Prevalence of Vertebral Fractures in Children with Suspected Osteoporosis

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Objectives To explore the prevalence and anatomic distribution of vertebral fractures in disease groups investigated for primary and secondary osteoporosis, using vertebral fracture assessment (VFA).

Study design VFA was performed independently by 2 nonradiologists, in 165 children (77 males, 88 females) as part of their investigation for osteoporosis. Vertebral bodies from T6 to L4 were assessed for vertebral fractures using the Genant scoring system. The common readings for the presence of vertebral fractures were used for evaluating the prevalence and anatomic distribution of vertebral fractures.

Results The median age of the subjects was 13.4 years (range, 3.6, 18). Of the 165 children, 24 (15%) were being investigated for primary bone disease, and the remainder had a range of chronic diseases known to affect bone health. Vertebral fractures were identified in 38 (23%) children. The distribution of the vertebral fractures was bimodal, with vertebral fractures peaks centered at T9 and L4. Conditions associated with increased odds for vertebral fractures were inflammatory bowel disease (OR, 3.3; 95% CI, 1.4, 8.0; $P = .018$) and osteogenesis imperfecta (OR, 2.3; 95% CI, 1.04, 5.8; $P = .022$). Among children with vertebral fractures, those with Duchenne muscular dystrophy ($P = .015$) and osteogenesis imperfecta ($P = .023$) demonstrated higher number of vertebral fractures than the other disease groups.

Conclusions VFA identified the presence of vertebral fractures, in a bimodal distribution, in both primary bone disease and chronic disease groups. VFA is a practical screening tool for identification of vertebral fractures in children and adolescents at risk of fragility fractures. *(J Pediatr 2016;179:219-25).*

In young people, vertebral fractures are increasingly recognized as an important marker of primary and secondary osteoporosis, spanning diverse groups of chronic illness, in particular those treated with glucocorticoids.[1-3] Vertebral fractures by themselves are indicative of severe bone fragility irrespective of the reported bone mineral density (BMD)[4] and, in both adults and children, are associated with a significant risk of further vertebral and nonvertebral fractures.[5-7] Early identification of vertebral fractures in children who are at risk of osteoporosis may influence the clinician's options for bone protection therapy, either through optimizing nutrition and limiting exposure to glucocorticoids or initiation of specific therapies, such as bisphosphonates, with a view to possible normalization of vertebral morphology during the years of active bone growth.[8,9]

The identification of vertebral fractures has been hampered by the availability of an imaging modality that provides adequate visualization of the thoracic and lumbar spine, is readily available in all centers, and is associated with suitably low levels of radiation exposure to allow for its use in screening and repeated studies. Information gathered on vertebral fractures anatomic distribution, from screening in different diseases, and readability at each vertebral level could aid clinical assessment and inform the choice of imaging modality, respectively.

Measurement of BMD by dual energy X-ray absorptiometry (DXA) is central to the comprehensive skeletal health assessment of children with an increased risk of fracture, both children presenting with suspected primary bone disorders and children with possible osteoporosis secondary to other chronic conditions.[2] Vertebral fracture assessment (VFA) is the assessment of lateral spine images acquired by DXA to detect vertebral fractures. VFA may prove to be a valuable screening tool for osteoporosis, particularly in the presence of normal bone density[10] and has recently been shown to be an accurate and reproducible method for assessing vertebral morphometry in children.[11] Preliminary data have highlighted its utility in young people with inflammatory bowel disease and anorexia nervosa.[12,13] The purpose of this study was to investigate the role of VFA in estimating the prevalence and the anatomic distribution of vertebral fractures in children and adolescents undergoing routine clinical assessment for osteoporosis.

Methods

The cohort consisted of 165 consecutive children and adolescents (77 males, 88 females) who had a DXA BMD measurement at the Royal Hospital for

BMC	Bone mineral content	DXA	Dual energy X-ray absorptiometry
BMD	Bone mineral density	TB	Total body
BMI	Body mass index	VFA	Vertebral fracture assessment

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Children, Glasgow, as part of their clinical evaluation for suspected or previously diagnosed osteoporosis, between July 2013 and May 2014. It has been standard practice from 2013 onward for all patients to have both BMD and VFA performed. Anthropometric measurements, height, and calculated body mass index (BMI), were obtained on the day of the DXA visit, and converted to SDS using 1990 United Kingdom standards.[14,15]

Image Acquisition and BMD Measurement

Lateral images of the thoracic–lumbar spine were obtained following BMD measurement of the lumbar spine (L2-L4) and total body (TB), using Lunar Prodigy (GE Medical Systems, Waukesha, Wisconsin) (**Figure 1**, A). The subject was placed in the left lateral decubitus position with hips, knees, and shoulders bent at 90 degrees. As outlined previously, reference data were used to calculate a predicted and a percentage predicted bone area for age and sex.[16,17] The reference data allowed for a comparison of the actual bone mineral content (BMC) of the individual with the predicted BMC of a subject of the same sex and bone area from which the percentage predicted BMC, expressed as an SDS (BMC SDS) could be calculated. The percent coefficient of variation of the device, calculated on repeated measurement of a phantom is 1%. The individual percent coefficient of variation calculated on repeated measurement of the lumbar spine in anterior-posterior view, in a group of 24 children, is <2.1%.

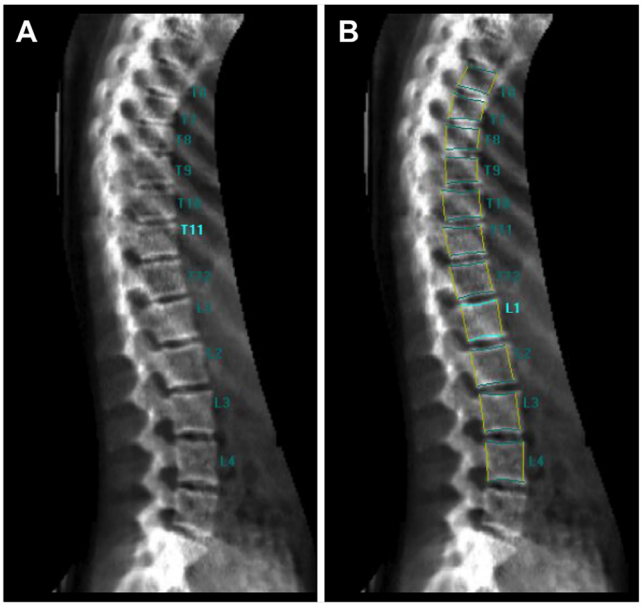

Figure 1. **A,** Lateral images of the thoracic–lumbar spine were obtained using DXA (Lunar Prodigy; GE Medical Systems). **B,** VFA: Each observer manually identified 6 landmarks corresponding to the 4 corners and the midpoints of the endplates, respectively, of each adequately visualized vertebral body starting at L4 and continuing through the thoracic spine up to T6 (Encore v 13).

VFA by DXA

Lateral spine images were analyzed independently by 2 nonradiologists, who performed VFA in all 165 subjects. Before the VFA analysis, the observers defined a common protocol for point placement on each vertebral body. Each observer manually identified 6 landmarks corresponding, to the 4 corners and the midpoints of the endplates, respectively, of each adequately visualized vertebral body starting at L4 and continuing through the thoracic spine (TS) up to T6 (**Figure 1**, B). From these points, the software (Encore v 13; GE Healthcare Lunar, Madison, Wisconsin) measured the anterior, middle, and posterior heights and calculated the anterior:posterior height and the middle:posterior height within a vertebral body. The observers also calculated the posterior:posterior height when comparing vertebrae above or below the one under examination. The vertebral bodies were classified, as either no fracture or vertebral fractures, according to the extent of any height reduction as expressed by the reduction in height ratios using the scoring system developed by Genant et al[18]: no fracture (grade 0) if the reduction in any height ratio was ≤20%, and vertebral fractures (inclusive of grade 1-3) if a height ratio reduction was greater than 20%. Interobserver agreement in vertebral readability was 94% (kappa, 0.73; 95% CI, 0.68, 0.73). Interobserver agreement for the presence of a vertebral fractures of any severity, in per-vertebra analysis was 99% (kappa, 0.85; 95% CI, 0.79, 0.91). In 20 children, VFA was compared with an assessment of lateral vertebral morphometry on a lateral spine radiograph. Per-vertebra agreement between lateral vertebral morphometry and VFA was 95% (kappa, 0.79; 95% CI, 0.62, 0.92), and per-subject agreement was 95% (kappa, 0.88; 95% CI, 0.58, 1.0). When analysis was based on the vertebral fractures grading, agreement was lower and reached 88% with kappa score of 0.55 (95% CI, 0.40, 0.68). Agreement on per-person basis between the 2 methods reached 95% (kappa, 0.88; 95% CI, 0.72, 1.0).[11]

Statistical Analyses

Analyses were conducted using SPSS v 20 (SPSS Inc, Chicago, Illinois). Population characteristics are expressed as median (range) for continuous variables, and categorical variables are expressed as the value (percentage frequency). Comparison between groups was performed by Mann-Whitney U test and Kruskal-Wallis test for continuous variables and by χ^2 test or Fisher exact test for categorical variables. All tests were 2 sided and P value of <.05 was considered significant. The common readings for the presence of vertebral fractures from the 2 observers were used for evaluating the prevalence of vertebral fractures in the population in total and in relation to the underlying chronic disease, and for determining the anatomic distribution of vertebral fractures. ORs were used to compare the relative odds of the occurrence of vertebral fractures on a vertebral level, with the odds of a vertebral fracture occurring on the rest of the vertebral levels from T6 to L4 and for the evaluation of the influence of the underlying condition on the occurrence of vertebral fractures. To overcome the obstacle of the variability in the number of the vertebrae per subject that were included in analysis for the estimation of the number of