# Effectiveness of teriparatide in in improving healing rates and bone-turnover markers of osteoporotic hip fracture: a meta-analysis

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## Abstract

**Objective:** To evaluate the effect of subcutaneous teriparatide therapy on fracture healing rate and change in bone mass density in osteoporotic hip fractures.

**Method:** The meta-analysis was done from September to December 2022, and comprised literature search on Wanfang, CNKI, VIP, PubMed, Embase, Cochrane Library, and Web of Science databases from the establishment of the respective database till December 2022. The relevant journals of the library of Macao University of Science and Technology, China, were manually searched for randomised controlled trials of teriparatide in the treatment of osteoporotic hip fractures. The shortlisted studies were subjectd to Cochrane Risk of Bias tool and the Jadad Rating Scale. Meta-analysis was done using the RevMan 5.4 software provided by the Cochrane Collaboration Network. Fracture healing rate and bone mineral density were the primary outcome measures, while mortality, adverse events, malformations, complications, subsequent fractures, timed-up-and-go test, visual analogue scale score, and procollagen type I N-terminal propeptide were the secondary outcome measures.

**Results:** Of the 1,094 articles retrieved, 8(0.7%) randomised controlled trials were analysed. There were 744 patients; 372(50%) in the teriparatide group and 372(50%) in the control group. Fracture healing rate was not significantly different ($p=0.82$), while bone mineral density was significantly different between the groups ($p<0.001$). Mortality, adverse events, deformity, and complications were not significantly different ($p>0.05$), while subsequent fractures, timed-up-and-go score, visual analogue scale score and procollagen type I N-terminal propeptide were significantly different between the groups ($p<0.05$).

**Conclusions:** The literature did not support teriparatide's ability to improve the healing rate of osteoporotic hip fractures, or to reduce mortality, adverse events, malformations, and complications. In addition, teriparatide could increase bone mineral density of osteoporotic hip fractures and the procollagen type I N-terminal propeptide value, alleviate hip pain, and reduce subsequent fracture rates. This trial is registered with PROSPERO with registration number CRD42022379832.


**Key Words:** Teriparatide, Osteoporosis, Hip fracture, The fracture healing rate, Bone-turnover markers, Bone density, Fracture union.

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## Introduction

The incidence rate of hip fracture in the elderly in the world is increasing year by year. It is estimated that by 2050, this number will reach approximately 6.26 million[1]. At the age of 50, the lifetime risk of hip fracture in men and women is reported to be as high as 5.6% and 20%, respectively[2]. Among people over 50 years of age, 53% are fractures caused by minor trauma, while among fractures in individuals over 70 years of age, the proportion is >80%[3]. Hip fractures mainly include femoral neck fractures and femoral intertrochanteric fractures. Osteoporosis is a common cause of such fractures and often complicates recovery post-fracture, leading to high incidence of loss of functionality and poor quality of life in the elderly that eventually leads to mortality[4], particularly in those living with multiple co-morbidities. The mortality rate is estimated to be 15- 20%[5,6] in this high-risk population, and it is also called the last fracture in life.

The drugs used to treat osteoporosis are generally divided into two categories: anti-absorption drugs, and anabolic drugs. In 2002, the United States Food and Drug Administration (FDA) approved teriparatide, a recombinant form of human parathyroid hormone, with a recommended adult dosage of 20mcg subcutaneously once a day[7]. Pre-clinical experiment studies on rats showed that teriparatide has the positive ability to improve fracture healing, promote callus volume, bone mineralisation, and strength[8]. The findings were controversial, as some clinical studies found that

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teriparatide could shorten the healing time and healing rate of osteoporotic vertebral fractures[9]. In a controlled trial of pelvic fracture patients, PTH1-84 also improved fracture healing[10].However, the systematic evaluation and meta-analysis by South Korean scholars[11] included [11] clinical research results, and the evaluation of the effect of teriparatide on fracture healing finally led to the conclusion that there was no difference in fracture healing. Literature showed that teriparatide reduced the healing time of hip fractures, but at 3-6 months, the fracture healing rate did not improve much[12].

Because teriparatide is expensive, it is necessary to further evaluate its efficacy and safety for osteoporotic hip fracture in order to provide the best treatment option for specific subgroups of patients. The current meta-analysis was planned to explore the efficacy of teriparatide in the treatment of hip fractures to reduce pain, improve mobility and prevent complications post-fracture.[13]

## Materials and Methods

The meta-analysis was conducted from September to December 2022. Two researchers independently searched Wanfang, CNKI, VIP, PubMed, Embase, Cochrane Library and Web of Science databases from the establishment of the respective databases to December 2022 as well as periodicals in the library of Macao University of Science and Technology, China. Key words and Boolean operators used were teriparatide, injection of teriparatide, hip fracture, femoral neck fracture, femoral intertrochanteric fracture, femoral fracture, iliac bone fracture, pelvic fracture, hPTH (1-34), human parathyroid hormone (1-34), oarathar, teriparatide acetate, forteo fractures, hip, trochanteric fractures, frames, trochanteric, intertrochanteric fractures, frames, intertrochanteric, subtrochanteric fractures, frames, subtrochanteric.

The articles retrieved were screened by two independent reviewers. Any discrepancy between the two were resolved in consultation with the third investigator.

Inclusion criteria in the meta-analysis comprised randomised controlled trials (RCTs), whether blind or not, published in mainstream scientific and technological journals in Chinese or English in which the patient was diagnosed as osteoporotic hip fracture and was treated with teriparatide (unlimited dose, usage, and course of treatment) + conventional therapy. Studies with missing data or serious data problems, animal experiments, reviews, case reports, conference papers were excluded, and so were studies whose data was not suitable for meta-analysis or could not be used for meta-analysis after conversion.

Patients diagnosed with osteoporotic hip fracture with other bone metabolic diseases, who had taken drugs that affected bone metabolism within 6 months, and patients with other major systemic diseases were excluded in the meta-analysis. The patients in the test group were treated with teriparatide (unlimited dose, usage, and course of treatment) + conventional therapy, while the patients in the control group were treated with conventional therapy alone.

The primary endpoints were fracture healing rate and bone mineral density (BMD), while the secondary outcome measures were mortality, adverse events, malformations, complications, subsequent fractures, Timed-Up-and-Go (TUG) test, visual analogue scale (VAS) score and procollagen type I N-terminal propeptide (PINP). At least one of the above evaluation indexes was selected in the RCTs analysed.

Review Manager 5.4 software of the Cochrane Collaboration Network was used for analysis.

Cochrane risk of bias assessment tool was used to evaluate the quality of the included literature[14]. The evaluation items included generation of random allocation method (control selection bias), concealment of allocation scheme (control selection bias), implementation of blind method (implementation bias), blind method of result evaluation (measurement bias), integrity of data (loss of interview bias), selective report (report bias) and other biases. The evaluation of each project was divided into "low risk", "unclear", and "high risk" categories.

The robustness of the results of the meta-analysis was assessed using the Trial Sequential analysis software TSA version 0.9.5.10 Beta, including subgroup and sensitivity analyses.

For binary outcomes, the odds ratio (OR) with 95% confidence interval (CI) were used as efficacy statistics. The outcome indicators with consistent units were expressed by mean difference (MD), and the measurement data with inconsistent units were expressed by standard mean difference (SMD). All data was expressed by 95% CI. For continuous outcomes, the change values before and after treatment were used for analysis. If the original text did not provide the change value before and after treatment, only pictures were provided, and Image J was used to extract the mean and standard deviation. Heterogeneity was tested using chi-square and $I^2$tests. When the heterogeneity existed ($I^2$ >50% or $p<0.1$), random effects model was applied to estimate the summary of relative ratio (RR), weighted

mean difference (WMD) and 95% CI, along with other standardised widely effective models for meta-analysis.

## Results

Of the 1,094 articles retrieved, 8(0.7%) RCTs were analysed (Figure 1). There were 2(25%) studies in the Chinese language and 6(75%) in English. There were 744 patients; 372(50%) in the teriparatide group and 372(50%) in the control group. The Jadad score was ≥4, showing a high quality of the studies. Out of the (shown in Table-1), patient diagnosis in 7(87.5%) trials was osteoporotic intertrochanteric fracture, and in 1(12.5%) it was osteoporotic femoral neck fracture. The number of patients in the selected trials ranged from 29 to 171. The studies used risedronate, calcium carbonate, vitamin D3, calcium agent and vitamin D as well teriparatide 20mcg subcutaneous injection per day in the intervention group with additional vitamin D and calcium, the use cycle of teriparatide ranges 4.75±2.1 months. Conservative treatment was adopted in the 2(25%) Chinese studies, and the rest opted for surgery. There was no significant methodological difference between the groups with respect to baseline data (Table 1).

**Table-1:** Characteristics of the studies analysed.

| Study ID | Design | Jadad Score | Diagnosis | No. Of Cases (n)(T/ C) | Interventions | | Dose (day) | Treatment Cycle (months) | Primary Outcomes | Treatment measures |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | T | C | | | | |
| Huang 2019[16] | RCT | 4 | Femoral intertroch-antericfracture | 40/40 | Teriparatide +control group | Conservative treatment | 20 μg/d | 3 | Non-surgical treatment | BMD,PINP,CTX-1 |
| Yin 2021[17] | RCT | 4 | Femoral intertroch-antericfracture | 35/35 | Teriparatide +control group | Calcium carbonate D3 | 20 μg/d | 1 | Non-surgical treatment | BMD,β-CTX,P1NPOCN |
| Bhandari 2016[15] | RCT | 4 | Femoral neckfracture | 78/81 | Teriparatide +control group | Ca+ vitD | 20 μg/d | 6 | Surgical treatment | Fracture healing,Reoperation,Complications,Adverse events,Death, Deformity |
| Malouf-Sierra J[30] | RCT | 5 | Femoral intertroch-antericfracture | 86/85 | Teriparatide +Ca+ vitD | Risedronate +Ca+ vitD | 20 μg/d | 6.5 | Surgical treatment | Fracture healing,BMD, ALP,VAS, TUG,Adverse events,Subsequent fracture |
| Aspenberg 2016[22] | RCT | 5 | Femoral intertroch-antericfracture | 86/85 | Teriparatide +Ca+ vitD | Risedronate +Ca+ vitD | 20 μg/d | 6.5 | Surgical treatment | Fracture healing,TUG, VAS,Death, Deformity,Adverse events,Subsequent fracture |
| Mishra 2022[23] | RCT | 4 | Femoral intertroch-antericfracture | 16/16 | Teriparatide + Ca+ vitD | Ca+ vitD | 20 μg/d | 6 | Surgical treatment | Fracture healing,BMD, Death,Complications |
| Rana 2021[19] | RCT | 5 | Femoral intertroch-antericfracture | 16/16 | Teriparatide +Ca+ vitD | Ca+ vitD | 20 μg/d | 6 | Surgical treatment | Fracture healing,BMD, Death,Complications |
| Chesser 2016[18] | RCT | 5 | Femoral intertroch-antericfracture | 15/14 | Teriparatide+ Ca+ vitD | Ca+ vitD | 20 μg/d | 3 | Surgical treatment | Fracture healing,Adverse events,Death, Complications |

**Table-2:** Methodological quality of the trials analysed.

| References | Random sequence generation | Allocation concealment | Blinding of participants and personnel | Blinding of outcome assessment | Incomplete outcome data | Selective reporting | Other bias |
|---|---|---|---|---|---|---|---|
| Aspenberg 2016[22] | + | + | + | + | + | + | + |
| Bhandari 2016[15] | + | + | + | + | + | + | ? |
| Chesser 2016[18] | + | + | ? | ? | + | + | ? |
| Huang 2019[16] | + | + | ? | ? | + | + | ? |
| Malouf-Sierra J[30] | - | - | - | - | - | - | - |
| Mishra 2022[23] | + | + | ? | ? | + | + | ? |
| Rana 2021[19] | + | + | ? | ? | + | + | ? |
| Yin 2021[17] | + | + | ? | ? | + | + | ? |

*+ =low risk of bias; ? =unclear risk of bias; - =high risk of bias.

**Table-3:** Details of the studies analysed.

| Outcome or subgroup | No. of studies | Participants | Statistical method | Effect size | P |
|---|---|---|---|---|---|
| Fracture healing rate RR (fixed), 95% CI | 6 | 563 | RR(fixed), 95% CI | 1.01[0.96,1.07] | p=0.69 |
| | | | OR(Random), 95% CI | 1.09 [0.72, 1.63] | P=0.69 |
| | | | RD(Random), 95% CI | 0.01[-0.03,0.05] | p=0.69 |
| BMD WMD(fixed), 95% CI | 5 | 336 | WMD(fixed), 95% CI | -0.30[-0.47,-0.12] | P=0.0008 |
| | | | SMD(fixed), 95% CI | -1.17[-1.46,-0.89] | P<0.00001* |
| Mortality RR(fixed), 95% CI | 6 | 684 | RR(fixed), 95% CI | 0.45[0.20,1.03] | P=0.06 |
| | | | OR(fixed), 95% CI | 0.44[0.19,1.03] | P=0.06 |
| | | | RD(fixed), 95% CI | -0.03[-0.06,-0.00] | P=0.05 |
| Adverse events OR(fixed), 95% CI | 4 | 244 | OR(fixed), 95% CI | 1.13 [0.80, 1.61] | P=0.49 |
| | | | RR(fixed), 95% CI | 1.07[0.89,1.27] | P=0.49 |
| | | | RD(fixed), 95% CI | 0.02[-0.05,0.10] | P=0.49 |
| Deformity OR(fixed), 95% CI | 2 | 285 | OR(fixed), 95% CI | 1.23[0.55,2.77] | P=0.61 |
| | | | RR(fixed), 95% CI | 1.21[0.58,2.51] | P=0.61 |
| | | | RD(fixed), 95% CI | 0.02[-0.05,0.08] | P=0.61 |
| Complication OR(fixed), 95% CI | 4 | 252 | OR(fixed), 95% CI | 1.80[0.91,3.57] | P=0.09 |
| | | | RR(fixed), 95% CI | 1.54[0.93,2.54] | P=0.09 |
| | | | RD(fixed), 95% CI | 0.08[-0.01,0.17] | P=0.06 |
| Subsequent fracture OR(fixed), 95% CI | 2 | 432 | OR(fixed), 95% CI | 0.39[0.17, 0.91] | P=0.03* |
| | | | RR(fixed), 95% CI | 0.42[0.19,0.92] | P=0.03* |
| | | | RD(fixed), 95% CI | -0.05[-0.10,-0.01] | P=0.02* |
| TUG WMD(fixed), 95% CI | 2 | 314 | WMD(fixed), 95% CI | -3.31[-4.23,-2.38] | P<0.00001* |
| | | | SMD(fixed), 95% CI | -0.77[-1.00,-0.54] | P<0.00001* |
| VAS WMD(fixed), 95% CI | 2 | 251 | WMD(fixed), 95% CI | -9.72[-11.81,-7.62] | P<0.00001* |
| | | | SMD(fixed), 95% CI | -1.14[-1.41,-0.87] | P<0.00001 |
| PINP WMD(fixed), 95% CI | 2 | 150 | WMD(fixed), 95% CI | -24.70[-31.76,-17.64] | P<0.00001* |
| | | | SMD(fixed), 95% CI | -0.97[-1.31,-0.62] | P<0.00001 |

OR: Odds ratio, RD: Risk difference, RR: Relative ratio, CI: Confidence interval, SMD: Standardised mean difference, WMD: Weighted mean difference, BMD: Bone mineral density, TUG: Timed-up-and-go; VAS, Visual analogue scale, PINP: Procollagen type I N-terminal propeptide.

° Favours treatment group with statistical significance.

Also, 3(37.5%) RCTs used the random number table method [15-17,] and 6(75%) RCTs used the random double-blind grouping method [15-20]. Safety evaluation was reported in 7 studies[15-19,22,23] (Table 2). The risk of bias was noted (Figures 2-3), and the outcome measures were summarised (Table 3).

With respect to fracture healing rate, 6(75%) studies[11-12,15-17,21] compared it after 3 or 6 months of medication between the two groups. The homogeneity statistic $I^2$ value was 0% (p=0.82). There was no statistically significant difference observed in fracture healing rate using the fixed effect model (RR=1.01, 95% CI: 0.96-1.07, p=0.82). Cumulative effect size was 0.39 (p=0.69). In the sensitivity analysis that excluded individual studies, the results remained stable (Figure 4).

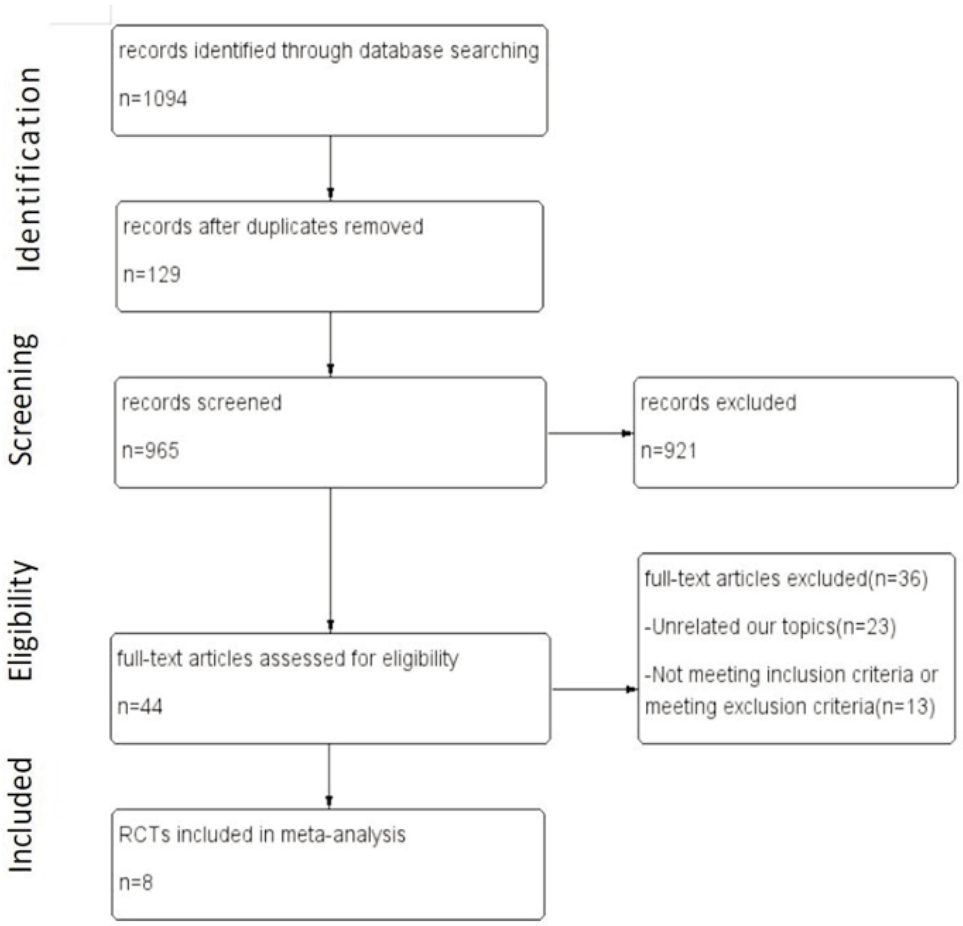


**Figure-1:** Study flow-chart.

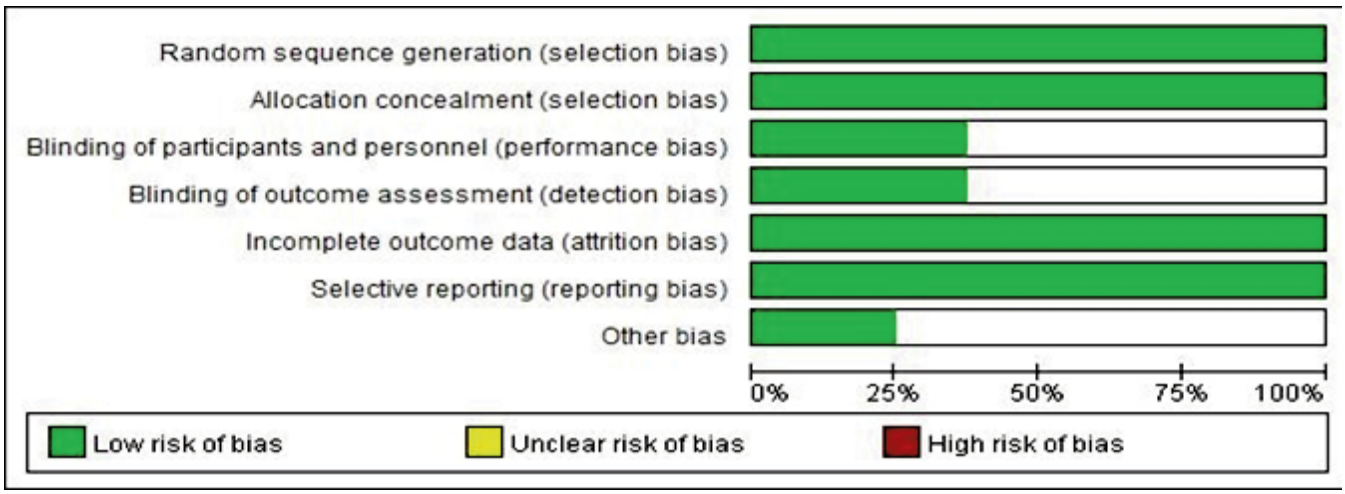


**Figure-2:** Risk of bias graph.

With regard to BMD, 5(62.5%) studies[16-20,21] reported the value before and after intervention. The value of $I^2$was 28% (p=0.24). Using the fixed response model, BMD of the teriparatide group was greater than that of the control group (SMD: -1.17, 95% CI: -1.46--0.89). Cumulative effect size was 0.86 (p<0.001), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 5).

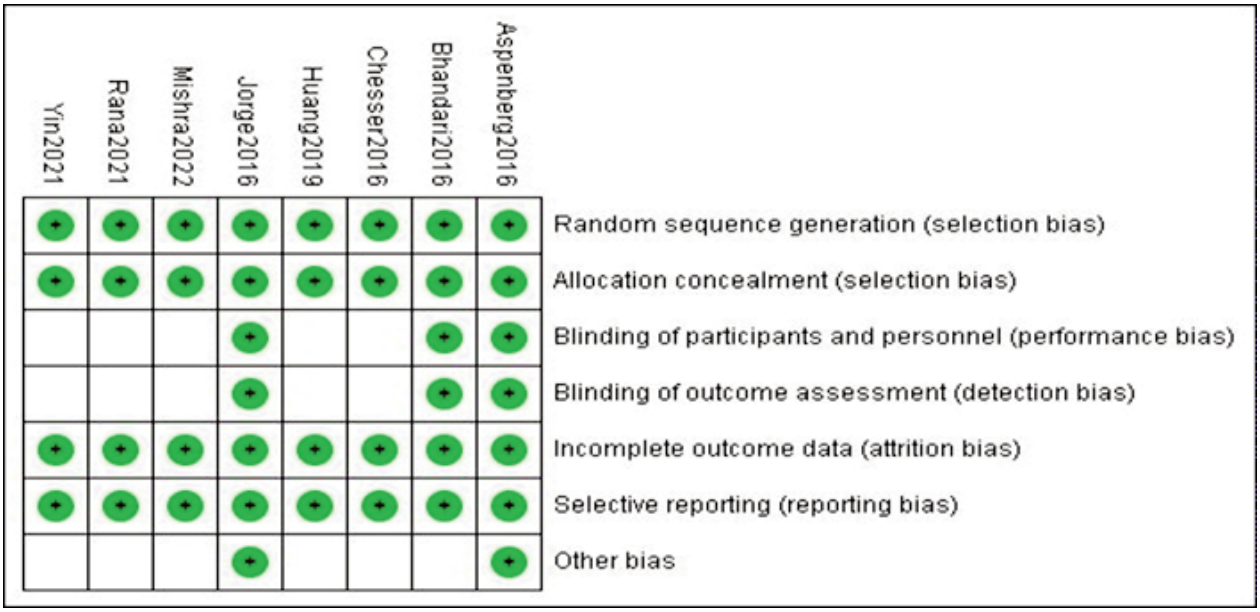


**Figure-3:** Risk of bias summary.

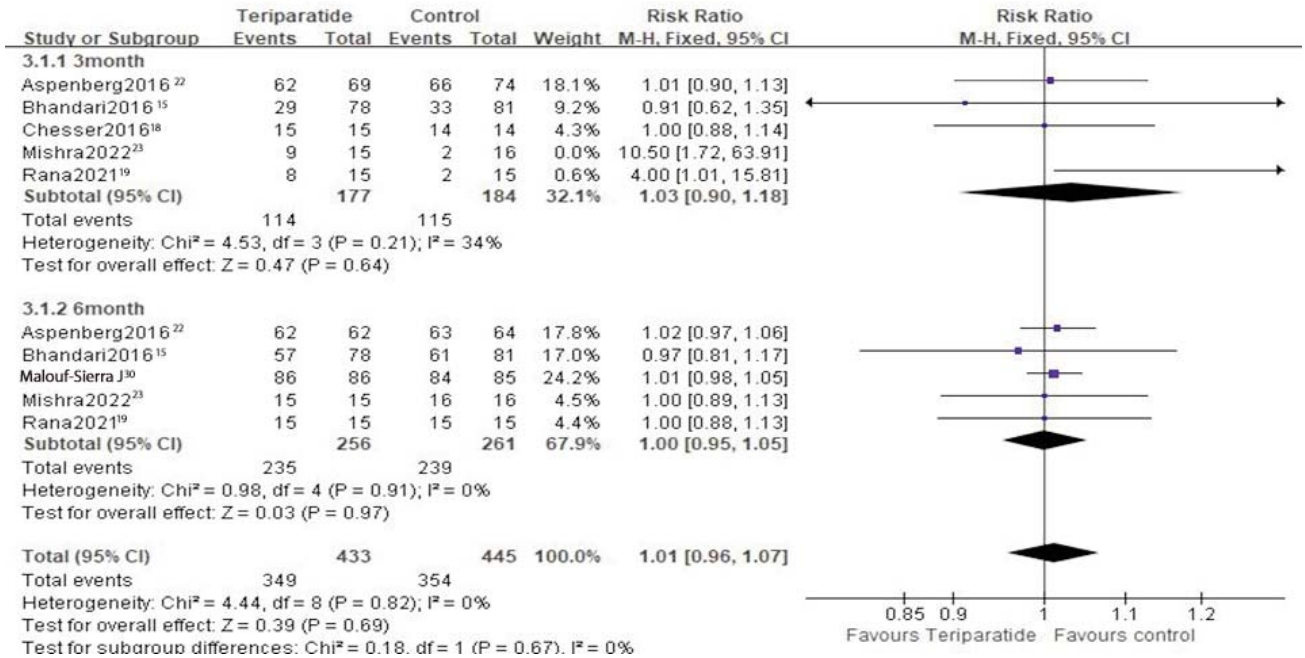


**Figure-4** Forest plot comparing the fracture healing rate between the teriparatide and control groups.

Mortality rates were reported by 6(75%) studies[15-20]. The heterogeneity value of $I^2$ was 0% (p=0.75). Using a fixed effect model, the trends showed a protective effect in the intervention group, but it did attain statistical significance between the two groups (OR: 0.44, 95% CI: 0.19-1.03). Cumulative effect size was 1.90 (p=0.06), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 6).

Adverse events were reported by 4(50%) studies[15-18]. The $I^2$ value was 0% (p=1.00). The fixed-effects model showed no significant difference between the two groups (OR: 1.13, 95% CI: 0.80-1.61). Cumulative effect size was 0.69 (p=0.49), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 7).

Deformity was reported by 2(25%) studies[15,22]. The $I^2$ value was 0% (p=0.37). The fixed effect model showed no

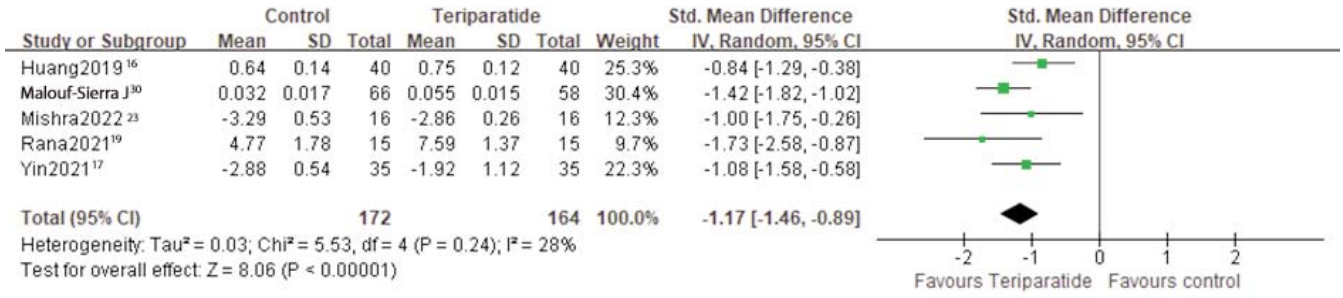


**Figure-5** Forest plots showing a significant improvement in bone mineral density (BMD) in the teriparatide group compared to the control group.

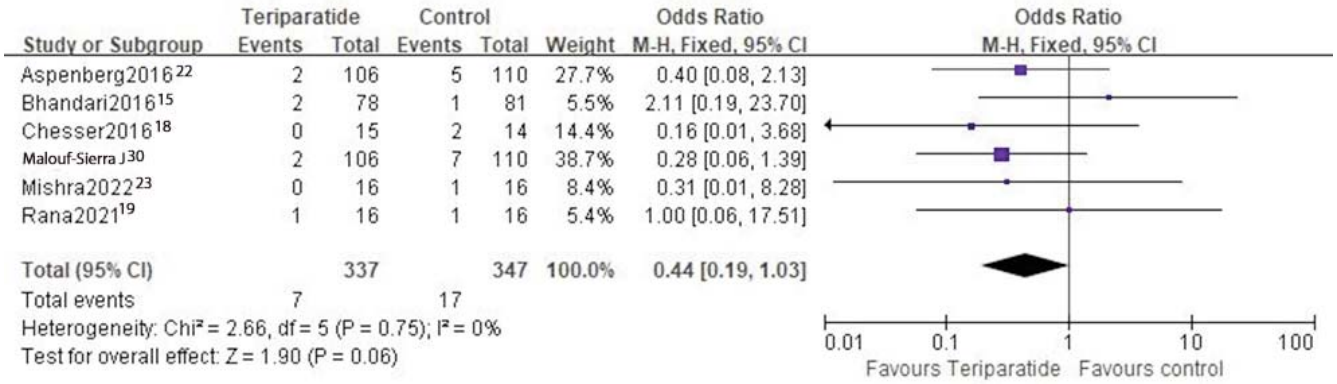


**Figure-6:** Forest plot showing no significant difference with respect to mortality rates between the teriparatide and control groups.

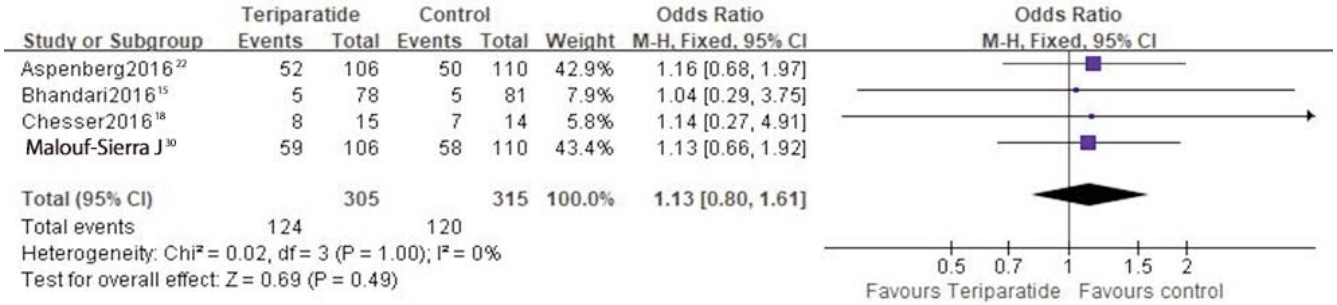


**Figure-7:** Forest plot showing no significant difference with respect to adverse events in the teriparatide and control groups.

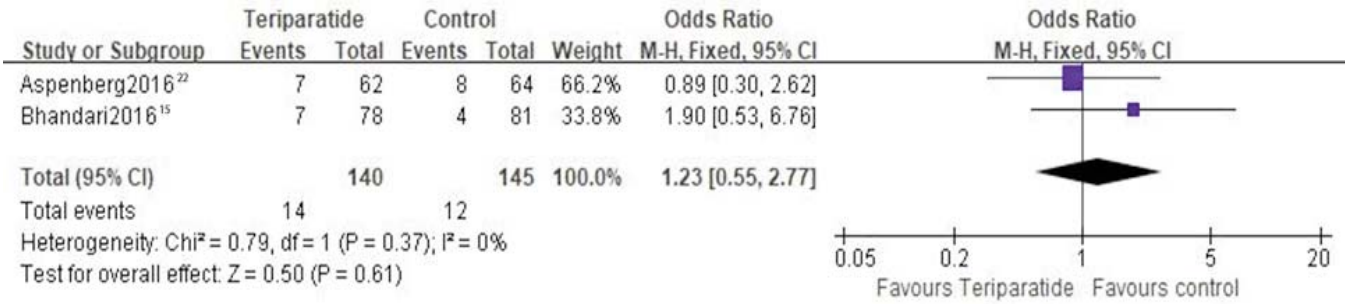


**Figure-8:** Forest plot showing no significant difference with respect to deformity in the teriparatide and control groups.

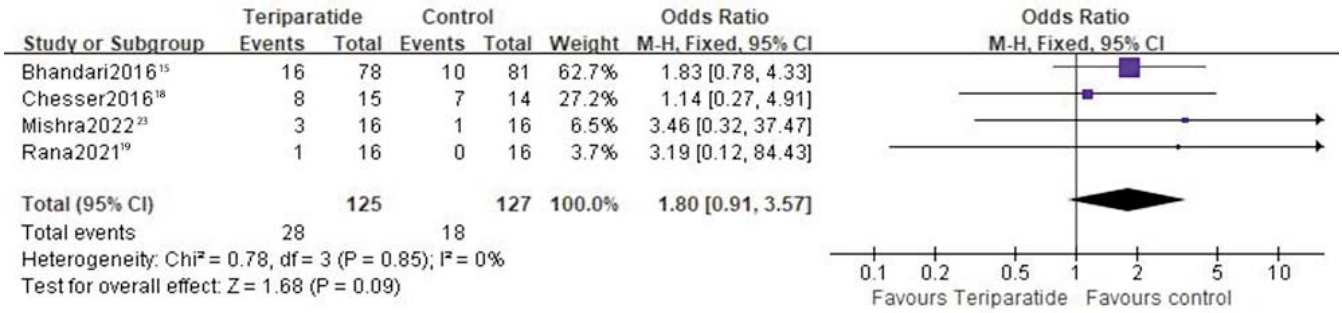


**Figure-9:** Forest plot showing no significant difference with respect to complications in the teriparatide and control groups.

significant difference in the appearance of malformations between the two groups (OR: 1.23, 95% CI: 0.55-2.77). Cumulative effect size was 0.50 (p=0.61), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 8).

Complication rates were reported by 4(50%) studies15,18-20. The value of $I^2$ was 0% (p=0.85). The fixed effect model findings were noted (OR: 1.80, 95% CI: 0.91-3.57). Cumulative effect size was 1.68 (p=0.09), Data that supported a trend of low complications in the control group (p=0.09) did not attain statistical significance. In the sensitivity analysis excluding individual studies, the results remained stable (Figure 9).

Subsequent fracture was report by 2(25%) studies[16,22]. The value of $I^2$ was 0% (p=0.92). Fixed effect model showed that the subsequent follow-up fractures in the teriparatide group were fewer than the control group (OR: 0.39, 95% CI: 0.17-0.91). Cumulative effect size was 2.18 (p=0.03). In the sensitivity analysis excluding individual studies, the results remained stable (Figure 10).

Walking TUG test scores were reported in 2(25%) studies[16,22]. The $I^2$ value was 0% (p=0.66). The fixed effect model showed a protective effect in the intervention group compared to the control group (WMD: -3.31, 95% CI: -4.23--2.38). Cumulative effect size was 7.03 (p<0.001), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 11).

VAS score was reported by 2(25%) studies[16,22]. The fixed


**Figure-10:** Forest plot showing a significant improvement in the subsequent fracture rate in the teriparatide group compared to the control group.

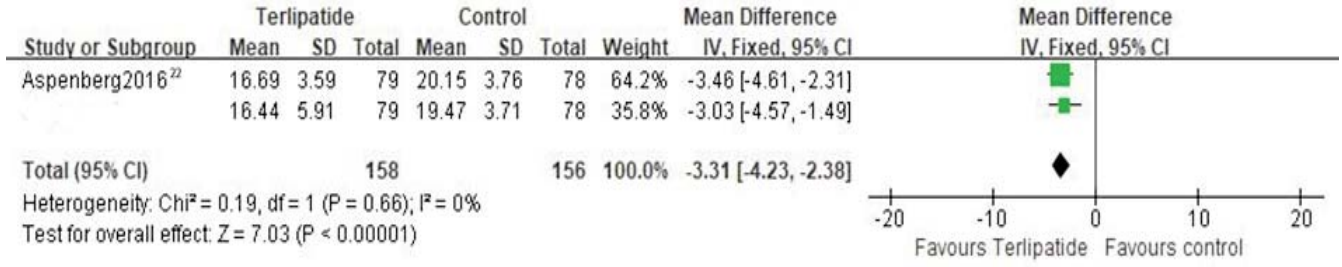


**Figure-11:** Forest plot showing a significant improvement in the timed-up-and-go (TUG) scores in the teriparatide group compared to the control group.

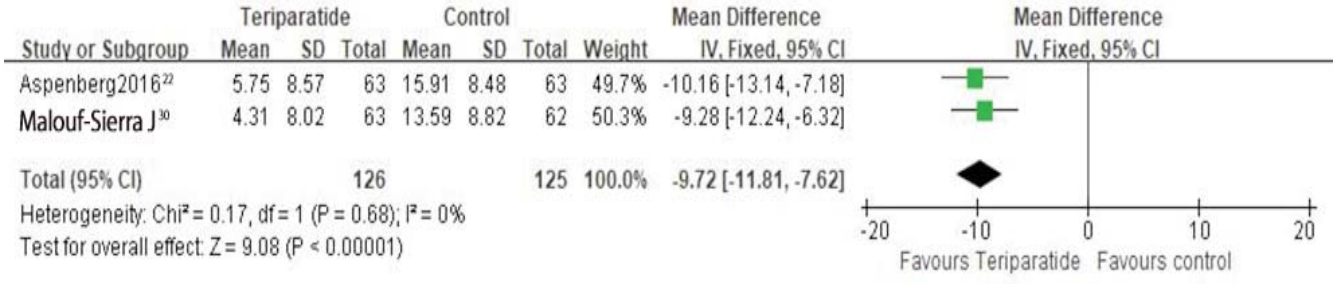


**Figure-12:** Forest plot showing a significant improvement in visual analogue scale (VAS) scores in the teriparatide group compared to the control group.

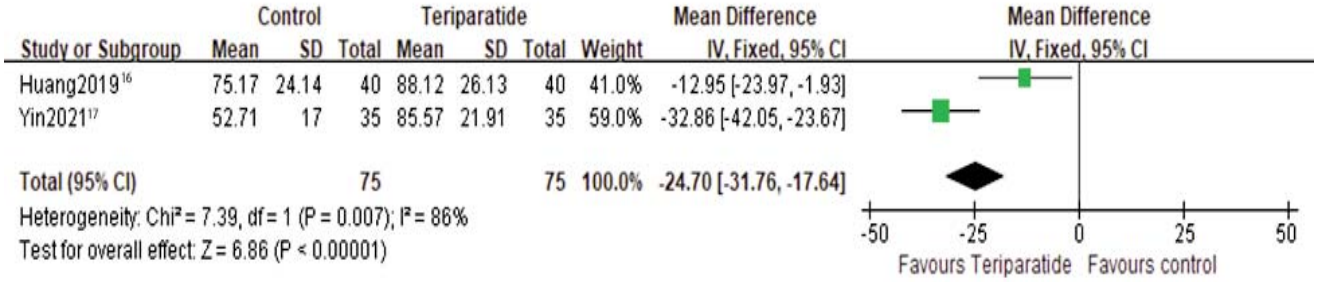


**Figure-13:** Forest plot showing a significant improvement in procollagen type I N-terminal propeptide (PINP) in the teriparatide group compared to the control group

effect model showed a significant reduction in the teriparatide group (MD: -9.72, 95% CI: -11.81--7.62). Cumulative effect size was 9.08 (p<0.001). In the sensitivity analysis excluding individual studies, the results remained stable (Figure 12).

PINP value was reported by 2(25%) studies[16,22]. The $I^2$ value was 26% (p=0.24). Fixed effect model showed that it was higher in the teriparatide group than the control group (MD: -24.70, 95% CI: -31.76--17.64). Cumulative effect size was 6.86 (p<0.001), In the sensitivity analysis excluding individual studies, the results remained stable (Figure 13).

Since the number of studies in the Meta-analysis was <10, no publication bias evaluation could be done as the number of studies was too small to find reasons for any asymmetry[20].

Generally, all the RCTs analysed had good homogeneity. There were no significant differences in the fracture healing rate of the primary endpoint between the 2

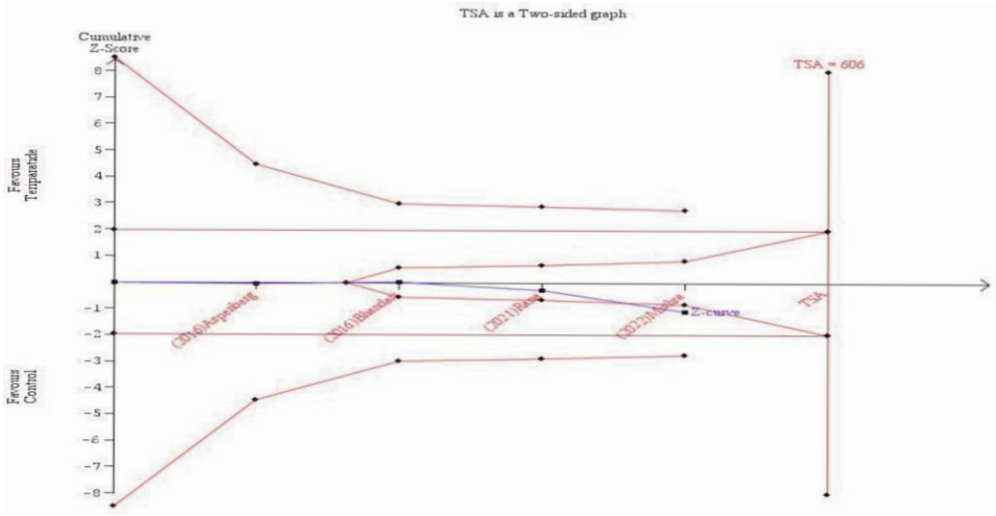


**Figure-14:** Sequential analysis of the fracture healing rate test showing that the cumulative amount of information did not meet expectations, and there were no significant differences with resoect to efficacy between terlipatide and control groups.

groups (RR: 1.01, 95% CI: 0.96-1.07, p=0.82). The overall results were divided into two subgroups. As the heterogeneity $I^2$ value at 3 months was 71% (p=0.01), a sensitivity analysis was performed. After excluding one study[23], the heterogeneity decreased significantly with $I^2$ value 34%, and it was 0% at 6 months. Subgroup analysis showed there were no significant difference in the fracture healing rate between the two groups at 3 months of treatment (RR: 1.03, 95% CI: 0.90-1.18, p=0.64) and 6 months of treatment (RR: 1.00, 95% CI: 0.95-1.05, p=0.97). The cumulative amount of information did not reach the expected amount of information, so there was no statistical difference in efficacy between the groups (Figure 14).

## Discussion

As one of the main complications of osteoporosis, the incidence and mortality of osteoporotic hip fracture are increasing every year. The focus of clinical treatment of osteoporotic hip fractures is to accelerate fracture healing, reduce complications, reduce mortality, and improve patient short-term quality of life. Osteoporosis has become an important reason that affects surgical efficacy and prognosis of patients, and it is among the important factors that lead to the loosening of internal fixation, fracture non-union, or surgical failure. Therefore, patients with osteoporotic hip fracture should adhere to long-term anti-osteoporosis treatment, improve bone density and bone strength, and reduce the possibility of fracture recurrence. Several studies have shown that teriparatide can improve the bone density of osteoporosis patients more efficiently and rapidly than other therapeutic drugs, and can improve the quality of life of patients[24]. In a controlled trial of pelvic fracture patients, PTH1-84 also improved fracture healing. The systematic evaluation and meta-analysis by South Korean scholars[11] included 11 clinical research results, and the evaluation of the effect of teriparatide on fracture healing finally led to the conclusion that there was no difference in fracture healing. Literature showed that teriparatide reduced the healing time of hip fractures, but at 3-6 months, the fracture healing rate did not improve much[12]. In a controlled trial of pelvic fracture patients, PTH1-84 also improved fracture healing. This is contrary to the current findings. A meta-analysis[25] aiming to determine the efficacy and safety of teriparatide verses bisphosphonate in postmenopausal women with osteoporosis found a significant reduction in vertebral and non-vertebral fractures and BMD in the teriparatide group compared to the bisphosphonate group. Manuele et al[26]. found that teriparatide not only reduced the incidence of fracture, but also significantly increased the bone density of the lumbar vertebrae and femoral neck during the treatment of senile osteoporosis. One study[27] showed that teriparatide can significantly reduce the degree of bone pain in the elderly with osteoporosis, but a few adverse reactions of the drug were also reported. Reducing bone pain was consistent with the current results, but adverse reactions were contrary. Only one study mentioned that the healing time of the fracture in the teriparatide group was reduced by approximately 2 weeks. The current study showed that teriparatide had no obvious advantage in reducing adverse events compared to alendronate, which was consistent with the conclusion of one meta-analysis[28]. The FDA believes that continuous use of teriparatide in clinical treatment should not exceed 2 years, as it may increase the risk of osteosarcoma and other toxic side effects, such as Osteomas[29].

The current meta-analysis has limitations. The research included has potential bias risk. The 2 RCTs from China did not explicitly report the concealment of allocation or the blinding method. Also, there was publication bias. Further, individual patient data was missing, leaving the overall dataset insufficient for hierarchical analysis. Besides, the sample size of the included RCTs was relatively small, and all the RCTs had been performed over a short period of time, which means long-term effects could not be evaluated.

Based on the current systematic evaluation, the future design of the teriparatide research method should be based on clinical research of large multicentre, prospective randomised double-blind, controlled trials, incorporating callus formation, disappearance time of radioactive X-ray fracture line, pain, TUG, bone formation markers, drug safety, adverse reactions, and serious side effects.

## Conclusion

Due to the heterogeneity and various biases, the current literature does not support the hypothesis that teriparatide can significantly improve the healing rate of osteoporotic hip fractures and BMD in the elderly.

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**LL:** Conceptualization, Methodology, Validation, Investigation, Formal analysis, Writing original draft.
**JL:** Validation, Investigation, Formal analysis, Writing review and editing.
**WM:** Writing review and editing, Supervision.
**JF:** Writing review and editing, Supervision, final approval.