Aseptic Nonunion of Long Bones in Children: A Report of Twelve Cases

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Conflict of Interest The authors report no conflicts of interest.

Funding The authors received no financial support for the research, authorship, or publication of this article.

ABSTRACT

Background: There are very few reports in the literature that directly address nonunion in children. The current study aimed to present a series of long bones nonunion in children following fractures and corrective osteotomies.

Methods: This was a retrospective study that included pediatric patients diagnosed with nonunion following long bone fractures or corrective osteotomies. Patients with nonunion following femoral neck or lateral humeral condyle fractures were excluded. The clinical and radiological records were retrospectively analyzed.

Results: Eight patients developed nonunion after fractures, while four patients had nonunion after corrective osteotomies. The mean age at the time of surgical procedure for nonunion was 10.8 years (range, 2 - 18). The tibia was the most common bone complicated by nonunion with 8 cases (66.6%). The mean time to diagnosis of nonunion was 7.9 months (range, 4 - 24). Five patients (41.6%) had multiple fractures or osteotomies. Two patients (16.6%) had a neurological deficit.

Conclusion: Pediatric nonunion is a rare entity. Possible risk factors include older children, open fractures, and co-existing neurological disorders. Further studies that include a comparative group and adequate sample size are needed to confirm these findings.

Keywords: Pediatric, Long Bones, Osteotomies, Fracture, Nonunion

INTRODUCTION

Bone healing is a complex physiological process. It includes different stages such as cellular activity, bone callus formation, and bone remodeling.[1] Any disturbances of these stages can lead to impaired healing response and subsequent delay in bone healing or nonunion.[2] Nonunion may have serious effects on the daily activities of children, and can cause loss of limb function, muscle atrophy, and stiffness of the adjacent joints.[2]

Nonunion is considered a rare complication of long bone fractures in the pediatric population. There are few studies in the literature reporting on the topic.[3,4] The studies discussing pediatric nonunion have been published as either case reports or as isolated entities in a larger series of predominantly adult fractures.[5] Moreover, there is a paucity of literature dealing with pediatric nonunion following corrective osteotomies.[6]

This study aimed to report the cases of nonunion after fractures and corrective osteotomies of long bones in children, and report the treatment plans and outcomes of such cases.

Patients and Methods

The authors obtained approval from our institution's Human Research Protective Program (HRPP #E18097). Records from over a 9-year span (Jan 2009-Jan 2018) were reviewed for pediatric patients treated for long bone nonunion at our institution. Inclusion criteria included patients younger than 18 years old who experienced nonunion of a long bone after fracture or corrective osteotomies. Exclusion criteria included any case of femoral neck or lateral humeral condyle nonunion or congenital pseudarthrosis of the tibia, because nonunions in these conditions are well documented in multiple studies.[7-10] Nonunion was defined by clinical and radiological factors. Clinical factors included persistent pain at the fracture site and impaired function of the extremity. Radiological factors included lack of bridging callus and persistent fracture lines in at least two of the orthogonal x-ray views. Lack of progressive radiological healing on consecutive radiographic imaging and at least 6 months from the injury were required to diagnose nonunion. Injuries with slow healing but less than 6 months from injury were classified as "delayed union," using the classification system by Weber and Cech.[11] The presence of infection or implant failure were also reported.

The data collected included patient age, gender, comorbidities, fracture characteristics, initial treatment, time to nonunion diagnosis, nonunion type, infection status, management, follow-up, and outcome. The study collected additional information for osteotomy patients, including initial diagnosis and management. Complications of the treatment were also reported.

The primary outcome of interest was the ability to treat the nonunion and achieve clinical and radiographic bone healing. Secondary outcomes were possible risk factors and treatment plans.

Table 1. Detailed Results of 13 pediatric cases who experienced non-union of long bones in the study

Patient #	Age	Gender	MOI	Fracture description	Initial treatment	Time from initial treatment to diagnose nonunion	Type of nonunion	Infection	Treatment of nonunion	Time to attain bony union -Follow up in months
1	16	M	MVA accident	Left open G IIIB distal both bone leg	Ring fixator	5 months	Atrophic	No	-Ring fixator -IM BG (RIA)	-5 months -34 months
				Left Closed transverse shaft femur	Antegrade IM nail	United				
				Left closed transverse proximal shaft humerus	2 Elastic IM nails	United				
2	12	F	MVA accident	Left closed transverse midshaft tibia	2 IM nails	4 months	Hypertrophic	No	-Compression plate -Synthetic, local BG -Fibular osteotomy	-3 months -14 months
3	11	F	Fall	Left open G II highly comminuted distal shaft humerus	Two 2.7 plates and one L. plate (synthes)	6 months	Oligotrophic	No	Posterolateral plate (S&N) -1/3 tubular plate -Synthetic BG	-4 months -6 months
	Patient had neurological deficit									
4	8	M	Fall	Right open G II distal ulna	One IM k-wire	6 months	Hypertrophic	No	-2 Compression plates -Synthetic and local BG	-3 months -11 months
				Right closed distal radius	2 lateral k-wires	6 months	Hypertrophic	No		
				Right closed SC humerus	2 lateral k-wires	United				
5	2	M	N/A	Right closed transverse midshaft femur	Plate fixation	8 months With implant failure	Atrophic	No	2 Elastic IM nails	-2 months -10 months
6	16	M	Fall	Right closed subtrochantric femur (Had retrograde Nail)	Retrograde removal and Reconstruction Nail applied	8 months	Oligotrophic	No	-Blade plate with retrograde nail for prophylaxis of distal femur -IM BG (RIA)	-1.5 months -12 months
	This patient had Osteogenesis imperfecta with multiple healed fractures									
7	18	M	N/A	Left closed transverse midshaft tibia	Kuntscher nail	2 years (late presentation)	Hypertrophic	No	-Ring Fixator -fibular osteotomy -RIA	-14 months -26 months
8	3	M	Fall	Left closed tibial shaft	Nonoperative	Exact timing cannot be determined as this is a child abuse case, however, radiologically it seems that it is over 6 months	Hyper-trophic	No	2 IM elastic nails	-2 month -7 months
				Multiple ribs	Nonoperative	United		This patient did not have congenital pseudo arthrosis of tibia or any manifestations of neurofibromatosis		

Table 1. *Detailed Results of 13 pediatric cases who experienced non-union of long bones in the study (continued)*

Patient #	Age	Gender	Comorbidity	Initial diagnosis	Initial surgical intervention	Time from initial treatment to diagnose nonunion	Infection	Type of non-union	Treatment of non-union	Time to attain bony union -Follow up
9	4	M	-Bilateral cleft feet -Developmental delay -Skeletal abnormalities	External rotation deformity of Rt tibia	Internal rotation osteotomy of the Rt tibia 30 degrees fixed by k wires	6 months	No	Hyper-trophic	-Compression plate -Synthetic BG	-5 months -56 months
10	10	F	-Juvenile RA -scleroderma -bilateral genu valgum	Right external tibial torsion	Right supra-malleolar 40-degrees derotational osteotomy Fixed by 2.7 plate (Synthes)	10 months	No	Oligo-trophic	-Double plating -Local BG	-3 months -9 months
11	18	F	-Achondoplasia -previous Bilateral femur, tibia and humerus lengthening	Valgus deformity of the Right tibia	Varus producing osteotomy fixed by ring fixator	6 months	No	Oligo-trophic	compression pate and synthetic BG.	-4 months -11 months
12	17	F	-Myelodysplasia -lower limbs neurological deficit	IR Right tibia	Right ER osteotomy Fixed by IM nail	United				
				ER Left tibia	Left IR osteotomy fixed by Plate	6 months	No	Oligo-trophic	IM nailing with synthetic BG	-3 months -63 months

Abbreviation: MOI, mechanism of injury; MVA, motor vehicle accident; N/A: not available; IM, intramedullary; TSF, Taylor spatial frame; BG, bone graft; SC, supracondylar; RA, rheumatoid arthritis; IR, internal rotation; ER, external rotation; RIA, reaming irrigation aspiration; G II, IIIB, Gastilo classification for open fractures

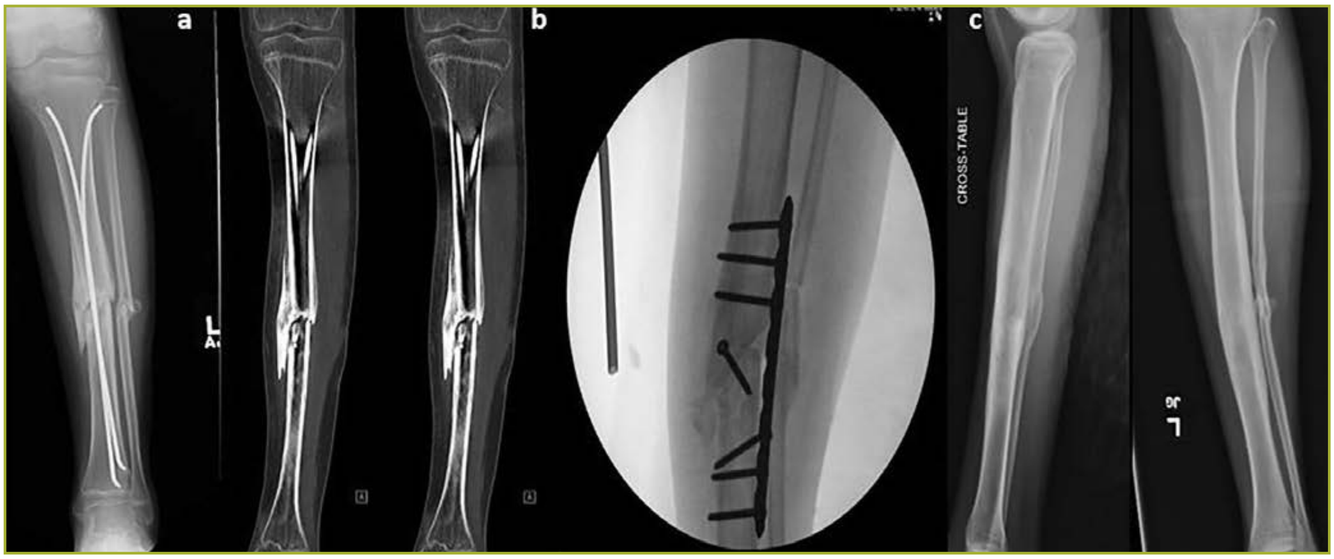

Figure 1. A) X-ray and computer tomography scan of left closed non-united transverse mid-shaft tibial fracture fixed by intramedullary nailing after 4 months of fixation. Patient was an 11-year-old adolescent girl. B) Intraoperative fluoroscopic image of a nonunion correction by open reduction and internal fixation using a compression plate with screws and bone graft (synthetic and local) with fibular osteotomy. C) Anteroposterior and lateral x-ray views after complete union and hardware removal.

Figure 2. A) Anteroposterior x-ray view of right distal both bone forearm (closed radius/open ulna G2), and supracondylar humerus fracture fixed by K-wires in cast. Patient was an 8-year-old boy (case 4). B) Follow up x-ray after 6 months showing non-united both bone forearm fracture. C) Anteroposterior x-ray view showing complete union of previous fracture fixed by 2 compression plates at 4 months postoperative period. D) Fluoroscopic image showing fracture union after implant removal.

Surgical Technique

Treatment was customized according to nonunion type, presence of infection, and implant failure. Fracture edges were exposed and freshened. All fibrous and sclerotic bone edges were excised. Drilling was applied to open the medulla to restore the medullary blood supply. Cultures were taken to rule out infection as appropriate.

Skeletal fixation was dependent on nonunion type. Eight cases were treated with compression plating of different types, according to fracture site and characteristics. When the compression plating modality could not be applied due to the nature of the fracture or the initial treatment plan, an alternative implant was used as another method of fixation. Two fractures were treated using elastic intramedullary nails, one osteotomy was treated with an interlocking nail for tibial nonunion, and two fracture nonunions were treated using a ring fixator.

Decortication was done to promote bone healing. Different types of bone grafting were used in eleven of the cases in this series. Demineralized bone matrix (DePuy Synthes Companies, Warsaw, PA) was used as a synthetic bone in five cases. In two cases, a combined local and synthetic graft was used. A local bone graft was used solely in one case. In three cases, intramedullary bone grafting using a reamer irrigator aspirator (DePuy Synthes Companies, Warsaw, PA) was used to harvest an autograft from the intramedullary canals of the femur and tibia.

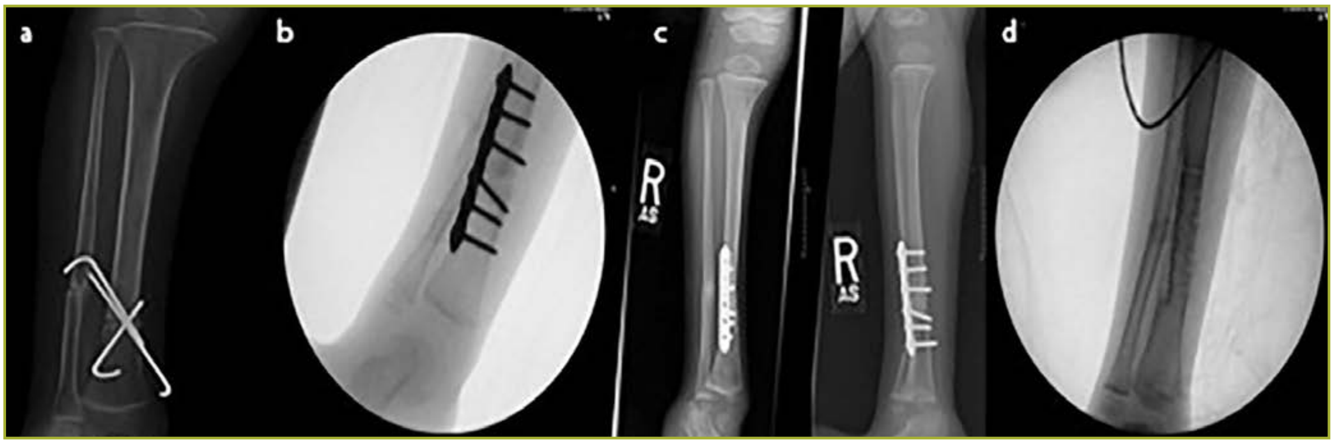

Figure 3. A) Anteroposterior x-ray view of non-united internal rotation osteotomy of the both bone right leg 30° fixed by K-wires. Patient is a 3-year-old boy who had external rotation deformity (case 9). B) Intraoperative fluoroscopic image of reoperation and fixation using compression plate and screws. C) Anteroposterior x-ray view showing complete bony union at 5 months of reoperation. D) Intraoperative fluoroscopic image after hardware removal

Figure 4. A) Anteroposterior x-ray view showing non-united varus producing osteotomy fixed by Taylor Spatial Frame for valgus deformity of the right tibia. Patient is an 18-year-old woman with achondroplasia (case 11). B) Intraoperative fluoroscopic image for reoperation and fixation using compression plate and screws. C) X-ray showing complete bony union after 4 months of reoperation. D) Intraoperative fluoroscopic solid union after hardware removal.

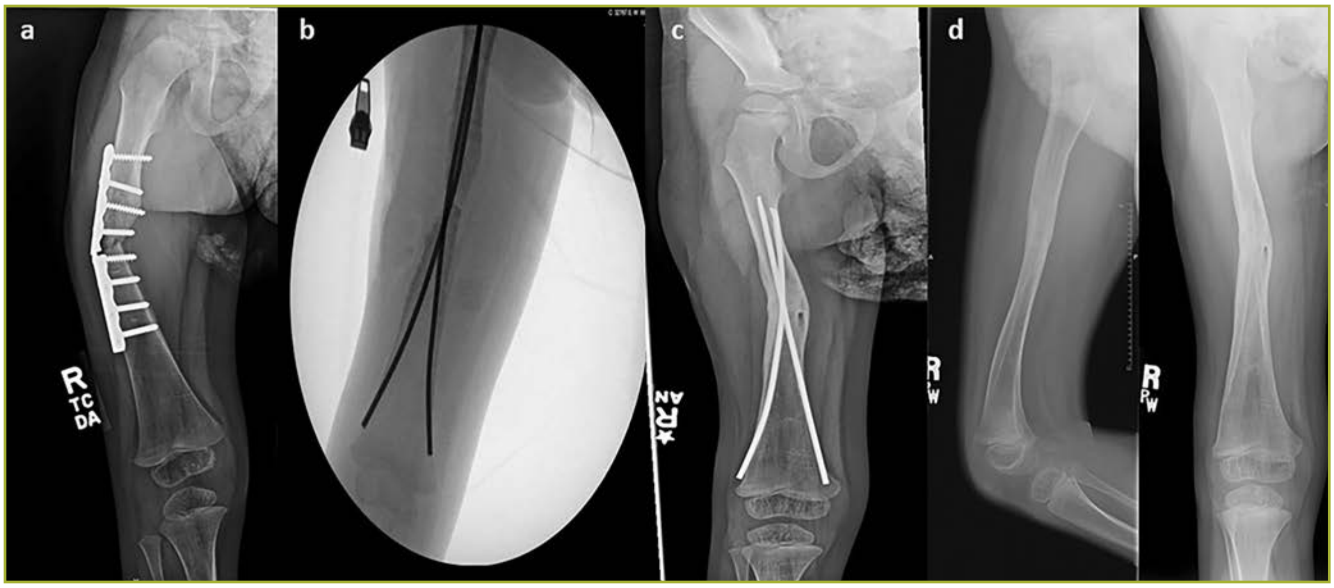

Figure 5. *A) X-ray (one view) of non-united closed transverse fracture of the mid-shaft right femur fixed by plate and screw 8 months postoperatively. Patient is a 2-year-old boy (case 5). Implant failure is evident. B) Intraoperative fluoroscopic image of reoperation using elastic intramedullary nails. C) Anteroposterior x-ray view showing complete bony union at 2 months of reoperation. D) X-ray showing complete union.*

Statistical Methods

This study used only descriptive statistics calculated using Microsoft Excel (Microsoft, Redmond, VA). Inferential statistics couldn't be used due to small sample size.

RESULTS

Table 1 details the results of the 12 cases. Eight patients developed nonunion after fracture, and four patients had nonunion following corrective osteotomy. Nonunion of the tibia was the most common, with a total of eight cases (Figures 1, 2, 3, and 4). Of these eight cases, four cases were post-traumatic and the other four cases were after osteotomy. There were two cases of femoral nonunion. The first of these cases was a shaft fracture that was initially treated using plate fixation, and it subsequently developed nonunion and the implant failed (case 5) (Figure 5). The second of these cases was a subtrochanteric fracture nonunion.

None of the patients in this study showed any clinical signs or laboratory findings suggestive of infection. No specific type of nonunion seemed to dominate. Four patients were polytrauma with multiple fractures at the time of presentation, and another patient had multiple osteotomies in the same setting. There were five fractures that were closed, and three open fractures (ie, tibia fracture, grade III B (case 1); distal shaft humerus fracture, grade II (case 3); and ulnar fracture, grade II (case 4). Two patients had an associated neurological deficit. One of these patients had three nerve palsies (ie, radial, ulnar, and partial median) that were associated with an open distal shaft humerus fracture (case 3). The other patient had a history of myelodysplasia with neurological deficit in the lower limbs (case 13). The average time to diagnosis

Table 2. *Summary of results.*

Age	10.8 (2-18)
Gender	7 Males; 5 Females
Fracture/Osteotomy Location	8/12 Tibia [66.6%] 1/12 Both bone forearm [8.3%] 1/12 Subtrochanteric femur [8.3%] 1/12 Shaft femur [8.3%] 1/12 Distal humerus [8.3%]
Nonunion Type	5/12 oligotrophic [41.6%] 2/12 atrophic [16.6%] 5/12 hypertrophic [41.6%]
Open Fractures/Total Fractures	3/8 [37.5%]
Associated Osteotomies/ Total Osteotomy Cases	1/4 [25%]
Associated Multiple Fractures/ Total Fractures	4/8 [50%]
Associated Neurological Deficit	2 /12 [16.6 %]
Method of Fixation	Compression plate 7/12 (58.3%) Elastic intramedullary nails 2/12 Interlocking Nail 1/12 Ring fixator 2/12
Bone Graft usage	Synthetic (DBM): 4 cases Local: 1 case Combined: 2 cases RIA: 3 cases None: 2 cases
Time to Diagnose Union	7.8 Months (4-24)
Follow-Up	21.6 Months (6-63)
Time to Attain Bony Union After Nonunion Treatment	4 Months (1.5-14)

of nonunion was 7.8 months (range, 4 - 24). No complications related to nonunion treatment were recorded in this study. All patients attained bony union within an average of 4 months (range, 1.5 - 14). A summary of results is included (Table 2).

DISCUSSION

Nonunion in children is a rare complication following long bone fractures and corrective osteotomies.[12] Mills and Simpson[13] estimated the incidence of nonunion in children. Their study examined the overall rate of nonunion in a large population of children and young adults. For patients under the age of 15 years, the risk of nonunion per fracture was approximately 1 in 500 for both boys and girls. For patients in the 15- to 19-year-old age group, the risk of nonunion per fracture was approximately 1 in 500 for girls and 1 in 200 for boys. During the study review, the authors identified only 12 cases of long bone nonunion over a span of 9 years. This reflected the rarity of this complication in the pediatric population. Highly comminuted fractures with or without bone defect, associated severe soft-tissue loss, presence of infection, and prior treatment with open reduction and internal fixation are well known risk factors for nonunion.[3]

Patient age, open fractures, technical errors, infection, polytrauma patients, or neurological disorders were reported as risk factors for nonunion in children. It has been reported that age and fracture pattern have a statistically significant association with developing nonunion. Older children over 12 years old are predisposed to nonunion.[3-12,14] Grimard et al[12] reported 10 cases with delayed union and 7 cases with nonunion, with all patients over 6 years of age. The study found that the age of the patient was a statistically significant factor associated with time to union. The authors reported from 12 years of age and older, and they found that delayed union and nonunion were seen at rates close to those in adults. Similarly, Kreder and Armstrong[14] found that age was a significant factor in the development of nonunion. Arslan et al[3] suggested that the incidence of nonunion increases after the age of 6 years. In a case series of 16 cases of pediatric nonunion, Yeo et al[4] had only one case below the age of 8 years. In our current study, only 3 patients (ie, 23%) were below the age of 8 years, which supports the previously published studies.

In a study by Grimard et al,[12] the authors found that open fractures were also considered a risk factor for delayed union. These authors found that the average union times for Gustilo-Anderson grade III fractures were significantly longer than those for grade I. The current study had three cases of open fractures (ie, 37.5%). Two cases were grade II (cases 3 and 4), which united at 4 and 3 months, respectively. The other case that was grade III B healed at 5 months.[12]

Technical error in surgery was considered another risk factor. In 1976, Weber stated the following statement, "Considerable skill is required to induce nonunion in a child, and its occurrence always results from a serious error in management."[11] In contrast, Arslan et al[3] disagreed with Weber's statement, and the authors found that it occured in children despite appropriate treatment. The author's observations suggested that the nonunion in pediatric fractures can occur because of the surgeons using a relatively less stable fixation method, and they feel falsely secured by favorable healing mechanisms present in children (Figures 1 and 3). Lack of sufficient attention to details and failure to achieve adequate fixation may cause nonunion.

The presence of infection adds to the complexity of nonunion. Treatment should include the controlling of the infection as well as treating the nonunion. In this study, we didn't encounter any fracture or osteotomy site infections. In contrast, Arslan et al[3] reported infections associated with pediatric nonunion in their study. However, our study results show that the majority of nonunions in children are not related to infection.

Zura et al[15] found that polytrauma patients were considered a risk factor for nonunion, with a reported odds ratio of 2.65 (95% CI, 2.34-2.99). In this study, four patients were categorized as polytrauma patients with multiple fractures, and another patient had multiple osteotomies in the same setting. The severity of the associated injuries and the fact that they had multiple healing sites may be a contributing risk factor.

Two cases in this study (ie, 15%) had associated neurological deficits, which may support the findings in the study conducted by Aro.[16] In his study, he demonstrated that sciatic denervation accompanying tibial fracture in rats had a negative effect on union.

Nonunion is not a rare occurrence in a child who has osteogenesis imperfecta.[17] Using a population of 52 osteogenesis imperfecta patients, Gamble et al[17] reported 12 nonunions in 10 patients. Similarly, in a case series of 44 osteogenesis imperfecta patients, Agarwal and Joseph[6] reported 9 nonunion in 8 patients, in which 4 nonunions developed at sites of osteotomies. Our study reports one case of proximal femur fracture nonunion in an osteogenesis imperfecta patient.

Bone quality and biology have a direct impact on the healing of bone. In inflammatory arthritis conditions, chronic use of glucocorticoids and immunomodulatory medications result in reduced bone mineral density and compromised bone growth and healing potentials.[18] One child with tibial osteotomy nonunion had an underlying connective tissue disease, scleroderma. This underlying disease, or the treatment of the disease, may have been a risk factor for the nonunion.

Children with the neurological disease myelomeningocele had bone mineral densities one to two standard deviations below the mean of the normal population.[19] Children with neuromuscular disorders, such as cerebral palsy and myelomeningocele, ambulate less than neurologically normal children. Additionally, the lack of the normal muscle tone in myelomeningocele patients further contributes to osteopenia. Compromised sensation and osteopenia in myelomeningocele patients could lead to an increased risk of hardware failure, malunion, or fracture.[20]

In this study, nonunion treatment consisted of bone edge refreshing, stable fixation using a plate, and bone grafting. These treatment options are similar to treatment for nonunion in adults. To support the poor biologic environment associated with atrophic nonunion, treatment included using a bone graft to ensure mechanical stability. Hypertrophic nonunion was addressed with better skeletal fixation. Bone grafting was used in eleven cases to enhance the union. This study used a reamer irrigation aspiration for autogenous bone grafting to treat pediatric nonunion in three cases without complications.

Despite being one of the largest case series in literature concerning pediatric nonunion, there are some limitations of this study. The small sample size of the study prevented a more advanced statistical analysis. However, the rarity of the aseptic nonunion in pediatric patients precluded obtaining a larger number of cases at one institution. Moreover, there are inherent limitations to the study due to the retrospective nature of this cohort. Further studies with a larger number of cases are needed to establish the risk factors and precautions that can be applied to avoid nonunion among this group of patients. The authors would also like to emphasize that our institution is a tertiary pediatric trauma service, and that these 12 cases represent a small fraction of the pediatric patients whom we treat.

In conclusion, surgeons dealing with pediatric orthopaedists and trauma should not expect successful bone healing in every child without paying attention to the details. Long bone nonunion in children is a rare complication after fractures and osteotomies. The orthopaedists treating nonunion in children should address it appropriately. Care and attention should be paid to the details in order to maintain fracture stability and promote bone healing, especially in patients with poor bone quality due to the associated medical comorbidities. Adequate stable revision fixation in addition to possible bone grafting can achieve union in cases of long bone nonunion in children.

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