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ORIGINAL STUDY

Staged bone grafting for the management of segmental long bone defects caused by trauma or infection using induced-membrane technique

Talaat Taher EL-HADIDI, Hesham Mesbah SOLIMAN, Hazem Ahmed FAROUK, Mustafa Abd El-Mogeeb RADWAN

From the Kasr Al Ainy Faculty of Medicine,

Treatment of segmental bone defects resulting from trauma or infection is extremely difficult. Bone segment transport with distraction osteogenesis and vascularized fibula transfer are the commonest used methods of treatment. Bone transport has problems with docking site. Vascularized fibula is technically demanding and hypertrophy occurs late. Induced membrane (Masquelet) technique is a relatively recent and simple treatment option consisting of two stages. A biological membrane is formed around cement spacer which is inserted in bone defect. In the second stage, the spacer is carefully removed and the membrane filled with autologous cancellous bone graft.

From May 2013 to October 2015, we treated 20 patients with post-traumatic and post-infectious bone defect using Masquelet technique. There were 17 males and 3 females, with an average age of 38 years (range 12-64). The etiology of defect was open fractures in 6 cases (30%), infected non union in 11 cases (55%) and aseptic atrophic nonunion in 3 cases (15%). The mean size of bone defect after debridement was 7.2 cm. Soft tissue defect was present in 3 cases which was reconstructed. In the first stage involves thorough debridement, stabilization of the bone (either external or internal) and insertion of antibiotic cement spacer. 2nd stage was done after 4 to 8 weeks with insertion of morselized cancellous bone graft harvested from iliac bone, then tight closure done. 17 cases (85%) united, 2 cases (10%) of graft resorption and 1 case (5%) of infected graft. The time to union ranged from 4 to 11 months after 2nd stage with mean 7.4 months.

In conclusion, induced membrane (Masquelet) technique is a safe, simple and reliable method for treating segmental bone defect. The major complications of this technique include infection and graft resorption.

Keywords : Segmental bone defects ; induced membrane ; Masquelet, cement spacer ; morselized cancellous bone graft ; graft resorptio.

INTRODUCTION

Large segmental bone defects are very difficult to treat because of the deranged mechanics and biology. In the early years of the 20th century, amputation was the management; however, limb salvage has become increasingly common. However, most techniques for reconstruction of significant bone loss are associated with lengthy healing or rehabilitation times and unpredictable union rates *(3)*.

Current management options include intercalary bone transport using distraction osteogenesis, vascularized bone transfer, massive cancellous

■ Talaat Taher El-Hadidi MD, Professor of orthopedic surgery.
■ Hesham Mesbah Soliman, MD, Professor of orthopedic surgery.
■ Hazem Ahmed Farouk, MD, Professor of orthopedic surgery.
■ Mustafa Abd El-Mogeeb Radwan, MD, Orthopedic consultant.
Kasr Al Ainy Faculty of Medicine.
E-mail : drhalawia@yahoo.com

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Table I — Etiology of the bone defect

Etiology	Number	Percentage
Trauma:	6	30%
1-Motor car accident	3	15%
2-Motorcycle accident	2	10%
3-Gunshot injury	1	5%
Aseptic nonunion	3	15%
Infected nonunion	11	55%
Total	**20**	**100%**

autograft transfer, and synthetic calcium-based fillers. These options may be supplemented with the addition of demineralized bone matrix, allograft, or bone morphogenetic protein (BMP) *(2)*.

Masquelet is the pioneer of developing use of induced membrane technique in 1986. He successfully managed defects ≤ 25 cm with associated severe soft-tissue injury by use of this technique. A bioactive membrane is created via placement of a temporary polymethyl methacrylate (PMMA) spacer, and the membrane is later filled with cancellous autograft. Reported advantages of this technique include protection against autograft resorption, maintenance of graft position and prevention of soft tissue interposition *(13)*.

Several animal studies have been done to detect the prosperities of this membrane. It was confirmed that it secretes substances that increase bone healing (e.g. bone morphogenetic protein). It is a fibrous membrane with high vascularity and looks like the periosteum *(18)*.

In the traditional technique described by Masquelet, external fixation was used with insertion of morselized iliac cancellous graft. Recently many authors use internal fixation and the new technique of harvesting medullary graft (Reamer Irrigator Aspirator or RIA) has overcome the limited amount of graft *(7)*.

The aim of this study is to assess the results of the induced membrane technique in management of segmental bone defects caused by trauma or infection.

PATIENTS AND METHOD

After approval of the ethical committee, we conducted prospective dual center study during the period, from May 2013 to October 2015 at Cairo University orthopedic department and Mansoura Health Insurance hospital orthopedic department. 20 patients with segmental bone loss were managed using the induced membrane (Masquelet) technique. There were 17 males (85%) and 3 females (15%) with male to female ratio 5.6. The age of patients ranged from 12 to 64 years old (mean 38 ± 18.32). The right side was affected in 7 patients (35%) and the left side in 13 patients (65%). The tibia was affected in 10 patients, the femur in 7 patients, the humerus in 2 patients and the ulna in one patient.

Among the tibial cases, defect was located in the upper third in 3 cases, in the middle third in 3 cases and in the distal third in 4 cases. Among the femoral cases the defect was located in the upper third in 1 case, in the middle third in 3 cases and in the distal third in 3 cases. In humeral cases the defect was located in the upper third in 1 case and in the middle third in the other case. The ulnar defect was at the lower third.

Etiology of bone loss was trauma in 6 cases, infected nonunion in 11 cases and aseptic nonunion

Table II — Incidence of infection

Infection	Number	Percentage
Active infection	3	15%
Quiescent infection	8	40%
No infection	9	45%
Total	20	100%

Table III. — Number of previous operations

Operation	Number
Debridement	4
External fixation	3
Removal of metal	4
Bone graft	4
Plastic surgery	1
Total	**16**

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Table IV. — Bone results

Bone results	No	%
excellent	15	75%
good	2	10%
poor	3	15%

in 3 cases. Mean diaphyseal bone loss was 7.2 cm (range, 5—15 cm), resulting directly from injury and debridement in six cases (mean, 8 cm; range, 6—12 cm), resection of necrotic bone for treatment of aseptic nonunion in two cases (5 cm), and resection of osteitic bone for treatment of septic nonunion and infected fractures in 11 cases (mean, 8 cm; range, 5—9 cm).

Mode of trauma was motor car accident in 3 cases, motorcycle accident in 2 cases and gunshot injury in 1 case. 3 cases of fracture were Gustilo and Anderson type III A and 3 cases type III B. Out of the 20 cases, 11 were infected and 9 were not infected. Two of the infected cases had active discharge at the time of surgery.

The time before first stage ranged from 1 day to 8 years with a mean of 11 months. Induced membrane technique was done as a primary management in only 6 cases (6 cases with open fractures). The majority of cases *(14)* underwent several previous operations before induced membrane technique including debridement and removal of infected implant, external fixation and bone graft (Table III). Soft tissue was deficient in 3 patients and required plastic surgery during first stage.

Fig. 1 — Excision of necrotic bone

Fig. 2 — Intraoperative measurement of the size of defect

In all infected 11 cases (55%), staphylococcus aureus was the causative organism in culture and sensitivity. All patients in this study were subjected to detailed history taking, pre-operative clinical examination and radiological examination.

Operative details

First stage:

Under general or spinal anaesthesia, patient was put supine on the ordinary table. Tourniquet was used in non-infected tibial cases and in case with ulnar defect. Cefotaxime was given 1gm IV within 1 hour preoperative. In infected cases the antibiotic was stopped 1 week preoperative to take intraoperative samples for culture and sensitivity. In most of cases we were obligated to follow the previous incisions and approaches in the limbs that have been operated on many times. We performed removal of infected metal (in cases with infected nonunion), thorough debridement of necrotic soft tissue and bone fragments (Figure 1). Debridement of devascularized, necrotic or infected bone was done using a rongeur, osteotome and hammer and drilling until reaching healthy bleeding bone (Paprika sign). Periosteum was stripped only from cortical bone intended for debridement, otherwise periosteum was preserved to protect the vascularity of bone. In cases with severe soft tissue loss, a plastic surgery team was present to cover the wound after fixation and insertion of bone cement spacer.

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Fig. 3 — Insertion of cement spacer in the defect

Samples from infected bone and soft tissue were taken for culture and sensitivity. Double set-up (change instruments, re-prep, re-drape, new gowns/gloves) was done in cases with infected nonunion and open fractures.

After diaphyseal washing, bone was stabilized. Plate and screw fixation (Orthomed-E, Egypt) was done in 7 cases, Ilizarov ring fixator (Orthomed-E, Egypt) in 12 cases and interlocking medullary nail in one case (Orthomed-E, Egypt). Limb length, alignment and rotation was regained based on preoperative planning and compared to the other limb taking care not to cause lengthening or excessively stretch the soft tissues. The length of the defect was then measured by metallic ruler (Figure 2).

Once stabilization was obtained, bone defect was filled with antibiotic impregnated cement. We added 2 gm vancomycine to each 40 gm cement (Cemex genta, TECRES, Italy) then mixed by hand. Cement was inserted in bone defect before hardening (Figure 3). Wash with saline was done over the cement to decrease the risk of heat injury to bone and soft tissue. We added vancomycine because it is eluted from cement spacer for a long duration, thermostable and highly effective antibiotic with wide spectrum of action. Cement was fashioned manually according to the shape and size of bone ends at the gap. In the case fixed with interlocking nail, cement was prefabricated on a nail with larger diameter on the instruments table and cut into 2 pieces before hardening to facilitate later extraction. Overfilling with cement was avoided to make extraction of the spacer in the 2nd stage easy because bone cement expands. In case of tourniquet, it was released and haemostasis done.

Table V — Functional results

Functional result	No	%
excellent	13	65%
good	2	10%
fair	2	10%
poor	3	15%

After that comes the step of soft tissue coverage. Closure of overlying muscles, subcutaneous tissue and skin was done. Plastic surgery performed by another surgical team of plastic surgeons in the same session, consisting in a rotational fasciocutaneous flap in 1 case and local muscle flap in 2 cases.

Postoperative antibiotic prophylaxis in aseptic cases 1gm IV Cefotaxime was administered twice daily for 24 hours. In open fractures associating 1.5gm Ampicillin/sulbctam IV every 8 hours, gentamicin 80 mg IV every 8 hours and flagyl 500 mg every 8 hours orally for 4 days followed by of amoxicillin / clavulanic acid per oral for approximately 3 weeks in cases of soft tissue flap until the flap is fully healed. For the 11 cases operated for septic nonunion with resection of osteitic bone, intravenous vancomycin treatment was initiated 1 week and replaced by oral antibiotic therapy adapted to the bacteria found (Ciprofloxacin and Amoxicillin/Clavulinic acid) for at least 6 weeks. Clearance of infection was confirmed by clinical examination of wound and trending level of acute inflammatory markers (ESR and CRP).

Second stage:

The second stage of bone reconstruction occurred a mean 6 weeks (range, 1—2 months) after the first stage. We were guided by the level of ESR and CRP, which should be normalized before 2nd stage. Also complete healing of soft tissues was an important determinant factor . Bone graft was harvested from the two anterosuperior iliac crests (18 cases), one anterosuperior iliac crest (1 case) and the two

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Fig. 4 — A) Preoperative clinical photograph of the right leg showing adherent scar and draining sinus, B) Preoperative lateral x. ray showing nonunion over plate fixation.

posterosuperior crests (1 case) because of previous graft taken from anterosuperior iliac crests in previous graft surgeries. Incision over the previous surgical scar was done, incising longitudinally of the self-induced membrane to extract the pieces of cement by fragmentation or en bloc.

Cancellous bone grafts were morselized into very small pieces (3-4 mm) using bone cutting forceps, then packed into the cavity bordered by the membrane. In the original technique size was 2 mm, however we did not have bone mill and 3 mm was the smallest size which we could gain. Morselizing the graft increases the surface area which in turn increases healing. In 1 case, B tricalcium phosphate bone substitute was added to expand the graft material because of low bone stock in iliac bone. Graft was packed against the fibula in tibial cases induce synostosis. Overfilling of the membrane was avoided to make its closure easy and not to affect graft vascularization. Then water tight closure of the induced membrane was done.

Analgesic anti-inflammatory drugs were given in the early postoperative period to relieve pain. In non infected cases 1st generation cephalosprin was given orally for 3 days postoperative. In infected cases antibiotic of the last culture and sensitivity was given for two weeks If ESR and CRP were normal. In cases with elevated ESR and CRP, antibiotic was given for 1 week after normalization of their level to eradicate any residual infection. The hospital stay after the first stage ranged from

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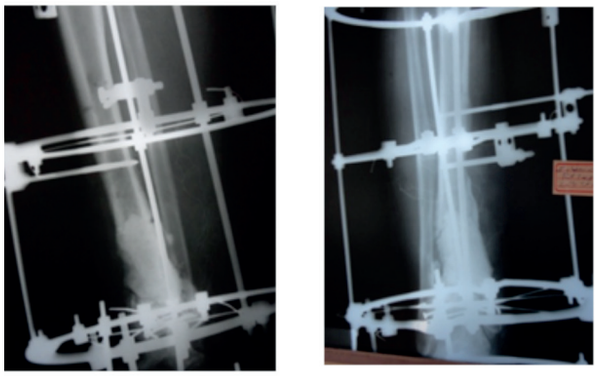
A



B

Fig. 5 — A) Intraoperative photograph showing the bone defect, B) Postoperative x rays after 1st stage.

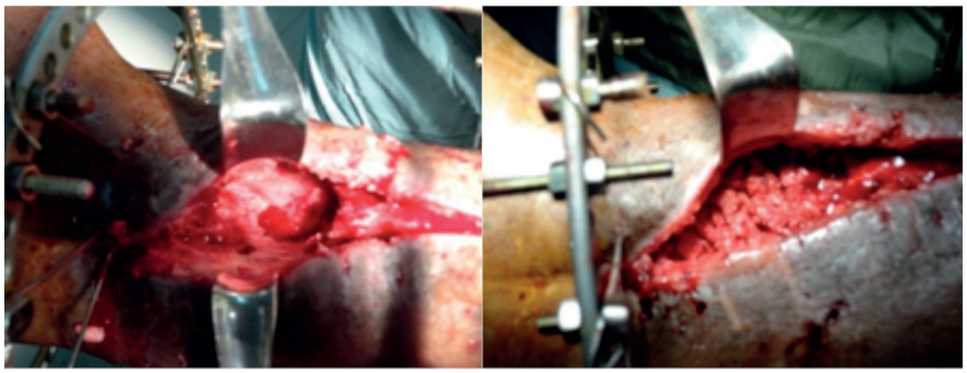
1 day to 2 weeks with a mean of 5 days. In the 2nd stage the hospital stay ranged from 1 day to 1 week with an average of 3 days. Low molecular weight heparin *(40)* units was given for cases of lower limb 12 hours preoperative then once daily postoperative until mobilization starts.

All patients were encouraged for immediate postoperative passive and active assisted range of motion. In cases of lower limb fixed with Ilizarov fixator, partial weight bearing was allowed because the apparatus is load sharing. Cases fixed with plate and screws started with toe touch then progressive protected weight bearing according to the progression of union.

The period of follow up ranged from 5 months to 26 months with a mean of 12 months. It was calculated after the second stage. During this period the patient was seen at 2 and 4 weeks postoperative then monthly until union then every 2 months. Every visit patient was assessed for union, ROM and any complication that may appear.

RESULTS

The end results were assessed according to the method adopted by Paley et al. in 1989 *(10)*. They divided the final results into bone results and functional results. We modified the functional results of this score for application in upper limb cases because DASH score is difficult to apply



A B

Fig. 6 — A) Intraoperative photograph during 2nd stage showing the defect surrounded with the membrane after cement removal, B) The defect filled with morcellized cancellous graft.

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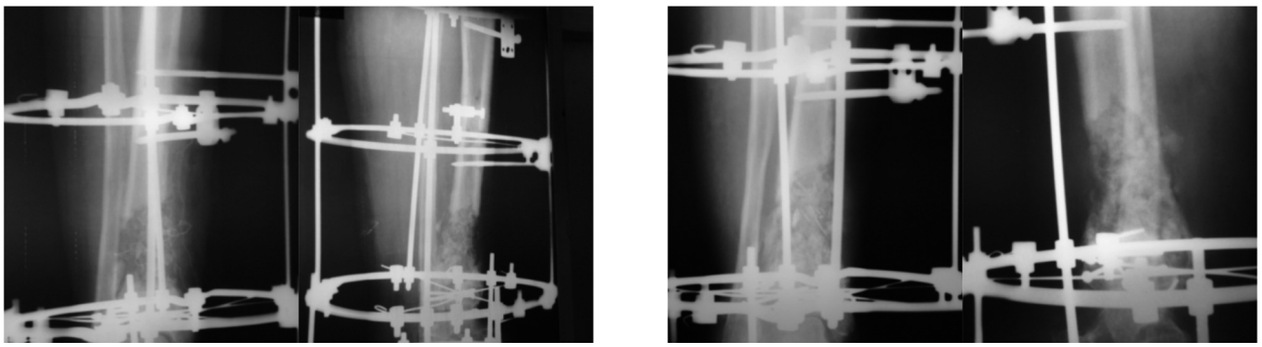

Fig. 7 — A) Immediate postoperative x. rays after 2nd stage, B) A.P. and lateral x rays 3 months postoperative showing good healing

for our patients because of cultural differences. Bone results depended on four criteria; bone union, infection, deformity and leg length discrepancy. An excellent bone results is one with bone union, no infection, deformity of less than 7 degrees and leg length discrepancy less than 2.5 cm. A good bone result is union, and any two of the others. A fair bone result is union, and any one of the others. A poor bone result is nonunion or refracture.

The functional results include five criteria (4 in upper limb), significant limp (not applicable in upper limb), joint stiffness (knee and/or ankle in lower limb) (shoulder and/or eblow and/or wrist in the upper limb), soft tissue dystrophy (skin hypersensitivity or insensitivity of sole), pain and inactivity (unemployment because of the limb injury or inability to return to daily activities because of the injured limb). An excellent functional result in the lower limb is an active individual with none of the following criteria (limp, stiffness, soft tissue dystrophy and significant pain). A good functional result is an active individual with one or two criteria. A fair result in the lower limb is an active individual with three or four criteria. An excellent functional result in the upper limb is an active individual with none of the following criteria (stiffness, soft tissue dystrophy and significant pain). A good functional result in the upper limb is an active individual with one criteria. A fair result in the upper limb is an active individual with two or three criteria A poor result in both limbs is an inactive individual regardless of the other criteria. According to bone results we had 15 patients with excellent results, 2

Fig. 8 — A. P. and lateral x rays 16 months postoperative showing corticalization of the graft and tibiofibular synostosis.

patients with good results and 3 patients with poor results. According to functional results we had 13 patients with excellent results, 2 patients with good results, 2 patients with fair results and 3 cases with poor results.

The mean follow up was 15 months (range, 5-26 months). Union occurred in all cases except 3, union time ranges from 4 months to 11 months

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Fig. 9. — Clinical photographs after removal of the frame showing excellent function

with mean time 7.4 months after the second stage. Severe infection occurred in one patient in The second week following bone grafting. After new debridement, including removal of the nail and the grafts, Ilizarov bone transport technique was performed. In another patient, she had fallen down on her arm and the plate humerus was bent. It was noted that the healing process is not progressing and graft resorption occurred at 5 months postoperative. She had refused to do any other surgery. In the third patient graft resorption occurred 6 months postoperative. The bone was fixed with Ilizarov fixator, so corticotomy and bone segment transport was done with the same frame in place.

After analysis of the previous results, it was found that there was no significant difference in

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accordance to the age, sex, etiology of the defect, soft tissue defect, size of the defect, number of previous surgeries and method of fixation where P value > 0.05.

There is significant correlation between functional and bony results where P value < 0.001

COMPLICATIONS

Donor site morbidity, injury of the lateral cutaneous nerve of the thigh occurred in one patient but symptoms improved after 2 months. In another patient infection occurred at one of the iliac bone and debridement was done. Non union occurred in three cases (15%) one case complete graft resorption occurred 2 months after falling down and bending of the plate, one case because of severe postoperative infection and the last case was heavy smoker. Delayed healing of the graft in one case, which was treated by another grafting 8 months after 2nd stage and encouraging the patient to bear weight progressively. After that the quality of the healing was improved. All cases fixed with Ilizarovring fixator complained of grade 1 pin tract infection, and was successfully managed with local care and antibiotics. No case of malunion, but in one case the deformity occurred after falling down and bending of the plate. We had two cases (10%) with > 2.5 cm shortening which was mainly due to the long interval between fracture and treatment so soft tissue contracture occurred and maintaining normal length was difficult. Two cases developed knee stiffness one of them because of ipsilateral fracture tibia and femur and the other one was not compliant to rehabilitation. Two cases developed equinus contracture (10%) at the end of follow up. Despite this equinus the functional results were good. One case recorded (5%) with severe postoperative infection 2 weeks after the 2nd stage, debridement was done, removal of interlocking nail, fixation by Ilizarov and corticotomy for bone transport.

DISCUSSION

The treatment of segmental bone loss caused by trauma or infection challenging particularly in the distal third of the leg because of the scarce soft tissue coverage and poor vascularization. Vascularized bone transfer and distraction osteogenesis are the most commonly used techniques. The main complications for vascularized bone transfer are that it is technically demanding, necrosis due to anastomosis failure, donor site morbidity and stress fracture. This procedure is not indicated in patients with arteriosclerosis, single-vessel leg and heavy smokers. The main complications for distraction osteogenesis are long periods of treatment, pain

Table VI. — Correlation between bone results and functional results

Functional results	Bone result						÷2	P
	poor		Good		excellent			
	No	%	No	%	No	%		
Fair	0	0%	1	5%	1	5%	28.667	(a) <0.001* (S)
Poor	3	15%	0	0%	0	0%		
Good	0	0%	1	5%	1	5%		
Excellent	0	0%	0	0%	13	65%		

(a): Chi - square (x2) likelihood ratio. (S) : Statistically highly significant difference

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Table VII. — :Comparison between the results of this study and other studies

Author/ year	Number of patients	cause of bone defect	Location (size) of bone defect	First stage	Second stage	Outcome	Complications
Apard [1]2010 Case series	12	Trauma, aseptic necrosis and infection	Tibia (8.7 cm; range: 6-15 cm)	static IM nailing and cement around the nail + free muscle flap or a pediculated fasciocutaneous flap	at 4 months (range: 2-6 months) with cancellous bone grafting (+ tricalcium phosphate substitute in 4 cases)	Complete weight-bearing at 4 months (range: 3-7 months)	5 deep infections (1 fixation failure, 2 exchange nailing, 2 prolonged antibiotic therapy
Flamans[6] 2010 Case series	11	Trauma (but intact pulp) and infection	Hand and wrist	stable fixation, flap if necessary, and PMMA spacer	at 2 months with cancellous bone	9 cases with union within 4 months	2 non-unions
Stafford[17]2010 Case series	25	Trauma and infection	Tibia and femur (range: 1-25 cm)	debridement, stable fixation (nail and/or plate, or extrernal fixation) and antibiotic-loaded PMMA spacer	at 6-8 weeks with RIA bone graft	(1 patient lost to FU)	1 non-union 1 deep infection requiring BKA
Woon[19] 2010 Case series	2	Infected non-unions	Tibia (4 and 6 cm)	Case 1 : IM nailing and antibiotic cement spacer Case 2: external fixation and cement	Case 1:at 2 months: with autologous iliac bone graft Case 2: at 11 weeks: ankle fusion with corticocancellous graft	Union at 9 months (case 1) and at 18 months (case 2)	Ankle stiffness and a claw-toe deformity (case 1) Case 2 required a second bone grafting procedure at 7 months
Masquelet[9]2008 Case series	11	Infected non-unions	Tibia, femur, humerus (10.5 cm; range 5-18 cm)	external fixation and cement spacer and muscle flaps	at 6-8 weeks with cancellous autograft augmented with BMP-7	10 cases of union at 11.5 months (6-18 months)	1 BKA for dystrophy of the foot and non-union
Roche[14] 2005 Case series	11	Humerus, femur, tibia (5.5 cm; range: 1.5-10 cm)	Infected non-unions	debridement, fixation and antibiotic-loaded cement	at two months and autologous bone graft	Union in all cases within 4.5 months (3-6 months)	No
Schottle[16]/ 2005 Case series	6	Tibia (6.5 cm; range: 5-8 cm)	Infected non-unions	debridement, external fixation antibiotic-loaded cement, and free microsurgical tissue transfer	at 105 days (91-119) with autologous bone graft (± allograft)	Union in 5 patients at 7 months (6-8 months)	2 superficial pin site infections 3 flap haematomas 1 refracture after fixator removal at 10 months
Pelissier[12]/ 2003 Case series	3	Tibia, calcaneus (7.6 cm)	Trauma and Osteomyelitis	cement spacer and external fixation	with cancellous bone graft	Union at 8 months (range, 5-10 months)	1 BKA for dystrophy of the foot and fixed ankle flexion

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Masquelet[8] 2000 Case series	35	Upper and lower limbs (range: 5-25 cm)	Trauma, infection	debridment, external fixation, and cement spacer	at 6-8 weeks with autologous cancellous bone graft ± allograft when required (to a maximum ratio of 1/3)	Average time to union 8.5 months (6-17 months) No recurrence of infection	4 stress fractures (2 early, 2 late)
Scholzl[15]/ 2015 Case series	8	Tibia, femur, radius, fibula and metatarsals. (8.08cm; range: 5.5 - 14.5cm)	Infected non-unions	debridment, external fixation, and cement spacer	at 8-14 weeks with autologous cancellous bone graft (in three cases, BMP-7 was added to the bone grafts).	union was found after 18.92 weeks (range 12 - 24 weeks).	1 case with knee stiffness and shortening 4 cm1 case with shortenng of radius and limited ROM of wrist
This study	20	Tibia, femur, humerus, radius and ulna. (7,4cm; range: 5 - 15cm)	Trauma, Infected nonunion and aseptic nonunion.	debridement, stable fixation (nail and/or plate, or external fixation) and antibiotic-loaded PMMA spacer	at 4-8 weeks with autologous cancellous iliac graft (B tricalcium phosphate was added in 1 case)	Union in 17 cases was found after 7,4 months (range 4-11 months).	2 cases with with graft resorption 1 case with uncontrolled infection after 2nd stage

accompanying the transport, pin tract infection, reflex sympathetic dystrophy and non-union at the docking site *(5)*.

The ''induced membrane'' technique was first described by Masquelet et al.. and consists of two surgical steps. The first step comprises soft tissue and bone debridement with implantation of a cement spacer that induces a pseudo synovial membrane, stabilization of the bony segment with an external fixation, and soft tissue coverage or free tissue transfer, if needed. The second step is performed approximately 2 months later and comprises removal of the cement spacer and filling of the cavity with morselized cancellous bone autograft harvested from the iliac crest *(4)*.

Karger et al. *(7)* reported on the largest case series that used this technique. This retrospective study included 84 posttraumatic diaphyseal long bone reconstructions (61 tibial, 13 femoral, 6 humeral and 4 in forearm) of which 50% were infected. Bone defect size ranged between <20 mm to 230 mm with a mean of 70 mm. The interval between initial trauma and treatment of bone defect was a mean 8 months. 46 cases required soft tissue coverage. Bone stabilization was done by external fixation in 46 cases, locked intramedullary nail in 19 cases and plates or pins in other cases. At a mean of 14.4 months after the first surgery, the authors observed union in 90% of cases. Eight patients (10%) were evaluated as failures and six patients required amputation. The authors concluded that reconstruction of large bone defects can be achieved with this procedure and its indications include non-traumatic bone defects .

The number of cases in this study is 20 patients, which is relatively large compared to other case series. Masquelet *(8)* reported a case series of 35 patients in 2000, Stafford *(17)* reported 25 cases in 2010. There are 4 case series with 11 to 12 cases. All other series have less than 5 cases and 6 case report studies.

Etiology of defect in this study was open fracture, infected nonunion and aseptic nonunion, which is consistent with the study done by Apard et al. *(1)* The etiology in the case series done by Flamans et al. *(6)*, Stafford et al. *(17)*, plessier et al. *(12)* and Masquelet et al. *(8)* was trauma and infection.

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Infected non-unions was the etiology in case series of Woon et al. *(19)*, Masquelet et al. *(9)* (2008), Roche et al. *(14)*, Schottle et al. *(16)* and Scholz et al. *(15)*.

The size of bone defect in this study ranged from 5cm to 15 cm (mean 7 cm) which is consistent with the size in the study of Apard et al. *(1)* (8.7 cm; range: 6-15 cm) and Scholz et al. *(15)* 8.08cm (range 5.5 - 14.5cm). The size of defect in the study done by Masquelet *(8)* in 2000 ranged from 5 to 25 cm and the study done by Masquelet *(9)* in 2008 was (10.5 cm;range 5-18 cm). In the study done by Roche et al. *(14)* the mean defect was (5.5 cm;range: 1.5-10 cm. In the study done by Schottle et al. *(16)* the mean size of defect was 6.5 cm (range: 5-8 cm).

In this study we used all methods of fixation (external fixator, plate and screws and static locked medullary nail), which is consistent with the study done by Stafford *(17)*. Masquelet *(8,9)* in his 2 case series, Plissier et al. *(12)*, Schottle et al. *(16)* and Scholz et al. *(15)* used external fixator. Aparad et al. *(1)* used intramedullary nailing.

The interval between 2 stages in this study ranged from 4 to 8 weeks (mean: 5 weeks). In the 2 studies done by Masquelet *(8,9)* and the study done by Stafford *(17)*, the interval was 6-8 weeks which is near to that of our study. In the study done by Scholz et al. *(15)* the time gap was 10 weeks (range: 8-14 week). In the study done by Apard et al. (1) and the study done by Schottle et al. *(16)* the interval was 4 months.

The graft used in this study was autologous cancellous iliac graft which is consistent with the studies done by Apard et al. *(1)*, Flamans et al. *(6)*, Masquelet *(9)* in 2008, Plissieret al. *(12)* and Roche et al. *(14)* and Scholz et al. *(15)*. In the study by Schottle et al. *(16)*, and Masquelet in 2000 *(8)*, they used autologous cancellous bone graft ± allograft when required (to a maximum ratio of 1/3). Stafford *(16)* used RIA bone graft.

In this study union occurred in 17 cases out of 20 (85%) which is consistent with the results of Flamans et al. *(6)* (9 out of 11) and Masquelet et al. *(9)* in 2008 (10 out of 11). Stafford et al. *(17)* reported union in 24 cases out of 25 cases (90%). Roche et al. *(14)* and Masquelet et al. *(8)* in 2000 reported union of all cases.

In this study union occurred at a mean of 7.4 months after 2nd stage which is consistent with most of other studies. A longer period to union was reported in the study of Masquelet in 2008 (9) (11.5 months, range: 6-18 months), despite adding BMP-7, which raises doubt about the value of BMP in this technique. In the study done by Woon et al. *(19)*, 1 case united after 11.5 months and this may be due to using corticocancellous graft which has less healing properties than pure cancellous graft. In the study done by Scholz et al. *(15)* union occurred after 4.5 months (range: 2.8-5.6 months).

The external fixator index in cases fixed with Ilizarov fixator in our study was 1.4 month per each cm of the defect. This is comparable to the index in distraction osteogenesis (1-1.5 months/cm). The induced membrane technique has the advantage that the frame is used only for stabilization. There is no lengthening, so the patient do not has to move the nuts 4 times daily, no pain from lengthening, no deformity and no joint stiffness. One patient required additional graft because of slow healing. The case fixed with interlocking nail developed severe infection 2 weeks after 2nd stage not responding to antibiotics. Debridement was done and Ilizarov bone segment transport in this case and another case with complete graft resorption after 7 months. 2 cases were complicated by shortening ≥ 2.5 cm and 4 cases with joint stiffness.

Although this study clearly showed the feasibility of induced membrane technique in patients with septic and traumatic long bone defects, there are some limitations. It is a non comparative study. There are non homogenous such as location, soft tissue defect, vascularity of the bone and bone defect size. Prospective studies on this field should focus on only one anatomic location.

CONCLUSIONS

The induced membrane technique is a simple, reliable and safe method for the treatment of post-traumatic and post infectious bone defects, with good results. Thorough debridement of necrotic bone and soft tissue is essential. Soft tissue coverage is a mandatory for this technique. The limited amount of bone graft can be solved by using the

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RIA system. The use of intramedullary nail with this technique carries the risk of infection and this may be due to more formation of biofilm on the outer and inner surface of the nail. Graft resorption and infection are the major complications of this technique. Despite the current evidence, further research is required to clarify issues regarding the use of the induced membrane technique in order to improve the clinical outcome. A first issue is the selection of the optimal type of spacer in an effort to induce a biologically active membrane. Currently, PMMA cement is used; but potentially another spacer may induce a more appropriate type of membrane. The ratio between autograft and allograft that not affect healing, the time between the two stages and the addition of BMP has to be further studied. Comparative studies are needed between this technique and other techniques.

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