Relationship between postoperative complications and fibular integrity in congenital pseudarthrosis of the tibia in children

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Background: **This study aimed to investigate the relationship between postoperative complications and fibular integrity in congenital pseudarthrosis of the tibia (CPT) in children.**

Methods: **A retrospective study was performed in 59 patients with Crawford type IV CPT who were treated with combined surgical technique from 2007 to 2011. The patients were divided into two groups, the CPT with fibular pseudarthrosis (group A) and CPT with intact fibula groups (group B), on the basis of fibula status after the union of CPT. The incidence rates of refracture, ankle valgus, tibial valgus, and limb length discrepancy in the two groups were investigated.**

Results: **In group A, 14 (36.8%) cases had refracture, 30 (78.9%) had ankle valgus; 27 (71%) exhibited tibial valgus with an average tibial valgus of 7° (6°-20°), and 24 (63.2%) had limb length discrepancy with an average limb length of 1.26 cm (0.6-4.4 cm). In group B, 2 (9.5%) cases had refracture, 11 (52.4%) had ankle valgus, 8 (42.9%) had tibial valgus with an average tibial valgus deformity of 2.9° (6°-13°), and 13 (61.9%) had limb length discrepancy with an average limb length of 1.48 cm (0.5-5 cm). Significant difference in refracture and ankle valgus was found between groups A and B (P<0.05).**

Conclusions: **After the union of CPT, patients with fibular pseudarthrosis showed higher incidence of refracture and ankle valgus than those with intact fibula. Attention should be paid to the presence of fibular pseudarthrosis when managing CPT.**

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complication;
congenital pseudarthrosis of the tibia;
fibula status;
pseudarthrosis

Introduction

Congenital pseudarthrosis of the tibia (CPT) is one of the most challenging problems confronting pediatric orthopedic surgery.[1-3] The goal of surgical management of congenital pseudarthrosis of the tibia is to obtain and maintain union while minimising deformity.[4] Various techniques have been described, including ipsilateral transfer of the fibula or contralateral free vascularized fibular transfer, circular external fixation, intramedullary rodding, periosteal grafting, and combined external fixation and intramedullary rodding.[5-9] More recently, bone morphogenic protein and bisphosphonate therapy have been used.[10,11] There is no optimal surgical treatment for the management of CPT now. The European Paediatric Orthopaedic Society (EPOS) multicenter study of 340 patients with CPT reported a healing rate of 75% with ilizarov external fixation.[12] Joseph et al[13] reported the union of the pseudarthrosis occurred in 12 of 13 children (92%) who were treated before 3 years of age by excision of the pseudarthrosis, intramedullary rodding, and dual-onlay cortical bone grafting. Paley[3] reported 15 cases treated by a shotgun approach (hamartoma resection, periosteal grafting, bone grafting, internal rodding, external fixation, tibio-fibular cross union, bone morphogenic protein and bisphosphonate pharmacologic manipulation). All patients united. There were no refractures with an average follow-up time of 2 years (1-4 years).

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Vanderstappen et al[14] reported the long-term follow up results of 12 patients with CPT treated with Ilizarov bone transport, the primary union rate was 83%, 6 patients (50%) experienced refracture. Refracture is the most serious complication and may result in pseudarthrosis reestablishment.[15] With the increase in success rate of CPT surgeries, the prevention and treatment of complications are more and more important. Determining the state of the fibula could be very helpful in the CPT prognosis. The reduction or prevention of postoperative complications requires not only treatment of tibial lesions but also careful examination of fibula status, the condition of the ipsilateral fibula (dysplasia, pseudarthrosis, normal etc.) could have important therapeutic implications in the treatment the CPT.[16] Many researchers have reported the relationship between the fibula and the prognosis of CPT. Many recent studies have focused on fibular stability in the treatment of CPT.[17-23] However, the status of the fibula in the prognosis of CPT remains controversial.[24]

Therefore, the present work reports a retrospective study which was conducted on 59 cases with Crawford type IV CPT who underwent combined surgery (excision of the fibrous hamartoma, excision of bone lesions, intramedullary rods, ilizarov fixator, and wrapping autogenic iliac bone graft), with a follow-up period of more than 3 years. The relationship between postoperative complications and fibula integrity in CPT was discussed.

Methods

Patients who were enrolled in this study met the following criteria: (1) Patients were followed up for more than 3 years; (2) The pseudarthrosis was located between the middle and distal third of the tibia in patients; (3) All operations were performed or supervised by a single surgeon; (4) Patients who were treated with combined surgical technique; (5) Patients were classified as Crawford type IV; (6) The data of patients were complete. The study was approved by Ethics Committee of Hunan Children's Hospital. The informed consent for participation in the study was obtained from the parents of children. Between 2007 and 2011, 59 patients (44 boys and 15 girls) with Crawford type IV CPT who were treated with combined surgical technique were analyzed.[1,25,26] The surgery was done on the right leg in 30 patients and on the left leg in 29 patients. Of the 59 patients, 10 had proximal tibia dysplasia. A total of 44 patients had no history of previous surgery, but 15 patients underwent one to four previous unsuccessful procedures in another hospital.

The average age during surgery was 3.8 years (3 years to 12 years 5 months). Fifty cases exhibited neurofibromatosis type 1, with an average follow-up time of 4.6 years (3-6.7 years). The average primary union time was 4.2 months (3-10 months), and the average retention time of external fixation was 4.3 months (3-10.4 months). Radiographic primary union was characterized by the presence of bridging callus across three of four visible cortices on anteroposterior and lateral views.[27] After primary union, patients were divided into the CPT with fibular pseudarthrosis group (group A, 38 cases) and the CPT with intact fibula group (group B, 21 cases, including 10 cases with fibular pseudarthrosis before the operation). Refracture was defined as an obvious fracture on a plain radiograph following the union at the site of the tibia. Picture Archiving and Communication System (PACS) was used to measure the length of the tibia (we measured the distance between the midpoint of the proximal tibial epiphyseal plate and the midpoint of distal tibia epiphyseal plate). In the present study, since the lengths of the femurs were equal, the data on limb length discrepancy (LLD) were obtained easily. Proximal tibial valgus was created by the intersection of a line parallel to the proximal physis and another line along the axis of the proximal third of diaphysis in the tibia. Ankle valgus was classified using Malhotra classification. Malhotra grades I, II, and III were believed to form in patients with ankle valgus.

Surgical technique

Harvesting autogenic iliac bone

The patient was placed in a supine position on a radiolucent operating table with a support beneath the hip. The iliac bone graft was harvested through a straight incision centered over the anterior superior iliac spine. The apophysis of the ilium was split and the outer table of the anterolateral surface of the ilium was exposed subperiosteal. A rectangular cortex of about 4 cm × 3 cm in size was obtained from the outer table of the ilium and most of the cancellous bone that can be obtained was curetted from the supra-acetabular region, while keeping the inner wall intact (Supplemental Fig. 1). Subsequently, a series of holes were made in the rectangular cortex using a fine Kirschner wire followed by weaving it with absorbable sutures in order to mold a cylindrical shape for wrapping graft (Supplemental Fig. 2).

Excision of pseudarthrosis, intramedullary rod insertion, and installation of Ilizarov's fixator

The tibia was approached through an anterior straight incision over the site of the pseudarthrosis and just lateral to the tibial crest. The excised pseudarthrosis exposed the abnormal periosteal, surrounding pathologic soft tissues and the sclerotic bone ending until normal tissue planes were encountered (Supplemental

Fig. 3). The medullary canal of both proximal and distal tibial fragment was opened with a drill until a proper rod could be inserted. The fibrous tissue at the site of pseudarthrosis of the fibula was also resected and fixed with an intramedullary Kirschner wire in patients with concomitant fibular pseudarthrosis in pre-operation. The implant used in the procedure depend on the age and the diameter of the CPT bone, making preoperative planning essential. The rod was then driven retrograde into the proximal tibial fragment, which was anatomically aligned to both the coronal and the sagittal planes. The alignment was verified using intraoperative imaging. After finishing the insertion of the intramedullary rod, the ilizarov's fixator was installed with one whole ring above the site of pseudarthrosis and one below. If the length of the distal tibial segment was less than 3 cm, a U-shaped ring was used to increase the distal stability.

Wrapping autogenic iliac bone graft

The previously harvested cylindrical cortex was wrapped around the site of pseudarthrosis of the tibial following application of the ilizarov fixator. Cancellous bone grafts were placed circumferentially between the grafted cortex and site of pseudarthrosis. The cortex was secured with tied absorbable sutures, which

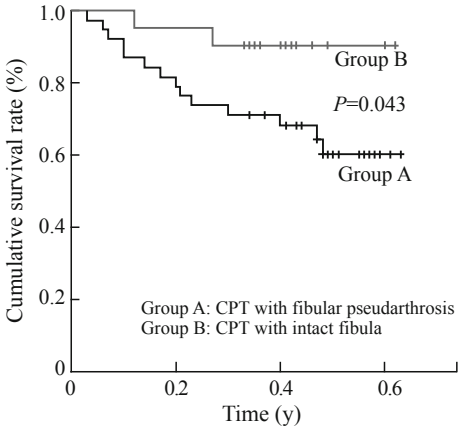

Fig. 1. The Kaplan-Meier analysis of refracture-free survival of patients in group A *vs.* those in group B. The refracture-free cumulative survival rate is 92% in group B at 2.7 years after surgery, whereas in group A, it dropped consistently to 60% at 4.8 years after surgery.

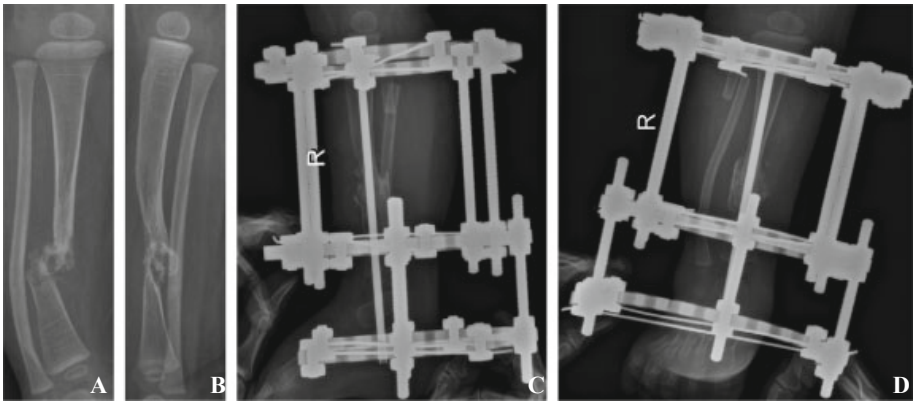

Fig. 2. X-ray of the site at 1 week pre-operation and post-operation. **A**: Anteroposterior of the tibia before surgery; **B**: Lateral of the tibia before surgery; C: Lateral radiography at one week after combined surgey; **D**: Anteroposterior radiograph of the same patient taken at one week after combined surgey.

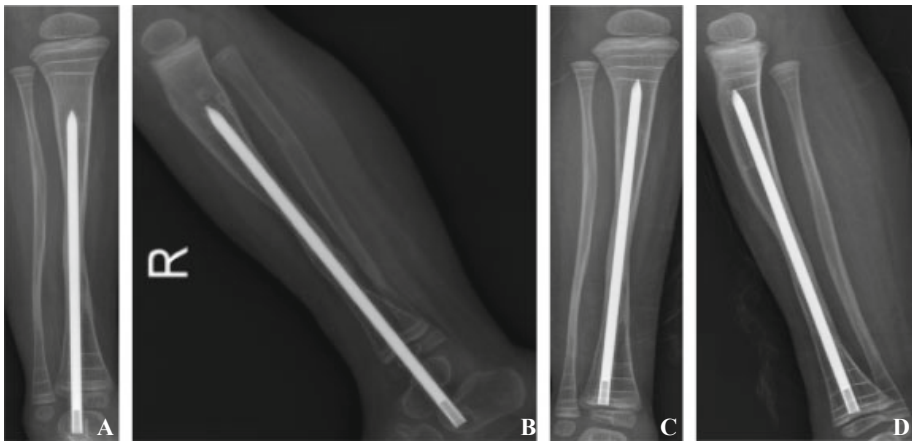

Fig. 3. A: Anteroposterior X-ray of 1 year post operation shows solid union of the pseudarthrosis with good alignment of the tibia; **B**: Lateral X-ray of 1 year post operation; **C**: The anteroposterior X-ray of the last follow-up; **D**: The lateral X-ray of the last follow-up.

were connected to the cortex on each corner, thereby establishing a sealing environment for enhancement of osteogenesis (Supplemental Fig. 4).

Pharmacologic protocol

One week prior or one week after the surgery, the patient was given pamidronate disodium intravenously over 3 hours. One hour later, calcium gluconate was given intravenously over the course of one hour. The patient was given elemental calcium for 7 days and vitamin D supplementation of 400 IU for 14 days. Pamidronate disodium was given with the index procedure and at the time of removal of the external fixation. The administration was performed once every 3-4 months and lasted for 2 years.

Postoperative management

The deep fascia of the anterior compartment was routinely divided longitudinally, before the closure of the wound to prevent compartment syndrome. When the pseudarthrosis of the tibia was consolidated, the ilizarov's fixator was removed and a long leg cast was applied for an average of 2.8 months (2-3 months). After the cast was removed, a protective knee-ankle-foot orthosis was used to protect the involved extremity with weight-bearing walking. The brace was worn at all times including during sleep and swimming until skeletal maturity was attained. The only time for taking off the brace was for bathing.

To minimize the duration of ankle joint immobilization and the potential damage to the articular cartilage with prolonged ankle transfixation of the intramedullary rod of the tibia, the rod across the ankle joint was surgically pushed into the epiphysis of the distal tibia at a mean period of 2 years following union of pseudarthrosis of the tibia. In some patients, the rod was located proximal to the ankle joint with growth of the tibia.

Statistical analysis

Chi-square test was used to compare the rates between the two groups, including the incidence of ankle valgus, tibial valgus, and LLD. Survival analysis was performed using the Kaplan-Meier method, and the log-rank test was used to compare the refracture-free survival rates of the 2 groups. Statistical analyses were performed using SPSS 18.0. Statistical significance was considered at $P<0.05$.

Results

Out of 38 patients, 34 (89%) patients achieved primary union in group A, and 19 out of 21 patients (90%) achieved primary union in group B ($P>0.05$, Chi-square test). Five cases exhibited pin tract infection, which were cured through antibiotic therapy. In group A, 14 (36.8%) cases showed refracture; 30 (78.9%) cases showed ankle valgus, including 8 grade 0 cases, 15 grade I cases, 3 grade II cases, and 12 grade III cases, 27 (71%) cases exhibited tibial valgus with the average tibial valgus deformity of 7° (6°- 20°); and 24 (63.2%) cases showed LLD with an average limb length of 1.26 cm (0.6-4.4 cm). In group B, 2 (9.5%) cases showed refracture; 11 (52.4%) cases showed ankle valgus with 10 grade 0 cases, 6 grade I cases, 3 grade II cases, and two grade III cases; 8 (42.9%) cases had tibial valgus with an average tibial valgus of 2.9° (6°-13°); and 13 (61.9%) cases exhibited LLD with an average limb length of 1.48 cm (0.5-5 cm). The Kaplan-Meier method revealed a refracture-free cumulative survival rate of 92% in Group B at 2.7 years after surgery, whereas in Group A, it reached 60% at 4.8 years (Fig. 1). Group A and group B differed significantly in refracture and ankle valgus ($P<0.05$) (Figs. 2&3).

Discussion

Significant difference in refracture and ankle valgus was found between group A and group B ($P<0.05$). After the primary union of CPT, patients with fibular pseudarthrosis showed higher incidence of refracture and ankle valgus than those with intact fibula.

In 2000, Tudisco et al[17] stated that a fibular pseudarthrosis appeared responsible for most of the poorest outcome. Persistent fibula pseudarthrosis was also found to be related to failure of tibia union[18,19] and progressive valgus of the ankle.[20] In 2002, Johnston[19] concluded that fibular osteotomy is necessary to achieve optimal limb alignment and union when the fibula is intact. The authors also recommended that a hypoplastic or bowed fibula suggested pseudarthrosis and should be resected. In 2004, Dobbs et al[21] reported that most of the ankle valgus deformities occurred in patients with concomitant fibular pseudarthrosis, even when the fibular lesion had been treated. Additionally, the prevalence of tibia refracture was found to be higher in patients in whom a fibular pseudarthrosis was not resected.

In 2008, Cho et al[22] disclosed that patients with an intact fibula or one stabilized by diaphyseal osteosynthesis or tibiofibular synostosis showed significantly better refracture-free survival than those with a pseudarthrotic fibula due to neglected or failed synostosis. In 2011, Choi et al[23] reported an increase in the refracture-free cumulative survival after starting applying multi-targeted, fibular status based algorithmic approach to atrophic-type CPT (since January 1999) and paying more attention to fibular management at the

time of tibial osteosynthesis. Nevertheless, Shah et al[28] found that the frequency of refracture and ankle valgus in CPT patients with persistent fibular nonunion was not higher than patients with fibular union. In addition, Keret et al[16] found in a multicenter study involving 250 patients who had been treated surgically that union of the pseudarthrosis occurred more frequently in children who had an associated fibular pseudarthrosis than in those with a normal fibula. This observation conflicts with the general impression that the prognosis of CPT is poorer when there is an associated fibular pseudarthrosis.[19]

In the present study, the incidence of ankle valgus was significantly higher in group A (78.9%) than in group B (52.4%) (P=0.034). The incidence of primary union was higher in group B (90%) than that in group A (89%), but the difference was not statistically significant. These results appear consistent with the earlier report of Johnston.[19]

The incidence of refracture was significantly higher in group A (36.8%) than that in group B (9.5%) (P=0.024). These results were consistent with some of the previous findings[22]. The incidence of tibial valgus was higher in group A (71%) than in group B (43%), which may be caused by the persistent fibular pseudarthrosis and increase of the stress in the tibia, while the difference was not statistically significant (P=0.051).

The incidence of limb length discrepancy was slightly higher in group A (63.2%) than that in group B (61.9%), but the difference was not statistically significant (P=0.57). To determine the relationship between tibial valgus, limb length and the states of the fibula after the initial healing in children, the patients with tibial valgus and LLD were continued to be observed until skeletal maturity was reached.

Refracture of the tibia and ankle valgus after successful osteosynthesis of the tibia in CPT is often associated with persistent pseudarthrosis of the fibula. In our experience, best treatment choice for patients with fibular pseudarthrosis is intramedullary nailing of the fibula coupled with circumferential bone grafting. Additionally, careful determination of fibula status at the time of osteosynthesis of the tibia is important. Intramedullary nail can be inserted in the fibula without difficulty when the diameter of the fibula is greater than 60% of that of the normal side in young children. This is the reason why status of the fibula should be taken into consideration when treating CPT.

In some patients with ankle valgus, the rod was not positioned in the exactly central portion of the tibial physis. The rod was located in the medial of the tibial physis in 16 patients (14 out of 16 patients exhibited ankle valgus). Meanwhile, the rod was positioned exactly in the central portion of the tibial physis in 43 patients (16 out of 43 patients exhibited ankle valgus) (P=0.001, Chi-square test). Therefore, the rod should be positioned exactly at the central portion of the tibial physis.

Patients who are treated with combined operation and achieve union with the fibula being intact may be able to resist strong mechanical stress; thereby reducing the risk of refracture. We recommend that the status of the tibia and fibula is considered rather than only focusing on the tibia. Fibular pseudoarthrosis is a very important indication of fibula status in CPT prognosis.

A progress has been achieved in the management of CPT in recent years, such as the development of masquelet surgery.[29] However, CPT still remains a very difficult problem,[30] and cases accompanied by proximal tibial dysplasia[31] or variable fibular states require individualized treatment.

The present study has several limitations. First, the sample size of 38 patients in group A and 21 patients in group B was small and could have led to a potential bias. Secondly, owing to its retrospective nature, and other confounding parameters, such as severity of the affected tibial segment, compliance with bracing, and level of daily activity, which have all been suggested to cause refracture, these could not be statistically analyzed. Thirdly, follow-up periods were not long enough to determine the actual refracture and ankle valgus rates. All the statistically significant results were obtained from a single institute directing to another possible limitation of the present study.

The prognosis of CPT in the different fibula forms still remains uncertain pointing towards the need of carrying out a large prospective multicenter study to investigate and address the issue. Long-term studies that monitor conditions until skeletal maturity are needed to evaluate the function of the fibula. Multicenter evaluation of the skeletal maturity with the uniform evaluation method is needed.

In conclusion, the present investigation showed that after union of CPT, patients with fibular pseudarthrosis had a high incidence of refracture and ankle valgus. Therefore, attention should be paid to the presence of fibular pseudarthrosis when managing CPT.

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