



## PERCUTANEOUS AUTOLOGOUS BONE MARROW INJECTION FOR DELAYED UNION OR NON-UNION OF FRACTURES AFTER INTERNAL FIXATION AND EXTERNAL FIXATION

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**ABSTRACT** Delayed union or non-union of bone fracture is becoming less frequent, but still remains a challenging clinical problem. Autologous cancellous bone grafting that is the gold standard method, often involves donor site morbidities and complications. Once these fractures have been mechanically stabilized, other local factors should be investigated to promote delayed healing. The aim of this study was to assess the results of percutaneous injection of autologous bone marrow in the treatment of fractures presenting with delayed union or non-union after internal fixation and external fixation. Twenty consecutive patients presenting to our orthopedics department with internally or externally fixed fractures with delayed union or non-union were included in the study. The time between the index surgery and the bone marrow injection ranged from 4 to 20 months with a mean of 8.75 months. The bone marrow aspirate was injected percutaneously into the fracture site. **Results:** Nineteen out of the twenty fractures achieved clinical and radiological union, on average after 2.65 months. **Conclusion:** The result of current study is encouraging in the initial outcome. Percutaneous autologous bone marrow injection could be an effective and safe option for the treatment of delayed or non-union fractures. The efficiency related to the population of progenitor cells in the concentrated bone marrow aspiration.

**KEYWORDS :** bone marrow; internal fixation; fractures; stem cell.

### INTRODUCTION

Fracture union is a complex process which starts with the initial injury and continues for several years after clinical and radiological union until the bone retains its original structure and function. Delayed union and non-union are two of the common problems that may face any surgeon dealing with fracture healing. Long bone diaphyseal fractures can be treated using the principle of relative stability using locking plates or nailing. Humerus and radius-ulna can be fixed using compression plating being non-weight bearing bones. Approximately 5% of all long bone fracture result in non-union and even more in delayed union. The reported incidence of non-union of femoral shaft fracture is less than 1% following nailing that tibia shaft fracture is 5-10%, humerus shaft fracture 5% following Delayed healing may be caused by several factors. Several methods of treatment have been adopted to overcome this problem.

Percutaneous bone grafting was first introduced by Herzog in 1951, with the use of a large bore needle and small cancellous chips to graft a non-union<sup>1</sup>. The bone marrow graft concept and the percutaneous grafting technique were subsequently combined in many studies, taking into account the fluid nature of the bone marrow. In 1998, Connolly<sup>2</sup> in a review of his 15 years research into various methods and techniques of using marrow osteoprogenitor cells showed that marrow injection in and about the nonunion site can be useful to treat numerous skeletal healing problems e.g., Tibial delayed unions or nonunion, either infected or not<sup>3,4</sup>. Based on this aim of this study was to assess the results of percutaneous injection of autologous bone marrow in the treatment of fractures presenting with delayed union or non-union after internal fixation and external fixation

### MATERIAL AND METHODOLOGY

The study included twenty consecutive patients who presented to department of orthopedics with delayed union or non-union of a closed fracture following internal fixation. The fracture was considered non united when there was no progression of union over the last three months, with a time lapse of more than six months since internal fixation. Exclusion criteria included fractures with delayed or non-union due to a mechanical cause related to the internal fixation necessitating revision of the fixation, active infection associated with the delayed union or the non-union necessitating removal of the fixation, and the presence of a gap at the fracture site more than 10 mm which needed to be filled with a structural graft.

Under general or spinal anesthesia, bone marrow was aspirated from the anterior iliac crest using a special bone marrow aspiration needle into heparinized syringes to avoid clotting of the aspirate. The aspirate was injected percutaneously into and around the fracture site under Radiological union of the fracture was assessed through serial monthly plain radiographs. The fracture was considered united radiographically

when callus was seen crossing the fracture line, indicating cortical union at least at three cortices in the two planes radiographs.

Association between categorical variables was tested using Chi-square test. For normally distributed data, comparison between two independent populations was done using independent t-test. The significance level was set at  $p < 0.05$ .

### RESULTS

In our study containing 20 patients, most common age group was 31-40 years with 9 cases followed by 21-30 years with 5 cases with mean age of 42.3. Coming to sex distribution 14 were male and 6 were female in our study.

Most common procedure underwent was Distal tibial locked plate in 9 patients, Proximal tibial locked plate in 4 patients, antegrade femoral nail in 2 patients, distal femoral locked plate in 2 patients, dynamic compression plate in 2 patients and retrograde femoral nail in one patient. Hence tibia being the commonest bone involved followed by femur and ulna.

In our study nineteen out of the twenty fractures went on to clinical and radiological union, and the patients were mobilizing without any walking aid or any support at the end of their follow-up with no pain or tenderness at the fracture site. One patient did not show any radiological evidence of new bone formation at his fracture site after three months and was considered a failure. The time to union following the bone marrow injection ranged from 2 to 5 months with an average of 2.65 months.

**Table I. — Relation between time to union and sex, age, type of fixation and bone affected**

	Time to union (months)	
	Mean $\pm$ SD	P value
	Sex	
Male	3.12 $\pm$ 0.87	0.033*
Female	2.25 $\pm$ 0.62	
	Type of fixation	
Femoral Nail	3.56 $\pm$ 0.65	0.156
DCP	2.45 $\pm$ 0.62	
DTLP	2.75 $\pm$ 0.71	
PTLP	3.12 $\pm$ 0.23	
DFLP	2.41 $\pm$ 0.56	
	Bone affected	
Femur	3.11 $\pm$ 0.82	0.232
Tibia	3.21 $\pm$ 1.0	
Ulna	2.65 $\pm$ 0.71	

The relation between the different factors and the time to union is presented in table I. Infection did not occur in any patient. There were no other complications related to either the donor site or the site of injection. All patients were safely discharged on the same day of the marrow injection.

## DISCUSSION

Delayed union or non-union of fractures has always been a challenging problem. Autogenous bone marrow injection has been the most commonly used method used in the surgical management up to now.

The time to union was significantly less in female patients compared to the male patients ( $p = 0.033$ ). The tibia represented 65% of the cases included in this study. The relatively high incidence of delayed and nonunion associated with tibial fractures compared to the other long bones fractures has been reported in previous studies<sup>5,6</sup>. The higher incidence of open tibial fractures due to their subcutaneous anatomical location as well as the specific aspects of vascularization of the tibia are among the important causes of this relatively frequent delay in healing.

This study included 15 fractures fixed with locked plates (13 tibial and 2 femoral plates). The relatively high proportion of delayed unions related to locked plating compared with intramedullary nailing has been noted and explained in previous studies by the fact that locked plating, if not performed using a MIS approach, damages the soft tissues much more than IM nailing done under fluoroscopy without opening the fracture site<sup>7</sup>.

The bone marrow aspirate can be used alone or as a composite graft e.g. with a synthetic scaffold. This composite graft is usually introduced using an open technique and is indicated in non-united fractures with gaps or in osteolytic lesions such as large bone cysts<sup>8</sup>.

Some authors have recommended the use of concentrated bone marrow obtained by centrifugation, in order to increase the number of osteoprogenitor cells in the bone marrow injected<sup>9</sup>. In other studies, the aspirate was cultured *in vitro* before injection of the osteoprogenitor cells into the fracture site<sup>10</sup>. Considering the increased cost and the risk of infection, we think that these techniques are more indicated in case of small bones nonunion e.g. scaphoid due to the limited space available to deliver the graft at the fracture site.

Muschler *et al*<sup>11</sup> have studied the effect of the aspiration volume on the concentration of the number of osteoprogenitor cells; they recommended the aspiration of the bone marrow from multiple sites to avoid its dilution with the peripheral blood. With 95% success to achieve union following the bone marrow injection, this study has showed the efficacy of autogenous bone marrow to accelerate fracture healing.

As for the complications, there was no reported infection or pain related to the donor sites or the injection sites. The use of bone marrow is considered a simple and minimally invasive technique. The bone marrow injection is safe, as the material injected is autologous, so there is no risk of disease transmission or immune reaction.

The use of bone marrow to accelerate fracture healing is one of the applications of the stem cell technology. It represents a promising method of application of tissue engineering in the orthopedic field, which avoids many of the complications of the traditional bone grafting method commonly used so far. We think that the good results achieved in this study were related to the good selection of cases, in which the causes for delayed union were essentially biological, thus excluding cases with mechanical causes for the delayed union or the non-union.

## CONCLUSION:

The result of current study is encouraging in the initial outcome. Percutaneous autologous bone marrow injection could be an effective and safe option for the treatment of delayed or non-union fractures. The efficiency related to the population of progenitor cells in the concentrated bone marrow aspiration.

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