harcke et al. [3]. Not all scans were performed on all patients; for example, spinal instrumentation precluded lumbar scanning. When multiple scans had been performed, the first scan date for each subject was used to avoid skewed findings by treatment effects.

Table 1. Demographics and neurofunctional level

Demographic	Value
Age at DXA scan	13.0 years (range, 4–22)
BMI	22.05 kg/m^2 (range, 11–49.5)
Gender	24 female; 13 male
Ethnicity	Hispanic: 19
	Native American: 4
	White: 11
	Hispanic/white: 3

Neurosegmental function	Number	Ambulatory
Thoracic level function	16	0/16
L1-2 function	7	0/7
L3-4 function	11	8/11
L5/sacral function	3	3/3

DXA = dual-energy xray absorptiometry; BMI = body mass index.

Data entered into a database included age, gender, height, weight, body mass index (weight/height^2), level of neurologic function as recommended by the International Myelodysplasia Study Group criteria [12], presence or absence of a shunt for hydrocephalus, ambulatory status, occurrence and number of fractures, and bone density in both grams/cm^2 and Z-scores as compared with age-and-sex-matched mean [2, 5]. Summary scores, including means and confidence intervals, were calculated using standard methods. Student's t-test was used to test the null hypothesis of Z-score = 0 (meaning that a normal population should have a mean Z-score of 0). Normal probability plots and the Wilk–Shapiro test were used to evaluate departure from normality. Fisher's exact test was used to compare fracture rates between ambulatory and nonambulatory children and to compare rates of low bone density in the study population with the expected rate of low bone density in a normal population. All hypothesis tests were two-tailed.

Results

Children who had contractures, scoliosis, and orthopaedic hardware that precluded whole body and lumbar spine scans were successfully studied using the lateral distal femoral scan.

BMD as measured by Z-score in this group differed from the age-and-sex-matched mean (Table 2). Twenty-four of the 37 patients (64.9%) patients had at least one Z-score less than 2 standard deviations below the age-and-sex-matched mean ($p < 0.002$). Four patients' Z-scores were predominantly above the mean (maximum 2.4 SD above the mean) (Table 3).

Twenty-five of 35 patients who answered the fracture question had experienced no fracture by history, seven had a history of one fracture, and three had two fractures. All were lower extremity fractures (Table 4).

Table 3. Details of children with spina bifida who had bone mineral density above the mean

Subject number	Ambulatory?	Body mass index (kg/m^2)	Maximum Z-score	Fractures?	Level
2	Yes	19	+1.1	0	L5
8	Yes	25	+2.0	1	L4
26	Yes	49	+1.3	1	L3
30	No	22	+2.4	0	T12

Table 4. Details of fractures

Patient number	Level	Ambulatory?	Fracture
3	T12	No	Birth fracture, tibia fracture
11	L2	No	"Spontaneous fracture tibia"
12	L1	No	"Charcot-like changes distal tibia," fracture femur
13	L2	No	Postoperative fracture femur
15	T12	No	Femur
22	T12	No	Distal femora: bilateral exuberant fracture callus
24	T12	No	Femoral physeal fracture
26	L3	Yes	Hematoma about distal femur
29	L4	Yes	Stress fracture metatarsal
30	T12	No	Femur

Table 2. Comparison of Z-scores with normal, comparison of Z-score ambulatory patients versus nonambulatory

Region of scan	Comparison with normal mean = 0	Ambulatory	Nonambulatory	p Value, difference between ambulatory versus nonambulatory
Lumbar	17	7	10	
"n"	−1.36	−1.05	−1.8	0.29
Mean Z-score (95% CI)	p = 0.0009 (−2.07 to −0.65)			
R1 "n"	35	11	24	0.004
Mean Z-score (95% CI)	−2.18	−1.00	−2.7	
	p = 0.000001 (−2.74 to −1.61)			
R2 "n"	35	11	24	0.01
Mean Z-score (95% CI)	−1.85	−0.8	−2.3	
	p = 0.0002 (−2.41 to −1.29)			
R3 "n"	35	11	24	0.025
Mean Z-score (95% CI)	−1.80	−0.7	−2.3	
	p = 0.00005 (−2.47 to −1.14)			

CI = confidence interval.

Discussion

The literature suggests patients with myelomeningocele are difficult to scan accurately using the suggested DXA regions of the whole body and lumbar spine [1, 14]; therefore, we posited that the LDF scan would accurately reflect bone density in most patients. Awareness of pitfalls in interpretation optimizes the scan value in these children, and the use of ISCD-recommended nomenclature, "low bone density for age," rather than "osteoporosis" or "osteopenia" should minimize errors in diagnosis [7]. We asked whether children with spina bifida who are nonambulatory or who have other bone health risk factors exhibit differences in BMD compared with an age-and-sex-matched population and whether Z-scores were related to extremity fractures scores.

We recognize certain limitations of our study. First, we used data supplied both by child or parent and from medical records, some of which conflicted. Patient or parent history was not always accurate such as misidentifying osteotomy as a fracture; accordingly, number and type of fracture were independently verified by medical records and radiographs. Second, the DXA scans examined here were studies that were clinically indicated. Although the policy of the spina bifida clinic at Carrie Tingley Hospital is to obtain scans on all nonambulatory children with spina bifida and those with other risk factors, those individuals who pursued the testing may have been more likely to have had fractures or bone fragility. However, it is rare for patients to decline DXA testing when recommended; parents are interested in their child's bone health, and the test is painless. Third, the exact number of children and adolescents with spina bifida that is followed at Carrie Tingley Hospital is unknown but estimated to be 250; the children who were studied with DXA were not necessarily a random or representative sampling. Finally, our subjects differed from many studies in that the majority was Hispanic. We do not know whether this would influence the generalizability of the findings.

We were able to perform a lateral distal femur scan on all of these patients, many of whom could not be studied using "standard" regions of interest. The current standard for measurement of pediatric bone density is DXA scan of the lumbar spine and whole body [7]. Both of these scans are problematic in children with myelodysplasia as a result of orthopaedic hardware that skews density reading and contractures making positioning difficult or impossible. Apkon et al. had to exclude six of 27 children with spina bifida because contractures precluded positioning for the scans [1]. The Apkon study asserted that scanning of the lumbar spine in these children is compromised by the anatomic abnormality of absent posterior elements as well as scoliosis or scoliosis hardware. In 20 of our 27 patients a spinal scan could not be done because of scoliosis or spinal instrumentation. Hip scans were attempted in all patients older than 8 years of age, but in only three patients was the hip scan of sufficient quality to be clinically useful. Thus, our study confirms Apkon et al.'s [1] suggestion that the lateral distal femoral scan, developed for use in children with cerebral palsy [3], was likely the most appropriate region to test in this patient population.

BMD as measured by Z-score in these children with spina bifida was indeed abnormal. Paradoxically, four of the 37 patients exhibited BMD above age-and-sex-matched mean, some as high as 2.4 SD above the mean (Table 3). The number of patients exhibiting BMD at or above the mean is too small for meaningful analysis but may relate to obesity [8] or precocious puberty [15]. The majority of subjects demonstrated Z-scores lower than age-and-sex-matched means (Table 2). Twenty-four of 37 children (64.8%) in the present study had at least one LDF Z-score less than 2 standard deviations below the age-and-sex-matched mean. Our observations confirm those of both Rosenstein et al. [11] and Quan et al. [10] looking at single photon absorptiometry. Apkon et al. [1], using DXA as we did, classified patients not according to ISCD recommendations for children (≤ -2 SD is "low bone density for age), but rather used the World Health Organization classification for postmenopausal females [2] (≤ -2.5 SD is "osteoporosis" and ≤ -1 SD is "osteopenia") [7]. Because of these differing definitions, our data are difficult to compare directly with those of Apkon et al. [1], but both studies agree that these individuals are at increased risk for low bone density. DXA scanning can identify those individuals who may benefit from a directed bone health program (maintaining vitamin $D > 40$ ng/mL, adequate calcium intake, and emphasis on weightbearing).

The question of a BMD relationship with fracture is a much more complex one that is not answered by this study; fracture as the end point in bone density studies requires very large numbers of subjects [9]. However, a few observations can be made. Ten of 35 children who answered the fracture question had experienced one or more fracture by history (Table 4); all fractures were in the lower extremities. The lateral distal femoral DXA scan reflects BMD in the legs, the regions most likely to incur fractures. Fractures in this population differed from fractures seen in other neuromuscular disorders such as cerebral palsy [4]; the nature of the radiographic changes suggested subperiosteal hemorrhage and Charcot-like changes in the physis, which might be attributed to chronic repetitive trauma and could not properly be described as an "insufficiency fracture." According to the ISCD, only children who have experienced an insufficiency fracture (a fracture occurring with minimal trauma) should be diagnosed with "osteoporosis." Children with a Z-score of less

than 2 SD below the mean who have not been documented to have an insufficiency fracture should be described as having "low bone density for age" [7]. The diagnosis of "insufficiency fracture" is hard to confirm in individuals with insensate limbs; a great deal of force could be applied to the limbs and not be perceived. This makes rendering a diagnosis of "osteoporosis" in these individuals very problematic.

In conclusion, the lateral distal femoral DXA scan provides data on the lower extremities, the most likely location for fracture in children with spina bifida. These patients, especially those who are nonambulatory, are likely to exhibit low bone density for age. A much larger series will be needed to correlate BMD with fracture in this population.

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