JRAAS
Special Issue in Medicine & Surgery
www.internationalmedicalpublishing.com

Research Article

Section: Orthopaedics

Effect of Teriparatide on Fracture Healing in Intertrochanteric Fractures Treated with Proximal Femoral Nailing: A Prospective Comparative Study

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HIGHLIGHTS

- Teriparatide accelerates fracture union
- Earlier recovery after PFN
- Improved early functional outcomes
- Enhanced healing in osteoporosis
- Similar long-term outcomes

Key Words:
Intertrochanteric fracture
Proximal femoral nail
Teriparatide
Fracture healing
Functional outcome

ABSTRACT

Introduction: Intertrochanteric fractures are common in the elderly and are associated with significant morbidity and delayed functional recovery. Proximal femoral nailing (PFN) is a standard method of fixation; however, fracture healing may be compromised in osteoporotic bone. Teriparatide, an anabolic agent, has been proposed to enhance fracture healing. **Aims & Objectives:** To evaluate the effect of adjunctive teriparatide therapy on radiological union and functional outcomes in intertrochanteric fractures treated with PFN. **Materials & Methods:** A prospective randomized comparative study was conducted on 30 patients with intertrochanteric fractures at a tertiary care hospital over a 24-month period. Patients were allocated into two groups: Group A (PFN with teriparatide, n=15) and Group B (PFN alone, n=15). Group A received subcutaneous teriparatide (20 µg/day) starting on postoperative day 7 for 24 weeks. Functional outcomes were assessed using the Visual Analogue Scale (VAS), Lower Extremity Functional Scale (LEFS), and Harris Hip Score (HHS). Radiological assessment included cortical bridging, tip-apex distance (TAD), femoral offset, and neck-shaft angle (NSA). **Results:** Group A demonstrated significantly earlier fracture union (mean 11.2 weeks) compared to Group B (13.4 weeks). Patients receiving teriparatide showed better pain relief and functional scores during early follow-up (1–3 months, $P < 0.05$). However, functional outcomes and radiological parameters (TAD, NSA, and femoral offset) were comparable between groups at 6 months ($P > 0.05$). Complication rates were similar in both groups. **Conclusion:** Adjunctive teriparatide therapy accelerates biological fracture healing and improves early functional recovery in osteoporotic intertrochanteric fractures treated with PFN, without affecting final structural outcomes or increasing complications.

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Article History: Received 28 May 2026; Received in Revised form 15 July 2026; Accepted 22 July 2026
How To Cite: Amit Ray, Piyush Patil, Yashdeep Dhouchak & Prakhar Mittal. Effect of Teriparatide on Fracture Healing in Intertrochanteric Fractures Treated with Proximal Femoral Nailing: A Prospective Comparative Study. *JRAAS : Special Issue in Medicine & Surgery.* 2026;41(2):1-9.
DOI: https://doi.org/10.71393/3d7sdm43

INTRODUCTION

Intertrochanteric (IT) femoral fractures constitute a significant percentage of hip fractures experienced in orthopedic practice. They cause substantial morbidity and mortality, especially among the older generation. These fractures occur in the region between the greater and lesser trochanters and are usually characterized by low-energy trauma in osteoporotic patients [1]. As life expectancy increases and the global population ages, the frequency of intertrochanteric fractures is steadily rising, presenting an increasing socioeconomic and healthcare liability worldwide [2]. Epidemiological estimates indicate that by 2050, the incidence of hip fractures globally could reach approximately 6.26 million cases per annum [3]. The lifetime risk of sustaining a hip fracture at age 50 stands at 5%–6% in men and nearly 20% in women [4]. Trivial falls in individuals above 70 years of age result in more than 80% of hip fractures, reflecting compromised bone quality and decreased protective reflexes [5].

Stable fixation that enables early mobilization & fewer complications is the major objective of management. Historically, conservative management with protracted traction resulted in unacceptably high complication rates and is no longer favored [7]. While extramedullary devices like the Dynamic Hip Screw (DHS) provide controlled fracture impaction in stable variants, they frequently experience overcollapsing, varus malalignment, and implant failure in unstable patterns [8]. Consequently, intramedullary devices like the Proximal Femoral Nail (PFN) have become popular for unstable intertrochanteric fractures. As load-sharing implants with a shorter lever arm, PFNs offer superior biomechanical stability, less bending stress, minimal soft-tissue dissection, and facilitate early weight-bearing [9].

In spite of these biomechanical advancements, post-fixation complications remain frequent in elderly osteoporotic patients, including delayed union, excessive fracture collapse, varus malalignment, screw cut-out, and functional impairment [10]. These challenges highlight the need for strategies that enhance not only mechanical stability but also biological fracture healing [11]. Osteoporosis impairs bone remodeling, leading to decreased mechanical purchase of implants and postponed healing [12]. Standard postoperative calcium and vitamin D supplementation alone is often insufficient to reverse this compromised osteogenic potential [13]. **Figure 1** compares fracture healing following PFN fixation alone and PFN fixation combined with teriparatide therapy. Teriparatide enhances osteoblastic activity, promotes callus formation and mineralization, improves trabecular architecture and biomechanical strength, and accelerates fracture union by stimulating osteoblast differentiation and extracellular matrix synthesis.

Teriparatide, a recombinant human parathyroid hormone (PTH 1-34), stimulates osteoblast proliferation, differentiation, and survival when administered intermittently [14]. Research indicates that teriparatide accelerates callus formation, mineralization, and biomechanical strength at the fracture site [15]. Clinical trials suggest it decreases the time to radiological union while improving early pain and functional scores in osteoporotic fractures [16]. However, localized clinical evidence regarding its efficacy alongside PFN fixation remains limited within the Indian population. The objective of this study is to evaluate the clinical, functional, and radiological outcomes of adjunctive teriparatide therapy combined with PFN versus PFN alone for managing intertrochanteric femur fractures.

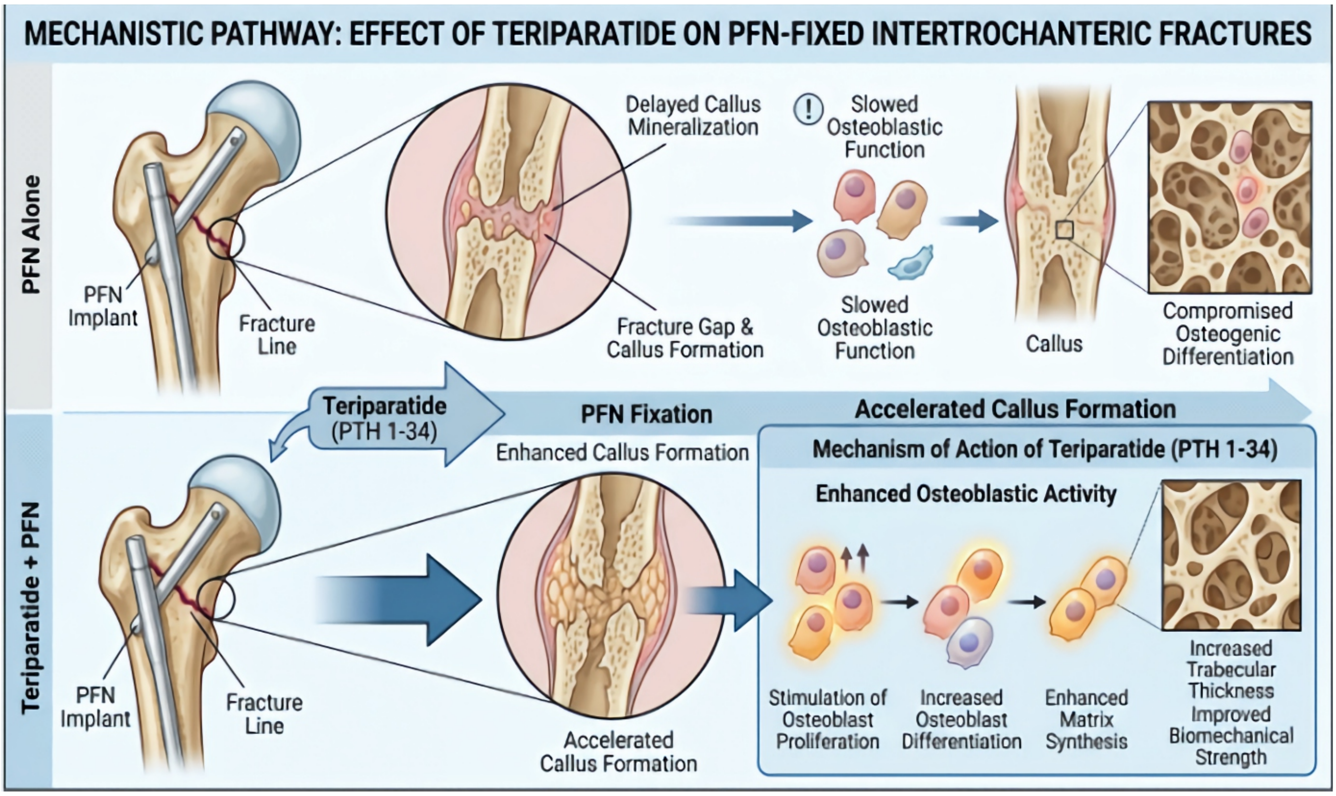

Figure 1: Mechanistic pathway illustrating the effect of teriparatide (PTH 1–34) on healing of proximal femoral nail (PFN)-fixed intertrochanteric fractures.

MATERIAL & METHODS

Study Design & Setting

This prospective randomized comparative study was conducted in the Department of Orthopaedics at K. D. Medical College, Hospital and Research Centre, Mathura, Uttar Pradesh, India. Institutional Ethics Committee approval was obtained prior to commencement (Ref. No: KDMCHRC/IEC/2024/19), and written informed consent was obtained from all participants. The study duration spanned 24 months, from February 2023 to January 2025, including patient recruitment and a 6-month follow-up period.

Patient Selection

A total of 30 patients presenting with isolated intertrochanteric femur fractures were enrolled based on strict selection criteria.

Inclusion Criteria

Patients aged >50 years, presenting with isolated intertrochanteric fractures classified as Boyd and Griffin Type II, III, or IV, who were ambulatory prior to injury, skeletally mature, medically fit for surgery, and willing to comply with the follow-up protocol.

Exclusion Criteria

Associated polytrauma or high-energy fractures, developmental anomalies or previous surgery on the affected hip, prior use of teriparatide, bisphosphonates, or calcitonin, unacceptable intraoperative fracture reduction, metabolic bone diseases other than osteoporosis, hypercalcemia, hyperparathyroidism, or a history of osteosarcoma.

Sample Size & Randomization

The sample size was calculated using the standard prevalence study formula:

Where Z = 1.96 (at a 5% type 1 error rate), p is the expected proportion based on pilot data, q = 1 - p, and d represents absolute precision. The calculation yielded n \approx 30, which was established as the final sample size.

Enrolled patients were allocated in a 1:1 ratio using simple randomization into two groups:

- Group A (Teriparatide Group, n=15): Received standard PFN fixation paired with adjunctive teriparatide therapy.
- Group B (Control Group, n=15): Received standard PFN fixation alone.

Intervention & Postoperative Protocol

All patients in both groups received standard daily oral calcium supplementation (1000 mg) and weekly Vitamin D_3 (60,000 IU). Patients in Group A additionally received teriparatide at a dose of 20 µg subcutaneously once daily for 24 weeks, initiated on the postoperative day 7.

Surgical Technique: Proximal Femoral Nailing

All surgeries were performed under spinal anesthesia with the patient positioned supine on a fracture table. The injured limb was placed in traction, abduction, and external rotation under fluoroscopic guidance to correct varus deformities and restore the posteromedial cortex [28]. Closed reduction was verified on both anteroposterior (AP) and lateral views to confirm anatomical neck-shaft angle restoration. A 5 cm longitudinal incision was made proximal to the tip of the greater trochanter. The tensor fascia lata was incised, and fibers of the gluteus medius were bluntly split. Under fluoroscopic control, an entry point was established at the tip of the greater trochanter using a bone awl. A guide wire was inserted across the fracture site into the distal femoral canal down to the upper pole of the patella. Reaming of the femoral canal was performed sequentially, followed by proximal reaming according to the nail system parameters.

The selected PFN was inserted over the guide wire using an insertion jig. Proximal locking was performed by placing the lag screw and anti-rotation screw into the femoral head, maintaining an optimal tip-apex distance (TAD). Distal locking was completed using a standard freehand technique. The surgical wound was irrigated, hemostasis secured, and closure completed in layers. Intravenous antibiotics were administered for 5 days postoperatively, followed by oral antibiotics until suture removal on day 12. Active quadriceps strengthening and ankle pump exercises were initiated on postoperative day 1, and mobilization using a walker commenced on day 2.

Follow-up and Outcome Assessments

Clinical, functional, and radiological parameters were evaluated on postoperative day 1 (POD 1), postoperative day 14 (POD 14), and at monthly intervals up to 6 months.

Pain Assessment

Quantified using the 10-point Visual Analogue Scale (VAS).

Functional Assessment

Evaluated using the Lower Extremity Functional Scale (LEFS, maximum score 80) and the Harris Hip Score (HHS, maximum score 100).

Radiological Assessment

Evaluated using serial AP and lateral plain radiographs of the affected hip. Fracture union was defined as the presence of bridging callus across at least three cortices. Structural stability was tracked by documenting the neck-shaft angle (NSA), femoral offset, and tip-apex distance (TAD) via Baumgaertner's method.

Statistical Analysis

Statistical analysis was conducted using SPSS software version 16.0. Continuous variables were presented as mean , standard deviation {SD} and evaluated using the unpaired Student's t-test.

Categorical data were presented as percentages and analyzed using the Chi-square or Fisher's exact test. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

The baseline demographics showed no significant difference between the two cohorts ($P > 0.05$). Group A comprised 6 males (40%) and 9 females (60%); Group B comprised 5 males (33.3%) and 10 females (66.7%). Both groups exhibited a female predominance, consistent with the epidemiology of osteoporotic fragility fractures.

Pain Scores (VAS)

No statistically significant difference in mean VAS scores was observed between the groups during the early postoperative period (POD 1 and POD 14, $P > 0.05$). However, Group A demonstrated significantly lower pain scores from the 1-month follow-up through the 3-month follow-up $P < 0.05$). From the 4-month mark onward, pain scores equalized, with no significant difference at the final 6-month evaluation ($P > 0.05$) **(Table 1)**. **Figure 2.** VAS Score Trends During Follow-up. Pain scores decreased progressively in both groups, with significantly lower VAS scores in the teriparatide group during the first 3 months.

Functional Progression (LEFS and HHS)

Functional scores tracked similarly to pain metrics. Early scores (POD 1 and POD 14) were statistically comparable between both cohorts ($P > 0.05$). Group A demonstrated significantly higher functional scores on both the LEFS and HHS from Month 1 through Month 3 ($P < 0.05$), indicating enhanced early functional recovery. By Month 4, scores began to equalize, showing no significant differences at the final 6-month endpoint ($P > 0.05$) **(Table 2)**. **Table 3.** Harris Hip Score (HHS) During Follow-up. HHS improved in both groups throughout follow-up. Patients receiving teriparatide showed significantly better functional scores during the first 3 months, while scores were comparable between groups by 6 months. **Figure 3.** Lower Extremity Functional Scale (LEFS) Scores During Follow-up. LEFS scores improved progressively in both groups, with significantly higher scores in the teriparatide group during the first 3 months, indicating enhanced early functional recovery. **Figure 4.** Harris Hip Score (HHS) During Follow-up. HHS improved steadily in both groups, with significantly higher scores in the teriparatide group during the first 3 months, reflecting better early hip function and recovery.

Radiological Union

No cortical bridging was observed in either group at POD 14. From Month 1 to Month 3, Group A demonstrated a significantly higher number of bridged cortices compared to Group B ($P < 0.05$). The mean overall time to definitive radiological union was significantly shorter in Group A (11.2 \text{ weeks}) than in Group B (13.4 \text{ weeks}, $P < 0.05$). At the 6-month endpoint, all patients in both arms achieved complete cortical union ($P > 0.05$) **(Figure 5 & Table 4)**.

Surgical Accuracy and Structural Stability

Radiological metrics associated with implant placement, including tip-apex distance (TAD), restoration of femoral offset, and neck-shaft angle (NSA), remained comparable between both arms across all follow-ups ($P > 0.05$). No hardware migration, implant breakage, or varus collapse occurred during the study period **(Table 5)**.

Table 1: Pain Assessment (VAS Score) Over Follow-up Intervals.

Follow-up	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
POD 1	7.9 ± 0.5	8.0 ± 0.6	> 0.05
POD 14	6.1 ± 0.7	6.5 ± 0.8	> 0.05
1 Month	4.2 ± 0.6	4.8 ± 0.7	0.03
2 Month	3.0 ± 0.6	3.6 ± 0.7	0.04
3 Month	1.6 ± 0.5	2.2 ± 0.6	0.04
4 Month	0.8 ± 0.4	1.1 ± 0.5	> 0.05
5 Month	0.4 ± 0.3	0.6 ± 0.4	> 0.05
6 Month	0.2 ± 0.3	0.3 ± 0.4	> 0.05

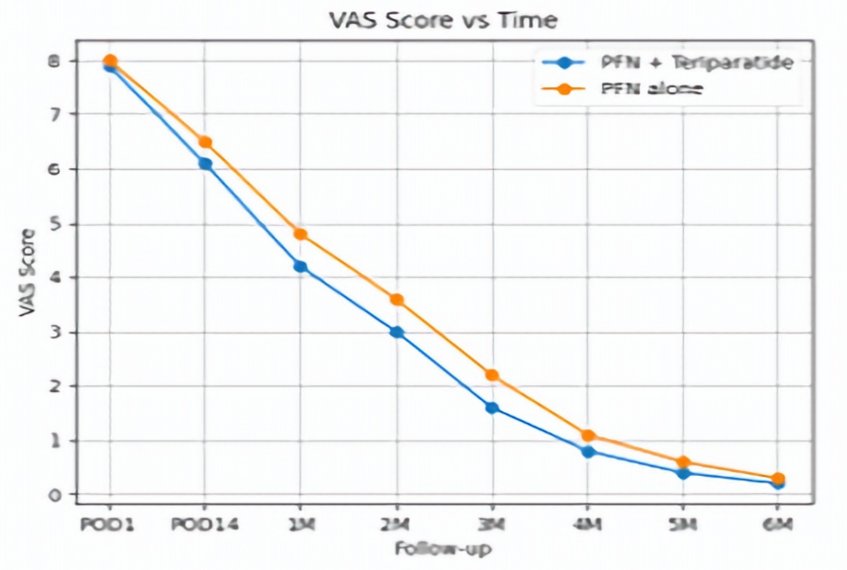

Figure 2: VAS vs Time

Table 2. Lower Extremity Functional Scale (LEFS) Score Over Follow-up.

Follow-up	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
POD 1	8.0 ± 2.9	6.9 ± 2.7	> 0.05
POD 14	19.0 ± 3.5	17.0 ± 3.3	> 0.05
1 Month	34.0 ± 4.1	30.0 ± 4.3	0.02
2 Month	51.0 ± 4.8	46.0 ± 5.0	0.03
3 Month	66.0 ± 5.2	60.0 ± 5.0	0.04
4 Month	71.0 ± 5.0	68.0 ± 5.3	> 0.05
5 Month	74.0 ± 5.2	71.0 ± 5.4	> 0.05
6 Month	75.0 ± 5.1	73.0 ± 5.4	> 0.05

Table 3: Harris Hip Score (HHS) Over Follow-up Intervals.

Follow-up	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
POD 1	24.0 ± 4.0	23.0 ± 4.1	> 0.05
POD 14	45.0 ± 5.2	43.0 ± 5.4	> 0.05
1 Month	63.0 ± 5.5	58.0 ± 5.8	0.02
2 Month	72.0 ± 5.8	68.0 ± 6.0	0.03
3 Month	83.0 ± 6.0	79.0 ± 6.3	0.04
4 Month	88.0 ± 5.1	86.0 ± 5.3	> 0.05
5 Month	92.0 ± 4.6	90.0 ± 4.8	> 0.05
6 Month	94.0 ± 4.2	92.0 ± 4.5	> 0.05

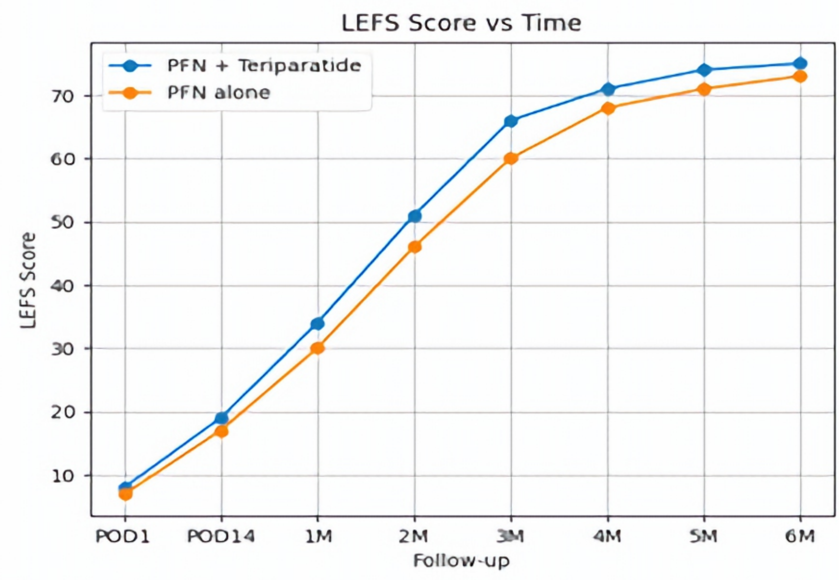

Figure 3: LEFS vs Time

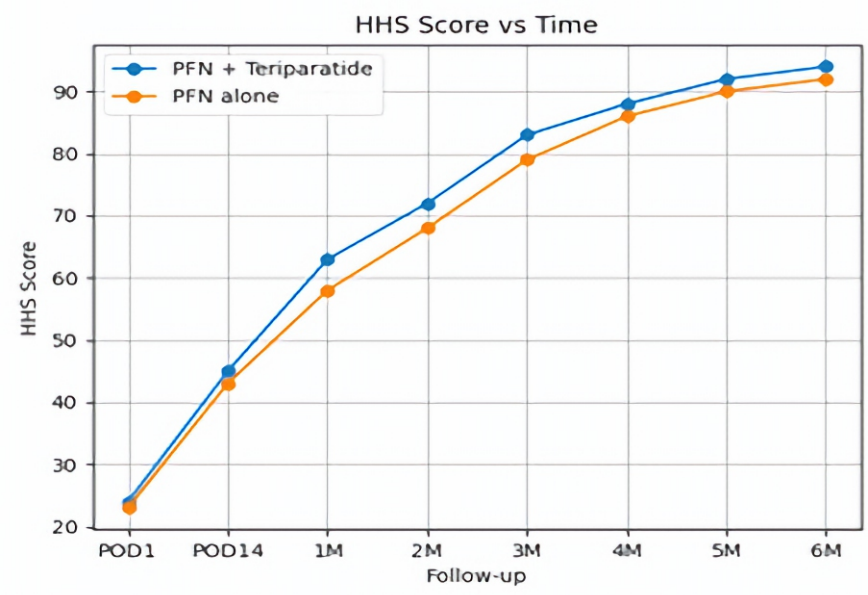

Figure 4: HHS vs Time

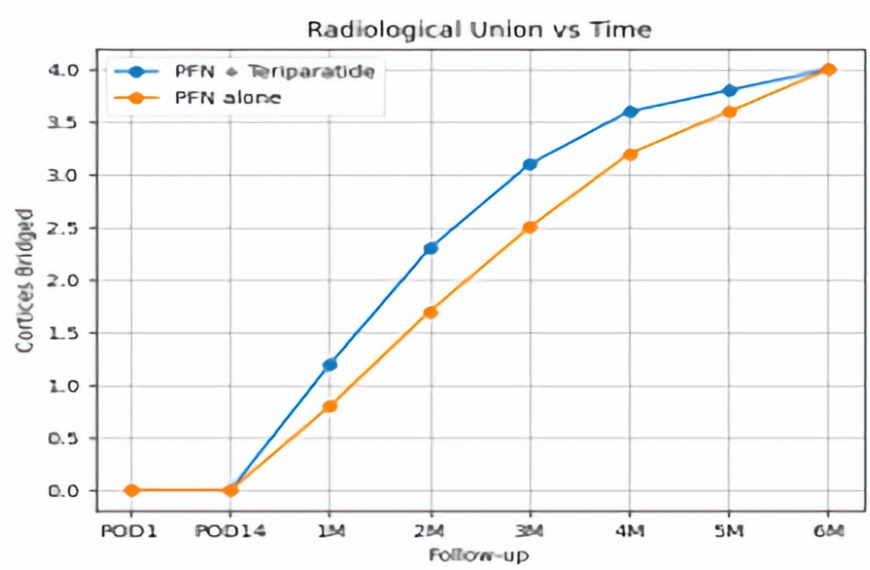

Figure 5: Radiological union vs Time

Table 4: Radiological Union (Number of Cortices United).

Follow-up	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
1 Month	1.2 ± 0.5	0.8 ± 0.4	0.02
2 Month	2.3 ± 0.6	1.7 ± 0.5	0.01
3 Month	3.1 ± 0.7	2.5 ± 0.6	0.03
4 Month	3.6 ± 0.5	3.2 ± 0.6	> 0.05
5 Month	3.8 ± 0.4	3.6 ± 0.5	> 0.05
6 Month	4.0 ± 0.0	4.0 ± 0.0	> 0.05

Table 5: Postoperative Structural and Surgical Parameters.

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	P-value
Femoral Offset (Final, mm)	40.8 ± 3.1	40.1 ± 3.2	> 0.05
Tip-Apex Distance (POD 1, mm)	20.1 ± 1.7	20.3 ± 1.8	> 0.05
Neck-Shaft Angle (POD 1, degrees)	130.8 ± 3.4	128.2 ± 3.5	> 0.05

DISCUSSION

Intertrochanteric fractures in elderly patients present significant biological challenges due to underlying osteoporosis and age-related osteogenic impairment [30]. While intramedullary options such as PFN provide standard mechanical stability [31], the rate of biological union often governs early recovery and overall post-surgical independence. This prospective study evaluated whether adjunctive teriparatide therapy alters these parameters.

The demographic trends observed here confirm a female predominance, consistent with global patterns of post-menopausal osteoporotic hip trauma [32]. Because immediate postoperative pain metrics did not show distinct variance between the groups, early postoperative discomfort appears primarily linked to direct surgical trauma and tissue manipulation. However, by the end of the first month, the teriparatide cohort demonstrated significantly lower VAS pain scores. This accelerated pain reduction is likely due to rapid callus stabilization and subsequent reductions in micromotion at the fracture line [34]. Landmark data indicate that intermittent parathyroid hormone delivery enhances osteoblastic function, directly advancing early bone consolidation [35].

Functional outcomes assessed using the LEFS and HHS showed a similar trend. While late functional outcomes at 6 months equalized between the cohorts, early functional scores (Months 1–3) were significantly higher in patients receiving teriparatide. This early acceleration in functional capacity is clinically valuable for elderly patients, as faster consolidation allows for definitive weight-bearing, reduces the duration of restricted mobility, and helps prevent prolonged recumbency complications [36, 37]. Radiologically, the teriparatide cohort achieved definitive union significantly faster than the control group (11.2 weeks {vs} 13.4 weeks). This reflects the anabolic mechanisms of teriparatide, which upregulates endochondral ossification, increases structural callus volume, and enhances local mineraliation patterns [35, 38].

The equalization of functional scores and radiological union at 6 months suggests that while PFN alone provides sufficient long-term mechanical stability for eventual union, adjunctive teriparatide accelerates the rate of biological healing [36, 39].

Crucially, structural measures such as the tip-apex distance, neck-shaft angle, and femoral offset remained highly consistent and showed no significant differences between the groups. Because these mechanical indicators are determined by intra-operative execution and screw positioning, they are unaffected by systemic pharmacological interventions [40, 41]. The consistency of these parameters between the groups confirms that the differences in pain relief and healing rates are attributable to the biological effects of teriparatide rather than confounding mechanical variations.

CONCLUSIONS

Proximal femoral nailing (PFN) provides stable fixation for unstable intertrochanteric fractures, resulting in satisfactory fracture union and maintenance of structural alignment. The addition of teriparatide therapy significantly accelerates biological fracture healing, leading to earlier radiological union and improved early clinical outcomes, including reduced pain and enhanced functional recovery as assessed by LEFS and Harris Hip Score during the first three postoperative months. However, long-term radiological and functional outcomes at 6 months were comparable between patients receiving teriparatide and those treated with PFN alone, indicating that teriparatide primarily hastens the healing process rather than altering the final outcome. Furthermore, postoperative mechanical parameters such as tip-apex distance, neck-shaft angle, and femoral offset were similar between groups, emphasizing that these factors depend mainly on surgical technique rather than pharmacological intervention. Overall, adjunctive teriparatide therapy appears to be a safe and effective strategy for enhancing early recovery in osteoporotic intertrochanteric fractures treated with PFN.

LIMITATIONS & FUTURE PERSPECTIVES

The study's limitations include a single-centre setting, a relatively small sample size, and a short study duration, which may limit the broader applicability of the results. Future studies should incorporate multicentre designs with larger populations to enhance validity, assess long-term outcomes, and investigate advanced diagnostic & management approaches. Such efforts will improve overall patient care & help minimize complications.

CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical health-.care, diagnosis, and treatment outcomes. By highlighting real-care applications. It emphasizes the importance of translating scientific observations into meaningful improvements in patientworld relevance, the study contributes to evidence based medical practice and supports informed clinical decision making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

ABBREVIATIONS

AP: Anteroposterior
HHS: Harris Hip Score
LEFS: Lower Extremity Functional Scale
NSA: Neck-Shaft Angle
PFN: Proximal Femoral Nailing
POD: Postoperative Day
PTH: Parathyroid Hormone
TAD: Tip-Apex Distance
VAS: Visual Analogue Scale

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AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

ACKNOWLEDGEMENT

The authors sincerely acknowledge the seniors of the Department of Orthopaedics, Kanti Devi Medical College Hospital & Research Center Mathura, India. We are grateful to our college for providing the necessary resources to carry out this work. We also extend our heartfelt thanks to our colleagues and technical staff for their valuable assistance during the study.

CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

FUNDING

None

ETHICAL APPROVAL & CONSENT TO PARTICIPATE

All necessary consent & approval was obtained by authors.

CONSENT FOR PUBLICATION

All necessary consent for publication was obtained by authors.

DATA AVAILABILITY

All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a re-asonable request.

USE OF ARTIFICIAL INTELLIGENCE (AI) & LARGE LANGUAGE MODEL (LLM)

The authors confirm that no AI & LLM tools were used in the writing or editing of the manuscript, and no images were altered or manipulated using AI & LLM.

AUTHOR'S NOTE

This article serves as an important educational tool for the scientific community, offering insights that may inspire future research diretions. However, they should not be relied upon independently when making treatment decisions or developing public health policies.

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