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ORIGINAL PAPER

Fibula regeneration following non-vascularized graft harvest in children

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Abstract
Background A peculiarity of non-vascularized fibular harvest is that the donor site regenerates new bone provided periosteum is preserved. We prospectively investigated the regenerated fibula quantitatively and studied clinical implications of non-regeneration.
Material and methods The fibula was harvested using a periosteum preserving technique. Only fibulae from healthy legs were harvested. X-rays were done pre- and post-operatively at three and six months. Clinical assessment of donor limb included pain, gait, motor and sensory examination. Fibular regeneration was quantified using defined length and width criteria.
Results There were 16 children with 21 harvested fibula. About 65 % of total fibular length was available for use as graft. There was regeneration of fibula similar to the pre-operative dimensions as early as six months in 71 % of cases. There were no clinical morbid findings as assessed at six months follow up despite non-continuity being observed in 29 % of cases. The predominant site for non-continuity was middle third-distal third junction.
Conclusions Periosteal preserving non-vascularized fibula grafting was a low morbidity procedure. In two-third of the cases, there was regeneration of fibula comparable to pre-operative dimensions as early as six months. The non-continuous regeneration had no clinical implications.

Keywords Fibula · Graft · Regeneration · Non-vascularized · Children

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Introduction

Bone grafting is widely used to fill bone defects arising from congenital defects, infections, trauma, or tumours [1]. Autogenous bone remains the ideal material for grafting because it is nonantigenic and has osteoinductive, osteoconductive and osteogenic properties [2, 3]. The limited availability of graft donor sites remains a major problem in children [3]. Fibula is an important graft among the available options because of its length characteristics and geometrical shape [4]. In addition to its structural strength, wherever required, dual graft from both legs can also be obtained.

There has been ample criticism in available literature on the harvesting of fibular graft due to findings of donor site morbidity [5–10]. Many of the above inferences had been drawn from anatomic or adult studies [5–10]. There are only a few studies in the pediatric population to testify for above inferences. Moreover, the main literature for donor site follow-up in the paediatric group has emerged from the vascularized fibular graft technique [11–17]. An important difference between vascularized and non-vascularized fibular graft is that the donor site following the latter regenerates new bone provided periosteum is preserved, and it can even be used for reharvest. In the present study we quantitatively investigated the regeneration at the harvest site of non-vascularised fibular graft and studied the clinical implications of non-regeneration of the fibula in the short term (6 months).

Material and methods

The prospective study was conducted at a tertiary care paediatric super specialty hospital in a low income country between January 2014 and December 2015. Ethical clearance for the study was obtained from the Institution's Scientific Committee. All patients with indications for bone grafting and giving informed consent for the index procedure and fibular bone grafting were included in the study. In all procedures, the maximum possible length of fibular graft available was harvested and utilized (Fig. 1). Criteria for exclusion were age more than 12 years, neuromuscular problems in donor leg or bony pathology in ipsilateral tibia or donor fibula. Clinical assessment of donor limb was performed at three and six months for pain (faces scale and need for medication), gait, motor (extensor hallucis longus, flexor hallucis longus, and the extensor and flexor of the digitorum longus) and sensory deficits (medial side of the foot). Plain X-rays of the donor leg were done post-operatively, as well as at three and six months. The follow-up radiographs were compared with the pre-operative radiographs of the leg from which fibula had been harvested. Radiological assessments included quantification of proximal and distal remnant and amount of fibular harvest in the immediate post-operative X-rays. Fibular regenerate at three and six months was quantified in plain radiographs using the criteria given in Fig. 2.

Technique of fibular harvesting: periosteum preserving technique [2] The fibular graft was obtained under tourniquet control. The fibular head and lateral malleoli were marked followed by longitudinal skin incision over palpable subcutaneous portions of fibula. The fascia was incised and a plane developed between peroneal longus and the soleus musculature. Muscular insertions on fibula were gently teased off. The periosteum was incised longitudinally and carefully dissected circumferentially around the bone to preserve its integrity as a continuous sleeve (Fig. 1). The fibula was then harvested preserving a minimum of 10 % of total length at either end to maintain ankle stability at distal and safely preserve deep peroneal nerve at the proximal end [18, 19]. The fascia was closed with interrupted sutures. No sutures were applied to the periosteal sleeve which gets approximated by fascial closure. Subcutaneous tissue and skin were subsequently closed in layers. Post-operatively, bulky dressings were given and weight bearing was allowed as pain subsided.

Measurement of fibula length and width All measurements were done on plain radiographs (Fig. 2). The fibular regenerate was measured longitudinally as continuity or non-continuity (nonunion) along with its width at two places. The total fibular length (AB) was measured from distal tip of lateral malleolus (point A) to the proximal most point on the head of the fibula (point B). Non-continuity was expressed in terms of the percentage of the total length of the fibula (AB), calculated from the distal (point K) and the proximal level (point L) of non-continuity, respectively. Thus, segment KL would represent the gap in regeneration.

For calculation of width of fibular regenerate, the total length of the fibula (AB) was divided into three equal parts (AH, HD, DB). Horizontal line segments (CD) and GH) were drawn across the width of fibula at the points D and H. The fibular region distal to GH represented distal third, between CD and GH middle third and proximal third was beyond segment CH. The segment GH and CD approximately represented the triangular and quadrilateral profiles of cross sectioned fibula observed intra-operatively [4]. Corresponding horizontal segments were then drawn on ipsilateral tibia, IJ and EF at fibular levels, GH and CD respectively. The widths of both fibula and tibia were then measured from these segments (for fibula GH and CD and, for tibia IJ and EF). A ratio of fibular to tibial width at above corresponding levels was calculated (distal GH/IJ and proximal CD/EF). Such ratios were calculated in pre-operative, three months and six months plain radiographs of all patients and statistically compared.

Statistical analysis Statistical relationships between measurements were calculated using paired t-tests and Pearson's coefficient on IBM SPSS Statistics 20 software.

The Pearson's coefficient was used to evaluate any correlation between:

1. Age and fibular/tibial width ratio (pre-operatively, 3 months and 6 months) at both proximal and distal levels.
2. Fibular/tibial width ratio at proximal and distal third junctions (3 months and 6 months).
3. Fibular/tibial width ratio at corresponding proximal third and distal third levels over time (3 months and 6 months).
4. Remnant fibular ratio was calculated as regenerated fibula at six months/ (residual proximal + distal fibula) and compared with age (in years). This ratio was also compared with regenerated fibula at six months.

Paired t-test was used to assess any significant difference in fibular width ratio between preoperative values when compared to regenerated fibular width at six months. A p value of <0.05 was taken as significant and <0.001 as highly significant.

Results

Total number of children (male:female = 9:7) in the study were 16 with 21 harvested fibulae. The mean age of the patients was six years (range, 2–10 years). Five fibular grafts were bilateral, each counted as two harvest cases. The indications for fibular harvest were spinal fusion in seven, filling of lytic cavities of extremities five, and augmentation of bony nonunion in nine cases. The corresponding width of normal preoperative fibula compared to ipsilateral tibia as calculated from pre-operative X-

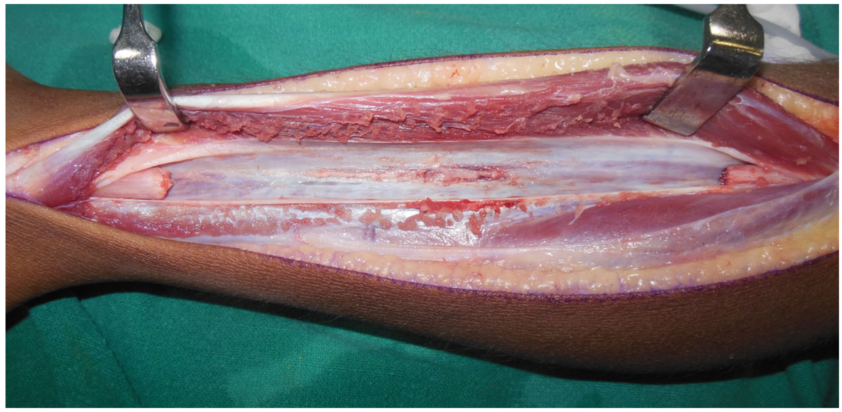

Fig. 1 An almost intact periosteal sleeve after harvesting of non-vascularized fibula

rays at proximal third level CD was 39 % (range, 32–47 %) and at distal third level GH was 48 % (range 40–74 %) (Fig. 2). The mean length of fibula harvest available was 64 % (SD 4) of total fibular length. The mean residual proximal and distal fibula segments were 17 % (SD 4) and 19 % (SD 3), respectively.

Partial weight bearing was possible in some patients as early as the next post-operative day. However, the two surgical incisions, namely, the index and harvesting procedure, necessitated initial pain management in these children. None of the children required analgesic supplementation beyond three weeks.

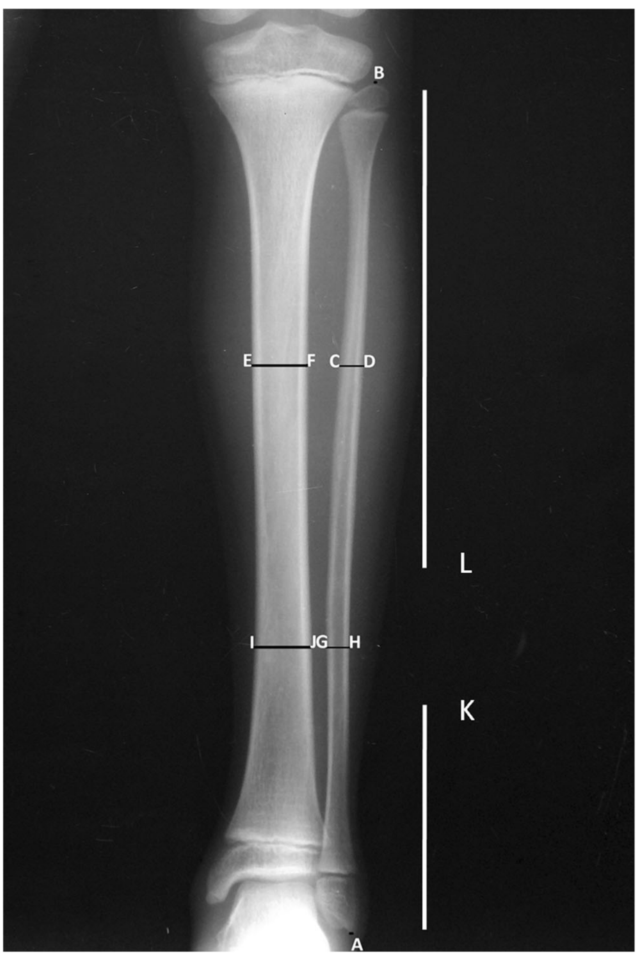

Fig. 2 The measurement of fibular length and width in plain radiographs. For explanation see *Material and methods*

The harvest site did not pose any clinical findings when examined at three months and all patients were full weight bearing on the donor leg at that time. Plain radiographs obtained at this time showed a thinner and irregular fibular regenerate (Fig. 3c).

The regenerate of fibula longitudinally was complete and continuous in 15 (71 %) and non-continuous in six cases (29 %) at six months. The mean width of fibula regenerate in continuous fibula in ratio to their corresponding tibial widths at six months at proximal and distal third were 43 % and 57 %, respectively (Fig. 3d) (see pre-operative values above). Therefore, in these cases, the measured dimensions of fibula had already regenerated radiologically. The medullary canal and cortical bone density in regenerated fibula was heterogeneous when compared to the adjacent tibia. The mean age in the continuous group (5.58 years; range 2–10) was lower than in the non-continuous group (7 years; range 4–10). The average length of gap non-continuity was 8 % of total fibular length (range, 5–16 %) (Fig. 4). Five out of six of these cases presented with non-continuity affection in the distal half. The distal non-continuity started at mean 35 % and ended at 42 % measured from the distal end of fibula, thereby indicating that the junction of the middle and distal third fibula was the predominant site for non-continuity. The only case with proximal non-continuity started at 62 % and ended at 67 % from the distal end of fibula. Clinical assessment of both continuous and non-continuous fibula at six months revealed no positive findings indicating no clinical implications of non-continuity. Full knee and ankle range of motion was preserved and no deformity (valgus/ varus) was present.

Statistical analysis

Statistical data are shown in Table 1.

- Age and fibular width: Age of child (in years) had no significant correlation with measured pre-operative fibular width, at either proximal (Pearson correlation 0.346, sig 0.125) or distal third (Pearson correlation 0.295, sig 0.195). However, the fibular/ tibial width ratio did show

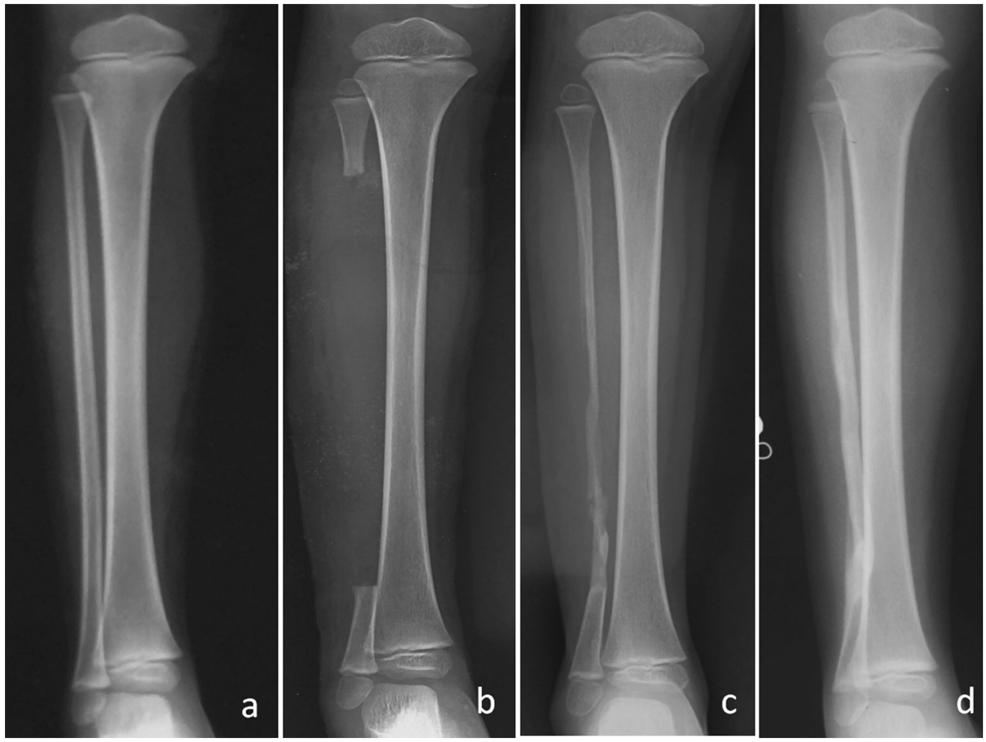

Fig. 3 Complete regeneration: A 3.6-year-old female who underwent fibular bone grafting from her right fibula for a localized bone defect. **a** Pre-operative radiograph of right leg showing original tibial and fibular width. **b** Immediate post-operative radiographs showing residual proximal and distal fibula and the total harvest. **c** Three-month radiograph of same leg showing early signs of complete linear regeneration. **d** Six-month radiograph showing complete linear regeneration with visibly thicker fibular width when compared to three-month radiograph and comparable fibular width to the pre-operative radiograph

a significant negative correlation with age at both three-month [proximal (Pearson correlation 0.553, sig 0.009), distal (Pearson correlation 0.575, sig 0.006)] and six-month radiographs [proximal (Pearson correlation 0.657, sig 0.001), distal (Pearson correlation 0.593, sig 0.005)]. With tibial width assumed constant at follow-up over a short interval of six months, these calculations suggest negative correlation between fibular width and age. The regeneration of fibular width thus declines with increasing age of children.

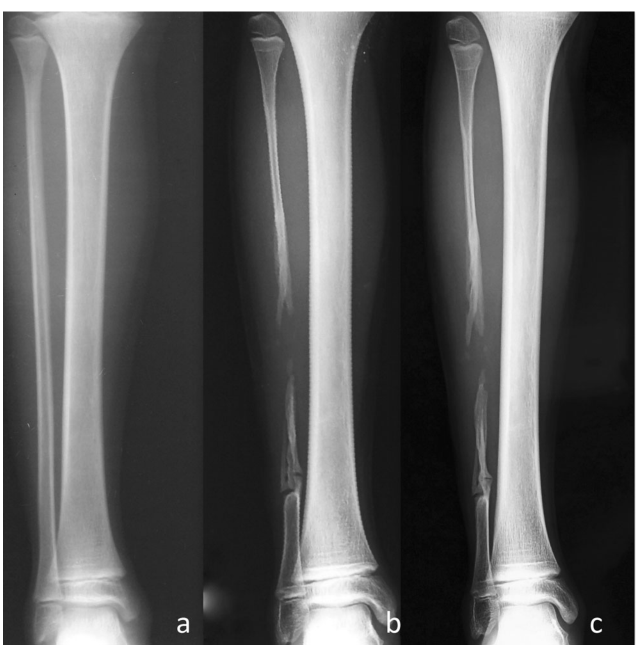

Fig. 4 Incomplete regeneration and non-continuity: A nine-year-old female who underwent fibular bone grafting from her right leg for spinal fusion. a Pre-operative radiograph of right leg showing original tibial and fibular width. b Three-month radiograph of same leg showing non continuous regeneration. c Six-month radiograph showing persistent non continuous regeneration

- Remnant fibula and regeneration of fibula at six months. No significant correlation could be found between remnant fibula ratio and age with weak negative correlation between them (Pearson correlation −0.099, sig 0.669). Also no significant correlation was found between remnant fibula ratio and regeneration of fibula at six months (Pearson correlation 0.011, sig 0.962).
- Ratio of fibular width at three and six months. Fibular regenerated width at proximal and distal third at three months showed significant correlation to observed widths at six months {(P3-P6 Pearson correlation 0.881, sig 0.000), (D3-D6 Pearson correlation 0.815, sig 0.000)}. This suggests that degree of width regeneration in fibula at three months radiographs would give a clue regarding degree of regeneration at six months.
- Ratio of fibular width at proximal and distal third. Ratio of fibular regenerated width at proximal and distal third showed significant correlation to each other at both three and six months {(P3-D3 Pearson correlation 0.654, sig 0.001), (P6-D6 Pearson correlation 0.627, sig 0.002). This suggests that regeneration of fibular width at proximal third goes in accordance with distal third.
- Pre-operative and regenerated fibula at six months. There was no significant statistical difference between fibular width at either proximal third (sig 0.738) or distal third

Table 1 Statistical data

Correlations			
Sl. number	Pairs	Pearson correlation	Significance
1	Age & P0	–0.346	0.125
2	Age & D0	–0.089	0.702
3	Age & P3	–0.553	0.009
4	Age & D3	–0.575	0.006
5	Age & P6	–0.657	0.001
6	Age & D6	–0.592	0.005
7	P3 & P6	0.881	0.000
8	D3 & D6	0.818	0.000
9	P3 & D3	0.654	0.001
10	P6 & D6	0.635	0.002
11	Remnant fibula ratio & age	–0.099	0.669
12	Remnant fibula ratio & regenerated fibula at six months	0.011	0.962
Pair t-test data			
Sl. number	Pairs	t-test	Significance
1	P0 & P6	0.340	0.738
2	D0 & D6	–0.450	0.657

P0: Proximal 3rd fibula/tibia percentage at pre-op

P3: Proximal 3rd fibula/tibia percentage at three months

P6: Proximal 3rd fibula/tibia percentage at six months

D0: Distal 3rd fibula/tibia percentage at pre-op

D3: Distal 3rd fibula/tibia percentage at three months

D6: Distal 3rd fibula/tibia percentage at six months

Remnant fibular ratio: Ratio regenerated fibula at six months/remnant fibula (residual proximal + distal fibula)
Please indicate the significance of the asterisks in the table or remove them.Removed asterisks

(sig 0.657) segments pre-operatively and at six months, suggesting regeneration of fibular width similar to the pre-operative dimensions at measured sites at six months follow up.

Discussion

Fibular bone has remained an important site for autogenous bone graft in children. Both vascularized and non-vascularized fibular grafting are frequently practised in paediatric orthopaedics centres. There has been an enhanced debate on several morbid findings found on radiological examinations of fibula donor sites and their clinical implications. Common complications of donor region reported are surgical scar, pain, ankle instability, motor-neural weaknesses, proximal migration of fibula, ankle valgus and deformities of the tibial shaft and ankle [11–17]. The recommendations of leaving a distal fibular remnant greater than 5–6 cm, distal tibiofibular arthodesis, and scheduling surgical harvest at age older than eight years emerged from these findings [11–14]. A close examination of literature on the subject showed that a majority of these results surfaced from vascularized fibula graft series where regeneration of donor fibula did not occur.

The non-vascularized fibular harvesting is simpler and economical. It does not require specialized microvascular skills or instruments. Only two dedicated paediatric series in recent indexed English literature discuss long-term impact of non-vascularized harvesting on fibular donor site [2, 20]. González-Herranz et al. studied 23 children (average age 8.9 years) who underwent 24 fibulae resections [20]. Major imaging findings in the series were distal migration of the fibula head in 18 cases (but without clinical relevance), lateral cortical thickening of tibia in five cases, talar tilt in 11 cases, proximal migration of the lateral malleolus in 13 cases, and diaphyseal valgus of the tibia in five cases. Two patients suffered a spiral diaphyseal fracture and another a slow physeal fracture of the distal tibia. The series however represented a heterogeneous data with harvest of different anatomical fibular regions (head, proximal diaphysis, middle diaphysis, distal diaphysis, lateral malleolus) and variable lengths of fibula (2–24 cm) [20]. There was primary tumour of fibula in seven cases. In half of their cases, the distal tibiofibular joint was stabilized with a supra syndesmal screw or a Kirschner wire. Periosteum preservation of fibula was not uniform in all cases.

The other paediatric study of non-vascularized fibula harvest studied a periosteum-preserving technique in 17 children with mean age 8.4 years [2]. Patients were divided into two groups—nine fibular graft sites filled with cancellous allograft and eight with calcium sulfate. Variable lengths of fibula were harvested with an average 28 % (range 10–58 %), and average length of distal fibula remnant was 28 % (15–47 %). At mean follow up of 31 months, all patients had complete regeneration of fibulae. No significant donor site complications were reported in this series [2].

The intact periosteum is one of the important contributors to osteogenesis. There are many clinical situations where this fact has been well documented, e.g. healing following fractures, tumour/ infection expansions, regenerations after rib harvest, etc. The fact that non-vascularized fibular donor sites regenerated fibula, especially if the enveloping periosteal sleeve was left intact, has also been long known [21]. But this particularly useful aspect of regeneration has never been studied in detail. Burchardt (1983) commented that the non-vascularized fibula in children undergoes spontaneous complete regeneration after resection if the periosteal sleeve is left intact but that it takes approximately two years [21]. In a series of seven cases of non-vascularised fibular grafting used for defects of long bones after sequestrectomy in children, Steinlechner and Mkandawire [22] had six fibulae regrowth in continuity at a mean follow up of 19.3 weeks (range, 6–75 weeks). Although they did not study regenerated fibula specifically, they opined that early restoration of bony continuity led to stabilization of the ankle in the donor leg. They even suggested the reuse of regenerated fibula for further bone grafting [22]. González-Herranz et al. reported 58 % incomplete regeneration or nonunion of harvested fibula at mean follow up of 6.2 years (range, 4–11 years) in their series [20]. The mean time to fibula regeneration reported in the Xin et al. pediatric series was just 12 weeks (range, 4–21 weeks) when the periosteal tube was filled with bone allograft or bone substitute [2]. Except for the Xin et al. series where donor site marrow density and cortical bone was matched with adjacent tibia, no other method to quantify regeneration of harvested fibula has been described. However, allograft or bone graft substitutes were used in their patients to fill the defect which makes comparisons difficult.

The strength of this study is the prospective evaluation of regeneration of fibula after harvesting a non-vacularized graft without addition of an allograft/ bone graft substitute. Our series is probably the first to quantify the regeneration in terms of longitudinal and transverse dimensions in the pediatric age group. The criteria of keeping minimal proximal and distal fibular residual lengths of 10 % did not pose any problems in our study. These indices in turn helped to obtain longer grafts in younger children. About 65 % of total fibular length was available for use as graft. There were no clinical morbid findings as assessed at six months follow-up despite the fact that non-continuity was observed in one third of cases (29 %). The predominant site (five cases; 83 %) for non-continuity was middle third-distal third junction. The statistical analysis in our series also showed that regeneration of fibular width declines with increasing age of children, a conclusion similar to the Xin et al. series [2]. A very important result of our study was regeneration of fibular width similar to the preoperative dimensions at measured sites as early as six months in 71 % of cases. The consistency of the radiologically measured fibula may not be equivalent to anatomical preharvested fibula, yet rapid restoration of dimensions of fibula, its muscle attachments and ankle mechanics may be the main reasons for minimal morbidity observed in our series. We had reharvested the regenerated fibular graft in several patients in subsequent follow ups. The reharvested graft, although irregular and slightly thinner, had characteristics very similar to the original graft.

The main limitations of our study were the small number of cases and shorter follow up. The six-months follow-up is probably short for evaluation of some clinical disorders like valgus of the ankle. Although our method for the levels of fibular width measurement on plain radiographs was based on anatomical criteria (see methods above), there are chances that the selected area may not be representative. The fibula has a three-dimensional structure and quantification of fibular dimensions on plain radiographs has its own limitations. Moreover, the fibular width on anteroposterior radiographs is not the same as lateral radiographs. Lateral profile of fibula could not be accounted for regeneration due to considerable overlap of radiological shadows obscuring radiological landmarks. Further, for statistical analysis purpose, it was assumed that the fibular dimensions did not alter significantly over a period of six months.

All fibulae were harvested from a healthy extremity with no obvious underlying pathology. There can be many possible factors for non-continuity of regenerated fibula. The periosteum thickness varies with age, with thicker periosteum available in younger children permitting better dissection. The mean age in a non-continuous group in our series was a bit higher (seven years) than mean age (5.58 years) in the continuous group. The differential thickness and firmness of periosteal attachment to fibula in different anatomical regions, especially middle lower third junction, could be another factor. Further, many other causes can contribute to non-continuity, e.g. bone, surrounding soft tissue and blood supply characteristics, intactness of the periosteal sleeve, total fibula length harvested and surgical skills and technique [4].

The children have tremendous remodelling potential and many cases of observed non-continuity at six months may recover later, e.g. in one case there was no radiological regenerate at three months in the distal third but it improved to 31 % at six months. The fibulae which have already regenerated were also expected to undergo remodelling [22]. It is therefore recommended to keep these children under regular follow up.

Conclusions

Periosteal preserving non-vascularized fibula grafting is a procedure with low morbidity. In the majority of cases (71 %), there was regeneration of fibula at the harvest site with dimensions of the regenerate comparable to preharvested fibula at six months. The non-continuous regeneration of the fibula had no clinical implications.

Compliance with ethical standards

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

Financial conflicts None.

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