CLINICAL AUDIT ON OSTEOGENESIS IMPERFECTA PATIENTS TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA FOR PAST 17 YEARS

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ABSTRAK

Pengenalan

Osteogenesis imperfecta (OI) adalah penyakit yang jarang dijumpai, mempunyai berbagai keterukan (*Sillence type I,2,3 and 4)* dan berjumpa doktor dengan berbagai keadaan. Ramai pakar bedah, walaupaun tanpa pengalaman yang baik dalam merawat pesakit, perlu merawat pesakit seperti ini kerana jumlah pakar bedah ortopedik pediatrik yang terhad. Kepatahan berulang, kecacatan, masalah yang berkaitan dengan Rod intramedullary, malrotasi, kepatahan tidak bercantum dan scoliosis adalah antara masalah yang dihadapi oleh pesakit tersebut. Kami mengkaji semua kes yang dirawat di institusi kami untuk mengetahui corak masalah,dan bentuk rawatan serta hasilnya.

Metodologi

Kami telah mengkaji semua pesakit osteogenesis imperfecta yang dirawat di hospital kami dari tahun 2003-2020. Pesakit dikesan dari pejabat rekod berdasarkan Klasifikasi Penyakit Antarabangsa, Semakan ke-10 (ICD -10). Maklumat klinikal yang diperlukan diperoleh dari rekod pesakit dan sistem komunikasi pengarkiban gambar General Healthcare Centricity^{tm} (PACS). Maklumat tersebut diteliti dan dipersembahkan secara deskriptif.

Keputusan

Kami telah merawat 27 pesakit selama 17 tahun yang lalu, namun 4 daripadanya hilang dari temujanji susulan. Sebilangan besar pesakit dengan *Sillence type III* dan 4 telah datang dengan kecacatan atau patah tulang panjang. Anatara penyebab pesakit *Sillence type I* datang berjumpa doktor adalah pinggul yang tercabut sejak lahir (2 orang), kepatahan *supracondylar humerus* jenis fleksi (2 orang) dan kepatahan *olecranon* (3 orang) . scoliosis ditemui berlaku kepada 4 orang pesakit OI Sillence *type III* dalam usia remaja. *Rush Rod* tunggal adalah jenis

pemegang tulang yang paling kerap digunakan untuk tulang femur. Semua femur pesakit *Sillence type III* dan 4 yang dirawat dengan batang rush sembuh dengan malrotasi. *Rush Rod* tunggal pada tulang femur perlu ditukar dalam tempoh 2 hingga 3 tahun kerana masalah yang berkaitan dengan pertumbuhan panjang tulang . *Rush Rod* berkembar dan rod boleh panjang tidak perlu ditukar semula untuk tempoh 5 tahun kerana kemampuannya memanjang bersama tulang. Rush rod yang dimasukkan melalui fossa Piriformis menyebabkan *Avascular Necrosis* pada kepala Femur yang perubahannya dapat dilihat secara radiologi. Teknik *Finidori* yang diubahsuai menggunakan *Rush Rod* dan *Kirschner wire* melalui leher femur mampu membetulkan coxa vara tetapi tidak dapat mengawal putaran. Baja tulang pesakit sendiri yang diambil dari puncak tulang iliac bagi tiga pesakit untuk merawat tulang tidak bercantum dan pemanjangan akut tidak memberi kesan sampingan lain pada mereka. Malrotasi dan anggota bawah pendek sebelah diperbetulkan dan dipanjangkan secara akut dengan *interlocking nail* pada usia matang. Ambulasi pesakit pada usia matang berkait dengan tahap keparahan penyakit bersarkan penkelasan *Sillence*.

Kesimpulannya

Rawatan pesakit osteogenesis imperfecta di institusi kami setanding dengan bukti yang ada dalam literatur.

Kata Kunci:

Baja tulang, Rush Rod berganda, rod yang boleh panjang, supracondylar jenis fleksi, intramedullary, malrotasin, tulang tidak bercantum,, olecranon. Osteogenesis Imperfecta, pembedahan ulangan, rod tunggal

ABSTRACT

Osteogenesis imperfecta is an uncommon disease that presented with different severities (*Sillence type I,II, III, and IV)* and condition. Many surgeons,even without good experience in treating osteogenesis imperfecta patients, need to treat these patients due to limited number of pediatric orthopedic surgeons. Recurrent fracture, deformity, problem related to intramedullary rod, malrotation, nonunion and scoliosis were among the problem faced by those patients. We reviewed all the cases treated in our institution to know the pattern of presentation and treatment with the outcome.

Methodology

We have reviewed all osteogenesis imperfecta patients treated in our hospital from 2003 - 2020. Patients were traced from record office based on International Classification of Disease, 10th Revision (ICD -10). The required clinical information was obtained from patients record and General Healthcare Centricity^{tm} picture archiving communication system (PACS). The information was scrutinized and presented with descriptive manner.

Results

We have treated 27 patients for the past 17 years, however 4 of them lost from follow up. Most of patients with Sillence type III and 4 presented with deformity or fracture shaft of long bones. Among the presentation of Sillence type I patient were developmental dislocated hip (2 patients), olecranon fracture (3 patients), flexion type supracondylar humerus fracture (2 patients). Scoliosis were found in 4 Sillence type III patients at adolescent age. Most common fixation for femur was single rush rod fixation. All femurs of Sillence type III and Sillence type IV patients treated with rush rod united with malrotation. Single rush rod in the femur required revision within 2 to 3 years due to problem related to growth. Double rush rod and expandable nail of femur did not require revision with 5 years. Rush rod through the

piriformis fossa did cause radiological changes of avascular necrosis of femoral head. Modified Finidori's technique using rush rod and wires through the neck of femur was able to correct Coxa Vara but not able to control rotation. Autogenous bone graft from iliac crest of four patient to treat nonunion and acute lengthening were successfully done without causing morbidity to the patients. Malrotation and short limb were derotated and acutely lengthened with interlocking nail at maturity. Ambulation of patient at maturity depend on the type of severity based on Sillence classification.

Conclusion

Treatment of osteogenesis imperfecta patients in our institution was comparable with available evidences in the literature.

Key Words:

Bone graft, Double rod, Expandable nail, flexion type supracondylar, intramedullary, malrotation, non union, olecranon. Osteogenesis Imperfecta, revision, Single rod

CHAPTER 1: INTRODUCTION

1.1 INTRODUCTION

Osteogenesis imperfecta (OI) is uncommon problem. Hospital Universiti Sains Malaysia (HUSM) treat patient from mainly from Terengganu and Kelantan. There have also been referral cases from other states in the country.

Many of them presented very late that associate with severe deformity and growth disturbances. Patient come at different age with different reason. The knowledge of the reasons may help us to provide future medical education to the society.

A few patients who had been walking in small age started to be wheelchair dependent after certain age making us wonder of the cause.

Malrotation is among the common presentation that even occur in post-operative patient. We hope to review the reason of this problem and find out whether modified techniques like interosseous wire loop, transfixing k wire and anti-rotational boot immobilizer that had been used was able to prevent malrotation.

The need of repeated surgery is common due to growth. However, many patients were not able to afford expendable nail. We had been using double rush rods as an alternative method; therefore, we need to know whether the outcome is comparable to expandable nail.

We also review on other associated conditions such as limb length discrepancy, avascular necrosis of the femoral head, Coxa Vara and our standard method of treatment.

CHAPTER 2: OBJECTIVE OF THE STUDY

OBJECTIVE

The general objective of this study was to compare the outcome of OI treatment in Hospital USM with the available evidences in the literature.

The specific objectives were to study the:

1. Pattern of clinical presentations
2. Occurrence of malrotation in patients treated with Rush rods
3. Frequency of revision surgery required for single Rush rod, double Rush rods and expandable nails
4. Outcome of acute lengthening
5. Occurrence of avascular necrosis in patients treated with intramedullary rodding
6. Final ambulatory status of patients

CHAPTER 3: MANUSCRIPT

3.1 TITLE

Clinical audit on Osteogenesis Imperfecta patients treated in Hospital Universiti Sains Malaysia for the past 17 years

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3.2 ABSTRACT

Introduction

Osteogenesis imperfecta (OI) is an uncommon disease that presented with different severities (Sillence type I,II, III, and IV) and condition. Many surgeons, without good experience in treating osteogenesis imperfecta patients, need to treat these patients due to limited number of pediatric orthopedic surgeons. Recurrent fracture, deformity, problem related to intramedullary rod, malrotation, nonunion and scoliosis were among the problem faced by those patients. We reviewed all the cases treated in our institution to know the pattern of presentation and treatment with the outcome.

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We have treated 27 patients for the past 17 years, however 4 of them lost from follow up. Most of patients with Sillence type III and 4 presented with deformity or fracture shaft of long bones. Among the presentation of Sillence type I patient were developmental dislocated hip (2 patients), olecranon fracture (3 patients), flexion type supracondylar humerus fracture (2 patients). Scoliosis were found in 4 Sillence type III patients at adolescent age. Most common

fixation for femur was single rush rod fixation. All femurs of type III and 4 patients treated with rush rod united with malrotation. Single rush rod in the femur required revision within 2 to 3 years due to problem related to growth. Double rush rod and expandable nail of femur did not require revision with 5 years. Rush rod through the piriformis fossa did cause radiological changes of avascular necrosis of femoral head. Modified Finidori's technique using rush rod and wires through the neck of femur was able to correct Coxa Vara but not able to control rotation. Autogenous bone graft from iliac crest of four patient to treat nonunion and acute lengthening were successfully done without causing morbidity to the patients. Malrotation and short limb were derotated and acutely lengthened with interlocking nail at maturity. Ambulation of patient at maturity depend on the type of severity based on Sillence classification.

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Treatment of osteogenesis imperfecta patients in our institution was comparable with available evidences in the literature.

Key Words:

Bone graft, Double rod, Expandable nail, flexion type supracondylar, intramedullary, malrotation, non-union, olecranon. Osteogenesis Imperfecta, revision, Single rod

3.3 INTRODUCTION

Osteogenesis Imperfecta (OI) is genetic disorder that cause abnormal formation of collagen type I that presented with various severity of brittle bone. It has been classified into 4 types [1]. It occurs in 1 in 15,000 – 20,000 birth and mostly is autosomal dominant inheritance [2]. Its rarity and varieties of severities make many surgeons has minimal experience in treating it. However, many surgeons still have to treat the disease from time to times due to logistic issues of many countries where there has been limited number of hospitals with pediatric orthopedic surgeons.

In our hospital we had been treating 27 patients until completion of study. Many of them presented with severe deformities and growth disturbances. Late in seeking for treatment or primarily treated elsewhere were among the cause of presentation with complex condition. There has been condition where walking patient during young age became wheelchair dependent after certain age. Malrotation had been among the common presentations. The most common implant used was intramedullary rush rod. Among the problem faced by patients with early operations using rush rod was the requirement of repeated surgeries following growth. Many patients were not able to afford expensive expendable nail. Intramedullary nailing through piriformis fossa in adolescent was reported to be associated with avascular necrosis (AVN) of femoral head [3]. It is not known whether intramedullary rush rod fixation through piriformis fossa done without reaming causes AVN of femoral head.

We conducted the audit to review the pattern of OI presentation, treatment and outcome. We also hope to find out the outcome of modified techniques of treatment like double rush rod, interosseous wire loop, transfixing k wire, anti-rotational boot, acute lengthening, malrotation correction technique and bone grafting.

3.4 METHODOLOGY

This is an audit on osteogenesis imperfecta patients treated in Hospital Universiti Sains Malaysia (HUSM). List of patients were obtained from record office according to ICD 10 classification of disease with the diagnosis of osteogenesis imperfecta regardless of the Sillence types treated in our center from 2003 until 2020.

Patients record were obtained from record office and studied. Sillence classification was referred to the record and reclassified based on time it started to fracture (before walking for Sillence type III, after walking for Sillence type IV and later in life for Sillence type I); limb deformity (bad in Sillence type III, mild in Sillence type IV, absent in Sillence type I); height (normal in Sillence type I). Blue sclera was used to differentiate Sillence type IV and Sillence type I (blue sclera for Sillence type I). History of disease in first degree relative was used to differentiate Sillence type IV and Sillence type III (positive history occurs in type IV). Patients with doubtful diagnosis was excluded from this study. Age of patients at presentation, gender, type of treatment either for fracture or deformity, administration of pamidronate, functional status at the point of assessment with the age were recorded. Other specific feature of assessment was avascular necrosis of femoral head (in intramedullary femoral fixation through piriformis fossa), malrotation and incidence of nonunion were also studied.

The clinical data from the record includes the x-ray which is obtained from our PACS system. From the x-ray we documented types of implant, complication of each implant usage, and anti-rotation method used, avascular necrosis of femoral head.

The data was tabulated to see the pattern of presentation, treatment and the outcome compared with available data in the literature.

3.5 RESULTS

There have been 27 patients with OI treated in our hospital from year 2003 to 2020. The male and female ratio was 2:1. Out of those patients, 24 patients came direct to HUSM and 3 patients were referred from other institutions.

Out of these patients, the most common type was Sillence type III (eleven patients), followed by Sillence type I (eight patients), Sillence type IV (seven patients) and Sillence type II (one patients). All patients were diagnosed based on clinical presentation by pediatrics orthopedic surgeon and clinical geneticist (figure 1).

Patients with Sillence type I presented with fracture at 19 months and above. The most common bone fracture was tibia. Most of upper limb deformity and non-unions were not corrected (figure 2). Only 2 fracture humerus with deformity corrected with Kirschner's wire (figure 3). Three patients presented with olecranon fracture were fixed with tension band wiring principle and united Two patients presented with flexion type supracondylar fracture at 4 years old. They underwent closed manipulative reduction and percutaneous pinning. Unfortunately, reduction was loss on follow up and the patients were left to unite in cubitus varus (figure4). Two patients had developmental hip dislocation. (figure 5).

One OI Sillence type II died after birth. The baby presented with breech presentation and was delivered via Caesarean section and due to intracranial bleeding and multiple long bone fractures (figure 1 b).

Four of eleven Sillence type III patient presented with long bone fractures within 12 months of age. Five of them presented between 2 to 15 years with deformities of femurs or tibiae because they seek initial treatment elsewhere. All of them were dependent on wheelchair. Four of them were noted to have scoliosis during adolescent age. Two patients

(female) had right long single thoracolumbar curve with vertebral rotation while the other two (male) had short left lumbar curve without rotation (figure 6). After going through treatment in our hospital, their limb deformities got corrected. Seven patients were available for follow up at adolescent and adulthood. All 5 adult patients were using wheel chair for community ambulation and able to walk a few steps with aid for transfer. Patient no.13 was still under treatment and depend on care giver to transfer from wheel chair.

All seven patient with Sillence type IV except patient no.24 presented after age of 2 years old with fracture of long bones. Patient no.24 was referred to us at birth due to tibia deformity without fracture. He had first fracture on the humerus at the age of one year old. Two patients had femoral deformity distal to intramedullary nail and required revision osteotomy with longer nail insertion. One patient (patient no.22) presented with severe proximal Femoral coxa vara that initially treated with Finidori's techniques. During last follow up, all of these patients were between 5 to 52 years old. Every one of them was community ambulatory.

Closed reduction and cast immobilization was used to treat femoral fracture in patient no.21 and no.24 at young age (2 years old). The youngest patient treated with open reduction and intra medullary Rush rod was patient no.27 at age of 3 years old. The most common intramedullary device used in OI treatment was single Rush rod (figure 7). All 8 Sillence type III patients that being follow up till age of 3 years or older required intramedullary femoral fixation either for fracture treatment or deformity correction. The other 4 patient loss to follow up by age of one or less. Three out of 7 Sillence type IV patients were treated with Rush rod between age of 4 to 7 years old.

All of the patients treated with Rush rod united with malrotation. There was no patient found to have avascular necrosis of femoral head. Double Rush rods were used in 2 femurs

(figure 8). Patient no.10 had expandable nail on his right femur and left tibia (figure 7). Patient no.14 had expandable nail on left femur and Double Rush rods on right femur.

We performed revision surgeries for 24 femurs and 6 tibiae on 12 patients with intramedullary rods. Most of the cases were due to bone outgrow the implant leading to deformity or fracture at the end of nail. Variability of revision interval ranged from 1 year (in patient no.24) up to 11 years (patient no.15). Twenty out of 24 single rods need revision after 1-4 years. Single Rush rod in Tibiae required revision between 2 to 4 years after the initial surgery Flexible nail failed as early as 5 months (figure 9). Double Rush rods in the femur were able to protect the femur and did not require revision up to 6 years (figure 8). None of the expandable nail case required revision (figure 7e).

Patient no.22 went through modified Finidori's technique at age of 15years old, followed by acute lengthening and malrotation correction with Interlocking nail fixation at age 16 years old (figure 10). Patient no.27 had acute lengthening, coxa vara correction and malrotation correction with ILN and autogenous bone graft at the age 18 years old (figure 11). Patient no.26, underwent femoral deformity correction with ILN fixation of both femur at age of 19. Patient no.25 underwent fracture treatment and coxa vara correction with two stages surgery. In the first stage hip plate with two screw to neck was inserted. A few weeks later retrograde Rush rod insertion was inserted to get combination of hip plate and intramedullary nail (figure 12). Patient no.23 underwent removal of plate followed by insertion of intramedullary nail and xenograft to treat nonunion of femur (figure 13). Tricortical iliac bone graft was used in our series. We took tricortical bone graft as a strut graft in 3 patients for treatment of nonunion and acute lengthening. No morbidity observed at the donor site. Xray pelvic shows healing of the donor site without complications (figure 14).

Six patients had pamidronate treatment. Four of them were from Sillence type IV group. Only 2 patients from Sillence type I received pamidronate. He was started on pamidronate because of increased frequency of fractures.

3.6 DISCUSSION

Osteogenesis imperfecta is a rare genetic bone disease that involves genetic abnormality in gene COL1A1 and COL1A2. It is either due to genetic mutation or inherited autosomal recessive or autosomal dominant. Confirmatory diagnosis is made based on either collagen culture or genetic testing. Since we have limited resource to do genetic testing for all the patients, clinical and radiological feature were used to diagnose and classified into 4 Sillence types as described by Sillence et al in 1978 [1]. More severe type of osteogenesis imperfecta which is Sillence type II and III is inherited recessively while less severe form, type I and IV were transmitted as autosomal dominant. In this study classification was decided based on assessment by pediatrics orthopedic surgeon and pediatrics geneticist.

OI Sillence Type I is supposed to be the most common Sillence type [4]. However, it was not the most common in our follow up. Among the reasons were due to treatment provided by other hospital. Sillence type I patients could have been underdiagnosed, as they have normal childhood milestone development, normal height without obvious skeletal deformity except recurrent fracture with less severe injury that went un noticed. Marked characteristic features of this Sillence type is blue sclerae. This feature however may disappear or less marked later in their life [1]. We only have one Sillence type II OI which was diagnosed antenatally with well counselled parents. Antenatal diagnosis is important for counselling but not for mode of delivery as caesarean section would not improve rate of fracture [5,6].

Unlike Sillence type I, all Sillence type III and 4 OI patients in our study presented with either lower limb fractures or deformities. Both type of patients may come with deformity as initial presentation. Most of our type III OI cases came with deformity with/without fracture

at younger age (before walking), while in Sillence type IV came with fracture or deformities at around older age (after walking).

Scoliosis was only found in Sillence type III in our series. We have 4 patients with scoliosis. The pattern was similar to adolescent idiopathic scoliosis with rotation and right thoracic curve in female patient. It is not like long curve of paralytic type of scoliosis. However, in male patient, the curve is left thoracic curve. We did not found association with bone fracture. Prevalence of scoliosis in our patients is relatively lower compared to other study [7]. Patient no 25 complain of back pain with association of compression fracture and kyphosis. There had been no report of high incidence associated spine fracture in OI, but kyphosis, scoliosis and craniocervical junction spine abnormalities are not uncommon. Wallace et al in their study advocate screening of craniocervical junction as early as 6 years old due to its high association with neurological symptoms especially with those who had dentinogenesis imperfecta [8,9].

Intramedullary rods were used for fixation of fractures or deformity correction because of its ability to protecting the whole length of bone as load sharing device [10]. It is preferred in comparison to cast fracture treatment because it will allow early rehabilitation and loading of the bone in preventing disuse osteoporosis that may further weaken an already weak bone [11]. In this series, we used cast treatment for patient younger than 3 years old. We were not keen to operate in young patients because availability of nail size, fragility of bone and bleeding. Availability of nail size is a well-known dilemma in operating a small child [12]. Anesthetic complication like possibility of malignant hyperthermia was also the factor. The youngest patient we inserted Rush rod was 3 years old. Hung et al performed k wire intramedullary at younger age (mean 27.4 months). Their indication for surgery was recurrent fracture with/without deformity. In their study, average patient had 3.2 times fracture before they decide to perform surgery (ranging from 1-5 times) [13]. Among the

reason for delay of operation in our patients were delayed in diagnosis that associated with unnoticeable blue sclerae in patients without similar family history.

Single non locking non elongating nail has been used widely as a classical option for intramedullary device after deformity correction. Bone growth will cause part of femur to be unprotected and lead stress concentration around tip of the implant [14]. Imajima et al on usage of non-elongating rods (K wires) in treating osteogenesis imperfecta patients found out 4 complications of using non elongating rods like transcortical migration, bent wire at fracture site, proximal back out and wire breakage at fracture site [15]. In this study total number of 24 single rods had been used and 20 of them required revision surgery due to complications like peri-implant fractures and transcortical migration. To prevent this fracture, they proposed early exchange of the rods before the wire length proportion drops to 70% or less [15].

This study showed that single rod required revision after 1-3 year while double Rush rods would be able to protect the bone for up to 6 years. It was similar to protection period provided by Fassier Duval expandable nail (patient no.10,18). The double rod will reciprocally migrate together with elongation of the bone thus minimized the need of exchanging rods. The similar concept used by the expensive telescoping nail. Joseph et al found that there was no significant advantage of using expandable nails compared to double rodding in term of revision surgeries required [16].

The two patients using expandable nail did not require revision surgery because the nails were inserted ta adolescent age. Unfortunately, only small number of usages of patients could afford to use expandable nail with the approximate cost of RM 12,000 each.

Interlocking nail especially with screw into the neck that used in mature patients were the final fixation in four of our Sillence type IV patients in the late adolescent age as the

medullary size were suitable for available nail size. It allowed angular and malrotation correction. Paphon et al advocated usage of humeral nail in smaller patient that require intramedullary fixation with locking mechanism [17]. In patient 22 and 27, acute distraction was done in getting additional elongation of 2cm. Even though there has been report of successful distraction osteogenesis over intramedullary nail in OI patient [18] we did choose the approach because the limb length discrepancy was only 3 cm.

It is known that extension type supracondylar humerus is a most common fracture in normal children [19,20]. Supracondylar fracture usually occurred on active patients while involving in activities like climbing and riding bicycle. In contrast, this study found olecranon fracture in 4 patients but supracondylar humerus fracture only in 2 patients. It is consistent with report of uncommon supracondylar fracture in OI patients [20]. Both of our patients had flexion type displacement. We postulated that the mechanism of injury to these fractures were direct injury rather than indirect injury. Olecranon fracture were known to be among the pattern of fracture in OI patients [20,21]. All olecranon fracture in our series united well with tension band wiring treatment like normal patients. We did not remove the tension band wiring as suggested by Gwynne-jones et al due high risk of re-fracture in OI patients after removal [22]. Unlike olecranon, both supracondylar fracture in our patients loss reduction despite having 3 and 4 percutaneous pins holding the fracture following closed manipulative reduction. There could be due to break of the exiting hole of the smooth K wire transfixing fracture at far cortex. It is also known that flexion type is a very unstable and frequently need open reduction in order to get precise reduction and stability [23]. Only 2 humerus were operated in this series due to fracture with deformities. Surgery rarely performed in the upper limb due to poor result of intramedullary rodding of the upper limb [24]. However, surgery is still indicated in severely impaired function patients [25]

Malrotation has not been well reported in literature could be due to its less visibility. In our series, patient no 22 had a very severe malrotation that affect walking and the correction showed significant improvement of ability to walk. Malrotations is only visible when it is more than 15^0 but it only starts to cause changes in biomechanics of walking if malrotation is more than 20^0 [26]. All of our Sillence type III and Sillence type IV patients presented with malrotation of the limbs on the most recent follow up. Inability of intramedullary device without interlocking screw like Rush rod is associated with external malrotation due to persistent external force from gravity on the leg. This study showed that interosseous wire crossings fracture site was not effective in controlling malrotation from occurring. Interosseous wire loop and transfixing k wires only control rotation at the fracture site, not the whole lower limb. Anti- rotational boot and cast offer control to the lower limb but less stable Cast/ boot also need to remove early to prevent complication of cast such as stiffness and discomfort to the patient. Occurrence of malrotation in spite present of transfixing wire, in Sillence type III and 4 but not in Sillence type I, may indicate gradual malrotation occurred along the whole length of bone over period of time due to persistent external rotation force by gravity during resting in supine position especially during sleep. Final correction could only be ensured with interlocking nail fixation during early adulthood like what was done on patient no.22,26 and 27.

We performed acute limb lengthening and malrotation correction using interlocking nail on 2 patients at the age of 16 years old. This procedure is only suitable in mature patients because of desired distal locking screw position at the end of femur. We did this as definitive fixation to support the bone without intention of removal. Gradual lengthening with distraction osteogenesis over intramedullary nail was known to be safe in OI patients [18,27]. Study by Saldanha et al in their series, they obtained up to 6.25cm lengthening through that method. Amount of acute lengthening in malunion of normal patient safe up to 5 cm [28]. We

only performed 2 cm acute lengthening in case no 22 and no 27 to avoid sudden over tension from the relatively short muscle that may break the bone distal or proximal to the nail. Acute malrotation correction in externally rotated femur of 45^0 did not cause any neurovascular injury in the two patients. We belief correcting malrotation due to fracture is much safer compare to correcting congenital malrotation. This principle is also applied in lengthening of limb length discrepancy due to malunion because the procedure would bring the muscle and neurovascular bundle to original length and position.

Nonunion is not a rare complication in osteogenesis imperfecta. Agrawal et al predicted that 20% of OI patients may develop nonunion in their long bones [29]. Gamble et al proposed that the important factor for malunion is inadequate control of rotational force [30] We encountered rotational instability of Rush rod in patient no.15 that eventually united with insertion of interosseous wire and autogenous bone graft. Removal of locking plate the caused fracture gap followed by insertion of reamed interlocking nail that provide endosteal bone graft with additional bridging strut cortical xenograft ensured union in patient no.23. Puvanesrajah et al reported the success of similar approach using sandwich allograft in treating nonunion in OI patients. Theoretical concern in this technique is devascularization of the bone by periosteal stripping and infection by allograft colonization [31]. Neither infection nor potential effect of periosteal devascularization were seen in our series. We did not operate on patient no 10 due to prolong nonunion of supracondylar fracture with stiff elbow joint. The nonunion side serve some movement. Treating humerus fracture in a small fragile bone is challenging. Shohei et al suggest a usage of mandible locking plate as a rigid more stable fixation for humerus fracture in OI [32].

Avascular necrosis of the femoral head as a complication of intramedullary nailing through medullary fossa is well known. It is due to its anatomy of the blood supply to the femoral head. The lateral femoral circumflex artery supplying the head is at risk during the

procedure. Most of the study don’t have AVN in their series [33]. However, there was a few cases reported in the literature noted there was AVN post intramedullary reaming in children [34,35,36]. Most of our intramedullary nailing to the femur were through piriformis fossa. It is advocated to monitor occurrence of AVN as it can occur up to 2 years after the injury [37]. We did not encounter any AVN in our patients.

3.7 CONCLUSION

We concluded that we are following the acceptable standard of practice comparing to the studies related to OI. Intramedullary Rush rods were the implant of choice with no evidence of AVN of femoral head. Malrotation and problem related to growth were the problems following fixation with Rush rod. Usage of double Rush rods or expandable nail delayed revision and minimized number of revisions required due to growth. Severe malrotation correction together with cute lengthening up to 2 cm and held with interlocking nail were safe choice when the patients reached maturity. Patients were able to ambulate with proper deformity correction and fracture fixation.

3.8 REFERENCES

1. Sillence D, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. Journal of medical genetics. 1979 Apr 1;16(2):101-16.
2. Forlino A, Cabral WA, Barnes AM, Marini JC. New perspectives on osteogenesis imperfecta. Nature Reviews Endocrinology. 2011 Sep;7(9):540.
3. MacNeil JA, Francis A, El-Hawary R. A systematic review of rigid, locked, intramedullary nail insertion sites and avascular necrosis of the femoral head in the skeletally immature. Journal of Pediatric Orthopaedics. 2011 Jun 1;31(4):377-80.
4. Martin E, Shapiro JR. Osteogenesis imperfecta: epidemiology and pathophysiology. Current osteoporosis reports. 2007 Sep 1;5(3):91-7.
5. Thompson EM. Non-invasive prenatal diagnosis of osteogenesis imperfecta. American journal of medical genetics. 1993 Jan 15;45(2):201-6.
6. Bellur S, Jain M, Cuthbertson D, Krakow D, Shapiro JR, Steiner RD, Smith PA, Bober MB, Hart T, Krischer J, Mullins M. Cesarean delivery is not associated with decreased at-birth fracture rates in osteogenesis imperfecta. Genetics in Medicine. 2016 Jun;18(6):570-6.
7. Anissipour AK, Hammerberg KW, Caudill A, Kostiuk T, Tarima S, Zhao HS, Krzak JJ, Smith PA. Behavior of scoliosis during growth in children with osteogenesis imperfecta. JBJS. 2014 Feb 5;96(3):237-43.
8. Wallace MJ, Kruse RW, Shah SA. The spine in patients with osteogenesis imperfecta. JAAOS-Journal of the American Academy of Orthopaedic Surgeons. 2017 Feb 1;25(2):100-9.
9. Sillence DO. Craniocervical abnormalities in osteogenesis imperfecta: genetic and molecular correlation. Pediatric radiology. 1994 Nov 1;24(6):427-30.
10. Fassier FR. Osteogenesis imperfecta. InPediatric lower limb deformities 2016 (pp. 255-265). Springer, Cham.
11. Sterian A, Balanescu R, Barbilian A, Tevanov I, Carp M, Nahoi C, Barbu M, Ulici A. Early telescopic rod osteosynthesis for Osteogenesis Imperfecta patients. Journal of medicine and life. 2015 Oct;8(4):544.
12. Fassier F, Esposito P, Sponseller P. Multicenter radiological assessment of the Fassier-Duval femoral rodding. InProceedings of the annual meeting of the pediatric orthopaedic society of North America (POSNA), San Diego, California 2006 May 3.

13. Hung NN, Tan D, Hien ND. The Use of Kirschner Wire Intramedullary in Pediatric Femur Fractures with Osteogenesis Imperfecta. International Journal of Orthopaedics. 2016 Dec 28;3(6):672-83.
14. Cho TJ, Kim JB, Lee JW, Lee K, Park MS, Yoo WJ, Chung CY, Choi IH. Fracture in long bones stabilised by telescopic intramedullary rods in patients with osteogenesis imperfecta. The Journal of bone and joint surgery. British volume. 2011 May;93(5):634-8.
15. Imajima Y, Kitano M, Ueda T. Intramedullary fixation using Kirschner wires in children with osteogenesis imperfecta. Journal of Pediatric Orthopaedics. 2015 Jun 1;35(4):431-4.
16. Joseph B, Rebello G, Kant BC. The choice of intramedullary devices for the femur and the tibia in osteogenesis imperfecta. Journal of Pediatric Orthopaedics B. 2005 Sep 1;14(5):311-9.
17. Sa-ngasoongsong P, Saisongcroh T, Angsanuntsukh C, Woratanarat P, Mulpruek P. Using humeral nail for surgical reconstruction of femur in adolescents with osteogenesis imperfecta. World journal of orthopedics. 2017 Sep 18;8(9):735.
18. Saldanha KA, Saleh M, Bell MJ, Fernandes JA. Limb lengthening and correction of deformity in the lower limbs of children with osteogenesis imperfecta. The Journal of bone and joint surgery. British volume. 2004 Mar;86(2):259-65.
19. Bracq H. Fractures of the olecranon. Revue de chirurgie orthopedique et reparatrice de l'appareil moteur. 1987;73(6):469.
20. Zionts LE, Moon CN. Olecranon apophysis fractures in children with osteogenesis imperfecta revisited. Journal of Pediatric Orthopaedics. 2002 Nov 1;22(6):745-50.
21. Peddada KV, Sullivan BT, Margalit A, Sponseller PD. Fracture patterns differ between osteogenesis imperfecta and routine pediatric fractures. Journal of Pediatric Orthopaedics. 2018 Apr 1;38(4):e207-12.
22. Gwynne-Jones DP. Displaced olecranon apophyseal fractures in children with osteogenesis imperfecta. Journal of Pediatric Orthopaedics. 2005 Mar 1;25(2):154-7.
23. Delniotis I, Dionellis P, Gekas CC, Arapoglou D, Tsantekidis D, Goulios V, Kantas T, Leidinger B, Galanis N. Flexion-Type Supracondylar Humeral Fracture with Ulnar Nerve Injury in Children: Two Case Reports and Review of the Literature. The American Journal of Case Reports. 2020;21:e921293-1.
24. Root LE. Upper limb surgery in osteogenesis imperfecta. Clinical orthopaedics and related research. 1981 Sep(159):141-6.