Acta Orthop. Belg., 2011, **77**, 506-515

ORIGINAL STUDY

Deep intramedullary infection in tibial lengthening over an intramedullary nail

Seung-Ju Kim, Gracia Cielo Balce, Young-Jae Huh, Sang-Yoon Song, Hae-Ryong Song, Seung-Ju Kim

From Korea University Medical Center, Guro Hospital, Seoul, South Korea

Tibial lengthening over an intramedullary (IM) device is associated with a risk of deep intramedullary infection ; there is so far no guideline for decision making between early removal and delayed removal of the nail.

Tibial lengthening over an intramedullary nail/Rush pin was performed in 118 limb segments (63 patients) from 2004 to 2008 in our institution. Fifty five patients had bilateral tibial lengthening. Ninety nine of the 118 segments went on to healing without infection, while 13 segments developed superficial infection and 6 segments developed deep infection. Among 6 patients with deep infection, 4 patients underwent early removal of the nail when deep infection signs and symptoms occurred and 2 patients underwent delayed removal of the nail at 11 months. The 6 segments with deep infection differed significantly with respect t to the callus pattern ($p < 0.05$) and density ($p = 0.0001$) from those without infection and with superficial infection.

In this small sugroup, removal of the nail was delayed in two patients as there was visible callus bridging at more than one cortex, and deep infection subsided after local drainage.

Keywords : deep infection ; tibial lengthening ; intramedullary nail.

INTRODUCTION

Lengthening over an intramedullary (IM) device was developed to decrease external fixation time and post-removal complications, such as fracture or angulation of the regenerate, associated with the traditional method (*2,3,8,9*). The technique is achieving greater acceptance due to its focus on patient comfort. However, the method is associated with many complications, the most devastating of which is intramedullary infection (*3,9*). The need for vigilant follow-up, quick detection and an effective treatment protocol to avert this possible obstacle (*7*) cannot be overemphasized.

Previous case series (*4,6*) describing experiences with tibial lengthening over IM devices have briefly described the occurrence and management of deep intramedullary infection, but none have described it in detail. There is also no consensus or guideline whether or not to remove or retain the IM device, and whether or not to do bone-grafting after resolution of infection.

■ Seung-Ju Kim, MD, Fellow.
■ Gracia Cielo Balce, MD, Fellow.
■ Young-Jae Huh, MD, Resident.
■ Sang-Yoon Song, College student.
■ Hae-Ryong Song, MD, PhD, Professor.
Institute for Rare Diseases, Department of Orthopaedic Surgery, Korea University Medical Center, Guro Hospital, Seoul, South Korea.
Correspondence : Professor Hae-Ryong Song, MD, PhD, Institute for Rare Diseases, Department of Orthopaedic Surgery, Korea University Medical Center, Guro Hospital, 80 Guro-dong, Guro-Gu, Seoul, 152-703, South Korea.
E-mail : songhae@korea.ac.kr

No benefits or funds were received in support of this study

Callus formation may be assessed from standard and digital radiographs, ultrasound, bone scans, CT and dual energy X-ray absorptiometry (DEXA). The latest approach that is being used to determine callus stiffness is to evaluate the pixel value ratio using a picture archiving and communication system (PACS) (*1,10*). The pixel value ratio is the ratio of the proximal segment to that of the regenerate, and it correlates well with the BMD ratio.

This study aimed to determine ways of enhancing timely radiographic detection of intramedullary infection in tibial lengthening cases over IM devices by reviewing if there are characteristic radiographic appearances in infected calluses, and if the evolution of their serial pixel value ratios (PVRs) is any different from that of non-infected ones. By evaluating our management of this complication, protocols may be either maintained or revised in order to produce better outcomes.

PATIENTS AND METHODS

Lengthening over an intramedullary nail/Rush pin was performed in 63 patients (118 tibial segments) between 2004 and 2008 in our institution ; 55 patients had bilateral lengthening. The mean age of the patients was 20.34 years (range : 13-48) at the time of the index procedure. The causes for short limbs were familial short stature (54 segments), Idiopathic short stature (23 segments), hypochondroplasia (10 segments), Osteogenesis Imperfecta (4 segments),vitamin D resistant rickets (6 segments), trauma resulting in epiphyseal injury (4 segments), Russell-Silver syndrome (2 segments), achondroplasia (2 segments), spondyloepiphyseal dysplasia (2 segments), short stature due to nephritic syndrome (2 segments), short stature due to adrenal hypertrophy (2 segments),Turner's syndrome (2 segments), congenital hemihypertrophy (2 segments), pseudoarthrosis (2 segments) and tibial dysostosis (1 segment).

Callus evaluation was done qualitatively using the Li classification (*7*), and quantitatively using serial pixel value ratios (PVRs) in a picture – archiving communication system (PACS).

All radiographs were analyzed retrospectively by three observers and regenerate characterization was done according to the Li classification system (*7*). Based on this system, the callus pattern was described as either sparse, homogeneous, heterogeneous, or lucent ; the callus shape was described as either fusiform, cylindrical, lateral, concave, or central ; and the callus density was described as either low, intermediate, or normal. These callus characteristics were noted in the pre-infection, infection, and post-infection radiographs of the six deep infected segments.

The PVR's (pixel value ratios) of the anterior, posterior, medial, and lateral cortices of the six infected calluses were measured, using the StarPACS (Infinitt, PiView Star, 5.0.6.0), at 4, 8, 12, 16, and 20 weeks after application of the Ilizarov fixator. These were plotted against the values taken from the contralateral uninfected tibial segments of the six patients with deep infection. Separate graphs were made for tibias that underwent post-infection bone-grafting and those that did not.

Immediate outcomes were measured and compared using the external fixation index (EFI), which was computed by dividing the total days the patient was treated in an external fixator by the final callus length (in centimeters). The external fixation index and the mean consolidation index were calculated.

RESULTS

Ninety nine of the 118 segments went on to healing without infection, while 13 segments developed superficial infection and 6 segments developed deep infection. In these 6 segments, a Rush nail was used in 2 segments and a rigid interlocking nail in 4 segments.

Among 6 patients with deep infection, 4 patients (3 with a Rush pin and 1 with a rigid interlocking nail) underwent early removal of the pin/nail when deep infection signs and symptoms occurred between 1 month and 6 months after the lengthening procedure and there was no callus bridging at any cortex. Vancomycin-impregnated PMMA beads were implanted if the IM device was removed. In the other 2 patients, both with a rigid interlocking nail, removal of the nail was delayed until 11 months, when bone consolidation involved at least 3 cortices. Three patients who had not achieved their lengthening goals underwent mid-diaphyseal tibial osteotomies for further lengthening. Culture-guided intravenous (IV) antibiotics were given for two weeks (Table I).

When serologic infection parameters, such as erythrocyte sedimentation rate (ESR) and CRP, had

Table I. — This table summarizes the details involving the six segments with deep intramedullary infection (IM = intramedullary ; EF = external fixator ; MRSA = methicillin-resistant *Staphylococcus aureus* ; MSSA = methicillin-sensitive *Staphylococcus aureus* ; F/C = fever and chills ; debt = debridement ; ABB = antibiotic beads ; EFI = external fixation index). Delays are in days

Case	age (yrs)	sex	length gain (cm)	IM device	infection detection (post-op day)	IM device removal (post-op day)	EF removal post-infection (days)	organism	CRP (mg/L)	Symptoms	treatment	bone graft	remarks	EFI (days/cm)
1	28	F	7.5	Rush	35	38	196	MRSA	227	F/C	debt + ABB	+	recovered	30
2	43	F	7.8	Nail	82	84	37	MRSA	124	-	debt + ABB	+	recovered	15
3	25	M	8	Nail	120	266	70	MSSA	76	-	debt	-	recovered	23
4	20	M	7.5	Nail	224	294	56	MSSA	154	F/C	debt	-	recovered	37
5	20	F	8	Nail	90	168	56	MSSA	299	F/C	debt	+	recovered	18
6	13	F	10	Rush	51	66	308	MSSA	54	-	debt	-	recovered	35

normalized, and the patient showed no clinical signs of infection, the decision to proceed to bone-grafting was made based on evaluation of the callus pattern.

Three patients with deep infection required bone grafting ; the other 3 patients with deep infection healed without bone grafting. One of these patients, a 13-year-old girl, showed spontaneous callus formation at the initial lengthening area – the proximal tibia – during the distraction period at midshaft (Fig. 1).

The two patients with delayed removal of the nail developed deep infection 4 months and 8 months respectively after the lengthening procedure and they had purulent discharge from the osteotomy site. After drainage and irrigation, intravenous administration of antibiotic was applied until ESR and CRP were normalized. They already demonstrated callus formation along the posterior and lateral cortices at the time of the drainage procedure. Therefore, the nail was not removed until 11 months postoperatively. Complete consolidation was obtained without bone grafting in these two patients (Fig. 2 & 3).

In patients with deep infection, all segments, except segment 4, which presented with a cylindrical, homogenous, low density callus, initially presented with cylindrical, lucent, low density calluses in the pre-infection period. During active infection, segments 1, 2, 5, and 6 had no identifiable changes. Segment 3, however, produced a heterogeneous pattern. Segment 4 presented with a lateral, heterogeneous, intermediate density callus during and after infection (Table II). The cylindrical, lucent segments 1, 2, and 5 eventually underwent bone grafting, and developed favorable callus characteristics : cylindrical turning into fusiform shape, homogeneous > heterogeneous patterns, and normal > intermediate densities (Table II). The mean EFI of the bone grafting group was 21 ± 6 days/cm.

Segments 3 and 4, which had calluses with cylindrical and lateral shapes respectively, and heterogeneous patterns during active infection, were not bone grafted. Their existing corticalized regenerates were allowed to consolidate without intervention. In contrast to the bone grafting group, they developed the following callus characteristics : lateral turning into cylindrical shapes, intermediate then normal densities, and all had heterogeneous patterns (Table II). The mean EFI of the non-bone-grafted group was 31 ± 6 days/cm.

We found that the mean consolidation index and the mean percentage gain in length (Table III) did not differ significantly among the patients. We also found the medial and anterior deficiency of the regenerates in patients with deep infection and most of callus type were heterogeneous.

All of the 6 patients with deep infection had bilateral lengthening. For the three tibial segments

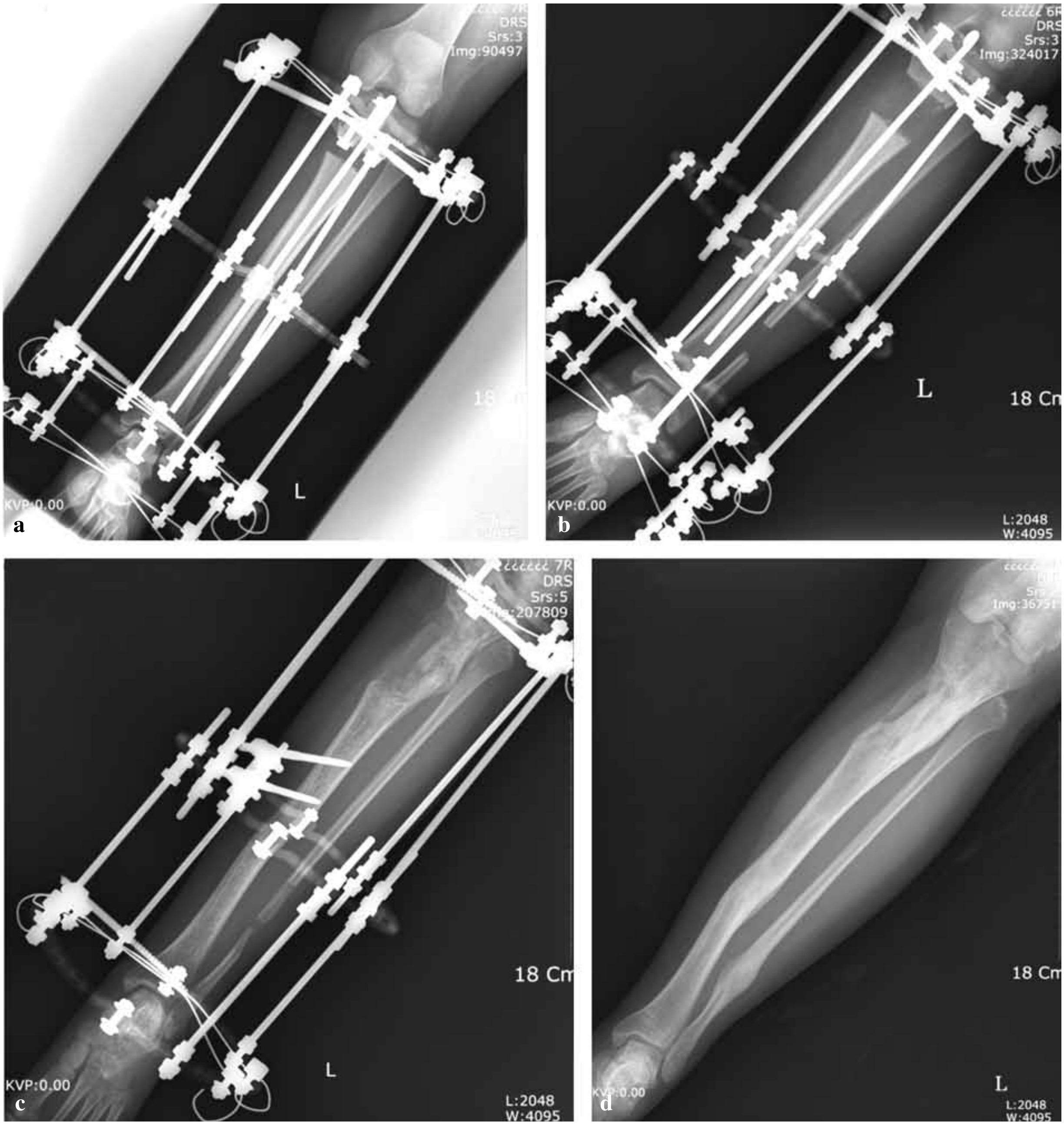

Fig. 1. — This figure shows the callus progression of case 6 (non-bone-grafted) through (a) preinfection, (b) active infection, and (c) post-infection phases. The most recent radiograph (d) still shows some anteromedial defect, and some valgus deformity at the mid-diaphyseal osteotomy site.

with deep infection that did not undergo bone grafting, the baseline PVRs at four weeks after Ilizarov application were consistent with those of the contralateral uninfected segments, except for the posterior cortices where they were markedly lower. At eight weeks, the lateral cortex PVRs started deviating from the normal and showed lower PVRs. At twelve weeks (84 days), which was much earlier

Fig. 2. — This figure shows the callus progression of case 3 (non-bone-grafted) through (a) preinfection, (b) active infection, and (c) post-infection phases. The most recent radiograph (d) shows full consolidation of the previous osteotomy site.

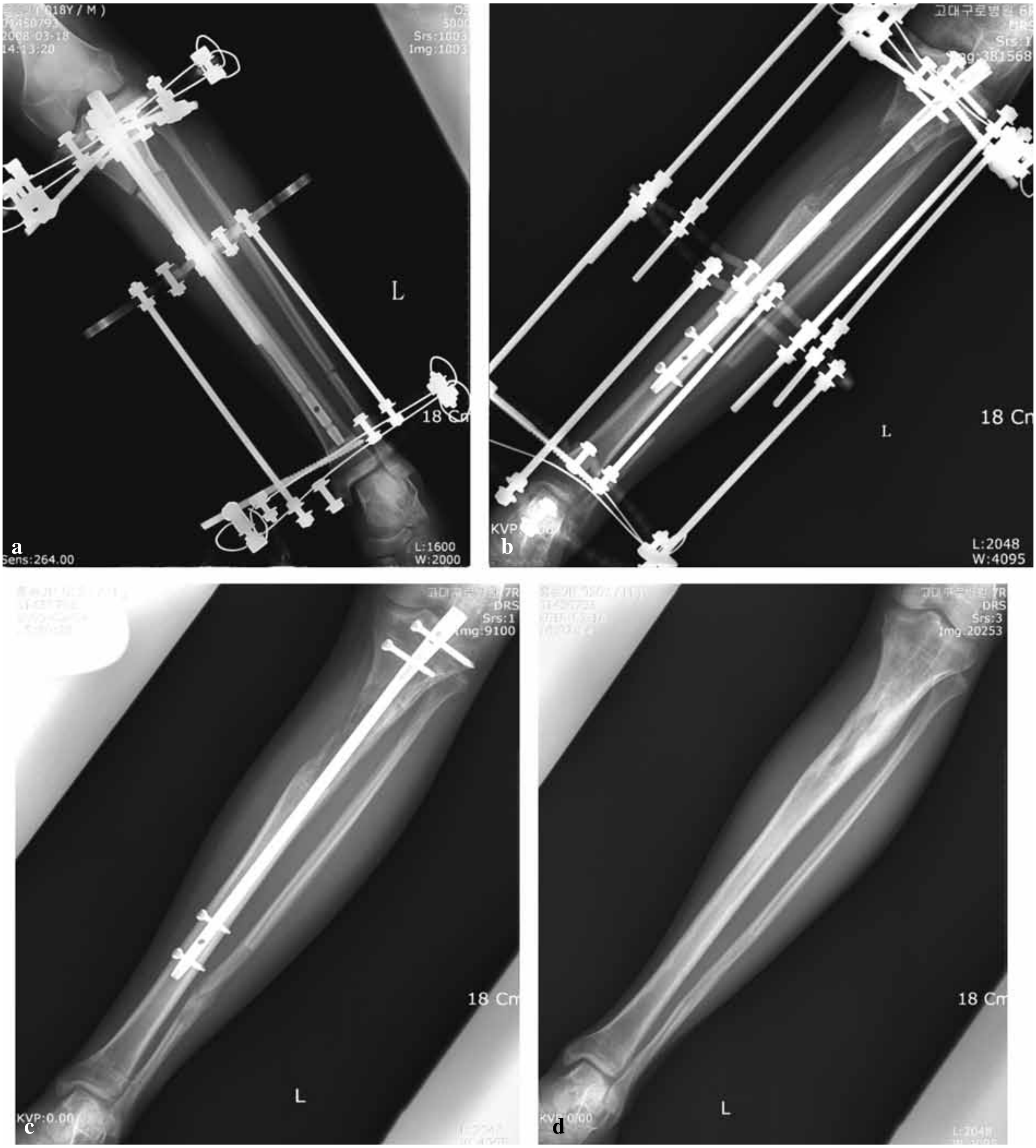

Fig. 3. — This figure shows the callus progression of case 4 (non-bone-grafted) through (a) preinfection, (b) active infection, and (c) post-infection phases. The most recent radiograph (d) shows full consolidation of the previous osteotomy site.

Table II. — This table shows the progression of callus characteristics of the six infected segments at pre-infection, active infection, and post-infection (post-bone-grafting for cases 1, 2, and 5) phases

Case	Pre-infection			Active Infection			Post-infection		
	shape	pattern	density	shape	pattern	density	shape	pattern	density
1	cylindrical	lucent	low	cylindrical	lucent	low	cylindrical	homogeneous	normal
2	cylindrical	lucent	low	cylindrical	lucent	low	fusiform	homogeneous	normal
3	cylindrical	lucent	low	cylindrical	heterogeneous	low	cylindrical	heterogeneous	normal
4	cylindrical	homogeneous	low	lateral	heterogeneous	low	lateral	heterogeneous	low
5	cylindrical	lucent	low	cylindrical	lucent	low	cylindrical	heterogeneous	intermediate
6	cylindrical	lucent	low	cylindrical	lucent	low	lateral	heterogeneous	intermediate

Table III. — This table shows the mean consolidation index, percentage gain in length and duration of procedure of the patients

	Patients without infection	Patients with superficial infection	Patients with deep infection	P value
Consolidation index Mean ± SD (range)	45.7 ± 38.8 (14.8-246)	54.7 ± 39.2 (20.4-167.6)	45.18 ± 6.38 (40.2-52.7)	0.24
Percentage gain in length Mean ± SD (range)	16.7 ± 5.08 (2.9-30)	15.6 ± 4.67 (6.25-23.6)	17.3 ± 5.42 (9.7-25)	0.55

than the mean infection detection time of 131 days, the PVR's of all cortices, especially that of the posterior cortex, have started declining. After management of infection with debridement, and intravenous and oral antibiotics, the PVR's of the infected segments increased, showing signs of callus recovery (Fig. 4).

For the three infected tibial segments that underwent bone grafting, the baseline PVRs four weeks after Ilizarov application were consistently higher than those of the contralateral uninfected segments, except for the anterior cortices which were lower. The posterior and medial cortex PVRs had declined sharply at the eighth week (56 days), which was prior to the mean infection detection time of 69 days. After treating the infection, and especially after bone grafting after the twelfth week, the PVRs have increased rapidly (Fig. 5).

DISCUSSION

One of the most troublesome complications of tibial lengthening over an IM device is intramedullary infection. There is however limited literature discussing this complication. Both Kristiansen *et al* (*4*) and Mathieu *et al* (*6*) reported deep intramedullary infection occurring in one out of nine tibial segments in lengthening over IM devices. Kristiansen *et al* (*4*) treated the deep infection by early nail removal, and Mathieu *et al* (*6*) treated their case by rod removal and 3-month antibiotic therapy. In our case series, the rate of deep intramedullary infection with this technique is relatively less at 5% (6/118 cases) versus the reported 11% (1/9 cases), perhaps due to our larger patient series.

Li *et al* (*5*) devised a callus classification system based on callus shape, pattern, and density, in order to predict healing patterns and provide a basis by which a therapeutic strategy may be made. This is usually employed in adjusting the rate of distraction during follow-ups in order to individualize the distraction protocol and maximize each patient's bone healing potential. We hypothesized that deep intramedullary infections should show radiographically different calluses.

Deep intramedullary infection in our experience was detected at a mean of 100 days after the index

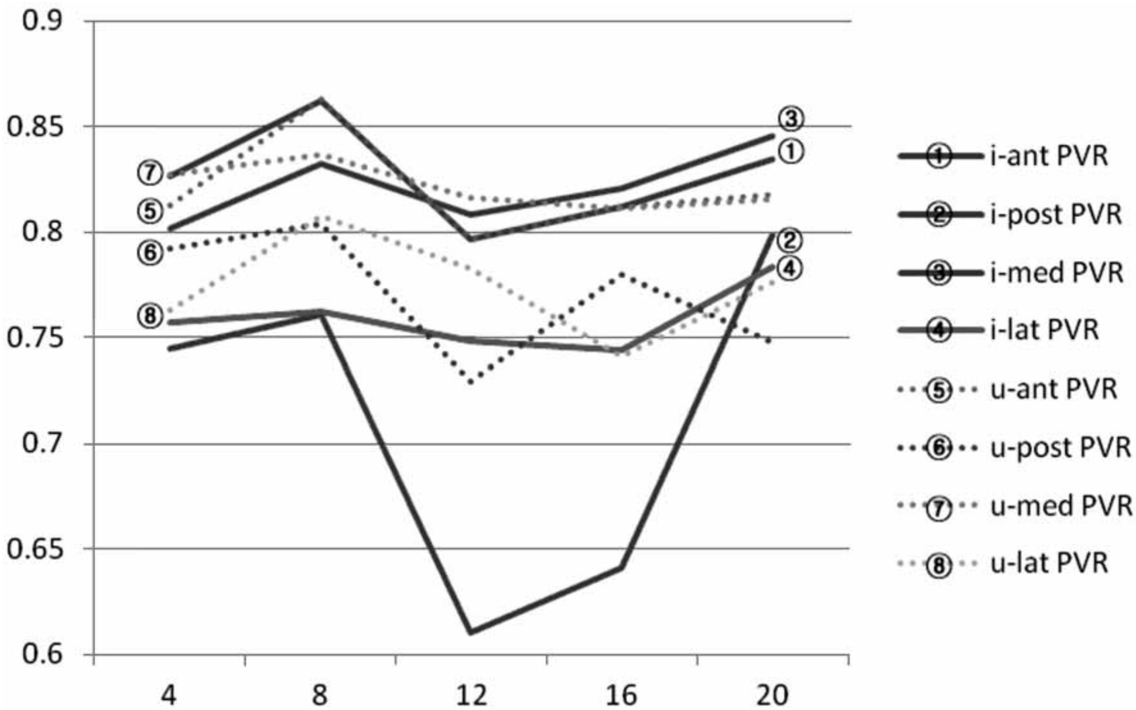

Fig. 4. — This graph shows the PVRs, through weeks 4 to 20, of the different cortices for the infected calluses that did not receive bone grafting (i, infected ; u, ininfected ; ant, anterior cortex ; post, posterior cortex ; med, medial cortex ; lat, lateral cortex).

procedure. The difference in callus patterns may be ascribed to the phase when the infection was discovered. Naturally, the earlier the infection is detected, the more lucent the callus pattern is. Those that were detected later during the consolidation phase had more heterogeneous patterns. There are no guidelines or any mention in current literature when a particular callus pattern should be addressed with bone grafting or not, especially after an intramedullary infection. We, however, opted to perform bone grafting for sparse or lucent callus patterns after infection had subsided. As expected, post-infection bone-grafting produced better calluses, higher PVRs, and faster EFIs than those that received no bone-grafting. The difference in EFIs between bone-grafted and non-bone-grafted groups is suggestive that bone-grafting might be beneficial for all post-debridement calluses, regardless of the callus pattern.

The medial and anterior deficiency in the density of the regenerates in patients with deep infection were most likely due to the subcutaneous location of the medial surface and anterior border of the tibia which causes differences in vascularisation due to a deficient muscle cover ; infectious discharge finds its way through this least resistant area, while this site is frequently used for the surgical approach. Thus, this area becomes deficient in callus due to drainage of infectious discharge, surgical intervention and this deficiency persists even after consolidation of the regenerate.

Lately, the Picture Archiving Communication System (PACS) has become quite useful because of its quantitative way of assessing cortical mineralization at the regenerate site (*1,10*). Since characterization of calluses using the Li classification (*5*) is subjective, we also measured serial PVR's of all four cortices to quantitatively assess changes in corticalization before, during, and after intramedullary infection. A sharp decline in serial PVR's may be indicative of a destructive, lytic process, such as an infection. The present data shows this sharp decline in PVR occurs a few weeks prior to the actual clinical detection of

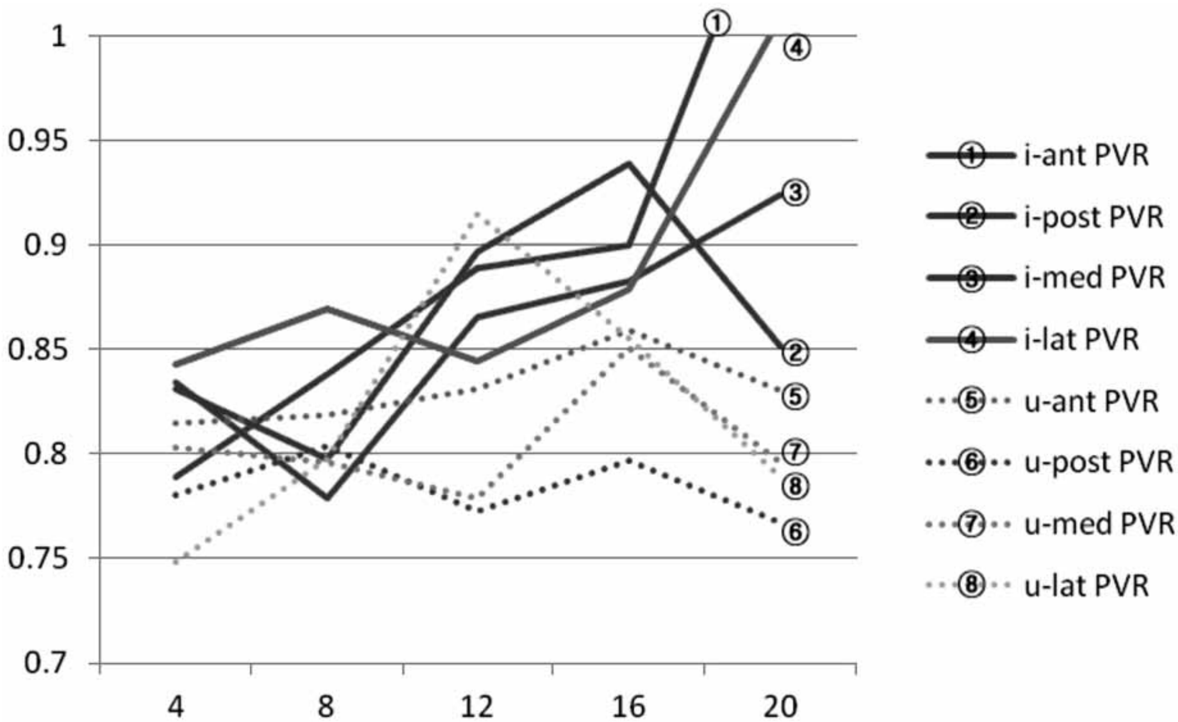

Fig. 5. — This line graph shows the PVRs, through weeks 4 to 20, of the different cortices of the infected calluses that received bone grafting (i, infected ; u, ininfected ; ant, anterior cortex ; post, posterior cortex ; med, medial cortex ; lat, lateral cortex).

infection. It seems that, among all four cortices, the posterior cortex exhibits the steepest decline and may be the most sensitive indication of a possible deep intramedullary infection.

The decision to remove or retain the IM device after deep infection was made according to the shape and pattern of callus formation and the improvement in systemic symptoms after the drainage procedure. In cases with cortical bridging at more than one cortex, we did not remove the device immediately after detection of infection, but waited for regenerate callus formation before removal of the device. If we would have removed the IM device immediately we would have had to put more pins and wires for the stability of the external fixator. This additional surgery would have compounded the problem of infection. We found that callus can be formed along the infected periosteum when there is visible callus at the other cortices provided the purulent discharge is drained to prevent further spread of the infection. This means that the deep infection was localized and the infected periosteum can retain healing potential originated from vascularization of the intact periosteum. But, if there is no visible callus formation at any cortex, we cannot expect a possibility of callus formation because the whole periosteum was infected and there is no resource for bone formation. This means that the deep infection was spreading to the whole intra-medullary area and there is no viable vascularization. In this situation, the nail should be removed to control infection.

The limitation of our study is that our conclusion is based on only two cases that developed deep infection and eventually healed in spite of delayed removal of the IM devices.

In summary, delayed removal of the nail could be another option to obtain bone union with a combined procedure such as drainage with or without bone grafting when there is deep intramedullary infection with visible callus formation. As compared with early removal of the nail, this method has some advantages such as avoidance of an additional stabilization procedure and preservation of the alignment.

Acknowledgement

This study was supported by a grant from the Korea Healthcare Technology R&D Project, Ministry for Health, Welfare & Family Affairs, Republic of Korea (A090084).

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