

Review article

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Clinical practice guidelines for optimizing bone health in Korean children and adolescents

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The Committee on Pediatric Bone Health of the Korean Society of Pediatric Endocrinology has newly developed evidence-based clinical practice guidelines for optimizing bone health in Korean children and adolescents. These guidelines present recommendations based on the Grading of Recommendations, which includes the quality of evidence. In the absence of sufficient evidence, conclusions were based on expert opinion. These guidelines include processes of bone acquisition, definition, and evaluation of low bone mineral density (BMD), causes of osteoporosis, methods for optimizing bone health, and pharmacological treatments for enhancing BMD in children and adolescents. While these guidelines provide current evidence-based recommendations, further research is required to strengthen these guidelines.

Keywords: Practice guidelines, Bone, Child, Adolescent, Korea

Highlights

- The Committee on Pediatric Bone Health of the Korean Society of Pediatric Endocrinology has newly developed evidence-based clinical practice guidelines for optimizing bone health in Korean children and adolescents. These guidelines include processes of bone acquisition, definition, and evaluation of low bone mineral density (BMD), causes of osteoporosis, methods for optimizing bone health, and pharmacological treatments for enhancing BMD in children and adolescents.

Introduction

Osteoporosis was previously thought to be a disease exclusive to older adults. However, it is now increasingly recognized in younger adults due, in part, to the longer survival of chronically ill children. Children with osteoporosis are at a high risk of skeletal morbidity not only during youth, but also in adult life.¹⁾ Bone mass attained in early life is thought to be the most important modifiable determinant of lifelong skeletal health.²⁾ In this context, the Committee on Pediatric Bone Health of the Korean Society of Pediatric Endocrinology recently developed evidence-based clinical practice guidelines for optimizing bone health in Korean children and adolescents. Recommendations were determined according to the quality of evidence graded by the steering committee on quality improvement and management in the American Academy of Pediatrics.³⁾

This guideline comprises the physiological processes of bone acquisition, definition, and evaluation of low bone mineral density (BMD), causes of osteoporosis, conservative management for optimizing bone health, and pharmacological treatments for enhancing BMD in children and adolescents.

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Bone acquisition and peak bone mass

Bone is a living structure comprising a matrix of collagen, hydroxyapatite crystals, and noncollagenous proteins. The matrix becomes mineralized with deposits of calcium and phosphate, which confer strength to the structure.¹⁾

Bone mineral deposition begins in utero, and bone mineral content increases 40-fold from birth to adulthood. BMD of the lumbar spine (BMDLS) showed the greatest increase from the age of 11 to 13 years in girls and from 12 to 14 years in boys. BMD of the total body less head (BMDTBLH) shows a relatively modest increase from the age of 10 to 15 years in girls and from 10 to 18 years in boys.^{4,5)} In Korea, peak bone mass is achieved at approximately 19 and 21 years of age in girls and boys, respectively.^{6,7)}

There are numerous factors that affect bone mineral deposition and bone mass formation. These are largely divided into 2 groups: nonmodifiable factors including genetics, sex, and ethnicity and modifiable factors including nutrition, exercise, lifestyle, body weight and composition, and hormonal status.⁸⁾

BMD measurement

BMD in children and adolescents is most commonly assessed with dual-energy x-ray absorptiometry (DXA) because it is less time-consuming and more precise and widely available, safer, and less costly than other options.⁹⁾ The posteroanterior lumbar spine and total body less head are the preferred skeletal sites for BMD measurement in most pediatric patients, while other sites are recommended only for specific cases.⁹⁾ BMDLS measurement is a feasible and reproducible method, especially for infants and young children aged 0–5 years. BMDTBLH measurement can be used for children aged 3 years and older.⁹⁾ The standard methods of BMD evaluation in children and adolescents are performed using BMD *z*-score calculations according to comparisons with reference data in children of each age, sex, pubertal stage, and ethnicity.^{6,7,9)} In children with short stature or growth delay, BMDLS should be adjusted with bone mineral apparent density or height *z*-score and BMDTBLH with the height *z*-score.⁹⁾

Two types of bone densitometers (GE Lunar Prodigy Advance bone densitometer, Absolute Medical Inc, Stony Point, NY, USA and Hologic QDR densitometer, Hologic Inc, Bedford, MA, USA) were used. Normal BMD reference values for Koreans were compared to each densitometry measurement.^{6,7)}

Definition of low BMD and osteoporosis

Low BMD is the preferred term for DXA reports in children when the BMD *z*-score is less than or equal to -2.0 standard deviation (SD).⁹⁾ Osteoporosis in children is defined as the presence of ≥ 1 vertebral compression fracture in the absence of local disease or high-energy trauma or the presence of both a clinically significant fracture history and a BMD *z*-score of -2.0 or lower. A clinically significant fracture history includes at least

Table 1. Causes of osteoporosis in children and adolescents

Primary
Osteogenesis imperfecta
Idiopathic juvenile osteoporosis
Fibrous dysplasia
Cleido-crainial dysplasia
Hajdu-Cheney syndrome
Osteoporosis-pseudoglioma syndrome
Ehlers-Danlos syndrome
Marfan syndrome
Calvarial doughnut lesions
Secondary
Endocrine disorders
Anorexia nervosa
Hypogonadism
Growth hormone deficiency
Hyperthyroidism
Hypothyroidism
Hyperparathyroidism
Cushing disease
Type I diabetes
Neuromuscular disorders
Cerebral palsy
Duchenne muscular dystrophy
Spinal muscular atrophy
Connective tissue disorders
Systemic lupus erythematosus
Juvenile idiopathic arthritis
Juvenile dermatomyositis
Gastrointestinal disorders
Inflammatory bowel disease
Celiac disease
Malabsorption
Milk intolerance
Chronic obstructive jaundice
Chronic hepatitis
Primary biliary cirrhosis and other cirrhosis
Hemato-oncologic disorders
Hemoglobinopathy
Leukemia
Lymphoma
Renal disorders
Chronic renal failure
Kidney transplantation
Others
Immobilization
Poor calcium intake
Inborn error of metabolism
Excessive exercise
Medication
Glucocorticoids
Anticonvulsants
Chemotherapeutic agents
Immune suppressants
Anticoagulant
Proton pump inhibitor
Selective serotonin reuptake inhibitor

one of the following: (1) ≥ 2 long bone fractures by the age of 10 years and (2) ≥ 3 long bone fractures at any age up to 19 years.⁹⁾

Conditions associated with low BMD

There are primary and secondary causes of reduced bone mass and increased fracture risk (Table 1). Primary osteoporosis occurs due to intrinsic skeletal defects originating from genetic or idiopathic causes, while secondary osteoporosis results from chronic systemic illnesses in children due to either the effects of the disease process on the skeleton or from treatment.^{8,10,11)}

1. Primary osteoporosis

1) Osteogenesis imperfecta

Osteogenesis imperfecta is a rare genetic disorder with an incidence of approximately 1/25,000. Clinical manifestations include low bone mass, frequent fractures, bone deformity, short stature, wormian bones, blue sclerae, hypermobility of joints, dentinogenesis imperfecta, and deafness. There are 5 types of osteogenesis imperfecta according to clinical severity. Type 1 is the least severe and nondeforming; type 2 is lethal in the perinatal period because of respiratory insufficiency due to multiple rib fractures; type 3 is associated with limb deformities and is progressively deforming; type 4 has an intermediate phenotype between types 1 and 3; and type 5 has a phenotype similar to that of type 4 but is associated with calcification of interosseous membranes and hypertrophic callus formation at healing fracture sites. The most common mutations in all types are found in *COL1A1* and *COL1A2*, but novel mutations in other genes have been found (Table 2).¹⁰⁾

2) Idiopathic juvenile osteoporosis

Idiopathic juvenile osteoporosis is a disease of unknown etiology that is considered genetically heterogeneous in origin. The clinical manifestations include bone pain and fractures with minimal trauma in girls or boys aged 8–12 years. Symptom severity tends to abate spontaneously with variable residual manifestations.^{10,12)} Differential diagnosis of osteogenesis imperfecta and idiopathic juvenile osteoporosis is shown in Table 3.

3) Osteoporosis-pseudoglioma syndrome

Osteoporosis-pseudoglioma syndrome is a congenital or

infantile-onset disease. Its clinical manifestations include severe visual impairment, bone fragility, ligamentous laxity, hypotonia, and cognitive impairment. It is transmitted as an autosomal recessive trait and is associated with several types of mutations in *LRP5*.¹⁰⁾

2. Secondary osteoporosis

1) Endocrine disorders

Hypogonadism, growth hormone (GH) deficiency, hyperthyroidism or hypothyroidism, hyperparathyroidism, diabetes mellitus (DM), and Cushing syndrome are associated with low bone mass.^{8,10,11)} Hypogonadism is associated with decreases in cortical width, trabecular number, and osteoid and mineralization activity because of the decreased lifespan of osteoblasts and osteocytes but increased lifespan of osteoclasts, histomorphometrically.¹³⁾ GH deficiency is associated with decreases in osteoblast differentiation and proliferation, osteoblast synthesis of insulin-like growth factor-I (IGF-I), insulin-like growth factor binding protein-3, osteocalcin, bone-specific alkaline phosphatase, procollagen type I, and osteoprotegerin.^{14,15)}

Thyroid disorders also lead to secondary osteoporosis in children. In hyperthyroidism, rates of cartilage maturation, bone turnover, and osteoclastogenic effects increase.¹⁶⁾ In hypothyroidism, cartilage maturation and endochondral bone formation decrease. Additionally, thyroid hormone deficiency in early life delays the development of epiphyseal centers of ossification.¹⁶⁾ In hyperparathyroidism, excess parathyroid

Table 3. Differential diagnosis between osteogenesis imperfecta and idiopathic juvenile osteoporosis

Characteristic	Osteogenesis imperfecta	Idiopathic juvenile osteoporosis
Family history	(+)	(-)
Genetic mutation	(+)	(-)
Clinical manifestation	Short stature, deafness, Dentinogenesis imperfecta Blue sclerae Hypermobility of joint	Scoliosis Abnormal gait pattern Bone pain
Radiographic findings	Thin bone and rib Pathologic fracture	Lumbar fracture Metaphyseal fracture
Disease duration	Life long	For 2–3 years (usually prepubertal)

Table 2. Types of osteogenesis imperfecta

Severity	Type	Inheritance	Genetic defect
Nondeforming form	1	AD	<i>COL1A1, COL1A2</i>
Perinatal lethal form	2	AD, AR	<i>COL1A1, COL1A2, CRTAP, LEPREL1, PPIB</i>
Progressively deforming form	3	AD, AR	<i>COL1A1, COL1A2, CRTAP, LEPREL1, PPIB, SERPINH1, BMP1, FKBP10, PLOD2, SERPINF1, SP7, WNT1, TMEM38B, CREB3L1, SEC24D</i>
Moderate form	4	AD, AR	<i>COL1A1, COL1A2, CRTAP, PPIB, FKBP10, SERPINF1, WNT1, SP7</i>
With calcification of the interosseous membranes and/or hypertrophic callus	5	AD	<i>IFITM5</i>

AD, autosomal dominant; AR, autosomal recessive.

hormone induces the production of receptor activator for nuclear factor κ B ligand (RANKL) and inhibits the production of osteoprotegerin, increasing osteoclastogenesis and bone resorption.¹¹⁾

In DM, hyperglycemia is related to accumulation of glycated proteins, which impairs differentiation of mesenchymal stem cells into chondrocytes and osteoblasts with decreased synthesis of osteocalcin.¹⁷⁾ Finally, in Cushing syndrome, glucocorticoid excess is directly associated with inhibition of osteoblastogenesis and promotion of osteoblast and osteocyte apoptosis. Further, the excess glucocorticoid indirectly impairs bone accretion by inhibiting secretion of IGF-I and intestinal calcium absorption.¹⁸⁻²⁰⁾

2) Neuromuscular disorders

Children with cerebral palsy, Duchenne muscular dystrophy, and spinal muscular atrophy cannot bear weight in the same way as children without these neuromuscular disorders, resulting in decreased bone formation with continued bone resorption and development of lower bone mass.²¹⁻²⁴⁾

3) Connective tissue disorders

In children with systemic lupus erythematosus, juvenile idiopathic arthritis, and juvenile dermatomyositis, bone mass is decreased due to chronic inflammation, production of pro-osteoclastic cytokines, and glucocorticoid therapy.^{25,26)}

4) Gastrointestinal disorders

Nutritional deficiency, secondary hyperparathyroidism,

chronic inflammatory state, and glucocorticoid therapy can decrease bone formation and increase bone resorption in children with chronic inflammatory bowel or celiac disease.²⁷⁻²⁹⁾

5) Hemato-oncologic disorders

Cytokine-induced osteoclastogenesis, radiation- or chemotherapeutic agent-induced bone injury, decreased physical activity, and nutritional deficiency result in diminished bone mass in children with leukemia or cancer.^{30,31)}

6) Renal disorders

Nutritional deficiency or immunosuppressive therapy can result in bone loss in children with chronic renal failure and kidney transplantation.^{32,33)}

7) Nutritional deprivation

Anorexia nervosa and female athlete triad are examples of both nutrition- and hormone-induced bone loss that can lead to early-onset osteoporosis.⁸⁾

8) Medications

Numerous medications such as glucocorticoids, anticonvulsants, chemotherapeutic agents, immunosuppressive agents, heparin, proton pump inhibitors, and selective serotonin reuptake inhibitors can increase the risk of low bone mass.⁸⁾ In children, studies have reported that use of oral glucocorticoids for more than 3 months reduced bone density and increased the risk of spinal compression fractures. Therefore, it is recommended that glucocorticoids be used in low doses every

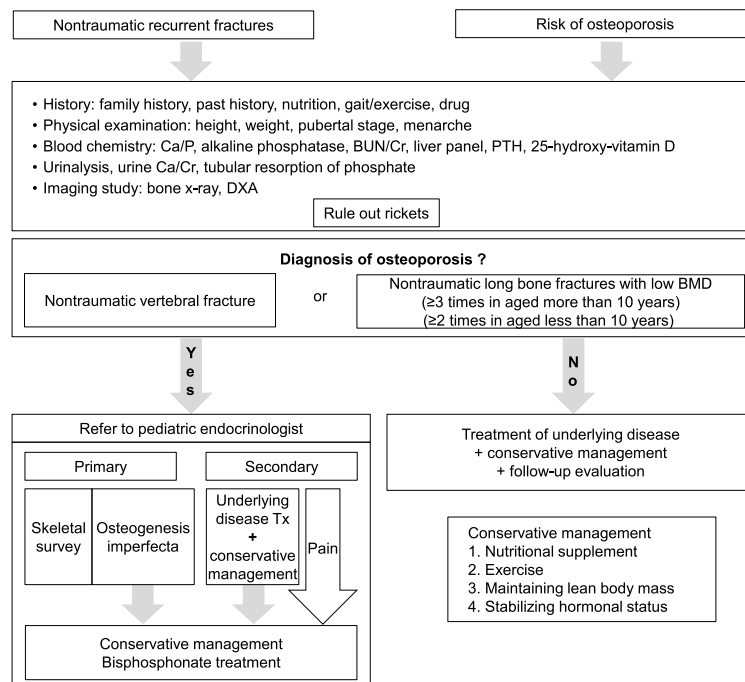


Fig. 1. The algorithm for assessment of bone health in children and adolescents. BUN, blood urea nitrogen; Cr, creatinine; PTH, parathyroid hormone; DXA, dual-energy x-ray absorptiometry; BMD, bone mineral density; Tx, treatment.

other day rather than every day, while maintaining calcium and vitamin D concentrations in the normal range. As short-term administration or inhaled formulations of corticosteroid can also affect bone density,¹⁾ it is difficult to recommend safe doses and durations.¹⁹⁾

Evaluation in patient with low BMD or increased risk of fracture

In pediatric patients with primary bone disease or those at risk of secondary bone disease, DXA should be performed when the patient might benefit from interventions to decrease the risk of clinically significant fracture. If follow-up DXA is indicated, the minimum interval between scans should be 6–12 months.⁹⁾ The evaluation processes according to risk of osteoporosis are shown in Fig. 1.

Conservative management for optimizing bone health

Modifiable determinants of bone mass include nutrition, exercise, lifestyle, body weight, lean body mass, and hormonal status. These conditions should be adequately maintained to optimize bone health.⁸⁾

1. Nutrition

Many studies have reported that calcium and vitamin D supplementation is helpful in increasing bone mass and BMD in children. These nutritional elements should be supplemented

Table 4. Dietary reference intake of calcium and vitamin D according to age

Age	Calcium (mg/day)		Vitamin D (IU/day)	
	RDA	UL	RDA	UL
0–6 Months	-	1,000		1,000
6–12 Months	-	1,500		1,500
1–2 Years	500	2,500		2,500
3–5 Years	600	2,500	400–600	3,000
6–8 Years	700	2,500		3,000
9–11 Years	800	3,000		4,000
12–14 Years	M, 1,000; F, 900	3,000		4,000
15–18 Years	M, 900; F, 800	3,000		4,000

RDA, recommended daily allowance; UL, upper limit; M, male; F, female.

Adapted from The Korean Nutrition Society. 2020 Dietary Reference Intakes for Koreans.³⁸⁾

using food rather than medicine in healthy children.³⁴⁻³⁷⁾ Many types of foods are good dietary sources of calcium and vitamin D. Human milk or infant formula is the primary source of calcium for healthy infants in the first year, and milk and other dairy products are the major sources of calcium after the first year of life. Other dietary sources include green leafy vegetables, legumes, nuts, cereal, and fruit juices. The bioavailability of calcium from vegetables is generally high but is reduced by binding with oxalate in spinach, collard greens, and beans and with phytate in whole bran cereals. Natural dietary sources of vitamin D include cod liver oil, salmon, sardines, tuna, and fortified foods. Exposure to ultraviolet B radiation from sunlight is the major source of vitamin D production.⁸⁾ The recommended daily allowance and upper limit of calcium and vitamin D are shown in Table 4.^{8,36-39)} If calcium or vitamin D deficiency causes low BMD, it should be administered at a therapeutic dosage (Table 5).^{8,40)} Several types of vitamin D prescriptions are available including ergocalciferol (vitamin D2), cholecalciferol (vitamin D3), alphacalcidol (1 α -hydroxyvitamin D3), and calcitriol (1,25-dihydroxyvitamin D3). Vitamin D3, an active form of vitamin D, is frequently used in children with vitamin D deficiencies. Alphacalcidol or calcitriol is used in children with renal diseases.⁸⁾

Ingestion of adequate amounts of calories, proteins, and vegetables or fruits containing high vitamin C, vitamin K, potassium, magnesium, copper, and manganese contents is also needed to maintain bone health in children.⁴¹⁾ The prescription forms of calcium are calcium carbonate (40% elemental calcium), calcium citrate (21% elemental calcium), calcium lactate (13% elemental calcium), and calcium glutamate (9% elemental calcium). Calcium carbonate should be taken with meals to promote absorption, but calcium citrate can be taken on an empty stomach. The adverse effects of consuming excessive calcium are dyspepsia, constipation, urinary stones, and hypercalcemia, especially when taken with vitamin D.⁸⁾

2. Exercise

Mechanical forces applied to the skeleton increase bone formation, and weight-bearing exercises improve bone mineral deposition.⁴²⁻⁴⁵⁾ High-impact and low-frequency exercises such as jumping, skipping, and hopping for 10 minutes 3 times per week increases the BMD of the femoral neck in healthy children.⁴⁶⁾ Weight-bearing exercises such as walking, jogging, jumping, and dancing are better than non-weight-bearing exercises such as swimming or bicycle riding.^{45,46)} However, excessive high-impact and prolonged exercises can increase

Table 5. Treatment of Vitamin D deficiency according to Guidelines

Age	Pediatric Endocrine Society	American Academy of Pediatrics
0–1 Month	1,000 IU daily, for 2–4 weeks	50,000 IU weekly, for 6 weeks or 2,000 IU daily for 6 weeks followed by a maintenance dose of 400–1,000 IU daily
1–12 Months	1,000–5,000 IU daily, for 2–4 weeks	
1–18 Years	More than 5,000 IU daily, For 2–4 weeks	50,000 IU weekly, for 6–8 weeks or 2,000 IU daily for 6–8 weeks followed by a maintenance dose of 600–1,000 IU daily

Adapted from Holick et al. J Clin Endocrinol Metab 2011;96:1911-30.⁴⁰⁾

fracture risk; therefore, children who want to participate in these sports should cross-train with low-impact activities.⁴⁷⁾

3. Lifestyle

Ingestion of fast food, alcohol, caffeine, and smoking can promote bone loss and should be avoided.⁴¹⁾ Sedentary activities, such as prolonged TV watching, internet gaming, and cellular phone use, also have negative effects on bone mass.^{8,46)}

4. Body weight and composition

Body mass index and lean body mass are directly correlated with BMD in most healthy adolescents; conversely, increased adiposity can be related with increased fracture risk. This implies the importance of maintaining healthy body composition during childhood and adolescence.^{8,48)}

5. Hormonal status

Estrogen, testosterone, GH, and IGF-I can promote bone formation, but excess glucocorticoid increases bone resorption.^{8,10,11)} Therefore, bone mineral depositions in children with endocrine disorders, such as hypogonadism, Turner syndrome, GH deficiency, and Cushing syndrome, should be carefully investigated and adequately maintained.

Pharmacological treatment for BMD enhancement

1. Bisphosphonate

1) Action mechanism and forms of bisphosphonate

Bisphosphonates inhibit osteoclast-mediated bone resorption and prevent osteoblast or osteocyte apoptosis. These medications have been used in children with osteogenesis imperfecta, diseases treated with corticosteroids, cerebral palsy, and connective tissue diseases. Bisphosphonates have been reported to increase BMD and decrease pain and fracture in children with these diseases. However, their use in children remains controversial because of long half-lives and potential adverse effects.⁴⁹⁾ The various prescription forms of bisphosphonates are shown in Table 6.

2) Indication for bisphosphonate treatment

(1) Primary osteoporosis

Bisphosphonates are commonly prescribed for individuals with osteogenesis imperfecta. Many reports have demonstrated that oral or intravenous bisphosphonates increase BMD in children and adults with this condition.^{50,51)} Most patients with idiopathic juvenile osteoporosis tend to remit spontaneously, but if there is a possibility of permanent deformity after vertebral or long bone fracture, bisphosphonate treatment should be considered.⁵²⁾

(2) Secondary osteoporosis

Bisphosphonates should be used in children with recurrent extremity fractures, symptomatic vertebral collapse, and severe bone pain caused by other clinical conditions but should not be used to treat asymptomatic reduction in bone mass in children.⁵³⁾ In addition, sufficient nutrition including calcium/vitamin D, adequate body weight, physical activity within the possible range, and supplementation in cases of hormone deficiencies should be prioritized over bisphosphonate treatment.⁵⁴⁾ Bisphosphonates have been reported to be effective for pediatric patients presenting with secondary osteoporosis with cerebral palsy, juvenile idiopathic arthritis, renal transplantation, renal disease with chronic steroid therapy, Crohn disease, Duchenne muscular dystrophy, leukemia or lymphoma with chemotherapy, or chronic graft-versus-host disease.⁵⁵⁻⁶⁴⁾

3) Practical bisphosphonate therapy

Although guideline consensus for bisphosphonate forms, dosage, treatment duration, and interval of administration is needed in children, pamidronate is often used in young children, followed by switching to zoledronate in older patients with moderate-to-severe disease.⁵⁴⁾ Pamidronate doses vary from 9 to 12 mg/kg/yr in 4 to 6 divided doses, and zoledronate is initiated at 0.1 mg/kg/yr in 2 divided doses. The starting doses for pamidronate and zoledronate are usually recommended to be reduced to 0.5 mg/kg and 0.0125 or 0.025 mg/kg respectively, to minimize acute-phase reactions and hypocalcemia. Maintenance therapy at reduced doses is determined by a combination of fracture history, bone pain, BMD, and growth. The maintenance dosages for pamidronate and zoledronate are 3.0 and 0.025 mg/kg/yr, respectively, administered in 2 divided doses.⁵⁴⁾ The typical treatment approaches for children with primary and secondary osteoporosis are shown in Fig. 2.

Contraindications for bisphosphonate therapy include

Table 6. Name, route of administration, dose, and relative potency of bisphosphonates

Name	Route	dose	Potency
Etidronate	PO	5–40 mg/kg/day for 2 weeks, every 3 months	1
Pamidronate	IV	0.5–1.5 mg/kg/day for 3 days, every 2–6 months (mixed with 200–250 mL of normal saline, infusion for 3 hr)	100
Alendronate	PO	1–2 mg/kg/wk or 5 mg/day (<20 kg) 10 mg/day (>20 kg)	100–1,000
Zoledronate	IV	0.015–0.05 mg/kg, every 3–6 months (mixed with 50 mL of normal saline, infusion for 30–45 minutes)	>10,000

PO, per os; IV, intravenous.

Adapted from Baroncelli and Bertelloni. *Horm Res Paediatr* 2014;82:290-302.⁴⁹⁾

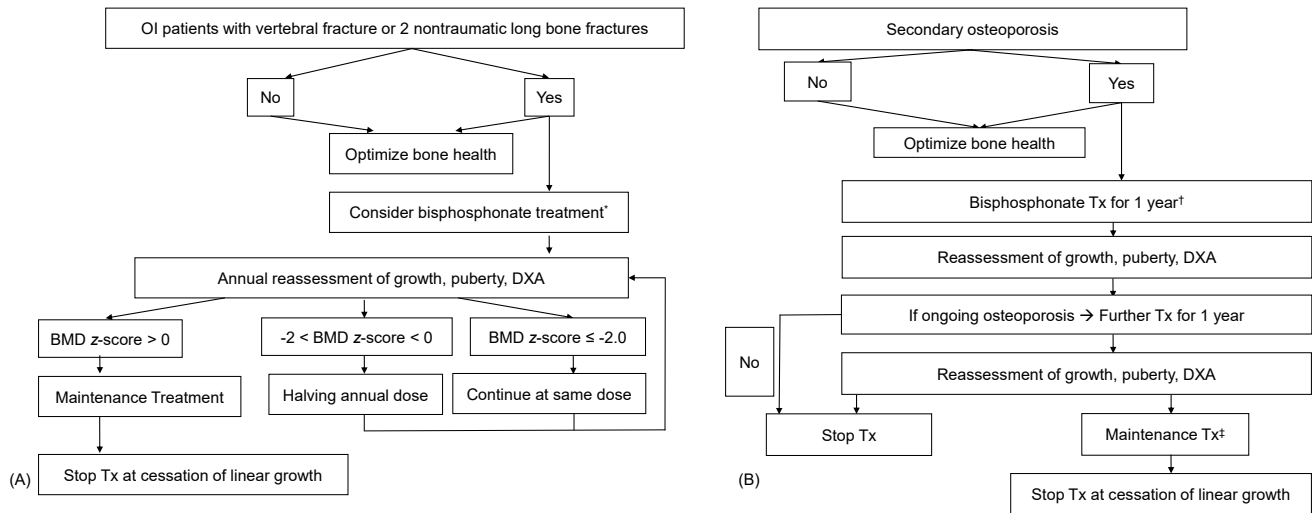


Fig. 2. (A) Bisphosphonate treatment in patients with osteogenesis imperfecta (OI). (B) Bisphosphonate treatment in patients with secondary osteoporosis. DXA, dual-energy x-ray absorptiometry; BMD, bone mineral density; Tx, treatment. [†]Pamidronate 9 mg/kg/yr, 4–6 divided doses or zoledronate 0.1 mg/kg/yr, 2 divided doses. [‡]Initial Tx of bisphosphonate, pamidronate 9 mg/kg/year, 4–6 divided doses or zoledronate 0.1 mg/kg/year, 2 divided doses. ^{*}Maintenance Tx, pamidronate 3 mg/kg/yr in 2 divided doses or zoledronate 0.025 mg/kg annually. Modified from Simm et al. *J Paediatr Child Health* 2018;54:223–33, with permission of Paediatrics and Child Health Division (The Royal Australasian College of Physicians).⁵⁴

pregnancy, severe renal disease, and active rickets. Reduced renal function is a relative contraindication because approximately 40%–60% of the dose is distributed to the bone; the remainder is excreted unaltered in the urine, with no substantial metabolism.^{65,66} The acute adverse effects of bisphosphonate treatment in pediatric patients are flu-like symptoms and hypocalcemia, with possible long-term effects of delayed bone healing, osteopetrosis, and gastroesophageal reflux. The potential side effects are atypical femoral fractures, osteonecrosis of the jaw, orbital inflammation, growth impairment, and teratogenicity.^{65,66} Therefore, clinical, biochemical, and imaging assessments must be performed.^{49,54} General clinical examination with growth and nutritional evaluation, dental and eye examination, complete blood cell count, electrolytes, alkaline phosphatase, bone turnover markers, liver function test, renal function test, serum vitamin D and parathyroid hormone levels, urine analysis, urinary calcium excretion, radiography of the wrist and knee, and BMD should be included in the assessments.^{49,54}

2. New therapeutic agents

Several new drugs, such as teriparatide (recombinant human parathyroid hormone), strontium ranelate, and denosumab (monoclonal anti-RANKL antibody), increase bone formation and decrease bone resorption. However, reports on the effect and safety of these medications in children are insufficient.^{10,11,67}

Conclusions

Bone mineral deposition shows the highest increase during the pubertal period in girls and boys and can be a major

determinant of BMD in later life. Therefore, modifiable determinants of bone mass, including nutrition, exercise, lifestyle, body weight, lean body mass, and hormonal status should be adequately maintained to optimize bone health in children and adolescents.

The definition of osteoporosis in children is different from that in adults. In pediatric patients with primary or secondary osteoporosis, underlying conditions should be treated first, and then conservative and pharmacologic therapies should be considered.

Notes

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Author contribution

Conceptualization: KSS; Data curation: AK, JHY, WKC; Formal analysis: JHK, JSL; Methodology: HN; Visualization: SYC; Writing - original draft: YA; Writing - review & editing: KSS

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