

# The Spine in Patients With Osteogenesis Imperfecta

Maegen J. Wallace, MD  
Richard W. Kruse, DO, MBA  
Suken A. Shah, MD

From the Department of Orthopedics, Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE.

Dr. Kruse or an immediate family member serves as an unpaid consultant to DePuy Synthes and serves as a board member, owner, officer, or committee member of the American Academy of Orthopaedic Surgeons and the Pediatric Orthopaedic Society of North America. Dr. Shah or an immediate family member has received royalties from Arthrex and DePuy Synthes; serves as a paid consultant to DePuy Synthes and Stryker; has stock or stock options held in Globus Medical; has received research or institutional support from DePuy Synthes; and serves as a board member, owner, officer, or committee member of the American Academy of Orthopaedic Surgeons, the Scoliosis Research Society, the Pediatric Orthopaedic Society of North America, and the Setting Scoliosis Straight Foundation. Neither Dr. Wallace nor any immediate family member has received anything of value from or has stock or stock options held in a commercial company or institution related directly or indirectly to the subject of this article.

*J Am Acad Orthop Surg* 2017;25:100-109

DOI: 10.5435/JAAOS-D-15-00169

Copyright 2016 by the American Academy of Orthopaedic Surgeons.

## Abstract

Osteogenesis imperfecta is a genetic disorder of type I collagen. Although multiple genotypes and phenotypes are associated with osteogenesis imperfecta, approximately 90% of the mutations are in the *COL1A1* and *COL1A2* genes. Osteogenesis imperfecta is characterized by bone fragility. Patients typically have multiple fractures or limb deformity; however, the spine can also be affected. Spinal manifestations include scoliosis, kyphosis, craniocervical junction abnormalities, and lumbosacral pathology. The incidence of lumbosacral spondylolysis and spondylolisthesis is higher in patients with osteogenesis imperfecta than in the general population. Use of diphosphonates has been found to decrease the rate of progression of scoliosis in patients with osteogenesis imperfecta. A lateral cervical radiograph is recommended in patients with this condition before age 6 years for surveillance of craniocervical junction abnormalities, such as basilar impression. Intraoperative and anesthetic considerations in patients with osteogenesis imperfecta include challenges related to fracture risk, airway management, pulmonary function, and blood loss.

Osteogenesis imperfecta (OI) is a genetic disorder of type I collagen, which is located mainly in bone, ligaments, dentin, and sclerae. Multiple genotypes and phenotypes are associated with OI, and the condition is characterized by bone fragility. Patients typically have multiple fractures or limb deformity; however, the spine can also be affected.<sup>1,2</sup> Spinal manifestations include scoliosis, kyphosis, craniocervical junction abnormalities, such as basilar impression, basilar invagination and platybasia, and lumbosacral pathology, such as spondylolisthesis.<sup>3</sup> Other clinical signs of OI include blue sclerae, early hearing loss, dentinogenesis imperfecta, joint hypermobility, and short stature.<sup>2</sup> Scoliosis, kyphosis, and craniocervical junction abnormalities

are more common in children with dentinogenesis imperfecta than in children without dentinogenesis imperfecta. Children with craniocervical junction abnormalities are not likely to have generalized hypermobility.<sup>4</sup> All children with OI should undergo regular physical examination of their extremities and spine to screen for and monitor progression of scoliosis.

Seventeen genetic causes of OI have been identified. Approximately 90% of the mutations are found in the *COL1A1* and *COL1A2* genes. *COL1A1* and *COL1A2* genes encode for the alpha-1 and alpha-2 chains of type I collagen.<sup>2</sup> The phenotypic expression of OI was originally classified by Sillence et al.<sup>1</sup> Type I is nondeforming OI with blue sclerae, type II is perinatally lethal OI

with multiple intrauterine fractures, type III can result in fractures at birth and causes progressive deformity, and type IV OI is characterized by normal sclerae and variable long bone deformities<sup>2</sup> (Table 1). Additional types have been described as knowledge of the genetics of OI has increased.

Diphosphonate therapy has been found to have a positive effect on vertebral morphology, including remodeling of deformed vertebrae in older children and preservation of vertebral shape when started early in life.<sup>5,6</sup> Diphosphonates are often started in infancy in patients with type III, type IV, or severe type I OI.<sup>7,8</sup> Kusumi et al<sup>8</sup> reported on a group of 18 patients with OI (5 type I, 7 type III, and 6 type IV) with an average age of 12 months (range, 11 days to 23 months). They showed considerable improvement in bone density via dual-energy x-ray absorptiometry (DEXA) and a decreased fracture rate with no major side effects of treatment. In one study, infants who were treated with diphosphonates showed no development of scoliosis, kyphosis, or craniocervical junction abnormalities during treatment or follow-up from age 3 to 6 years, although clinically relevant scoliosis generally is not seen before 6 years of age.<sup>7,9</sup> Furthermore, all 11 children who were treated in the study (average age, 4.8 years) were ambulatory. In a historical cohort of children with OI of similar severity who were not treated with diphosphonates, only 2 of 11 children could walk at an average age of 4.6 years, and 6 other children had lost a motor milestone previously gained during childhood.<sup>7</sup>

### Kyphoscoliosis

The prevalence of scoliosis in the population of patients with OI ranges from 39% to 80%, depending on the

**Table 1**

#### Sillence Classification of Osteogenesis Imperfecta<sup>1,2</sup>

Type	Severity	Features	Inheritance
I	Mild	Blue sclerae, mild bone fragility, fractures after walking, minimal deformity	Autosomal dominant or new mutations
II	Lethal	Blue sclerae, multiple intrauterine fractures, severe deformity, stillbirth or neonatal death	Autosomal recessive or new mutations
III	Severe deforming	Normal sclerae, dentinogenesis imperfecta, frequent fractures, deformity of long bones, short stature, scoliosis	Autosomal recessive or new mutations
IV	Intermediate	Normal sclerae, moderate bone fragility, moderate deformity, short stature, possible dentinogenesis imperfecta	Autosomal dominant or new mutations

study.<sup>3</sup> Scoliosis is rarely observed in patients younger than 6 years and can progress rapidly after it is diagnosed.<sup>9</sup> Engelbert et al<sup>10</sup> and others<sup>11</sup> showed that children with OI in whom scoliosis developed had markedly lower DEXA Z scores compared with those of children with OI in whom scoliosis did not develop. Single thoracic curves are the most frequent type of scoliosis curve found in patients with type I OI: 97% of curves in patients with type I OI who have scoliosis are single thoracic curves, whereas in patients with type III OI, 58% of curves are in the thoracic region.<sup>12</sup>

### Etiology

The etiology of scoliosis in patients with OI is controversial, with theories including vertebral body fragility, vertebral body shape, ligamentous laxity, muscle weakness, limb-length discrepancy, and pelvic obliquity.<sup>11,13</sup> Vertebral fractures are thought to be a leading cause of scoliosis because of the severe fragility of the vertebral growth plates and the progression that occurs with continued growth.<sup>14</sup> Benson and Newman<sup>9</sup> and Engelbert et al<sup>10</sup>

theorized that ligamentous laxity plays a substantial role because the lack of stability between vertebrae allows scoliosis to progress.

### Progression

Untreated scoliosis is known to progress in growing children with OI and even into adulthood.<sup>13</sup> Scoliosis curve progression can be as high as 6° per year in patients with type III OI, 4° per year in patients with type IV OI, and as low as 1° per year in patients with type I OI<sup>12</sup> (Table 2). Watanabe et al<sup>11</sup> found that, as the DEXA Z score worsened, the scoliosis progressed, suggesting that poorer bone quality leads to more severe scoliosis. Ishikawa et al<sup>14</sup> found that biconcave vertebrae, in which the height of the midportion of the body is <70% of the mean of the anterior and posterior vertebral body heights, were common in patients with OI (Figure 1). The presence of six or more biconcave vertebrae before puberty suggested that severe scoliosis would develop.

Anissipour et al<sup>12</sup> found that patients with type III OI who began diphosphonate treatment before age 6 years had slower curve progression

Table 2

Prevalence of and Progression of Scoliosis in Patients With Osteogenesis Imperfecta<sup>12</sup>

Type of Osteogenesis Imperfecta	Prevalence of Scoliosis	No Diphosphonate Treatment Before Age 6 Years		Diphosphonate Treatment Before Age 6 Years	
		Rate of Scoliosis Progression (degrees/yr)	P Value	Rate of Scoliosis Progression (degrees/yr)	P Value
I	39%	1	0.01	2.3	0.19
III	68%	6	<0.01	2.3	0.01
IV	54%	4	<0.01	3.1	0.91

Figure 1



Lateral spine radiograph demonstrating osteogenesis imperfecta in a 5-year-old boy. The patient has multiple biconcave vertebrae. For T7, the anterior vertebral body height is 11 mm, the posterior vertebral body height is 6.9 mm, and the midportion vertebral body height is 4.6 mm. Black lines indicate vertebral body height measurement locations. The height of the midportion of the body is 51% of the mean of the anterior and posterior vertebral body heights.

after the development of scoliosis than did patients who started diphosphonate treatment after age 6 years (2.3° per year versus 6° per year). Diphosphonate treatment started after age 6 years or in

patients with type I or IV OI did not have a statistically significant effect on the progression of scoliosis.

### Pulmonary Function

Widmann et al<sup>3</sup> evaluated patients with OI and found that increasing severity of scoliosis correlated with a decrease in pulmonary function, specifically the vital capacity, leading to restrictive lung disease. Vital capacity was 78% predicted when thoracic scoliosis was <40° and dropped to 41% predicted when thoracic scoliosis was >60°. The authors did not find a correlation between pulmonary function and kyphosis or chest wall deformity.

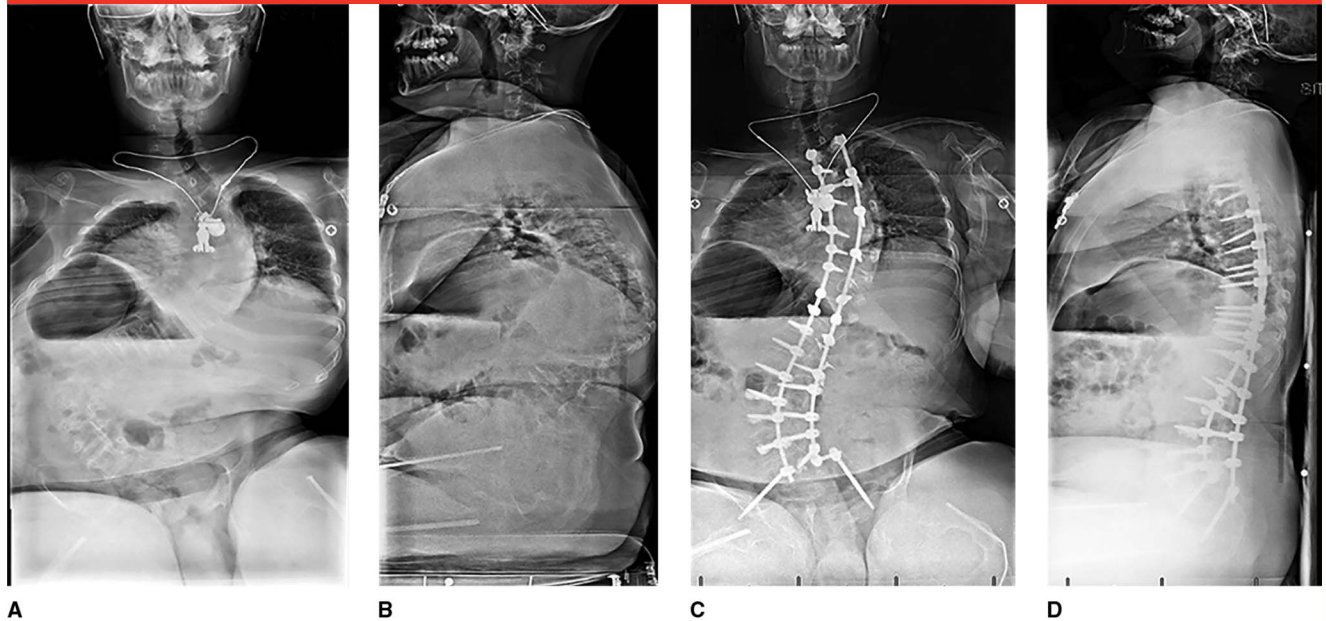
### Treatment Strategies

Treatment of scoliosis in patients with OI can be difficult mostly because of poor bone quality and the rigidity of the deformity. Brace treatment has not been found to be effective and is difficult to use because of the fragility of the rib cage. Chest wall deformity secondary to Milwaukee bracing has been reported, and progression of curves despite bracing appears to be the norm.<sup>15</sup> In some patients, a soft thoracolumbosacral orthosis can be used for supported sitting to assist with functional activities, but no assurance should be given with regard to curve progression.

Surgical spinal fusion to halt curve progression is considered when

curves reach 45°, but the patient's age and truncal height need to be taken into account to avoid thoracic insufficiency syndrome. One report indicated that children with severe OI may benefit from fusion when curves are 35°,<sup>16</sup> but we prefer to avoid fusion in young children when possible because contemporary techniques make correction of larger curves at a later stage more feasible. Although historical methods of fusion have not been found to improve lung volumes, contemporary techniques may improve results, and fusion can prevent progressive respiratory decline resulting from thoracic insufficiency syndrome.<sup>3</sup>

Previous methods of treatment, including noninstrumented fusion, Harrington rods, and Luque instrumentation, have shown modest or no correction of curves, little improvement in physical function, and up to 50% complication rates. Cristofaro et al<sup>17</sup> performed spinal fusion in eight patients who had OI and scoliosis. Five patients underwent fusion with Harrington instrumentation, and three patients underwent noninstrumented fusion. All eight patients were placed in casts or braces postoperatively, and all patients attained fusion by 10.3 months postoperatively. No patient had any correction of the scoliosis or change of ambulatory status. In 1982, Yong-Hing and MacEwen<sup>13</sup> published data from a survey of pediatric orthopaedic and spine

**Figure 2**

PA (A) and lateral (B) radiographs demonstrating severe osteogenesis imperfecta in a 16-year-old boy with an 87° thoracic curve, a 115° thoracolumbar curve, and substantial pelvic obliquity. PA (C) and lateral (D) radiographs obtained 2.5 years postoperatively demonstrate spinal fusion from T1 to the sacrum with cement-augmented pedicle screws and pelvic fixation.

surgeons regarding their patients with OI and scoliosis. The report included 60 patients who were treated surgically, including 39 who underwent posterior fusion with Harrington rods, 16 who underwent noninstrumented posterior fusion, 4 who underwent anterior fusion, and 1 who underwent combined anterior and posterior fusion. They found an average correction of 27° (36%). Compared with patients who underwent noninstrumented posterior fusion, patients treated with instrumented posterior fusion had 7% better correction. The complication rate was >50%; 33 of 60 patients had complications, mainly intraoperative bleeding and implant-related problems.<sup>10</sup>

In a series of spinal fusions in patients with OI, Benson and Newman<sup>9</sup> reported postoperative curve progression of 16° in the noninstrumented fusion group and 8° in the instrumented fusion group. In that study, instrumentation

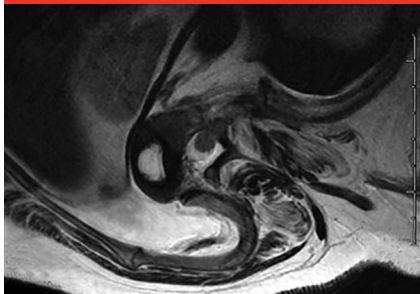
usually consisted of one Harrington rod and hooks supplemented with methyl methacrylate. Hanscom et al<sup>18</sup> reported on 13 patients with OI and scoliosis. One patient underwent noninstrumented fusion, five patients underwent fusion with Harrington rods, and seven patients underwent fusion with Luque instrumentation. The authors reported minimal correction at the time of surgery with loss of correction on follow-up, one instance of pseudarthrosis, and overall good outcomes.

Janus et al<sup>19</sup> evaluated 20 consecutive patients with OI who underwent treatment for scoliosis with preoperative halo gravity traction followed by in situ fusion, with Cotrel-Dubouset instrumentation in 18 patients and Harrington instrumentation in 2 patients. All patients used body jackets for 7.5 to 18 months postoperatively. The authors found 32% improvement in the scoliosis with traction, which subsided to 25% correction after fusion and

long-term follow-up. Two patients sustained intraoperative lamina fractures that required hook placement at an adjacent level. Three patients had failure of instrumentation at 1 to 4 years postoperatively. The authors reported functional improvements, with 7 of 20 patients upgrading their ambulation level and none having a decrease in functional level.

Recent evaluation of contemporary instrumentation and correction techniques at our institution, such as the use of pedicle screws with cement augmentation, has shown improved outcomes. Yilmaz et al<sup>20</sup> reviewed a series of 10 patients with OI who underwent posterior spinal fusion for the treatment of scoliosis. All of the patients underwent preoperative pamidronate therapy. Seven patients had cement-augmented pedicle screw instrumentation at the proximal and distal foundations (Figure 2). These authors were the first to report the difficulty of exposure of the thoracic

**Figure 3**



Preoperative T2-weighted axial magnetic resonance image demonstrating type III osteogenesis imperfecta in a 19-year-old man. Note the severe rib deformities that made access to the posterior spinal elements challenging. Multiple rib osteotomies were required during posterior spinal fusion to gain adequate access to the posterior elements for pedicle screw placement and Ponte osteotomies to aid in correction of the deformity.

spine because of rib overgrowth and thoracic lordosis (Figure 3). They routinely performed rib and posterior Ponte osteotomies at the apex of the thoracic curve to aid in adequate exposure and to increase flexibility of the curve in the coronal and sagittal planes to allow correction. Cement augmentation of the proximal and distal screws was used to increase pullout strength of fixation in bone and prevent pullout. The authors reported average correction of 48% with no loss of correction at follow-up, no neurologic deficits, and no implant failures. They also noted improved quality of life scores, pain, and sitting tolerance in these patients.<sup>20</sup>

### Authors' Preferred Treatment Strategy

Children with OI are followed at least annually for clinical signs of spinal deformity. For those with curves  $>30^\circ$ , more frequent follow-up is recommended, especially during peak height velocity. Current indications for fusion are

curves  $>50^\circ$  in patients who are past peak height velocity or in patients with substantial curve progression after skeletal maturity because these curves can continue to progress in adulthood. Curve rigidity is an important factor in the timing of surgical treatment and is evaluated clinically. We will observe curves that progress during growth if they remain flexible. The proximal extent of instrumentation and fusion is usually T2, T3, or T4 and depends on the stable vertebra in the coronal plane and the extent of proximal thoracic kyphosis. The distal extent of fusion is the vertebra that is stable on the erect radiograph, unless examination of the sagittal plane demonstrates an indication for lower fusion, such as thoracolumbar junctional kyphosis. In addition to apical lordosis, compensatory kyphosis above and below the apex of the thoracic and thoracolumbar curves can be problematic and needs to be addressed in the selection of fusion levels. Proximal instrumentation and fusion to T2, T3, or T4 is frequently needed to control the sagittal plane and prevent proximal junctional kyphosis. Pelvic fixation is sometimes indicated for the management of severe pelvic obliquity.

In patients with rigid, severe ( $90^\circ$ ) curves, preoperative traction is occasionally used to avoid the need for three-column osteotomy and to achieve slow correction over time. Intraoperative traction is used commonly in these patients to achieve slow correction with release of the facets and intersegmental ligaments (eg, interspinous, ligamentum flavum) and viscoelastic creep and to address the deformity in all three planes. We think that traction is a useful adjunct for correction because it decreases the force that the instrumentation needs to exert on the spinal column. Exposure of the

spine in patients with severe rib deformity, especially those with thoracic lordosis, sometimes requires rib osteotomy and retraction. All patients are monitored intraoperatively with multimodal spinal cord monitoring consisting of transcranial motor-evoked potentials, somatosensory-evoked potentials, and electromyography.

In our opinion, pamidronate therapy results in more robust cortical bone in the spine and improves pullout strength of pedicle screw fixation when screws appropriately fill the pedicle. Pamidronate therapy does not seem to affect the intraoperative appearance of the bone or the risk of bleeding. Because diphosphonates affect bone remodeling, continuation of pamidronate therapy can theoretically affect the quality of the fusion. However, no evidence-based guidelines in the literature address the postoperative use of diphosphonates. On the basis of personal preferences and our experience with the healing of long bones, we prefer to withhold pamidronate for 4 months postoperatively to facilitate partial resumption of osteoclast function to allow for remodeling of the fusion mass. If postoperative surveillance radiographs indicate early signs of fusion and the implants are stable, pamidronate therapy is resumed. Our experience with patients who have never received pamidronate therapy is limited; most patients treated at our institution are on a routine infusion schedule or are given pamidronate preoperatively.

### Craniocervical Junction Abnormalities

Craniocervical junction abnormalities have been observed in 37% of patients with OI; these abnormalities include basilar invagination, basilar impression, and platybasia (seen in

13%, 15%, and 29% of patients with OI, respectively), as well as secondary hydrocephalus.<sup>21</sup> Basilar invagination is the protrusion of the uppermost cervical structures into the foramen magnum with projection of the tip of the dens axis >5 mm above the Chamberlain line (from the posterior nasal spine to the posterior lip of the foramen magnum) or >7 mm above the McGregor line (from the posterior nasal spine to the most caudal portion of the posterior cranial base). Basilar impression is the relative lowering of the cranial base (occipital condyles and foramen magnum) with resultant positioning of the uppermost cervical vertebral structures above the caudal border of the skull. Platybasia is flattening of the cranial base.<sup>21,22</sup> A study demonstrated skull base abnormalities in all four types of OI.<sup>23</sup> The authors reported that 26% of patients had at least one abnormality; specifically, 16% had platybasia, 6% had basilar impression, and 4% had basilar invagination. Increased clinical severity of OI was the strongest predictor of skull base anomalies. This retrospective review demonstrated that treatment within the first year of life with diphosphonates did not decrease the prevalence of skull base abnormalities later in life. In a different study, Sillence<sup>22</sup> found that 71% of patients with type IV OI who also had dentinogenesis imperfecta had basilar impression, and 50% of patients with type IV OI and dentinogenesis imperfecta had neurologic symptoms. Overall, 25% of patients with OI had basilar impression, and 8% of patients with OI had neurologic symptoms.<sup>22</sup> Sillence<sup>22</sup> recommended that independent upright posture be delayed in all patients with OI, especially those with type IV OI, until age 18 months in an attempt to prevent basilar impression.

Basilar impression results in characteristic features of the skull. These features include overhang of the temporal and occipital bones, termed the “tam-o’-shanter” or “Darth Vader” skull.<sup>24</sup> Clinical presentation of craniocervical junction problems can range from no symptoms to brain stem compression, restriction of cerebrospinal fluid circulation resulting in hydrocephalus, and impingement of cranial nerves.<sup>25</sup> Baseline lateral skull/cervical spine radiographs are recommended in all patients with OI before they reach age 6 years. Basilar impression may be clearly visible on a lateral radiograph with upward migration of the cervical spine into the base of the skull. In more subtle cases, the diagnosis of basilar invagination is made when the odontoid bone protrudes above the Chamberlain, McRae, and McGregor lines on the lateral radiograph<sup>24</sup> (Figure 4, A and B). Drawing the recommended lines on plain radiographs can be challenging because of the deformity and overlapping bony detail. If craniocervical abnormalities are a substantial concern, we recommend obtaining an MRI and drawing the lines on those images (Figure 4, C).

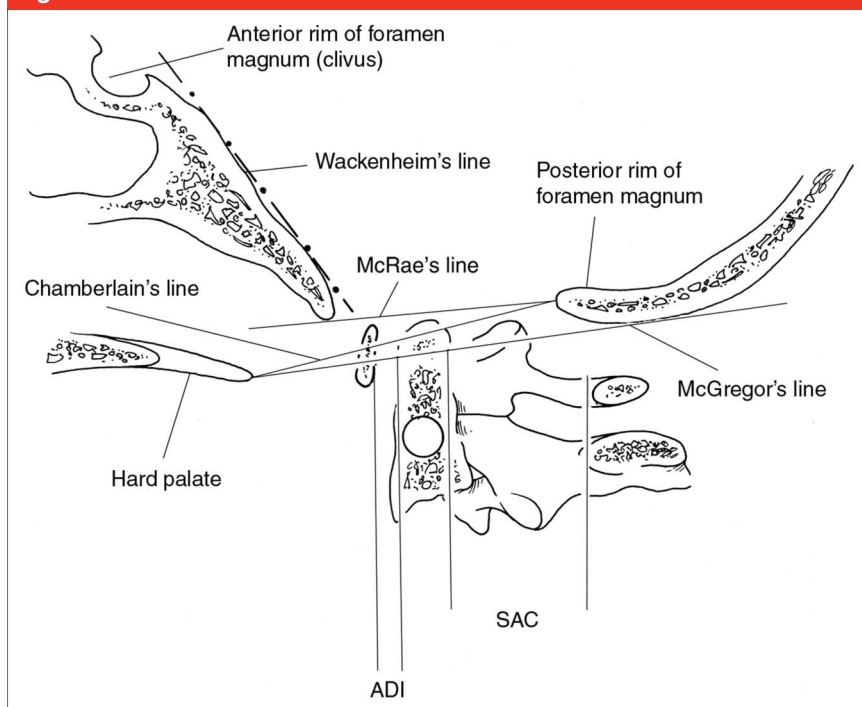
### Treatment of Craniocervical Junction Abnormalities

Treatment of symptomatic craniocervical junction problems includes craniocervical fusion with or without traction (Figure 5). Sawin and Menezes<sup>26</sup> reported on 25 patients with basilar invagination, 18 of whom had OI. Of the 25 patients, 56% were aged 11 and 15 years, and 44% also had symptoms of hydrocephalus. Patients with asymptomatic basilar invagination were treated with external orthotic immobilization. Symptomatic patients with hydrocephalus underwent ventriculoperitoneal shunt placement before treatment of basilar invagination.

The treatment of the craniocervical junction abnormality depended on whether the basilar invagination was successfully reduced with preoperative traction. The patients in whom reduction occurred (40%) were treated with posterior decompression and occipitocervical fusion with or without instrumentation. The patients in whom reduction did not occur (60%) underwent transoral or transnasal anterior decompression, followed by posterior occipitocervical fusion. These patients were treated with in situ occipitocervical fusion with autogenous rib strut grafting with sublaminar cables or contoured loop instrumentation. Postoperatively, all patients used either a halo vest or modified Minerva braces until solid union was observed. Contemporary rigid occipitocervical instrumentation was not used in this series. Although successful fusion occurred at an average of 8.2 months postoperatively, progression of the basilar invagination was observed in 80% of the patients. Of the 20 patients with progression, 6 were symptomatic, including 4 with recurrent headache/neck pain, 1 with dysphagia, and 1 with myelopathy; these patients were treated with prolonged external bracing, with improvement over time.<sup>26</sup>

In 2007, Ibrahim and Crockard<sup>27</sup> reported on their long-term experience treating 20 patients with basilar invagination and OI with ventral decompression and dorsal occipitocervical fixation. The average age of the patients was 27 years. Ten patients had type III OI, five patients had type IV OI, and five patients had type I OI. All of the patients underwent anterior decompression through an extended maxillotomy approach and elective tracheostomy. In a second surgical procedure 1 week later, the patients underwent posterior occipitocervical fusion from the occiput to C7, T1, or T2. The fixation

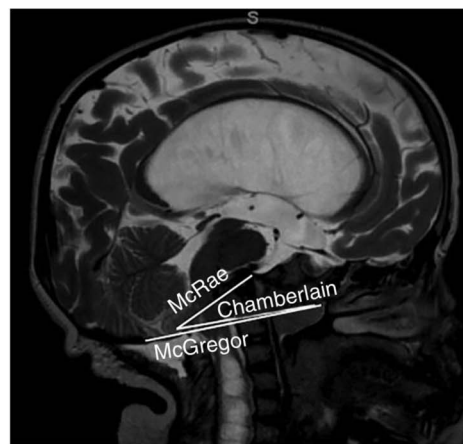
**Figure 4**



**A**



**B**



**C**

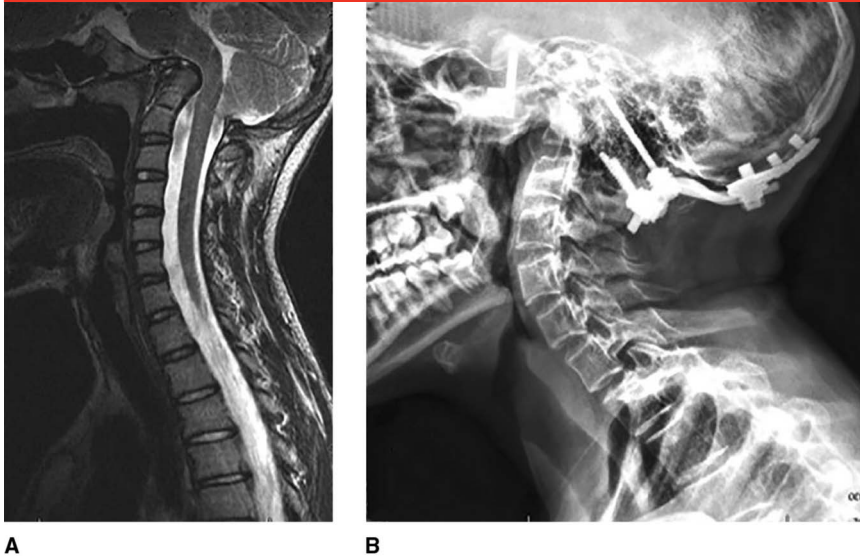
**A**, Diagram depicting the Chamberlain line, which extends from the posterior nasal spine to the posterior lip of the foramen magnum; the McRae line, which joins the anterior and posterior margins of the foramen magnum; and the McGregor line, which extends from the posterior nasal spine to the most caudal portion of the posterior cranial base. **B**, Lateral radiograph of the cervical spine demonstrating type III osteogenesis imperfecta in a 12-year-old girl. This image demonstrates the difficulty of drawing the McGregor, Chamberlain, and McRae lines. The McRae line was difficult to draw because the anterior and posterior aspects of the foramen magnum were difficult to visualize. **C**, Sagittal T2-weighted magnetic resonance image was obtained for further evaluation of the same patient. The McGregor, Chamberlain, and McRae lines are drawn. Hydrocephalus and syrinx are present. ADI = atlanto-dens interval, SAC = space available for spinal cord (Panel A reproduced from Willis BP, Dormans JP: Nontraumatic upper cervical spine instability in children. *J Am Acad Orthop Surg* 2006;14:233-245.)

instrumentation used in these procedures varied, with modern occipito-cervical instrumentation used in more recent procedures. At hospital discharge, 80% of the patients showed clinical improvement or no deterioration of high-level function, compared with their preoperative neurologic symptoms. In three patients, clinical symptoms recurred at 2, 10, and 15 years postoperatively. At long-term follow-up, 15% of patients showed no clinical improvement, and 25% of the patients who had a recurrence of symptoms had died. The authors concluded that aggressive ventral decompression with the use of modern dorsal occipitocervical instrumentation can halt progression of basilar invagination in the long term.<sup>27</sup>

### Authors' Preferred Treatment Strategy

Surgical treatment of craniocervical junction abnormalities is generally reserved for basilar invagination with clinical symptoms, which most commonly includes headaches, cranial nerve palsy, dysphagia, and symptoms of myelopathy, such as hyperreflexia, quadriparesis, and gait abnormality. In patients with basilar invagination, hydrocephalus can be very dangerous and must be treated before any other intervention is performed. The natural history of basilar invagination can include progressive deformity and neurologic dysfunction, creating the controversy of whether prophylactic treatment is indicated in asymptomatic patients with basilar invagination evident on imaging. We take a conservative stance and prefer to monitor these patients for development of neurologic symptoms, which can be subtle and can progress slowly. We currently do not prescribe orthotic braces for patients with OI who have asymptomatic basilar invagination because we do not believe there is

Figure 5



A

B

T2-weighted sagittal magnetic resonance image of the cervical spine demonstrating progressive basilar invagination in a 14-year-old boy with osteogenesis imperfecta. The patient had headaches, neck pain, and decreased endurance but no overt symptoms of myelopathy. **B**, Postoperative lateral radiograph of the cervical spine in the same patient demonstrating occiput to C2 fusion, which was performed with intraoperative traction.

convincing evidence in the literature that the use of a cervical brace prevents progression of basilar invagination or prevents symptomatic basilar invagination from occurring. We also do not counsel patients to delay independent upright posture until 18 months of age. No definitive evidence in the literature has proven that delayed sitting decreases the risk of basilar invagination, and delaying independent upright posture is nearly impossible in most patients with OI because many of these children are motivated to sit, crawl, scoot, or stand at or near normal developmental milestones.

### Lumbosacral Pathology

Spondylolysis and spondylolisthesis have been found in patients with OI almost exclusively at the L5 level. In the literature, incidence rates range from 5.3% to 10.9%.<sup>28,29</sup> Abelin

et al<sup>30</sup> compared the sagittal balance of the spine in patients with OI and a normal cohort. They found an increase in T5-T12 kyphosis in the patients with OI and equal lumbar lordosis compared with that of the control group. They found no difference in sacral slope, pelvic tilt, or pelvic incidence in the patients with OI compared with the control group. They concluded that patients with OI have increased thoracic kyphosis with lumbar lordosis that is unable to compensate for the kyphosis, resulting in overall anterior sagittal balance.

Hatz et al<sup>29</sup> evaluated lateral radiographs of the spine in 110 patients with OI to characterize lumbar deformities and spondylolysis/spondylolisthesis. They found an 8.2% incidence of spondylolysis at an average age of 7.5 years, with all nine of those patients ambulatory. Spondylolisthesis occurred in 12 patients (10.9%) at an average age of 6.4 years, with 92% of those

Figure 6



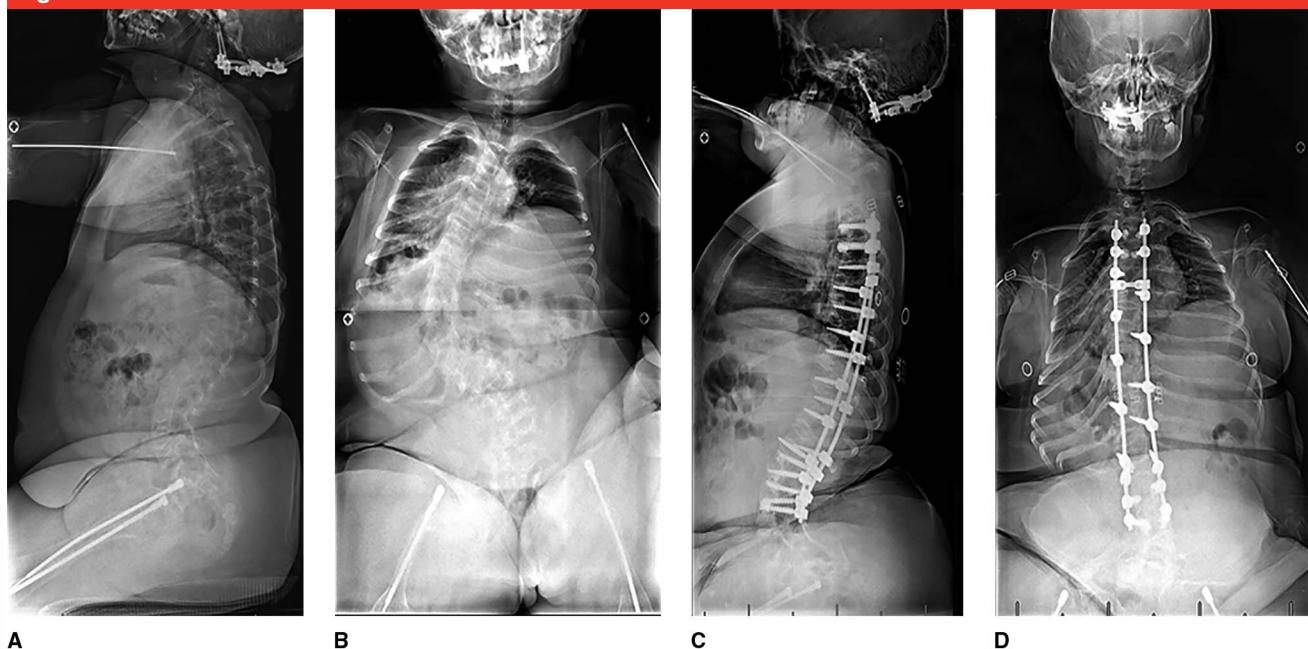
Lateral lumbar spine radiograph demonstrating osteogenesis imperfecta in a 20-year-old woman who reported increasing low back pain. The patient has substantial lumbar lordosis, elongated pedicles, and a horizontal sacrum with sacral deformity.

patients ambulatory. Spondylolisthesis occurred at L5/S1 in 11 of 12 patients and at S1/S2 in 1 patient. Nine patients had isthmic spondylolisthesis, and three were dysplastic. The grade was low in 10 patients and high in 2 patients. The authors did not find that one specific type of OI had a higher incidence of spondylolisthesis than did other types, although seven of the nine patients with spondylolysis had type III OI.<sup>29</sup>

The clinical relevance and natural history of spondylolysis and spondylolisthesis in patients with OI are not clear in the literature, and information on surgical indications and techniques is available only in sparse case reports. In our experience, many patients with OI do not have normal pelvic parameters and often have increased lumbar lordosis, and an increase in lumbar lordosis can even develop at the distal end of a fusion construct (Figures 6 and 7). The practitioner also needs to be aware of hip flexion contractures and the possibility of acetabular protrusion.



Figure 7



Lateral (A) and PA (B) radiographs of the spine demonstrating increased lumbar lordosis in a 16-year-old girl with osteogenesis imperfecta and scoliosis. Postoperative lateral (C) and PA (D) radiographs of the spine obtained 2 years after fusion demonstrate distal lordosis at the end of the fusion construct.

### Anesthetic and Intraoperative Considerations

The surgeon must be aware of several anesthetic and intraoperative considerations in patients with OI. Fractures can occur when patients are transferred to the surgical table, positioned during the procedure, and transferred to the postoperative bed. In severely affected patients, fractures can result from the use of blood pressure cuffs and from tourniquets used for insertion of intravenous lines. Airway management in anesthesia is challenging because these patients often have large heads, large tongues, and short necks. They also have poor pulmonary function as a result of chest wall deformities. Normal lung predictions based on age and size are not accurate in patients with OI because of their stature. Hyperthermia and diaphoresis tend to occur in these patients. The use of

succinylcholine should be avoided because fasciculations can cause fractures in severely affected patients.<sup>24</sup> Patients with OI can lose substantial amounts of blood during spinal surgery; therefore, blood should be available for transfusion if required. Controlled hypotension during the spinal exposure and the use of tranexamic acid can decrease blood loss and have been shown to be effective in the surgical management of complex pediatric spinal deformity.<sup>31</sup>

### Summary

The spine is commonly affected in patients with OI. Early identification of scoliosis, kyphosis, and craniocervical junction abnormalities is important. By age 6 years, patients should be screened with a clinical examination, including a neurologic examination and a lateral cervical spine radiograph to

identify asymptomatic craniocervical pathology. Early diphosphonate treatment in patients with OI has been shown to be beneficial for the extremities and the spine by decreasing the progression of scoliosis and improving bone quality.

### References

*Evidence-based Medicine:* Levels of evidence are described in the table of contents. In this article, reference 7 is a level II study. References 5, 6, 8, 13, 16, 23, 24, and 30 are level III studies. References 1-4, 9-12, 14, 15, 17-21, and 25-29 are level IV studies.

References printed in **bold type** are those published within the past 5 years.

1. Sillence DO, Senn A, Danks DM: Genetic heterogeneity in osteogenesis imperfecta. *J Med Genet* 1979;16(2):101-116.
2. Van Dijk FS, Sillence DO: Osteogenesis imperfecta: Clinical diagnosis,

- nomenclature and severity assessment [published correction appears in *Am J Med Genet A* 2015;167(5):1178]. *Am J Med Genet A* 2014;164(6):1470-1481.
3. Widmann RF, Bitan FD, Laplaza FJ, Burke SW, DiMaio MF, Schneider R: Spinal deformity, pulmonary compromise, and quality of life in osteogenesis imperfecta. *Spine (Phila Pa 1976)* 1999;24(16):1673-1678.
  4. Engelbert RH, Gerver WJ, Breslau-Siderius LJ, et al: Spinal complications in osteogenesis imperfecta: 47 patients 1-16 years of age. *Acta Orthop Scand* 1998;69(3):283-286.
  5. Land C, Rauch F, Munns CF, Sahebjam S, Glorieux FH: Vertebral morphometry in children and adolescents with osteogenesis imperfecta: Effect of intravenous pamidronate treatment. *Bone* 2006;39(4):901-906.
  6. Semler O, Beccard R, Palmisano D, et al: Reshaping of vertebrae during treatment with neridronate or pamidronate in children with osteogenesis imperfecta. *Horm Res Paediatr* 2011;76(5):321-327.
  7. Aström E, Jorulf H, Söderhäll S: Intravenous pamidronate treatment of infants with severe osteogenesis imperfecta. *Arch Dis Child* 2007;92(4):332-338.
  8. Kusumi K, Ayoob R, Bowden SA, Ingraham S, Mahan JD: Beneficial effects of intravenous pamidronate treatment in children with osteogenesis imperfecta under 24 months of age. *J Bone Miner Metab* 2015;33(5):560-568.
  9. Benson DR, Newman DC: The spine and surgical treatment in osteogenesis imperfecta. *Clin Orthop Relat Res* 1981;159:147-153.
  10. Engelbert RH, Uiterwaal CS, van der Hulst A, Witjes B, Helders PJ, Pruijs HE: Scoliosis in children with osteogenesis imperfecta: Influence of severity of disease and age of reaching motor milestones. *Eur Spine J* 2003;12(2):130-134.
  11. Watanabe G, Kawaguchi S, Matsuyama T, Yamashita T: Correlation of scoliotic curvature with Z-score bone mineral density and body mass index in patients with osteogenesis imperfecta. *Spine (Phila Pa 1976)* 2007;32(17):E488-E494.
  12. Anissipour AK, Hammerberg KW, Caudill A, et al: Behavior of scoliosis during growth in children with osteogenesis imperfecta. *J Bone Joint Surg Am* 2014;96(3):237-243.
  13. Yong-Hing K, MacEwen GD: Scoliosis associated with osteogenesis imperfecta. *J Bone Joint Surg Br* 1982;64(1):36-43.
  14. Ishikawa S, Kumar SJ, Takahashi HE, Homma M: Vertebral body shape as a predictor of spinal deformity in osteogenesis imperfecta. *J Bone Joint Surg Am* 1996;78(2):212-219.
  15. Benson DR, Donaldson DH, Millar EA: The spine in osteogenesis imperfecta. *J Bone Joint Surg Am* 1978;60(7):925-929.
  16. Kocher MS, Shapiro F: Osteogenesis imperfecta. *J Am Acad Orthop Surg* 1998;6(4):225-236.
  17. Cristofaro RL, Hoek KJ, Bonnett CA, Brown JC: Operative treatment of spine deformity in osteogenesis imperfecta. *Clin Orthop Relat Res* 1979;139:40-48.
  18. Hanscom DA, Winter RB, Lutter L, Lonstein JE, Bloom BA, Bradford DS: Osteogenesis imperfecta: Radiographic classification, natural history, and treatment of spinal deformities. *J Bone Joint Surg Am* 1992;74(4):598-616.
  19. Janus GJ, Finidori G, Engelbert RH, Poulouen M, Pruijs JE: Operative treatment of severe scoliosis in osteogenesis imperfecta: Results of 20 patients after halo traction and posterior spondylosis with instrumentation. *Eur Spine J* 2000;9(6):486-491.
  20. Yilmaz G, Hwang S, Oto M, et al: Surgical treatment of scoliosis in osteogenesis imperfecta with cement-augmented pedicle screw instrumentation. *J Spinal Disord Tech* 2014;27(3):174-180.
  21. Arponen H, Mäkitie O, Haukka J, et al: Prevalence and natural course of craniocervical junction anomalies during growth in patients with osteogenesis imperfecta. *J Bone Miner Res* 2012;27(5):1142-1149.
  22. Sillence DO: Craniocervical abnormalities in osteogenesis imperfecta: Genetic and molecular correlation. *Pediatr Radiol* 1994;24(6):427-430.
  23. Cheung MS, Arponen H, Roughley P, et al: Cranial base abnormalities in osteogenesis imperfecta: Phenotypic and genotypic determinants. *J Bone Miner Res* 2011;26(2):405-413.
  24. Lubicky JP: The spine in osteogenesis imperfecta, in Weinstein SL, ed: *The Pediatric Spine: Principles and Practice*, ed 1. New York, NY, Raven Press, 1994, pp 943-958.
  25. Khandanpour N, Connolly DJ, Raghavan A, Griffiths PD, Hoggard N: Craniospinal abnormalities and neurologic complications of osteogenesis imperfecta: Imaging overview. *Radiographics* 2012;32(7):2101-2112.
  26. Sawin PD, Menezes AH: Basilar invagination in osteogenesis imperfecta and related osteochondrodysplasias: Medical and surgical management. *J Neurosurg* 1997;86(6):950-960.
  27. Ibrahim AG, Crockard HA: Basilar impression and osteogenesis imperfecta: A 21-year retrospective review of outcomes in 20 patients. *J Neurosurg Spine* 2007;7(6):594-600.
  28. Verra WC, Pruijs HJ, Beek EJ, Castelein RM: Prevalence of vertebral pars defects (spondylolysis) in a population with osteogenesis imperfecta. *Spine (Phila Pa 1976)* 2009;34(13):1399-1401.
  29. Hatz D, Esposito PW, Schroeder B, Burke B, Lutz R, Hasley BP: The incidence of spondylolysis and spondylolisthesis in children with osteogenesis imperfecta. *J Pediatr Orthop* 2011;31(6):655-660.
  30. Abelin K, Vialle R, Lenoir T, Thévenin-Lemoine C, Damsin JP, Forin V: The sagittal balance of the spine in children and adolescents with osteogenesis imperfecta. *Eur Spine J* 2008;17(12):1697-1704.
  31. Dhawale AA, Shah SA, Sponseller PD, et al: Are antifibrinolytics helpful in decreasing blood loss and transfusions during spinal fusion surgery in children with cerebral palsy scoliosis? *Spine (Phila Pa 1976)* 2012;37(9):E549-E555.