

# Management of congenital pseudarthrosis of the tibia with the Ilizarov method in a paediatric population: influence of aetiological factors

Dmitry Y. Borzunov<sup>1</sup> · Alexander Y. Chevardin<sup>1</sup> · Alexander I. Mitrofanov<sup>1</sup>

Received: 15 July 2015 / Accepted: 21 October 2015 / Published online: 7 November 2015  
© SICOT aisbl 2015

## Abstract

**Purpose** Our study compared the rates of union achieved with the Ilizarov method in congenital pseudarthrosis of the tibia (CPT) associated with neurofibromatosis type 1 (NF1) or CPT of idiopathic origin in paediatric patients.

**Methods** We studied the outcomes of 28 children that were treated for CPT between 2005 and 2013. Group 1 included children ( $n=14$ , mean age=9.7 years) with CPT associated with NF1 while group 2 were CPT cases that had radiographic confirmation of dysplastic lesions in the tibia but lacked clinical NF1 manifestations ( $n=14$ , mean age=8.6 years). There was no statistical difference between the groups regarding their age or number of previous operations per patient. Individual technical solutions were planned for each patient but coaptation of bone fragments and autologous local tissue grafting to achieve a greater bone thickness and contact area at the pseudarthrosis level were mainly used. Refracture-free rate after the first operation, number of re-operations per patient, and union rates in the groups were compared.

**Results** Bone union and weight bearing were obtained in all the cases after the first operation. Refracture-free rate was 42.86 % in group 1 and 35.71% in group 2 (no statistical difference,  $p>0.05$ ). Mean number of re-operations per patient was 1.07 and 0.78 respectively ( $p>0.05$ ). Subsequent treatment for refractures with the Ilizarov techniques gained 92.86% of union in both groups at the follow-ups by completion of the study (range, 2–9 years).

**Conclusions** The Ilizarov method yields comparable results in the management of CPT associated with NF1 or tibial dysplasia of idiopathic origin in paediatric cases. Further research should focus on the ways to support the Ilizarov method in order to reduce the number of repetitive surgeries or eliminate them.

**Keywords** Congenital pseudarthrosis of the tibia · Neurofibromatosis type 1 · Tibial dysplasia · Ilizarov method

## Introduction

The aetiology of congenital pseudarthrosis of the tibia (CPT) has not been clearly understood yet but its association with neurofibromatosis type 1 (NF1), fibrous dysplasia or osseofibrous dysplasia is known [1–3]. Numerous studies reported on the outcomes of its management with the use of available operative techniques that include autologous free bone grafting, vascularized fibular grafting, and the Ilizarov method that are supported by internal fixation and adjuvant chemical, physical and biological means [2–9].

The Ilizarov method and vascularized fibular grafting are the two alternative methods that are able to provide better bone union rates in the treatment of CPT. They are based on the use of a tissue complex that is capable of preserving blood supply [2, 4, 5]. However, the Ilizarov method was recognized as the optimal one, having the highest rate of fusion (75.5%) as well as success in bone lengthening, correction of the associated deformities and foot malposition [10]. Intramedullary nailing was added to the arsenal of the Ilizarov method for stability and retaining the union achieved [6–8].

Repetitive operations are quite frequent in the management of CPT due to the severity of its pathological complex. Dysplastic changes in the bone tissue of the tibia and fibula, limb-

✉ Alexander Y. Chevardin  
alexander.chevardin@mail.ru

<sup>1</sup> Russian Ilizarov Scientific Centre for Restorative Traumatology and Orthopaedics, 6, M. Ulianova Street, Kurgan 640014, Russian Federation

length discrepancy (LLD), residual tibial deformities and foot malposition are their main causes [2–5]. Therefore, management of this multi-component orthopaedic pathology in a paediatric population remains challenging and needs further study and discussion [8].

Our work was aimed at a comparative analysis of the outcomes (refracture-free rate, number of reoperations per patient, union rate by the completion of the study) achieved with the Ilizarov techniques in the management of CPT that was associated with NF1 versus CPT and featured tibial dysplasia, but its aetiology was idiopathic or unconfirmed.

## Materials and methods

We retrospectively studied the outcomes of CPT management with the Ilizarov method in 28 patients who had been treated between 2005 and 2013 by our team. Inclusion criteria were paediatric age and CPT that was associated either with NF1 (group 1,  $n=14$ , mean age=9.7) established according to the guidelines of the National Institutes of Health Consensus Development Conference Statement on neurofibromatosis 1 [11], or tibial dysplasia due to idiopathic or unconfirmed aetiology (group 2,  $n=14$ , mean age=8.6). Group 2 patients had radiographic confirmation of dysplastic bone lesions in the tibia and fibula but lacked specific clinical NF1 manifestations. The demographic data and pre-operative findings are given in Tables 1 and 2. There was no statistical difference in the mean age and number of operations per patient before admission (2.4 operations in group 1 versus 2.0 in group 2,  $p>0.05$ ).

Medical records and radiographs were examined. Radiographic findings revealed that CPT was located in the middle or distal third of the tibia (the middle third was involved in one case of group 1 and in six cases of group 2). Three cases were bowed dysplastic tibias that were not fractured (a latent type). Twenty-four cases were atrophic CPT (Crawford Type IV) associated with fibular pseudarthrosis. They featured tibial bone osteoporosis, local areas of sclerosis, bone marrow canal eburnation of different extension, cortical resorption, and sclerotic end plates on the non-united fragments that had the ends which were incongruent in shape. Clinical examination revealed that 75% of patients had rough soft tissue scars due to previous operations at other hospitals. According to Dopplerography, blood flow in the anterior and posterior tibial arteries was compromised in atrophic CPT type.

Clinical goals were bone union, correction of tibial deformities and of foot malposition, as well as complete or partial LLD compensation in order to achieve weight bearing.

Ilizarov method technical solutions for implementing these goals are presented in Table 1 and Table 2. Individual technical solutions were planned for each patient. Coaptation of tibial fragments aimed to thicken the tibia and increase the contact area of the fragments at the nonunion level in atrophic

CPT as well as deformity correction were the means to achieve union and weight-bearing. Open coaptation was a preferable method. It included refreshment of sclerotic end plates and two variants of their plunging into each other: (1) the sharper bone fragment end into the wider one (Fig. 1) or (2) splitting of each bone fragment end into two parts (“swallow’s tail”) for mutual introduction. Extensive resections were not used as most of the patients had had them at previous operations. A local split from the proximal tibial area was gradually transported using wire traction to the pseudarthrosis site to serve as a local autologous graft in one case of group 1. An autologous fibular graft to cover the pseudarthrosis and intramedullary wires were applied in one case of group 2. Khakhutov’s bone plasty with a local rotational tibial graft to bridge the pseudarthrosis was performed in one case of group 2. Acute compression was produced intraoperatively. Supportive compression was maintained every week or two weeks (Fig. 2). LLD was compensated by lengthening in the tibial metaphysis of a longer bone fragment after its osteotomy (Fig. 3) but bone union and correction of deformities was a priority to lengthening in eight patients who suffered severe conditions (Fig. 4). Twenty-two patients needed correction of associated deformities.

The Ilizarov apparatus was removed based on a clinical test for absence of pathological movements at the pseudarthrosis level and pain during axial loading. Radiographic union was judged by an interrupted continuity of the cortex at the fragments junction and along the regenerated bone and by similar bone density in the regenerated area to the adjacent tibial areas. Orthotic bracing was advised for a minimum of four months following treatment.

Re-fracture-free rate, number of re-operations per patient in the groups, CPT union in the age subgroups under ten and  $\leq$ ten years of age after the index operation, as well as union rate by the completion of this study were compared between the groups. Pearson’s chi-squared and Mann–Whitney tests were used for revealing the significance of difference between the groups.

Informed consent statements were given by children’s parents. The study was approved by the ethic committee of our institution and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## Results

### Outcomes after the index operation

Bone union was obtained in all the cases after the first operation. However, eight patients of group 1 and nine patients in group 2 had re-fractures within a year post-operatively (Table 1 and Table 2). The refracture-free rate was higher in group 1 versus group 2 after the first operation (42.86 % and 35.71% respectively) but it was not statistically significant ( $p>0.05$ ).

**Table 1** Group I patients' data

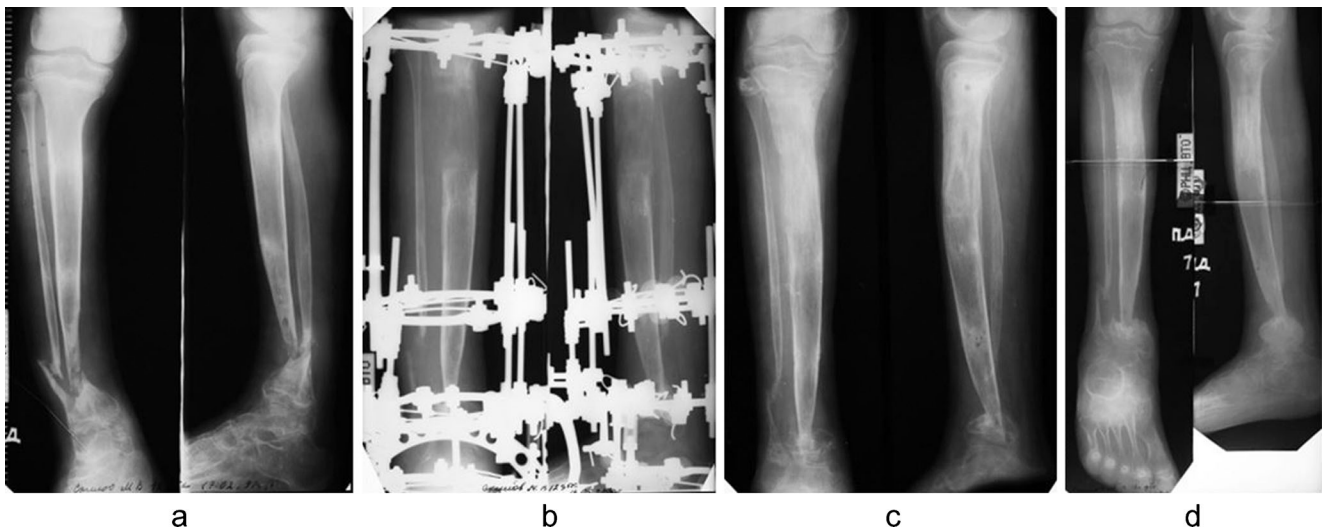
Age at index operation, demographic and orthopaedic data										First operation by our team			Subsequent operations by our team		
Case	Age (years)	Sex	CTP type	Previous operations	Initial deformity (degrees)	Initial LLD (cm)	Procedures	Total duration (days)	Outcome	Residual LLD (cm)	Number	Outcome			
1.	3	F	L	0	Valgus/recurvatum 160	3	Osteotomy, compression	286	H	0	0				
2.	4	F	A	0	Varus/ antecurvatum 160	2	Coaptation, bone plasty with a split from the proximal fragment	116	R	2	2	Discontinued treatment			
3.	7	M	A, bilateral	3	Valgus/antecurvatum 150/160	2	Coaptation, correction	335	H	0	0	Lengthening			
4.	8	M	A	2	Varus 160	7	Coaptation	228	R	5	2	H			
5.	8	M	A	2	Varus 160	12	Coaptation, osteotomy	93	R	7	1	H			
6.	8	F	A	3	0	8	Coaptation, osteotomy for lengthening	149	R	7	1	H			
7.	11	F	A	1	Valgus/antecurvatum 80/160	13	Coaptation, gradual correction	252	H	13	0				
8.	11	M	A	2	Varus /antecurvatum 160	9	Coaptation, osteotomy for lengthening	163	R	0	3	H			
9.	11	M	A	7	0	11	Coaptation	241	H	11		Lengthening (twice)			
10.	12	M	A	3	Varus/antecurvatum 150	4	Closed gradual correction	130	R	6	1	H			
11.	13	M	A	1	Recurvatum 150	9	Coaptation, osteotomy for lengthening and correction	136	R	6	2	H			
12.	13	F	A	4	Recurvatum 160	18	Coaptation	182	H	18	0	Lengthening (twice)			
13.	13	F	A	2	Varus /antecurvatum 140/15	10	Coaptation, gradual correction	273	R	15	2	H			
14.	14	M	A	4	Recurvatum 170	17	Coaptation, fibular osteotomy	245	H	17	0				

F female, M male, L latent, A atrophic, N normotrophic, LLD leg length discrepancy, IMN intramedullary nailing, H healing, R refracture

**Table 2** Group 2 patients' data

Age at index operation, demographic and orthopaedic data										First operation by our team			Subsequent operations by our team		
Case	Age (years)	Sex	CTP type	Previous operations	Initial deformity (degrees)	Initial LLD (cm)	Procedures	Total time in frame (days)	Outcome	Residual LLD (cm)	Number	Outcome			
1.	2	F	L	0	Valgus/recurvatum 160	4	Double osteotomy	133	H	0	0				
2.	3	M	A	2	0	3	Coaptation	197	R	2	1	Continues treatment			
3.	3	F	A	2	0	2	Coaptation	84	R	2	1	H			
4.	4	M	A	1	Varus/anteurcurvatum 160	4	Coaptation	219	R	4	1	H			
5.	5	M	L	0	Varus/anteurcurvatum 160	1	Osteotomy for acute correction	133	R	0	2	H			
6.	6	M	A	0	Anteaurcurvatum 160	0	Coaptation	215	R	2	1	H			
7.	7	M	A	2	Valgus/anteurcurvatum	0	Coaptation, osteotomy for lengthening	169	R	14	1	H			
8.	10	M	A	7	0	6	Coaptation	244	R	12	2	H			
9.	11	M	A	3	0	1.5	Khahutov bone plasty, gradual compression	114	R	4	1	H			
10.	12	M	A	7	Varus/anteurcurvatum 160	7	Coaptation, osteotomy, acute correction	188	H	2	0				
11.	13	F	N	1	Varus/anteurcurvatum 150	2	Coaptation, gradual correction	217	H	0	0				
12.	15	F	A	3	Anteaurcurvatum 90	8	Coaptation, gradual correction	411	H	6	0				
13.	15	M	A	2	Varus/anteurcurvatum 160	8	Resection, fibular autograft, osteotomy, IMN	163	R	8	1	H			
14.	15	M	A	1	Anteaurcurvatum 160	4	Coaptation, osteotomy for lengthening and correction	291	H	2	0				

F female, M male, L latent, A atrophic, N normotrophic, LLD leg length discrepancy, IMN intramedullary nailing, H healing, R refracture



**Fig. 1** Coaptation by plunging a sharper bone fragment end into a wider one in a 12-year-old male patient (Table 2, case 10) with CPT in the distal right tibia due to nonspecific tibial dysplasia (a–b) treated in 2010. X-rays

show the outcomes following the removal of the apparatus (c) and at a one year follow-up (d)

Within the subgroups, two children aged  $\geq$ three years with a latent CPT type who underwent their first treatment recovered completely. Only one case healed in the age from three to ten years that had bilateral involvement. In children aged  $\leq$  ten years, re-fractures did not happen in 50% (4 out of 8 cases) and 57% (4 out of 7 cases) in group 1 and group 2, respectively.

The union achieved in 11 patients after the first operation was preserved at follow-ups (range, 2–9 years).

Axial deformities were corrected in all the cases. LLD was compensated completely or partially in six patients of group 1 and in seven patients of group 2.

### Outcomes of subsequent operations

In group 1, refractures resulted in a greater number of reoperations as compared to group 2 (14 versus 11) over the period studied but the difference between the groups was not statistically significant (1.07 and 0.78 re-operations per patient respectively,  $p > 0.05$ ).

Thirteen patients (92.86%) out of 14 in each group retained bone union by the completion of this study (follow-up range, 2–9 years).

Three patients in group 1 that had achieved complete union after the first operation underwent only lengthening procedures at subsequent stages.

One patient discontinued treatment. None of the patients had amputation.

### Complications

Complications other than refracture were residual deformities and LLD. Wire-tract infection was observed but it was

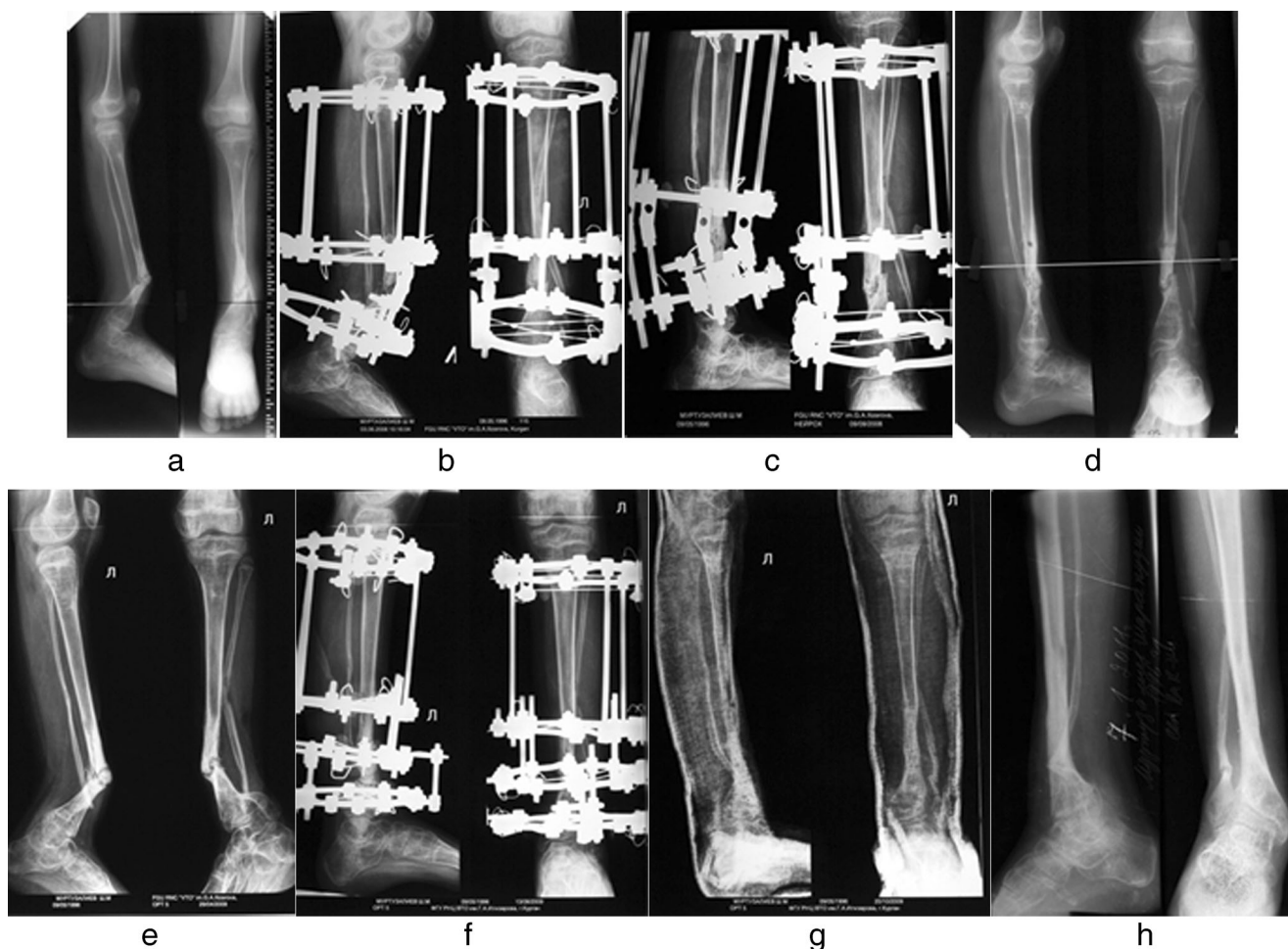
resolved using local anti-infection injections, wire removal or its reinsertion.

### Discussion

Histological examinations in 192 patients from several countries showed a nonspecific CPT appearance in 45.3% of cases, resemblance to fibrous dysplasia in 15.6%, and in 39% there was a histologic evidence of neurofibromatosis [3]. Tibial dysplasia in children with NF1, osseous fibrous or fibrous dysplasia frequently results in tibial bowing and a pathological fracture as these children grow [12, 13]. Treatment of pseudarthrosis starts before skeletal maturity but often fails and results in repetitive operations in the paediatric population. As the research showed, the problems of bone reconstruction in CPT are related to a low bone tissue potential for regeneration though the aetiological causes of this affected capacity to regenerate differ [14–17]. Recent innovations in molecular and histological studies have helped in understanding the aetiological mechanisms of the CPT pathogenesis but an appropriate treatment method has not been found. Therefore, surgical interventions with the objective to achieve union, salvage the limb, and improve patients' quality of life remain the main means.

The two alternative ways of CPT management that yield better outcomes are vascularized fibular autologous grafting and the Ilizarov method [4]. This fact can be explained by the main feature of the techniques: they both use a complex of tissues that preserves blood supply to the nonunion area.

Ilizarov proposed his method for CPT treatment in the early 1970s and described residual angulations and refractures in cases of thinned tibial fragments that happened within five



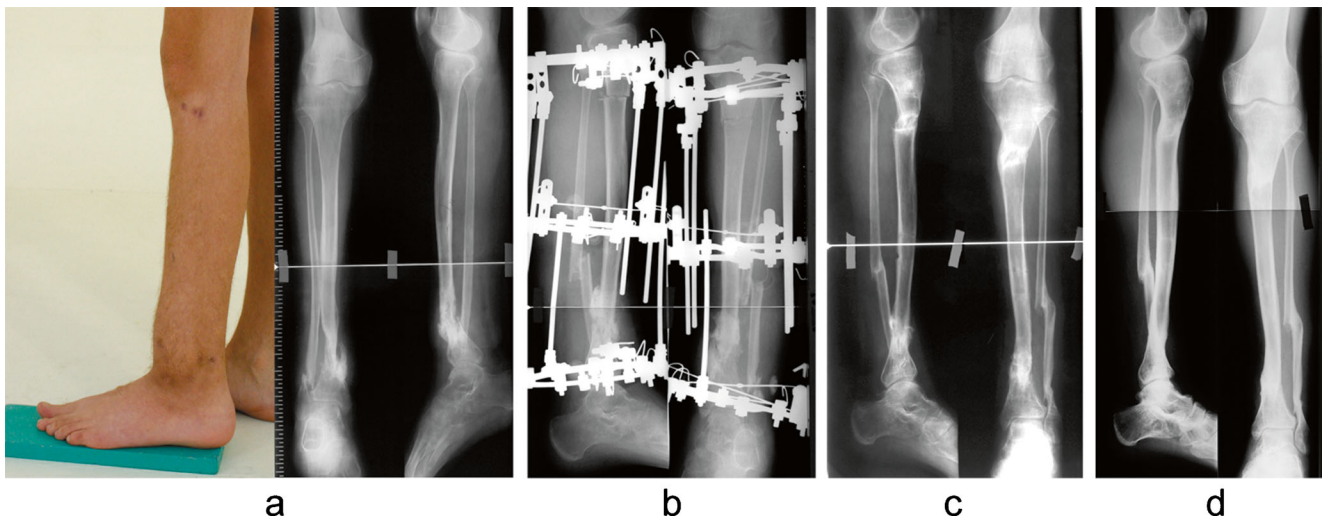
**Fig. 2** A 12-year-old female patient (Table 1, case 10) with CPT Crowfoot type IV associated with NF1 (a) who had three failed operations at another hospital was treated in 2008 by closed osteosynthesis with the Ilizarov apparatus (b) and gradual correction of the deformity for 30 days (c). X-rays show the outcome after 100 days of fixation following deformity correction (d). Re-fracture occurred

seven months after the removal of the apparatus (e). Re-operation comprised spared resection and coaptation of fragments (f). Supportive compression of 1 mm every two weeks was maintained at the fragments contact. Consolidation was obtained after 130 days (g); the leg was immobilized with a plaster cast. X-rays of the outcome in 2011 (h) demonstrate the healing

to six months after frame removal [18]. There is no doubt that the Ilizarov method is capable of producing rigid and controlled fixation for compression, distraction, bone transport to the resection defect, lengthening, deformity correction, and union. However, considerable changes in the bone tissue of the tibia make proper consolidation difficult. Therefore, refractures are frequently inevitable [15, 19]. The largest multicentre study of CPT treatment found that the Ilizarov method was the most optimal method for CPT management as far as it provides a comprehensive approach to the pathological complex [3, 4]. It was concluded that segmental bone transport alone resulted in a lower fusion rate when compared with either: (1) simple resection, acute shortening, compression; or (2) resection, acute shortening, metaphyseal lengthening [10].

**Our groups matched in CPT types, mean age and number of previous operations per patient** Several technical

approaches with the Ilizarov method were used in our series after having considered the individual condition in each of the patients. Unfortunately, the orthopaedic pathology had been worsened by previous operations in the majority of the cases. We did not do extensive resections in the pseudarthrosis area but largely used coaptation of bone fragments and various types of bridging the nonunion with local tissues to thicken the bone and increase the fragments contact area in atrophic cases, corrected deformities and lengthened in the metaphyseal area. In our opinion, bone union and axial alignment are of primary goals. Lengthening can be postponed to the next stage in severe atrophic CPT cases, in particular after multiple previous surgery [19–21]. However, our approaches did not gain the outcomes that would satisfy us as the refracture rate was rather high. Altogether, CPT consolidated in 11 children after the first intervention and in 26 cases out of the total of 28 in the period studied.



**Fig. 3** A 15-year-old male patient (Table 2, case 14) with CPT due to nonspecific tibial dysplasia (a) treated in 2012 by coaptation and lengthening in the tibial metaphysis of a longer bone fragment and

simultaneous deformity correction (b). X-rays after the apparatus removal (c) and at one-year follow-up show good healing (d)

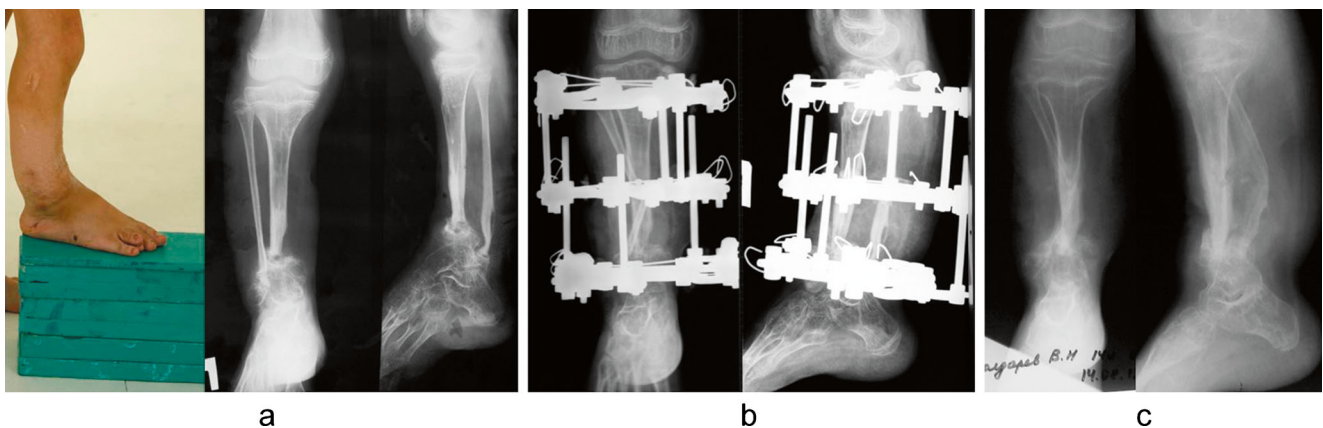
It was advised that the surgery for CPT should be avoided before the third year of life [10, 21]. We cannot draw conclusions for outcomes at this early age as far since there were few cases of this age. The risk of re-fracture was significantly higher in children under the age of ten years in cases when the tibial cross-section at the pseudarthrosis was narrow and CPT was associated with persistent fibular pseudarthrosis. We should acknowledge that the results were poor in this age subgroup. We should also admit that patients should be braced for a longer period upon initial union if complete bone remodeling does not happen in the pseudarthrosis area, or even through skeletal maturity [7].

Most of the latest studies agree that the Ilizarov method was more efficient when it was supported by intramedullary nailing [6, 9]. The advantages of both methods such as high union rate with alignment control achieved with the Ilizarov method and protection against refracture provided by intramedullary nailing are combined together. Nevertheless,

the reported rates of union and re-fracture differ in the available literature that studied combined fixation [2, 9, 21, 22]. Infected cases have also been reported [2, 9].

A combination of biological and mechanical solutions was suggested for CPT healing which included a free periosteal autologous graft along with bone graft, internal nailing and Ilizarov fixation [7]. The periosteal graft was used as a biological envelope to promote osteogenesis. However, the rate of refractures in that study was also high. It is remarkable that all the patients in our study and in the study mentioned [7] obtained union after the primary operation. It proves the fact that a greater volume of bone tissue that is achieved either by autologous free grafting or local tissues around the nonunion plays a positive role [9]. Unfortunately, it is not sufficient for the resolution of the disease as far as the tibial bone tissue remains pathological.

The search for new optimal methods of improving bone tissue quality in CPT continues [20]. It seems mandatory to



**Fig. 4** A 14-year-old patient (Table 1, case 14) with CPT associated with NF1 (a) operated in 2013. Osteosynthesis with the Ilizarov apparatus continued for 245 days (b). X-rays of a one-year outcome show good consolidation (c)

study the effects of the Masquelet two-stage membrane technique using an autologous graft and internal fixation as a procedure to be recommended for consideration in achieving and maintaining union in the early age [8, 23], an “unexpected effect” of CPT healing by lengthening over a rod without compression of the nonunion [24], and to test the benefits from regenerative strategies based on mesenchymal stromal cells, platelet-rich fibrin [25], rh-BMP-7 [26, 27], or calcium and vitamin D supplementation [28].

Nevertheless, currently in the hands of clinicians the Ilizarov method alone or supported by IMN and autologous grafting remains a method of choice for CPT treatment in children.

To our knowledge, our study is one of the latest studies of a large group of children with CPT and the first one that compared the results of CPT management with the Ilizarov techniques according to the etiological factor. We have found that the treatment does not result in a significant difference between the group of CPT with NF1 and the group without it.

## Conclusion

The unsupported Ilizarov method for management of CPT that is associated with NF1 and CPT of nonspecific or unconfirmed origin yields comparable outcomes: high rate of bone union but high re-fracture rate. More research is necessary to seek optimal solutions to support the Ilizarov method in order to reduce the number of repetitive surgery or eliminate them.

**Conflict of interest statement** The authors declare that they have no competing interests.

**Funding** The authors received no funding for doing this study.

## References

- Andersen KS (1976) Congenital pseudarthrosis of the tibia and neurofibromatosis. *Acta Orthop Scand* 47(1):108–111
- Vander Have KL, Hensinger RN, Caird M, Johnston C, Farley FA (2008) Congenital pseudarthrosis of the tibia. *J Am Acad Orthop Surg* 16(4):228–236
- Hefti F, Bollini G, Dungal P, Fixsen J, Grill F, Ippolito E, Romanus B, Tudisco C, Wientroub S (2000) Congenital pseudarthrosis of the tibia: history, etiology, classification and epidemiologic data. *J Pediatr Orthop B* 9(1):11–15
- Ohnishi I, Sato W, Matsuyama J, Yajima H, Haga N, Kamegaya M, Minami A, Sato M, Yoshino S, Oki T, Nakamura K (2005) Treatment of congenital pseudarthrosis of the tibia: a multicenter study in Japan. *J Pediatr Orthop* 25(2):219–224
- Sakamoto A, Yoshida T, Uchida Y, Kojima T, Kubota H, Iwamoto Y (2008) Long-term follow-up on the use of vascularized fibular graft for the treatment of congenital pseudarthrosis of the tibia. *J Orthop Surg Res* 3:13
- Mathieu L, Vialle R, Thevenin-Lemoine C, Mary P, Damsin JP (2008) Association of Ilizarov’s technique and intramedullary rodding in the treatment of congenital pseudarthrosis of the tibia. *J Child Orthop* 2(6):449–455
- Thabet AM, Paley D, Kocaoglu M, Eralp L, Herzenberg JE, Ergin ON (2008) Periosteal grafting for congenital pseudarthrosis of the tibia: a preliminary report. *Clin Orthop* 466:2981–2994
- Gouron R, Deroussen F, Juvet M, Ursu C, Plancq MC, Collet LM (2011) Early resection of congenital pseudarthrosis of the tibia and successful reconstruction using the Masquelet technique. *J Bone Joint Surg (Br)* 93(4):552–554
- Johnston CE, Birch JG (2008) A tale of two tibias: a review of treatment options for congenital pseudarthrosis of the tibia. *J Child Orthop* 2:133–149
- Grill F, Bollini G, Dungal P, Fixsen J, Hefti F, Ippolito E, Romanus B, Tudisco C, Wientroub S (2000) Treatment approaches for congenital pseudarthrosis of tibia: results of the EPOS multicenter study. European paediatric orthopaedic society (EPOS). *J Pediatr Orthop B* 9(2):75–89
- Ferner RE, Huson SM, Thomas N, Moss C, Willshaw H, Evans DG et al (2007) Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. *J Med Genet* 44(2):81–88
- Crawford AH, Schorry EK (1999) Neurofibromatosis in children: the role of the orthopaedist. *J Am Acad Orthop Surg* 7(4):217–230
- Exner GU, von Hochstetter AR (1995) Fibrous dysplasia and osteofibrous dysplasia. *Orthopade* 24(1):50–56
- Cho TJ, Seo JB, Lee HR, Yoo WJ, Chung CY, Choi IH (2008) Biologic characteristics of fibrous hamartoma from congenital pseudarthrosis of the tibia associated with neurofibromatosis type 1. *J Bone Joint Surg Am* 90(12):2735–2744
- Lee DY, Cho TJ, Lee HR, Lee K, Moon HJ, Park MS, Yoo WJ, Chung CY, Choi IH (2011) Disturbed osteoblastic differentiation of fibrous hamartoma cell from congenital pseudarthrosis of the tibia associated with neurofibromatosis type I. *Clin Orthop Surg* 3(3):230–237
- Riddle ND, Bui MM (2013) Fibrous dysplasia. *Arch Pathol Lab Med* 137(1):134–138
- Sakamoto A, Oda Y, Iwamoto Y, Tsuneyoshi M (2000) A comparative study of fibrous dysplasia and osteofibrous dysplasia with regard to GSA mutation at the Arg201 Codon. *J Mol Diagn* 2(2):67–72
- Ilizarov GA, Gracheva VI (1971) Bloodless treatment of congenital pseudarthrosis of the crus with simultaneous elimination of shortening using dosed distraction. *Ortop Travmatol Protez* 32(2):42–46
- Horn J, Steen H, Terjesen T (2013) Epidemiology and treatment outcome of congenital pseudarthrosis of the tibia. *J Child Orthop* 7(2):157–166
- Khan T, Joseph B (2013) Controversies in the management of congenital pseudarthrosis of the tibia and fibula. *Bone Joint J* 95-B(8):1027–1034
- Cho TJ, Choi IH, Lee SM, Chung CY, Yoo WJ, Lee DY, Lee JW (2008) Refracture after Ilizarov osteosynthesis in atrophic-type congenital pseudarthrosis of the tibia. *J Bone Joint Surg (Br)* 90(4):488–493
- Agashe MV, Song SH, Refai MA, Park KW, Song HR (2012) Congenital pseudarthrosis of the tibia treated with a combination of Ilizarov’s technique and intramedullary rodding. *Acta Orthop* 83(5):515–522
- Pannier S, Pejcin Z, Dana C, Masquelet AC, Glorion C (2013) Induced membrane technique for the treatment of congenital pseudarthrosis of the tibia: preliminary results of five cases. *J Child Orthop* 7(6):477–485
- Muhammad Abdul Jamil MK, Abdul Rashid AH, Ibrahim S (2013) Congenital pseudarthrosis of the tibia: healing by lengthening over a rod without compression of the nonunion. a preliminary report. *J Pediatr Orthop B* 22(3):207–212



25. Granchi D, Devescovi V, Baglio SR, Magnani M, Donzelli O, Baldini N (2012) A regenerative approach for bone repair in congenital pseudarthrosis of the tibia associated or not associated with type 1 neurofibromatosis: correlation between laboratory findings and clinical outcome. *Cytotherapy* 14(3):306–314
26. Das SP, Ganesh S, Pradhan S, Singh D, Mohanty RN (2014) Effectiveness of recombinant human bone morphogenetic protein-7 in the management of congenital pseudarthrosis of the tibia: a randomised controlled trial. *Int Orthop* 38(9):1987–1992
27. Dohin B, Kohler R (2012) Masquelet's procedure and bone morphogenetic protein in congenital pseudarthrosis of the tibia in children: a case series and meta-analysis. *J Child Orthop* 6(4):297–306. doi:[10.1007/s11832-012-0421-3](https://doi.org/10.1007/s11832-012-0421-3)
28. Petramala L, Giustini S, Zinamosca L, Marinelli C, Colangelo L, Cilenti G, Formicuccia MC, D'Erasmus E, Calvieri S, Letizia C (2012) Bone mineral metabolism in patients with neurofibromatosis type 1 (von Recklinghausen disease). *Arch Dermatol Res* 304(4):325–331