

# Surgical treatment of osteogenesis imperfecta: current concepts

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### Purpose of review

The treatment of osteogenesis imperfecta requires a multidisciplinary team to maximize function and comfort, and decrease fracture incidence. Medical treatment with bisphosphonates has allowed for safer, more effective surgical management of children with osteogenesis imperfecta. The purpose of this review is to outline treatment indications and choices of surgical techniques based on recent clinical studies, and in addition to identify persistent clinical problems addressed in recent literature.

### Recent findings

Several new intramedullary rodding surgical techniques and modifications of older techniques have been developed to correct deformities of the long bones. These techniques decrease the trauma associated with surgical treatment. The newer techniques limit postoperative immobilization, enabling earlier rehabilitation, and allowing for treatment of multiple bones simultaneously.

### Summary

Recent medical and surgical advances have allowed improved safety, function and comfort in treating children with osteogenesis imperfecta. The selection of surgical techniques is dependent on surgeon experience, severity of disease and patient function, and availability of specific instrumentation. Intramedullary fixation rather than plating is preferred, and allowing early protected weight bearing and rehabilitation of children with ambulatory potential is the ideal goal.

### Keywords

osteogenesis imperfecta, osteotomy, pamidronate, telescoping nails

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## Introduction

Osteogenesis imperfecta is a group of heterogenous disorders with the common feature of congenital bone fragility caused by mutations in the genes that codify for type I procollagen (COL1A1 and COL1A2) [1]. These two genes are located in chromosomes 7 and 17. In the vast majority of cases, osteogenesis imperfecta is inherited in a dominant fashion or is caused by a new mutation. The prevalence of osteogenesis imperfecta is estimated to be one in 20 000–50 000 infants, but the incidence is probably higher because, since it is a heterogenous condition, misdiagnosis is frequent [2]. Recent advances in medical and surgical treatment of children have had an impact on the comfort and quality of life of these children.

## Classification

The classification systems available, which divide osteogenesis imperfecta into specific types, are problematic in that they do not necessarily predict long-term function or response to medical and surgical management. The Sillence classification, as modified by Rauch and Glorieux, is most widely referenced. Briefly, type I includes individuals without major boney deformities with

variable numbers of fractures throughout their lives. Type II is often lethal in the perinatal period, but now with treatment with bisphosphonates some individuals survive for several years. Patients with type III usually have severe limb and spine deformities and fractures, while individuals with moderate deformities and fracture rates are classified as having type IV. These four types of classic osteogenesis imperfecta occur secondary to mutations in the genes responsible for production of type I procollagen.

Other more recently described types of osteogenesis imperfecta – V, VI and VII – are not caused by abnormalities in these specific genes and have other specific associated findings not seen in types I–IV [3•]. Plotkin [1] has stated that these and many other syndromes with brittle bones might better be described as syndromes resembling osteogenesis imperfecta. Treatment is based on clinical presentation and severity rather than classification [4••].

## Medical treatment

The only documented medical treatment shown to have a consistent, positive effect on comfort, fracture rate, pain, and function in children with osteogenesis imperfecta is

bisphosphonates, which clearly increase cortical thickness [3<sup>•</sup>,5<sup>•</sup>]. This treatment does not cause preexisting boney deformities to resolve, but does decrease fracture incidence. Bisphosphonates actually increase bone density by reducing bone turnover, which may inhibit spontaneous correction of preexisting deformity [6]. The mechanism and effects of bisphosphonates were reviewed recently by Morris and Einhorn [7].

Bisphosphonates, most commonly IV pamidronate in children, clearly increase areal bone density [8], especially in the first year of treatment [9]. Pamidronate has also been shown to improve vertebral height and development in children with compressed vertebral bodies [10]. Treatment in very young infants with severe osteogenesis imperfecta has been shown to be safe, at least in the short term, improve mobility, and prevent some secondary deformities [11<sup>•</sup>,12]. The ideal indications for treatment and dosing regimen have not been determined [13]. Bone density has been shown to correlate with disease severity and may be predictive of long-term outcome [14]. Whether achieving 'normal' age-matched bone density is optimal is not clear. The ultimate goal is to decrease fracture incidence regardless of bone density Z-score, which has been shown to be possible with 'low-dose' treatment [15]. Excessively dense bone may be predisposed to fracture by becoming more 'brittle'.

The long-term deleterious effects of bisphosphonate treatment are unknown, and for that reason treatment is not recommended in 'mild' osteogenesis imperfecta, except for children with recurrent fractures, significant deformity, and pain. Some centers are recommending that treatment be stopped after several years. The concern with this approach is that subsequent bone that is formed will not be treated and fractures will then occur at the transition zone where new bone is forming [16,17<sup>•</sup>,18]. Although this has been seen clinically, it has not been documented extensively in the literature. Nonunion and delayed union are common in osteogenesis imperfecta, especially in the distal humerus. Nonunion after intramedullary rodding is frequently asymptomatic [19].

The timing of bisphosphonate treatment relative to surgery is important. One study demonstrated that, with the Montreal protocol, osteotomy, but not fracture healing, was delayed with perioperative pamidronate treatment [20]. Confounding factors in the Montreal study were that the osteotomies in this series were done with an oscillating saw, which generates thermal injury and can slow healing. Another study [21] did not show problems with bone healing in patients receiving bisphosphonates. The expected occurrence of nonunion fractures is about 15% of patients, regardless of treatment. It is unclear if lower doses of pamidronate will also show the same effect

on healing of osteotomies. El Sobky *et al.* [22<sup>•</sup>] documented that children treated with pamidronate prior to surgery and afterwards do better than children treated with surgery alone. Discontinuing pamidronate post-operatively can lead to increased pain and fractures in some patients.

### Operative indications

Indications for surgical realignment and intramedullary rodding are recurrent fractures and severe bowing deformities in children with severe osteogenesis imperfecta who are attempting to stand. The lower extremities are typically involved to a greater extent than the upper extremities functionally. Medical treatment alone may not decrease lower extremity fracture rates [23]. Realignment and rodding of these children not only decrease pain and reduce the incidence of fractures, but also enhance the child's overall function, comfort, development, and ability to stand and walk. There rarely are indications for operative intervention prior to attempts at standing, but, based on recent studies, there is no advantage to delaying surgery until some arbitrary older age if the child has bone with adequately-sized medullary canals to accommodate available rods [24,25<sup>•</sup>].

Surgical treatment at a younger age may require revision sooner than surgery done in an older child. This relative disadvantage is clearly countered by the enhanced growth, development and quality of life gained through early surgical stabilization. In some cases, children with mild osteogenesis imperfecta may develop recurrent fractures and bowing deformities that warrant operative realignment and intramedullary fixation.

### Surgical principles

The goals of any surgery are to obtain optimal alignment with full correction of deformity, utilizing an intramedullary device to maintain alignment, and to act as an internal splint. Intramedullary devices are designed to be load-sharing and should never be rigid, as rigidity may lead to complete bone resorption. If bowing persists despite utilizing an appropriate intramedullary rod, whether telescoping or not, recurrent fracture or nonunion will occur at a high rate.

### Operative techniques

Preoperative evaluation is critical, including evaluation for cranial cervical abnormalities. There is a somewhat unpredictable tendency to bleeding, and many of the children tend to run an elevated temperature throughout the operation, although malignant hyperthermia is not a recognized problem with osteogenesis imperfecta.

Stabilization of the neck by the surgeon assisting anesthesiology during intubation is critical.

The entire operative team, as well as the preoperative and postoperative nursing staff, must be educated in the care, monitoring, and handling of these children to prevent fractures.

Postoperative pain management is also challenging, as many of the children have been exposed to pain medications throughout their lives. Spasm is often a major component of postoperative discomfort and short-term, low-dose diazepam can be quite beneficial.

### Specific devices and techniques

Plates and screws are rarely indicated in treating fractures in children with osteogenesis imperfecta and should be avoided if at all possible. They predictably fail and predispose to recurrent fractures at the ends of the plates [26].

Variations of the Bailey Dubow telescoping rod have T-shaped ends that are buried in the subchondral epiphyseal bone of the knee and ankle, as well as in the greater trochanter, and have been used successfully in many centers for decades [27]. They have historically been used in conjunction with extensive surgical approaches, and require that an arthrotomy of the knee be performed for insertion in the femur and tibia, and an extensive arthrotomy of the ankle to insert this device in the tibia. Cho *et al.* [28] have developed a variant of this system that does not require arthrotomies, but does require a small partially threaded wire to engage a small hole in the distal end of the male nail in the distal femoral epiphysis or distal tibial epiphysis, respectively [28]. To cross-link wire, theoretically, could cause disruption to growth if they do not telescope and the rod migrates proximally through the physis.

Variations of the Metaizeu technique, using flexible nails as well as the double Rush rods technique, have also been successfully utilized in osteogenesis imperfecta [29]. These are complex procedures that frequently require open reaming and extensive open osteotomies to perform, and require postoperative cast immobilization. These techniques have the distinct advantage in some parts of the world in terms of cost and availability of the intramedullary devices [30]. With growth, bowing in the central segment of the rodded bone can occur with transcortical migration of the rods and ultimately fracture. Single Rush rods, or even k-wires in the tibias of small children, can be used, but revision is necessary sooner than it is with telescoping nails or double Rush rodding. Percutaneous osteotomies and medullary fixation are an important development. Recent advances in technology

have improved the ability to minimize surgical exposure and hence trauma to these patients [31].

The Fassier–Duval telescoping nail is a recent design inserted through small incisions under fluoroscopic control in conjunction with percutaneous osteotomies whenever possible. This is the authors' preferred technique. Arthrotomies of the knees and ankles are not required, and rigid postoperative immobilization is typically not needed as the soft tissue envelope around the bone is maintained. The procedure does require meticulous technique and experience to ensure proper correction of all the deformity, and for appropriate placement of the rods [24]. One of the main advantages of this technique is that multiple bones may be treated at the same surgical setting, limiting the number of surgical procedures and reducing the rehabilitation that these children endure [32\*].

Osteotomies ideally are performed percutaneously with an osteotome or drill and not an oscillating or reciprocating saw to minimize soft tissue trauma and thermal injury. In the femur, the rod is placed through the greater trochanter. In some small children the piriformis fossa is entered but no cases of avascular necrosis (AVN) have been reported. There are typically significant areas of bowing in the proximal femur in the subtrochanteric region, often mimicking a true coxa vara. These deformities may approach 90°, and are commonly bowed both anteriorly and laterally and may require two to three osteotomies to correct. Often, a more subtle, less apparent bow is found just above the supracondylar region that requires an osteotomy to avoid anterior penetration regardless of which nail is utilized. If the nail is not placed in the center–center position on the anteroposterior and lateral views of the distal femoral epiphysis, cut out and migration are more likely to occur. Overgrowth of the proximal nail by the greater trochanter can occur.

Placement of the Fassier–Duval telescoping nail in the tibia does not require arthrotomy of the knee or ankle, with the proximal entry point just posterior to the patellar tendon. Osteotomies are done through small open incisions, causing as little periosteal disruption as possible. Sclerotic areas in the tibia and femur may require limited open reaming to avoid thermal injury and to allow passage of the guide wire. The fibula can be treated with a closed osteoclisis if small and spindly, or through an open osteotomy if it is substantial in size.

The revision rate in an early multicenter series is lower with the Fassier–Duval telescoping nail in the femur than other reported series [25\*]. Findings following treatment of tibial deformities with this system have not been reported yet. When revision is required with this system, extraction is facilitated with a specially designed

extraction instrument. With significant bending or breakage of any of the rodding systems, open techniques may be necessary to remove the rods.

The typical postoperative management following Fassier-Duval telescoping nailing is splinting the child with a light long-leg splint or brace for 3–4 weeks. Some centers place a bar between the legs to avoid the tendency for external rotation. Casts are rarely necessary. Most of the children will attempt to stand approximately 3–4 weeks postoperatively as they have a remarkable ability to judge when it is safe and comfortable to weight-bear. The efficacy for long-term bracing, in terms of improving long-term function and preventing recurrent deformity and fracture, has not been demonstrated (Figs 1–3).

When nontelescoping rods are used, or when a telescoping nail does not lengthen with growth, many of the children functionally do well for variable lengths of time. Revision may be required for persistent pain, progression of deformity, progressive signs of stress reaction, or if the

**Figure 1** Preoperative anteroposterior radiograph demonstrates apparent coxa vara, secondary to subtrochanteric bowing, recurrent fractures of the right femur



Pamidronate lines indicate multiple treatments.

**Figure 2** Significant anterior bowing with evidence of recurrent episodes of modeling



This image also demonstrates the anterior bowing that is present, especially in the femurs, in addition to the lateral bowing.

child sustains a fracture. Fractures most commonly occur just distal to the end of the proximally migrating nail, or near the junction of the male/female nails as they elongate. Anecdotally, bending of the nails is becoming more of a problem as children with more severe osteogenesis imperfecta are becoming significantly more active because of their improved function and comfort with medical and surgical management.

True coxa vara occurs commonly in children with moderate to severe osteogenesis imperfecta [33]. This can be effectively treated at the same time as the diaphyseal deformity with a modification of the Wagner and Finidori technique [24]. Two small, smooth wires are placed in the femoral neck, across the physis. Osteotomy is then performed below the lesser trochanter. A drill is passed through the medial aspect of the greater trochanter through the lateral cortex and then into the canal of the femoral shaft. A telescoping nail is then placed between the two smooth pins after correcting the varus and securing the osteotomy. Any remaining distal deformities are then treated as described above. The pins are then bent over and secured to the proximal shaft with cerclage wires.

**Figure 3 Postoperative osteotomies demonstrating correction of the apparent but not true coxa vara**



The femoral nails are placed deeper than they would be at the present time, which may avoid overgrowth of the trochanter around the proximal threaded nail. The prominence of the male nail in the gluteal region usually does not cause significant symptoms but allows for increased growth. The limitation of the tibial nail is the length of the threaded portion distally but can be extended just to the tip of the subchondral bone. Lightweight radiolucent splint is also demonstrated, which can be utilized with an abduction pillow for comfort for the initial few weeks.

### Upper extremity surgery

The treatment with pamidronate in children and adolescents with severe forms of osteogenesis imperfecta has been shown to increase grip strength [34]. Significant bowing deformities or recurrent fractures, especially of the humerus, can impair functional activities and the ability to transfer [35]. Intramedullary alignment and rodding with either telescoping or single Rush rods can improve function. Open osteotomies are necessary in the humerus to avoid neurovascular injury. The device must not impinge in the shoulder, and full motion should be demonstrated at the completion of the procedure. Distal fixation is in the lateral condyle. Bipolar elastic nailing may also be useful. Patients presenting with a nonunion of the distal humerus following fracture are a vexing problem, which, at this time, does not have a predictable surgical solution and may be best treated with bracing if symptomatic [36].

Olecranon fractures are much more common in children with type I osteogenesis imperfecta than they are in

normal children, occur at an earlier age, and can involve both elbows. They require operative fixation with a tension band technique if at all displaced. Due to problems with the intramedullary wire backing out, utilizing a long intramedullary wire, with an absorbable suture rather than a tension wire, should be considered.

Great care should be undertaken in approaching operative correction of the forearm. Ulnar deformities can be corrected with an intramedullary wire, but osteotomy and intramedullary fixation of the radius are very difficult. The entry point near the radial styloid relies on the ability to bounce off the opposite radial cortex. In children with osteogenesis imperfecta the wire may pass directly through the opposite cortex without any sensation of resistance and potentially lead to significant complications. These wires also have a tendency to 'back out' and cause skin irritation if not obvious protrusion through the skin.

### Conclusion

Medical management with pamidronate, while not a cure, has allowed improved operative treatment and function for children that were unimaginable even 10 years ago. Children with severe osteogenesis imperfecta, many of whom in the past were wheelchair-bound with almost constant fractures and persistent pain, are much more active in many instances. This has created new challenges for the treating physicians. Treatment does not make these children fracture-free. Surgical realignment and intramedullary stabilization decrease the incidence of fractures and make these fractures more manageable for many carefully selected patients. Future efforts must be directed to finding a genetic 'cure' for the underlying causes of the collagen abnormalities. Improved methods of fixation, which emphasize minimization of soft tissue injury, telescoping rods, and avoidance of postoperative casting, have also diminished the trauma and frequency of operative treatment. Many questions remain, including the optimal doses and duration of bisphosphonates, especially around the time of surgery. The causes of delayed union and nonunion in children with osteogenesis imperfecta are not fully elucidated.

### References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 113–114).

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