

The Use of Kirschner Wire Intramedullary in Pediatric Femur Fractures with Osteogenesis Imperfecta

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ABSTRACT

BACKGROUND: Surgical treatment for osteogenesis imperfecta (OI) remains controversial. The use of nonelongating rods is considered to be the classic method. This older method is still used by surgeons who are concerned about the possibility of trauma or who are working in developing countries with fewer resources. We are among those who prefer the use of Kirschner wire (K-W). This article presents the results of intramedullary fixation using K-W and Bisphosphonate treatment in children with OI and the proper timing of wire exchange to prevent further fracture.

METHODS: We treated 29 femora in 24 patients with OI by means of stabilization using K-W. The patients divided two Variant: (1)

Variant 1: femoral fractures fixed by K-W only (10 patients); (2) Variant 2: femoral fractures fixed by K-W and combined treated with bisphosphonates (14 patients). Sillence classification of OI with 4 Types and the features: Type I: Osseous fragility, Adulthood hearing loss, Blue sclera; Type II: Extremely severe osseous fragility, Perinatally lethal; Type III: Moderate to severe osseous fragility, Normal sclera, Severe deformity of the long bones and spine, Variable clinical and radiographic phenotypes; Type IV: Osseous fragility, General normal sclera, Severe deformity of long bones and spine. Our Surgical treatment for acute fracture and for angular deformity correction if present on patients with OI is based on the classic Sofield-Millar technique, evaluating treatment according to El Sobky.

RESULTS: Indications for the primary surgery included: fracture were 4 fracture only, and Fracture and deform were 25. There were 24 Patients, Right/left/Bilateral fracture femur in 12/7/5; Total fracture femur 29. There were 45.8% in Type 1, 33.4% in Type 3, and 20.8% in Type 4. The male to female ratio was 1: 1.7. There were 5 (20.8%) patients with family history. The mean age at the primary procedure for K-W was 27.9 months old (range, 18-43 months old). The mean follow-up period was 75.5 months (range, 62 months to 89 months). In this study, Variant 2 (accepted was 57.1%) better than Variant 1 (accepted was 20%).

CONCLUSIONS: Documented that children treated with Bisphosphonate prior to surgery and afterwards do better than children treated with surgery alone. We suggested that a surgical treatment using non-extensible nails is indicated when complications such as fractures and/ or deformities are present, based on the fact that these nails do not follow bone growth, if early implanted, complications will eventually occur, resulting in a larger number of review surgeries.

Key words: Osteogenesis imperfect; Nonelongating rod; Atypical femoral fractures; Bisphosphonates; Pamidronate; Proximal migration

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INTRODUCTION

Osteogenesis imperfecta, according to Melebranche, in 1684, Ekman, in 1788, Lobstein, in 1834, Vrolick, in 1845, and Porak-Durante, in 1905 and Correa *et al*^[1] was described as a syndrome caused by a change on the connective tissue involving type-I collagen, which is the organic component of the bone. However, with the recent DNA studies, it was proven that many patients with Osteogenesis Imperfecta did not show changes on the genes codifying collagen production^[2]. Today, the concept has been broadened, being defined as a syndrome caused by a genetic change and with variable complexity levels. Diagnosis is pretty much provided by clinical examination and X-ray tests. The classification by Sillence^[3], published in 1979, has been employed for grouping these patients.

The orthopaedic treatment, both for fractures and for deformities correction, which consists of corrective osteotomy and stabilization of those bones, using several kinds of implant materials for osteosynthesis has been used by a number of authors^[2]. Osteosynthesis can be made with fixed or non extensible nails, which may present complications due to bone growth, such as nail protrusion through cortical, with recurrence of deformity, and extensible nails with different fixation techniques on the epiphyseal region of the long bones, targeting nail stretching as the bone grows, thus avoiding complications and reducing the required time between procedures.

Surgical treatment for children with osteogenesis im-perfecta (OI) has changed in the past half century, but there is still no standard treatment. In 1959, Sofield and Millar^[4] introduced corrective osteotomies and intramedullary fixation with a nonelongating rod. Then elongating rod was invented by Bailey and Dubow^[5] to resolve problems that arose with the nonelongating rod, namely the need for frequent rod exchanges due to the patient's growth and the fixed length of the rod. The elongating rod has undergone some improvements and is presently becoming a mainstay for the treatment. In addition, a study by Cho *et al*^[6] provided useful tips for obtaining better results with the elongating rod.

In reality, none elongating rods such as K-W or Rush pins have also been used by surgeons who are concerned about the possibility of trauma on the articular surface at the insertion of the elongating rod or who are working in developing countries with fewer resources^[7,8].

Osteogenesis imperfecta (OI) is an inherited bone and connective tissue disorder caused by defect in type I collagen synthesis and function. More than 200 mutations have so far been identified in the COL1A1 and COL1A2 genes^[9]. Bisphosphonates (BP) are now considered the standard of care in the medical treatment of children with OI.2. Cyclic administration of pamidronate has been shown to increase bone mineral density; however, this has not been consistently translated into decreased fracture risk^[9].

Long-term consequences of BP treatment in young children during the growing years are not known yet^[10]. Complications such as osteopetrosis from osteoclast suppression have been reported in children^[11]. Other reported complications with prolonged treatment in postmenopausal women include osteonecrosis of the jaw^[12] and the risk of atypical femoral fractures, likely caused by suppression of remodeling^[13]. Recently, there are increasing concerns about the adverse effects of long term suppression of bone remodeling and its contribution to micro damage accumulation and increased bone fragility^[14]. This may be particularly important in children with growing bones because BP remain bound to their skeleton for many years following discontinuation^[15].

The American Society of Bone and Mineral Research (ASBMR)

has recently published 2 consensus reports to define the criteria used for diagnosis of atypical femoral fractures with BP treatment^[16]. A description of a change in femoral fracture location, with more proximal third fractures in BP treated children, has also been recently published^[17].

The objective of this study evaluating results and clarify the features of intramedullary fixation using K-wires and long time consequence of Bisphosphonate treatment in children with OI.

MATERIALS AND METHODS

A retrospective study was carried out to evaluate the results of surgical techniques performed from December 2001 to August 2012 in 24 patients (29 femurs) with femoral fractures in Children with osteogenesis imperfecta. The operations were performed by single surgeon (Author).

The study had the approval of the Ethical Review Committee of our Institute and was carried out in accordance with the tenets of the Declaration of Helsinki.

Medical files and X-ray images of all patients with femoral fractures and Osteogenesis Imperfecta submitted to bone realignment with fixed (non-extensible) intramedullary nails on femurs by (K-W) were reviewed at the National Hospital for Pediatrics, between 2001 and 2012. Thirty-one patients were treated according to this procedure. Of these, five were excluded due to a postoperative follow-up inferior to five years, remain twenty-four patients in this study.

Patients with femoral fractures associated ipsilateral or contralateral tibial fractures, pathological fractures, neuromuscular disease and metabolic bone disease were excluded.

There were 24 Patients, Right/left/Bilateral fracture femur in 12/7/5; Total fracture femur 29 (see Table 1). The average age for primary surgery was 27.4 months old (range, 18-43). The average follow-up period was 75.5 months (range, 62-89 months). Mean Healing time 14.7 weeks (range, 12-16 weeks). 14 patients received bisphosphonate treatment. The indication for primary surgery was recurrent femoral fracture with or without associated deformity, and the indication for revision surgery was a fracture with a bent or cutout wire, or a displaced fracture.

All fractures were analyzed in detail, that is, fracture site, treatment, complications, and wire length ratio.

The 24 remaining patients (fifteen boys and nine girls) were classified according to the criteria described by Sillence^[3]. Type I (11); Type III (8); Type IV (5). (Table 2).

Type I is the most prevalent form, including the milder bone weakness forms, with few fractures, no significant deformities and with normal height. We had eight patients, seven of which in IA, with normal dentinogenesis, and one patient in IB com dentinogenesis imperfecta. Type II includes the most life threatening kind, with a significant incidence of death at birth, with serious bone weakness, in which a number of intrauterine and delivery fractures can occur. Death usually occurs during delivery or on the first days after birth. We had no patients included in this group. Type III includes classic cases showing significant bone weakness and deformity; the patients are usually short and show dentinogenesis imperfecta. We had four patients included in this group. Type IV includes patients with bone weakness, normal sclera, and skeletal deformity with short heights, which is subdivided into IVA with normal dentinogenesis and IVB, with dentinogenesis imperfecta.

Demographic details were recorded, including the age of the patients, the gender, mechanism of injury, weight at the time of

surgery and the time between injury and operation. We assumed that the patients did not have a preoperative leg length discrepancy because their guardians did not inform us of this.

Height was measured with a Harpenden stadiometer when patients were able to stand. Children unable to stand were measured in the supine position after gentle traction was applied. In cases of leg length discrepancy or contractures, the longest leg was used for measurements. Weight was measured using digital electronic scales for infants and mechanic scales for children and adolescents.

The patients divided two Variant: (1) Variant 1: femoral fractures fixed by Kirschner wire only in 10 patients with 12 femoral fractures; (2) Variant 2: femoral fractures fixed by Kirschner wire and combined treated with bisphosphonates in 14 patients with 17 femoral fractures.

All patients were available for follow-up, and underwent physical examination and radiographic assessment at follow-ups every 6 to 12 months. Immediate postoperative radiographs served as the baseline against which all subsequent radiographs were compared.

The purpose of the index surgery was recorded whether it was performed for internal fixation of an acute fracture and for angular deformity correction if present.

Angular deformity of the femur was defined as a line connecting the center of intramedullary cavity at the lesser trochanter and at the distal physis levels overlapped with or crossed the diaphyseal cortices, on either anteroposterior or lateral projections of radiographs. Optimal position of the K-W at the distal physis was defined as the middle one third of width on radiographs of both anteroposterior and lateral, projection had femoral bowing greater than 20°^[18].

All the patients had multiple fractures before surgery average 3.2 times (range 1-5 times) (see Table 3).

Preoperative physical examination was done and radiographs taken to precisely measure the shaft length and the degree of deformity and to map out the exact size of the bone wedge to be removed. The operation was done under an epidural anesthesia or general anesthesia. The patient was positioned on the fracture table to allow use of a C-arm machine.

Operative technique

Our Surgical treatment for acute fracture and for angular deformity correction if present on patients with OI is based on the classic Sofield-Millar technique, described in 1959^[4] and modified technique by Williams^[19] consists of multiple osteotomies of the bowed long bones if bowing bone more 20 degree followed by intramedullary K-W. The bone was exposed subperiosteally, either directly at the convexity of the bone or through the appropriate surgical anatomical planes. The curved part of the shaft was cut with a bone cutter or oscillating saw into several fragments to achieve correction. Williams recommended that it was better to err on the side of too many osteotomies than too few. Each fragment must be sufficiently straight to allow passage of the rod. An intramedullary nail of the largest possible diameter was then passed through the fragments. The middiaphyseal portion was sometimes sclerotic and required reaming. A rod was passed retrogradely as a guide through the proximal fragment and then an intramedullary nail of the correct length was inserted antegrade through all the osteotomised fragments. K-W was used in our series depending on the size of the intramedullary canal. If severe bowing was present, the bone was shortened to reduce the soft tissue tension. The distal end of the rod was positioned centrally in the bone. The periosteum was then closed if possible. A cast was applied after operation in most patients.

Modified Sofield-Millar operation in the femur. The patient was

placed in a supine position with the operative side elevated by a sandbag. An image intensifier was used to guide the entry of the nail and to monitor the progress of the osteotomies. The tip of the greater trochanter was exposed and reamed as for closed insertion of an intramedullary nail. A reamer of the same size as the femoral canal was inserted through the greater trochanter. The progress of the reamer stopped at the first site of angulation of the femur which was confirmed using the image intensifier. Here, a small lateral incision, about 2 cm in length, was made to expose a small portion of the femur. The periosteum was incised longitudinally, elevated and protected. A small lateral wedge of bone was removed to correct the angulation using a bone cutter or oscillating saw. The medial cortex was left intact to provide stability. The deformity was then reduced and the nail advanced more distally. Usually a second block then occurred and the same procedure was repeated. Normally, two osteotomies were sufficient to correct the deformity and to allow the nail to be passed through to the condylar region.

Occasionally, a third osteotomy was necessary. Ideally, the end of the K-W should be in the middle of the femoral condyles. The periosteum was sutured if possible, the wound closed and a hip spica applied. Immobilisation in plaster was limited to eight weeks and the patient was allowed to bear weight as soon as possible.

The use of an image intensifier allowed us to identify the most suitable sites for the osteotomies and to keep their number to a minimum. Exposure can be direct with short incisions minimising surgical trauma.

Postoperative examinations included a careful assessment of knee motion, limb length inequality, limb rotation and alignment, and signs of irritation from the K-W tip.

Post-operative management

Following femoral intramedullary, the limb was immobilized in a single hip spica cast, a groin-to-toe cast was applied. The casts were retained for 8 weeks, after which gentle non weight bearing mobilization exercises were begun. Weight bearing was permitted after sound union of all the fracture and osteotomy sites.

The possible complications K-W are the following: migration, fractures on K-W, lesions of the growth plates, bending of the rod, rotation disorders of the operated segment, infections.

Radiographs

The pre-operative anteroposterior (AP) and lateral radiographs of the injured femur were reviewed to determine the characteristics of the fractures, The location of the fracture was classified as proximal, middle or distal, third.

Post-operative radiographs were analysed for angulation, delayed union, shortening at the fracture site or changes in the position of the nails. Union was determined by bridging callus across four cortices. For the evaluation of femoral overgrowth and leg length discrepancy, scanograms were taken at the last follow-up.

In order to evaluate the risk factors for femoral over-growth, we divided our patients into those with femoral overgrowth of < 1 cm or ≥ 1 cm on the final scanograms, according to Flynn's guidelines^[20].

Usually radiographs were taken both in the anterior-posterior and lateral views with the patient in the standing or in the supine position. Unless requested otherwise by the treating physician, femora and tibiae were included on a single cassette (lower-extremity radiograph).

Radiographs were evaluated for alignment, callus formation, and change in K-W position. Scanograms were performed if a clinically significant leg length inequality was noted on physical examination.

Cases were followed up to their clinical end point of fracture union and return to full activity, typically several months after nail removal (i.e., about 1 year after implantation).

Medical threat

Pamidronate therapy before operation delivered 1 mg/kg/day in 250–500 ml of normal saline administered over 8 h for three consecutive days and repeated at 3–4-monthly intervals [21]. Younger patients were started on pamidronate treatment at a dose ranging from 1.5 to 3.0 mg/kg per treatment cycle. Dose and interval depended on age, leading to an annual dose of 9 mg/kg/y for all subjects. Older children received alendronate at a single daily dose of 5 mg for subjects 30 kg and under or 10 mg for subjects above 30 kg. Time during treatment before surgery and side effects were documented for the purposes of the study. Orthopaedic surgery was performed based on the needs of each child, and therefore the time under treatment before surgery varied widely. Surgery was chosen based on the occurrence of acute fractures requiring intervention, or elective surgery because of significant functional deficit due to deformity and established a limit of 6 months as a definition of delayed fracture healing.

Evaluate result according to El Sobk *et al* [22] scoring system, a grade of excellent was given to results above 15 points, good between 11 and 15 points, fair between 6 and 10 points while grading was poor if the score was 5 points or less.

1 Ambulation:

- Walking without aid 5 Points
- Use of frames or crutches 3 Points
- Wheelchair bound 1 Point
- Recumbent 0 Point

2. Activities:

- Regula employee of student, 3 Points
- Appointed as handicapped or at special school, 2 Points
- Home activities, 1 Points
- No activities and need full-time care, 0 Point

3. Clinical deformities:

- No deformities, 3 Points
- Deformity in one limb, 2 Points
- Deformities in two limbs, 1 Point
- Deformities in more than two limbs, 0 Point

4. Incidence of revision surgery in one segment:

- No revision with regular follow-up, 3 Points
- Less than two revision surgeries with regular follow-up, 2 Points
- Two to four revisions with regular follow-up, 1 Point
- More than four revisions or no regular follow-up, 0 Point

5. Limb length discrepancy:

- No limb length discrepancy, 3 Points
- Less than 2 cm shortening, 2 Points
- 2-4 cm shortening, 1 Point
- More than 4 cm shortening, 0 Point

6. Subjective evaluation:

- Better than before surgery, 3 Points
- Improved after surgery but deteriorated later, 2 Points
- The same, 1 Point
- Worse, 0 Point

Statistical Analysis

The paired-samples t-test was used for comparison between the pre-operative and the final ROM of the knee. Univariate regression analysis was performed to determine whether there was a significant association between each of the pre-operative and operation-related variables and the final gain in flexion. All analyses were performed with SPSS, version 12.0 (SPSS Inc., Chicago, Illinois) and a *p*-value

Table 1 Distribution of the operated cases with regard to sex.

	Variant 1				Variant 2			
	No of Patients	Right	Left	Bilateral	No of Patients	Right	Left	Bilateral
Male	6	3	2	1	9	4	3	2
Female	4	2	1	1	5	3	1	1
Total	10	5	3	2	14	7	4	3

In the Variant 1: There were 10 Patients, Right/left/Bilateral fracture femur in 5/3/2; Total fracture femur 12; In the Variant 2: There were 14 Patients; Right/left/Bilateral fracture femur in 7/4/3; Total fracture femur 17. Total Right 12, Left 7, and Bilateral 5.

Table 2 Number and percentage of different Types and sex.

Type of Patients	Variant 1			Variant 2		
	Male	Female	Total (%)	Male	Female	Total (%)
Type I	3	2	5 (50%)	4	2	6 (42.9%)
Type III	2	1	3 (30%)	3	2	5 (35.7%)
Type IV	1	1	2 (20%)	2	1	3 (21.4%)
Total	6	4	10 (100%)	9	5	14 (100%)

In the Variant 1: There were Male 6 and Female 4; Type I: 5, Type III: 3, and Type IV: 2 In the Variant 2: There were Male 9 and Female 5; Type I: 6, Type III: 5, and Type IV: 3. Total Male 15, Female 9. Type I: 11 (45.8%), Type III: 8 (33.4%), Type IV: 5 (20.8%).

Table 3A Different Type of Variant 1 related Family history and Age at first fracture (months).

Patients	Sex	Type	Family history	Age at first fracture (months)	Previous fracture
1	M	I	No	36	4
2	M	III+III	No	16	2+1
3	F	III	Yes	12	2
4	M	I+I	No	20+22	4+3
5	F	I	No	18	3
6	F	IV	No	12	1
7	M	IV	No	24	4
8	F	I	No	14	2
9	M	I	Yes	19	5
10	M	III	No	24	4

In the Variant 1: There were mean fractures: 3 time (range, 1-5 time); Age at first fracture (months) mean 18 (range, 12-36); There were 2 patients with family history.

<0.05 was considered significant.

RESULT

Indications for the primary surgery included: fracture were 4 fractures only, and Fracture and deform were 25. The mean age at the primary procedure for K-W was 27.9 months old (range, 18-43 months old). The mean follow-up period was 75.5 months (range, 62 months to 89 months).

There were 2 fixation by K-W only for Subtrochanteric fracture; remaining 10 femoral fracture combined Kirschner and Osteotomy; There were 2 fixation by Kirschner only for Subtrochanteric fracture; remaining 10 femoral fracture combined K-W and Osteotomy. Mean healing time: 15.3 months (range, 12-18); mean bending angle: 46.5° (range, 23-62); Fracture level with Subtrochanteric: 2 and Mid-shaft: 10; Fracture pattern with Short Oblique: 3 and transverse: 9. Mean surgical age 27.4 months (range, 20-43). Mean Healing time 15.3 weeks (range, 12-16 weeks). Mean follow-up 77.6 months (range, 68-89 months).

There were 2 fixation by Kirschner only for Subtrochanteric fracture; remaining 15 femoral fracture combined K-W and

Osteotomy; mean healing time: 14.1 months (range, 12-16); mean bending angle: 47.2° (range, 22-60); Frature level with Subtrochanteric: 2 and Mid-shaft: 15; Fracture pattern with Short Oblique: 4 and transverse: 13. Mean surgical age 28.4 months (range, 18-35). Mean Healing time 14.1 weeks (range, 12-16 weeks). Mean follow-up 73.3 months (range, 62-85 months).

All of these fractures were transverse or short oblique, located in the mid – three or subtrochanteric area. All patients with atypical fractures presented with acute pain on the day of pain onset or within a few days.

The total number of recurrent fractures that occurred after primary surgery was 9 of 29 femora (31.0%), six recurrent fractures (20.7%) occurred at the wire site, two of them (16.7%) at the wire tip, and one of them (8.3%) at a non wire site. Proximal migration of the K-W 50.0% in Variant 1, 17.7 in variant 2 (*P* Value: 0.123363).

Mean Time of fractures at previous osteotomy were 16.3 months (range, 10-23) in Variant1, and 19.6 months (range, 16-24) in Variant 2. The recurrent fractures were at the same place as the previous osteotomy in Variant 1: Proximal/Mid/Distal –three were 8.3%/25.0%/0%, in Variant 2 in Proximal/Mid/Distal –three were 0/17.6%/0%. Mean Time of fractures at previous osteotomy were 17 months (range, 10-24). The seven recurrent fractures were at the same place as the previous osteotomy. The recurrent fractures were at the same place as the previous osteotomy 40% in Variant 1, 20.0% in

Table 3B Different Type of Variant 2 related Family history and Age at first fracture (months).

Patients	Sex	Type	Family history	Age at first fracture (months)	Previous fracture	Receiving Bisphosphonate (months)
1	M	I+I	No	32+38	5+4	22
2	F	I	No	19	3	21
3	M	I	Yes	15	3	17
4	M	III	No	24	4	28
5	F	III+III	No	22+26	2+4	26
6	M	I	No	17	2	16
7	M	III	No	26	5	20
8	M	IV	No	18	3	18
9	F	IV	Yes	16	4	14
10	M	IV	Yes	24	3	25
11	M	I+I	No	20+24	3+4	21
12	F	I	No	24	2	22
13	F	III	No	34	4	29
14	M	III	No	42	3	32

In the Variant 2: There were mean fractures: 3.4 (range, 2-5); Age at first fracture (months) mean 24.8 (range, 15-42); There were 3 patients with family history; All patients in the Variant 2, they had surgery immediately before the start of operative treatment. Corrective orthopaedic surgery was performed after a mean of 23.6 months under treatment.

Table 4 A Different fracture pattern, level, Bending angle and Operative approach in Variant 1.

Patients	Fracture pattern	Fracture Level	Bending angle (°)	Surgical age (m)	Operative Approachs	Healing time (w)	Follow up (m)
1	Short Oblique	Mid-shaft	62	32	KW+ 2 Ost.	14	68
2	Transverse	Mid-shaft+	53+	28+	KW+2 Ost.	16+17	70
		Mid-shaft	55	29	KW+2 Ost.		
3	Transverse	Subtrochanteric	25	22	KW	15	76
4	Transverse	Mid-shaft+	48+	42+	KW+Ost.	15+14	78
		Mid-shaft	48	43	KW+Ost.		
5	Transverse	Mid-shaft	46	24	KW+Ost.	16	78
6	Transverse	Mid-shaft	39	16	KW+Ost.	14	73
7	Short Oblique	Mid-shaft	42	18	KW+Ost.	12	82
8	Transverse	Mid-shaft	61	20	KW+ 2 Ost.	17	89
9	Transverse	Subtrochanteric	23	26	KW	16	77
10	Short Oblique	Mid-shaft	56	29	KW+2 Ost.	18	85

KW+Ost.: Kirschner and Osteotomy; KW+ 2 Ost: Kirschner and 2 Osteotomy site.

Table 4 B Different fracture pattern, level, Bending angle and Operative approach in Variant 2.

Patients	Fracture pattern	Fracture Level	Bending angle (°)	Surgical age (m)	Operative Approachs	Healing time (W)	Followup (m)
1	Transverse	Mid-shaft+	53+	29+	KW+ 2 Ost.	13+14	79
		Mid-shaft	53	30	KW+ 2 Ost		
2	Short Oblique	Mid-shaft	54	28	KW+2 Ost.	15	76
3	Transverse	Mid-shaft	50	33	KW+ 2 Ost.	16	78
4	Transverse	Mid-shaft	45	26	KW+Ost.	14+15	69
5	Transverse	Mid-shaft+	45+	18+	KW+Ost.	12+12	68
		Mid-shaft	44	19	KW+Ost		
6	Transverse	Mid-shaft	32	34	KW+Ost.	13	78
7	Short Oblique	Subtrochanteric	25	31	KW	12	71
8	Transverse	Mid-shaft	56	29	KW+ 2 Ost.	13	76
9	Transverse	Subtrochanteric	22	22	KW	12	85
10	Short Oblique	Mid-shaft	52	34	KW+2 Ost.	14	79
11	Transverse	Mid-shaft+	45+	34+	KW+Ost.	13+13	73
		Mid-shaft	45	35	KW+Ost		
12	Transverse	Mid-shaft	42	28	KW+Ost.	12	68
13	Transverse	Mid-shaft	60	26	KW+ 2 Ost.	13	62
14	Short Oblique	Mid-shaft	34	26	KW+Ost.	13	64

KW+Ost.: Kirschner and Osteotomy; KW+ 2 Ost: Kirschner and 2 Osteotomy site.

Variant 2 (*P* Value 0.524471).

Of the 29 femora included in the analysis, 9 femora showed proximal K-W migration during the follow-up period. Mean time interval from index operation to proximal migration was 14.6 months (range, 5.6 to 34.6 mo). None of the cases show any evidence of avascular necrosis of the femoral head.

All the surgical wounds healed with primary intention. Neurovascular complications or infections did not occur in any patient. All the patients healed well, with an average healing time of 14 weeks (range 12-16 weeks) and the callus gray density increased with the passing of time. After surgery, the deformity and mobility significantly improved.

Concerning operative complications with the use of K-W was none of the patients was submitted to blood transfusion. Osteotomies showed an union rate of 100%. In the present study, the procedure has been shown not to interfere with physis, because we had no patient with physeal changes. We didn't find growth disorders inherent to the adopted procedure. No postoperative infection case was found.

DISCUSSION

Osteogenesis imperfecta occurs about once in every 10.000 births worldwide. Most cases of osteogenesis imperfecta are caused by autosomal dominant defect. Some children inherit the disorder from a parent. Other children are born with osteogenesis imperfecta even though there is no family history of the disorder. In these children, the genetic defect occurred as a spontaneous mutation^[23].

Although there is considerable variability in bone fragility and fracture frequency within the same type of Sillence classification^[3], we adopted this system to categorize patients according to disease severity type I as mild, type IV as moderate, and type III as severe. Proximal migration seems to be associated with moderate to severe disease.

Our patients were classified according to the Classification by Sillence^[3], which, in spite of not presenting clearness between groups, was the way we found to differentiate and evaluate our patients. Our series encompassed types I, III and IV of the classification by Sillence^[3]. In this study, 45.8% in Type 1, 33.4% in Type 3, and 20.8% in Type 4 (see Table 1).

The clinical evaluation of patients in our study revealed that In the Variant 1: There were 10 Patients, Right/left/Bilateral fracture femur in 5/3/2; and in the Variant 2: There were 14 Patients; Right/left/ Bilateral fracture femur in 7/4/3 (see Table 1). The male to female ratio was 1: 1.7 (see Table 2), which is identical to the ratio in the Daly *et al*^[24], King and Bobecko^[25] and Khoshal and Ellis^[26] series while it was 1: 2 in the Hanscom *et al*^[27] and Li *et al*^[28] series. In other series the ratio was different; it was 1: 5 in the study by Gamble *et al*^[29] and 1: 4 in the study by Mulpuri and Joseph^[30]. We cannot correlate the incidence of osteogenesis imperfecta to sex according to the different incidence in the literature.

Positive family history was presented in 20.8% of patients in our study (see Table 3). This was 37%, almost the same, in the Yong Hing and Mac Ewen^[31] series and 43% in the Li *et al*^[14] series.

Nicolaou *et al*^[17] suggest that combined surgical and medical treatment should be started at the age of 1-2 years (age of walking) or once progressive deformity appears, especially in types III and IV, to help them pull themselves up to a standing position and to break the cycle of fracture osteoporosis refracturel. Now, our protocol is to give bisphosphonate for at least four cycles prior to surgery if the patient presents early, as this improves the final outcome. In this study, corrective orthopaedic surgery was performed after a mean of 22.2 months under treatment (see Table 3B) and surgical age mean 27.9

Table 5 Assessment was carried out according to the El Sobky *et al*^[2].

	Excellent (%)	Good (%)	Fair (%)	Poor (%)
Variant 1		2	5	3
n=10		20	50	30
Variant 2	5	3	5	1
n=14	35.7	21.4	35.7	7.2

In the Variant 1: Good result 2 (20%), Fair 5 (50.0%), and Poor 3 (30%); ccepted 2 (20%). In the Variant 2: Excellent 5 (35.7%), Good 3 (21.4%), Fair 5 (35.7%), and Poor 1 (7.2%). Accept 8 (57.1%).

Table 6 Complications of the Kirschner wire and fracture site.

	Variant 1 (n=12) (%)	Variant 2 (n=17) (%)	Total (n=29) (%)	Mean Time Recurrent fractures
Proximal Migration of the K-W	2; 16.7	1; 5.9	3; 10.3	15 mo.; (range 11 - 16)
Bent wire at fracture	2; 16.7	1; 5.9	3; 10.3	18 mo.; (range 13 - 20)
Proximal Migration of the K-W and wire tip fracture	1; 8.3	1; 5.9	2; 6.9	15 mo.; (range 14 - 16)
Wire breakage at fracture	1; 8.3	0	1; 3.5	20 mo.
Total	6; 50.0	3; 17.7	9; 31.0	17 mo.; (range 14 - 20)

Proximal Migration of the K-W: 3 (10.3%), Bent wire at fracture 3 (10.3%), Proximal Migration of the K-W and wire tip fracture 2 (6.9%), and Wire breakage at fracture: 1 (3.5%). Total Proximal Migration of the K-W 9 of 29 (31.1%). Mean Time Recurrent fractures were 17 months (range 14 - 20).

Table 7 The recurrent fractures were at the same place as the previous osteotomy.

	Recurrent Fracture site			Total	Mean Time fractures at previous osteo*.
	Proximal-three (%)	Mid-three (%)	Distal-three (%)		
Variant 1	1	3	0	4	16.3 mo.
n = 10	10	30		40	(range, 10-23)
Variant 2		3		3	19.6 mo.
n = 15		15		20	(range, 16-24)
Total	1	6	0	7	17 mo.
n = 25	3.4	24	0	28	(range, 10-24)

There were 10 in Variant 1 and 15 Variant 2, they had to Osteotomy (see Table 4).

Table 8 Comparision some Technique for femoral fracture in Children with Osteogenesis Imperfecta.

Technique	Efficacy of preventing fracture	Longevity (1)	Frequency of complication	Esease of surgery	Cost (2)
Syngle Rush rod	Poor	Low	High	Easy	Low
Dual Rush rod	Good	High	Low	Most difficult	Low/ High (3)
Sheffield telescoping rod	Good	High	Low	Difficult	High

(1) Longevity refers to the interval between rod insertion and rod revision. (2) Cost includes the cost of the rod, operating times cost and cost of surgery for dealing with complications. (3) The overall cost would be low if theatre time costs are low, while the overall cost would be high if the theatre time cost is high.

months (range, 18-35) (see Table 4).

Bisphosphonate treatment for OI has been reported to be beneficial, resulting in increased vertebral bone mass and reduced fracture rates, and has become a mainstream pediatric treatment^[32]. More

recently, negative effects of this treatment, including delayed healing of the osteotomy site and a changing pattern of fractures, have been reported^[33].

We have not only experienced cases that exhibited these negative effects, but also cases involving inadequate intramedullary canal formation as a consequence of bisphosphonate. We think that such cases may increase in the future, and some of them are hard to treat with elongating rods because of the narrowness of the canal. In such cases, K-W in a variety of sizes will be helpful, and the findings of this study could be useful information.

Improved bone quality with pamidronate treatment allows better stability of rods in the bone, and improved design of rods reduces the rate of mechanical complications^[34] and Graff *et al.*^[35] shown that bisphosphonates can significantly reduce the number of outpatient department consultations and operative interventions in patients with OI.

Glorieux *et al.*^[36] were pioneers in bisphosphonate treatment of children with OI. Their first patient received pamidronate in the Shriners Hospital, Montreal in 1992. In the study they published in 1998 cyclic intravenous pamidronate treatment was administered to 30 children older than 3 years with severe OI, during 1.3-5 years. Pamidronate was given in cycles of three consecutive days at 4-6 month intervals in a mean dose of 6.8 mg/kg per year.

The response to treatment appeared to be faster and more pronounced in infants under 2 years of age than in older children. Relief of bone pain and increase in movement activity occurred within days after beginning of pamidronate administration. Early bisphosphonate treatment did not completely prevent long bone bowing deformities. However, by the increase of vertebral height, improvement of growth and decrease of fracture rate, it obviously ameliorated the development of a severe OI phenotype. Safety issues of bisphosphonate use in children were addressed in these studies and in others. Linear growth was not affected by pamidronate, growth plate appearance was not altered and fracture healing was not delayed^[36].

Several bisphosphonates are currently used in children to treat different osteoporotic conditions, including OI and cerebral palsy^[37]. Pamidronate, alendronate, and risedronate are the bisphosphonates most commonly mentioned in the literature. These are second generation bisphosphonates. The inhibitory effect of bisphosphonates on bone resorption is thought to be mediated by actions on both osteoblasts^[38] and osteoclasts^[39,40]. Previous reports suggested that treatment of children with OI with pamidronate produces an increase in age corrected bone mineral density (Z score) and metacarpal cortical thickness, and the number of radiologically confirmed fractures decreases significantly^[41,36]. Growth appears to happen at the same rate or faster when compared with that of non treated children with OI^[42]. El Sobky *et al.*^[43] shown that the ambulatory status of the patients improves after the telescopic rod surgery, especially when it is associated with the intravenous administration of bisphosphonates.

El Sobky *et al.*^[43], Nicolaou *et al.*^[17], Emad *et al.*^[44], documented that children treated with pamidronate prior to surgery and afterwards do better than children treated with surgery alone. In this study, Variant 2 with accepted was 57.1% and Variant 1 accepted was 20%; but no meaningful comparison (*P* Value: 0.853100) (see Table 5). The effects of the treatments on the ambulatory status were also analyzed. This way, after the reconstructive surgery for the lower limbs, done in 24 patients with moderate and severe forms of OI, we have noticed that 10 patients are able to walk with support (crutches or walking frames), 10 are walking independently, while 4 are still wheelchair bound.

with K-W migration, which included residual or developing angular deformity (Figure 3), eccentric K-W position at the distal physis, and persistent cortical gap at the fracture/osteotomy site. However, multivariate Cox regression model indicated that eccentric rod position at the distal physis is the only significant predisposing factor for proximal migration. We interpret the reason for such results of multivariate analysis is because the risk factors confirmed as significant from univariate analysis are associated with each other to some extent.

We have shown that 2 major findings with KW. First, a decrease in the ratio of the intramedullary wire length to the femoral length, which we defined as “wire length ratio,” was related to a risk of wire-tip fracture. Second, wire-tip fractures tended to require surgery because they were often displaced fractures due to a loss of wire support (Figure 4); K-W through cortical bone a loss of wire support to (Figure 5).

In other words, extra wire-tip fractures could be prevented by proper wire exchange to maintain a high wire length ratio. Cho *et al.*^[6] speculated that a stress concentration occurs at the tip area, where the mechanical properties change abruptly. When the bone outgrows the wire, the unsupported non wire locations are easily displaced and require surgery once they are fractured. This kind of surgery can become invasive and complicated. Although outgrowth of the wire and wire exchange surgery are unavoidable when we adopt non elongating rods such as K-W^[5] most wire exchange surgery performed with no fracture present is less difficult than surgery performed to treat a displaced wire-tip fracture. Therefore, it is important to determine the proper timing of the wire exchange before a wire tip fracture occurs.

Wire length ratios were assessed at 5% increments, and a significant difference was observed in the incidence of wire-tip fractures and other fractures between ratios of 65% and 75% (Figure 6), we shown 31.1% in this study (see, Tables 5 and 6). Therefore, we consider that a wire length ratio of 70% could be set as the cut off point clinically. Using this cut off point, wire exchange surgery could be scheduled regularly. Such scheduled surgery is strongly preferable to urgent surgery, both for the patients and the medical team.

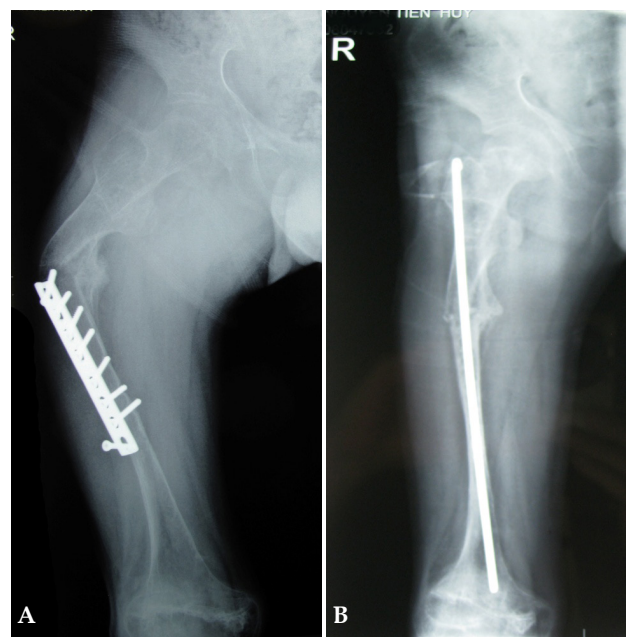


Figure 1 (A B). A: the plate and screw fixation is poor; B: Postoperative changing plate and screw by K-W 6 months.

All fractures occurred without trauma or with only minimal trauma. Five patients reported a small fall from standing height, one had a single fracture without trauma. In all cases the fractures presented with acute pain and with tenderness at the fracture site. None of the fractures displaced. All were treated by operation, and all healed.

All fractures were either short oblique (24.1%) or transverse (75.9%). Those included in this group were injuries where a definite fall had occurred that could cause a fracture in an unaffected individual. Low energy injuries included all fractures where the mechanism would not be associated with a fracture in an unaffected individual. In one cases there was no history of injury prior to the onset of pain, after which the fracture was diagnosed.

Union was defined as bridging callus visible on four cortices on an AP and lateral radiograph of the femur^[45]. Fractures tended to be associated with pancortical thickening of subtrochanteric bone, although due to the small differences in the amount of thickening and despite standardised views the absence of a calibration.

The osteotomies (one or several) are made through the skin cuts according to the classic Sofield-Millar technique^[4]. The advantage of such a method is reduced blood loss, decreased time of operation, less pain, better post-operative mobility and small scars. However, this is a difficult technique with a steep learning curve.

Straightening and fixation of the long bones with intramedullary rodding has been widely accepted for limb stabilization^[4]. Intramedullary fixation is preferred to plate and screws as the latter would invite refracture or angulation at the tip of the plate because of stress riser effect^[46]. External support with plates is contraindicated because the fracture risk below and above the plate is high and screw fixation is poor^[47] (Figure 1).

Proximal migration of the rod into the gluteal region is the most

common complication of the intramedullary telescopic rodding in the femur of OI patients^[5, 48-50], in this study Proximal migration of the KW with 31.1%. Complications of the Kirschner wire and fracture site with proximal K-W 50% in Variant 1, and 17.7% in Variant 2, but but no meaningful comparison (*P* Valuate: 0.123363) (see Table 5 and 6) (Figure 2). The most common complication reported in the femur is proximal migration of the rod into the gluteal region^[51,52]. Proximal migration of the rod may produce symptoms from irritation of the soft tissue at the gluteal region, and even result in disassembly of the telescopic rods, thus creating an unprotected segment at the femur. However, mechanism of proximal migration has not been well elucidated, and it is difficult to understand intuitively as it is against gravitational force. There were 7 Proximal migration of the KW and the recurrent fractures were at the same place as the previous osteotomy with 40.0% in Variant 1, and 20.0% in Variant 2 but no meaningful comparison (*P* Valuate 0.524471) (see Table 7).

Some authors asserted that insertion of the proximal T-piece below the surface of the greater trochanter rather than within the piriformis recess or at the top of the trochanter might aid in avoiding the proximal migration^[48]. However, such an approach runs a risk of migration of the T-piece into proximal femoral medullary cavity. We concur with Wilkinson *et al*^[53] in that revision for distal migration of the sleeve with T-piece into the intramedullary cavity would demand higher dimension surgery than revision for proximal migration. Therefore, we chose to place the T-piece over the greater trochanter. Lee *et al*^[54] had 14% proximal migration.

Mechanism of proximal migration has not been well elucidated, and it is difficult to understand intuitively as it is against gravitational force. We analyzed several possible risk factors for proximal migration by Kaplan-Meier survival and univariate Cox regression models, and noticed few factors that were significantly associated



Figure 2 Proximal imigation of the K-W.



Figure 3 Included residual fracture.

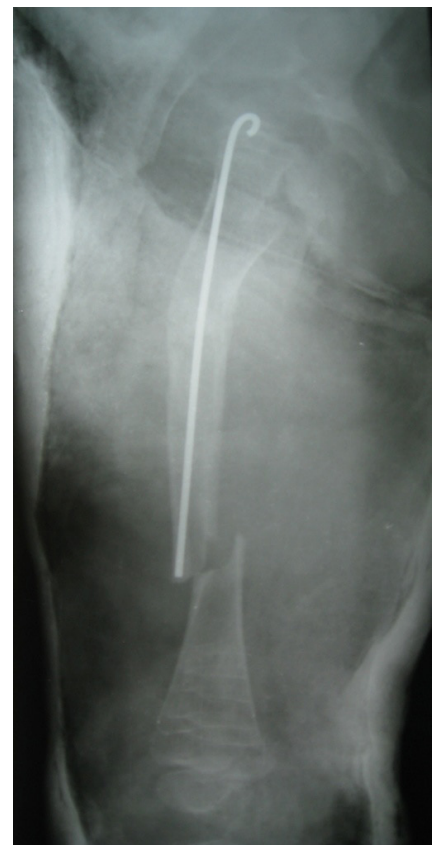


Figure 4 Fractures due to a loss of wire support.

Other factors involved in the prevention of further fractures, such as the diameter of the wire or the materials it is made from, should also be considered. The results of flexible intramedullary nailing have suggested that a low ratio of the diameter of the nail to the femoral canal was an indicator of an unstable configuration^[55,56]. Green *et al*^[57] reported that 80% canal fill improved the overall biomechanical stability of the fractured femur. Although this finding cannot be directly extrapolated to patients in the present study because patients with abnormal bone fragility were not included and the implants adopted were not K-W in their study, we believe that the previous finding was generally applicable in our cases. We did not investigate such other factors, so they cannot be ruled out as having had an effect in the present study. However, we inserted wires with the largest diameter possible relative to the femoral isthmus: the average canal fill was 71%. The actual diameter of the femoral isthmus for OI patients tends to be narrower than that measured in preoperative X-rays as a result of frequent fractures and prolonged bisphosphonate treatment^[58].

We agree Imajima's opinion that methods will not have an adverse effect on fracture prevention even though we used K-W with small diameters such as 2.0 or 3.0 mm. In contrast, the material of the wire may be a factor in preventing further fracture and warrants further research^[59].

Comparison of variables was to be considered while choosing the implant for the femur in children with osteogenesis imperfecta (Table 8). Single Rush rod with ease of surgery and low cost; Dual Rush rod with good efficacy of preventing fractures, high longevity, lower frequency of complications, most difficult of surgery, and Low/high cost; Sheffield telescoping rod with good efficacy of Preventing fractures, high Longevity lower frequency of complications, difficult of surgery, and high cost.

In patients where femoral fracture and angular deformity correction was the purpose of insertion K-W, it is likely to leave some residual angular deformity because the number of osteotomies tended to be less than enough for complete correction of preexisting angular deformity. After acute correction of severe angular deformity, the stretched muscles and fasciae may act as deforming force to result in loss of correction during healing period. Such deforming force may also develop recurrent angular deformity by a minimally displaced fracture.

If some angular deformity remains after corrective osteotomy, it is very likely to place the K-W through an eccentric position of the distal femoral physis. Developing angular deformity may also drive the K-W, which was initially placed through the center of distal physis, into an eccentric position. In evaluating the angular deformity of the femur, we devised an axis connecting the mid-points at the lesser trochanter and distal physis that would represent the intramedullary rod placed in the medullary cavity. If this axis overlapped with or crossed the diaphyseal cortices, the femur was considered to be angulated, and the rod inside was either bent or malpositioned^[60].

Muscle mass and strength have a powerful stimulating effect on bone formation^[61]. Prolonged and repeated immobilization of OI patients as a result of fractures, surgeries, chronic bone pain and parental overprotection severely affects trabecular bone volume and cortical thickness, giving rise to the vicious circle of 'fracture - immobilization-fracture'. The only way to improve the strength of a long bone with thin cortices, formed from weak material, is to increase its diameter. Unfortunately, in most cases of OI the diaphyseal diameter of long bones is decreased, as discussed in the previous paragraph. This compromises further the strength of the

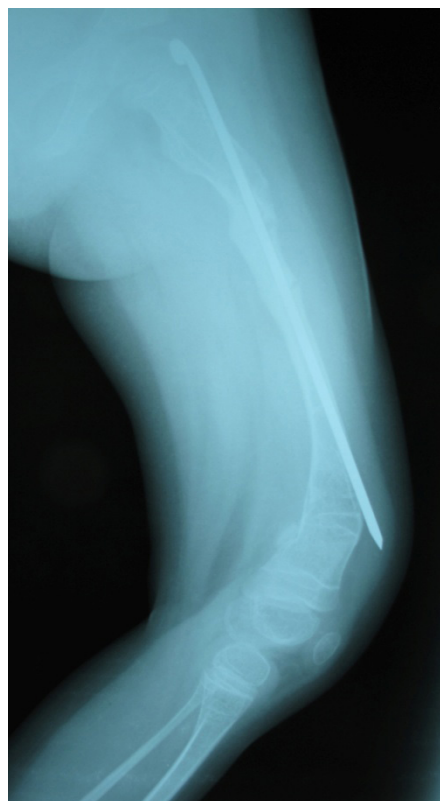


Figure 5 K-W through cortical bone a loss of wire support to.

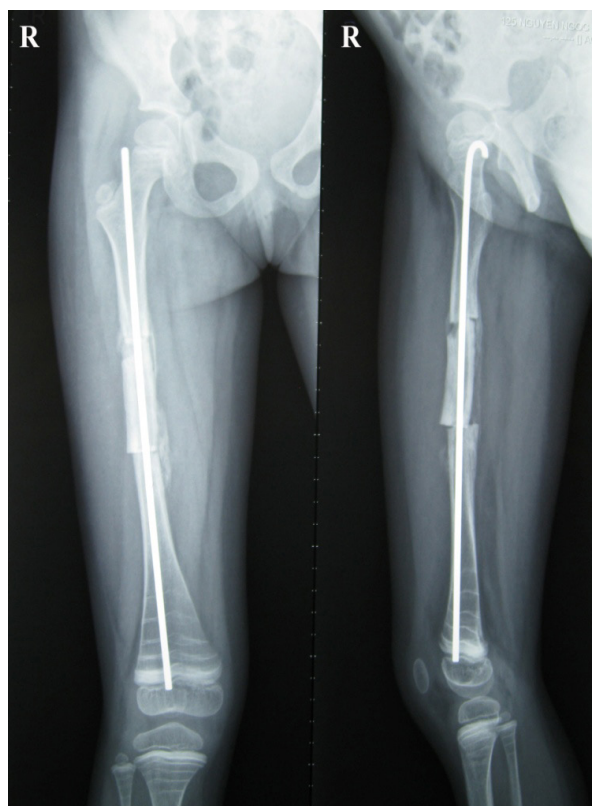


Figure 6 Wire length ratios were assessed at 5% increments.

long bones^[47].

The other very frequent geometric problems in OI are bowing deformities of the extremities that predispose the long bones to repeated fractures at the top of deformity until the angulation is

corrected by surgery^[47].

We assert that to prevent proximal migration of the KW in the femur, angular deformity should be corrected as completely as possible and the KW should be placed in the optimal position, that is, through the center of distal physis, especially in severely affected cases. These data also imply that minimally displaced fractures occurring at femoral segments with a rod in situ could develop angular deformity during healing process, finally resulting in proximal rod migration. In case with developing angular deformity or persistent osteotomy/fracture gap, possibility of proximal migration of the rod should always be kept in mind during follow-up.

Leonid *et al*^[47] immobilization after surgery should be as short as possible to prevent post-operative bone loss. Spica casts are not used unless the osteotomy sites are grossly unstable. To prevent rotation of femoral osteotomies, the two long leg casts are linked (like an A-frame). This allows the patient to sit. Usually 8 weeks after surgery the casts are removed, long leg plastic braces are fitted and gradual verticalization of the patients begins. We performed spica casts for all patients in this study.

The procedure of conducting surgical treatment fractures and multiple osteotomies fixated with intramedullary nails in order to fix deformities and prevent recurrent fractures on patients with Osteogenesis Imperfecta has been accepted since 1959, when Sofield and Millar^[4] described this procedure. It has been modified by a number of surgeons^[20,62,63], but its principle, which consists of multiple osteotomies, realignment and fixation with intramedullary nail on long bones, remains the same.

This procedure improves the quality of life for these patients, although complications are commonly seen, such as bone segments deprived of nail protection due to bone growth, enabling the occurrence of fractures or recurrent deformities, nail migration, pseudoarthrosis and union delay^[4, 64]. Indeed, with a continuous growth, bone segments exceeding the nail can be deprived of protection, favoring deformities and nail protrusion through the cortical. The bone can either fracture or deform at this level, requiring nail replacement by a longer one and a new realignment of the limb. In our study, nine nails required review (see table 6 and 7), six as a result of deformities and three as a result of fractures. The mean time for nails review was 75.5 months (range 62-85 months).

The procedure is associated to a low morbidity rate. Osteotomies showed union in all patients, no blood transfusion was required, and no infection or anesthetic complications cases were found.

Regarding the best time for surgery, literature does not indicate a consistent concept about the best age to fix deformities or the best time to prevent recurrent fractures. Ryoppy *et al*^[49] recommend interventions in children using non-extensible nails, emphasizing that the early realignment and stabilization of the lower limbs improves motor development, with no minimum age for surgery.

We suggested that a surgical treatment using non-extensible nails is indicated when complications such as fractures and/ or deformities are present, based on the fact that these nails do not follow bone growth, if early implanted, complications will eventually occur, resulting in a larger number of review surgeries.

Comprehensive rehabilitation programs for children with OI were developed in the pre-bisphosphonate era^[65]. They have become more effective now, when decreased bone fragility and a better prognosis for standing or walking can be achieved with bisphosphonate treatment.

The child with OI may be affected with bowing of the long bones, vertebral compressions, spinal deformities, muscle weakness secondary to disuse, plagiocephaly, externally rotated and flexed hips

(frog-leg) and equines feet. These problems may limit acquisition of motor skills, in particular, head and trunk control, sitting, crawling, standing and walking. Fear of handling and overprotection by caregivers are also limitations to functional independence.

The main goals of rehabilitation for infants and children with OI are (1) to promote the acquisition of gross motor development; (2) to facilitate all safe forms of active movement and (3) to maximize functional independence and thereby quality of life. The rehabilitation strategies change with age^[19,66].

In early infancy, parents are encouraged to gently handle their babies to promote bonding. Positioning, in the form of alternate side lying, was assists in preventing occipital flattening, torticollis and the frog leg position of the hips. If possible, the prone position is recommended during waking hours only. Parents are shown how to stimulate active upper and lower extremity motions. Gentle movements of the limbs may be assisted by the parents, but aggressive, diagonal and rotational movements should be avoided due to the risk of fracture.

During the crawling period, any means of locomotion (scooting, snaking or reciprocal crawling) are promoted. While the ability to reciprocal crawl is not essential for eventual standing and ambulation, weight bearing on upper extremities assists in transfers, propelling a wheel chair or ambulating with walking aids.

CONCLUSION

The last decade was very productive in the field of OI. Our understanding of why bones in OI are brittle has seen significant progress. Modern multidisciplinary approaches, including early started bisphosphonate treatment, timely orthopedic surgery and rehabilitation, have changed the natural history of brittle bone disease. Surgical realignment and intramedullary stabilization decrease the incidence of fractures and make these fractures more manageable for many carefully selected patients. Improved methods of fixation, which emphasize minimization of soft tissue injury, and avoidance of the trauma and frequency of operative treatment. Many questions remain, including the optimal doses and duration of bisphosphonates, especially around the time of surgery. One disadvantage would be bone growth enabling the emergence of areas without protection of the internal fixation, which might cause recurrence of deformities, fractures and wire migration. These complications usually require review surgeries. The causes of delayed union and nonunion in children with osteogenesis imperfecta are not fully elucidated.

Limitations of this study include the small cohort of patients and the number of segments with proximal migration was too small to perform parametric statistical analysis. Second, this is an interim outcome report as most patients were not followed-up until skeletal maturity. Third, the subjects of this study were not homogenous in terms of the implants used. Fourth, compare results between cases with and without bisphosphonate treatment all equally no value. Fifth, A review of radiographs is not guaranteed to identify all femoral fractures.

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