Antibiotic Cement Spacer and Induced Membrane Bone Grafting in Open Fractures with Bone Loss: A Case Series

Abstract

Background: Open fractures are a difficult entity, often complicated by infection and nonunion. Bone loss in such fractures adds to the complexity. Conventional techniques of bone defect management are mainly directed toward fracture union but not against preventing infection or joint stiffness. In this case series, we evaluated Masquelet's technique for management of open fractures with bone loss. **Materials and Methods:** Twenty seven open fractures with bone defect, which presented within 3 days of trauma were planned for treatment by Masquelet's technique. Followup ranged from 21 to 60 months. **Results:** Average length of bone defect was 6 cm. Radiological union was obtained at a mean of 280 days since first stage of surgery. Time for union was not related to the size of defect. Union was faster in metaphyseal region (265.6 ± 38.8 days) as compared to diaphysis (300.9 ± 58.6 days). No patient had residual infection after stage 1. All the patients were able to mobilize with full weight bearing after radiological union with a satisfactory range of motion of adjacent joints. **Conclusion:** This technique can be routinely applied in compound fractures with bone loss with good results. Chances of infection are reduced using antibiotic cement spacer as an adjunct to thorough debridement. Induced biomembrane revascularizes the graft. Union can be expected in most of the cases, however, long time to union is a limitation. Technique is cost-effective and does not require special training or instrumentation. Although it is a two-stage surgery, requirement of multiple surgeries, as may be needed in conventional methods, is avoided.

Keywords: *Antibiotic cement spacer, induced biomembrane bone grafting, management of bone defect, management of compound fractures, Masquelet technique*

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Introduction

Management of open fractures has always been a challenging problem for trauma surgeons. Despite the improvements in technology and surgical techniques, rates of infection and nonunion are still troublesome.[1-4] Bone loss in open fractures, due to trauma or during debridement, add to complexity of the problem. For managing bone defects, various techniques such as limb lengthening by Ilizarov ring fixator or limb reconstruction system (LRS), fibular grafting, cancellous, or cortical bone grafting have been in use with their particular advantages and disadvantages.[5-8]

Traditional bone grafting techniques are limited by uncontrollable graft resorption. Vascularized bone grafting is technically demanding.[5,6] Ilizarov technique has been associated with adjacent joint stiffness, neurological injuries, premature, or delayed

consolidation.[7,8] And importantly, none of the techniques are directed against infection and can be used only when chances of infection have been ruled out.

In 1986, French surgeon A. C. Masquelet conceived and developed a two-stage technique for the management of large bone defects.[9] First stage consists of debridement and antibiotic cement spacer application. Second stage consists of cement spacer removal and filling of bone graft in the biomembrane envelope that forms around the spacer as a foreign body reaction to it. Conventionally, this technique has been used mostly for infected gap nonunions,[9] with limited application in fresh trauma.

Treating open fractures with bone loss, with the Masquelet's technique can decrease the incidence of infection and help in achieving a functionally viable limb with fewer complications. Here, in this prospective study we evaluated the effectiveness of the Masquelet's technique.

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Materials and Methods

Twenty seven patients with open fractures with bone defect who presented within 3 days of trauma, from January 2012 to April 2015, treated by the Masquelet's technique are included in this prospective study. All the patients were operated by the lead author (SK). All the patients were taken up for first stage of surgery immediately after presentation. Details of the type of injury, location, soft-tissue condition, length of bone defect, type of fixation, time difference between antibiotic cement spacer placement and bone grafting, and time to union were documented [Table 1]. Length of bone defect was taken to be mean of gap between all the four cortices. Patient classification was also done depending on the amount of cortical continuity after debridement [Table 2]. If a fractured segment or comminution was retained and maintained continuity of the proximal and distal fragments, it was not accounted as loss of cortex. Only the amount of actual cortical bone loss was taken into consideration.

Type I: Less than 25% loss of circumferential cortex
Type II: 25%–50% loss of circumferential cortex
Type III: Greater than 50% loss of circumferential cortex
Type IV: Segmental loss of bone.

Operative procedure

First stage

After regular painting and draping, open wound was meticulously debrided. Bone edges were washed and debrided whenever they were contaminated. It was ensured to achieve a viable bleeding bed. Fixation was undertaken after acceptable reduction was achieved, ensuring anatomic length, alignment, and rotation. A little reduction in length (up to 2 cm) was accepted if size of the defect was huge. Method of fixation depended on the soft-tissue condition, location, and type of defect. After satisfactory debridement, aim was to go for internal fixation. In cases where soft-tissue status precluded internal fixation, external fixation was done, and efforts were made to provide stability to the cement spacer using rush nail or k-wire, as this was considered essential by the surgeon to eliminate the chances of infection. After fixation, defect was filled with antibiotic cement spacer which was made by mixing 4 g of vancomycin in 40 g of poly-methyl-meth-acrylate preloaded with 500 mg of gentamicin (Palacos R + G, Zimmer, Wehrheim, Germany). Shaping of cement spacer was done to match contour of the bone. Overstuffing of the defect was avoided to accommodate soft-tissue coverage. Continuous irrigation with normal saline was done during setting of cement to avoid thermal damage to tissues. Vascularized wound coverage was given either by existing soft tissues or by myofasciocutaneous local flaps or distant flaps by the plastic surgeon.

Second stage

Second stage was planned after 6 weeks. Prerequisite for second stage was healed wound without any inflammation or edema. If wound healing was not satisfactory, or, if any edema was present, it was decided to wait. White blood cell (WBC) count and erythrocyte sedimentation rate (ESR) were monitored during this interval. After they reached normal range or exhibited a downward trend with near normal values, second stage was undertaken with the intent of bone grafting. In cases where WBC count and ESR may not show a downward trend till 8 weeks, it was decided that spacer exchange would be considered.

In second-stage surgery, first the bone defect was approached by careful dissection protecting the healed wound edges. Sharp incision was made over the induced biomembrane [Figure 1]. The cement spacer was broken with osteotome and removed in a piecemeal fashion. Biomembrane was irrigated to remove debris. Cancellous autograft was harvested from iliac crest. If the bone defect was too large, allograft was mixed, making up to 33% of volume of the graft. Allograft was freeze-dried bone graft procured from bone bank of the institute. In a few cases, cortical slivers from the iliac crest were also mixed with the graft. Then, entire void was filled with the graft, engulfing the bone ends by at least 5 mm. The biomembrane was repaired with absorbable vicryl sutures if possible; otherwise, the soft tissues over it were repaired making the membrane fall back into place covering the graft completely. Watertight fascial closure was done, followed by skin closure using nylon.

Postoperative protocol

Patients were allowed immediate passive and active motion and nonweight bearing mobilization. Toe touch weight bearing was started after 12 weeks of second stage. Full-weight bearing was allowed after obtaining radiological union. A few patients in the study had multiple trauma. For such patients, mobilization and weight bearing were delayed as required. However, all efforts were aimed at aggressive physiotherapy and early mobilization.

Followup was done up to a minimum of 21 months for evaluating the results. Radiological outcome was measured as time to bony union. Union was considered when anteroposterior and lateral radiographs of affected part showed continuity of three cortices. Functional outcome was evaluated as range of motion (ROM) of adjacent joints, ability to bear weight, and carry out routine activities.

Results

The case series includes a total of 27 patients, in the age group of 20–58 years. 24 were male and three were female. Mode of injury was road traffic accident in all. All the patients had Gustilo and Anderson Type III b injury. A total of 24 patients presented on the same day to the hospital. Three patients were referred from the periphery and presented late, but all within 3 days of initial trauma.

Table 1: Fracture pattern, size of defect, type of fixation, time interval between two stages, time to union, and range of motion of adjacent joint

Type of fracture	Part of bone	Defect size (cm)	Bone loss	Articular/ extraarticular	Fixation	Time interval between cement spacer placement and bone grafting (days)	Time to radiological union (days)	ROM of adjacent joints	ROM (percentage), as compared to normal limb
Distal femur	Meta-dia	8	Type IV	EA	Plate/k-wire	38	300	0-130 (knee)	93
Distal femur	Dia	10	Type IV	EA	Plate	42	360	0-140 (knee)	100
Distal femur	Meta	5	Type II	A	Plate	44	200	10-100 (knee)	69
Distal femur	Meta-dia	6	Type III	EA	Plate	38	240	0-120 (knee)	92
Distal femur	Dia	10	Type IV	EA	Plate/k-wire	42	330	0-140 (knee)	93
Distal femur	Dia	7	Type IV	EA	Plate	42	300	0-150 (knee)	100
Distal femur	Meta-dia	8	Type IV	EA	External fixator/k-wires Plate	42	300	0-120 (knee)	86
Distal femur	Meta-dia	9	Type IV	EA	Plate	44	330	0-130 (knee)	96
Distal femur	Meta-dia	6	Type IV	EA	External fixator/k-wire Plate	48	300	10-130 (knee)	89
Distal femur	Meta-dia	7	Type IV	EA	Plate	42	300	0-120 (knee)	89
Distal femur	Meta-dia	5	Type III	A	Plate	44	270	0-130 (knee)	100
Distal femur	Dia	6	Type IV	EA	External fixator/k-wire Plate	46	330	0-120 (knee)	92
Distal femur	Meta-dia	5	Type III	A	Plate	40	270	10-120 (knee)	85
Distal femur	Dia	7	Type IV	EA	External fixator/k-wire Plate	44	330	10-110 (knee)	77
Shaft femur	Dia	6	Type IV	EA	External fixator/k-wire Plate	48	330	0-120 (knee)	92
Tibia shaft middle 1/3rd	Dia	6	Type III	EA	External fixator Nail	38	270	0-140 (knee)	100
Tibia distal 1/3rd	Dia	4	Type IV	EA	External fixator/k-wire Nail	36	310	30/10 (ankle) (plantar/ dorsiflexion)	62
Tibia distal 1/3rd	Dia	3	Type IV	EA	External fixator External fixator Nail	48	360	30/0 (ankle) (plantar/ dorsiflexion)	50
Proximal Tibia	Meta	5	Type III	A	Plate	38	240	0-100 (knee)	80
Proximal Tibia	Meta-dia	8	Type III	EA	External fixator Plate	45	270	0-120 (knee)	92.3
Proximal Tibia	Meta	4	Type IV	A	External fixator/k-wires Plate	42	270	0-110 (knee)	79
Proximal tibia	Meta-dia	5	Type III	EA	Plate	40	270	0-135 (knee)	100

Contd...

Table 1: Contd...

Type of fracture	Part of bone	Defect size (cm)	Bone loss	Articular/ extraarticular	Fixation	Time interval between cement spacer placement and bone grafting (days)	Time to radiological union (days)	ROM of adjacent joints	ROM (percentage), as compared to normal limb
Proximal tibia	Meta-dia	6	Type IV	EA	Plate	42	270	5-130 (knee)	96
Proximal tibia	Meta	4	Type III	A	Plate	44	240	0-135 (knee)	100
Proximal Humerus	Meta	4	Type III	A	Rusch nail/k-wire Plate	46	180	40/30 (shoulder) (flex/ex), 30/60 (add/ abd), 70/20 (IR/ER)	54, 49, 75
Humerus shaft middle 1/3rd	Dia	4	Type IV	EA	Plate	52	210	0-120 (elbow)	92
Ulna	Dia	4	Type IV	EA	Plate	40	180	50/60 (forearm) (supination/ pronation)	69

EA=Extraarticular, ROM=Range of motion

Fracture of distal femur was the most commonly encountered injury. Size of the bone defect was measured intraoperatively after debridement and it ranged from 3 to 10 cm, averaging at 6 cm. All the wounds were covered during the first-stage surgery. For ten cases, primary wound closure could be obtained, nine of which were fractures of femur. Skin grafting was done for nine cases and flap coverage was given for eight cases [Table 3].

Average followup was 30 months (range 21–60 months). Mean time interval between cement spacer placement and bone grafting was 42.8 days (range 38-52 days). No correlation was found between the time interval between two stages and time to union, correlation coefficient, $r = -0.05$. Average time to radiological union was 280 days since first stage of surgery (range 180–360 days) [Table 1]. Union was faster in metaphyseal and meta-diaphyseal region (265.6 ± 38.8 days) as compared to diaphyseal region (300.9 ± 58.6 days); however, the difference was not statistically significant ($P = 0.07$). Time to union seemed not to be dependent on the length of bone defect in a particular region. No statistical analysis was performed due to small sample size. Fractures with Type IV bone loss (segmental loss) united slower than fractures having some cortical continuity (Type II and III), $P = 0.003$. In Type IV, bone loss average time to union was 300.6 ± 47.5 days, whereas in Type III and II, it was 250 ± 30 and 200, respectively. In the first stage, internal fixation was done in 17 cases, and external fixation was done in ten, which was later converted to internal fixation. In patients with internal fixation, time to union was 264.1 ± 52.9 days, whereas for patients with external fixation it was 307 ± 30.9 days. This difference was found to be statistically significant, $P = 0.028$. This could be attributed to more extensive soft-tissue injury in patients selected for external fixation. No patients had infection after the first stage of surgery. Hence, all the patients were considered for second

Table 2: Categorization depending on loss of cortices after debridement

Type of bone loss	Number of cases
Type I	0
Type II	1
Type III	8
Type IV	18

Table 3: Bones affected and type of coverage attained for wound

Bone affected	Number of cases	Primary closure	Skin grafting	Flap coverage
Femur	15	9	4	2
Tibia	9	0	3	6
Humerus	2	1	1	0
Ulna	1	0	1	0

stage without the need for any additional surgery after the first stage. One patient had required an additional surgery after the second stage to correct the deformity. All the patients were able to mobilize with full-weight bearing after radiological union and had achieved functional ROM of adjacent joints. Some limitation of movement at joints was observed which could be because of initial soft-tissue injury or intraarticular nature of fracture. At followup of 18 months, comparison of ROM of the joint nearest to the injury site was done with the same joint on unaffected extremity by paired *t*-test. ROM on the affected side was significantly lower ($P = 0.0001$), but none required any additional surgery and all were able to carry out routine activities. No correlation was seen between ROM and amount of bone loss. Shortening of the limb was noted in four patients, all <2 cm, for which shoe raise was prescribed case examples are shown in Figures 2-20.
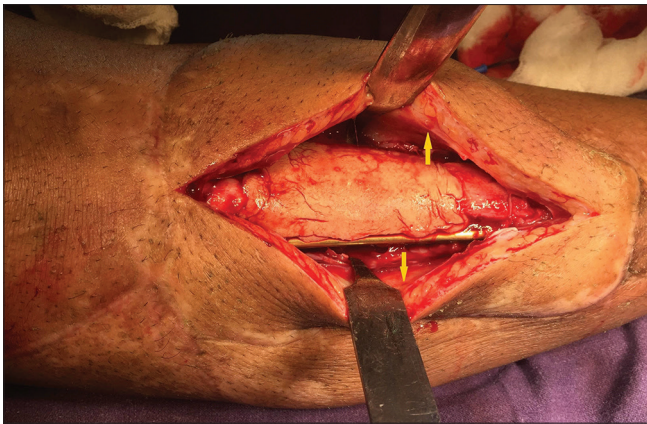
Figure 1: Intraoperative image during second stage of a tibia fracture showing biomembrane (yellow arrows). After a sharp incision, membrane is lifted off the cement spacer
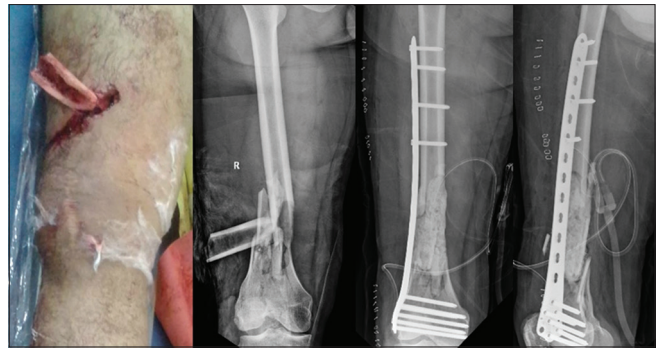

Figure 2: Case A, Compound Grade III b distal femur fracture. Preoperative clinical image shows extruded bone fragment and x-ray shows communuited fracture of shaft of distal-third femur. After thorough debridement, fixation with distal femur locking plate and antibiotic cement spacer placement was done. Primary wound closure was obtained in this case. Figure also shows x-rays after stage 1 surgery
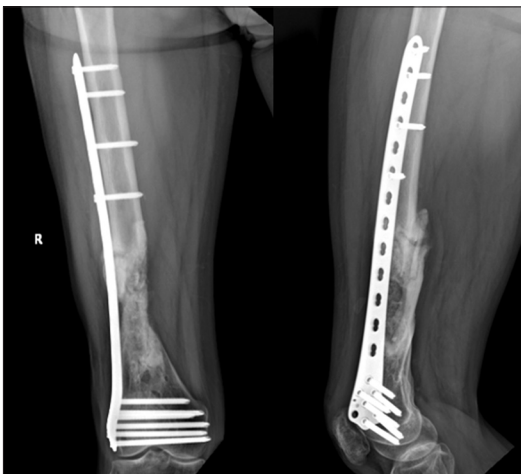
Figure 3: Case A, x-rays at 9 months followup

Figure 4: Case A, Function at 9 months

Figure 5: Case B, Compound Grade III c distal tibia fracture, preoperative clinical image showing extensive tissue damage. X-rays show communuited fracture of distal shaft of tibia

Figure 6: Case B, postoperative clinical image and x-ray. Thorough debridement of the wound, stabilization with an external fixator and cement spacer placement was done. Wound coverage was done by free flap and skin grafting

As mentioned above, one patient required an additional surgery after the second stage, due to development of deformity. This patient had a distal tibia fracture which was managed by debridement, antibiotic cement spacer, external fixator, and primary coverage by flap. In second stage, spacer was replaced by bone graft and external fixator continued. At followup of 6 months, p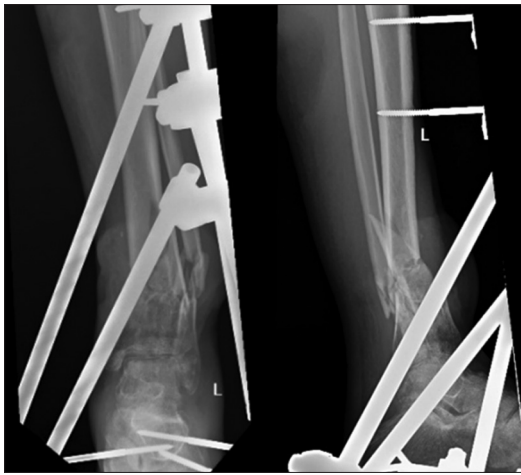atient was found to have developed varus and recurvatum malalignment. External fixator was removed and after 1 week, intramedullary nailing was done with bone in acceptable alignment. Additional bone grafting was also done. Fracture went onto heal in acceptable position by 12 months [Figures 5-8].

Discussion

Segmental bone defects, of whatever etiology, have severe negative long term impact on patient's lives.[10] Reconstruction is extremely difficult and functional outcome is usually less than satisfactory as compared to bony outcome. There is no single technique that is absolutely successful for the management of long-bone defects. The technique of induced membrane bone grafting, as put forth by A. C. Masquelet offers an alternative and viable management strategy for treatment of large bone defects.[9]

Figure 7: Case B, Fixation was not changed during stage 2 surgery. Patient developed varus and recurvatum malalignment as shown in the x-rays
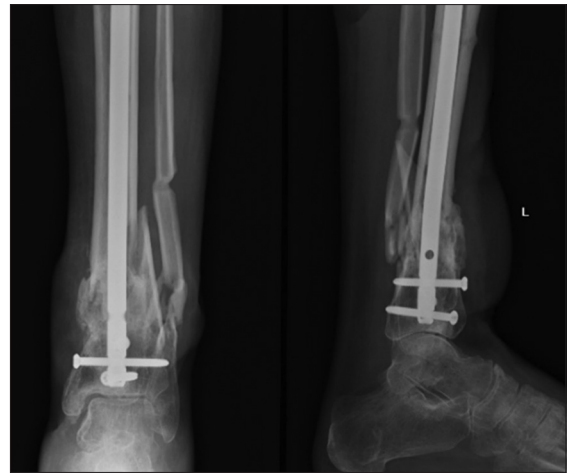

Figure 8: Case B, Fixator was removed and nailing in correct alignment along with bone grafting was done. X-rays show healed fracture at 12 months from initiation of treatment

Figure 9: Case C, x-rays show an intraarticular distal femur fracture with metaphyseal communuition

Figure 10: Case C, clinical image before and after debridement of the wound

Figure 11: Case C, postoperative x-rays after stage 1 surgery. Internal fixation with distal femur locking plate was done and antibiotic cement spacer was placed
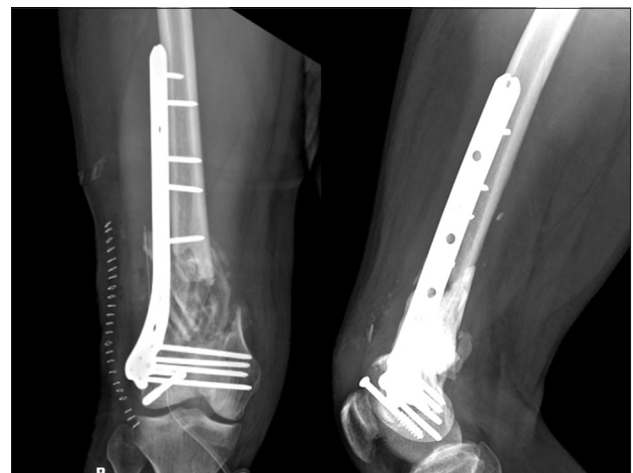

Figure 12: Case C, postoperative x-rays after stage 2 surgery showing bone graft in the bone defect

This procedure has distinct advantage in cases of open fractures as chances of infection have been reported upto 10%–50%.[1-3] Thorough debridement is of utmost importance in preventing infection, but nonetheless,

antibiotic cement acts as a useful adjunct. Although leeching of antibiotic from the cement is limited to a few days,[11] it helps in preventing the wound getting infected in crucial initial period. In our case series of 27 compound fractures, none of the cases got infected.

This cement spacer also induces the formation of biomembrane as a foreign body reaction to itself. It prevents ingrowth of fibrous tissue and maintains a well-defined
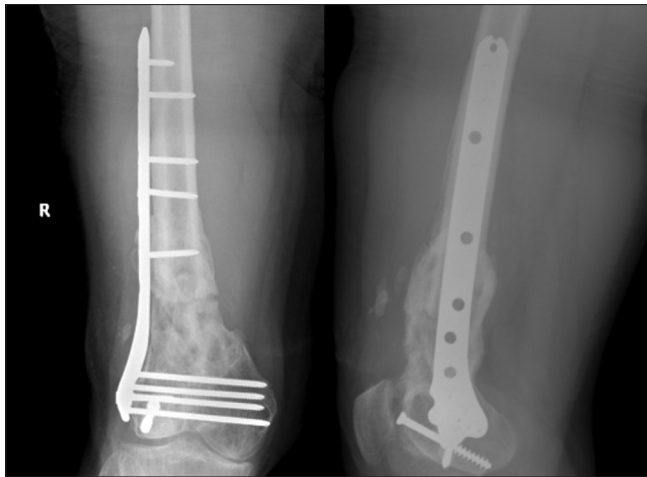
Figure 13: Case C, Followup x-rays at 9 months showing consolidation of the graft and union

Figure 14: Case D, preoperative clinical image of compound grade III fracture of shaft of tibia showing extensive soft tissue loss, and x-rays show communuition with segmental bone defect
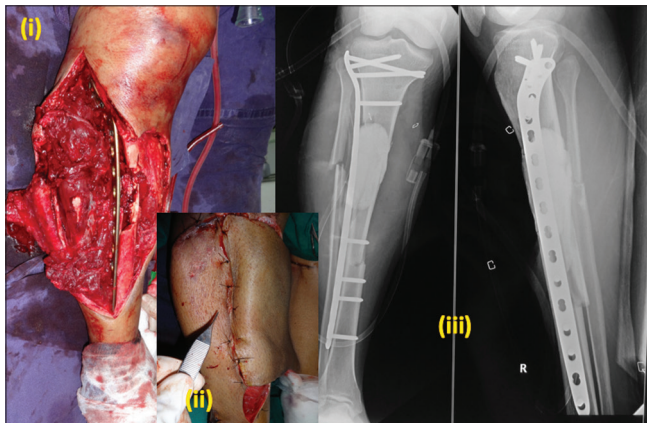

Figure 15: Case D, (i) intraoperative image after debridement and fixation with a locking plate (ii) image after coverage of wound on anterior aspect of middle of leg by a cross-leg flap (iii) X-rays after stage 1 surgery showing fixation and antibiotic cement spacer in the bone defect
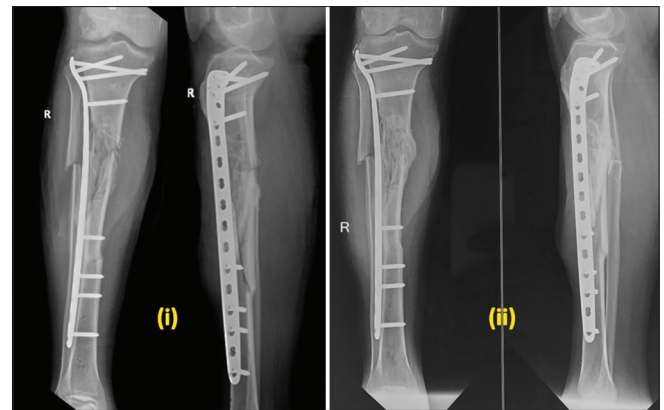

Figure 16: Case D, (i) X-rays after stage 2 surgery showing bone grafting after removal of spacer. Cortical slivers were grafted in this case along with cancellous bone graft (ii) X-rays at followup of 12 months showing union

void for later placement of graft and also gives structural support to the construct.[9,12,13] In addition, it helps the plastic surgeon by eliminating dead space and providing a base for putting up flaps for wound coverage.

Biomembrane is the workhorse in this technique, characteristics of which have been highlighted by various researchers. It prevents graft resorption, promotes vascularity, and corticalization.[9,12,14] Histologic and immunochemistry studies were performed and the following data have been established:[13-15]

- The membrane is richly vascularized in all its layers
- The inner part (face to the cement) is a synovial-like epithelium with regular arrangement of fibroblasts. Fibroblasts orientation becomes random and collagen fibers become more on going away from the spacer
- The membrane secretes growth factors: High concentration of VEGF and TGF β-1 were observed as early as the 2nd week and remain significantly high till 6 weeks. Bone morphogenetic protein 2 (BMP-2) is at its highest level at the 4th week. The membrane also secreted interleukin (IL)-6 and IL-8.

The mechanism of action of induced membrane in bone repair was studied by Aho *et al*.[16] According to their study, optimum time for grafting is at around 4–6 weeks when vascularity, expression of VEGF, IL-6, and col-1 is at peak. In our case series, the time interval between two stages ranged from 38 to 52 days and no correlation to time to union was seen. Hence, we conclude that around 6 weeks is an optimum time window for undertaking the second stage of surgery.

As shown by a case report, after healing, macroscopic examination of transverse section of the healed bone graft exhibits normal bone anatomy, and the junction between the normal bone and the graft was difficult to see by macroscopic examination of longitudinal sections.[14]

The technique as described by Masquelet relies on the placement of moreselized cancellous autograft harvested from iliac crest. If the amount was inadequate, demineralized allograft was added to the autograft in a ratio that does not exceed 1:3.[9] The guideline is empirical. However, there are no studies that compared different auto or allograft compositions. In our study, if the defect required

Figure 17: Case D, clinical image of healed flap and functional outcome at 12 months
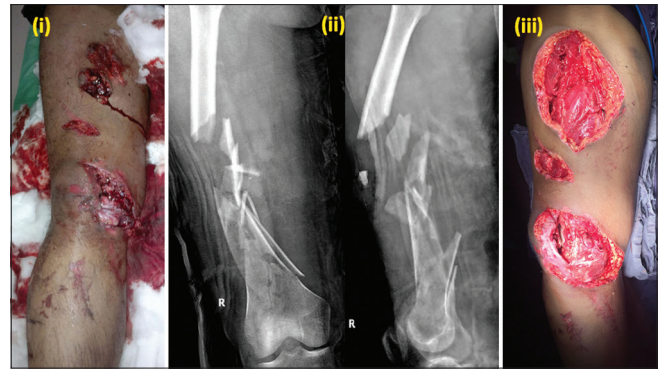

Figure 18: Case E, (i) clinical image of a compound grade 3 shaft of femur fracture at presentation (ii) preoperative x-rays showing communuition with segmental bone loss (iii) intra-operative image after debridement of wound

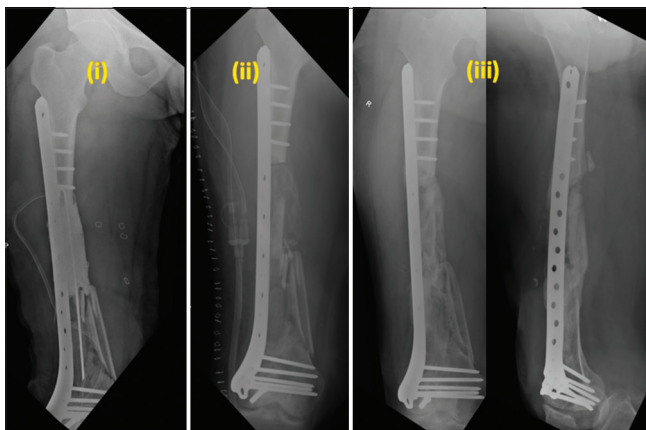Figure 20: Case E, clinical image, and functional outcome at 12 months followup

Figure 19: Case E, (i) postoperative x-ray after Stage 1 surgery, notice stabilization of cement spacer with a k-wire (ii) postoperative X-ray after stage 2 surgery (iii) X-rays at 12 months followup showing consolidation of bone graft

larger volume of graft, we have mixed allograft to autograft up to a ratio of 1:2 and there is a slight increase in time to union than expected. In our series, in two cases, we used cortical slivers of iliac crest to make up the volume of the graft and provide structural support. We have not utilized any additional growth factors or osteoinductive agents along with the cancellous bone graft. Previous studies done in this direction have been inconclusive. As studied by Masquelet and Begue, use of BMP-7 along with bone graft has not given encouraging results.[9] No other studies have established the benefit of supplementary growth factors.

Originally, the technique was described for infected gap nonunions with occasional application in cases of open fractures. In recent literature, there are a few cases reported, describing use of this technique in acute traumatic bone loss.[17,18] Encouraging results from our case series allude that it can be routinely used for such cases. Original description of the technique emphasized stabilization of the bone with an external fixator.[9] In few other reported cases, internal fixation has also been used with success.[19] In our series, for the majority of cases, we have used primary internal fixation with good results and without any residual infection after the first stage of debridement and antibiotic cement spacer application. In carefully selected cases, primary internal fixation is advisable as it allows for early joint mobility and better functional outcome. Internal fixation also provides certain amount of stability to the spacer, which the authors consider important. It prevents propagation of infection by preventing unwanted mobility of the spacer. Hence, even if an external fixator is used for skeletal stabilization, a rush nail, or k-wires should be used to keep the cement spacer fixed in place.

Management of open fractures with bone loss by limb lengthening techniques such as Ilizarov or LRS runs risk of

complications such as persistence of infection and stiffness of adjacent joints. Both these issues are addressed by Masquelet's technique.

Along with all the advantages mentioned, there are certain drawbacks as well. Long healing time and donor site morbidity at iliac crests are of concern. In addition, in some studies, development of deformity has been reported after the patient starts weight bearing.[20] This complication could have occurred due to initiating weight bearing before fracture healing and a nonrigid construct. One such complication occurred in our series as well which has been described in the results section.

One important feature of this technique is that it can be merged with other techniques of extremity reconstruction if required. In cases with unexpected or unacceptable outcomes, the technique can be improvized and direction of treatment can be modified to obtain desired results. Hence, there is still scope left for optimization of the technique in different clinical scenarios.

Conclusion

Management of open fractures with bone loss requires multiple surgeries and causes significant morbidity to the patient. This causes immense financial and mental strain on the patient and burdens the already overcrowded health facilities. With this two-stage technique, number of surgeries and duration of hospital stay can be reduced with optimum functional recovery. In addition, this procedure does not require any sophisticated or costly instruments or implants which make it feasible to be performed everywhere.

Patient declaration statement

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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