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Original Research Article

Accelerating Fracture Healing in Delayed Uniting Fractures: A Clinical Study

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Abstract: ***Background:*** Delayed union fractures pose a significant clinical challenge, often requiring enhanced treatment modalities to accelerate healing and improve patient outcomes. Various techniques, including autologous bone grafting and biologic agents like platelet-rich plasma (PRP) and bone morphogenetic proteins (BMPs), have been employed to stimulate bone regeneration. However, the optimal approach remains debated. ***Objective:*** This study aimed to compare the efficacy of autologous bone grafting, biologic agents, and combined therapies in promoting fracture healing, reducing pain, improving functional outcomes, and enhancing patient satisfaction in delayed union fractures. ***Methods:*** A prospective study was conducted on 80 patients with delayed union fractures. Patients were randomly assigned to one of four groups: standard care (control), autologous bone grafting, biologic agents (PRP and BMPs), or a combination of bone grafting and biologic agents. Radiographic healing was assessed at 6, 12, and 24 weeks. Pain intensity was measured using the Visual Analog Scale (VAS), functional outcomes were assessed using the AAOS lower limb function scale, and patient satisfaction was evaluated using a Likert scale. ***Results:*** The combined therapy group exhibited significantly faster radiographic healing, with 80% of patients showing callus formation at 6 weeks and 95% achieving complete union at 24 weeks, compared to 35% in the control group. The combined group also reported the greatest reduction in VAS pain scores, with a mean decrease from 7.8 to 1.5 at 24 weeks ($p<0.001$). Functional outcomes were significantly improved in the combined group, with a mean AAOS score of 100 at 24 weeks, compared to 70 in the control group ($p<0.001$). Additionally, 90% of patients in the combined group reported high satisfaction, compared to 40% in the control group. ***Conclusion:*** The combination of autologous bone grafting and biologic agents, such as PRP and BMPs, significantly accelerates fracture healing, reduces pain, improves function, and enhances patient satisfaction in delayed union fractures. This multimodal approach should be considered in cases where traditional methods are insufficient. Further research is warranted to assess the long-term benefits and cost-effectiveness of these interventions.

Keywords: Delayed Union, Fracture Healing, Bone Grafting, Platelet-Rich Plasma, Biologic Agents, Orthopedic Surgery.

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INTRODUCTION

Fractures are one of the most common musculoskeletal injuries, affecting individuals across various age groups and activity levels. While most fractures heal successfully within the expected timeframe, a subset of patients experience delayed union, defined as the failure of a fracture to progress towards healing after a defined period. Delayed union can lead to prolonged pain, increased healthcare costs, and a

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significant impact on patients' quality of life. Identifying effective interventions to accelerate fracture healing in these cases is crucial to improving patient outcomes and reducing the burden on healthcare systems [1].

The process of bone healing is complex and involves a series of biological and mechanical events that promote the regeneration of bone tissue. The healing process typically occurs in three phases: the inflammatory phase, the reparative phase, and the remodeling phase. During the inflammatory phase, the fracture site becomes vascularized, and inflammatory cells migrate to the area, laying the groundwork for subsequent healing. In the reparative phase, mesenchymal stem cells differentiate into chondrocytes and osteoblasts, producing a soft callus that is later replaced by a hard callus. Finally, the remodeling phase involves the gradual replacement of woven bone with lamellar bone, restoring the original bone architecture [2].

Several factors can contribute to delayed union, including the severity of the fracture, patient comorbidities, and the presence of infection or other complications. Local biological factors such as inadequate blood supply, poor bone quality, and the mechanical environment at the fracture site also play significant roles in the healing process. In cases where standard conservative management fails to achieve satisfactory healing, more aggressive interventions may be required to stimulate bone regeneration [3].

Recent advancements in orthopedic treatment modalities have introduced various strategies to enhance fracture healing. One such approach involves the use of biologic agents, including platelet-rich plasma (PRP) and bone morphogenetic proteins (BMPs), which have been shown to promote osteogenesis and enhance the healing environment. PRP is derived from the patient's own blood and contains a high concentration of growth factors that can stimulate cellular activities critical for bone repair. Similarly, BMPs are proteins that have the ability to induce bone formation and can be applied directly at the fracture site to promote healing [4].

In addition to biologic agents, surgical interventions such as bone grafting have also gained traction in managing delayed union fractures. Autologous bone grafts, harvested from the patient's own body, provide a biological scaffold that supports new bone formation and enhances vascularization at the fracture site. This method not only improves the likelihood of healing but also decreases the risk of complications associated with foreign materials [5].

A multidisciplinary approach, combining surgical intervention and biologic agents, is increasingly recognized as an effective strategy for treating delayed union fractures. This approach aims to create an optimal healing environment by addressing both mechanical stability and biological factors. Evidence from recent clinical studies suggests that the combined use of bone grafting and biologic agents can significantly accelerate fracture healing and improve functional outcomes [6].

Despite the promising results from previous studies, the exact mechanisms by which these interventions enhance healing remain poorly understood. Additionally, variability in treatment protocols and patient populations complicates the generalization of findings across different settings. Thus, further investigation is warranted to elucidate the most effective combinations of interventions for patients with delayed union fractures.

The current study aims to evaluate the effectiveness of a multidisciplinary treatment approach that includes surgical bone grafting combined with biologic agents in accelerating fracture healing in patients diagnosed with delayed union. By assessing clinical and radiographic outcomes, this study seeks to contribute to the growing body of literature on optimal strategies for managing delayed union fractures and improving patient care in orthopedic practice.

METHODS

Study Design

This study was designed as a prospective, randomized, comparative trial conducted over a period of 12 months at a tertiary care orthopedic center. The objective was to evaluate the effectiveness of a multidisciplinary approach to accelerate fracture healing in patients diagnosed with delayed union fractures. This approach involved the use of surgical intervention, specifically autologous bone grafting, in combination with biologic agents, including platelet-rich plasma (PRP) and bone morphogenetic proteins (BMPs).

Participants

A total of 80 patients with delayed union fractures were enrolled in the study. The diagnosis of delayed union was confirmed through clinical assessment and radiographic evaluation, where fractures had not shown signs of progression toward healing after a minimum of 12 weeks of conservative treatment. Patients eligible for inclusion were aged between 18 and 65 years and had stable fractures without any significant comorbidities that could affect healing.

Exclusion criteria included patients with active infections, malignancies, metabolic bone disorders, previous non-union surgeries, or those undergoing anticoagulant therapy. Additionally, patients with a history of substance abuse or non-compliance with medical advice were also excluded to ensure the integrity of the study results.

Sampling Procedure

Participants were randomly assigned to one of four treatment groups using a computer-generated

randomization sequence to ensure unbiased allocation. The randomization process aimed to create equivalent groups in terms of demographic characteristics and fracture types to minimize confounding variables.

1. **Control Group (n=20)**: Received standard care with immobilization using a cast or splint.
2. **Bone Grafting Group (n=20)**: Underwent surgical intervention involving autologous bone grafting in addition to standard care.
3. **Biologic Agents Group (n=20)**: Received PRP and BMP treatment alongside standard care.
4. **Combined Therapy Group (n=20)**: Received both autologous bone grafting and biologic agents in addition to standard care.

Study Procedure

Control Group: Patients in this group received standard immobilization of the fracture using either a cast or a splint, along with pain management and regular follow-ups to monitor healing.

Bone Grafting Group: Patients underwent surgical intervention where autologous bone grafts were harvested from the iliac crest. The graft was then applied to the fracture site during open reduction and internal fixation (ORIF) surgery. The surgical procedure involved careful exposure of the fracture site, followed by the placement of the graft to enhance the biological healing process.

Biologic Agents Group: This group received a combination of PRP and BMPs. PRP was prepared from the patient's own blood using a centrifuge to concentrate on the platelets. This concentrated PRP was injected directly into the fracture site at the time of surgery. BMPs, specifically BMP-2, were also applied to the fracture site to stimulate osteogenesis and promote healing.

Combined Therapy Group: Patients in this group underwent the same surgical procedure as the bone grafting group but also received PRP and BMPs. The application of both bone grafting and biologic agents aimed to maximize the potential for bone regeneration and enhance healing outcomes.

Outcome Measures

The primary outcomes assessed in this study were:

1. **Radiographic Healing**: Fracture healing was evaluated radiographically at 6-, 12-, and 24-weeks post-treatment. Radiographs were examined for evidence of callus formation, alignment, and bridging across the fracture site by two independent radiologists who were blinded to group allocation. The presence of bridging callus and cortical continuity was used as the criteria for determining fracture union.
2. **Pain Assessment**: Pain intensity was measured using the Visual Analog Scale (VAS) before treatment and at each follow-up interval (6, 12, and 24 weeks). Patients rated their pain on a scale from 0 (no pain) to 10 (worst pain imaginable).
3. **Functional Outcomes**: Functional improvement was assessed using the American Academy of Orthopaedic Surgeons (AAOS) lower limb function scale and the range of motion (ROM) at the fracture site. These assessments were conducted at the same intervals as pain assessments.
4. **Patient Satisfaction**: At the 24-week follow-up, patient satisfaction was evaluated using a five-point Likert scale, ranging from "very dissatisfied" to "very satisfied." This measure aimed to capture patients' perceptions of their recovery and overall treatment experience.

Data Analysis

Statistical analysis was performed using SPSS software (version 26.0). Descriptive statistics, including means and standard deviations, were calculated for demographic and clinical variables. Differences among groups in terms of radiographic healing, pain scores, and functional outcomes were assessed using Analysis of Variance (ANOVA) for continuous variables, with post-hoc testing conducted where applicable. Chi-square tests were used to analyze categorical variables such as patient satisfaction.

Intra-group comparisons (baseline to follow-up changes) were analyzed using paired t-tests. Statistical significance was established at a p-value of <0.05. A power analysis was performed prior to the study to ensure that the sample size was adequate to detect clinically significant differences between groups.

RESULTS

A total of 80 patients were enrolled in the study, with an equal number of participants (n=20) in each treatment group. The demographic characteristics of patients, including age and gender, are presented in Table 1. The mean age of participants was similar across all groups, and there was no significant difference in gender distribution ($p>0.05$). The majority of the patients were male, accounting for about 60-65% in each group. (Table 1)

Table 1: Demographic Profile of the Study Patients

Characteristic	Control Group (n=20)	Bone Grafting Group (n=20)	Biologic Agents Group (n=20)	Combined Therapy Group (n=20)	p-value
Mean Age (years)	42.8 ± 10.5	43.3 ± 9.8	42.6 ± 11.1	43.0 ± 10.0	0.75
Gender Male Female	 12(60%) 8(40%)	 13(65%) 7(35%)	 12(60%) 8(40%)	 13(65%) 7(35%)	0.82

Radiographic healing was assessed at 6, 12, and 24 weeks post-treatment. The proportion of patients showing evidence of callus formation and fractured union in each group is shown in Table 2. At the 6-week mark, the combined therapy group had the highest percentage of patients demonstrating callus formation (80%), significantly higher than the control group (25%) ($p<0.01$). By 24 weeks, 95% of patients in the combined therapy group achieved fracture union compared to only 35% in the control group ($p<0.001$). (Table 2)

Table 2: Radiographic Healing of the Study Patients

Time Point	Control Group (n=20)	Bone Grafting Group (n=20)	Biologic Agents Group (n=20)	Combined Therapy Group (n=20)	p-value
Callus Formation at 6 weeks (%)	25%	45%	40%	80%	<0.01
Fracture Union at 12 weeks (%)	35%	70%	60%	95%	<0.001
Fracture Union at 24 weeks (%)	35%	85%	80%	95%	<0.001

Pain levels were assessed using the Visual Analog Scale (VAS). The mean VAS scores for each group at baseline, 6, 12, and 24 weeks are displayed in Table 3. Patients in the combined therapy group showed the greatest reduction in pain, with mean VAS scores decreasing from 7.5 at baseline to 2.0 at 12 weeks, and further to 1.5 at 24 weeks ($p<0.001$). In contrast, the control group reported a more modest reduction in pain, with VAS scores decreasing from 7.4 to 5.5 at 24 weeks ($p<0.05$). (Table 3)

Table 3: Pain Reduction Level of the Study Patients

Time Point	Control Group (n=20)	Bone Grafting Group (n=20)	Biologic Agents Group (n=20)	Combined Therapy Group (n=20)	p-value
Baseline VAS Score	7.4 ± 1.2	7.5 ± 1.1	7.3 ± 1.3	7.5 ± 1.2	0.88
VAS at 6 weeks	6.5 ± 1.0	5.0 ± 1.1	5.2 ± 1.0	3.5 ± 1.1	<0.05
VAS at 12 weeks	5.8 ± 1.2	4.0 ± 1.2	4.3 ± 1.1	2.0 ± 0.8	<0.01
VAS at 24 weeks	5.5 ± 1.1	3.5 ± 1.0	3.8 ± 0.9	1.5 ± 0.7	<0.001

Functional improvement was measured using the American Academy of Orthopaedic Surgeons (AAOS) lower limb function scale. The results are presented in Table 4. At 24 weeks, the combined therapy group showed the greatest improvement in functional scores, with a mean increase of 60 points from baseline, compared to an improvement of only 30 points in the control group ($p<0.001$). (Table 4)

Table 4: Functional Improvement of the Study Patients

Time Point	Control Group (n=20)	Bone Grafting Group (n=20)	Biologic Agents Group (n=20)	Combined Therapy Group (n=20)	p-value
Baseline AAOS Score	40 ± 10	39 ± 11	41 ± 9	40 ± 10	0.75
AAOS at 12 weeks	55 ± 12	65 ± 10	63 ± 11	75 ± 9	<0.01
AAOS at 24 weeks	70 ± 10	85 ± 8	83 ± 9	100 ± 5	<0.001

At the 24-week follow-up, patient satisfaction was assessed using a Likert scale. The combined therapy group reported the highest satisfaction rates, with 90% of patients rating their satisfaction as "very satisfied" or "satisfied," compared to 40% in the control group ($p<0.001$) (Table 5).

Table 5: Satisfaction Level of the Study Patients

Satisfaction Level	Control Group (n=20)	Bone Grafting Group (n=20)	Biologic Agents Group (n=20)	Combined Therapy Group (n=20)	p-value
Very satisfied (%)	20%	55%	60%	75%	<0.01
Satisfied (%)	20%	25%	25%	15%	<0.05
Neutral or Dissatisfied (%)	60%	20%	15%	10%	<0.001

DISCUSSION

The primary goal of this study was to evaluate the efficacy of different treatment modalities, standard care, autologous bone grafting, biologic agents, and combined therapy in promoting fracture healing in patients with delayed union fractures. Our results demonstrated that the combined approach of using autologous bone grafting along with biologic agents

(PRP and BMPs) resulted in significantly faster fracture healing, greater pain reduction, improved functional outcomes, and higher patient satisfaction compared to standard care or the use of either modality alone. These findings align with and expand upon existing literature on fracture management, further reinforcing the role of combined interventions in accelerating bone healing.

The radiographic assessment of fracture healing revealed that the combined therapy group had the highest percentage of patients demonstrating callus formation at 6 weeks (80%), and 95% of these patients achieved complete fracture union by 24 weeks. This outcome is consistent with findings from previous studies that have demonstrated the synergistic effects of combining autologous bone grafting with biologic agents. In a study reported that the use of BMPs in conjunction with bone grafts resulted in enhanced callus formation and faster fracture consolidation compared to bone grafts alone [7]. The application of PRP and BMPs in non-union fractures, concluding that patients receiving both interventions showed significantly faster healing than those treated with either PRP or BMPs alone. In our study, the group receiving biologic agents alone (PRP and BMPs) also showed a higher rate of fracture union (80%) by 24 weeks compared to the control group (35%), highlighting the effectiveness of these agents in enhancing osteogenesis. However, when used in combination with bone grafting, the benefits were even more pronounced [8].

This synergistic effect can be attributed to the complementary mechanisms of bone grafting and biologic agents. Autologous bone grafts provide a scaffold for new bone formation, while PRP and BMPs act as biological stimulators that enhance cell proliferation, differentiation, and angiogenesis at the fracture site. These combined effects accelerate the bone remodeling process, leading to faster and more robust healing.

Pain reduction, as measured by the Visual Analog Scale (VAS), was significantly greater in the combined therapy group compared to all other groups. At 24 weeks, the mean VAS score in the combined group was 1.5, compared to 5.5 in the control group. This significant reduction in pain aligns with the results of previous studies that have evaluated the analgesic effects of PRP and BMPs in fracture management. Patients treated with PRP reported faster pain relief compared to those treated with conventional methods, due to PRP's anti-inflammatory properties and its ability to enhance tissue regeneration [9]. The use of BMPs not only accelerates fracture healing but also reduces the need for secondary interventions and pain management, likely due to the faster restoration of structural integrity at the fracture site [10]. Our study's findings are consistent with this literature, suggesting that biologic agents, particularly when combined with bone grafts, may offer a dual benefit of reducing pain and promoting faster healing.

Functional outcomes, as assessed by the AAOS lower limb function scale, further highlighted the superiority of combined therapy. At 24 weeks, the mean AAOS score in the combined group was 100, indicating near-complete functional recovery, compared to 70 in the control group. This significant improvement in function can be attributed to faster fracture healing and reduced pain, which allowed patients in the combined therapy group to resume normal activities more quickly.

Some other study reported that patients treated with bone grafts and BMPs show greater improvements in mobility and functional outcomes compared to those receiving standard care. These studies highlighted that biologic agent, such as BMPs, promote not only bone healing but also soft tissue regeneration, which may contribute to improved function in the affected limb. In our study, the bone grafting and biologic agent groups also demonstrated significant functional improvements (AAOS scores of 85 and 83, respectively), although these improvements were not as pronounced as in the combined group [11].

Patient satisfaction at the 24-week follow-up further supported the effectiveness of the combined approach. A total of 90% of patients in the combined therapy group rated their satisfaction as "very satisfied" or "satisfied," compared to only 40% in the control group. This finding is in line with some other studies who found that patients receiving biologic therapies, such as PRP and BMPs, were more satisfied with their treatment outcomes due to faster recovery times and less post-treatment pain [12,13].

Interestingly, patient satisfaction correlated closely with both functional outcomes and pain reduction, suggesting that the faster return to daily activities and lower levels of discomfort were key drivers of satisfaction. While both the bone grafting and biologic agent groups reported higher satisfaction than the control group, the combination of these two interventions appeared to provide the most substantial benefits in terms of overall recovery, thus leading to higher levels of patient-reported satisfaction.

CONCLUSION

In conclusion, this study provides strong evidence that the combination of autologous bone grafting and biologic agents, such as PRP and BMPs, is highly effective in accelerating fracture healing, reducing pain, and improving functional outcomes in patients with delayed union fractures. These findings are consistent with other published studies and suggest that a multimodal approach should be considered in challenging cases of fracturing non-union or delayed union. Future research should focus on the long-term

outcomes of these interventions and explore their cost-effectiveness to further guide clinical decision-making.

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