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Pediatric Dual-Energy X-Ray Absorptiometry in Japan: A Proposal for Shared Access to Equipment

Toru Igarashi[1], Syuji Takei[2], Eriko Tanaka[3], Utako Kaneko[4], Tomohiro Kubota[2], Keisuke Okamoto[5], Shiro Ohshima[6] and Masaaki Mori[7]

[1]Department of Pediatrics, Nippon Medical School, Tokyo, Japan
[2]Department of Pediatrics, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan
[3]Department of Pediatrics, Kyorin University School of Medicine, Tokyo, Japan
[4]Department of Pediatrics, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
[5]Department of Pediatrics and Developmental Biology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan
[6]Department of Rheumatology, National Hospital Organization, Osaka-Minami Medical Center, Osaka, Japan
[7]Department of Lifetime Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Background: Regular assessment of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is essential for detecting glucocorticoid-induced osteoporosis in juvenile-onset autoimmune diseases. Z-score is used to standardize osteoporosis assessment in children and is evaluated with only one of three devices in Japan. The purpose of this study was to determine how many Japanese medical facilities for pediatric rheumatic diseases were unable to use Z-scores to evaluate osteoporosis.
Methods: Electronic questionnaires were distributed between 2017 and 2019 to hospitals belonging to the Pediatric Rheumatology Association of Japan and to university hospitals and public children's hospitals that provide medical care for pediatric rheumatic diseases. The questionnaire inquired about the location of DXA measurement, manufacturer (Hologic, GE healthcare, Hitachi), and measurement site, and the answers were collected using Google Forms. Statcel 4 was used for analysis.
Results: Overall, 120 facilities responded to the survey, of which 117 had DXA. In the remaining three facilities, DXA was not installed in two and was out of order in one. Bone loss in childhood was evaluated using a Z-score calculated from age-based reference values; however, 30% of hospitals without HOLOGIC DXA could not evaluate osteoporosis by Z-score in Japanese childhood. The characteristics of the hospitals enrolled in this study did not bias the selection of Hologic DXA.
Conclusions: Neighboring institutions should consider sharing access to Hologic DXA equipment, to ensure use of uniform reference values. GE BMD reference values should be established for Japanese children. (J Nippon Med Sch 2021; 88: 296–300)

Key words: dual-energy X-ray absorptiometry, corticosteroid, osteoporosis, systemic lupus erythematosus

Introduction

Juvenile-onset autoimmune diseases such as rheumatic diseases and systemic lupus erythematosus (SLE) have a long disease duration, resulting in prolonged corticosteroid use and, potentially, osteoporosis. Female patients with juvenile-onset SLE who do not have adequate bone mass and with bone loss after menopause may develop osteoporosis. Because SLE is more common in females and bone mass reaches its peak in childhood and adolescence, regular assessment of bone mineral density (BMD)

Correspondence to Toru Igarashi, Department of Pediatrics, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: iga@nms.ac.jp
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is essential in the treatment course of juvenile-onset SLE, to detect onset of glucocorticoid-induced osteoporosis.

Bone strength is determined by BMD (70%) and bone quality (30%). BMD is measured using dual-energy X-ray absorptiometry (DXA), and bone quality is determined by the degree of bone structure, bone turnover, bone fatigue/microfracture, and bone calcification[1]. Lumbar DXA is frequently used to determine BMD values; however, BMD values from different DXA devices cannot be compared; thus, another parameter has been proposed[2]. In adults, the T-score (calculated as [patient BMD - mean BMD values for healthy young adults]/standard deviation for healthy young adults) compares an individual's BMD with the mean value of a young healthy reference population; the difference is expressed as a standard deviation. Because the healthy reference population comprises those between the ages of 20 and 44 years, the T-score cannot be calculated for individuals <20 years. Therefore, the Z-score, which is the standard deviation between the individual's BMD and that of the age- and sex-matched population, is used in individuals <20 years. However, only the DXA from Hologic has incorporated pediatric reference values (provided by Nishiyama and colleagues)[3,4]. Other devices do not have standard values for Japanese children; therefore, Z-scores cannot be calculated for those younger than 20 years, making it difficult for physicians to assess bone density.

Pediatric rheumatologists aim to use Z-score in children for standardization of osteoporosis assessment. Only one of the three models in Japan can evaluate Z-score in children. The purpose of this study was to determine how many domestic medical facilities for pediatric rheumatic diseases were unable to evaluate osteoporosis with Z-scores. In addition, when a nearby facility had installed a HOLOGIC DXA that can calculate Z-scores, we recommend that it be shared.

Materials and Methods

In this descriptive study, electronic questionnaires were distributed between 2017 and 2019 to pediatricians and internists at nine hospitals that belong to the Pediatric Rheumatology Association of Japan, as well as to main and branch university hospitals and public children's hospitals that provide medical care for pediatric rheumatic diseases. The questionnaire inquired about the location of DXA measurement (within their facility or in an outside facility), manufacturer (Hologic, Inc. Marlborough, MA, US; GE Healthcare, Madison, WI, US; or Hitachi, Ltd. Tokyo, Japan), and measurement site (lumbar spine or radius). The answers were collected by using Google Forms. Facilities that did not respond to the survey were telephoned.

This study was approved by the Ethics Committee of Nippon Medical School Musashi Kosugi Hospital (no. 519-31-48). Patients were given the opportunity to refuse participation in studies by using an opt-out form. Categorical variables were analyzed with the chi-square test or Fisher's exact test. A p-value <0.05 was considered to indicate statistical significance. Statcel 4 software (OMS Publishing Inc., Saitama, Japan) was used for the analyses.

Table 1. Dual-energy X-ray absorptiometry (DXA) installation by type of facility (n = 120)

	Hologic	Other than Hologic
Hospital type[a)]		
Private hospitals (n = 46)	27	19
Public hospitals (n = 71)	51	20
Provision of care for pediatric rheumatic diseases		
Core facilities[b)] (n = 58)	40	15
Noncore facilities (n = 62)	38	24
Hospital expertise		
University hospital (n = 90)	58	32
Children's hospital[c)] (n = 12)	11	1

a) Private hospitals include private university hospitals; public hospitals include national/prefectural university hospitals and children's hospitals.
b) In the core facilities, DXA was not installed in two facilities and out of order in one. One facility was using digital image processing.
c) Two children's hospitals have access to Hologic at a partner hospital.

Results

The details of the DXA installation status for the 120 facilities are shown in **Table 1**. A total of 117 facilities had DXA; however, in the three remaining facilities DXA was not installed in two and was not functioning in one. One facility with no DXA was performing radiographic absorptiometry of the metacarpal bone through digital image processing.

The DXAs were from Hologic (n = 78; 67%), GE (n = 39; 33%), and Hitachi (n = 3; 2%). Two university branch hospitals and one municipal hospital were using Hitachi DXA. Of the three facilities using Hitachi DXA, two were for the radius and one was for the lumbar spine. One facility had a radius DXA and a Hologic DXA; this facility was thus registered twice.

For adults, a formula can convert values between Hologic and GE devices; however, there is no formula to convert values between Hitachi devices and other devices. Therefore, we classified the hospitals into two groups: those with Hologic devices and those with other devices. We then examined equipment installation conditions in relation to type of facility (private vs. public hospitals; core vs. noncore facilities; university vs. children's hospitals).

Table 1 shows that the characteristics of the hospitals enrolled in this study did not bias the selection of Hologic DXA. Fisher's exact test showed no difference in the percentage of Hologic installations between public and private hospitals (p=0.95), between core and noncore facilities (p=0.13), or between university hospitals and children's hospitals (p=0.05).

Discussion

The Z-score, which is widely used in monitoring glucocorticoid-induced osteoporosis, is used to compare a child's BMD value with the BMD values of age-matched healthy children. Because lumbar DXA is frequently used to determine BMD, we examined DXA installation conditions in hospitals in Japan.

The American College of Rheumatology has published recommendations for prevention and treatment of glucocorticoid-induced osteoporosis[5]. The committee recommends obtaining a baseline BMD measurement at the lumbar spine and/or hip when initiating long-term (>6 months) glucocorticoid therapy. The Japanese guidelines for glucocorticoid-induced osteoporosis were issued in 2004 and revised in 2014. The 2004 guidelines for glucocorticoid-induced osteoporosis targeted patients aged ≥18 years. If oral glucocorticoids were used for ≥3 months, BMD was assessed in comparison with the young adult mean (YAM), which is the mean BMD of young adults aged 20 to 44 years (%YAM). If the %YAM is <80%, the use of bisphosphonates as the first choice and active vitamin D3 as the second choice is indicated. A similar treatment was recommended for those with %YAM ≥80 if the mean daily dose of prednisolone (PSL) was ≥5 mg[6]. The Japanese 2014 revised guidelines are for patients aged ≥17 years[7]. The revised guidelines assess risk factors for bone fractures, including prior fragility and fracture, age (years), glucocorticoid dose (PSL equivalent mg/day), and lumbar BMD (%YAM), which are used to calculate the scores. Drug therapy is required if the score is ≥3. When assessing BMD in patients aged ≤17 years, separate age-specific reference values are required for male and female patients. In pediatric patients, the Z-score is used instead of the T-score. To calculate the Z-score in children, it is necessary to use DXA with pediatric reference values.

Surveys conducted by the Japan Osteoporosis Foundation in 1996 and 2006[8], and the present survey, found that DXA devices are constantly updated, leading to difficulty in comparing BMD values. In Japan, the reference values for the Hologic system were obtained from a study conducted by the Kumamoto University Group. Outside of Japan, DXA performed using the Hologic system calculates BMD values in relation to age, sex, and race[9,10].

Our results indicate that Hologic equipment accounts for two-thirds of all DXAs in Japan, indicating that a multicenter DXA study in children is possible. However, in the remaining one-third of all DXAs, Z-scores cannot be promptly calculated in one-third of facilities. The GE DXA has no reference BMD values for Japanese children; however, pediatric BMDs using DXA measured by the GE equipment have been reported overseas. A study using the GE Lunar Prodigy yielded lumbar spine BMD values in 155 Canadian children (77 boys) who were younger than age 5 years[11]. Another study, using the GE Luna DPX Pro, yielded reference values for lumbar spine BMD according to sex in 920 Indian children (480 boys and 440 girls) aged 5 to 17 years[12]. A study using the GE Lunar Prodigy yielded normal reference values for total body DXA in 877 Chinese children (505 boys and 372 girls) aged 5 to 13 years[13]. These studies suggest that pediatric Z-scores can be calculated with GE equipment.

DCS-600EX series devices by Hitachi, which measure radius BMD, have standard values according to sex for children aged 9 to 17 years. Because the standard values are not incorporated into the device, Z-scores are calculated manually. Although this DXA has pediatric reference values, it is unclear if it is appropriate for monitoring treatment course.

Although we did not survey installation in this study, radius DXA and calcaneal quantitative ultrasound are also used for osteoporosis screening but are unsuitable for monitoring treatment course.

To evaluate DXA values in patients younger than 20 years with juvenile-onset SLE, devices can be shared through medical cooperation. Even in the absence of reference values, if a nearby hospital has Hologic DXA, measurement results can be determined. GE systems account for 30% of DXA devices in Japan. It may become necessary in the future to measure the DXA of healthy children by using the GE Lunar Prodigy and to establish

reference values similar to those reported for other countries. Until then, if patients tested in facilities using the GE system have significantly lower BMD values, osteoporosis should be diagnosed.

A limitation of our study is that the patients with low BMD values do not always experience fractures. Occasionally, a BMD value obtained does not provide information on the absolute risk of bone fracture of an individual patient. In addition to BMD, clinical fracture risks include age, sex, degree of obesity, body mass index, family history of bone fracture, corticosteroid use, and rheumatoid arthritis.

This is the first study reporting that 30% of hospitals could not use Z-scores for BMD in the field of pediatric rheumatology. We propose enabling joint access of DXA equipment among neighboring hospitals. Such shared access to the Hologic DXA would facilitate use of standard reference values, which can aid in monitoring glucocorticoid-induced osteoporosis. Beginning evaluation of steroid-induced osteoporosis in childhood is important for quality of life in adulthood. In May 2020, we published the Japanese Guide for Clinicians to Support Transition of Pediatric Rheumatic Diseases[14], which provides recommendations for using DXA to evaluate child-onset steroid-induced osteoporosis. With all DXA models installed in Japan, our future goal is to be able to diagnose osteoporosis in children younger than 20 years.

Although the World Health Organization has developed a fracture risk prediction tool for adults (the Fracture Risk Assessment Tool)[2], a similar tool that is suitable for use in children is needed. Further studies of the relationship between bone mineral quantification and fracture in pediatric rheumatic diseases, including SLE, during the transition to adulthood and the association between renal function and bone fracture are needed.

Conclusion

In this study, we surveyed the use of DXA in children. Although the Hologic system, which is being used by two-thirds of physicians in Japan, can calculate age-specific Z-scores, the remaining one-third of physicians use GE devices. Therefore, it is necessary to consider providing shared access of Hologic DXA to neighboring hospitals, to obtain standard reference values. Furthermore, we recommend establishing BMD reference values for Japanese children assessed with GE systems, so that Z-scores can be used for pediatric patients, as they are in other countries.

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