Post-Traumatic Bone and Soft-Tissue Defects Treated with the Masquelet Induced-Membrane Technique: A Review of Technique and Outcomes

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ABSTRACT

Introduction: Post-traumatic bone and soft tissue defects can be managed by combining Masquelet induced membrane technique (MIMT) with local flaps. Compared to Ilizarov's technique, this technique heals independent of defect length with no or short frame time. In this case series, we describe this technique's critical steps and reviewed the outcomes.
Materials and methods: This is a single surgeon retrospective review, between July 2021 and June 2023. Two stages MIMT were performed on nine cases of bone defect with or without soft tissue defect, either due to index trauma or fracture related infection. In first stage, bone was debrided and stabilised with various fixation techniques followed by cementation, local flaps applied if indicated. Once soft tissue equilibrium achieved, second stage replaced cement with quantified amount of bone grafts, and bone fixation was revised accordingly.
Results: Bone defects length ranged from 4 to 9cm while bone grafts volume ranged from 17 to 41cc. Stage 1 fixation choices include Ilizarov or conventional external fixator, intercalary cemented intramedullary rod with Ilizarov hinges, plate and nail, while stage 2 includes plate and nail as definitive fixation. Time between two stages ranges from one to five months, bone union achieved between four and nine months. Out of nine cases, eight had excellent ASAMI bony outcome, six had excellent ASAMI functional outcome.
Conclusion: Bone grafts quantification allows appropriate autologous to total graft ratio, avoids excessive or inadequate bone graft harvesting. Different bone fixation choices have their own advantages. MIMT with local flap is a strategic combination.

Keywords:
Masquelet technique, bone defect, induced membrane technique, bone cement, bone graft

INTRODUCTION

Post-traumatic bone defects, either during index trauma itself, or secondary to infection that requires resection, need careful surgical strategies to achieve a good clinical outcome. This is made more complicated, when there is accompanied soft tissue defect and infection. Ilizarov's technique of distraction osteogenesis is able to tackle all the issues above. However, it has its unique limitations, such as adjacent joint stiffness especially if the defect is periarticularly, duration of bone defect healing that is length dependent, and pin wire sites infection along with cumbersome external devices. Masquelet's induced membrane technique (MIMT) offers an alternative to address the same, while potentially having fewer of the problems associated with Ilizarov's technique[1]. It comprises of two-stage operations[2]. The first stage operation fills up bone defect gap with bone cement, along with soft tissue reconstruction with flaps if necessary and skeletal stabilisation. The second stage operation replaces the bone cement with bone graft with careful preservation of the fibrous tissue-like induced membrane, that is formed around the bone cement.

We aim to review the outcome of our case series using MIMT in bone defect management and describe its technicalities and surgical strategies applied in these case series.

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MATERIALS AND METHODS

This is a single surgeon retrospective review of MIMT cases done between July 2021 and June 2023. A total of nine cases were identified, distributed in two tertiary trauma hospitals. After approval from the institutional ethics committee, data were collected with Microsoft Excel on table form, and was analysed using IBM SPSS, by an independent assessor. Age, gender, cause, location, bone defect type and length, soft tissue defect status, fixation choices in stage 1 and stage 2, time between the stages, details of quantity and quality of bone grafts used in stage 2, were collected. The type of bone defect is divided into 2 types, intercalary and critical size bone defects. Intercalary bone defect has bone defect circumferentially while critical size bone defect[3] involves circumferential fracture with significant cortical bone loss but with at least one of the cortex could still be restored in length after reduction. Outcomes were measured by unions time in months, ASAMI bony scores, ASAMI functional scores[4] as well as descriptions of complications observed. The union is defined by radiological achievement of mRUST score of 13 or higher[5-7], in months, by the follow-up radiograph. On last follow-up, the patient's ASAMI scores were evaluated. Data are presented in Table I and subgroup analysis presented in Table II. Written consents were obtained from the patients for publication.

During stage 1 surgery, the surgical wound was extended adequately to evaluate fracture and the bone defect. It was debrided adequately, and various site tissue and bone culture samples were sent if that was not first index trauma surgery. The bone was stabilized with restoration of length and alignment, either with nail, intercalary intramedullary Ilizarov cemented threaded rod with hinge component[8], Ilizarov external fixator or conventional fixator, with or without crossing the adjacent joints depending on stability (Fig. 1). Either 1 or two packs of 40g bone cement, with or without addition of 2g of vancomycin over each pack, depending on if the cause was infective in nature, were prepared and mixed. It was then packed into the bone defect site by hand packing during working phase of the cement, taking care to cover edge of fracture ends circumferentially[9]. The diameter of the cement packed in, was intentionally kept larger than the adjacent bone end, to allow containment of more bone grafts in future. In soft tissue defect cases, local flaps were raised and applied over soft tissue defect, preventing exposure of bone or cement.

In between stage 1 and 2, in the case with infection, antibiotic was given based on deep tissue and bone culture sensitivity, for a duration of 6 weeks, with minimum of 2 weeks to be given intravenously. If necessary, stage 1 operation could be repeated, to exchange bone cement with internal fixation device or conversion to external fixator, and repeat the cultures, in order to effectively treat the infection[9]. External fixator was removed at least 2 weeks prior to stage 2 to allow healing of pin and wire site if it had crossed the same bone and fall within future fixation zone. Stage 2 operation was performed once soft tissue equilibrium and CRP baseline achieved.

In stage 2 surgery (Fig. 2), previous surgical incision was revisited, and carefully dissected in order to create a plane over membrane induced by the bone cement, to facilitate later repair. The dissected membrane capsule was vertically incised and elevated circumferentially from the junction of cement and bone edges to reveal entire bone cement. The cement could be removed by piecemeal after being broken into pieces using osteotome and mallet. Bone defect size is estimated by bone cement volume measurement, using water submersion technique. A gallipot full of normal saline was prepared on an empty kidney dish, all the cements removed were inserted into the gallipot, and spill over saline was aspirated with syringe to quantify the volume displaced. This technique quantifies bone cement volume, allows estimation of bone defect size. The bone edges were debrided, intramedullary canals were cleared and curetted, tissue and bone cultures were taken. The fracture was then stabilised with plate or nail if it was yet to be internally fixed (if previously was on external fixator). Autologous bone grafts were harvested from either of these sites: corticocancellous or cancellous iliac crest graft, and proximal tibia cancellous graft from tibia interlocking nail entry point. These autologous bone grafts were milled with bone miller or fine cut manually with bonecutter and packed densely while squeezing out excessive blood using 10cc syringe. Non-autologous bone grafts were also prepared in 10cc syringes, these include demineralised bone matrix, allograft corticocancellous bone chips, synthetic bone grafts such as tricalcium phosphasegranules [chronOS™ DePuy Synthes], with or without 1cc of rhBMP-2 loaded hydroxyapatite granules [Novosis™]. Quantifying and compacting the bone grafts are keys to allow dense bone graft packing over the bone defects site, in the right amount of ratio. We prefer to use at least 30% of autologous bone grafts, with addition of 1cc of Novosis along with other bone graft substitutes. These bone grafts were then mixed evenly in a gallipot, applied over bone defect area, and packed densely with fingers, including over the edge of bone end, evenly over all surface of bone defects, with its diameter larger than the previous bone defects whenever possible. The induced membrane capsule was repaired with absorbable suture securely to contain the bone grafts before the surgical incision was closed with or without a drain outside the capsule. If post-operative culture was positive, suitable antibiotic was given for a duration of at least 12 weeks, with initial at least 2 weeks being given intravenously. The patients were follow-up monthly for first three months, then three monthly until a year at least (Fig. 3), with serial radiographs and CRP to monitor infection.

Table I: Data sheet of 9 cases of bone defects managed with Masquelet induced membrane technique, aetiology, location and degree of bone defect, soft tissue defect, fixation strategies used in stage 1 and stage 2, timing between stage, quality and quantity of bone grafts used, and outcome measured with union time, and ASAMI bony and functional scores.

Case	1	2	3	4	5	6	7	8	9
Age (years)	49	22	58	36	37	31	38	18	40
Gender	Male	Male	Male	Male	Male	Male	Male	Female	Male
Cause	trauma	infection	infection	trauma	infection	trauma	infection	infection	trauma
Location	distal M T	D T	DT	proximal M T	D T	D T	D T	D U	proximal M T
BD type	intercalary	intercalary	intercalary	CSBD	intercalary	CSBD	intercalary	intercalary	CSBD
BD length (cm)	4	7	8.5	9	4	5	7	5	7
Soft tissue defect	medial hemisoleus flap	absence	pedicle advancement flap	abscence	medial hemisoleus flap	absence	absence	absence	Medial gastrocnemius flap
Stage 1	cross ankle IEF	cross ankle EF	interlocking nail, repeat stage 1 with exchange nail	cross knee EF	tibia IEF	nail	intercalary cemented intramedullary rod with ilizarov hinges	plate	tibia EF, repeat stage 1 with nail
Stage 2	plate	nail	exchange nail	plate	plate	no exchange	nail	no exchange	no exchange
Time between 2 stages (month)	5	3	5	1	2	2	3	2	5
BG volume (cc)	10cc ICCC 10cc chronOS	15cc ICCC 20cc chronOS	15cc ICCC 20cc chronOS	15cc ICCC 20cc chronOS	10cc ICC 10cc chronOS	6cc PTC 10cc AL 1cc Novosis	15cc PTC 10cc IC 15cc AL 1cc Novosis	6cc ICC 5cc Demineralized bone maxtrix	5cc IC 10cc AL 1cc Novosis
Total volume (cc)	20	35	35	35	20	17	41	11	16
Autologous: Total BG	0.50	0.43	0.43	0.43	0.50	0.35	0.61	0.55	0.31
Union in months post stage 2 - mRUST>12	5	5	4	5	7	4	9	4	5
ASAMI bony outcome	good	excellent	excellent	excellent	excellent	excellent	excellent	excellent	excellent
ASAMI function outcome	good	good	excellent	excellent	excellent	excellent	excellent	excellent	good
Compilations	delay junctional union, broken plate, 2.5cm residual shortening		repeated stage 1 with repeat debridement		require remova of plate post union due to infection				limping gait

Abbreviations - AL: allograft cancellous, ASAMI: International Association for Study and Application of Methods of Ilizarov, BD: Bone Defect, CSBD: critical size bone defect, D: diaphyseal, DBX: maxtrix, EF: external fixator, IEF: Ilizarov external fixator, ICCC: iliac crest corticocancellous, ICC: iliac crest cancellous, M: metaphyseal, mRUST: modified Radiological Union Score for Tibia, Novosis: recombinant human Bone Morphogenetic Protein-2 with hydroxyapatite carrier, PTC: proximal tibia cancellous, T: tibia, U: ulna

Table II: Subgroup analysis of flap and no flap, trauma and infection, and bone defect type subgroups. The flap group requires longer duration between two stages, attributed by extra time needed to achieve soft tissue equilibrium. The infection group requires significant more bone graft volume as compared to index trauma group.

	Age (years)	Bone Defect Length (cm)	Time between 2 stages (months)	Total bone graft volume (cc)	Union time
Total n=9	36.6 ± 11.3	6.3 ± 1.9	3.1 ± 1.5	25.6 ± 10.7	5.3 ± 1.6
Flap and no flap group comparison					
Flap Group n=4	41.0 ± 8.9	6.4 ± 2.1	4.3 ± 1.7	22.8 ± 8.5	5.5 ± 1.3
No flap Group n=5	33.4 ± 12.3	6.2 ± 1.9	2.4 ± 0.9	27.6 ± 12.5	5.2 ± 1.9
Mann-Whitney U test	P = 0.251	P = 0.881	P = 0.034*	P = 0.468	P = 0.762
Trauma and infection group comparison					
Trauma Group n=4	38.8 ± 7.5	6.3 ± 2.2	2.5 ± 1.7	17.0 ± 2.2	4.8 ± 0.5
Infection Group n=5	35.0 ± 13.7	6.3 ± 1.8	3.4 ± 1.3	30.6 ± 10.9	5.8 ± 1.9
Mann-Whitney U test	P = 0.584	P = 0.964	P = 0.334	P = 0.018*	P = 0.273
Bone defect type: intercalary and CSBD group comparison					
Intercalary Group n=6	35.1 ± 13.3	5.9 ± 1.6	3.4 ± 1.4	26.3 ± 10.6	5.6 ± 1.6
CSBD Group n=3	38.0 ± 5.7	7.0 ± 2.7	2.3 ± 1.5	22.7 ± 6.7	4.7 ± 0.6
Mann-Whitney U test	P = 0.703	P = 0.424	P = 0.253	P = 0.563	P = 0.293

Remarks: value in mean ± standard deviation,
Mann-Whitney U test used due to small sample size and potential non-normal distribution, P value <0.05 is significant

RESULTS

There were 9 bone defects cases treated over the span of two years, their age ranges from 18 to 58 [mean 36.6, standard deviation (SD) ± 11.3] years, 8 out of 9 were males. Four cases were due to primary trauma while other five cases were complication of post-traumatic fracture related infection, requiring debridement of soft tissue and bone resection. A total of 33% of the cases were located at metaphysis while the rest were involving diaphysis. All cases involved tibia except one case that involved ulna. Four of nine cases needed soft tissue coverage procedures due to soft tissue defects, during first stage operation. The mean bone defect sizes were 6.4 (SD±2.1) cm and 6.2 (SD±1.9) cm in length for those required soft tissue coverage and those that did not need, respectively. The bone grafts volume used on each case ranges between 11 and 41cc, with autologous bone graft ratio proportion over total bone graft volume ranges between 0.31 and 0.61. The mean time between first and second stage were 4.3 (SD±1.7) months and 2.4 (SD±0.9) months for those that needed soft tissue procedures and those that did not need, respectively. The duration between two stages for the flap group was statistically longer, attributed by extra time needed for soft tissue equilibrium (Table II). Unions were achieved between 4 to 9 months, with mean of 5.3 (SD±1.6) months, those with intercalary defects took 5.6 (SD±1.6) months in average to achieve union while those with critical size bone defects took 4.7(SD±0.6) months in average. Interestingly, though bone defect length for both trauma and infection groups were comparable with mean of 6.3(SD±2.2) and 6.3((SD±1.8) cm respectively, their total bone graft volume required were statistically significant, with mean 17.0 (SD±2.2) and 30.6(SD±10.9) cc, respectively. This could be possibly due to more bone resection was needed for infection group as compared to those done masquelet stage 1 during index trauma itself. Eight out of nine patients achieved excellent ASAMI bone scores. Seven out of nine patients achieved excellent ASAMI functional scores. There was one patient had delayed junctional non-union which resolved at nine months without further intervention, the same patient also had broken plate at two months post second stage operation, but no revision was done as the patient was tolerating full weigh bearing without pain. Two of the cases required repeated stage 1, with cement spacer exchange due to infection inadequately controlled, while one patient required removal of plate after union achieved. All patients achieved infection-free state at the final follow-up.

DISCUSSION

Choice of bone fixation plays a major role in MIMT. In the first stage operation in the setting of acute trauma with metaphyseal bone loss, peri-articular stabilisation with stable fixation adjunct with bone cement augmentation to provide meta-diaphyseal stability allows faster bone and soft tissue healing and earlier functional rehabilitation. This often can be achieved with peri-articular locking plate or newer design nail that offersmulti-directional angular stable interlocking screw. The use of modular Ilizarov external fixator as temporary measure also helps in wound management especially involving flaps. It provides adequate stability and allows threaded rods positional change if necessary to have better wound access. The antibiotic bone cement also provides antibiotic elution and dead space management in open fractures cases. Musa *et al*[10] reported successful treatment of 10 distal femoral opened fractures with metaphyseal bone loss treated with plate fixation in stage 1, using MIMT. A total of 4g of vancomycin and 6ml of gentamicin were added to each pack of bone cement

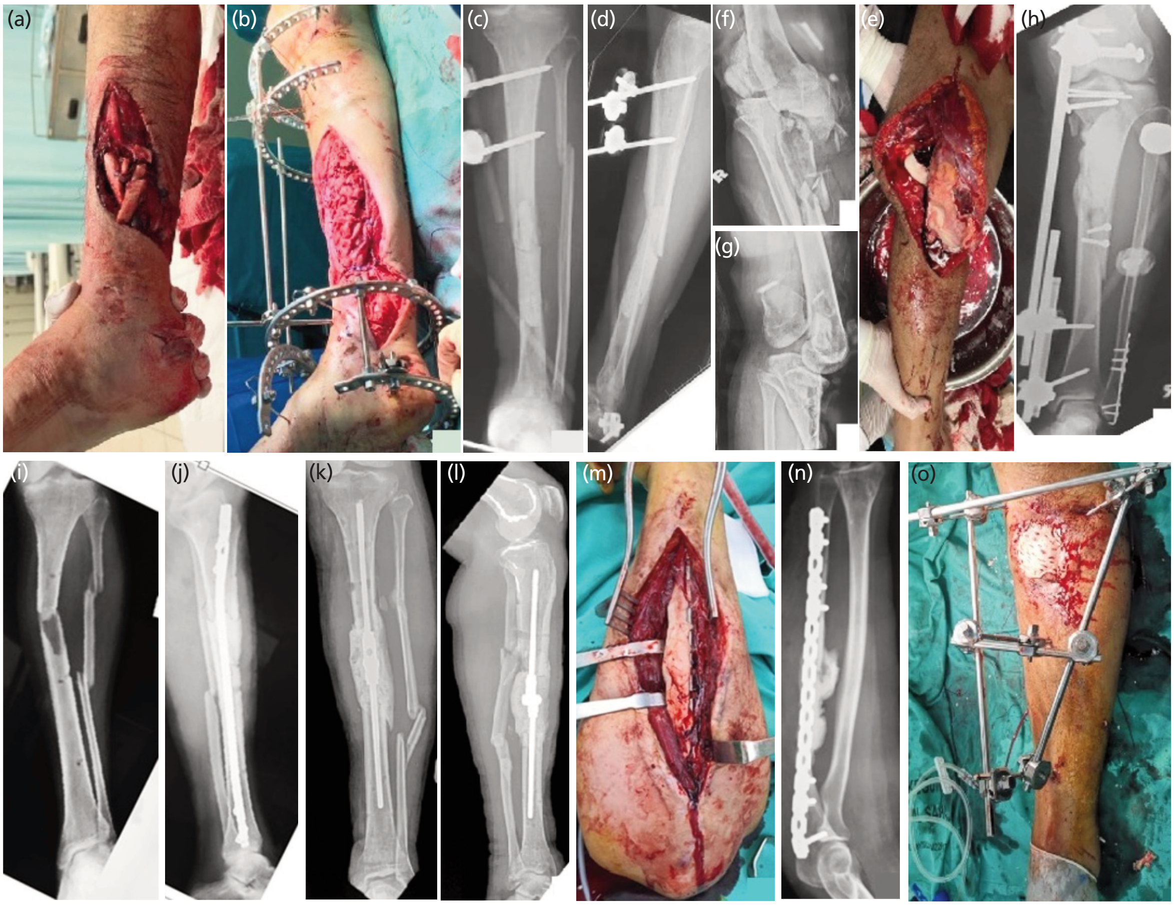

Fig. 1: Different fixation choices for Stage 1. (a) Belongs to Case 1 and shows a Gustilo–Anderson Grade IIIB open distal tibial fracture with a soft-tissue defect and bone comminution before debridement. (b) Also belongs to Case 1 and shows a cross-ankle Ilizarov external fixator with a medial hemisoleus flap covering the cement spacer over the bone defect. (c, d) Belong to Case 2, a tibial fracture-related infection that required bone resection, and are anteroposterior (AP) and lateral radiographs of the tibia showing a cross-ankle external fixator and an intercalary cement spacer. (e) Belongs to Case 4 and shows a severe open fracture-dislocation of the knee. (f, g) Also belong to Case 4 and are radiographs of the knee demonstrating the fracture-dislocation associated with severe tibial metaphyseal bone loss. (h) Belongs to Case 4 and shows the post-operative radiograph following fixation of the distal femur and proximal tibial articular surfaces with screws, reconstruction of the metaphyseal bone defect with bone cement, and application of a cross-knee external fixator. (i) Belongs to Case 6, an open tibial fracture with a critical-sized bone defect, and shows a radiograph of the tibia demonstrating the bone defect. (j) Shows the Stage 1 fixation using an intramedullary nail and bone cement to fill the defect. (k, l) Belong to Case 7, a tibial fracture-related infection associated with an intercalary bone defect, and show radiographs obtained after Stage 1 surgery, demonstrating an intercalary cement spacer with a cement-coated threaded rod and an Ilizarov hinge. (m) Belongs to Case 8, an ulnar fracture-related infection with a bone defect, and shows plate fixation with a cement spacer. (n) Also belongs to Case 8 and shows the post-operative Stage 1 radiograph of the oversized cement spacer. (o) Belongs to Case 9, a Gustilo–Anderson Grade IIIB open proximal tibial fracture with associated bone and soft-tissue defects. A medial gastrocnemius flap was used to cover the bone cement spacer, which was stabilised with a tibial external fixator.

according to their case series. Cho *et al* described an innovative technique of using Ilizarov component of cemented threaded rod, coupled with hinge and interlock with bolt and nut followed by intercalary cement[8]. In stage 2, intramedullary nail offers several advantages over plate fixation[11], such as reduction of central canal volume needed for bone grafting, being a load sharing device which allows earlier weigh bearing and offer simultaneous proximal tibia bone graft harvesting from its entry point during tibial nailing procedure[12]. Plate, however, will be mandatory when fracture fixation is not being able to be achieved by nail, such as peri-articular fracture.

In cases with bone defects associated with infection, it is necessary to debride the diseased bone adequately and manage the dead space with bone cements, which also allows elution of antibiotic and provide local stability to the adjacent bone ends[13]. Vancomycin and gentamicin loaded antibiotic cement spacer have no adverse impact on osteogenicity according to a study[14]. If clinical condition or inflammatory markers do not achieve baseline, repeat of stage 1 operation will be necessary to perform re-debridement, to obtain a new set of samples and to exchange the cement spacer which will be potentially colonised with inadequately treated infection and a course of targeted

Fig. 2: Steps of stage 2. (a) Dissection of previous surgical incision, into the plane of induced membrane capsule. (b) Vertical incision made over the capsule to access bone cement spacer. Removal of bone cements in piecemeal, volumetric measurement of cement by submerging to gallipot full of normal saline, and measure the spillover saline in volume, helps to determine volume of bone grafts needed. Bone graft was harvested from site of choice, in this case, entry point of the tibia nail, and cancellous iliac crest. Nail was inserted to restore appropriate length and alignment. (c) The bone graft was densely packed into bone defect cavity evenly, and to cover edge of fracture end to prevent junctional non-union, prior to repair of the capsule. (d) Autologous grafts were collected into 10cc syringe and were squeezed dried to allow dense impaction of graft later. (e) Volume of bone grafts were estimated prior to mixing with other bone graft expander in a gallipot, (f) to obtain appropriate autologous to total bone graft ratio.

antibiotic based on the culture[15]. If clinical and laboratory markers are favourable, internal fixation with exchange cement spacer can be done as early as three weeks, and four weeks in the case of with flap, followed by another stage of replacing the cement with bone graft later. A Korean study[16] reviewed their own surgical strategy protocol in 140 patients that were treated with multiple staged MIMT. It highlights the importance of inflammatory markers being normalised prior to stage 2 operation, and compliance to protocol, to lower the risk infection recurrence following stage 2 operation.

Quantifying the bone cement volume with the water submersion technique allows estimation of bone grafts needed, to prevent excessive autologous bone graft harvesting leading to donor morbidity[17]. This study[18] highlighted bone graft weighing and estimating bone defect through radiological measurement. Compared to the study,

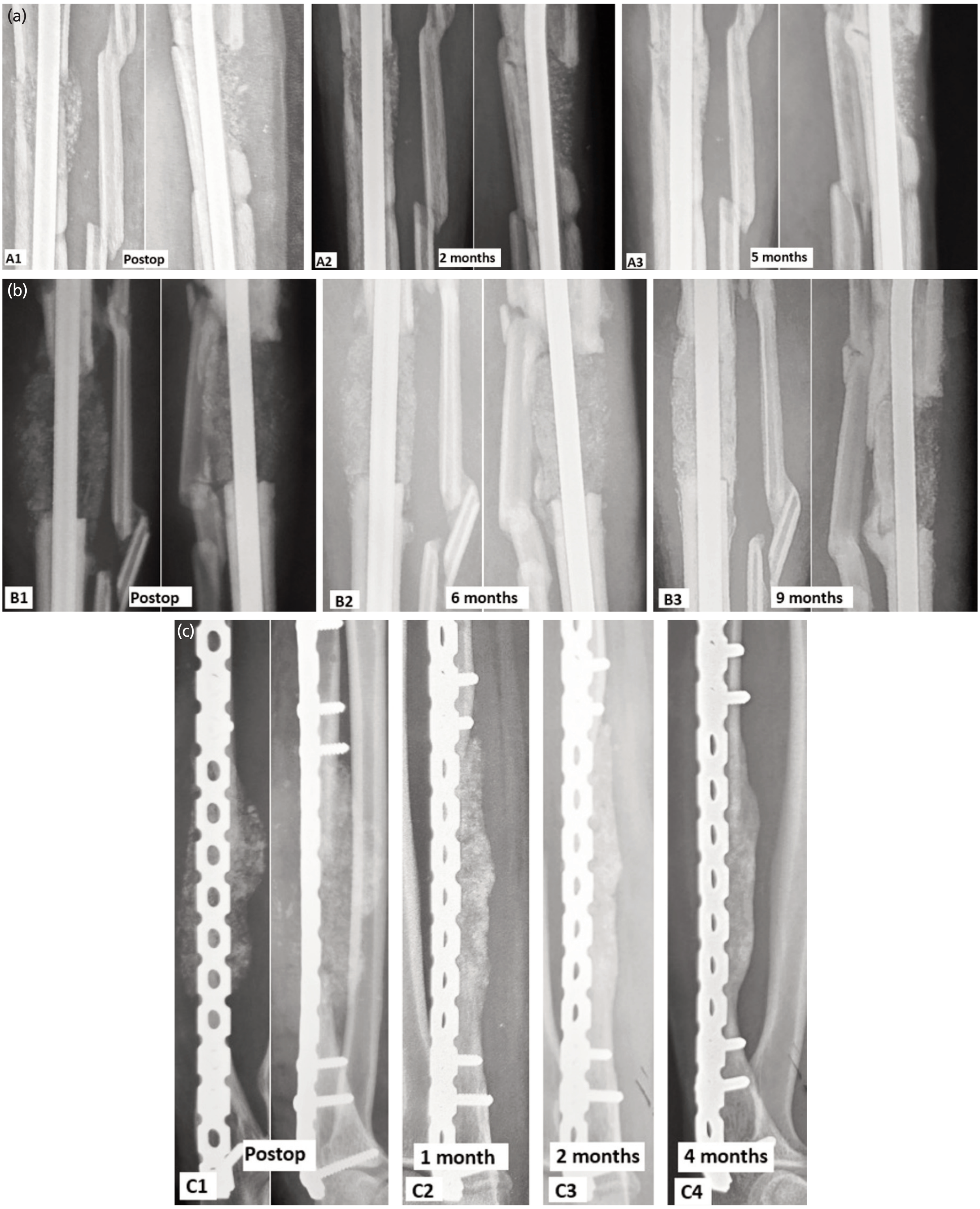

Fig. 3: Bone grafting with Masquelet technique shows remodelling over time. (a) Figures belongs to Case 3, A1 shows AP and lateral tibia radiographs immediate after bone grafting. A2 and A3 are 2 and 5 months follow up radiographs. (b) Figure belongs to Case 7, B1 shows AP and lateral tibia radiographs immediate after bone grafting. B2 and B3 are 6 and 9 months follow up radiographs. (c) Figure belongs to Case 8, C1 shows AP and lateral ulna radiographs immediate after bone grafting. C2, C3, C4 are 1, 2, 4 months follow up radiographs, respectively. Common findings are initial shrinkage of bone graft size in diameter, gradual smoothening of graft edges that suggests remodelling, and corticalization of graft demonstrated by radio-opacification matching that of the cortex. Note that the anterior cortex of the tibia (A3, B3) tends to regenerate with thinner bone as compared to other wall of the cortexes.

our technique is direct and reproducible, allowing direct estimation of bone defect size which could be irregular in critical size bone defects, or intercalary bone defects that have oblique bone end surfaces. The use of bone graft volume expander, such as synthetic bone graft and allograft have been well supported by literature[2]. Current literatures suggest addition of recombinant human bone morphogenetic protein-2(rhBMP-2) with hydroxyapatite(HA) carrier enhances bone healing in MIMT[19,20]. In our case series, we observed earlier corticalization of cases using a small quantity of rhBMP-2 with HA carrier [1cc of Novosis™] but no significant earlier union. As compared to the previous study[20] that used 1:1 autologous graft rhBMP-2 ratio, low dose of 1cc rhBMP-2 with HA carrier shows potential effect that warrants further study to evaluate its cost efficiency in surgical strategy of managing non-union cases. In our series, we observed that anterior cortex tends to consolidate slower and thinner, as compared to the other cortexes (Fig. 3). This is consistent with a study[9] that analysed 111 computed tomography of 37 patients and noted lower healing over anteromedial aspect of the tibia, in term of bone regenerate volume, density as well as corticalization. The finding however does not adversely affect our cases outcome.

Soft tissue defect management in conjunction with MIMT has been well demonstrated by previous studies[21-23]. Orthoplastic limb reconstruction is emerging in modern orthopaedic trauma surgery, however in Malaysia, the plastic service is still very limited and orthopaedic surgeons have to take effort to master this art[24]. With local flap, a larger circumference bone cement can be filled without concern of inadequate soft tissue closure. This is a great advantage to allow larger bone grafting chamber in stage 2 operation, as bone graft tends to shrink in size during the initial first few months (Fig. 3). As compared to cases without the need of flap, the stage 2 operations that needed soft tissue reconstruction are usually delayed achieving flap healing and soft tissue equilibrium[25], and it has not been shown to affect the time it takes to achieve union in our series.

The limitation of this retrospective case review includes variables on the choice of fixation, surgical technique applied such as bone graft harvesting site and type of bone graft use, location of bone defects, and low number of cases reviewed and relative short follow-up period to observe long term complication such as bone graft site re-fracture, relapse of infection.

CONCLUSION

The measurement techniques of bone defect size and bone graft volume allow optimal autologous to total graft ratio, with accurate bone graft quantity harvesting. This avoids excessive graft harvesting that has donor site morbidity, or underharvesting that potentially compromises bone healing. The technique is highly versatile, allowing various fixation choices depending on clinical situation, with each having their own perks. MIMT with local flap is a strategic combination that not just solves the bone and soft tissue defect but also allows larger bone graft chamber creation, permitting more bone grafts to be packed in later. It is thus an advantage for orthopaedic trauma surgeon to equip the skill to perform flaps or develop collaboration with plastic counterpart. There is yet a gold standard MIMT to be followed, and development of local protocol with regular review of its outcome is necessary to achieve good outcome.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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