## Review Paper

# Exploring the Role of Orthobiologic Agents in Promoting Scaphoid Nonunion Healing: A Narrative Review

**Morteza Behjat[1], Alireza Pahlevan Sabagh[1*]**

*1. Department of Orthopedics, Bone and Joint Reconstruction Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.*

Use your device to scan and read the article online

**Citation** Behjat M, Pahlevan Sabagh A. Exploring the Role of Orthobiologic Agents in Promoting Scaphoid Nonunion Healing: A Narrative Review. Journal of Research in Orthopedic Science. 2024; 11(2):77-82. http://dx.doi.org/10.32598/JROSJ.11.2.1358.3

**http://dx.doi.org/10.32598/JROSJ.11.2.1358.3**

**Article info:**
Received: 18 Jan 2024
Revised: 29 Jan 2024
Accepted: 25 Feb 2024
Available Online: 01 May 2024

**Keywords:**
Orthobiologic, Scaphoid fracture, Nonunion, Platelet-rich plasma (PRP), Bone morphogenetic protein (BMP)

## ABSTRACT

Scaphoid fractures are common carpal fractures that often result in associated nonunion or delayed union. Traditional treatment typically involves prolonged immobilization with a cast, which can result in joint stiffness and reduced mobility. Currently, fixation with a headless compression screw is the standard treatment for scaphoid fractures, often combined with volar plates for added stability. Orthobiologic therapies, such as platelet-rich plasma (PRP) and bone morphogenetic proteins (BMPs), have shown promise in enhancing fracture union and improving long-term patient outcomes. However, the use of orthobiologics in treating scaphoid nonunion yields contradictory results, making it difficult to draw a definitive conclusion.

*** Corresponding Author:**
*Alireza Pahlevan Sabagh, Associate Professor.*
***Address:*** *Department of Orthopedics, Bone and Joint Reconstruction Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.*
***Phone:*** *+98 (913) 1156477*
***E-mail:*** *pahlevansabagh@gmail.com*

## Introduction

Scaphoid fractures are among the most frequently encountered carpal fractures, often accompanied by complications such as nonunion or delayed union [1]. These fractures are highly prevalent and typically present with pain, functional impairment, and limited wrist mobility [2]. Conventional treatment often involves prolonged immobilization with a cast, which can lead to joint stiffness, further motion restriction, and delays in returning to work or daily activities [3, 4].

To address these challenges, novel orthobiologic therapies have been investigated, demonstrating the potential to accelerate fracture and nonunion healing. Platelet-rich plasma (PRP) is one such treatment that has shown promise in a limited number of studies for enhancing fracture union and improving long-term patient outcomes [5, 6]. Additionally, bone morphogenetic proteins (BMPs) have been utilized to promote union in lumbar fusions and tibial fractures [7, 8]. However, their effectiveness in reducing scaphoid nonunion has produced mixed results.

This narrative review aims to evaluate the clinical and functional outcomes reported in studies examining the application of orthobiologic therapies in the management of scaphoid nonunions.

### Current treatment of scaphoid fracture and nonunion

If a scaphoid fracture is minimally displaced, immobilization through casting or a splint is a common treatment approach [9]. However, fracture union with this method typically requires 8 to 12 weeks, a duration that may be inconvenient for young and active individuals [10]. Once a union is achieved, hand physiotherapy can commence to restore function [9]. However, complications such as muscle atrophy, joint stiffness, and diminished grip strength may arise, potentially delaying the patient's return to work and normal daily activities [11].

Various surgical fixation methods, including screws, bone grafts, and alternative approaches, have been discussed in the literature [12, 13]. Bone grafting, often sourced from the radius, is employed to enhance blood supply to the fracture site [14]. Screw fixation, particularly with headless compression screws inserted along the central longitudinal axis of the scaphoid, provides structural stability by compressing fracture fragments and preventing bending at the site [15]. This method is the most common fixation technique for scaphoid fractures [12]. Kirschner wires (K-wires) may also be used for stabilization, particularly in cases of ligamentous instability or minor soft tissue injuries [11]. However, K-wires are associated with risks such as pin site infections, stiffness, and the potential need for reoperation [12]. For fractures with significant comminution or bone loss, volar plating can provide additional support [14].

Overall, internal fixation methods achieve high union rates, typically ranging from 85% to 90%, and enable an earlier return to activity compared to non-surgical approaches [11, 15]. Nevertheless, complications such as vascular injury or fracture instability can contribute to nonunion, requiring advanced treatment strategies [12]. In cases of nonunion, salvage procedures such as proximal row carpectomy, scaphoid excision with arthrodesis, or total wrist fusion may be necessary. However, these methods often result in permanent limitations to wrist function [14].

Currently, fixation with a headless compression screw, with or without bone grafting, is considered the standard treatment for scaphoid fractures [14, 16]. If additional stability is required, a volar plate can be combined with screw fixation to provide extra support [14]. These combined techniques aim to address both the structural and vascular challenges associated with scaphoid fractures while minimizing long-term complications.

### BMP for scaphoid nonunion

Bilic et al. [17] conducted a study in 2006 involving 17 patients diagnosed with proximal scaphoid nonunion. The participants were randomly allocated into three distinct treatment groups: 6 patients received an autologous iliac crest bone graft, another 6 received an autologous iliac crest bone graft supplemented with osteogenic protein 1 (OP-1, also known as BMP-7), and the remaining 5 were treated with an allogenic iliac crest bone graft combined with OP-1. Radiographic and clinical evaluations were performed over a 24-month follow-up period. The findings demonstrated that human recombinant OP-1 (or BMP-7) facilitated the repair of proximal scaphoid nonunions by promoting bone angiogenesis and replacing sclerotic bone caused by avascular necrosis. Patients treated with autologous bone and OP-1 showed significantly enhanced radiological healing and reduced healing times, achieving union in 4 weeks compared to 9 weeks for those treated with autologous bone alone. This reduction in healing time has the potential to shorten the immobilization period, thereby decreasing the risk of complications such as radiocarpal and radioulnar arthritis, joint stiffness, and Sudeck's atrophy. It also minimizes muscle atrophy in the forearm and hand, allowing for a quicker return to work. In group 3 (allogenic graft with OP-1), radiographic improvement was observed at 8 weeks post-surgery, outperforming group 1 (autologous graft alone). This result suggests that combining allogenic bone grafts with OP-1 can eliminate the need for autologous grafts, which are associated with donor site complications, including increased surgical blood loss, postoperative pain, and an increased risk of infection. Additionally, OP-1 significantly improved the functional performance of the injured hand compared to autologous grafting alone.

Conversely, a study by Chevet-Noël et al. [18] investigated 5 patients (mean age: 32 years, range: 21–44 years) with old scaphoid nonunion (over 24 months) following unsuccessful autograft treatment. The treatment involved reaming the nonunion site, applying a bone autograft supplemented with BMP-7 at the defect, and stabilizing it with a screw or K-wire, followed by postoperative immobilization. Despite a long average follow-up of 10 years (ranging from 80 to 143 months), only one patient (20%) achieved bone union. Functional outcomes revealed an average flexion-extension loss of 16.68 degrees (range: 0–30 degrees) and average hand strength reductions of 450 g (range: 0–2000 g) for pinch and 12.1 kg (range: 0–29 kg) for grip compared to the contralateral hand. The mean patient-rated wrist evaluation (PRWE) score was 28.9 (range: 10.5–49), and the mean QuickDASH (disabilities of the arm, shoulder, and hand) score was 28.6 (range: 9.09–61.36). The study concluded that BMP-7 offered no significant advantages for treating old scaphoid nonunion, particularly given its high cost and limited success.

In 2015, Ablove et al. [19] performed a retrospective analysis to assess the outcomes of 4 patients who experienced failed open reduction and internal fixation (ORIF) for scaphoid fractures. Of these cases, three involved fractures at the scaphoid waist, while one was located at the proximal pole. All patients underwent screw replacement and placement with the addition of BMP-2, without the need for supplementary bone grafting. Patients were immobilized for four weeks, with serial radiographs taken for all and follow-up computed tomography (CT) scans in three cases. Union was achieved in all patients within an average of 53 days post-surgery, and they eventually returned to full, pain-free activity. No complications were reported, and the use of BMP-2 and screw exchange resulted in a 100% union rate. Although the study was limited by its small sample size and retrospective design, it highlights a potentially effective approach for managing scaphoid nonunion.

In a 2016 retrospective study by Brannan et al. [20], 6 cases of revision surgery for scaphoid nonunion were examined. These patients, who had persistent nonunion following initial ORIF for scaphoid fractures, were treated with revision screw surgery, bone grafting, and recombinant human BMP-2 (rhBMP-2). Union was confirmed via CT scans in all cases. However, complications were common, including persistent nonunion (2 cases), significant heterotopic ossification (4 cases, with 1 requiring revision surgery), and loss of functional movement (1 case). Two patients with persistent nonunion underwent scaphoidectomy and midcarpal arthrodesis. Notably, delayed wound healing was not observed in any of the cases. Only 1 out of 6 patients healed without complications. The time between the initial injury and the first ORIF ranged from 3 months to 4 years, with an average of 24 months. Despite the high union rate, the study highlighted significant challenges, particularly the high prevalence of heterotopic ossification and other complications. These findings suggest that while rhBMP-2 shows potential in scaphoid nonunion revision surgeries, its risks and limitations warrant further investigation.

### PRP for scaphoid nonunion

In a 2016 study by Namazi et al. [21], a randomized controlled trial was conducted involving 14 patients with Herbert type B2 scaphoid fractures. Participants were divided into two groups, with one group receiving intra-articular injections of 1.5 mL PRP and the other receiving 1.5 mL normal saline. Both groups were subsequently immobilized with long-arm casts. Radiological evaluations were performed at 2-week and 2-month follow-ups, and CT scans were conducted at the 2-month follow-up to assess fracture union. Clinical assessments were performed using the PRWE questionnaire for pain and functional outcomes, as well as measurements of range of motion at 3 and 6 months post-treatment. The results demonstrated significant improvements in pain at rest and during specific activities in the PRP group compared to the control group. However, no statistically significant differences were observed in wrist movements, including radial and ulnar deviation, flexion, and extension, except for an improvement in ulnar deviation at the 3-month follow-up. Although scaphoid union appeared to occur earlier in the PRP group, the difference was not statistically significant.

In a separate study by de Vitis et al. [22] in 2020, patients undergoing surgical treatment for scaphoid fractures were divided into two groups. Group A underwent osteosynthesis via the volar approach using shape memory staples (SMS), while Group B received SMS combined with gelled PRP (GPRP) at the bone defect site. Both groups underwent cast immobilization (without including the thumb) for 4 weeks. Outcomes were assessed based on pain levels, QuickDASH scores, Mayo wrist scores, and radiographic evaluations. Bone union was observed in 95.2% of patients in group A (40 out of 42) and in 100% of patients in group B (45 out of 45). Group B demonstrated a statistically significant improvement in the Mayo wrist score, QuickDASH score, and pain levels (as measured by the visual analog scale, [VAS]) at 3 months post-surgery (P = 0.02). These findings suggest that the addition of GPRP to SMS osteosynthesis may enhance both clinical and functional outcomes in the treatment of scaphoid fractures.

In a retrospective study conducted by Zhong et al. [23] in 2023, patients with grade III (25 patients) and grade IV (28 patients) scaphoid nonunions (SNU) were evaluated based on the Slade and Dodds classification. The study included patients treated between January 2015 and May 2020 using three different methods: Open bone grafting (BG) and internal fixation (group A), percutaneous screw fixation (group B), and percutaneous screw fixation combined with PRP injection (group C). Outcomes were assessed by comparing the fracture stabilization rate, VAS score for pain, and Mayo wrist function score among the three groups. The union rates for SNU grades III and IV did not differ significantly between the groups. However, patients in group C reported significantly less pain and better wrist function 7 days post-surgery compared to patients in groups A and B, for both grades of nonunion. At the 3-month follow-up, group C showed significantly superior VAS and Mayo wrist scores compared to group A across both grades, and also outperformed group B in cases of grade IV SNU. At 6 and 12 months after surgery, patients with grade IV SNU in groups A and C continued to exhibit notably better VAS and Mayo wrist scores than those in group B. In a case series by Aslam et al. [24], conducted from 2007 to 2011 at Hong Kong Hospital, 4 patients with scaphoid fractures were treated with ORIF, BG from the iliac crest, and PRP injections. The study included patients with an average age of 35.7±7.7 years (range: 31 to 47 years) and an average follow-up of 21.75±14.97 months (range: 5 months to 3.5 years). Clinical and radiological evaluations were conducted to assess union and pain-free range of motion. The results showed that all patients achieved union and restored pain-free wrist mobility, highlighting the potential of this combined approach in managing scaphoid fractures.

## Conclusion

After reviewing the articles mentioned above, it is evident that the use of orthobiologics in treating scaphoid nonunion yields contradictory results, making it difficult to draw a definitive conclusion. While some studies report improved union rates following the use of PRP or BMP, others show no significant differences in outcomes with the application of these agents. Moreover, potential complications associated with orthobiologics, such as heterotopic ossification and reduced wrist motion, warrant careful consideration. A major limitation of the current evidence lies in the retrospective nature and small sample sizes of most studies, which reduce the reliability and generalizability of their findings. To address these shortcomings, future research should prioritize well-designed randomized controlled trials with larger sample sizes to provide more robust and conclusive evidence. Additionally, further exploration of innovative therapeutic strategies is recommended. Potential strategies may involve creating advanced scaffolds that integrate vascular endothelial growth factor (VEGF) and BMPs or exploring the effectiveness of different BMP variants. These approaches have the potential to enhance the efficacy of orthobiologics in treating scaphoid nonunion while minimizing associated complications.

## Ethical Considerations

### Compliance with ethical guidelines

This article is a meta-analysis with no human or animal sample.

### Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

### Authors' contributions

Conceptualization, methodology, software, validation, formal analysis, investigation, resources, data curation, visualization and writing the original draft: Morteza Behjat; Supervision, project administration, funding acquisition, review and editing: Alireza Pahlevansabagh.

### Conflict of interest

The authors declared no conflict of interest.

## References

[1] Hackney LA, Dodds SD. Assessment of scaphoid fracture healing. Curr Rev Musculoskelet Med. 2011; 4(1):16-22. [DOI:10.1007/s12178-011-9072-0] [PMID]

[2] Al-Jabri T, Mannan A, Giannoudis P. The use of the free vascularised bone graft for nonunion of the scaphoid: A systematic review. J Orthop Surg Res. 2014; 9:21. [DOI:10.1186/1749-799X-9-21] [PMID]

[3] Bond CD, Shin AY, McBride MT, Dao KD. Percutaneous screw fixation or cast immobilization for nondisplaced scaphoid fractures. J Bone Joint Surg Am. 2001; 83(4):483-8. [DOI:10.2106/00004623-200104000-00001] [PMID]

[4] McQueen MM, Gelbke MK, Wakefield A, Will EM, Gaebler C. Percutaneous screw fixation versus conservative treatment for fractures of the waist of the scaphoid: A prospective randomised study. J Bone Joint Surg Br. 2008; 90(1):66-71. [DOI:10.1302/0301-620X.90B1.19767] [PMID]

[5] Murray DJ, Javed S, Jain N, Kemp S, Watts AC. Platelet-Rich-Plasma Injections in Treating Lateral Epicondylosis: A review of the recent evidence. J Hand Microsurg. 2015; 7(2):320-5. [DOI:10.1007/s12593-015-0193-3] [PMID]

[6] Namazi H, Mehbudi A. Investigating the effect of intra-articular PRP injection on pain and function improvement in patients with distal radius fracture. Orthop Traumatol Surg Res. 2016; 102(1):47-52. [DOI:10.1016/j.otsr.2015.11.002] [PMID]

[7] Dai J, Li L, Jiang C, Wang C, Chen H, Chai Y. Bone morphogenetic protein for the healing of tibial fracture: A meta-analysis of randomized controlled trials. Plos One. 2015; 10(10):e0141670. [DOI:10.1371/journal.pone.0141670] [PMID]

[8] Ong KL, Villarraga ML, Lau E, Carreon LY, Kurtz SM, Glassman SD. Off-label use of bone morphogenetic proteins in the United States using administrative data. Spine (Phila Pa 1976). 2010; 35(19):1794-800. [PMID]

[9] Suh N, Grewal R. Controversies and best practices for acute scaphoid fracture management. J Hand Surg Eur. 2018; 43(1):4-12. [DOI:10.1177/1753193417735973]

[10] Moatshe G, Godin JA, Chahla J, Cinque ME, Kennedy NI, Sanchez G, et al. Clinical and radiologic outcomes after scaphoid fracture: Injury and treatment patterns in national football league combine athletes between 2009 and 2014. Arthroscopy. 2017; 33(12):2154-8. [DOI:10.1016/j.arthro.2017.08.259] [PMID]

[11] Hohenberger GM, Berzins U, Bakota B, Holweg P, Clement B, Grechenig S. Scaphoid screw placement under minimal radiation exposure. Injury. 2017; 48(Suppl 5):S47-50. [PMID]

[12] Allon R, Kramer A, Wollstein R. Intramedullary Screw and Kirschner Wire Fixation for Unstable Scaphoid Non:union. J Hand Microsurg. 2016; 8(3):150-4. [DOI:10.1055/s-0036-1597550]

[13] Dedeoğlu SS, İmren Y, Çabuk H, Tekin AC, Türe YC, Gürbüz H. Results of percutaneous fixation and distal radius core decompression in scaphoid waist non-unions treated without grafting. Hand Surg Rehabil. 2018; 37(1):43-47. [DOI:10.1016/j.hansur.2017.11.001] [PMID]

[14] Dodds SD, Williams JB, Seiter M, Chen C. Lessons learned from volar plate fixation of scaphoid fracture non:union:s. J Hand Surg Eur Vol, 2017; 43(1):57-65. [DOI:10.1177/1753193417743636]

[15] Patel S, Tiedeken N, Qvick L, Debski RE, Kaufmann R, Fowler JR. Interfragmentary compression forces vary based on scaphoid bone screw type and fracture location. Hand. 2017; 14(3):371-6. [DOI:10.1177/1558944717745663]

[16] Luchetti TJ, Rao AJ, Fernandez JJ, Cohen MS, Wysocki RW. Fixation of proximal pole scaphoid nonunion: With non-vascularized cancellous autograft. J Hand Surg. 2017; 43(1):66-72. [DOI:10.1177/1753193417743438]

[17] Bilic R, Simic P, Jelic M, Stern-Padovan R, Dodig D, van Meerdervoort HP, et al. Osteogenic protein-1 (BMP-7) accelerates healing of scaphoid non-union with proximal pole sclerosis. Int Orthop. 2006; 30(2):128-34. [DOI:10.1007/s00264-005-0045-z] [PMID]

[18] Chevet-Noël A, Delord M, Bertrand D, Obert L, Lepage D, Pluvy I, et al. RhBMP7 use for treating scaphoid non-union: 5 cases assessed at 10 years' follow-up. Hand Surg Rehabil. 2020; 39(5):383-8. [DOI:10.1016/j.hansur.2020.06.001] [PMID]

[19] Ablove RH, Abrams SS. The use of BMP-2 and screw exchange in the treatment of scaphoid fracture non-union. Hand Surg. 2015; 20(1):167-71. [DOI:10.1142/S0218810415970023]

[20] Brannan PS, Gaston RG, Loeffler BJ, Lewis DR. Complications with the use of bmp-2 in scaphoid nonunion surgery. J Hand Surg Am. 2016; 41(5):602-8. [DOI:10.1016/j.jhsa.2016.01.013] [PMID]

[21] Namazi H, Kayedi T. Investigating the Effect of intra-articular platelet-rich plasma injection on union: Pain and function improvement in patients with scaphoid fracture. J Hand Microsurg. 2016; 8(3):140-4. [DOI:10.1055/s-0036-1597088]

[22] De Vitis R, Passiatore M, Perna A, Fioravanti Cinci G, Taccardo G. Comparison of shape memory staple and gelled platelet-rich plasma versus shape memory staple alone for the treatment of waist scaphoid nonunion: A single-center experience. Joints. 2020; 7(3):84-90. [DOI:10.1055/s-0040-1710387]

[23] Zhong Z, Wei M, Jiang Z, Chen J, He Y, Lin K. Comparative effectiveness of three treatment options for slade and dodds grade III-IV scaphoid nonunion: A retrospective study. BMC Musculoskelet Disord. 2023; 24(1):204. [DOI:10.1186/s12891-023-06320-1] [PMID]

[24] Aslam MZ, Ip J, Ahmed SK, Fung B. Role of platelet rich plasma in fracture non-union of scaphoid - case series. J Pak Med Assoc. 2021; 71(Suppl 5)(8):S103-6. **[PMID]**

This Page Intentionally Left Blank