Traumatology and Orthopaedics of Kazakhstan
ISSN - e2789-9640

Review

Congenital Pseudoarthrosis of the Tibia: Current Treatment Strategies and Outcomes. Literature Review

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Received: 20 October 2025
Revised: 23 November 2025
Accepted: 02 December 2025
Published: 30 December 2025

Citation: Arsen Kaliyev, Dina Saginova, Agabek Chikinayev. Congenital Pseudoarthrosis of the Tibia: Current Treatment Strategies and Outcomes. Literature Review. Trauma & Ortho Kaz, 2025, 76 (6), jto032.
https://doi.org/10.52889/1684-9280-2025-76-6-jto032

Abstract

Congenital pseudarthrosis of the tibia is a rare but clinically significant condition that leads to progressive deformity of the lower limb, impaired bone regeneration, repeated fractures, and substantial long-term functional limitations in affected children. Although the disorder has been described for more than a century, its underlying mechanisms remain incompletely understood, and current evidence points to a complex interaction of genetic, molecular, and biomechanical factors that contribute to the formation of fibrous nonunion. A wide range of therapeutic strategies has been proposed, including intramedullary fixation, circular external fixation using the Ilizarov technique, vascularized bone grafts, combined surgical approaches, and modern procedures aimed at creating a stable tibiofibular bone block. Despite significant progress in surgical management, the risks of persistent nonunion, recurrent deformity, and refracture remain considerable. Parallel to surgical advances, biological and pharmacological methods intended to enhance bone healing—such as bone morphogenetic proteins, bisphosphonates, platelet-rich plasma, cellular therapies, and engineered osteogenic constructs—are being actively explored, although current clinical evidence remains heterogeneous. Given the variability of treatment protocols and the limited number of high-quality comparative studies, a comprehensive synthesis of available data is essential for identifying the most effective approaches and guiding future research. This review summarizes contemporary knowledge on the pathogenesis, clinical presentation, and treatment strategies for congenital pseudarthrosis of the tibia and highlights the need for standardized protocols and multicenter studies to improve long-term outcomes in pediatric patients.

Keywords: congenital pseudarthrosis of the tibia, Ilizarov apparatus, intramedullary rod, cross-union.

1. Introduction

Congenital pseudarthrosis of the tibia (CPT) is a rare and severe form of tibial dysplasia and remains one of the most challenging conditions in pediatric orthopedics due to its resistance to treatment and high

recurrence rates [1,2]. The condition typically presents with anterolateral tibial bowing that progresses to spontaneous or low-energy fractures and nonunion, ultimately leading to functional impairment and limb deformity [1,3,4]. Reported incidence ranges from 1 per 140,000 to 1 per 250,000 live births [1].

A strong association between CPT and neurofibromatosis type 1 (NF1) has been well documented, with NF1 present in 38–90% of affected children [5-12]. Recent genetic and molecular studies have demonstrated that dysregulation of the rat sarcoma–mitogen-activated protein kinase kinase–extracellular signal-regulated kinase (RAS–MEK–ERK) signaling pathway, NF1 germline mutations, somatic mosaicism, and altered osteoblastic differentiation play a central role in CPT pathogenesis [13-17]. Histologically, CPT is characterized by a fibrous hamartoma with low osteogenic and high osteoclastogenic potential, explaining the high risk of nonunion even after adequate surgical management [18-24]. Furthermore, several studies have revealed alterations in serum growth factor profiles, periosteal proteomics, and exosome-mediated signaling, which contribute to impaired bone regeneration in these patients [18,25,26].

Clinically, CPT manifests with progressive tibial deformity, limb shortening, ankle valgus, and functional impairment, while bilateral involvement remains extremely rare [10,11,27-29]. In addition to orthopedic complications, CPT imposes a significant psychosocial burden on children and their caregivers [8].

Despite advances in orthopedic surgery, achieving durable bone union and preventing refracture remain challenging. Numerous surgical strategies have been proposed, including intramedullary fixation, circular external fixation using the Ilizarov method, vascularized bone grafts, combined fixation techniques, and the more recent cross-union protocol [30-57]. The introduction of biological and pharmacological adjuvants – such as bisphosphonates, bone morphogenetic proteins, platelet-rich plasma, and osteogenic organoids—has expanded therapeutic possibilities; however, available evidence remains heterogeneous and is based mostly on small, non-comparative studies [58-81].

Given the variability in treatment protocols and the limited number of high-quality studies, a structured synthesis of current evidence is needed. Therefore, the objective of this review was to summarize contemporary surgical and biological treatment strategies for CPT in children, compare their reported outcomes, and identify factors associated with treatment success and refracture.

2. Methodology

This review involves data collected from various studies, and some of the references have been taken from articles published in journals like PubMed, Scopus, and Web of Science and utilized the keywords to sensitize or search: congenital pseudarthrosis of the tibia, Ilizarov apparatus, intramedullary rod, cross-union. We excluded the article that was incomplete, not in the English language, or duplicate. Studies have been made on patients presenting with CPT.

3. Etiology and Pathogenesis

CPT is recognized as a genetic disorder with incompletely understood pathogenetic mechanisms. According to Agrawal et al. and Yang G et al., in 38–90% of cases, the disease is associated with NF1, and fibular anomalies are observed in 60–90% of cases [9-11]. The findings of Zhu et al. further support a strong association with NF1: among 75 patients with CPT, up to 84% showed clinical signs of NF1 [12]. Mutations in the NF1 gene lead to increased activation of the RAS pathway and subsequent clinical consequences. Elevated levels of active RAS protein trigger the MEK–ERK signaling cascade [13]. Single-cell sequencing of samples obtained from pseudarthrosis sites and iliac crest bone identified expression signatures indicating upregulated MAPK pathway activity in pseudarthrosis-derived cells [14].

Zheng et al. reported the presence of somatic mosaicism in this patient population: monoallelic NF1 inactivation was found in 21% of patients without NF1, whereas biallelic inactivation was detected in 83.3% of patients with NF1-associated CPT in pseudarthrosis tissue. These findings highlight that both germline and somatic alterations in NF1 may play critical roles in disease pathogenesis [15].

The study by Wang et al. expanded current knowledge of the genetic background of CPT. In a cohort of 159 patients, whole-exome sequencing identified rare loss-of-function (LoF) variants affecting NF1, GLI3, MRC2, PTH1R, RYR1, NPR2, and ITGA11.

These mutations are associated with disturbances in osteogenesis and ossification processes, suggesting their contribution to the complex molecular network underlying CPT [16]. Xu et al. identified a novel p.E291* mutation resulting in the loss of multiple functional domains, including CSRD, GRD, TBD, SEC14-PH, CTD, and NLS, which may explain the severe clinical manifestations observed in CPT [17].

Liu et al. reported proteomic differences in CPT patients: 347 proteins were differentially expressed in NF1-associated cases, and 467 in non-NF1 cases, with 231 proteins overlapping between the two groups, suggesting shared pathogenic mechanisms [18]. The remaining differences support the existence of multiple pathogenic phenotypes that require further clarification [19]. Lee D.Y. et al. demonstrated that circ_0000888 suppresses miR-338-3p activity and enhances PTN expression, thereby increasing the viability and osteogenic differentiation capacity of CPT-dPMSCs [22]. Perrin showed that combined MEK–SHP2 inhibition prevents fibrous nonunion in an NF1 model [14]. Novel regulators of osteogenesis have been identified, including METTL3 (enhancing MSC differentiation through the HOXD8/ITGA5 axis), miR-30a (inhibiting osteogenesis by suppressing HOXD8/RUNX2), and circ_0000888/miR-338-3p/PTN (modulating osteogenic activity) [21].

The primary lesion in CPT is a hamartoma, a dysontogenetic formation characterized by low osteogenic and high osteoclastogenic potential. Hamartoma develops due to aberrant growth of periosteal cells that fail to undergo terminal osteoblastic differentiation and arrest at a specific stage of this process [22]. Diaz-Solano et al. conducted histological studies of hamartomas and found spindle-shaped mesenchymal cells, but no osteoblasts, osteoclasts, chondrocytes, or adipocytes responsible for osteogenesis were detected [23].

Several studies indicate that mesenchymal stem cells (MSCs) are not the primary cause of impaired bone regeneration in CPT patients [10,22]. Cho et al. investigated the immunophenotype of hamartoma cells compared to periosteal cells from non-CPT patients and analyzed mRNA expression of BMP-2, BMP-4, and their receptors using reverse transcription PCR. They found that hamartoma cells did not undergo osteoblastic differentiation in response to BMP stimulation and exhibited higher osteoclastogenic potential compared to control periosteal cells [24].

Patients with CPT demonstrate low bone regenerative capacity, serum TGF (transforming growth factor) imbalance, and impaired collagen synthesis [25]. Differences in serum-derived exosomal proteins (SDEs) have also been noted between healthy children, CPT patients, and those with NF1. These differentially expressed proteins in CPT-SDEs worsen trabecular bone microarchitecture by inhibiting bone formation and promoting bone resorption [26].

4. Clinical manifestations

CPT is most commonly localized in the middle or distal third of the tibia, while bilateral involvement is exceptionally rare [10,11,27]. The primary clinical sign is anterolateral bowing of the tibia (ALBT), which manifests as varus–procurvatum deformity of the distal third of the diaphysis combined with valgus–recurvatum deformity of the proximal third. In newborns and infants, the condition may present as a marked limb deformity or leg shortening, which becomes apparent at birth or within the first months of life. As the child grows, particularly with the onset of walking, the deformity tends to progress, frequently resulting in spontaneous or pathological fractures that form a pseudarthrosis and lead to loss of weight-bearing function of the affected limb.

Combined fractures of the fibula and tibia often lead to proximal migration of the distal fibular fragment, contributing to valgus deformity and instability of the ankle joint [4,28]. Valgus deformities of the knee and ankle are observed in 38.11% of patients, while limb shortening occurs in 35.69% of cases [29].

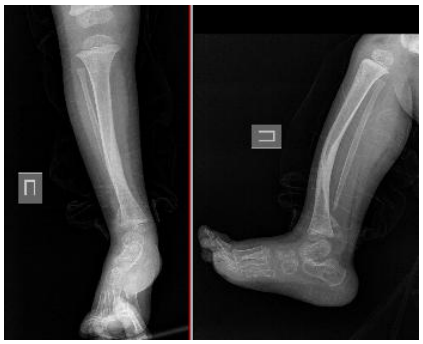

Figure 1 – X-ray of the right lower leg and foot in two projections shows anterolateral tibial deformity, fibular pseudarthrosis, and valgus deformity of the ankle joint

ALBT leads to reduced tone of the posterior compartment muscles of the lower leg, which in turn contributes to the development of calcaneocavus deformity of the foot. The combination of deformity, impaired muscle function, and lack of weight-bearing results in slowed tibial growth and limb shortening [29,30]. In response, compensatory hypertrophy of the ipsilateral femur and valgus deformity of the femoral neck may develop, which can ultimately lead to secondary hip dysplasia [31].

Diagnosis

The "gold standard" for diagnosing CPT is standard radiography of the affected limb. Radiographs typically reveal bowing of the tibia and fibula, thinning of the cortical bone, sclerosis of the bone, or signs of stress fracture. In newborns, marked deformity with limb shortening may already be evident. Over time, a pseudarthrosis forms, often accompanied by calcification of the fibrous tissue. The distal third of the tibia is most commonly affected, and the fibula is almost always involved [3].

Densitometry data show a statistically significant reduction in cortical bone density in the affected tibia of all CPT patients prior to treatment. Following treatment, bone density approaches normal values [32].

Magnetic resonance imaging (MRI) plays an important role in preoperative planning by accurately defining the resection margins and detecting subtle soft tissue changes. Additionally, intravenous contrast administration allows visualization of bone perfusion, which can be useful for assessing vascularization defects and determining the appropriate resection volume [33].

5. Classifications of CPT

Several classification systems for CPT have been proposed, but the most widely used remains the Crawford classification, which is based on radiographic appearance:

Crawford Classification (1986):

Type 1: Anterior bowing with increased cortical density and a narrow medullary canal.

Type 2: Anterior bowing with sclerotic bone and a narrow elongated medullary canal.

Type 3: Anterior bowing associated with a cyst.

Type 4: Anterior bowing with an obvious fracture and pseudarthrosis involving both the tibia and fibula [34].

In clinical practice, the Paley classification is also used. This system takes into account the integrity of the tibia and fibula, the presence or absence of proximal migration of the distal fibula, and the size of the bone defect. These factors influence the treatment protocol for CPT [30].

Paley Classification (2019):

Type 1: Both tibia and fibula are intact with anterolateral bowing.

Type 2: Tibia intact, fibula fractured.

2A: Fibula remains in place (no migration).

2B: Fibula fractured with proximal migration.

Type 3: Tibial fracture with intact fibula.

Type 4: Both tibia and fibula fractured.

4A: Both bones fractured, but fibula remains in place.

4B: Both bones fractured with proximal migration of the fibula.

4C: Both bones fractured, with a significant tibial defect and proximal fibular migration.

Other classifications, including those proposed by El-Rosasy, Boyd, and Anderson, also exist but are less commonly used in clinical practice [2,3,74].

6. Treatment

Conservative Treatment

Conservative treatment of CPT involves orthotic management of the limb, aimed at preventing fractures and the progression of deformity [37,38]. Physical therapy is prescribed to maintain the range of motion and strengthen the muscles, while ensuring adequate levels of vitamin D, calcium, and phosphorus is also recommended.

Surgical Treatment

Surgical treatment remains the mainstay of therapy for CPT, with the goals of achieving bone union, restoring limb function, and preventing refracture. The best outcomes are achieved when surgery is performed before the age of three and in the absence of previous surgical interventions [39]. A variety of surgical techniques have been employed, including intramedullary fixation, use of the Ilizarov apparatus, combined methods, plate and screw

fixation, vascularized bone grafting, and the cross-union technique.

The use of intramedullary rods was introduced in the mid-20th century. However, its effectiveness has been limited by high rates of nonunion [40,41]. According to a systematic review by Aiona et al. including 22 studies, the mean primary union rate with intramedullary fixation was 64%, while refracture rates reached 35–40% [42]. Similarly, Ong et al. reported a low rate of stable union (22.2%) with isolated intramedullary fixation during long-term follow-up [43].

Vascularized fibular bone grafting with microvascular anastomoses was first described by Judet and Gilbert in 1978 [44]. In a meta-analysis by Madhuri et al. of 14 studies, union rates ranged from 87% to 95%, although stress fractures of the graft occurred in approximately 20% of patients [39,45,46]. Costa et al. and Soldado et al. confirmed that this technique offers the best outcomes in younger children but is technically demanding and carries a significant risk of donor-site morbidity [47,48].

The Ilizarov method remains one of the most commonly used techniques for surgical correction of CPT, providing stability and the possibility of limb lengthening. In a meta-analysis by Zhu et al. including over 200 patients, the mean union rate ranged from 82% to 85% [49]. A major advantage of the Ilizarov method is the ability to address limb shortening, with a recommended distraction rate of 0.5 mm per day [50,51].

Among traditional techniques, the combination of intramedullary fixation with the Ilizarov apparatus has been shown to be the most effective. A systematic review by Tan et al. and a meta-analysis by Jing et al. demonstrated primary union rates of 88–92% and refracture rates reduced to 15–20%. This combined approach has a higher level of evidence (Level II) and is recommended as the standard treatment, especially for revision cases [52-56]. Popkov et al. evaluated the use of hydroxyapatite-coated intramedullary nails combined with the Ilizarov method in six patients with CPT and reported no refractures during a mean follow-up of 2.1 years, indicating promising outcomes [57].

In recent years, a promising surgical approach has been the cross-union technique, developed by Paley. This protocol involves creating a tibiofibular synostosis to enhance stability and biological healing. \

The procedure includes:

- Preoperative zoledronic acid infusion;
- Excision of hamartomatous tissue around the tibia and fibula with interosseous membrane resection;
- Tibial fixation using a telescopic growing rod and fibular fixation with a Kirschner wire;
- Harvesting of cancellous bone graft;
- Placement of a three-layer graft consisting of (i) periosteum around the pseudarthrosis site, (ii) cancellous bone between and around the tibia and fibula, and (iii) BMP-2 anteriorly and posteriorly, covered by soft tissues.

Initially, external fixation with the Ilizarov apparatus is applied to provide compression and rotational stability, although the smooth, unlocked telescopic rod only provides angular support. In 2017, the external fixator was replaced with an internal locking plate. In Paley's study, the primary union rate was 100%, with refractures occurring in less than 25% of cases [30]. The use of biological adjuvants, such as bone morphogenetic proteins (BMP), platelet-rich plasma (PRP), and bisphosphonates, has been shown to enhance the effectiveness of surgical treatment [58–63]. However, authors emphasize that current evidence is based mainly on case series and medium-term follow-up (up to 10 years). Large multicenter randomized controlled trials are needed to confirm the long-term efficacy of these combined protocols [30,64].

Table 1 – Comparative characteristics of surgical methods for the treatment of CPT

Method	Primary union	Final union	Time to union	Nonunion rate
Intramedullary nailing (IMN)	67,7%	76,5%	12,6 months	17,0%
Ilizarov apparatus	84.2%	81,5%	9,3 months	13,6%
IMN + Ilizarov apparatus	83.7%	92,4%	5,3 months	6,0%
Vascularized bone graft	65.3%	87,1%	9,5 months	7,9%
Cross-union technique	100%	100%	4,5 months	

During surgery, proper positioning of the operated limb is crucial to avoid new complications during the treatment process. Seo et al. emphasize the importance of early stabilization and preservation of ankle joint

mobility during and after surgery, which is considered critical for maintaining joint function in patients with CPT [65].

ALBT is regarded as a distinct pre-fracture condition. Recent studies have demonstrated that guided growth techniques can improve alignment, reduce the risk of fracture, and, in many cases, prevent the development of pseudarthrosis. The principle of this technique involves temporary tethering of the lateral column of the distal tibial physis using a plate, staples, or screws. This is a minimally invasive, simple, and effective corrective procedure that can delay or even prevent the progression to CPT [66–69].

7. Biological Therapy and Cellular Technologies

Given the complexity of treating CPT, a comprehensive therapeutic approach is essential. Numerous studies have investigated the impact of orthobiological and pharmacological agents on the treatment process of tibial pseudarthrosis. Evidence suggests that bisphosphonates enhance the proliferation and osteogenic differentiation of MSCs in CPT through activation of the p38/ERK1/2 signaling pathways and modulation of the RANKL/OPG axis [16]. However, some studies have reported that bisphosphonates used in monotherapy are insufficient to induce complete osteogenesis [70]. The Paley protocol incorporates the use of bone BMPs; however, the application of rhBMP-2 and BMP-7 has yielded mixed results. While consolidation was achieved in some patients, several studies have described complications and high recurrence rates [71–76]. In a meta-analysis, Kesireddy et al. found no significant advantage of BMP use compared to combined Ilizarov fixation and intramedullary nailing [77]. In a randomized controlled trial, Das et al. evaluated the efficacy of recombinant human BMP-7 (rhBMP-7) in the treatment of CPT and concluded that BMP-7 combined with autologous bone grafting offers no clear benefit over autologous grafting alone [78].

The use of vasoactive intestinal peptide (VIP) has also been explored in combined CPT treatment protocols. VIP was found to inhibit osteoclast differentiation via the RANKL/OPG and NF-κB pathways, making it a potentially attractive therapeutic option that warrants further investigation [79].

Additionally, osteogenic organoids (OstO) composed of allogeneic bone marrow MSCs, PRP clot, and collagen microgranules have been investigated. Their application during surgery led to union of CPT within six months [80]. Meselhy et al. studied the use of induced biomembrane techniques in 19 patients with recurrent CPT and reported successful consolidation in all patients, each of whom had previously undergone unsuccessful surgical interventions [81].

Thus, a variety of biological agents have been explored as part of the comprehensive management of CPT, many of which show promising potential for future research and clinical application. Nevertheless, a wide range of known orthobiological compounds remain unstudied in the context of CPT treatment, highlighting the need for further investigation in this area.

8. Discussion

This review summarizes current surgical and biological strategies for managing CPT. Despite advances in operative techniques, achieving reliable union and preventing refracture remain major challenges.

Across the included studies, isolated intramedullary fixation demonstrated the lowest union rates and the highest risk of refracture, confirming that it should not be used as a standalone treatment. The Ilizarov method showed better outcomes due to controlled compression, deformity correction, and stimulation of osteogenesis; however, complications such as pin tract infection and joint stiffness remain common.

Combined fixation using intramedullary nails together with the Ilizarov apparatus consistently produced higher primary and final union rates and lower refracture rates than either technique alone. This approach currently represents one of the most reliable treatment options, especially in recurrent cases.

Vascularized bone grafting demonstrated high union rates, particularly in younger children, though its complexity and donor-site morbidity limit its use. The cross-union technique (Paley protocol) achieved the most favorable outcomes, including 100% primary union in several studies, likely due to enhanced mechanical stability and a broad biological environment for healing.

Biological adjuvants such as bisphosphonates, BMPs, PRP, and cellular technologies have shown variable results. While some studies report enhanced osteogenesis, the overall evidence remains heterogeneous and largely limited to small case series.

Factors associated with better outcomes include younger age at surgery, stable fixation, intact or reconstructed fibular alignment, and prolonged postoperative protection. Refracture continues to be a significant concern, emphasizing the need for long-term follow-up and orthotic support throughout growth.

Overall, modern surgical strategies—especially combined fixation and the cross-union technique—have substantially improved outcomes, but CPT remains a biologically challenging condition. Further prospective and comparative studies are required to establish standardized treatment protocols and evaluate the long-term effectiveness of emerging biological therapies.

9. Conclusions

CPT remains one of the most difficult conditions in pediatric orthopedics due to its complex biological background and high risk of recurrent nonunion. Modern surgical approaches—particularly combined intramedullary fixation with the Ilizarov method and the cross-union technique—demonstrate the most consistent and reliable outcomes, offering high union rates and reduced refracture risk. Biological adjuvants such as bisphosphonates, BMPs, PRP, and cellular technologies may enhance healing but require further validation. Long-term protection, correction of associated deformities, and careful follow-up through skeletal maturity remain essential components of successful treatment. Continued development of standardized protocols and prospective multicenter studies is necessary to further improve long-term outcomes for children with CPT.

Conflict of interest. The authors declare that there is no conflict of interest.

Acknowledgments. The authors express their gratitude to the institutions and colleagues who contributed to the research and preparation of this article.

Funding. This research received no external funding.

Authors contributions: Conceptualization – A.K.; Methodology – D.S.; Validation – A.K.; Formal analysis – A.K., D.S., and A.Ch.; Writing – original draft – A.K.; Writing – review and editing – D.S. All authors have read and approved the final version of the manuscript and signed the copyright transfer form.

References

1. Hefti, F., Bollini, G., Dungl, 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. Journal of pediatric orthopedics. Part B, 9(1), 11–15. https://doi.org/10.1097/01202412-200001000-00003
2. Boyd H. B. (1982). Pathology and natural history of congenital pseudarthrosis of the tibia. Clinical orthopaedics and related research, (166), 5–13.
3. El-Rosasy, M. A. (2025). Congenital Pseudarthrosis Tibia (El-Rosasy–Paley Type 2). In Limb Lengthening and Reconstruction Surgery Case Atlas: Pediatric Deformity (pp. 167-171). Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-77359-4_279
4. Zhou, Y., Tan, Q., Liu, K., Liu, Y., Zhu, G., Mei, H., & Yang, G. (2022). Epidemiological and clinical characteristics of congenital pseudarthrosis of the tibia in China. Frontiers in pediatrics, 10, 943917. https://doi.org/10.3389/fped.2022.943917
5. Van Den Heuvel, S. C. M., Winters, H. A. H., Ultee, K. H., Zijlstra-Koenrades, N., & Sakkers, R. J. B. (2020). Combined massive allograft and intramedullary vascularized fibula transfer: the Capanna technique for treatment of congenital pseudarthrosis of the tibia. Acta orthopaedica, 91(5), 605–610. https://doi.org/10.1080/17453674.2020.1773670
6. O'Donnell, C., Foster, J., Mooney, R., Beebe, C., Donaldson, N., & Heare, T. (2017). Congenital Pseudarthrosis of the Tibia. JBJS reviews, 5(4), e3. https://doi.org/10.2106/JBJS.RVW.16.00068
7. Westberry, D. E., Carpenter, A. M., Tisch, J., & Wack, L. I. (2018). Amputation Outcomes in Congenital Pseudarthrosis of the Tibia. Journal of pediatric orthopedics, 38(8), e475–e481. https://doi.org/10.1097/BPO.0000000000001211
8. Xie, J. H., Mei, H. B., Liu, K., Zhu, G. H., Ouyang, Y. Q., Huang, Y., Hou, S. T., Wang, L. Y., & Yi, Y. Z. (2022). Analysis of related factors of behavioral problems in children with congenital pseudarthrosis of tibia. Revista da Associacao Medica Brasileira (1992), 68(7), 893–897. https://doi.org/10.1590/1806-9282.20211197

9. Van Royen, K., Brems, H., Legius, E., Lammens, J., & Laumen, A. (2016). Prevalence of neurofibromatosis type 1 in congenital pseudarthrosis of the tibia. European journal of pediatrics, 175(9), 1193–1198. https://doi.org/10.1007/s00431-016-2757-z

10. Agrawal, U., & Tiwari, V. (2023). Congenital Tibial Pseudarthrosis. In StatPearls. StatPearls Publishing.

11. Yang, G., Xu, S., Mei, H., Zhu, G., Liu, Y., Tan, Q., & Yu, H. (2022). Are Children Suffering From Congenital Pseudarthrosis of the Tibia Associated With Decreased Bone Strength?. Frontiers in pediatrics, 10, 859580. https://doi.org/10.3389/fped.2022.859580

12. Zhu, G., Zheng, Y., Liu, Y., Yan, A., Hu, Z., Yang, Y., Xiang, S., Li, L., Chen, W., Peng, Y., Zhong, N., & Mei, H. (2019). Identification and characterization of NF1 and non-NF1 congenital pseudarthrosis of the tibia based on germline NF1 variants: genetic and clinical analysis of 75 patients. Orphanet journal of rare diseases, 14(1), 221. https://doi.org/10.1186/s13023-019-1196-0

13. Khalid, A., Paria, N., & Rios, J. J. (2025). Molecular Basis of Fracture Pseudarthrosis Associated with Neurofibromatosis Type 1. Journal of the Pediatric Orthopaedic Society of North America, 12, 100202. https://doi.org/10.1016/j.jposna.2025.100202

14. Perrin, S., Protic, S., Bretegnier, V., Laurendeau, I., de Lageneste, O. D., Panara, N., Ruckebusch, O., Luka, M., Masson, C., Maillard, T., Coulpier, F., Pannier, S., Wicart, P., Hadj-Rabia, S., Radomska, K. J., Zarhrate, M., Ménager, M., Vidaud, D., Topilko, P., Parfait, B., … Colnot, C. (2024). MEK-SHP2 inhibition prevents tibial pseudarthrosis caused by NF1 loss in Schwann cells and skeletal stem/progenitor cells. Science translational medicine, 16(753), eadj1597. https://doi.org/10.1126/scitranslmed.adj1597

15. Zheng, Y., Zhu, G., Liu, Y., Zhao, W., Yang, Y., Luo, Z., Fu, Y., Mei, H., & Hu, Z. (2022). Case series of congenital pseudarthrosis of the tibia unfulfilling neurofibromatosis type 1 diagnosis: 21% with somatic NF1 haploinsufficiency in the periosteum. Human genetics, 141(8), 1371–1383. https://doi.org/10.1007/s00439-021-02429-2

16. Wang, R., Zheng, Y., Yang, G., Xu, Z., Liu, Y., Zhao, W., Wang, H., Mei, H., & Zhu, G. (2025). Unraveling the molecular landscape of congenital pseudoarthrosis of the tibia: insights from a comprehensive analysis of 159 probands. Orphanet journal of rare diseases, 20(1), 269. https://doi.org/10.1186/s13023-025-03759-4

17. Xu, J., Zhang, Y., Zhu, K., Li, J., Guan, Y., He, X., Jin, X., Bai, G., & Hu, L. (2022). Clinical characteristics and in silico analysis of congenital pseudarthrosis of the tibia combined with neurofibromatosis type 1 caused by a novel NF1 mutation. Frontiers in genetics, 13, 991314. https://doi.org/10.3389/fgene.2022.991314

18. Liu, Y., Qin, Z. Q., Zheng, Y., Wu, J., Yang, G., Tan, Q., Zhu, G., Liu, K., & Mei, H. (2022). New insights into pathogenesis of congenital pseudarthrosis of tibia in children using periosteum proteomics analysis. Rapid communications in mass spectrometry: RCM, 36(21), e9374. https://doi.org/10.1002/rcm.9374

19. Liu, Y., Mei, H., Zhu, G., Liu, K., Wu, J., Tang, J., & He, R. (2018). Congenital pseudarthrosis of the tibia in children: should we defer surgery until 3 years old?. Journal of pediatric orthopedics. Part B, 27(1), 17–25. https://doi.org/10.1097/BPB.0000000000000468

20. Li, Z., Liu, Y., Huang, Y., Tan, Q., Mei, H., Zhu, G., Liu, K., & Yang, G. (2023). Circ_0000888 regulates osteogenic differentiation of periosteal mesenchymal stem cells in congenital pseudarthrosis of the tibia. iScience, 26(10), 107923. https://doi.org/10.1016/j.isci.2023.107923

21. Ye, W., Liu, Z., Liu, Y., Xiao, H., Tan, Q., Yan, A., & Zhu, G. (2024). METTL3 promotes the osteogenic differentiation of periosteum-derived MSCs via regulation of the HOXD8/ITGA5 axis in congenital pseudarthrosis. Regenerative therapy, 26, 42–49. https://doi.org/10.1016/j.reth.2024.04.004

22. Lee, D. Y., Cho, T. J., Lee, H. R., Lee, K., Moon, H. J., Park, M. S., Yoo, W. J., Chung, C. Y., & Choi, I. H. (2011). Disturbed osteoblastic differentiation of fibrous hamartoma cell from congenital pseudarthrosis of the tibia associated with neurofibromatosis type I. Clinics in orthopedic surgery, 3(3), 230–237. https://doi.org/10.4055/cios.2011.3.3.230

23. Diaz-Solano, D., Wittig, O., Mota, J. D., & Cardier, J. E. (2015). Isolation and Characterization of Multipotential Mesenchymal Stromal Cells from Congenital Pseudoarthrosis of the Tibia: Case Report. Anatomical record (Hoboken, N.J. : 2007), 298(10), 1804–1814. https://doi.org/10.1002/ar.23198

24. Cho, T. J., Seo, J. B., Lee, H. R., Yoo, W. J., Chung, C. Y., & Choi, I. H. (2008). Biologic characteristics of fibrous hamartoma from congenital pseudarthrosis of the tibia associated with neurofibromatosis type 1. The Journal of bone and joint surgery. American volume, 90(12), 2735–2744. https://doi.org/10.2106/JBJS.H.00014

25. Vykhovanets, E. P., Luneva, S. N., Nakoskina, N. V., Borzunov, D. Y., & Mokhovikov, D. S. (2018). Soderzhanie nekotorykh osteotropnykh faktorov rosta, markerov osteogeneza i biologicheski aktivnykh molekul v krovi patsientov s vrozhdennym lozhnym sustavom goleni pri ortopedicheskom lechenii s ispol'zovaniem kombinirovannykh tekhnologiĭ (Concentration of several osteotropic growth factors, markers of osteogenesis and biologically active molecules in the blood serum of patients with congenital pseudarthrosis of tibia during orthopaedic treatment with combined technologies) [in Russian]. Biomeditsinskaia khimiia, 64(6), 525–533. https://doi.org/10.18097/PBMC20186406525

26. Yang, G., Yu, H., Liu, Y., Ye, W., Zhu, G., Yan, A., Tan, Q., & Mei, H. (2021). Serum-derived exosomes from neurofibromatosis type 1 congenital tibial pseudarthrosis impaired bone by promoting osteoclastogenesis and

inhibiting osteogenesis. Experimental biology and medicine (Maywood, N.J.), 246(2), 130–141. https://doi.org/10.1177/1535370220962737

27. Chand, S., Afaque, S. F., & Singh, R. K. (2024). Bilateral congenital pseudoarthrosis of the tibia: A case report and literature review. Journal of clinical orthopaedics and trauma, 58, 102769. https://doi.org/10.1016/j.jcot.2024.102769

28. Zargarbashi, R., Bagherpour, A., Keshavarz-Fathi, M., Panjavi, B., & Bagherpour Zarchi, M. (2021). Prognosis of Congenital Pseudarthrosis of the Tibia: Effect of Site of Tibial Pseudarthrososis and Fibular Involvement. Journal of pediatric orthopedics, 41(7), 422–427. https://doi.org/10.1097/BPO.0000000000001861

29. Khan, T., & Joseph, B. (2013). Controversies in the management of congenital pseudarthrosis of the tibia and fibula. The bone & joint journal, 95-B(8), 1027–1034. https://doi.org/10.1302/0301-620X.95B8.31434

30. Paley D. (2019). Congenital pseudarthrosis of the tibia: biological and biomechanical considerations to achieve union and prevent refracture. Journal of children's orthopaedics, 13(2), 120–133. https://doi.org/10.1302/1863-2548.13.180147

31. Liu, Y. X., Yang, G., Hu, X. K., Tan, Q., Pan, H., Liu, K., ... & Mei, H. B. (2023). Long term follow-up evaluation of combined surgery for congenital tibial pseudarthrosis in children. Zhonghua wai ke za zhi [Chinese Journal of Surgery], 61(8), 675-680. https://doi.org/10.3760/cma.j.cn112139-20230205-00051

32. Khmyzov, S. O., Katsalap, Y. S., Karpinsky, M. J., & Karpinska, O. (2022). Experimental study of bone density in patients with congenital pseudoarthrosis of the tibia before and after surgery. Wiad Lek, 75(9 pt 1), 2112-20. https://doi.org/10.36740/WLek202209112

33. Cariello, V., Smaldone, M. C., Durante, A., Pizzicato, P., Rossi, A., Minelli, R., Ferrara, D., Esposito, F., Zeccolini, M., & Rossi, E. (2024). Congenital tibial pseudarthrosis: A challenge in pediatric radiology. Radiology case reports, 19(6), 2502–2507. https://doi.org/10.1016/j.radcr.2024.03.045

34. Crawford A. H. (1986). Neurofibromatosis in children. Acta orthopaedica Scandinavica. Supplementum, 218, 1–60.

36. Andersen K. S. (1973). Radiological classification of congenital pseudarthrosis of the tibia. Acta orthopaedica Scandinavica, 44(6), 719–727. https://doi.org/10.3109/17453677308989112

37. Laufer, A., Frommer, A., Gosheger, G., Roedl, R., Schiedel, F., Broeking, J. N., Toporowski, G., Rachbauer, A., Antfang, C., & Vogt, B. (2020). Reconstructive Approaches in Surgical Management of Congenital Pseudarthrosis of the Tibia. Journal of clinical medicine, 9(12), 4132. https://doi.org/10.3390/jcm9124132

38. Dong, C., Li, C., Brückner, U., Hellmich, H., & Krieg, A. H. (2024). Preventing of nonunion in congenital pseudarthrosis of the tibia cases of Crawford Type I and II through the use of allograft bypass and a brace: Midterm findings. Journal of children's orthopaedics, 18(2), 187–199. https://doi.org/10.1177/18632521241228168

39. El-Gammal, T. A., Ali, A. E., Kotb, M. M., Saleh, W. R., Ragheb, Y. F., Refai, O. A., Morsy, M. M., & El-Gammal, Y. T. (2023). Congenital Pseudarthrosis of the Tibia: Long-term Outcome of Treatment With Intramedullary Vascularized Fibular Graft Combined With Ilizarov Distraction. Journal of pediatric orthopedics, 43(6), e487–e492. https://doi.org/10.1097/BPO.0000000000002399

40. Johnston, C. E. (2025). Congenital Pseudarthrosis of the Fibula. In Limb Lengthening and Reconstruction Surgery Case Atlas: Pediatric Deformity (pp. 149-153). Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-77359-4_331

41. Singer, D., & Johnston, C. E. (2019). Congenital Pseudarthrosis of the Tibia: Results, at Skeletal Maturity, of the Charnley-Williams Procedure. JB & JS open access, 4(2), e0004. https://doi.org/10.2106/JBJS.OA.19.00004

42. Aiona, M. (2025). Congenital Tibial Pseudarthrosis Managed with Ipsilateral Vascularized Fibula Transfer. In Limb Lengthening and Reconstruction Surgery Case Atlas: Pediatric Deformity (pp. 179-183). Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-77359-4_329

43. Ong, T. J., Jamil, K., Abd-Rasid, A. F., Abdul-Rashid, A. H., & Ibrahim, S. (2025). Long-term Surgical Outcome of Congenital Pseudarthrosis of the Tibia. Malaysian orthopaedic journal, 19(2), 73–81. https://doi.org/10.5704/MOJ.2507.010

44. Chou, T. A., Liu, T. Y., Wang, M. N., & Yang, C. Y. (2023). Treatment of Refractory Congenital Pseudoarthrosis of Tibia with Contralateral Vascularized Fibular Bone Graft and Anatomic Distal Tibial Locking Plate: A Case Series and Literature Review. Children (Basel, Switzerland), 10(3), 503. https://doi.org/10.3390/children10030503

45. Madhuri, V., Ramesh, S., Sahoo, B., Sivadasan, S. B., Rajagopal, K., Kandagaddala, M., ... & Varma, H. (2025). Safety Evaluation of Autologous Human Bone Marrow-derived MSCs on Hydroxyapatite-based Scaffold for Congenital Pseudarthrosis of the Tibia: A Pilot Clinical Trial. Regenerative Engineering and Translational Medicine, 1-10. https://doi.org/10.1007/s40883-025-00402-3

46. Sing, Q. Y., Pai, A. A., Geeroms, M., Cha, S. M., & Lin, C. H. (2024). Free Fibula Flap for Congenital Pseudarthrosis of the Tibia: Indications and Challenges. JPRAS open, 40, 305–319. https://doi.org/10.1016/j.jpra.2024.02.007

47. da Costa, A. C., Romero-Larrauri, P., Rojas-Neira, J., Gonzalez-Morgado, D., Fouad, A., Alves, C., & Soldado, F. (2025). Vascularized Deep Femoral Periosteal Flap: Anatomical Study and Clinical Application in Congenital Pseudarthrosis of the Tibia in Two Cases. Microsurgery, 45(2), e70043. https://doi.org/10.1002/micr.70043

48. Soldado, F., Rivas-Nicolls, D., Rojas-Neira, J., Sevilla-Tirado, J. J., Nguyen, T. Q., & Knorr, J. (2024). Vascularized Femoral Myo-Periosteal Graft for Congenital Pseudarthrosis of the Tibia: A Case Report. Microsurgery, 44(6), e31218. https://doi.org/10.1002/micr.31218

49. Zhu, G. H., Mei, H. B., He, R. G., Liu, Y. X., Liu, K., Tang, J., & Wu, J. Y. (2016). Combination of intramedullary rod, wrapping bone grafting and Ilizarov's fixator for the treatment of Crawford type IV congenital pseudarthrosis of the tibia: mid-term follow up of 56 cases. BMC musculoskeletal disorders, 17(1), 443. https://doi.org/10.1186/s12891-016-1295-1

50. Balci, H. İ., Bayram, S., Pehlivanoglu, T., Anarat, F. B., Eralp, L., Şen, C., & Kocaoğlu, M. (2021). Effect of lengthening speed on the quality of callus and complications in patients with congenital pseudarthrosis of tibia. International orthopaedics, 45(6), 1517–1522. https://doi.org/10.1007/s00264-021-05011-7

51. Jang, W. Y., Choi, Y. H., Park, M. S., Yoo, W. J., Cho, T. J., & Choi, I. H. (2019). Physeal and Subphyseal Distraction Osteogenesis in Atrophic-type Congenital Pseudarthrosis of the Tibia: Efficacy and Safety. Journal of pediatric orthopedics, 39(8), 422–428. https://doi.org/10.1097/BPO.0000000000000979

52. Tan, S. H. S., Pei, Y., Chan, C. X., Pang, K. C., Lim, A. K. S., Hui, J. H., & Ning, B. (2024). A good index surgery for congenital pseudarthrosis of the tibia minimizes complications following surgery. Bone & joint open, 5(11), 999–1003. https://doi.org/10.1302/2633-1462.511.BJO-2024-0045.R1

53. Jing, Y., Wang, D., Wu, C., Zhang, Z., Mo, Y., & Ning, B. (2025). Efficacy of the cross-union protocol in the treatment of congenital tibial pseudarthrosis: a comparative study. BMC musculoskeletal disorders, 26(1), 3. https://doi.org/10.1186/s12891-024-08257-5

54. Song, W., Zhou, R., Liu, P., Guo, Y., Shao, L., Liu, D., Xu, J., Wu, T., Bai, Z., Su, C., Liu, F., Liu, J., Kang, Q., & Lu, S. (2025). Surgical treatment of congenital pseudarthrosis of the tibia in children: CPAM-LRC consensus and guidelines. International journal of surgery (London, England), 111(2), 1689–1698. https://doi.org/10.1097/JS9.0000000000002211

55. Yalikun, A., Yushan, M., Hamiti, Y., Lu, C., & Yusufu, A. (2022). Combination of the Ilizarov Method and Intramedullary Fixation for the Treatment of Congenital Pseudarthrosis of the Tibia in Children: A Retrospective Observational Study. Frontiers in surgery, 9, 901262. https://doi.org/10.3389/fsurg.2022.901262

56. Kale, A., Patil, V. S., Singh, P., Jr, Raithatha, H., Shah, M., & Aggarwal, R. (2023). Congenital Pseudoarthrosis of Tibia With Anterolateral Bowing Treated With Ilizarov Ring Fixator: A Case Report. Cureus, 15(10), e47615. https://doi.org/10.7759/cureus.47615

57. Popkov, D., Popkov, A., Dučić, S., Lazović, M., & Lascombes, P. (2019). Combined technique with hydroxyapatite coated intramedullary nails in treatment of anterolateral bowing of congenital pseudarthrosis of tibia. Journal of orthopaedics, 19, 189–193. https://doi.org/10.1016/j.jor.2019.11.017

58. Lippross, S., Tsaknakis, K., Lorenz, H. M., & Hell, A. K. (2021). Kongenitale Pseudarthrose der Tibia : Ein seltenes, oft unterschätztes Krankheitsbild [Congenital pseudarthrosis of the tibia : A rare often underestimated disorder]. Der Unfallchirurg, 124(9), 755–767. https://doi.org/10.1007/s00113-021-01061-z

59. Shannon, C. E., Huser, A. J., & Paley, D. (2021). Cross-Union Surgery for Congenital Pseudarthrosis of the Tibia. Children (Basel, Switzerland), 8(7), 547. https://doi.org/10.3390/children8070547

60. Siebert, M. J., & Makarewich, C. A. (2022). Anterolateral Tibial Bowing and Congenital Pseudoarthrosis of the Tibia: Current Concept Review and Future Directions. Current reviews in musculoskeletal medicine, 15(6), 438–446. https://doi.org/10.1007/s12178-022-09779-y

61. Wu, C., Zheng, G., Wang, D., Paley, D., & Ning, B. (2022). Combination Treatment by Cross-Union of the Tibia and Fibula, Autogenic Iliac Bone Grafting, Reliable Fixation and Bone Morphogenetic Proteins for the Treatment of Refractory Congenital Pseudarthrosis of the Tibia. Journal of pediatric orthopedics, 42(6), e623–e629. https://doi.org/10.1097/BPO.0000000000002138

62. Vaidya, S. V., Aroojis, A., Mehta, R., Agashe, M. V., Dhawale, A., Bansal, A. V., & Sarathy, K. (2019). Short Term Results of a New Comprehensive Protocol for the Management of Congenital Pseudarthrosis of the Tibia. Indian journal of orthopaedics, 53(6), 736–744. https://doi.org/10.4103/ortho.IJOrtho_155_19

63. Liu, X., Liu, K., & Zhu, G. (2025). Combined surgery with intramedullary rod fixation across the ankle for the treatment of Crawford IV congenital pseudarthrosis of the tibia: a long-term follow-up study. Orphanet journal of rare diseases, 20(1), 343. https://doi.org/10.1186/s13023-025-03873-3

64. Rastogi, A., & Agarwal, A. (2022). Surgical treatment options for congenital pseudarthrosis of tibia in children: cross-union versus other options: a systematic review. Journal of pediatric orthopedics. Part B, 31(2), 139–149. https://doi.org/10.1097/BPB.0000000000000924

65. Seo, S. G., Lee, D. Y., Kim, Y. S., Yoo, W. J., Cho, T. J., & Choi, I. H. (2016). Foot and Ankle Function at Maturity After Ilizarov Treatment for Atrophic-Type Congenital Pseudarthrosis of the Tibia: A Comprehensive

Outcome Comparison with Normal Controls. The Journal of bone and joint surgery. American volume, 98(6), 490–498. https://doi.org/10.2106/JBJS.15.00964

66. Laine, J. C., Novotny, S. A., Weber, E. W., Georgiadis, A. G., & Dahl, M. T. (2020). Distal Tibial Guided Growth for Anterolateral Bowing of the Tibia: Fracture May Be Prevented. The Journal of bone and joint surgery. American volume, 102(23), 2077–2086. https://doi.org/10.2106/JBJS.20.00657

67. Zhou, X., Liu, Y., Chen, H., Hu, X., Zhu, G., Liu, K., Jiang, Z., Xiao, H., & Mei, H. (2025). Clinical study of the 'U'-shaped staple-guided growth technique in the treatment of congenital anterolateral bowing of the tibia in children. Journal of pediatric orthopedics. Part B, 34(6), 608–615. https://doi.org/10.1097/BPB.0000000000001237

68. Todderud, J. E., Carlson, S. W., & Larson, A. N. (2024). Guided Growth to Treat Anterolateral Tibial Bowing Associated with Congenital Pseudarthrosis of the Tibia. Journal of pediatric orthopedics, 44(6), e560–e565. https://doi.org/10.1097/BPO.0000000000002683

69. Hu, X., Li, A., Liu, K., & Mei, H. (2022). Efficacy Comparison of 3 Kinds of Distal Tibial Hemiepiphyseal Implants in the Treatment of Postoperative Ankle Valgus of Congenital Pseudarthrosis of the Tibia. Journal of pediatric orthopedics, 42(5), e441–e447. https://doi.org/10.1097/BPO.0000000000002101

70. Madhuri, V., Mathew, S. E., Rajagopal, K., Ramesh, S., & Antonisamy, B. (2016). Does pamidronate enhance the osteogenesis in mesenchymal stem cells derived from fibrous hamartoma in congenital pseudarthrosis of the tibia?. Bone reports, 5, 292–298. https://doi.org/10.1016/j.bonr.2016.10.003

71. Hamdy, R. C. (2025). Fourteen Year Old Patient with Severe Congenital Pseudarthrosis of the Tibia. In Limb Lengthening and Reconstruction Surgery Case Atlas: Pediatric Deformity (pp. 197-203). Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-77359-4_23

72. Yan, A., Mei, H. B., Liu, K., Wu, J. Y., Tang, J., Zhu, G. H., & Ye, W. H. (2017). Wrapping grafting for congenital pseudarthrosis of the tibia: A preliminary report. Medicine, 96(48), e8835. https://doi.org/10.1097/MD.0000000000008835

73. Stiel, N., Hissnauer, T. N., Rupprecht, M., Babin, K., Schlickewei, C. W., Rueger, J. M., Stuecker, R., & Spiro, A. S. (2016). Evaluation of complications associated with off-label use of recombinant human bone morphogenetic protein-2 (rhBMP-2) in pediatric orthopaedics. Journal of materials science. Materials in medicine, 27(12), 184. https://doi.org/10.1007/s10856-016-5800-8

74. Richards, B. S., & Anderson, T. D. (2018). rhBMP-2 and Intramedullary Fixation in Congenital Pseudarthrosis of the Tibia. Journal of pediatric orthopedics, 38(4), 230–238. https://doi.org/10.1097/BPO.0000000000000789

75. Shah, H., Joseph, B., Nair, B. V. S., Kotian, D. B., Choi, I. H., Richards, B. S., Johnston, C., Madhuri, V., Dobbs, M. B., & Dahl, M. (2018). What Factors Influence Union and Refracture of Congenital Pseudarthrosis of the Tibia? A Multicenter Long-term Study. Journal of pediatric orthopedics, 38(6), e332–e337. https://doi.org/10.1097/BPO.0000000000001172

76. Hissnauer, T. N., Stiel, N., Babin, K., Rupprecht, M., Hoffmann, M., Rueger, J. M., Stuecker, R., & Spiro, A. S. (2017). Bone morphogenetic protein-2 for the treatment of congenital pseudarthrosis of the tibia or persistent tibial nonunion in children and adolescents: A retrospective study with a minimum 2-year follow-up. Journal of materials science. Materials in medicine, 28(4), 60. https://doi.org/10.1007/s10856-017-5868-9

77. Kesireddy, N., Kheireldin, R. K., Lu, A., Cooper, J., Liu, J., & Ebraheim, N. A. (2018). Current treatment of congenital pseudarthrosis of the tibia: a systematic review and meta-analysis. Journal of pediatric orthopedics. Part B, 27(6), 541–550. https://doi.org/10.1097/BPB.0000000000000524

78. Das, S. P., Ganesh, S., Pradhan, S., Singh, D., & Mohanty, R. N. (2014). Effectiveness of recombinant human bone morphogenetic protein-7 in the management of congenital pseudoarthrosis of the tibia: a randomised controlled trial. International orthopaedics, 38(9), 1987–1992. https://doi.org/10.1007/s00264-014-2361-7

79. Qu, H., Zhuang, Y., Zhu, L., Zhao, Z., & Wang, K. (2021). The effects of vasoactive intestinal peptide on RANKL-induced osteoclast formation. Annals of translational medicine, 9(2), 127. https://doi.org/10.21037/atm-20-7607

80. Cardier, J. E., Diaz-Solano, D., Wittig, O., Sierra, G., Pulido, J., Moreno, R., Fuentes, S., & Leal, F. (2024). Osteogenic organoid for bone regeneration: Healing of bone defect in congenital pseudoarthrosis of the tibia. The International journal of artificial organs, 47(2), 107–114. https://doi.org/10.1177/03913988231220844

81. Meselhy, M. A., Elhammady, A. S., & Singer, M. S. (2020). Outcome of Induced Membrane Technique in Treatment of failed previously operated Congenital Pseudarthrosis of the Tibia. Orthopaedics & traumatology, surgery & research: OTSR, 106(5), 813–818. https://doi.org/10.1016/j.otsr.2019.11.033

Туа біткен асықты жіліктің жалған буыны: Қазіргі емдеу стратегиялары мен нәтижелері. Әдебиетке шолу

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Түйіндеме

Туа біткен асық жіліктің жалған буыны – сирек кездесетін, бірақ клиникалық тұрғыдан маңызды патологиялық жағдай. Ол аяқтың үдемелі деформациясына, сүйек регенерациясының бұзылуына, қайталанатын сынықтарға және балаларда ұзақ мерзімді функционалдық шектеулерге алып келеді. Бұл ауру жүз жылдан астам уақыт бұрын сипатталғанымен, оның даму тетіктері толық зерттелмеген. Қазіргі ғылыми деректер генетикалық, молекулалық және биомеханикалық факторлардың күрделі өзара әрекеттесуі фиброздық бірлесудің қалыптасуына ықпал ететінін көрсетеді. Емдеудің кең ауқымды тәсілдері ұсынылған, олардың ішінде сүйекті ішкі фиксациялау интрамедуллярлық бекіту, Илизаров техникасын қолдана отырып сыртқы шеңберлі фиксация, тамырлы сүйек трансплантаттары, біріктірілген хирургиялық әдістер және тұрақты тибиофибулярлық сүйек блогын құруға бағытталған заманауи тәсілдер бар. Хирургиялық әдістердің дамуына қарамастан, тұрақты жазылмау, деформацияның қайта пайда болуы және қайталама сынықтар қаупі жоғары болып қала береді. Хирургиялық жетістіктермен қатар сүйектің сауығуын күшейтуге бағытталған биологиялық және фармакологиялық әдістер – сүйек морфогенетикалық ақуыздары, бисфосфонаттар, тромбоцитке бай плазма, жасушалық терапиялар және остеогендік инженерлік құрылымдар – белсенді зерттелуде, алайда клиникалық деректер әлі де бірыңғай емес. Емдеу хаттамаларының әртүрлілігі мен сапалы салыстырмалы зерттеулердің аздығы қолжетімді деректерді жүйелі талдауды қажет етеді, бұл ең тиімді тәсілдерді анықтауға және болашақ зерттеулерге бағыт беруге мүмкіндік береді. Бұл шолу туа біткен асық жіліктің жалған буынының патогенезі, клиникалық көріністері және емдеу стратегиялары жөніндегі қазіргі мәліметтерді жинақтап, хаттамаларды стандартизациялау және көпорталықтық зерттеулер жүргізу қажеттілігін ерекше атап көрсетеді.

Түйін сөздер: туа біткен асықты жілік сүйегінің жалған буыны, Илизаров аппараты, интрамедуллярлық өзек.

Врожденный псевдоартроз большеберцовой кости: Современные стратегии лечения и результаты. Обзор литературы

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Резюме

Врожденный ложный сустав большеберцовой кости представляет собой редкое, но клинически значимое заболевание, приводящее к прогрессирующей деформации нижней конечности, нарушению костной регенерации, повторным переломам и выраженным долгосрочным функциональным ограничениям у детей. Несмотря на то, что это заболевание описано более ста лет назад, его патогенез остаются неполностью изученными, а современные данные указывают на сложное взаимодействие генетических, молекулярных и биомеханических факторов, способствующих формированию фиброзного несращения. Для лечения предложен широкий спектр терапевтических подходов, включая внутрикостную фиксацию, круговую внешнюю фиксацию с использованием техники Илизарова, васкуляризованные костные трансплантаты, комбинированные хирургические методы и современные процедуры, направленные на создание стабильного тибиофибулярного костного блока. Несмотря на значительный прогресс в хирургическом лечении,

https://doi.org/10.52889/1684-9280-2025-76-6-jto032

сохраняются высокий риск стойкого несращения, рецидивирующей деформации и повторных переломов. Наряду с хирургическими методами активно изучаются биологические и фармакологические методы, направленные на усиление костного заживления, такие как костные морфогенетические белки, бисфосфонаты, обогащенную тромбоцитами плазма, клеточные технологии и инженерные остеогенные конструкции, хотя имеющиеся клинические данные остаются неоднородными. Учитывая вариабельность лечебных протоколов и ограниченное количество качественных сравнительных исследований, комплексный анализ доступных данных необходим для определения наиболее эффективных подходов и направлений будущих исследований. Данный обзор обобщает современные сведения о патогенезе, клинических проявлениях и методах лечения врожденного ложного сустава большеберцовой кости и подчеркивает необходимость стандартизации протоколов и проведения многоцентровых исследований для улучшения долгосрочных результатов.

Ключевые слова: врожденный ложный сустав большеберцовой кости, аппарат Илизарова, интрамедуллярный стержень.