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Original Research Article

Effectiveness of percutaneous autologous bone marrow injection in delayed and non-union of long bones after definitive fixation

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ABSTRACT

Background: Delayed and non-union of long bones remain challenging complications despite stable fixation. Percutaneous autologous bone marrow injection (PABMI) provides osteogenic stimulation without the morbidity of open grafting.
Methods: This prospective observational study included 32 patients with delayed or non-union following internal fixation. Forty to sixty milliliters of autologous bone marrow aspirate was collected from the anterior iliac crest and injected percutaneously around the non-union site under fluoroscopic guidance. Patients were followed clinically and radiologically at 4, 8, 16, and 24 weeks.
Results: Radiological union improved progressively, from 3.1% at 4 weeks to 87.5% at 24 weeks (p=0.02). Patients operated within 1 week of injury and those presenting within 12 months of fixation had significantly higher union rates (p=0.021 and p=0.0038). No major complications were observed apart from transient donor-site pain.
Conclusion: PABMI is a safe, simple, and effective biological method for achieving union in delayed and non-union of long bones, with earlier intervention significantly improving outcomes.

Keywords: Percutaneous autologous bone marrow injection, Non-union, Delayed union, Long bones, Osteogenesis

INTRODUCTION

Fracture healing is a complex biological process that may be impaired by several factors, resulting in delayed or non-union. Despite advances in fixation techniques and implant design, the incidence of non-union in long bones continues to range between 5–10%, posing a significant challenge to orthopaedic surgeons. Failure of fracture healing not only prolongs disability but also imposes a substantial socioeconomic burden due to repeated hospitalizations, prolonged rehabilitation, and loss of productivity.

The success of fracture union depends on both mechanical stability and biological viability at the fracture site. When mechanical factors are adequate, biological stimulation becomes crucial for achieving union. Autologous cancellous bone grafting has long been considered the gold standard for enhancing osteogenesis; however, it requires open surgery, is associated with donor-site morbidity, and may not always be feasible, particularly in elderly or medically compromised patients.

To overcome these limitations, attention has shifted toward biological augmentation techniques that stimulate osteogenesis without the morbidity of open graft harvesting. One such promising approach is percutaneous autologous bone marrow injection (PABMI). Bone marrow aspirate contains mesenchymal stem cells, osteoprogenitor cells, and various growth factors that play a pivotal role in new bone formation. Injecting these osteogenic cells directly into the fracture gap can initiate and accelerate healing, even in a biologically inactive environment.

Previous studies, including those by Connolly et al, Hernigou et al, Garg et al and Goel et al, have reported

union rates of 75–90% in long bone non-unions following bone marrow injection.[1-4] However, there remains limited literature from Indian tertiary centers validating these outcomes under local clinical conditions and patient profiles. The present study aims to evaluate the effectiveness of percutaneous autologous bone marrow injection in the treatment of delayed and non-union of long bones following internal fixation, with emphasis on radiological progression of union, influence of time factors, and overall clinical outcome.

Literature survey

The concept of using bone marrow aspirate as a source of osteogenic cells for fracture healing was first described by Guthe and later popularized by Connolly et al, who demonstrated an 85% union rate in tibial non-unions treated with autologous bone marrow injection. Hernigou et al further quantified the concentration of progenitor cells and reported up to 90% success when adequate cell counts were delivered, establishing bone marrow concentrate as a potent biological stimulant. Garg et al reported a union rate of ~85%, while Goel et al reported ~75%. Thus, Indian series generally show union rates ranging from ~75% to ~88%, depending on patient factors and technique, validating its efficacy in the Indian population. When mechanical stability is adequate, biological stimulation becomes the key determinant for achieving union.[5] Subsequent studies confirmed that the marrow aspirate contains mesenchymal stem cells (MSCs) capable of differentiating into osteoblasts and promoting callus formation at the fracture site.[6] Compared to open bone grafting, PABMI offers several advantages—minimal morbidity, repeatability, shorter hospitalization, and early mobilization—making it an appealing first-line biological adjunct for delayed and non-union of long bones.[7]

METHODS

A prospective observational study was carried out on 32 patients aged between 18 and 75 years presenting with delayed or non-union of long bones following definitive internal fixation.

The study was conducted at the Department of Orthopaedics, Patna Medical College and Hospital, Patna, between December 2022 to March 2025.

Inclusion criteria

Patients with radiologically confirmed delayed or non-union of long bones (humerus, forearm, femur, tibia) who had undergone internal fixation and had no signs of infection were included.

Exclusion criteria

Cases with active infection, pathological fractures, metabolic bone disease, or those unfit for the procedure were excluded.

Procedure

After obtaining informed consent, approximately 40–60 ml of bone marrow aspirate was collected aseptically from the anterior iliac crest using a bone marrow aspiration needle under local anesthesia. The aspirate was then percutaneously injected at multiple sites around the non-union or delayed union site under fluoroscopic guidance. No additional bone grafting or internal fixation procedure was performed during this session.

Follow-up and evaluation

Patients were followed up clinically and radiologically at 4-,8-,16-, and 24-weeks post-injection, clinical union was defined by the absence of pain and abnormal mobility at the fracture site and radiological union was defined as the presence of bridging callus across at least three cortices on orthogonal X-rays.

Demographic and clinical profile

The mean age of the study population was 32.24±11.82 years, with the majority (56%) aged between 21 and 40 years (Table 1). The average time from fixation to presentation with non-union or delayed union was 11.5±3.84 months (Table 2).

Table 1: Age distribution of patients (n=32).

Age group (years)	Number of patients	Mean age (years)	SD
<20	7		
21–30	9		
31–40	9		
41–50	1		
51–60	1		
61–75	0		
Total	32	32.24	11.82

Table 2: Time lapsed to presentation with non-union/delayed union after fixation.

Time (months)	No. of patients
4-6	1
6-9	8
9-12	12
12-18	9
>18	2

The distribution of bones involved is shown in Table 3. The tibia was the most affected bone (14 cases), followed by the humerus and forearm bones (7 cases each), and the femur (4 cases).

Statistical analysis

Data were analyzed using the Cochran's Q test to evaluate the relationship between radiological union and follow-up

time intervals. A $p<0.05$ was considered statistically significant.

Table 3: Bone presented with delayed/non-union.

Bone type	N
Humerus	7
Forearm (BBFA/single bone)	7
Femur	4
Tibia	14

RESULTS

A total of 32 patients with delayed or non-union of long bones were treated with PABMI and followed up radiologically for 24 weeks.

Progression of radiological union

Radiological union progressively improved over time following PABMI (Table 4 and Figure 1).

Table 4: Radiological union of the non-union/delayed union sites at various stages of follow-up.

Stage of follow-up	Radiological union	No radiological union	Total
1 month (4 weeks)	1	31	32
2 months (8 weeks)	7	25	32
4 months (16 weeks)	21	11	32
6 months (24 weeks)	28	4	32

*Using the Cochran's Q test, the calculated p 0.02 which is more than the permissible limit of 0.05. This suggests there is a very strong relationship between the radiological union and PABMI

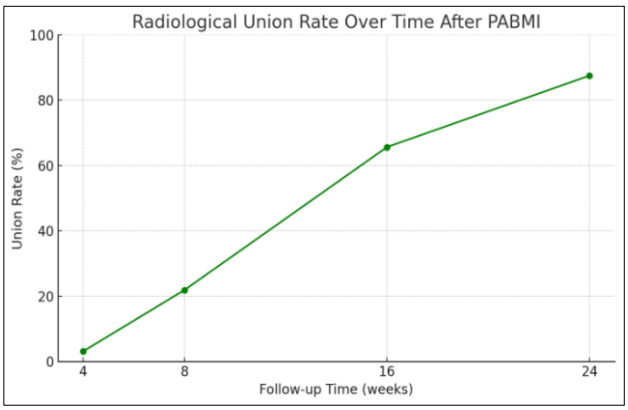

Figure 1: Radiological union progression at 4, 8, 16 and 24 weeks following PABMI.

At 4 weeks, only 1 patient (3.1%) showed early callus formation.

By 8 weeks, 7 patients (21.9%) demonstrated partial bridging callus, and by 16 weeks, 21 patients (65.6%) achieved radiological union. At the end of 24 weeks, 28 patients (87.5%) showed complete union with bridging of at least three cortices on X-rays (Figure 2).

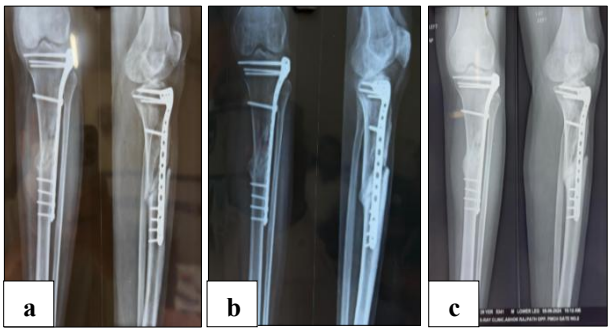

Figure 2: Representative case showing tibial delayed union before and after PABMI (24 weeks), (a) initial presentation, (b) 8-weeks follow-up (progression of callus), and (c) 24-weeks follow-up (complete union at ¾ cortices).

Using the Cochran's Q test, the calculated p-value was 0.02, indicating a statistically significant correlation between the duration of follow-up and the rate of radiological union (Figure 1).

Effect of time to surgery

A statistically significant relationship was observed between the time interval from injury to surgery and the rate of radiological union (Table 5).

Table 5: Relationship between radiological union and time lapsed to fixation from injury.

Time to surgery (weeks)	Total cases	Radiological union
<1	11	11
1–2	15	14
2–4	4	2
>4	2	1

P value is 0.021, the result is statistically significant. This suggests a significant association between time lapsed to surgery and radiological union—in other words, delaying surgery may negatively impact union rates

Patients who underwent surgery within 1 week of injury showed 100% union (11/11), while those operated after 4 weeks had only 50% union (1/2).

Overall, patients treated earlier after injury demonstrated superior healing outcomes compared to those with delayed fixation ($p=0.021$). This suggests that early surgical intervention optimizes bone biology, thereby enhancing the subsequent response to PABMI.

Effect of time to presentation with non-union

The time elapsed from initial fixation to presentation with delayed/non-union was found to have a strong influence on healing (Table 6). Patients who presented within 6–9 months of fixation achieved 100% union (8/8), those presenting after >18 months showed 0% union (0/2) and the mean duration from fixation to presentation was 11.5±3.84 months.

Statistical analysis using the Chi-square test revealed a highly significant association (p=0.0038), confirming that earlier presentation and intervention with PABMI leads to higher success rates.

Summary of radiological outcome

Overall radiological union rate was 87.5% (28/32), mean time to union was 16–24 weeks, significant factors; follow-up duration (p=0.02), time to surgery (p=0.021), and time to presentation (p=0.0038) and no infection, neurovascular injury, or donor site morbidity reported.

Table 6: Relationship between radiological union and time lapsed to presentation with non-union/delayed union after fixation.

Time to presentation (months)	Total cases	Radiological union
4–6	1	1
6–9	8	8
9–12	12	11
12–18	9	8
>18	2	0

Chi-square test results, p value is highly significant (p=0.0038), indicating a strong association between time to presentation with non-union/delayed union and the likelihood of radiological union after bone marrow injection. The earlier the patient presents with non-union or delayed union, the higher the chance of successful radiological healing.

DISCUSSION

The management of delayed and non-union of long bones continues to pose a significant challenge in orthopaedic practice, particularly when mechanical stability is adequate, but biological activity at the fracture site is diminished. The present study demonstrates that PABMI is an effective and minimally invasive biological augmentation technique for achieving union in such cases.

Efficacy of PABMI

In this series, radiological unions were achieved in 87.5% of cases within 24 weeks of PABMI. The rate of union progressively increased with follow-up duration — from 3.1% at 4 weeks to 87.5% at 24 weeks (p=0.02). These findings corroborate the observations of Connolly et al who reported an 85% success rate using bone marrow aspirate for tibial non-union, and Hernigou et al who achieved 90% union in long bone non-unions with bone marrow concentrate. The results thus reinforce that adequate osteoprogenitor cell content in the aspirate can initiate and sustain bone healing in a biologically compromised environment.[8,9]

Influence of timing

The current study highlights the critical importance of timing in both surgical fixation and biological intervention. Patients operated within 1 week of injury achieved 100% union, compared to 50% in those treated after 4 weeks (p=0.021). Similarly, earlier presentation for PABMI (<12 months) yielded significantly higher union rates (p=0.0038).

These findings are consistent with the principle that earlier stimulation of the osteogenic cascade enhances marrow-derived cellular response, while delayed intervention allows progressive biological exhaustion and fibrous tissue maturation at the fracture gap.[9]

Comparison with previous studies

The union rate of 87.5% in this study compares favorably with previous reports. Connolly et al reported 85% union rate in tibial non-unions treated with bone marrow aspirate, Hernigou et al reported 90% success rate with concentrated bone marrow injections and Garg et al reported 86% radiological union in long bone delayed unions.

Minor variations in reported rates may be attributed to differences in patient selection, injection volume, and concentration of osteoprogenitor cells used.

Mechanism of healing

Bone marrow aspirate contains mesenchymal stem cells (MSCs), osteoprogenitor cells, and growth factors such as BMPs and PDGF, which act synergistically to promote osteogenesis. When injected into the fracture site, these cells differentiate into osteoblasts and enhance callus formation.[10-14] This mechanism explains the gradual but steady improvement in union rates observed between 8 and 24 weeks in this study.

Safety and advantages

No major complications were observed in this series. Only mild transient donor-site pain was noted in a few cases, which resolved spontaneously. The procedure avoids donor-site morbidity, extensive dissection, and risks associated with open bone grafting. It is minimally invasive, repeatable, and cost-effective, making it suitable for resource-limited settings.[15,16]

Limitations

The primary limitation of this study is the relatively small sample size and short follow-up period. Quantitative assessment of the cellular content of the aspirate was not performed, which might influence the reproducibility of results. Future studies incorporating bone marrow concentration techniques and objective cellular quantification could provide greater insight into dose-response relationships.[17-19]

CONCLUSION

PABMI is a safe, simple, and effective biological method for promoting fracture healing in cases of delayed and non-union of long bones. The technique provides a minimally invasive alternative to open bone grafting, with negligible morbidity and no requirement for additional fixation procedures.

In this study, a progressive increase in radiological unions was observed over 24 weeks, achieving an overall success rate of 87.5%. The results demonstrate that earlier intervention after fixation and timely presentation for treatment significantly improve union rates.

PABMI effectively harnesses the osteogenic potential of autologous marrow cells to reactivate biological activity at the fracture site, thereby enhancing consolidation without surgical morbidity. Hence, it should be considered a first-line biological adjunct in the management of delayed and non-union of long bones before resorting to open grafting procedures.

Recommendations

Further research with larger sample sizes, longer follow-up durations, and quantitative analysis of osteoprogenitor cell concentration is warranted to better define the biological dose–response relationship of PABMI. The incorporation of bone marrow concentration techniques, growth factor assays, and comparative studies with platelet-rich plasma or stem cell grafting could provide deeper insight into optimizing outcomes. Future studies should also explore cost-effectiveness, repeat injection protocols, and the potential of image-guided precision delivery to further enhance the success of this minimally invasive technique.

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