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Original Article

# Antibiotic Cement Spacer and Induced Membrane Bone Grafting in Open Distal End Femur Fractures with Bone Loss; Radiographic and Functional Outcomes: A Retrospective Study

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#### 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.

Objectives: In this study, we evaluated Masquelet's technique for the management of open distal end Femur fractures with bone loss.

**Methods:** Twenty-two patients with open distal end fractures with bone defects who presented within 3 days of trauma from January 2015 to December 2018, treated by the Masquelet's technique are included in this study. All the patients were operated on by the same surgeon. All the patients were taken up for the first stage of surgery immediately after the presentation. Details of the type of injury, location, soft-tissue condition, length of bone defect, type of fixation, the time difference between antibiotic cement spacer placement and bone grafting, and time to the union were documented.

**Results:** 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, the bone loss average time to union was 316.6±44.5 days, whereas, in Type III and II, it was 240±30 and 180, respectively. In the first stage, internal fixation with antibiotics cement spacer was done in all cases. In patients with internal fixation with 2<sup>nd</sup> stage spacer removal plus bone grafting done, time to union was 244.1±42.9 days. No patients had an infection after the first stage of surgery.

**Conclusion:** The technique of delayed bone grafting after the initial placement of a cement spacer provides a reasonable alternative for the challenging problem of significant bone loss in extremity reconstruction. This technique can be used in either an acute or delayed fashion with equally promising results. The bioactivity of the membrane created by filling large bony defects with cement leads to a favorable environment for bone formation and osseous consolidation of a large void. As this technique becomes more widely applied, the answer to which graft substances to place in the void may become clearer. Increasing clinical evidence will also help support the use of this technique in treating segmental bone loss.

Keywords: Induce membrane, Distal femur, Antibiotic cement spacer, Bone graft.

## 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.<sup>1-4</sup> 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.<sup>5-8</sup>

Traditional bone grafting techniques are limited by uncontrollable graft resorption. Vascularized bone grafting is technically demanding.<sup>5,6</sup> Ilizarov technique has been associated with adjacent joint stiffness, neurological injuries, premature, or delayed consolidation.<sup>7,8</sup> 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.<sup>9</sup> 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 <sup>9</sup> with limited application in fresh trauma.

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#### Objectives

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 retrospective study we evaluated the effectiveness of the Masquelet's technique and functional outcomes.

## **Materials and Methods**

Twenty two patients with open fractures with bone defect who presented within 3 days of trauma, from January 2015 to December 2018, treated by the Masquelet's technique are included in this study. All the patients were operated by same surgeon. 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.

Table-1.	Fracture pattern,	size of defect, ty	pe of fixation,	, time interval	l between two	stages, time to	union, an	d range of	f motion o	of adjacent
	-	,	1			ç		0		

					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
			Type-2	Α	_	60			80
		3		EA	_	40	180-240		70
			Type-3	A	_	62			95
	Meta			EA	_	48	300		85
Distal		4	Туре-4	EA		48	320		80
end		4	Туре-3	А	_	40	240	0-	69
femur			_	A	Plate	44	280	130(knee)	90
		5	Type-4	А	_	55	300		85
			Type-3	А	_	48	240		92
	Meta-	6	Type-4	A	_	38	320		80
	Dia			EA	_	50	280		92
		8	Type-4	A	_	46			85
				EA	_	55	360		75
		10	Type-4	A		55	320		80

Type of bone loss	Number of cases
Туре І	0
Type II	4
Type III	9
Type IV	9

# 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 polymethyl-meth-acrylate preloaded with 500 mg of gentamicin. 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 if required.

## Second stage

Second stage was planned after 6-8 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 with medial plate augmentation. 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. Then medial plate augmentation done for additional bone support. Watertight fascial closure was done, followed by skin closure using nylon.

#### Postoperative protocol

Patients were allowed immediate passive and active motion and non-weight bearing mobilization. Toe touch weight bearing was started after 12 weeks of second stage. Fullweight 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.

Follow-up 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

In this study includes a total of 22 patients, in the age group of 16–65 years. 20 were male and two 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 19 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.

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 5 cm. All the wounds were covered during the first-stage surgery.

For 21 cases, primary wound closure could be obtained, Skin grafting was done for 1 cases.



Figure-1. Intraoperative image during second stage of a distal end Femur fracture showing biomembrane (BM-White arrows). After a sharp incision, membrane is lifted off the cement spacer

Average follow up was 30 months (range 21–60 months). Mean time interval between cement spacer placement and bone grafting was 47.6 days (range 38-62 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 274 days since first stage of surgery (range 180–360 days) (Table-1). 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 316.6±44.5 days, where as in Type III and III, it was 240±30 and 180, respectively.

In the first stage, internal fixation with antibiotics cement spacer was done in all cases. In patients with internal fixation, time to union was 244.1±42.9 days. No patients had infection after the first stage of surgery.

Hence, all the patients were considered for second stage without the need for any additional surgery after the first stage. 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 softtissue injury or intra-articular nature of fracture. At follow up 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 two patients, all <2 cm, for which shoe raise, and was prescribed case examples are shown in Figure-2 and Figure-3 and Figure-4 and Figure-5 and Figure-6 and Figure-7 and Figure-8 and Figure-9, Figure-10.

## Discussion

Segmental bone defects, of whatever etiology, have severe negative long term impact on patient's lives.<sup>10</sup> 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.<sup>9</sup>

This procedure has distinct advantage in cases of open fractures as chances of infection have been reported upto 10%-50%.<sup>1-3</sup>

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,<sup>11</sup> it helps in preventing the wound getting infected in crucial initial period. In our study of 22 open distal femur 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 void for later placement of graft and also gives structural support to the construct.<sup>9,12,13</sup> 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.<sup>9,12,14</sup> Histologic and immunochemistry studies were performed and the following data have been established:<sup>13-15</sup>



Figure-2. Case-1, Compound Grade IIIB 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-1, Follow-up x-rays at 9 months showing consolidation of the graft and union.

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Figure-4. Case-1, Image showing Extension and Flexion at 9 months follow-up.



**Figure-5. Case-2,** Compound Grade IIIB distal femur fracture. Preoperative clinical image shows Multiple Wound with loose bone fragment removed while debridement 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. Initially Partial wound closure was obtained in this case and SSG done after 48hrs. Figure also shows x-rays after stage 1 surgery.



Figure-6. Case-2, Follow-up x-rays at 11 months showing consolidation of the graft and union.

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Figure-7. Case-2, Image showing Extension and Flexion at 11 months follow-up with SSG scar present.



**Figure-8. Case-3,** Compound Grade IIIB Intra-articular distal end femur fracture. Preoperative clinical image shows wound with bone fragment exposed. X-ray and CT scan shows communuited intra-articular fracture of distal end 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-9. Case-3, Follow-up x-rays at 9 months showing consolidation of the graft and union.



Figure-10. Case-3, Image showing Extension and Flexion at 9 months follow-up.

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  $\beta$ -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.<sup>16</sup> 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 study, the time interval between two stages ranged from 38 to 62 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.<sup>14</sup>

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.<sup>9</sup> The guideline is empirical. However, there are no studies that compared different auto or allograft compositions. In our study, if the defect required 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.<sup>9</sup> No other studies have established the benefit of supplementary growth factors.

Originally, the technique was described for infected gap nonunion 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.<sup>17,18</sup> 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.<sup>19</sup> In our study, all 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.<sup>20</sup> This complication could have occurred due to initiating weight bearing before fracture healing and a non-rigid 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.

#### Conclusions

The technique of delayed bone grafting after initial placement of a cement spacer provides a reasonable alternative for the challenging problem of significant bone loss in extremity reconstruction. This technique can be used in either an acute or delayed fashion with equally promising results. The bioactivity of the membrane created by filling large bony defects with cement leads to a favorable environment for bone formation and osseous consolidation of a large void. As this technique becomes more widely applied, the answer to which graft substances to place in the void may become clearer. Increasing clinical evidence will also help support the use of this technique in treating segmental bone loss.

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## **Authors' Contribution**

All authors pass the four criteria for authorship contribution based on the International Committee of Medical Journal Editors (ICMJE) recommendations.

#### **Conflict of Interests**

The authors declare that they have no conflict of interest.

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