Non-Vascularized Fibular Strut Grafting in Infected Gap Non-Union of Long Bones in Paediatric Population

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ABSTRACT
Management of infected gap non-unions of long bones has always been a challenging undertaking. Issues like compromised vascularity of bone, poor soft tissue envelop, persistent infection along with bone gap makes treatment complex. Staged treatment with fibular graft is a promising method for bridging the gap in bone defects created by debridement and sequestrectomy. Therefore, the objective of our study was to evaluate the outcome of non-vascularized fibular strut grafting in the management of infected gap non-union of long bones in paediatric patients. The prospective study included patients ≤ 14 years, with an infected gap non-union of long bones due to haematogenous osteomyelitis. Non-unions due to trauma, tumour, or other causes were excluded. Pre-operative evaluation of the patient included age, sex, anatomic site, and size of the bone gap. Staged treatment protocol for adequate healing of the infection as well as non-union was undertaken. The primary outcome measure was bone healing which was defined as complete fracture union with fibular graft incorporation and hypertrophy. Secondary outcome measures were mal-union, delayed union, peri-implant fracture, and re-activation of infection. Nine patients underwent staged treatment for infected gap non-unions with a mean age of 5.78 years. The average size of the bone gap was 5.83 cm. The average time between stage I and II surgeries was 3.56 months. The mean follow-up was 32 months. The most common bone involved was the femur (n = 6). Successful eradication of infection and consequent healing of non-union occurred in 7 (77.8%) patients. Non-union was seen in two (22.2%) patients. Stable fixation of graft with plate resulted in better outcome. Average time of radiological union was 6.5 months (range 5 - 9 months). Hypertrophy of fibula was evident radiologically at one-year follow-up in all of the patients, except two with graft failure. Delayed union and reactivation of infection were seen in one patient each. Limb-length discrepancy (mean = 5.5 cm) was seen in all patients with lower-limb involvement. Regrowth of the fibula was seen in all patients, and no patient developed common peroneal palsy. The use of non-vascularized fibular graft as a staged procedure for the treatment of infected gap non-union in children is a promising technique, which brings forth predictable and reproducible outcomes in all hands without the need for any microsurgical expertise. In addition, it has a minimal complication rate. Finally, the role of stable fixation in graft incorporation warrants further study.

KEYWORDS: Infected Gap Non-Union; Debridement; Sequestrectomy; Fibular Strut Graft; Non-Vascularized.

1. INTRODUCTION

Management of bone gaps has always been a challenging undertaking for an orthopaedic surgeon especially in infected gap non-unions of long bones where the persistence of infection, soft-tissue compromise, and damage to periosteal sleeve complicate the treatment [1,2]. For adequate healing of osteomyelitis, protracted treatment with antibiotics, serial staged debridement along with sequestrectomy are obligatory [3-5]. The outcome of serial staged debridement and sequestrectomy is healing of infection. However, in doing so, the result is the development of gap non-unions, often with large gaps. There are only limited options for the management of such large bone gaps, especially in paediatric patients. Issues like compromised vascularity of bone, poor soft tissue envelop, persistent infection along with bone gap makes it challenging to achieve a satisfactory outcome. Moreover, the problem is of special apprehension in developing nations where due to unawareness, poverty, prevalent quackery, and deficient health care facilities leads to neglect of such patients. An ideal surgical technique to manage such gap non-unions should not only be simple, easy to administer without necessitating sophisticated infrastructure, cost-effective but also reproducible technique in all hands to deliver painless, mobile, functional extremity with acceptable length and alignment. Various surgical techniques available to satisfy the above-stated principles are indigenous bone grafting (cancellous bone grafting and fibular strut grafting), distraction osteogenesis, and induced membrane technique [3-12]. Nevertheless, each of these surgical techniques has its own merits and demerits and cannot be practiced unanimously. Distraction osteogenesis necessitates a prolonged treatment with a ring or railroad fixator with its potential complications including poor tolerance, joint stiffness, deformities, and others [3,5,8-10]. The cancellous bone graft can be used for small gaps with sufficient remnants of native bone at the ends [11]. However, this requires a large amount of cancellous bone, and often more than one harvest site is required, making its limited application in children [4,12,13]. Fibular strut grafting is a promising method for bridging the gap in bone defects created by serial staged debridement and sequestrectomy [14,15]. Controversy exists between the vascularized and non-vascularized nature of fibular strut grafts with their potential advantages and disadvantages in managing large gaps. The former is technically demanding, costly, and requires microsurgical expertise, with good outcomes reported in the literature [4,16-18]. While non-vascularized fibular strut graft is a simple, cost-effective procedure with almost similar results claimed in literature [5,19,20]. Therefore, the objective of our study was to evaluate the outcome of non-vascularized fibular strut grafting in the management of infected gap non-union of long bones in paediatric patients.

2. METHOD(S)

The present study is a prospective study to evaluate the outcome of non-vascularized fibular strut grafting in infected gap non-union of long bones in paediatric patients. The duration of the study was four years extending from January 2014 to December 2018. The inclusion criteria were patients ≤ 14 years of age, with infected gap non-union of long bones as a consequence of haematogenous osteomyelitis. Gap non-unions due to trauma, tumour, or other causes were excluded. Informed consent was obtained in all patients. The study was permitted by the ethical board of our hospital. The study was performed consonant with the moral standards of the 1964 Declaration of Helsinki as revised in 2000. During the study period, 9 patients met the inclusion criteria and thus were enrolled for treatment of infected gap non-union. A custom orthogonal radiographic analysis of the involved extremity was done for each patient. Routine blood investigations including blood counts with general blood picture, ESR, and CRP were done. ESR and CRP were used as inflammatory markers in our study. Pre-operative evaluation of the patient included age, sex, anatomic site of infection, and size of the bone gap (Table – 1).

Table 1. Clinical details along with the outcome of patients managed with staged fibular strut grafting.

Case No.	Age (years) /Gender	Gap size (cm)	Anatomical site of infection	Interval between stage I and Stage II surgery	Outcome	Repeat Surgery
1	1.5/F	10	Femur, Middle 1/3rd	3	Graft Failure leading to non-union	Patient refused
2	3/M	6	Femur, Middle 1/3rd	4	Union	-
3	12/M	3	Humerus, Prox.1/3rd	4	Union	-
4	2/F	5	Femur, Middle 1/3rd	3.5	Union	Implant Removal
5	7/F	5	Radius, Middle 1/3rd	5	Union	-
6	5/M	7	Femur, Middle 1/3rd	3	Graft Failure leading to non-union + Re-infection	Implant removal & Debridement
7	14/M	4	Humerus, Prox. 1/3rd	4	Union	-
8	3/F	6	Femur, Middle 1/3rd	3.5	Union	-
9	4.5/M	6.5	Femur, Lower 1/2	4	Union	-

Invariably all patients presented with discharging sinus with a variable segment of diaphyseal sequestration evident on orthogonal views (Figure – 1a). We followed staged treatment protocol for adequate healing of the infection as well as non-union. Initial treatment at presentation to our hospital involved meticulous debridement and sequestrectomy (stage-I). Following comprehensive debridement and removal of the loose sequestrum, the proximal and distal segments of bone were debrided of leftovers of infected granulation tissue and sequestrum, pending punctate bleeding bone was appreciated. The medullary canal was also opened and thoroughly washed to eradicate any intramedullary infective focus. Excision of the whole sinus tract was done, along with the release of soft tissue adhesions. Per-operatively tissue was collected and sent for microbial analysis (Gram stain and culture). After stage I surgery, the operated extremity was elevated and supported in the splint. Appropriate antibiotics were given on the basis of the culture sensitivity reports.

A triple check was ensured prior to the second stage surgery, which included settling of clinical, radiological, and inflammatory parameters of infection. Clinically, healing of infection was indicated by the healing of the sinus tract along with surgical wound. Radiologically, the absence of any periosteal reaction, sequestrum, and cavities were indicators of healing of infection. Normalization of inflammatory markers (ESR and CRP), were also suggestive of healing of infection. When the infection was inactive as indicated by clinical, radiological, and inflammatory markers, non-vascularized fibular strut grafting augmented with internal fixation either by plate osteosynthesis or by Kirschner wires was performed (stage-II). Second stage surgery involved the freshening of the bone ends and preparing of the medullary canal for inserting the harvested fibular strut graft. The middle portion of fibular diaphysis was harvested from the leg, utilizing the posterolateral approach. Graft harvesting was performed subperiosteally, leaving the periosteal sleeve intact. Augmentation of the fibular graft was provided by internal fixation using K-wire or plate. Only one patient was fixed with K-wire and the remaining were fixed with plating. The fibular strut graft was longer than the dimension of the gap to permit it to telescope on either side of the gap non-union site. Additional cancellous bone grafting from the iliac crest was done in two cases in a relatively older patient (≥ 12 years). Postoperatively the limb was immobilized in plaster slab/cast/spica for 3 to 4 months. After that, the patient was provided with an appropriate caliper or brace for initiating mobilization. In the case of the lower extremity, the commencement of protected weight-bearing progressing to full weight bearing was dependent on the clinico-radiological union.

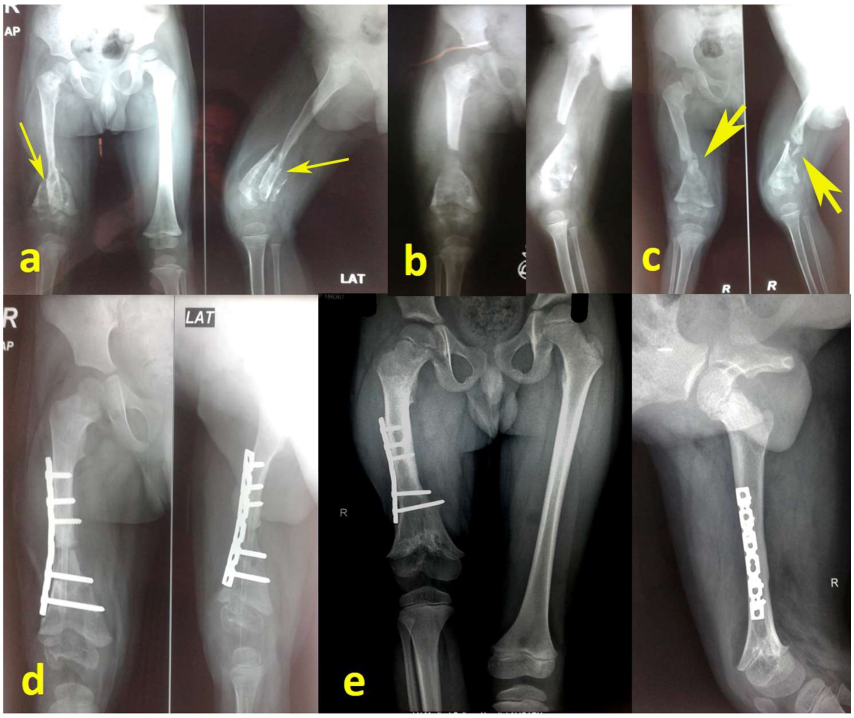
Patients were regularly followed up in the outpatient department at an interval of 1 month for the first six months, 2 monthly for the next 6 months or till union, and 6 monthly thereafter. The clinico-radiological assessment was performed at each follow-up visit, which included parameters like fracture healing, fibular graft incorporation and hypertrophy, any deformity development at the fracture site (varus or valgus), re-infection, fibular graft failure or implant failure, and limb length discrepancy. The follow-up period ranged from 15 to 48 months (mean of 32 months).

The primary outcome measure was bone healing which was defined as complete fracture union with fibular graft incorporation. Secondary outcome measures were mal-union, delayed union, peri-implant fracture, and re-activation of infection (superficial or deep; deep infection was defined as requiring revision surgery for control of infection, Table – 1).

3. RESULTS

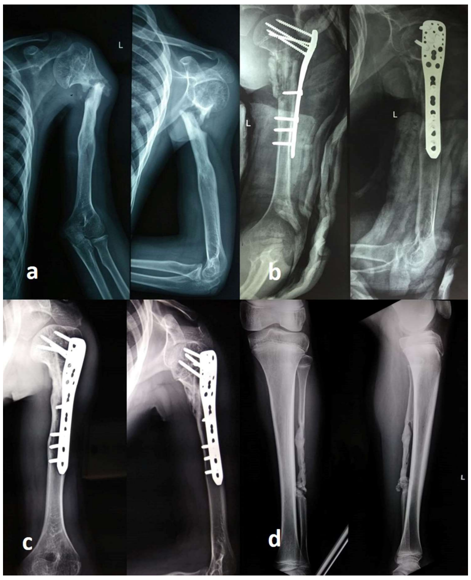
The study included 9 patients with 5 boys and 4 girls. The mean age was 5.78 years (range = 1.5 to 14 years). The mean follow-up was 32 months with a range from 15-48 months. The average size of the bone defect was 5.83 cm (range 3 to 10 cm). The most common bone involved was the femur (n = 6 Cases). The most common site of diaphyseal sequestration was the middle third of the femur just reaching distal metaphysis. All the patients (n = 9) underwent staged treatment. Stage I was done at the presentation of the patient at our hospital. The average time between stage I and II surgeries was 3.56 months (range 3 to 5 months, Table – 1). Intra-operative tissue cultures for stage I surgery were negative in all patients except two. However, at the second stage of surgery, all patients exhibited negative cultures. For our primary outcome measure, successful eradication of infection and consequent healing of non-union occurred in 7 (77.8%) out of 9 patients. Non-union was seen in two (22.2%) patients. The average time of radiological union was 6.5 months (range 5 - 9 months), following second-stage surgery. Figures 1 and 2 show serial radiographs of two patients in our series. Incorporation of the fibula was evident radiologically at one-year follow-up in all patients, except two patients with graft failure. Among the two failure cases, one patient was with a 10 cm segmental gap in the femur, bridged by fibular graft fixed with K-wire (Case – 1). The patient developed stress fracture of the fibula and subsequent graft failure (Figure – 3). The second failure (Case – 6) was having a 7 cm gap in the femur, bridged by fibular graft and fixed with plate developed non-union at the distal end of the grafted fibula and subsequent graft failure. This patient also developed re-activation of infection. Both these patients were explained for revision surgery. The first patient refused revision surgery due to some personal issues and was given a long-leg calliper. The second patient (Case – 6) underwent implant removal and debridement and subsequently given a long leg calliper.

Figure 1



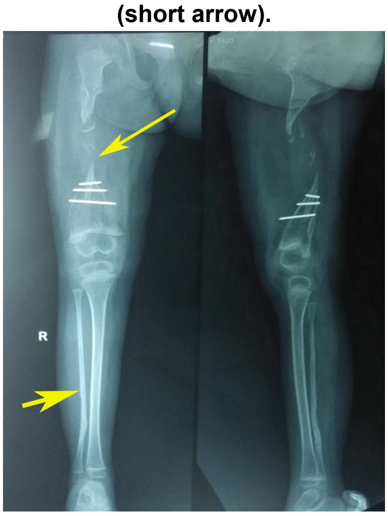
1a: Plain radiograph of a 3-year-old male patient (Case – 2) showing chronic osteomyelitis of femur with pathological fracture, diaphyseal sequestration, and cavitation (long arrows).
1b: Immediate post-op radiograph following debridement and sequestrectomy (stage I).
1c: Radiograph of the patient at 4 months after stage I surgery showing gap non-union with the collapse of the gap non-union site (short arrows).
1d: Radiograph following stage II surgery showing fibular strut graft fixed with a plate.
1e: Radiograph of a patient at union and complete incorporation of the fibula. Also, note on pelvis radiograph including both femora demonstrating limb length discrepancy.

Figure 2



2a: Plain radiograph of a 14-year-old male patient (Case – 7) showing gap non-union of proximal third of the humerus.
2b: Immediate post-op radiograph following stage II surgery showing fibular strut and cancellous bone grafting. The stability of the graft was augmented with plate osteosynthesis.
2c: Plain radiograph of a patient at union and complete incorporation of the fibula.
2d: Plain radiograph of the leg of a patient showing reformation of the fibula.

Figure 3. Plain radiograph of a 1.5-year-old female patient (Case – 1) showing graft failure with resorption of the fibula and ensuing gap non-union (long arrow). Also, note the complete formation of the harvested fibula (short arrow).



Delayed union was seen at the lower end of the fibular graft incorporation in one patient with femur bone involvement (Case – 4). Development of varus mal-alignment and secondary instability due to discrepancy between the dimensions of the native bone and the graft might be responsible for delayed union and incorporation of the fibula. The patient was managed with protected weight-bearing with calliper, which resulted in a successful union. In our series, physeal arrest was seen in two patients (Case – 2 and 7; Figure – 1e and 2c). This could be the result of premature physeal closure due to infection. Limb-length discrepancy (mean, 5.5 cm; range, 2 to 9 cm) was seen in all patients with lower-limb involvement and was treated with a shoe raise. Patients with distal femoral physeal arrest developed the maximum amount of limb length discrepancy in our study (Case – 2). The patient was offered a limb lengthening procedure. Limb length discrepancy was not measured in patients with upper extremity involvement. However, the shortening was present in the upper extremity also. The plate was removed in one patient at 2 years of second-stage surgery (Case – 4). There were no cases of plate breakage. Regrowth of the fibula was seen in all patients (Figure – 2d and 3), and no patient developed common peroneal palsy or other graft-related morbidities. At the time of the latest follow-up, all patients with lower extremity involvement were ambulating securely (with or without shoe raise alone) and had full range of motion, compared with that in the opposite extremity at the joints adjacent to the bone gap. No patient with upper extremity involvement had any functional restriction.

4. DISCUSSION

Although bone infection with extensive sequestration is infrequent in developed nations but is not rare in developing nations [5,21]. Neglect of the disease and delayed presentation is associated with variable length of diaphyseal sequestration, which requires sequestrectomy resulting in substantial bone gap and non-union. Reconstruction of bone gaps along with union has been a leading challenge for orthopaedic surgeons, especially in developing nations due to limited resources. Non-vascularized fibular strut grafting has been used to manage gap non-unions because of its simplicity, cost-effectiveness, ease of administration, and reproducibility. Moreover, the harvest of fibular strut graft does not cause any significant morbidity in the donor's leg. It has been used successfully in post-traumatic gap non-unions, tumour resections, congenital pseudoarthrosis, and as a staged procedure in infected gap non-unions with reported success as high as 92% [5,8,14,19,20,22-24]. Results of several studies including the current study are presented in Table – 2, describing the number of patients, age group, etiology, additional bone grafting, union rates, the time required for union, and complications associated with non-vascularized fibular strut grafting [5,8,14,19,20,22-24]. On appraising the above-cited literature, the studies done exclusively for infected gap non-unions in paediatric patients were of Steinlechner *et al*., 2005, Patwardhan *et al*., 2013, and Swamy *et al*., 2013 [5,19,20].

Table 2. Literature review describing the number of patients, age group, etiology, additional bone grafting, union rates, the time required for union, and complications associated with non-vascularized fibular strut grafting.

Study	No. of patients	Age group (years)	Etiology	Gap size	Additional bone grafting	Successful union	Time required for union	Complications
Current study	9	5.78 years (1.5-14 years)	Chronic osteomyelitis	5.83 cms (3-10 cms)	In 2 cases	7/9 (77.8%)	6.5 months (5-9 months)	Graft failure = 2 deep infection = 1
Swamy *et al*., 2013 [20]	20	1 to 12 years	Chronic osteomyelitis & Tumour	8 cms (6-12 cms)	+	16/20 (80%)	22 weeks (12-32 weeks)	Resorption = 2 Stress fracture = 1 Superficial infection = 2
Patwardhan *et al*., 2013 [19]	26	6.8 +/- 2.33 (3 to 12 years)	Chronic osteomyelitis	5.11 +/- 1.43 (3.5-9 cms)	+	22/26 (84.6%)	38.76 weeks (15-60 weeks)	Delayed union = 4 Re-infection = 1
Steinlechner *et al*., 2005 [5]	8	6 years & 2 months (2 to 14 years)	Infection	7 cms (4-12 cms)	+	6/7 (85.7%)	10 weeks (6 to 12 weeks)	Non-union = 1 Re-infection = 1
El. Sayed *et al*., 2007 [22]	12	25 years (12-40)	Trauma	7 cms (6-10 cms)	+	11/12 (92%)	4 months	Non-union = 1
S. Al-Zahrani *et al*., 1993 [14]	27	22.7 years (2-70)	Trauma, Tumour Infection, Bone cyst Psuedoarthrosis	9.1 cms (4-16 cms)	+	25/27 (92%)	6 to 11 months	Stress fracture = 7 Failures after primary surgery = 2
Lawal *et al*., 2011 [23]	10	24-60 years	Trauma and oncological resections	6.5 cms	+	8/10 (80%)	-	Infection and graft lysis = 2 patients
Omolou *et al*., 2002 [24]	2	8 years & 30 years	Trauma & Infection	-	-	2/2 (100%)	-	-
Morsi, 2002 [8]	7	39.3 years (20-52 years)	Trauma	4.7 cms	-	6/7 (85.7%)	4.5 months (3 to 6 months)	Pseudoarthrosis in one patient

For infected gap, non-unions staged management is generally encouraged, with debridement and sequestrectomy in the first stage for healing of infection followed by management of the bone gap in the second stage [5,19,20,25] as was done in our study. The studies in the past have reported the interval between first and second-stage surgery should be dictated by clinical parameters and normalization of the serum CRP level. The serum CRP level is a good indicator of the healing of infection [1,19,26-28]. We used clinical, radiological, and lab markers (CRP and ESR) as a triple check for healing of infection. In our study, the mean interval between the two stages was 3.56 months (range 3 to 5 months, Table – 1), with 11.1% recurrence of infection. While, the mean interval in Steinlechner *et al*., and Patwardhan *et al*. study was 5.7 weeks and 6 months with 29% and 4% infection rates respectively [5,19]. The infection rate was relatively more in Steinlechner *et al*. study [5]. The possible explanation for this is a relatively short interval between the two stages and relying on clinical parameters alone for healing of infection. Whereas the interval was long (mean = 3.56 months) in our study and we have utilized clinical, radiological, and lab markers for healing of infection. In our study seven of the nine patients achieved union in 5 to 9 months, with a union rate of 77.8%. While, Steinlechner *et al*., Patwardhan *et al*., and Swamy *et al*., reported a union rate of 85.7%, 80%, and 84.6% respectively.

The important complication that we encountered in our series was fibular graft failure leading to non-union (n=2). In both these cases potential instability either due to poor fixation or mismatch between the size of the fibular graft and the native bone led to delayed incorporation and ultimately failure (Case – 1 and 6). Additionally, deep infection recurred in Case - 6. Implant removal along with debridement was done. Currently, the patient is on a long-leg calliper and is being planned for revision surgery. Hence large bone defects with potential instability warrant the use of augmented support with an external fixator, till fibular incorporation and union as reported by Patwardhan *et al*. [19]. In Case 4, varus deformity occurred at the lower end of the fibular graft due to delayed incorporation. Protected weight bearing using long leg calliper resulted in successful graft incorporation and union. Shortening of the limb by 2 to 9 cm was observed in patients with lower extremity involvement. This was attributed to the growth arrest and/or restricted growth of the extremity because of the limited weight-bearing stresses on the extremity. Additionally, some docking of the fragments also contributed to the shortening of extremity. Significant symptomatic shortening of the limb warrants limb lengthening procedures in the future. The mode of fixation for fibular graft, as described in the literature is K-wire or plate or external fixator or a combination [5,19,20]. As reported by Swamy *et al*., plate as a fixation device produced good results precluding the need for revision surgery when compared to fixation with K-wires. In our study, we used K-wire in one patient and plate in the rest of the patients (n=8). One failure from each group was encountered. This observation further boosted the role of stable fixation for achieving bone healing. In our series harvest of the fibular strut, graft does not lead to any significant morbidity. Moreover, as the fibula was harvested subperiosteally, the fibula reformed in all our patients with its near-normal appearance and function (Figure 2d and 3).

Admittedly, the results presented here originated from a small and heterogeneous sample, which limits the strength of conclusions that can be derived from our study. However, long follow-up and inclusion of only infected non-unions cases are the strength of the current study. Therefore, comparative studies with a large sample size should be the next step. Additionally, a combination of Masquelet technique and fibular strut grafting is recommended. Likewise, the lack of consistent documentation on whether the stable fixation has a good outcome and reduces graft failure merits additional evaluation.

5. CONCLUSION

To conclude, the use of non-vascularized fibular graft as a staged procedure for the treatment of infected gap non-union in children is a promising technique, which brings forth predictable and reproducible outcomes without the need for any microsurgical expertise. In addition, it has a minimal complication rate. Finally, the role of stable fixation in bone healing and thus decreasing the need for revision surgery warrants further study.

CONFLICT OF INTEREST

None.

REFERENCES

1. Agus H, Kalenderer O, Ozcalabi IT, Arslantas M. Treatment of infected defect pseudoarthrosis of the tibia by in situ fibular transfer in children. Injury. 2005 Dec;36(12):1476-9.
2. Daoud A, Saighi-Bouaouina A. Treatment of sequestra, pseudarthroses, and defects in the long bones of children who have chronic hematogenous osteomyelitis. J Bone Joint Surg Am. 1989 Dec;71(10):1448-68.
3. Kucukkaya M, Kabukcuoglu Y, Tezer M, Kuzgun U. Management of childhood chronic tibial osteomyelitis with the Ilizarov method. J Pediatr Orthop. 2002 Sep-Oct;22(5):632-7.
4. Spiegel DA, Penny JN. Chronic osteomyelitis in children. Tech Orthop.2005;20(2):142-52.
5. Steinlechner CW, Mkandawire NC. Non-vascularised fibular transfer in the management of defects of long bones after sequestrectomy in children. J Bone Joint Surg Br. 2005 Sep;87(9):1259-63.
6. Morelli I, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? A systematic review and meta-analysis. Injury. 2016; 47 Suppl 6:S68-S76. doi:10.1016/S0020-1383(16)30842-7

7. Morelli I, Drago L, George DA, Romanò D, Romanò CL. Managing large bone defects in children: a systematic review of the 'induced membrane technique'. J Pediatr Orthop B. 2018; 27(5):443-455. doi:10.1097
8. Morsi E. Tibial reconstruction using a non-vascularised fibular transfer. Int Orthop. 2002;26(6):377-80.
9. Dendrinos GK, Kontos S, Lyritsis E. Use of the Ilizarov technique for treatment of non-union of the tibia associated with infection. J Bone Joint Surg Am. 1995 Jun;77(6):835-46.
10. Blum AL, Bongio-Vanni JC, Morgan SJ, Flierl MA, dos Reis FB. Complications associated with distraction osteogenesis for infected nonunion of the femoral shaft in the presence of a bone defect: a retrospective series. J Bone Joint Surg Br. 2010 Apr;92(4):565-70.
11. Fowles JV, Lehoux J, Zlitni M, Kassab MT, Nolan B. Tibial defect due to acute haematogenous osteomyelitis: treatment and results in twenty-one children. J Bone Joint Surg Br. 1979 Feb;61(1):77-81.
12. Mumford JE, Simpson AHWR. Management of bone defects: a review of available techniques. Iowa Orthop J. 1992;12:42-9.
13. Malkawi H, Shannak A, Sunna P. Active treatment of segmental defects of long bones with established infection. A prospective study. Clin Orthop Relat Res. 1984 Apr;184:241-8.
14. Al-Zahrani S, Harding MG, Kremli M, Khan FA, Ikram A, Takroni T. Free fibular graft still has a place in the treatment of bone defects. Injury. 1993;24:551e554.
15. Tuli SM. Bridging of bone defects by massive bone gaps in tumorous conditions and in osteomyelitis. Clin Orthop.1972;87:60-73.
16. Marino JT, Ziran BH. Use of solid and cancellous autologous bone graft for fractures and non-unions. Orthop Clin North Am. 2010 Jan;41(1):15-26.
17. Daecke W, Marzi I, Frank J. Reconstruction of lower extremity fractures with soft tissue defects. Eur J Trauma Emerg Surg. 2007;33(1):24-32.
18. Beris AE, Lykissas MG, Korompilias AV, Vekris MD, Mitsionis GI, Malizos KN, *et al*. Vascularized fibula transfer for lower limb reconstruction. Microsurgery. 2011 Mar;31(3):205-11.
19. Patwardhan S, Shyam AK, Mody RA, Sancheti PK, Mehta R. Reconstruction of bone defects after osteomyelitis with nonvascularized fibular graft: a retrospective stuyd in twenty-six children. J Bone Joint Surg Am. 2013;95:e561–566.
20. Swamy, Akhilesh R, Gupta V. Results of non-vascularised fibular grafting in gap non-union of long bones in paediatric age group. J Clin Orthop Trauma. 2013;4(4):180–184. DOI:10.1016/j.jcot.2013.09.001PMCID:PMC3880954.
21. Agiza AR. Treatment of tibial osteomyelitic defects and infected pseudarthroses by the Huntington fibular transference operation. J Bone Joint Surg Am. 1981 Jun;63(5):814-9.
22. El-Sayed M, El-Hadidi M, El Adl Wael. Free non-vascularised fibular graft for treatment of post-traumatic bone defects. Acta Orthop Belg. 2007;73:70e76.
23. Lawal YZ, Garba ES, Ogirima MO. Use of non-vascularized autologous fibula strut graft in the treatment of segmental bone loss. Ann Afr Med. 2011;10(1):25e28.
24. Omolou B, Ogunlade SO, Alonge TO. Limb conservation using non-vascularised fibular grafts. West Afr J Med. 2002;21:347-349.
25. Zahiri CA, Zahiri H, Tehrany F. Limb salvage in advanced chronic osteomyelitis in children. Int Orthop. 1997;21(4):249-52.
26. Maak P, Benitz WE. Limitations of C-reactive protein in diagnosis of neonatal infection caused by coagulase-negative staphylococcus. J Perinatol. 2011;31:S83.
27. Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics. 1998 Oct;102(4):E41.
28. Pourcyrous M, Bada HS, Korones SB, Baselski V, Wong SP. Significance of serial C-reactive protein responses in neonatal infection and other disorders. Pediatrics. 1993 Sep;92(3):431-5.