

The orthopaedic management of long bone deformities in genetically and acquired generalized bone weakening conditions

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Abstract

Purpose Diseases such as osteogenesis imperfecta, fibrous dysplasia, hypophosphataemic rickets and others lead to soft and weak bones and long bone deformity in affected patients. As a consequence, these patients lose their walking capacity and functional abilities of the upper extremities as well.

Methods In combination with bisphosphonate treatment and physical rehabilitation programmes surgical interventions are being applied to correct and stabilize the deformed and less mechanically resistant long bones. Intramedullary devices, ideally with an elongating telescopic mechanism, have proven to be the most suitable implants.

Results The surgical correction and stabilization of deformed bones in weak bone diseases is very beneficial to the patients. Pain restriction, reduction of fracture events, minimization of consequences of traumatic events and falls have resulted in a significant functional improvement. The patients live on a better activity level with a much-improved individual independence. Despite a high complication and revision rate of the intramedullary rods the gain of quality of life outweighs these negative aspects by far.

Conclusion Orthopaedic surgical treatment for deformed bones in patients with weak bone diseases has changed the life of the patients and plays a very important role in the disease management protocols.

This paper was written under the guidance of the Study Group Genetics and Metabolic Diseases of the European Paediatric Orthopaedic Society.

Cite this article: Wirth T. The orthopaedic management of long bone deformities in genetically and acquired generalized bone weakening conditions. *J Child Orthop* 2019;13:12-21. DOI: 10.1302/1863-2548.13.180184

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Keywords: osteogenesis imperfecta; fibrous dysplasia; hypophosphataemic rickets; bone deformity

Introduction

A variety of congenital and acquired conditions lead to a localized or general bone weakness which may result in more or less severe long bone deformities. The most important and most frequent diseases are hypophosphataemic rickets, fibrous dysplasia and osteogenesis imperfecta (OI) representing examples of genetically determined entities and rickets and osteopenia due to malabsorption syndromes as typical causes of acquired diseases (Table 1).^{1,2}

All these bone weakening conditions are subject to a higher fracture rate, mainly from low energy and inadequate injuries, and to gradual development of bone deformities. The muscular forces generated along the upper and lower limbs' long bones are stronger than the biomechanically transmitted tensile strengths of the bones themselves. Among typical resulting deformities are a varus deviation of the distal humerus or a varus and flexion deformity of the femur. The clinical implications are severe axial deformities with considerable functional impairment. Severe forearm deformity, for example, may lead to a complete restriction of pro- and supination. Serious deformations of the lower extremity may be associated with the inability to stand or walk, or trigger the loss of pre-existing walking capacities.^{3,4} As a consequence of bone deformation fractures may develop at the site of maximum curvature.

The treatment of weak bones diseases has made significant progress in the past years both through improved medical and surgical strategies. The introduction of bisphosphonate treatment for patients suffering from moderate and severe forms of OI has reduced the fracture rate and improved bone stability.⁵⁻⁸ Increasingly enzyme and antibody treatment will be available for these conditions in order to reduce their clinical symptoms, as it is currently already available for hypophosphatasia⁹ and hypophosphataemic rickets.¹⁰ In the orthopaedic field, improved surgical techniques such as minimally invasive procedures and better and more sophisticated implants, have facilitated correction and stabilization of long bone deformities and furthermore even extended indications for surgical

Table 1 Genetically determined diseases leading to soft bones and its consequences

Disease	Genetics	Main deformity	Conservative treatment	Surgical treatment
Fibrous dysplasia	GNAS gene	All bones affected	Bisphosphonates	Intramedullary stabilization
Hypophosphatasia	TNSALP gene	Long bones affected	Asfotase Alfa	Intramedullary stabilization, growth modulation
Hypophosphataemic rickets	PHEX gene	Lower limbs, bow legs	Burosumab	Intramedullary stabilization, growth modulation
Osteogenesis imperfecta, type I to V(1, 2)	Col 1A1, Col 1A2, dominant	All long bones affected	Bisphosphonates, physiotherapy	Intramedullary stabilization
Osteogenesis imperfecta, type IV to XVII(2)	Many gene locations, autosomal recessive	All long bones affected	Bisphosphonates, physiotherapy	Intramedullary stabilization

GNAS, Guanine Nucleotide Binding Protein (G Protein), alpha stimulating activity; TNSALP, tissue-nonspecific alkaline phosphatase; PHEX, Phosphate regulating endopeptidase homolog X-linked; Col 1A1, collagen 1A1; Col 1A2, collagen 1A2

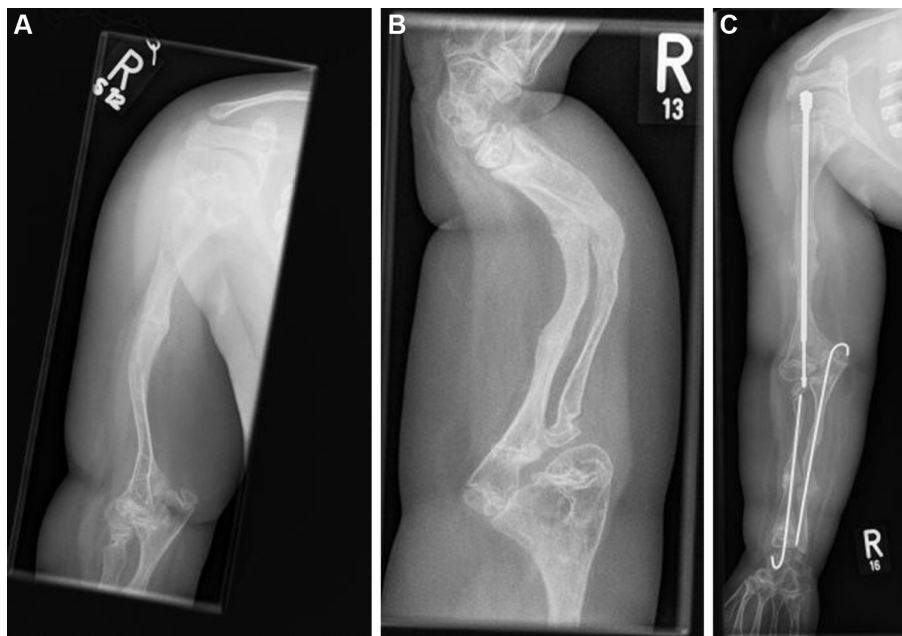


Fig. 1 Severely affected osteogenesis imperfecta patient with significant deformity of the right humerus (a) and right forearm (b). A simultaneous correction of both the right humerus and forearm was performed using multiple osteotomies; telescopic nail for humerus; and Kirschner-wires in the radius and ulna (c).

interventions.^{11,12} This work on current orthopaedic treatment in weak long bones was inspired by the symposium on key aspects of OI at the 37th Annual Meeting of the European Paediatric Orthopaedic Society in Oslo/Norway (13 April 2018).

Upper extremity

Deformities of the upper extremities seem to occur less frequently and to play a less significant role than lower limb deformities. Why do we then need to pay attention to them, if their functional impairment does not seem to be such an obvious issue? With increasing degrees of severity, the extent of deformity progresses and the subsequent fractures risk increases. The larger number of fractures and the development of more pronounced deformities do inflict on the functionality of the elbow joint and forearm

movements.⁴ Mainly patients with fibrous dysplasia and, in particular, moderately and severely affected children with OI require surgical interventions for upper extremity deformities.^{13,14}

In general, the well-known principles of deformity correction apply. The osteotomies are being placed at the apex of the deformity, and the number of osteotomies are chosen according to the number of apices (Fig. 1). The choice of the right implant may pose another difficulty. In growing patients, telescoping implants are mostly used, if the diameter of the bones allows them to be fitted. In the upper extremity, however, telescoping nails are only usable for humeral rodding.¹⁵ The radius and ulna do not generally accept telescoping nails due to the small diameters of the intramedullary canal and the difficult accessibility of the radius. Hence, flexible intramedullary nails, Rush rods or Kirschner (K)-wires

of appropriate sizes are the implant of choice for forearm correction and stabilization (Fig. 1). In patients with fibrous dysplasia, it is usually larger bones that are affected, and several suitable intramedullary implants can be utilized. Plates are not chosen routinely but they may be helpful to fix rotationally unstable osteotomies. Small tubular plates or small locking plates with use of single cortex screw fixation are very useful in this context. If plates are chosen for fixing osteotomies or fractures, they should be removed soon after completion of bony healing. Because of the increased stability of the plated bone area, stress risers are created above and below with predictable deformity occurrence, if they are kept in place as a single implant.

While humerus corrections in OI patients are mostly possible from the age of three years,¹⁵ forearm correction requires a minimum size of both bones and the intramedullary canal. The indication for upper extremity correction is currently worked out with the patients themselves and their parents. They can identify the difficulties of daily living best and judge the impairment and disability caused by the present deformity. It is on the orthopaedic surgeon to outline treatment and offer strategies to overcome the patient's problems, and to warn them from subsequent surgeries, if difficulties arise.

There are several strategies to address the upper extremity problem of OI patients. If the humerus is the only bone affected, unilateral or simultaneous bilateral corrective osteotomies are possible. If the upper arm and forearm need to be corrected, a side-by-side intervention is preferable. Forearm correction can be very tricky, requiring many osteotomies and meticulous surgical procedure. It is best to start with the humerus first, followed by radius and ulnar correction (Fig. 1). In severe deformities both bones must be corrected simultaneously through separate incisions. If you try to correct them one-by-one the intact bone may prevent adequate alignment of the osteotomized bone. Postoperatively a split above the elbow cast may be necessary for four weeks, if some instability persists.

Lower extremity

The functionality of the lower limbs in OI patients focuses on all aspects of verticalization and implicates, therefore, different goals than described for the upper extremity. In mildly and moderately affected patients walking in an as normal a way possible must be the main goal of treatment, with the aim to prevent fractures particularly in the latter group. In the severely affected patients the avoidance of multiple fracture episodes and the stabilization of the weak bones to allow safe standing, transfer at home and maybe some walking with use of aids for

short distances are most important. A whole variety of implants have been used and developed with the third generation of telescopic nails being the most up-to-date implant.^{11,16-19} Accordingly, surgical intervention for deformity correction and long bone stabilization starts earlier than upper extremity surgery.

In other weak bone diseases, the development of lower limb deformities occurs at a slower rate and later in life. Consequently, the indication for surgical interventions is very closely linked to the clinical effect of the developing deformity and is timed to the needs of the patients.^{13,20}

The primary goal in most of these patients, namely early verticalization and weight bearing, requires bones which can be biomechanically highly loaded from the beginning. Due to soft bone quality and microfracturing transmitted by the muscular force alone the long bones show some deformity at walking age already. With increasing load, the deformation continues to worsen, ultimately resulting in fatigue or acute fractures at or near the apex of the deformity. This process is highly dependent on the severity of the disease and the associated bone quality. Ideal timing of any corrective procedure in the lower extremity includes the assessment of deformity, bone size and quality to fit the best suitable implant, in order to schedule it prior to any expected acute incident.²¹

Any conceivable deformity is possible in both the femur and tibia in all patients with OI. However, femur varum and antecurvatum and tibia vara and antecurvata are the predominant deformities with the varus angulation of the tibia being rather distal. The strongest muscles of every long bone segment act as the most significant deforming forces bending it away from the largest muscle mass. The femoral neck area is another weak point with a trend to coxa vara development. In addition, there is a tendency to femoral retroversion which has a clear trend to recur after correction.²² In fibrous dysplasia coxa vara, femur antecurvatum and varum are the typical deformity configurations. In the tibia, increased antecurvatum is the predominant finding. In hypophosphataemic rickets we mostly find long C-shaped varus deformities of both the femur and the tibia²⁰ (Fig. 2).

As early as age two years, first considerations for correcting deformed bones in OI patients arise. The well-known principles of deformity correction apply to all procedures. Single or multiple osteotomies are being performed, depending on the numbers of apices in the bent bone, to straighten it out. It is very important to plan the procedure thoroughly, because the placement of the osteotomy is crucial for achieving optimal alignment. Further, choosing the right implant is not always easy. Ideally intramedullary devices with elongating capacities are utilized in growing patients (Fig. 3). These are telescoping rods or flexible intramedullary nails inserted in opposite direction.^{11,19} In cases of too small a medullary

canal for insertion of such implants simple K-wires or Rush rods can also be used without exhibiting the telescoping effect.¹⁸ Despite similar clinical outcomes compared with telescopic nails, their protecting effect is limited to the length of the implant causing secondary deformities above and below in the growth period.²³ In adult patients,

custom-made or readily available small intramedullary locking nails are very suitable implants. In all of these corrective surgeries special attention has to be paid to the correct rotational alignment, particularly in the femur. All patients tend to present with femoral retroversion, which should be corrected during the procedure. If the osteotomy or the fixation do not provide rotational stability the application of a small tubular or locking plate with unicortical screw fixation solves this problem.²⁴

A specific issue of the femur applies to the area of the proximal femur and femoral neck. There is a great tendency of the femoral neck to gradually deviate into varus and retroversion while supporting the development of acetabular protrusion and high riding trochanter. When should it be protected and when should coxa vara be corrected? There are no general guidelines available. In cases with a neck-shaft angle of below 120° and the need for a very proximal femoral osteotomy, a support of the femoral neck by two K-wires which are attached to the lateral femoral cortex by circular wires²² is recommended. In severe coxa vara (neck-shaft angle below 100°) and an obvious proximal femoral deformity, surgical correction should also be strongly considered, using the same fixation. In older children with larger bones special implants that allow screw fixation of the femoral neck are available and very useful. In all other patients the clinical symptoms and the chronological changes over time should be used as guidance for indicating operative correction.

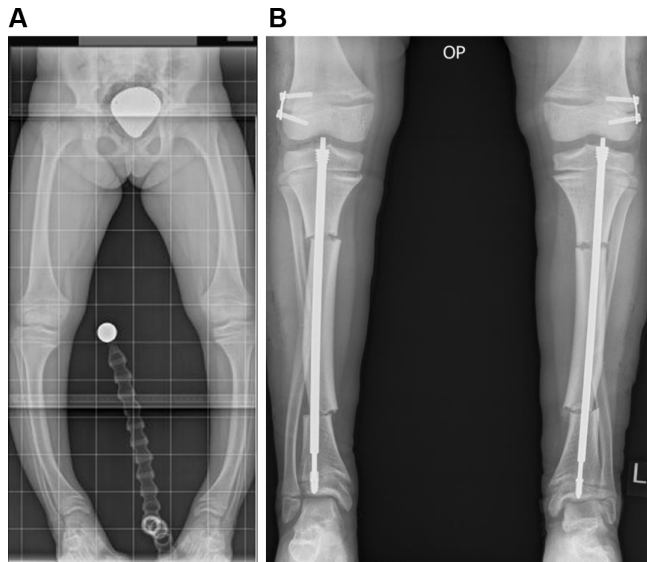


Fig. 2 Typical long bone deformity in a patient with hypophosphataemic rickets, both tibiae more affected than both femurs (a). Simultaneous bilateral correction by guided growth (femur) and double osteotomies of the tibiae (b).

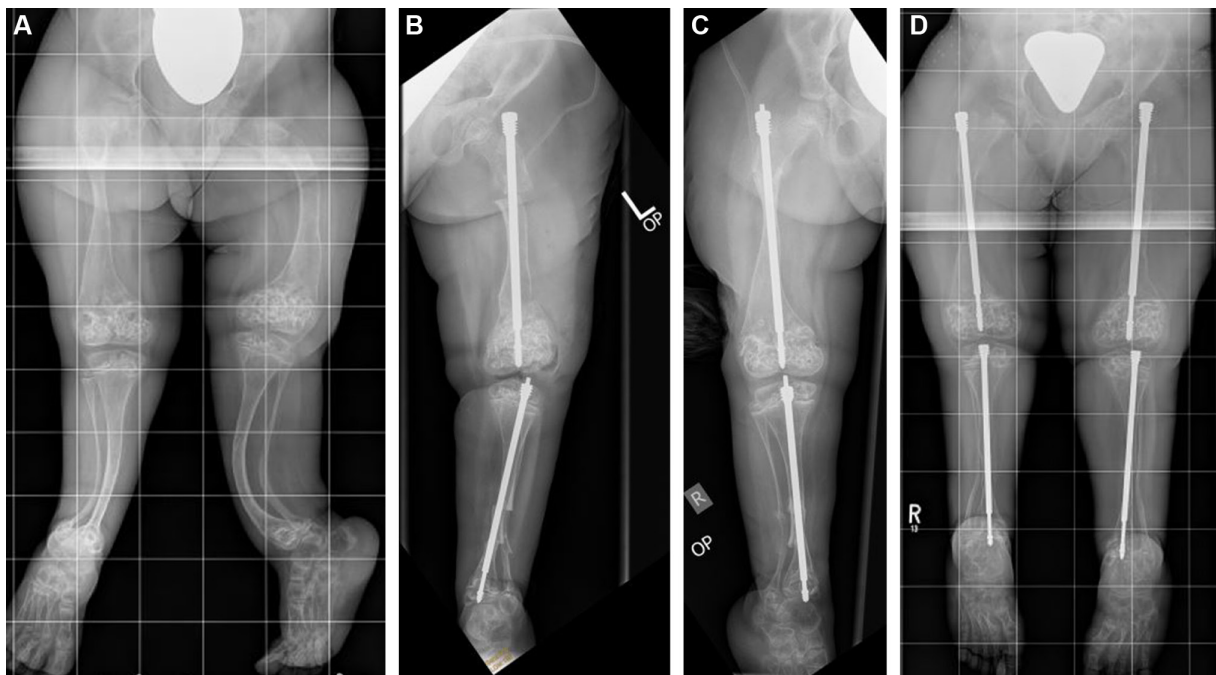


Fig. 3 Two stage surgical interventions in a one leg at a time technique for deformed lower limbs in a severely affected osteogenesis imperfecta patient. Surgery was performed one week apart. Pre- (a) and postoperative results (b and c) with a one-year follow-up (d).

There are two techniques of performing the operation: minimal-invasive and open approaches. In straight forward cases with moderate deformities the osteotomies can be done percutaneously through a small incision by drilling the bone and osteotomizing it with a chisel. Patients with severe deformities and patients without an intramedullary canal may not be suitable for the technique and need open approaches. The medullary cavity has to be recreated to accept a nail. Sometimes shortening of the bones is inevitable for proper realignment, and this requires longer incisions. To use or mix several percutaneous and formal incisions of appropriate length may be the best pragmatic principle.¹¹

Most patients, regardless of which underlying pathology causes the deformity, are in need of having several bones corrected: both femurs, both tibias or all four long

bones. While bilateral correction of the tibia rarely poses problems, bilateral correction of the femur may be unwise in frail and severely affected children. In fibrous dysplasia patients with whole bone involvement and in older children bilateral surgery may be problematic also and should be avoided (Fig. 4). In healthy OI patients, correction and rodding of all four bones of the lower extremity in one session can be done in principle. Because of associated medical issues in many of these children, my preferable strategies for first time correction of the lower extremity in OI patients are two-fold: first step aim for bilateral femoral correction followed by bilateral tibial interventions six to eight weeks later. Or, one leg after the other, two to three months apart. If difficulties in the first femoral correction are being encountered, i.e. horrible bone quality, bleeding issues and others, the surgery should be limited to one



Fig. 4 Symptomatic fibrous dysplasia of the proximal right femur in an adolescent patient (a and b). Stabilization by conventional interlocking gamma nail (c and d).

side only and a three-step approach should be taken with the second femur to be done in a separate intervention (see Fig. 2).

Complications and causes of revision surgery

Complications and the need for revisions are connected to disease-related factors such as poor bone quality and softness, which impedes anchorage of the implants, to technical issues in conjunction with the operation and to implant-related issues (Fig. 5).

Most of the problems are associated with loss of fixation of the distal and proximal anchorage.^{25,26} The risk of losing this fixation is higher in patients with poor bone quality and smaller epiphyses that require implants with shorter threads. There are techniques which allow improved fixation by additionally applying cross-wires and locking screws to prevent the nail from disengagement from the original position^{11,27,28} (Fig. 5). Telescoping nails may not extend with growth as expected due to too high internal friction or insufficient fixation to the bone. This may lead to gradual deformity development at the junction of the non-protected bone and require revision.²⁹⁻³² Falls or permanent stress on the weak bones may also generate enough energy to acutely or slowly bend the nails with subsequent jamming of the transport mechanism³³ (Fig. 5).

The healing of the osteotomies may be delayed by intrinsic or extrinsic factors. This is a specific issue in OI patients. If the periosteum is protected, the osteotomy healing is not generally compromised, however, it may take longer. Most of the children with OI have been given bisphosphonates which is known to interfere with the consolidation process of osteotomies³⁴ and resulted in a four-month bisphosphonate free interval after surgery. My current recommendation and practice to pause the administration of bisphosphonates about four to six weeks prior to the operation and restore this treatment when clear signs of bone healing can be picked up on the follow-up radiographs is based on new findings with a different bisphosphonate.³⁵ Some children, in the majority the older ones, may show a lack of osteotomy healing and develop a pseudarthrosis. It occurs more frequently at the tibia than at the other long bones (Fig. 6). The revision is only indicated if the patient reports related symptoms, or if the implant fails and breaks.³⁶

The revision rates of telescopic nails in OI patients have been reported to be as high as 45% to 50% in femoral rodding and 50% in the tibia.^{25,28,30} In the humerus a revision rate of 34% to 57% was recorded.^{15,29} With the improvement of the implants and implication of more advanced surgical techniques the complication and reoperation rates are thought to be less. The reality, however, is that with the improvement of the global medical care in those patients, the activity levels rise. Consequently, this leads to increasing forces on the bones and implants with higher

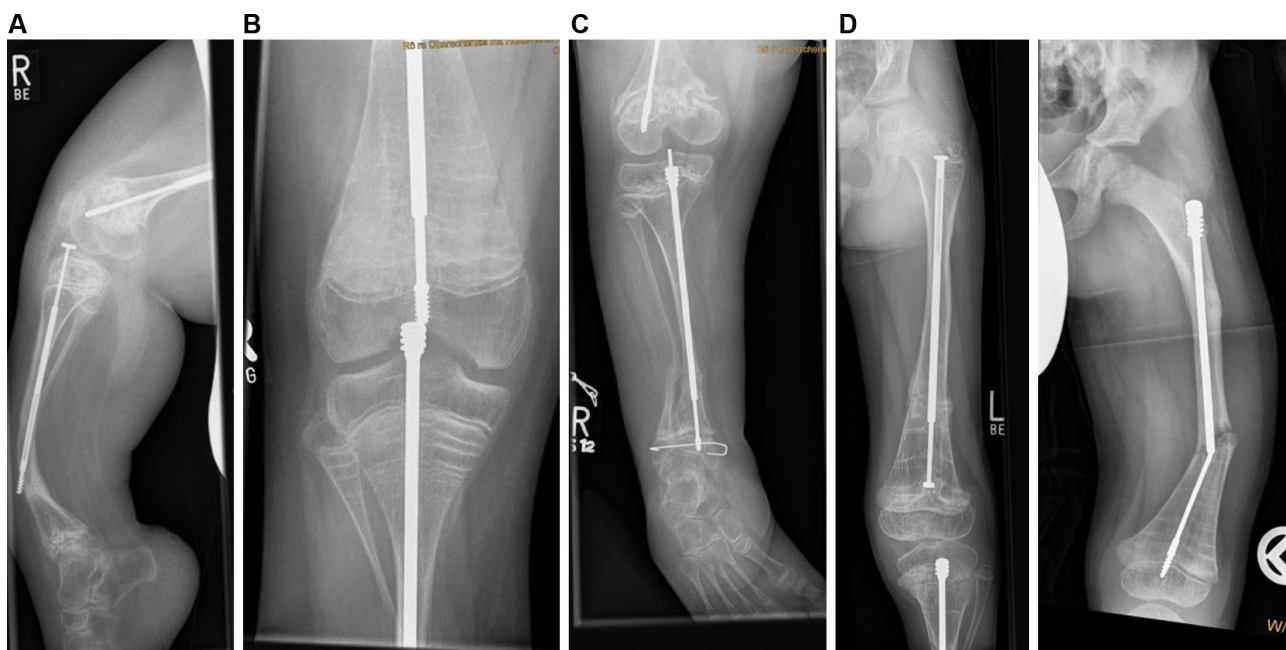


Fig. 5 Typical complications after insertion of telescopic nails for deformity correction in soft bones: loss of distal (a) and proximal (b) fixation, to be avoided by distal wire locking technique (c). Jammed sliding mechanism (d) and bent nail after a fall (e).

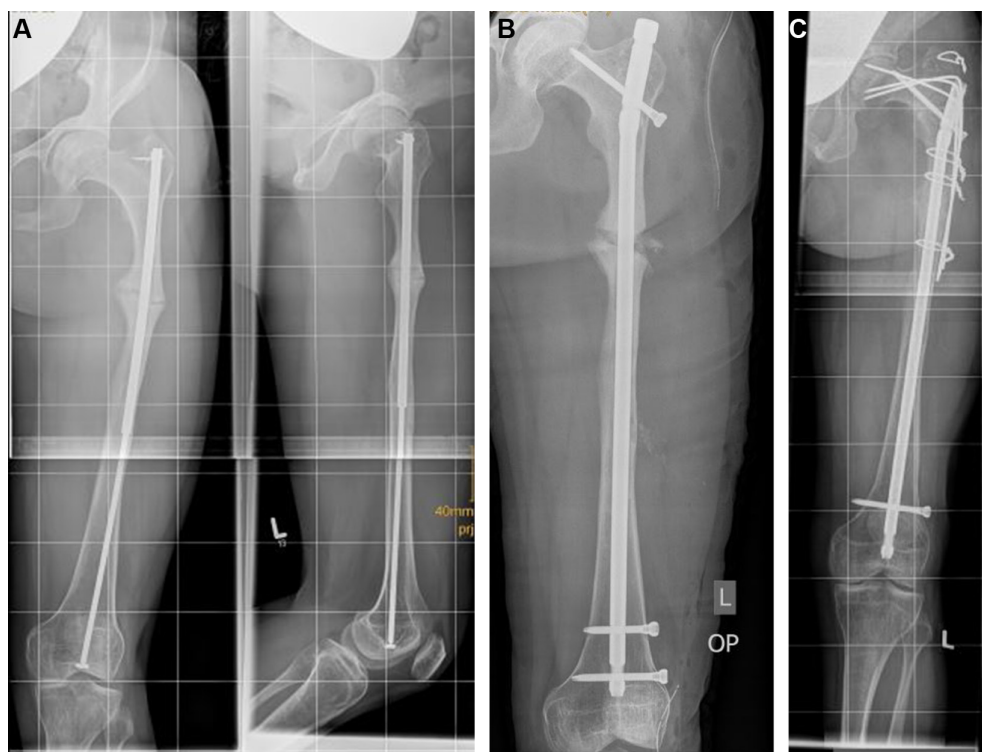


Fig. 6 Symptomatic pseudarthrosis in a young adult osteogenesis imperfecta patients (a). Surgical correction and stabilization with an interlocking gamma nail (b). Healed pseudarthrosis after numerous revisions (c).

Table 2 Comparison of lower limb revision rates of different studies using telescoping nails

Study	Patients (n)	Primary rod insertions (n)	Mean follow-up (yrs)	Implant	Complication rate (femur) (%)	Complication rate (tibia) (%)	Revision rate (femur) (%)	Revision rate (tibia) (%)
Karbowski et al 2000 ²⁹	63	186	5.6	Bailey-Dubow	21	52.1	17.8	29.6
Nicolaou et al 2011 ³⁰	22	66	19	Sheffield rod	50 (no specification)	50 (no specification)	50 (no specification)	50 (no specification)
Rosemberg et al 2018 ²⁵	21	52	9.96	TIR Sao Paulo	50	n/a	50	n/a
Shin et al 2018 ²⁷	17/17	29/26	5.3/9.6	Single/dual interlocking telescoping rod	n/a	81/54	n/a	n/a
Birke et al 2011 ³¹	15	24	1 to 2.4	Fassier-Duval	40	40	13	13
Azzam et al 2018 ²⁸	58	179	5	Fassier-Duval	45	34	45	34

TIR, telescopic intramedullary rod

rates of implant failure. In my experience the overall revision rate has, therefore, not changed. Not surprisingly, short-term follow-up series report much better results than mid-term and long-term outcome studies (Table 2).

Functional outcome

The three principal treatment modalities for patients with OI, bisphosphonates, physical rehabilitation programmes and orthopaedic surgery, have been reported to improve

the functional status of almost all of these children. The gain of functional abilities with regards to walking, transfer and individual household mobility is related to the severity of the disease. Type III OI patients do not benefit from this therapy as much as type IV patients do.³⁷ Both parents of and patients with severely affected OI diagnosis take a long and often painful time to adapt to their life, but they do experience positive moments, which may be directly related to functional improvement.³⁸ At one year after femoral rodding of a group of patients, who were also treated with bisphosphonates, a significant improvement was

noticed in range of movement of hip and knee joints and in the Functional Ability Questionnaire Score.³² Crawling, standing, walking and running as well as all domains of the Gross Motor Function Measure and the Pediatric Evaluation of Disability Inventory mobility and self-care scores changed considerably in favour of functionality. Greater severity of the disease and body weight were negative predictors for a more favourable outcome of this type of surgery.³² The lesser improvement of function in OI type III patients has prompted the idea of focusing on the upper extremity being vital for mastering daily activities and self-care in the severely affected individuals. Upper extremity surgery was found to be very beneficial to them.³⁹ The greater the deformity the more disabling and functionally impairing the clinical implication was.⁴ The great benefit of upper limb surgery could be proven to be significant as well as the sustainable improvement of the self-care and mobility scores tested by the Pediatric Evaluation of Disability Inventory.^{40,41}

Discussion

Surgical stabilization and deformity correction of weak bones, regardless of the underlying disease has become the main stake in all recently published consensus statements on their treatment, particularly true for OI.^{42,43} The lower limb has been the focus of surgical interventions since the beginning in order to allow the patients to stand and walk on stable lower extremities. The choice of implant was always in favour of intramedullary devices. Although double Rush rods in the femur and single Rush rods in the tibia were identified to yield comparable results with telescoping rods,²³ telescopic nails became the standard implant. The Bailey-Dubow, Sheffield, Fassier-Duval and other rods have clearly set aside other intramedullary devices.^{11,17,27,30} Only in very small bones that cannot accommodate telescoping rods or specific anatomic locations like the forearm are K-wires and small Rush rods needed. Larger long bones, mostly found in adolescent patients with mild OI or fibrous dysplasia and hypophosphataemic rickets, are predisposed to small interlocking nails.^{13,20}

The timing of the procedures should be individually planned and discussed with the patients. When it is evident that corrective surgery for both the lower and upper limb is inevitable, a time plan should be set up with the parents. A one leg at a time approach may be a very useful tactic to deal with the problem in a reasonable time period. This includes a detailed and individually tailored postoperative rehabilitation programme, to minimize the immobilization period.⁴³ Depending on the size of the bone and the overall condition of the child, surgery can be scheduled as early as the second year of life. Upper limb surgery has come into focus more and more in recent

years¹⁵ on the same principal approach as in the lower extremities and a considerably older age at surgery. The outcomes are very promising.^{15,39-41}

In all the years, despite improved surgical techniques and more sophisticated implants, the overall complication and reoperation rate has not changed a lot.^{25,27-29,31} The causes of failure have not changed either: distal and proximal rod migration, jamming of the telescoping mechanism, bending rods due to the operating mechanical and muscular forces and technical issues with the operation.^{25,27-29,31} Most of these problems are caused by the weak bones; the disease itself. Despite of all these negative points the overall activity level of our patients with weak bones has clearly improved. Mildly affected patients can lead an almost normal life, including participation in sports activities. Severely affected patients can manage transfer and short distance walks in their homes by themselves and have reached a greater degree of independence. They accept the high revision rate, because they know that they gain mobility and quality of life.

Received 12 November 2018; accepted 30 November 2018.

COMPLIANCE WITH ETHICAL STANDARDS

FUNDING STATEMENT

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

OA LICENCE TEXT

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ETHICAL STATEMENT

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent: Not required for this work.

ICMJE CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest.

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