Original Research

TERIPARATIDE-ASSISTED UNION IN DELAYED UNION AND INFECTED DELAYED UNION OF LONG-BONE SHAFT FRACTURES: A RETROSPECTIVE OBSERVATIONAL STUDY

Dr. Arjun A.[1], Dr. Mahesh J. Nerkar[2], Dr. Nitin N. Sunku[3], Dr. Prashanth Reddy P.[4*]

[1]Assistant Professor, Department of Orthopedic, Farookh Academy of Medical Education Hospital and Research Institute, Mysuru, Karnataka, India.

[2]Assistant Professor, Department of General Medicine, Farookh Academy of Medical Education Hospital and Research Institute, Mysuru, Karnataka, India.

[3]Assistant Professor, Department of Orthopedics, The Oxford Medical College, Hospital & Research Centre, Bangalore, Karnataka, India.

[4*]Assistant Professor, Department of Orthopedics, Farookh Academy of Medical Education Hospital and Research Institute, Mysuru, Karnataka, India.

Corresponding Author: Dr. Prashanth Reddy P.,
Assistant Professor, Department of Orthopedics, Farookh Academy of Medical Education Hospital and Research Institute, Mysuru, Karnataka, India.

ABSTRACT

Background: Delayed union of long-bone shaft fractures remains a persistent problem in trauma practice, especially in tibia and femur injuries with soft-tissue compromise. Teriparatide is a biologically plausible adjunct for fracture healing, but real-world evidence in delayed union cohorts remains heterogeneous.

Methods: We conducted a retrospective observational study of 50 adults with delayed union or infected delayed union of long-bone shaft fractures managed with stable fixation and teriparatide. Only diaphyseal fractures were included; intra-articular and metaphyseal fractures were excluded. Fractures were classified using Gustilo-Anderson (open fractures) and AO classification.

Results: Mean time from fracture to teriparatide initiation was 3.6+/-0.4 months. Mean radiological union time from teriparatide start was 3.5+/-0.6 months, and complete union from index surgery was 15.1+/-1.8 months overall. Six cases required revision surgery (femur n=3, tibia n=2, radius n=1); these showed prolonged union from index surgery (18.7+/-1.5 months) but achieved union within 5.0+/-0.6 months after revision.

Conclusion: Teriparatide may support fracture healing in delayed union when mechanical stability is maintained; open injuries and infected delayed union remain slower-healing subgroups.

Keywords: Teriparatide, Delayed Union, Infected Delayed Union, Long-Bone Shaft Fracture, Fracture Healing.

INTRODUCTION

Fracture healing is an ordered biologic process that depends on local stability, vascularity, and host response, progressing from inflammation to callus formation and remodeling.[1] When this progression slows or stalls, the clinician enters the difficult territory of delayed union, where radiographs show incomplete progression and confidence in spontaneous healing declines.

Definitions of delayed union and nonunion vary across studies, and this variation complicates direct comparison of treatment outcomes.[2]

In routine trauma practice, the distinction is often made pragmatically using serial radiographic stagnation, persistent pain on loading, and absence of progressive cortical bridging.

www.ajmrhs.com
eISSN: 2583-7761

Date of Received: 29-01-2026
Date Acceptance: 20-03-2026
Date of Publication: 25-03-2026

Open fractures add a separate layer of complexity because soft-tissue injury, contamination burden, and infection risk directly influence healing biology. The Gustilo-Anderson system continues to be the most widely used clinical framework for grading open injuries and anticipating complications.[3,4]

Risk-factor syntheses consistently identify infection, smoking, diabetes, and higher open-fracture severity as major contributors to delayed or failed union after surgical fixation.[5] Epidemiologic data also show that tibia and femur fractures contribute disproportionately to the nonunion burden.[6]

Teriparatide (recombinant human PTH 1-34) is established in osteoporosis treatment, but intermittent PTH signaling also supports osteoblast activity and callus maturation, making it biologically relevant to fracture repair.[7] Human clinical evidence remains mixed but encouraging, with randomized and observational studies suggesting faster radiological healing in selected fracture settings and delayed union cohorts.[8-10]

In this study, we aligned a retrospective cohort dataset to examine teriparatide-assisted healing in delayed union and infected delayed union of long-bone shaft fractures, with particular attention to timelines from index surgery, timelines from teriparatide initiation, and a separate revision timeline for cases requiring exchange fixation or grafting.

MATERIALS AND METHODS

Study Design and Setting: This was a retrospective observational study conducted in a tertiary orthopaedic trauma unit. Records of patients treated for delayed union of long-bone shaft fractures and prescribed teriparatide were reviewed.

Participants: Adults aged 18 years or older with long-bone shaft fractures showing delayed union or infected delayed union were eligible. Cases were included when stable fixation was present and serial follow-up radiographs were available.

Exclusion Criteria: Intra-articular fractures, metaphyseal fractures, pathological fractures, and isolated ulna fractures were excluded. The study cohort was restricted to long-bone shaft fractures only.

Fracture Classification: Open fractures were classified using the Gustilo-Anderson classification. Fracture morphology and shaft location were documented using AO classification. Tibia and femur cases included mid-shaft, distal-third shaft, and segmental patterns. Upper-limb cases included humeral shaft fractures and forearm fractures represented as radius-dominant shaft fixation in the dataset.

Fixation Method: Tibia and femur fractures were managed predominantly by closed reduction and intramedullary nailing (CRIF with nailing). Humerus and radius shaft fractures were managed by open reduction and internal fixation with plate constructs. External fixation was not used as the final fixation category in the aligned analysis dataset.

Teriparatide Protocol: Teriparatide was initiated after recognition of delayed union, typically around 3 to 5 months from the index fracture event. Timing from fracture to initiation was recorded in months.

Outcome Measures: Primary outcomes were radiological union timing and complete union timing. Radiological union was documented both from index surgery and from teriparatide initiation. Complete union from surgery was recorded for all cases. For revision cases, a separate field (complete union from revision surgery) was used to avoid timeline contradiction.

Revision-Case Handling: Cases requiring revision surgery were analyzed separately. This separation allowed biologically plausible reporting of prolonged union from index surgery and shorter union intervals after exchange nailing or revision plating with bone grafting.

Radiological Assessment Approach: Union was assessed on serial radiographs using cortical bridging progression and clinical correlation. A structured radiographic interpretation approach was used, and future prospective work should standardize scoring (for example, RUST/mRUST for tibia and adapted cortical bridging scoring for other shaft bones).

Statistical Analysis: Continuous variables are presented as mean +/- standard deviation and categorical variables as count (percentage). Subgroup comparisons for union duration were assessed using non-parametric testing where appropriate.

RESULTS

A total of 50 patients were included. The cohort was tibia-predominant, followed by femur fractures, which is consistent with long-bone delayed-union patterns in tertiary trauma practice.

Variable	Value
Age (years), mean +/- SD (range)	38.6 +/- 9.4 (22-60)
Sex: Male	42 (84.0%)
Sex: Female	8 (16.0%)
Bone involved: Tibia	20 (40.0%)
Bone involved: Femur	15 (30.0%)
Bone involved: Humerus	7 (14.0%)
Bone involved: Radius	8 (16.0%)
Fracture type: Closed	25 (50.0%)
Fracture type: Open	25 (50.0%)
Open fracture subtype: Gustilo Type I	11 (22.0%)
Open fracture subtype: Gustilo Type II	10 (20.0%)
Open fracture subtype: Gustilo Type IIIA	4 (8.0%)
Status at enrollment: Delayed union	44 (88.0%)
Status at enrollment: Infected delayed union	6 (12.0%)

Table 1. Baseline Demographics and Fracture Profile (N=50)

Table 1 summarizes the cohort composition. Tibia and femur together formed the majority of cases, and infected delayed union represented the revision subgroup in the aligned dataset.

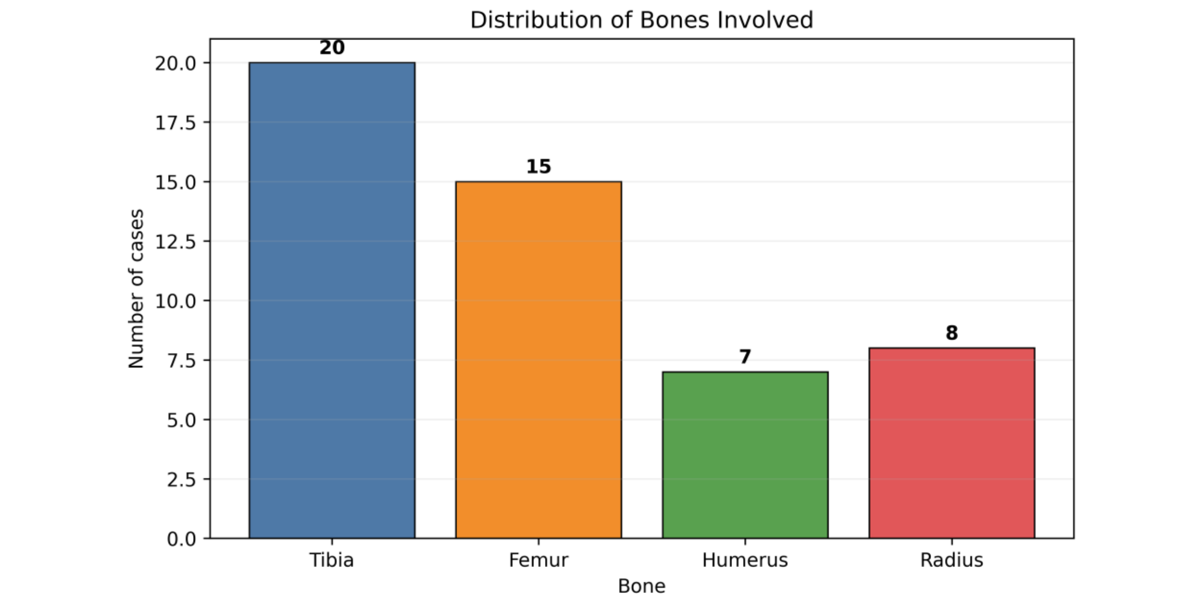

Figure 1. Distribution of bones involved in the cohort (bar chart with counts above bars)

The figure uses distinct colors for each bone category and shows the exact count over each bar for rapid visual reading.

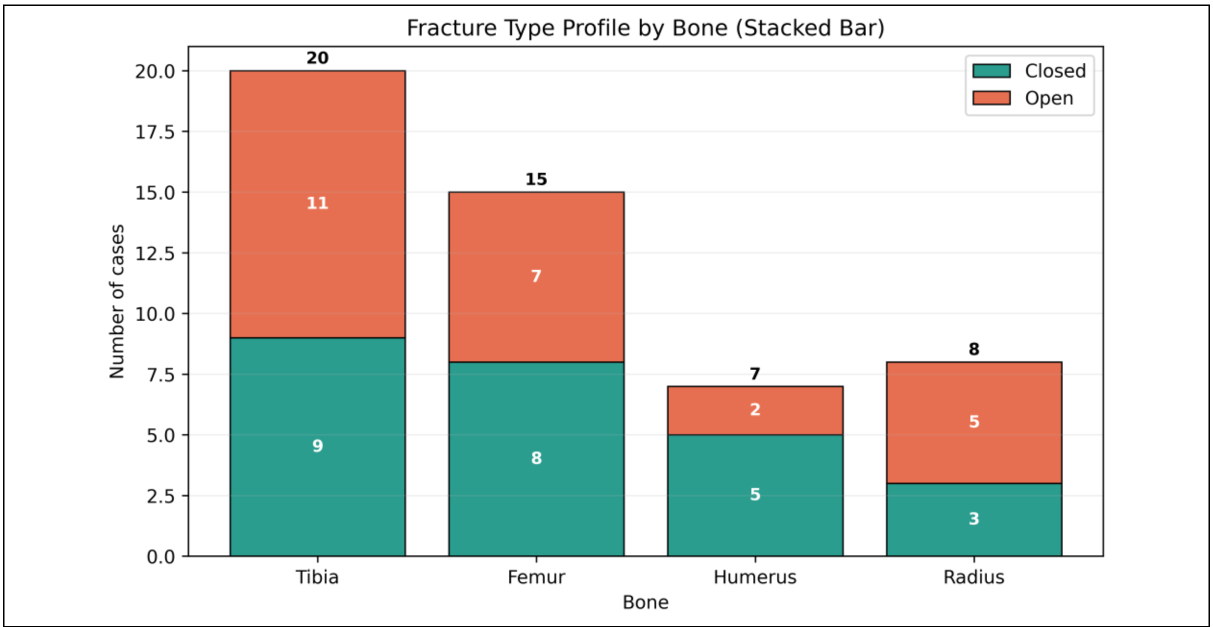

Figure 2. Fracture type profile by bone (stacked bar chart showing closed and open fractures)

Closed and open components are color-separated for each bone, with segment values and total counts displayed for immediate interpretation.

Bone	Fracture Segment Profile	Common AO Classes	Fixation Pattern	Open Fractures, N
Tibia	Distal third: 7; Mid shaft: 7; Segmental: 6	42-C (7), 42-B (7), 42-A (6)	IM Nailing (CRIF) (20)	11
Femur	Distal third: 3; Mid shaft: 6;	32-A (7), 32-C (5), 32-	IM Nailing (CRIF) (15)	7

	Segmental: 6	B (3)		
Humerus	Shaft: 7	12-C (6), 12-A (1)	ORIF with Plate (7)	2
Radius	Shaft: 8	22-C (5), 22-B (2), 22-A (1)	ORIF with Plate (8)	5

Table 2. Fracture Segment, Classification, and Fixation Summary by Bone

Table 2 Reflects the Updated Manuscript Plan Shaft-only fractures, inclusion of segmental tibia and femur patterns, no isolated ulna category, and fixation grouped into stable intramedullary nailing versus plate fixation.

Union Timelines and Treatment Interval

Mean interval from fracture to teriparatide initiation was 3.6+/-0.4 months. Mean radiological union time was 3.5+/-0.6 months from teriparatide initiation and 7.0+/-1.1 months from index surgery.

Mean complete union from index surgery was 15.1+/-1.8 months overall.

Non-revision cases (n=44) achieved complete union in 14.6+/-1.2 months from index surgery. Revision cases (n=6) showed prolonged complete union from index surgery (18.7+/-1.5 months), but union after revision occurred in 5.0+/-0.6 months.

Exploratory subgroup testing showed longer complete-union duration in open versus closed fractures (Mann-Whitney U, p=0.801) and in infected delayed union versus delayed union (Mann-Whitney U, p=0.000139).

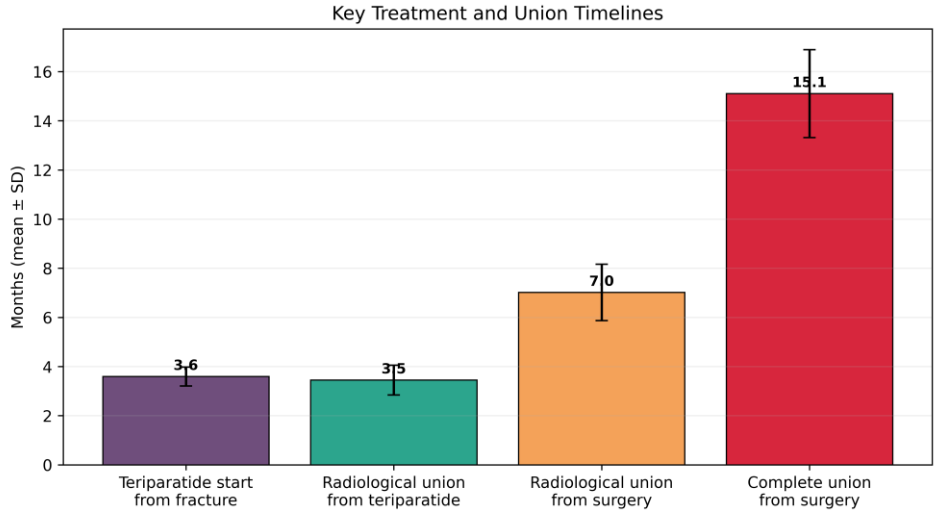

Figure 3. Key treatment and union timelines (grouped bar chart with mean values and SD error bars)

Each timeline parameter is color-coded separately, and numeric values are placed above each bar to support quick clinical interpretation.

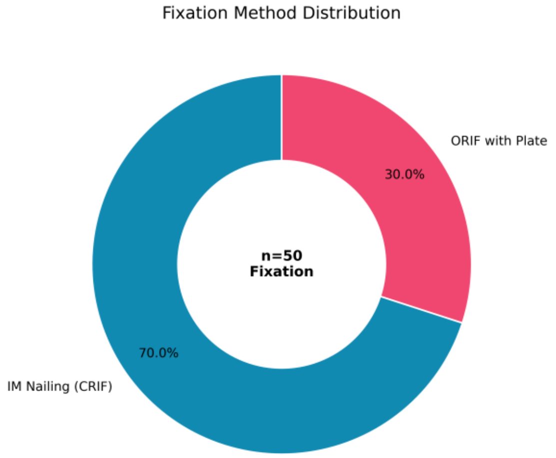

Figure 4. Fixation Method Distribution (Donut Chart)

The donut chart provides a simple overview of fixation strategy composition in the cohort while keeping the central sample size visible.

Case ID	Bone	Complete Union From Index Surgery (Months)	Complete Union From Revision Surgery (Months)	Revision Details
10	Femur	19.0	5.0	Exchange nailing + iliac crest bone graft
26	Femur	18.0	6.0	Exchange nailing + iliac crest bone graft
29	Femur	20.0	5.0	Exchange nailing + iliac crest bone graft
43	Radius	19.0	5.0	Revision long plating + bone graft (implant failure)
13	Tibia	20.0	5.0	Exchange nailing + iliac crest bone graft
28	Tibia	16.0	4.0	Exchange nailing + iliac crest bone graft

Table 3. Revision-Surgery Analysis with Separate Post-Revision Union Timeline

Six cases required revision surgery with bone grafting (femur n=3, tibia n=2, radius n=1). These cases demonstrated prolonged time to union from the index surgery. However, following revision, union was achieved within a shorter duration from the time of revision. This corrected timeline structure removes a major dataset contradiction.

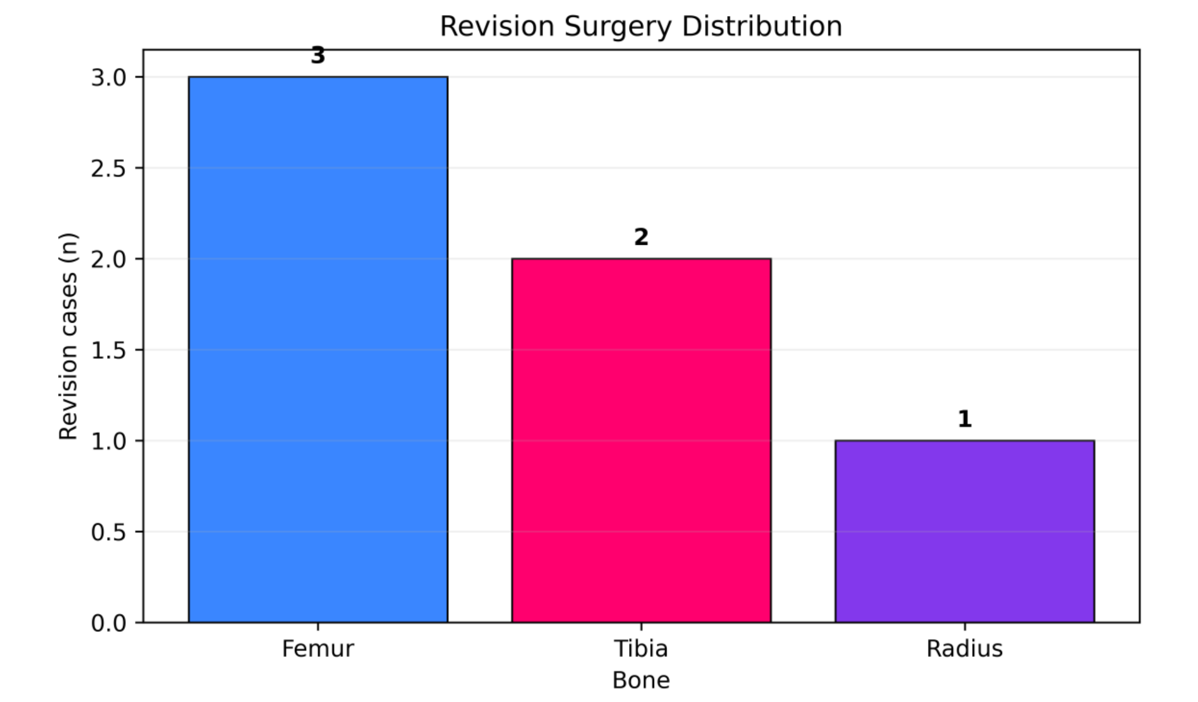

Figure 5. Revision Surgery Distribution by Bone (Bar Chart with Values above Bars)

The revision burden clustered in femur and tibia, with a single radius case requiring revision plating and grafting.

Image 1: Before Teriparatide

Image 2: 3 Months From the Date of Teriparatide

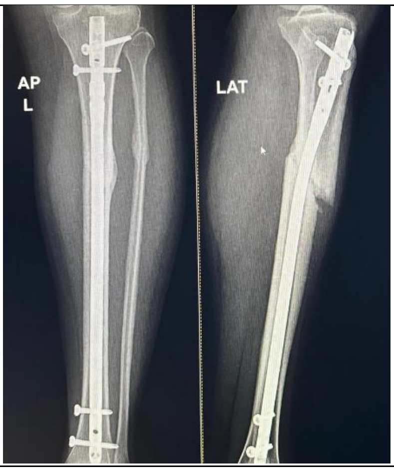

Image 3: 5 Months From the Date of Teriparatide

Image 4: Pre Op and Immediate Post Op

Image 5: Pre Op and Immediate Post Op

Image 6: 5 Months from the Teriparatide

Image 7: 3 Months From the Date of Teriparatide

Image 8: Union of Infected Case

DISCUSSION

The Updated Analysis Resolves a Common Problem in Retrospective Fracture-Healing Datasets: revision cases should not be forced into the same single union endpoint used for uncomplicated cases. By separating complete union from index surgery and complete union from revision surgery, the healing trajectory remains biologically plausible and statistically interpretable.

In this cohort, radiological union occurred at a mean of 3.5 months after teriparatide initiation, while complete union from index surgery occurred later in the expected delayed-union range. Longer healing in open fractures and infected delayed union is consistent with the biological impact of soft-tissue injury and infection on fracture repair.[5,12]

Teriparatide is best interpreted as a biologic adjunct rather than a replacement for mechanical stability. Intermittent PTH signaling supports osteoblast differentiation and callus maturation, which may improve radiological progression when adequate fixation and local biology are present.[7,8,13]

The revision subgroup reinforces this layered interpretation. Exchange nailing or revision plating with iliac crest grafting likely restored a more favorable mechanical-biological environment, after which union progressed over a shorter post-revision interval. This does not negate the role of teriparatide; rather, it shows that pharmacologic augmentation and revision surgery often act together in difficult cases.

Radiographic assessment in retrospective studies is often pragmatic. Future studies should pre-specify RUST or modified RUST scoring for tibia fractures and adapted scoring frameworks for other shaft bones to improve reproducibility and subgroup comparisons.[14]

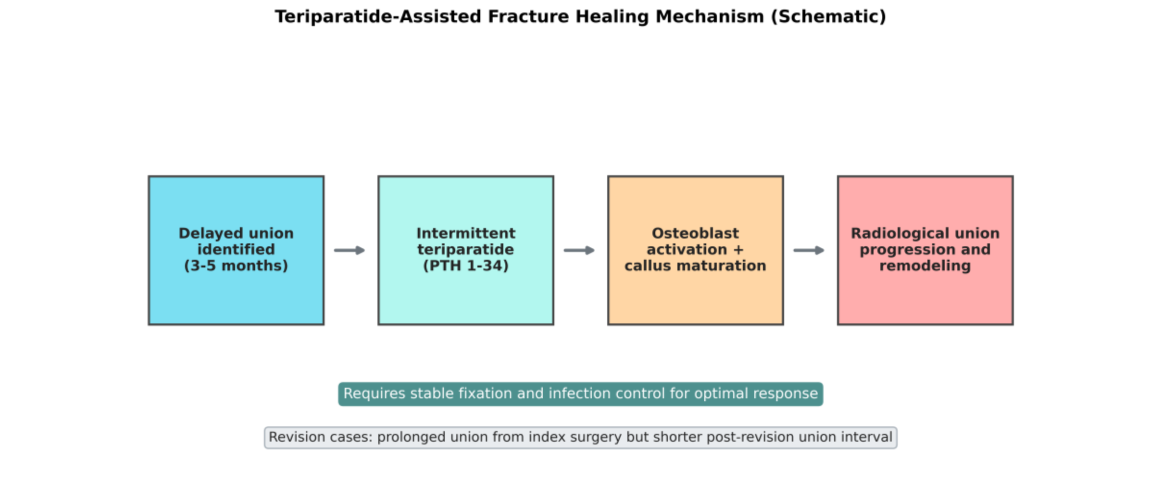

Figure 6. Colorful Schematic of Teriparatide-Assisted Fracture Healing Pathway

The schematic highlights intermittent teriparatide signaling as an adjunct to stable fixation and infection control, progressing toward callus maturation and radiological union.

Limitations

This study is retrospective and lacks a contemporaneous control group. The sample size is limited for detailed multivariable analysis. Causes of delayed union were not systematically subclassified beyond the aligned infected delayed union grouping, and host factors such as smoking burden, glycaemic control, and vitamin D status were not consistently available. Radiological assessment was structured but not fully standardized to a single validated score across all bones.

CONCLUSION

In this aligned retrospective cohort of long-bone shaft delayed union, teriparatide was associated with radiological progression within a clinically meaningful interval after treatment initiation. The key methodological strength of the corrected dataset is separation of revision timelines from primary healing timelines, which preserves biological plausibility and improves interpretability. Open fractures and infected delayed union remained slower-healing subgroups, emphasizing that teriparatide should be used as an adjunct within a framework of stable fixation and infection control.

REFERENCES

1. Marsell R, Einhorn TA. The biology of fracture healing. Injury 2011;42(6):551-5.
2. Wittauer M, Burch MA, McNally M, et al. Definition of long-bone nonunion: A scoping review of prospective clinical trials to evaluate current practice. Injury 2021;52(11):3200-5.
3. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 1976;58(4):453-8.
4. Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984;24(8):742-6.
5. Jensen SS, Jensen NM, Gundtoft PH, et al. Risk factors for nonunion following surgically managed, traumatic, diaphyseal fractures: a systematic review and meta-analysis. EFORT Open Rev 2022;7(7):516-25.
6. Zura R, Xiong Z, Einhorn T, et al. Epidemiology of fracture nonunion in 18 human bones. JAMA Surg 2016;151(11):e162775.
7. Aspenberg P, Genant HK, Johansson T, et al. Teriparatide for acceleration of fracture repair in humans: a prospective, randomized, double-blind study of 102 postmenopausal women with distal radial fractures. J Bone Miner Res 2010;25(2):404-14.
8. Canintika AF, Dilogo IH. Teriparatide for treating delayed union and nonunion: a systematic review. J Clin Orthop Traum. 2020;11(Suppl 1):S107-12.
9. Aspenberg P, Johansson T. Teriparatide improves early callus formation in distal radial fractures. Acta Orthop 2010;81(2):234-6.
10. Mancilla EE, Brodsky JL, Mehta S, et al. Teriparatide as a systemic treatment for lower extremity nonunion fractures: a case series. Endocr Pract 2015;21(2):136-42.

11. Leow JM. The radiographic union scale in tibial (RUST) fractures: Reliability of the outcome measure at an independent centre. Bone Joint Res 2016;5:116-21.
12. Coppola C, Del Buono A, Maffulli N. Teriparatide in fracture non-unions. Transl Med UniSa 2014;12:47-53.
13. Gariffo G, Bottai V, Falcinelli F, et al. Use of teriparatide in preventing delayed bone healing and nonunion: a multicentric study on a series of 20 patients. BMC Musculoskelet Disord 2023;24(1):184.
14. Fiset S, Godbout C, Crookshank MC, et al. Experimental validation of the Radiographic Union Score for Tibial Fractures (RUST) using micro-computed tomography scanning and biomechanical testing in an in-vivo rat model. J Bone Joint Surg Am 2018;100(21):1871-8.

How to cite this article: Dr. Arjun A., Dr. Mahesh J. Nerkar, Dr. Nitin N. Sunku, Dr. Prashanth Reddy P., TERIPARATIDE-ASSISTED UNION IN DELAYED UNION AND INFECTED DELAYED UNION OF LONG-BONE SHAFT FRACTURES: A RETROSPECTIVE OBSERVATIONAL STUDY, Asian J. Med. Res. Health Sci., 2026; 4 (1):778-486.

Source of Support: Nil, Conflicts of Interest: None declared.