Am J Transl Res 2025;17(10):7886-7896
www.ajtr.org /ISSN:1943-8141/AJTR0166234

Original Article

Denosumab improves bone mineral density, promotes fracture healing, and reduces recurrent fractures in patients with osteoporotic fractures

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Received May 21, 2025; Accepted September 12, 2025; Epub October 15, 2025; Published October 30, 2025

Abstract: Objective: To evaluate the effects of denosumab on bone mineral density (BMD), fracture healing, recurrent-fracture risk, pain, and safety in patients with osteoporotic fractures. Methods: This retrospective cohort study included 216 patients with osteoporotic fractures treated between January 2019 and June 2023. Patients received either denosumab (60 mg subcutaneously every 6 months; n = 113) or zoledronic acid (5 mg intravenously once annually; n = 103), alongside calcium and calcitriol supplementation. The primary endpoint was the change in lumbar-spine, femoral-neck, and total-hip BMD at 6 and 12 months. Secondary endpoints included serum bone-turnover markers [C-terminal telopeptide of type I collagen (CTX), bone-specific alkaline phosphatase (BALP), procollagen type I N-terminal propeptide (P1NP)], fracture-healing time, 12-month recurrent fracture incidence, pain intensity [Visual Analog Scale (VAS)], function by the Oswestry Disability Index (ODI), analgesic use, and adverse events. Pearson correlation was used to evaluate associations between bone turnover markers and BMD. Results: At 12 months, denosumab significantly increased lumbar-spine, femoral-neck, and total-hip BMD compared to zoledronic acid ($P < 0.05$). CTX and P1NP were significantly lower after 6 and 12 months ($P < 0.05$) and were inversely correlated with BMD gains ($P < 0.05$), while BALP showed no correlation. Denosumab significantly shortened fracture-healing time ($P < 0.05$), improved complete-healing rate ($P < 0.05$), and reduced recurrence ($P < 0.05$). VAS, ODI, and analgesic use were all lower in the denosumab group ($P < 0.05$). The incidence of adverse events was comparable between the two groups ($P > 0.05$). Conclusion: Denosumab substantially enhanced BMD, accelerated fracture healing, reduced recurrent fracture risk, and alleviated pain in patients with osteoporotic fracture, with a safety profile comparable to zoledronic acid.

Keywords: Denosumab, osteoporotic fracture, bone mineral density, pain

Introduction

With the global population aging at an unprecedented rate, osteoporosis and its associated fragility fractures have emerged as critical public health challenges [1]. In the United States, approximately 10 million people aged over 50 already have osteoporosis, and another 34 million are at increased risk [2]. Epidemiologic data from the United Kingdom indicate that one in two women and one in five men over 50 will sustain an osteoporotic fracture during their lifetime [3]. In China, nearly 70 million people are affected, with prevalence rates of 20.7% in women and 14.4% in men over 50; these rates rise sharply after age 60, especially among women [4].

Current management of osteoporotic fractures typically involves surgical fixation combined with conventional anti-osteoporotic therapies, including calcium supplementation, active vitamin D analogues, and bisphosphonates [5, 6]. However, these approaches often fail to markedly improve bone mineral density (BMD) or effectively reduce the risk of subsequent fractures. Indeed, bisphosphonates may inadequately suppress high bone turnover, leading to

https://doi.org/10.62347/SDNL9227

elevated recurrence rates within two years of treatment [7]. Moreover, excessive inhibition of bone remodeling during the healing phase can delay callus formation and increase the risk of atypical fractures [8]. Consequently, there is an urgent need for novel therapies that can both rapidly stabilize bone metabolism and promote efficient fracture repair.

Osteoporotic fractures result from reduced bone mass and deterioration of bone microarchitecture. Effective prevention and treatment depend on suppressing osteoclastic bone resorption, stimulating osteoblastic bone formation, and enhancing overall bone strength [9]. Denosumab, a fully human monoclonal antibody against RANKL, blocks the RANKL-RANK interaction on osteoclast precursors, thereby potently inhibiting osteoclast differentiation and activity while improving bone microstructure [10]. Clinical trials have demonstrated that denosumab reduces vertebral fracture risk in postmenopausal women and is effective in elderly men and in patients with glucocorticoid-induced osteoporosis [11].

However, most existing studies have focused on primary prevention in patients without prior fractures. Data on denosumab's role in secondary prevention, - specifically its effects on fracture healing, dynamic BMD changes, and long-term recurrence risk in patients with established osteoporotic fractures - remain scarce. Patients with fracture often exhibit unique bone metabolic profiles, characterized by accelerated bone resorption during the acute phase and increased demand for bone formation during repair [12]. These alterations may influence both the efficacy and safety of denosumab in this population. Furthermore, the long-term impact of denosumab on healing speed, recurrent fracture rates, and its modulation of bone-turnover markers has not been fully characterized, limiting its use in early post-fracture interventions.

Patients and methods

Study design and data sources

This retrospective study included 216 patients hospitalized with osteoporotic fractures at Affiliated Hospital of Yan'an University between January 2019 and June 2023. Patients were divided into two groups based on treatment modality: the study group (denosumab, n = 113) and the control group (zoledronic acid, n = 103). Data were extracted from the hospital's electronic medical record system and follow-up database. This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Affiliated Hospital of Yan'an University.

Inclusion criteria: Age > 40 years; Clinically confirmed osteoporotic fracture with a clear fracture type; Diagnosis of osteoporosis confirmed by imaging and bone mineral density (BMD) assessment; No severe comorbidities, with ability to tolerate the planned treatment regimen; Complete medical records and follow-up data.

Exclusion criteria: Severe systemic diseases (e.g., severe hepatic or renal insufficiency); Fractures due to other conditions such as malignant tumors; Use of calcitonin, bone formation-promoting drugs, bisphosphonates, estrogen, or selective estrogen receptor modulators within 12 months before treatment; Pregnancy or lactation.

Treatment regimen

All patients received basic therapy with oral calcium (calcium carbonate and vitamin D3 tablets, each containing 500 mg calcium and 200 IU vitamin D3, two tablets per day) and calcitriol (0.25 μg per capsule, one capsule daily). In addition, patients in the study group received subcutaneous injections of denosumab (60 mg) once every 6 months. The control group received an intravenous infusion of zoledronic acid (5 mg in 100 mL), diluted in 1000 mL of 0.9% sodium chloride solution, once per year. Both groups were treated for one year.

Data collection

Baseline data were extracted from the electronic medical records and included: Demographic information: age, sex, smoking history, alcohol consumption, and past medical history (e.g., diabetes, history of fractures, corticosteroid use); Clinical data: fracture type and location, interval from fracture to treatment, comorbidities (e.g., diabetes, hypertension), body mass index (BMI); Laboratory and imaging data: pre-treatment BMD of the lumbar spine, femoral neck, and total hip, measured using dual-

energy X-ray absorptiometry (DXA, device: GE Lunar Prodigy).

Bone turnover markers before treatment: serum bone-specific alkaline phosphatase (BALP), C-terminal telopeptide of type I collagen (CTX), and procollagen type I N-terminal propeptide (P1NP), measured by enzyme-linked immunosorbent assay (ELISA). Serum calcium and phosphorus levels (mmol/L) measured using a fully automatic biochemical analyzer (Roche Cobas 8000).

Outcome measures

Primary outcome measures: 1. Dynamic changes in BMD: BMD was assessed at baseline, 6 months, and 12 months using the same DXA scanner by a single experienced technician. Each site was measured three times, and the mean value was used for analysis. Measurement sites included lumbar spine (L1-L4), femoral neck, total hip, with positioning standardized according to the International Society for Clinical Densitometry (ISCD). 2. Fracture healing and recurrent fractures: Fracture healing time: defined as the interval from initial treatment to radiographic confirmation of healing, characterized by blurring of the fracture line and formation of continuous callus on X-ray. 12-month complete healing rate: proportion of patients showing radiographic disappearance of the fracture line, accompanied by absence of local tenderness or percussion pain. Recurrent fracture rate: incidence of new fragility fractures (excluding traumatic fractures) during follow-up, recorded at 6 and 12 months through outpatient review or telephone follow-up.

Secondary outcome measures: 1. Bone turnover markers: Serum samples were collected at the same time points as BMD assessments. Five milliliters of fasting venous blood were collected, centrifuged for serum separation, and stored at -80°C for batch analysis. 2. Adverse events: Adverse events during treatment included gastrointestinal symptoms (nausea, vomiting, diarrhea), hepatic or renal function dysfunction (ALT/AST > 2× upper normal limit or Scr > 1.5× baseline), rash, musculoskeletal pain, fatigue, etc. For each event, onset time, duration, and management were recorded. 3. Pain assessment: Pain intensity was evaluated using the Visual Analog Scale (VAS, 0-10; 0 = no pain, 10 = worst pain) at baseline, 6 months, and 12 months. 4. Functional assessment: Lumbar dysfunction was assessed with the Oswestry Disability Index (ODI, 0%-100%), a 10-item questionnaire where higher scores indicate more severe dysfunction. Scores were collected with guidance from trained nurses. 5. Analgesic usage: The proportion of patients requiring analgesics (NSAIDs such as ibuprofen or opioids such as tramadol) for pain relief during follow-up was recorded.

Statistical analysis

All statistical analyses were performed using SPSS 26.0. Continuous variables were expressed as mean ± standard deviation (SD) and compared using independent-samples t-tests or repeated-measures ANOVA followed by the least significant difference (LSD) test. Categorical data were expressed as frequencies (percentage) and analyzed using chi-square tests. Pearson correlation analysis was used to assess associations between changes in bone turnover markers and BMD improvement. A P-value < 0.05 was considered significant.

Results

Baseline data

Baseline characteristics were comparable between the two groups, with no significant differences in age, sex, smoking history, interval from fracture to treatment, prior fractures, corticosteroid use, diabetes mellitus, number of fracture sites, prior osteoporosis therapy, BMI, or fracture location (all P > 0.05; **Table 1**).

Changes in BMD

At baseline, BMD values at the total hip, femoral neck, and lumbar spine did not differ significantly between the two groups (all P > 0.05). Six months after treatment, lumbar spine BMD remained comparable (P > 0.05), whereas total hip and femoral neck BMD were significantly higher in the study group than in the control group (P < 0.05). At 12 months, the study group demonstrated significantly higher BMD at all three sites compared to the control group (all P < 0.05) (**Table 2**).

Changes in bone metabolism markers

Baseline levels of bone turnover markers (BALP, CTX, and P1NP), as well as serum calcium and

Table 1. Baseline data

	Study Group (n = 113)	Control Group (n = 103)	χ^2	P
Age			0.117	0.732
≤ 65 years	37 (32.74)	36 (34.95)		
> 65 years	76 (67.26)	67 (65.05)		
Gender			0.725	0.395
Male	20 (17.70)	23 (22.33)		
Female	93 (82.30)	80 (77.67)		
Smoking History			0.669	0.413
Yes	15 (13.27)	10 (9.71)		
No	98 (86.73)	93 (90.29)		
Interval from Fracture to Treatment			0.533	0.465
≤ 72 h	46 (40.71)	47 (45.63)		
> 72 h	67 (59.29)	56 (54.37)		
Previous Fracture History			0.24	0.624
Yes	63 (55.75)	54 (52.43)		
No	50 (44.25)	49 (47.57)		
Corticosteroid Use History			1.061	0.303
Yes	17 (15.04)	21 (20.39)		
No	96 (84.96)	82 (79.61)		
Presence of Diabetes			0.449	0.503
Yes	25 (22.12)	19 (18.45)		
No	88 (77.88)	84 (81.55)		
Number of Fracture Sites			0.528	0.467
Single	84 (74.34)	72 (69.90)		
Multiple	29 (25.66)	31 (30.10)		
Previous Osteoporosis Treatment			1.07	0.301
Yes	29 (25.66)	33 (32.04)		
No	84 (74.34)	70 (67.96)		
BMI			2.42	0.298
< 18.5 kg/m^2	30 (26.55)	19 (18.45)		
18.5-23.9 kg/m^2	66 (58.41)	70 (67.96)		
> 23.9 kg/m^2	17 (15.04)	14 (13.59)		
Fracture Site			0.536	0.765
Spine	63 (55.75)	60 (58.25)		
Hip	33 (28.70)	31 (30.10)		
Radius	17 (15.04)	12 (11.65)		

Note: BMI, body mass index.

phosphorus levels, did not differ significantly between the two groups (all P > 0.05). At 6 months post-treatment, the study group showed marked reductions in CTX, BALP, and P1NP compared with the control group (P < 0.05). Serum calcium was also significantly lower in the study cohort (P < 0.05), while phosphorus levels remained comparable (P > 0.05). After 12 months of therapy, these bone turnover markers remained significantly lower in the study group (all P < 0.05), with no significant intergroup differences in serum calcium or phosphorus (both P > 0.05) (**Table 3**).

Fracture healing and recurrent fracture rates

The study group achieved significantly shorter fracture union times compared to the control group (P < 0.05). By 12 months, a higher proportion of patients in the study group achieved complete healing (P < 0.05). Recurrent fracture rates at 6 months did not differ significantly

Table 2. Changes in BMD

	Before treatment	6 months after treatment	12 months after treatment	F	P
BMD of the total hip (g/cm^2)					
Study Group (n = 113)	0.78±0.08	0.81±0.07	0.84±0.06	20.477	< 0.001
Control Group (n = 103)	0.79±0.10	0.77±0.09	0.80±0.07	3.135	0.045
t	0.815	3.663	4.520		
P	0.416	< 0.001	< 0.001		
BMD of the lumbar spine (g/cm^2)					
Study Group (n = 113)	0.81±0.09	0.85±0.09	0.91±0.07	40.701	< 0.001
Control Group (n = 103)	0.80±0.10	0.84±0.09	0.86±0.07	12.539	< 0.001
t	0.774	0.816	5.243		
P	0.440	0.416	< 0.001		
BMD of the femoral neck (g/cm^2)					
Study Group (n = 113)	0.73±0.07	0.77±0.06	0.80±0.06	34.554	< 0.001
Control Group (n = 103)	0.72±0.10	0.74±0.07	0.75±0.07	3.995	0.019
	0.857	3.390	5.650		
	0.392	< 0.001	< 0.001		

Note: BMD, bone mineral density.

Table 3. Changes in bone metabolism markers

	Before treatment	6 months after treatment	12 months after treatment	F	P
CTX (ng/mL)					
Study Group (n = 113)	0.53±0.15	0.33±0.07	0.23±0.05	264.55	< 0.001
Control Group (n = 103)	0.51±0.16	0.46±0.15	0.38±0.10	22.869	< 0.001
t	0.948	8.278	14.127		
P	0.344	< 0.001	< 0.001		
P1NP (μg/L)					
Study Group (n = 113)	69.70±15.39	42.61±12.15	36.09±11.42	209.15	< 0.001
Control Group (n = 103)	67.43±14.81	50.46±12.50	48.06±12.20	65.691	< 0.001
t	1.102	4.678	7.447		
P	0.272	< 0.001	< 0.001		
BALP (μg/L)					
Study Group (n = 113)	29.83±9.69	16.81±6.83	13.86±7.10	128.20	< 0.001
Control Group (n = 103)	28.48±7.72	21.41±7.84	19.74±6.77	39.856	< 0.001
t	1.125	4.607	6.215		
P	0.262	< 0.001	< 0.001		
Serum calcium (mmol/L)					
Study Group (n = 113)	2.27±0.12	2.18±0.11	2.17±0.09	27.720	< 0.001
Control Group (n = 103)	2.25±0.10	2.21±0.09	2.19±0.08	8.240	< 0.001
t	1.324	2.181	1.720		
P	0.187	0.030	0.087		
Serum phosphorus (mmol/L)					
Study Group (n = 113)	1.16±0.15	1.08±0.15	1.07±0.11	14.447	< 0.001
Control Group (n = 103)	1.13±0.12	1.11±0.13	1.09±0.13	2.564	0.078
t	1.613	1.563	1.224		
P	0.108	0.119	0.222		

Note: CTX, C-terminal telopeptide of type I collagen, P1NP, procollagen type I N-terminal propeptide, BALP, bone-specific alkaline phosphatase.

Table 4. Fracture healing and recurrent fracture rates

	Study Group (n = 113)	Control Group (n = 103)	χ^2	P
Complete Healing at Post-treatment 12 months	104 (92.04)	82 (79.61)	6.954	0.008
Recurrent Fracture during 6-month follow-up	4 (3.54)	6 (5.83)	0.637	0.425
Recurrent Fracture during 12-month follow-up	7 (6.19)	16 (15.53)	4.940	0.026

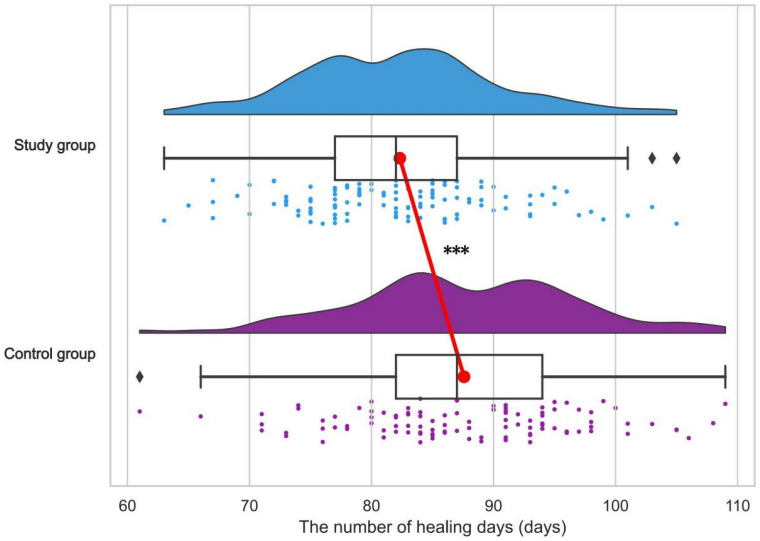

Figure 1. Comparison of fracture healing times between the two groups. Note: ***P < 0.001.

between groups (P > 0.05); however, at 12 months, the recurrence rate was significantly lower in the study than in control group (P < 0.05) (**Table 4**; **Figure 1**).

Adverse events

Adverse events reported in the study group included gastrointestinal reactions, hepatic and renal function abnormalities, rash, musculoskeletal pain, and fatigue; however, no rash or hepatic/renal function abnormalities were observed in the control group. The overall incidence of adverse events was 18.58% in the study group and 11.65% in the control group, with no significant difference between the groups (P > 0.05; **Table 5**).

Pain level and functional outcomes

At baseline, VAS scores or ODI values did not differ significantly between cohorts (both P > 0.05). At both 6- and 12-month post-treatment, the study group reported significantly lower VAS scores compared to the control group (P < 0.05). Concurrently, ODI values were significantly improved in the study group at these time points, with values markedly lower than those in the control group (P < 0.05). Moreover, the proportion of patients requiring analgesic medications was significantly lower in the study cohort at both 6 and 12 months (P < 0.05; **Table 6**).

Correlation between changes in bone metabolism markers and BMD

Pearson correlation analysis revealed that reductions in CTX and P1NP were strongly and inversely associated with increases in BMD at the lumbar spine, femoral neck, and total hip (all P < 0.001). In contrast, alterations in BALP did not correlate significantly with BMD improvements at any sites (all P > 0.05; **Figure 2**).

Discussion

The management of osteoporotic fractures necessitates a dual focus on fracture healing and bone quality reconstruction, as both are critical determinants of patient outcomes. In this retrospective study, denosumab demonstrated significant clinical benefits in patients with osteoporotic fractures. Specifically, it significantly improved BMD, accelerated fracture healing, lowered the 12-month recurrent fracture risk, and enhanced pain relief and functional recovery. These findings are consistent with previous studies, further supporting the effectiveness of denosumab in the management of osteoporosis [13].

A prominent finding of this study is the superior effect of denosumab on BMD compared to

Table 5. Adverse events

	Study Group (n = 113)	Control Group (n = 103)	χ^2	P
Gastrointestinal Reactions	6 (5.31)	3 (2.91)		
Hepatic/Renal Function Abnormalities	2 (1.77)	0 (0.00)		
Rash	2 (1.77)	0 (0.00)		
Musculoskeletal Pain	8 (7.08)	5 (4.85)		
Fatigue	3 (2.65)	4 (3.88)		
Total Adverse Events	21 (18.58)	12 (11.65)	2.001	0.157

Table 6. Comparison of pain level and functional improvement between the two groups

	Before treatment	6 months after treatment	12 months after treatment	F	P
		VAS score			
Study Group (n = 113)	6.84±1.38	4.21±1.90	2.51±0.88	256.55	< 0.001
Control Group (n = 103)	6.64±1.44	6.06±1.51	4.98±1.28	36.600	< 0.001
t	1.042	7.872	16.647		
P	0.299	< 0.001	< 0.001		
		ODI			
Study Group (n = 113)	37.13±6.50	24.66±8.11	23.53±8.19	110.27	< 0.001
Control Group (n = 103)	36.57±8.51	31.86±7.70	29.81±7.2	20.225	< 0.001
t	0.546	6.676	5.961		
P	0.586	< 0.001	< 0.001		
		Pain Medication Usage Rate			
Study Group (n = 113)		51 (45.13)	25 (22.12)		
Control Group (n = 103)		65 (63.11)	40 (38.83)		
χ^2		7.002	7.153		
P		0.008	0.008		

Note: VAS, visual analogue scale, ODI, oswestry disability index.

zoledronic acid. After 6 months of treatment, the denosumab group showed significantly higher BMD at the femoral neck and total hip, and by 12 months, this advantage extended to the lumbar spine as well. These outcomes are in line with earlier research. For example, Greenspan et al. reported that long-term denosumab use in elderly patients increased spine and hip BMD by 7.4% and 4.6%, respectively [14]. Similarly, a cohort study by Curtis et al. demonstrated that compared with alendronate, denosumab significantly reduced hip fracture risk by 36%, with long-term use (≥ 5 years) further lowering the incidence of fractures [15]. The mechanism underlying these benefits is related to denosumab's potent inhibition of osteoclast activity, thereby reducing bone resorption. In fracture patients, this action rapidly corrects post-injury metabolic imbalance and facilitates BMD recovery during the healing phase [16]. In contrast, traditional bisphosphonates like zoledronic acid can also improve BMD, but their effects are slower in high bone-turnover states and, with prolonged use, may excessively suppress bone remodeling, potentially hindering fracture healing [17]. Rotman-Pikielny et al. found that although both denosumab and zoledronic acid induced a similar rise of parathyroid hormone (approximately 20%), denosumab did not significantly affect bone metabolic homeostasis [18]. This indicates that denosumab modulates bone metabolism more precisely, making it more effective in improving BMD and reducing fracture risk in fracture patients.

Fracture healing is a crucial issue in the treatment of osteoporotic fractures, and the results of this study highlight the favorable effect of denosumab on this process. Patients in the denosumab group experienced significantly shorter fracture healing times than those in the

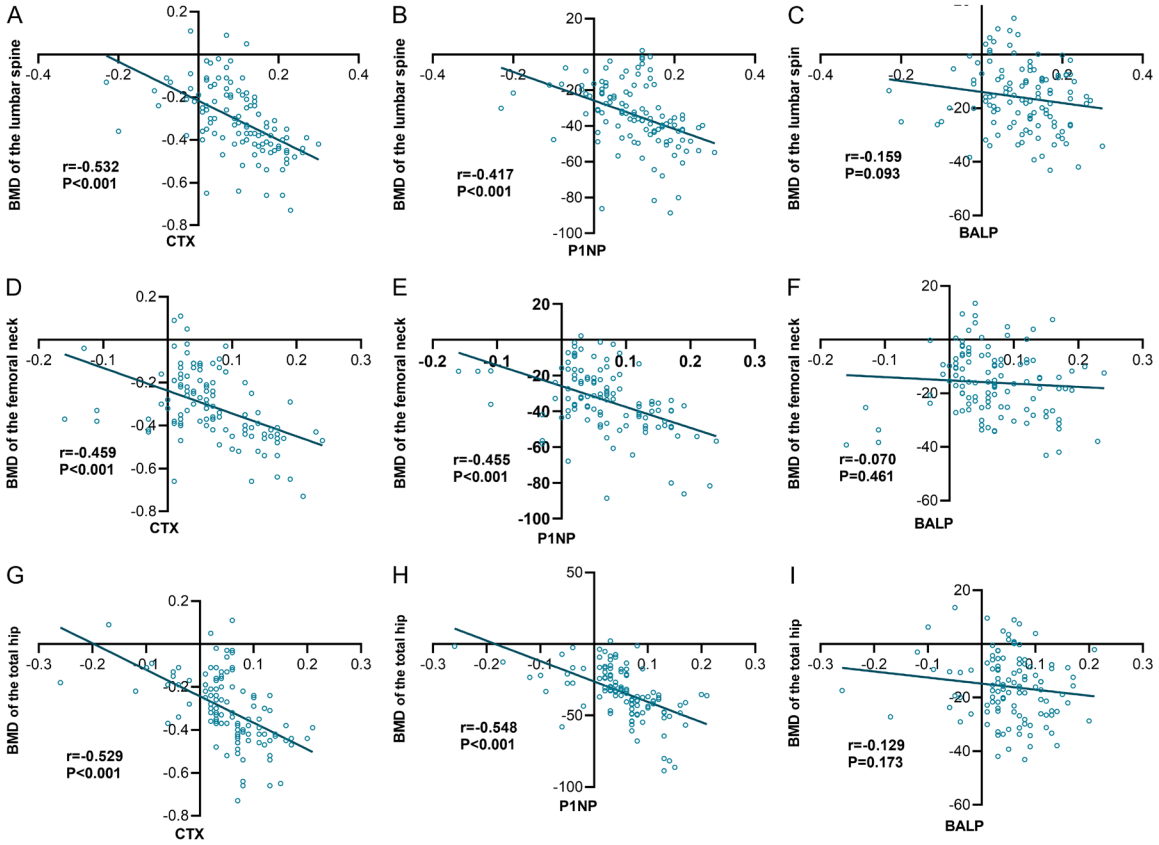

Figure 2. Correlation between changes in bone metabolism markers and bone mineral density increase. A. There was a negative correlation between the increase in lumbar spine BMD and the change in CTX before and after treatment (r = -0.532, P < 0.001). B. There was a negative correlation between the increase in lumbar spine BMD and the change in P1NP before and after treatment (r = -0.417, P < 0.001). C. There was no significant correlation between the increase in lumbar spine BMD and the change in BALP before and after treatment (r = -0.159, P = 0.093). D. There was a negative correlation between the increase in femoral neck BMD and the change in CTX before and after treatment (r = -0.459, P < 0.001). E. There was a negative correlation between the increase in femoral neck BMD and the change in P1NP before and after treatment (r = -0.445, P < 0.001). F. There was no significant correlation between the increase in femoral neck BMD and the change in BALP before and after treatment (r = -0.070, P = 0.461). G. There was a negative correlation between the increase in total hip BMD and the change in CTX before and after treatment (r = -0.539, P < 0.001). H. There was a negative correlation between the increase in total hip BMD and the change in P1NP before and after treatment (r = -0.548, P < 0.001). I. There was no significant correlation between the increase in total hip BMD and the change in BALP before and after treatment (r = -0.129, P = 0.173). Note: BMD, bone mineral density, CTX, C-terminal telopeptide of type I collagen, P1NP, procollagen type I N-terminal propeptide, BALP, bone-specific alkaline phosphatase.

control group, and a higher proportion achieved complete fracture healing within 12 months (92.04% vs. 79.61%). This is particularly meaningful, as traditional bisphosphonates, while inhibiting bone resorption, has been associated with excessive bone hardening, delayed callus formation, and increased risk of atypical fractures [19]. In contrast, denosumab acts directly on the RANKL-RANK signaling pathway, inhibiting bone resorption without affecting bone formation during the healing phase [20]. Through selective regulation of bone metabolism, denosumab reduces excessive resorption without impeding osteogenesis, thus avoiding the adverse effects associated with bisphosphonates. Additionally, a cohort study by Lyu et al. pointed out that delaying denosumab injection by more than 16 weeks significantly increased the risk of vertebral fractures (HR = 3.91) [21], highlighting the importance of maintaining timely dosing to sustain therapeutic efficacy. Taken together, these findings suggest that denosumab accelerates fracture healing by stabilizing bone metabolism and

enhancing bone microstructure, thereby creating a more favorable environment for fracture healing.

In terms of the risk of recurrent fractures, no significant difference was observed between the two groups at 6 months; however, by 12 months, the re-fracture rate in the denosumab group was significantly lower than that in the control group (6.19% vs. 15.53%). This finding further confirms the potential of denosumab in preventing recurrent osteoporotic fractures. Relevant literature indicates that 5 years of denosumab treatment reduces the risk of major osteoporotic fractures by 31%, highlighting its long-term protective effects [15]. These results collectively suggest that denosumab reduces the risk of recurrent fractures through multiple mechanisms, including improving BMD, promoting fracture healing, and reducing bone resorption, with more pronounced efficacy in long-term interventions.

This study also explored dynamic changes in bone metabolism markers, providing insights into the mechanisms underlying denosumab's action. At post-treatment 6 months, the denosumab group had significantly lower levels of the bone resorption marker CTX and the bone formation markers BALP and P1NP compared to the control group, indicating that denosumab effectively suppresses bone turnover. Pearson correlation analysis further revealed that changes in CTX and P1NP were significantly and negatively correlated with increases in BMD, whereas changes in BALP showed no significant correlation with BMD increase. This suggests that the dynamic changes in bone resorption and bone formation directly affect BMD, and highlights the unique role of denosumab in regulating bone metabolism - its inhibition of bone resorption play key roles in increasing BMD. Additionally, the denosumab group showed a modest reduction in serum calcium at post-treatment 6 months compare with the control group, while phosphate levels remained comparable. It is worth noting that literature has shown that sequential treatment with teriparatide and denosumab can further enhance spinal BMD by 21.9% [22], suggesting that combination therapy may further optimize the bone metabolic environment, which is a direction worthy of exploration in future research.

Pain relief is an important therapeutic goal in the management of osteoporotic fractures. In this study, patients treated with denosumab reported significantly lower VAS scores and better ODI scores at both 6 and 12 months compared with controls, along with a lower proportion of patients requiring analgesics. These findings are supported by a clinical trial conducted by Tsai et al., which showed that denosumab combined with high-dose teriparatide significantly alleviated pain (with a VAS score reduction of more than 30%) [23]. These results indicate that denosumab not only improves BMD and promotes fracture healing but also effectively alleviates pain and enhances quality of life, reinforcing its potential as a preferred treatment option for osteoporotic fractures.

Several limitations of this study should be acknowledged. First, due to the study's retrospective nature, it is difficult to fully control confounding factors such as calcium intake and fall risk, which may have an impact on the outcomes. Second, bone microstructure (such as HR-pQCT) and biomechanical parameters were not included, which limits deeper understanding of denosumab's effects on bone quality. Future research should conduct multi-center prospective randomized controlled trials with larger cohorts and longer follow-up to validate these findings. In addition, sequential treatment strategies deserve further exploration. Evidence suggests that switching from teriparatide to denosumab can maintain an 18.3% increase in spinal BMD, whereas the reverse sequence may lead to bone loss [24]. Evaluating follow-up beyond 24 months will also be essential to assess long-term efficacy and capture rare adverse events.

In conclusion, denosumab demonstrates significant efficacy in the treatment of osteoporotic fractures. It effectively improves BMD, accelerates fracture healing, reduces the risk of recurrent fractures, alleviates pain, and enhances functional recovery, making it a valuable therapeutic option in clinical practice.

Acknowledgements

This study was supported by the Key R&D projects in Yan'an City (2024SLSFGG-102).

Disclosure of conflict of interest

None.

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