Systematic Review and Meta-Analysis

Medicine®

OPEN

Effects of teriparatide versus alendronate for treatment of postmenopausal osteoporosis

A meta-analysis of randomized controlled trials

Ya-Kang Wang, MD*, Si-Qing Qin, MD, Tao Ma, MD, Wei Song, MD, Ren-Qi Jiang, MD, Jian-Bin Guo, MD, Kun Li, MD, Yu-Min Zhang, MD*

Abstract

Objectives: Osteoporosis remains a clinical challenge. Teriparatide is an anabolic drug and alendronate is an antiresorptive agent; both are used in the treatment of osteoporosis. Comprehensive reviews investigating the comparative safety and efficacy of teriparatide versus alendronate are scarce. Therefore, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the safety and efficacy of teriparatide versus alendronate for the treatment of postmenopausal osteoporosis.

Methods: We conducted a comprehensive literature review of the PubMed, EMBASE, Cochrane Controlled Trials Registry, and the China Academic Journal Network Publishing databases for relevant RCTs of teriparatide versus alendronate in postmenopausal osteoporosis patients. Outcome measures were percentage change in lumbar spine and femoral neck bone mineral density (BMD) and incidence of vertebral and nonvertebral fractures. Effect size was reported as weighted mean differences (WMDs) for continuous outcomes and odds ratios (OR) for dichotomous outcomes, with associated 95% confidence intervals (CIs).

Results: Six trials involving 618 patients were included. The meta-analysis demonstrated a significant increase in lumbar spine BMD (WMD: 3.46, 95% CI: 2.15–4.77, $P < .00001$), but not femoral neck BMD (WMD = 1.50, 95% CI: 0.04–2.95, $P = .04$), in postmenopausal osteoporosis patients treated with teriparatide compared with alendronate for 6 to 18 months. These beneficial effects were apparent in the lumbar spine at 12 months of treatment (WMD: 4.49, 95% CI: 2.57–6.40, $P < .01$). Teriparatide was not superior to alendronate in reducing fracture risk (OR: −0.03, 95% CI: −0.12 to 0.07; $P = .52$).

Conclusion: Teriparatide may be superior to alendronate for increasing lumbar spine BMD in postmenopausal osteoporosis. The efficacy and safety of long-term teriparatide and alendronate treatment in postmenopausal osteoporosis should be further investigated in clinical trials.

Abbreviations: BMD = bone mineral density, CI = confidence interval, OR = odds ratio, PTH = parathyroid hormone, QALY = quality-adjusted life year, RCTs = randomized controlled trials, WMD = weighted mean difference.

Keywords: alendronate, meta-analysis, osteoporosis, postmenopausal, teriparatide

1. Introduction

Osteoporosis is a persistent public health problem that is common in older women. Approximately 30% of postmenopausal women have osteoporosis according to the World Health Organization definition of osteoporosis.[1,2] Despite therapy, fractures frequently occur in trabecular bone, predominantly in the lumbar spine and the femoral neck.[3,4] The most common osteoporotic fractures in postmenopausal women occur in the spine and hip. Among these, nonvertebral fractures are associated with the highest morbidity and mortality. The annual disability and mortality rates associated with hip fractures are estimated at 50% and 20%, respectively.[5]

Parathyroid hormone (PTH) is an anabolic agent that has widespread clinical application.[6] Teriparatide is a PTH that is approved for use in osteoporosis. Teriparatide induces the production of osteoblasts and inhibits osteoblast apoptosis, resulting in a rapid increase in bone microstructure and strength.[7] Bisphosphonates are widely used to prevent or treat osteoporosis as they induce osteoclast apoptosis and inhibit bone resorption.[8] Alendronate, a second-generation bisphosphonate, inhibits osteoclast activity, reduces bone resorption, and maintains the balance of bone resorption and formation. Alendronate may also stimulate osteoblast differentiation, and prevent or mitigate osteocyte and osteoblast apoptosis.[9,10] Alendronate is an effective and well-tolerated drug for prevention and treatment of postmenopausal osteoporosis, maintaining bone mineral density (BMD) and fracture benefits for up to 2 years.[3,11]

BMD is a major determinant of fractures and an essential parameter for the evaluation of anabolic and antiosteoporotic drugs used in clinical therapy. An increasing number of studies

Editor: Yi Shu.

The authors have no funding and conflicts of interest to disclose.

Department of Joint Surgery, Hong-Hui Hospital, Xi'an Jiaotong University College of Medicine, Xi'an, China.

* Correspondence: Ya-Kang Wang, Hong-Hui Hospital, Xi'an Jiaotong University College of Medicine, Xi'an 710054, China (e-mail: wangyakangde@163.com), Yu-Min Zhang, Hong-Hui, Hospital Xi'an Jiaotong University College of Medicine, Xi'an 710054, China (e-mail: zym2666@163.com).

Medicine (2017) 96:21(e6970)

Received: 20 October 2016 / Received in final form: 28 April 2017 / Accepted: 3 May 2017

http://dx.doi.org/10.1097/MD.0000000000006970

comparing the effects of PTH and bisphosphonates on BMD in osteoporosis patients are available; however, meta-analyses comparing the safety and efficacy of teriparatide versus alendronate in postmenopausal osteoporosis are scarce.

We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) of teriparatide versus alendronate to fully characterize the effect of teriparatide and alendronate on changes in lumbar spine and femoral neck BMD and incidence of vertebral and nonvertebral fractures in postmenopausal osteoporosis.

2. Materials and methods

2.1. Search strategy

Two researchers (Y-KW and WS) independently searched PubMed, EMBASE, the Cochrane Controlled Trials Registry, and the China Academic Journal Network Publishing Database from inception to March 1, 2015 using the following Keywords: osteoporosis; alendronate; teriparatide; bone mineral density or BMD; postmenopausal. Searches were restricted to studies published in the English language.

2.2. Inclusion and exclusion criteria

Inclusion criteria were RCTs of teriparatide versus alendronate, involving postmenopausal adult osteoporosis patients, treated for at least 6 months, and presenting changes in lumbar spine and femoral neck BMD and the incidence of vertebral and non-vertebral factures as outcomes data, and reporting adverse effects of treatment. Corresponding authors of RCTs that presented incomplete data were contacted to obtain missing information, when necessary.

Exclusion criteria were RCTs that included children; RCTs that included patients with secondary osteoporosis caused by fatal diseases, or organ transplant recipients; RCTs that included patients with primary osteoporosis treated with other drugs that affected BMD; and non-RCTs, case reports, conference abstracts, or review articles.

Disagreement about study selection was resolved by discussion with a review author (Y-MZ) until consensus was reached.

2.3. Data extraction

Two researchers (Y-KW and WS) independently performed data extraction. Means were obtained from data tables or figures if no direct data were available from the article text or the corresponding author. Within-group and between-group standard deviations and the standard error of the difference in means were calculated according to the Cochrane Handbook for Systematic Reviews of Interventions (www.handbook.cochrone.org). Disagreements about data extraction were resolved by discussion with a review author (Y-MZ) until consensus was reached.

2.4. Assessment of study quality

Two researchers (Y-KW and WS) independently assessed the quality of the included studies. Risk of bias was evaluated using the modified Jadad scale.[12] Categories included: "Was the study described as randomized?," "Was the method used to generate the sequence of randomization described and appropriate (random numbers, computer-generated, etc.)?," "Was the study described as double-blind?," "Was the method of double-blinding described and appropriate (identical placebo, active placebo, dummy, etc.)?," and "Was there a description of withdrawals and drop-outs?" The Jadad scale is a 5-point scale; a score of 0 indicates poor quality evidence and a score of 5 indicates high-quality evidence; therefore, trials with a score of 4 or 5 were considered high methodological quality (Table 1). Disagreements about study quality were resolved by discussion with a review author (Y-MZ) until consensus was reached.

Table 1

Jadad score[12].

Random allocation	Cited +1	Described and appropriate +1	Nonappropriate −1
Double blind	Cited +1	Described and appropriate +1	Nonappropriate −1
Dropouts and withdrawals	Described +1		

2.5. Statistical analysis

Data were analyzed using the Cochrane Collaboration software Review Manager 5.2. Weighted mean differences (WMDs) and their associated 95% confidence intervals (CIs) were calculated for the continuous outcome, change in BMD, while odds ratios (OR) and their associated 95% CIs were calculated for the dichotomous outcomes, incidence of bone fractures and adverse effects.

Heterogeneity was assessed using the I^2 test. A fixed-effects model was used to pool data if there was no evidence of significant heterogeneity ($I^2 \leq 50\%$). Otherwise, a random-effects model was used. Publication bias was assessed with funnel plots. Subgroup analyses were stratified by treatment duration (6, 12, and 24 months) and dose.

Ethics committee and/or institutional board approval was not required for this study.

3. Results

3.1. Trial characteristics

The searches identified 145 relevant articles. Of these, 6 RCTs were found eligible for inclusion according to our criteria for considering studies for this review[13–18] (Fig. 1). A total of 618 patients with postmenopausal osteoporosis were included in the analyses. Among the 6 included trials, 4 were multicenter trials[13–16] and 2 were single-center trials.[17,18] Twenty micrograms teriparatide was administered in 3 trials,[14,15,18] 40 μg teriparatide was administered in 3 trials,[13,16,17] 10 mg/d alendronate was administered in 5 trials,[13–17] and 70 mg/wk alendronate was administered in 1 trial. These trials were considered comparable as evidence suggests that the efficacy of alendronate in the treatment of osteoporosis is equivalent when administered at a dose of 70 mg/wk or 10 mg/d.[19,20] Trial duration ranged from 18 to 30 months. The characteristics of the 6 included trials are summarized in Table 2.

3.2. BMD of the lumbar spine

Percentage change in lumbar spine BMD in postmenopausal osteoporosis patients treated with teriparatide versus alendronate for 6, 12, and 18 months is described in all 6 included trials (n = 574 patients).[13–18] The meta-analysis demonstrated that the percentage change in lumbar spine BMD was significantly greater

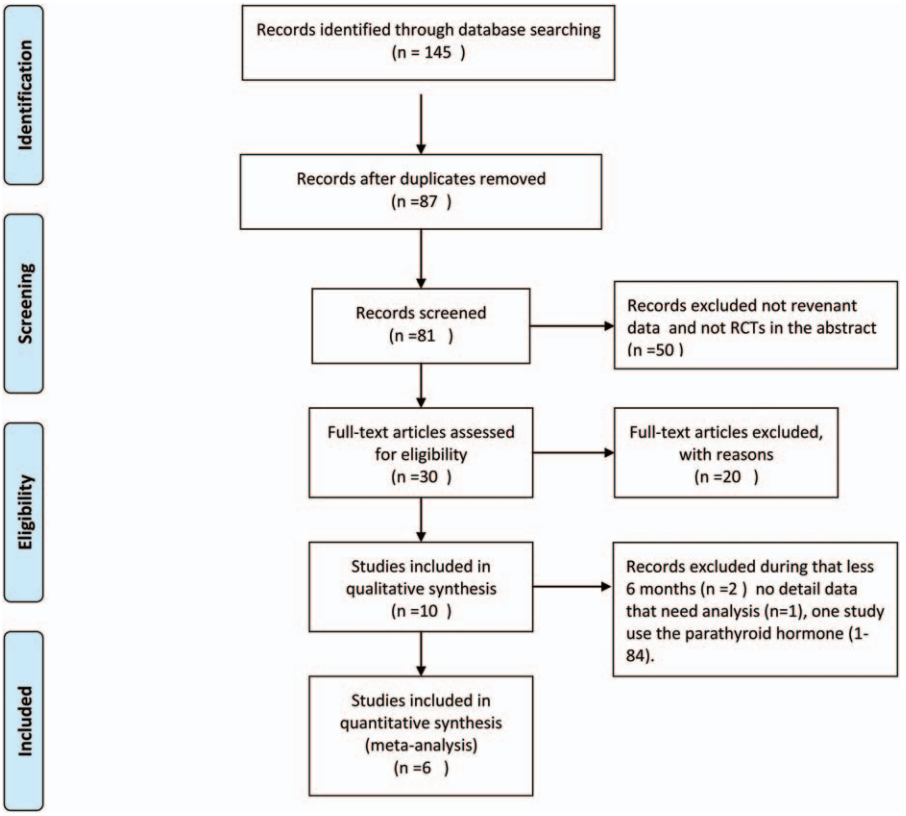

Figure 1. Flowchart of the article screening and selection process.

in postmenopausal osteoporosis patients administered teriparatid compared to those administered alendronate (WMD: 3.46, 95% CI: 2.15–4.77, $P < .00001$; Fig. 2). There was evidence of significant heterogeneity between trials ($P = .02$, $I^2 = 51\%$).

3.3. BMD of the femoral neck

Percentage change in femoral neck BMD in postmenopausal osteoporosis patients treated with teriparatide versus alendronate for 12 and 18 months is also described in all 6 trials (n = 574 patients).[13–18] The meta-analysis demonstrated no significant difference in the percentage change in femoral neck BMD in postmenopausal osteoporosis patients administered teriparatide compared to those administered alendronate (WMD = 1.50, 95% CI: 0.04–2.95, $P = .04$; Fig. 3). There was no evidence of significant heterogeneity between trials ($P = .17$, $I^2 = 34\%$).

3.4. Incidence of vertebral and nonvertebral fractures

The incidence of vertebral and nonvertebral fractures in postmenopausal osteoporosis patients treated with teriparatide versus alendronate for 6 to 24 months is described in 3 trials (n = 430 patients).[13,15,18] The meta-analysis demonstrated no significant difference in the incidence of vertebral and/or nonvertebral fractures in postmenopausal osteoporosis patients administered teriparatide compared to those administered alendronate (overall OR: −0.03, 95% CI: −0.12 to 0.07; $P = .52$; Fig. 4). There was evidence of significant heterogeneity between trials ($P = .0006$, $I^2 = 76\%$).

3.5. Subgroup and sensitivity analysis

Subgroup analyses stratified by treatment duration indicated that the percentage change in lumbar spine BMD was significantly

Table 2

Study characteristics.

Study	Design	Mean age, y (alendronate/ teriparatide)	Mean BMI, kg/m^2 (alendronate/ teriparatide)	Type of population studied (teriparatide/alendronate)	Teriparatide, μg/d	Alendronate, mg/d	Duration, mo	Jadad scores
Body 2002	RCT	65/66	24.4/23.9	12 study sites (73/73)	40	10	24	4
Arlot 2005	RCT	66/61	25.3/25.7	6 clinical sites (21/21)	20	10	18	5
McClung 2005	RCT	67/65	24.7/26.6	19 clinical trial sites (102/101)	20	10	18	3
Keaveny 2007	RCT	63/65	26.3/26.5	19 clinical trial sites (28/25)	40	10	18	5
Finkelstein 2010	RCT	64/65	25.6/24.9	Single university hospital (20/29)	40	10	30	3
Panico 2011	RCT	60/65	22.8/24.5	Single university hospital (42/39)	20	70 mg/wk	18	4

BMD = body mass index, RCT = randomized controlled trial.

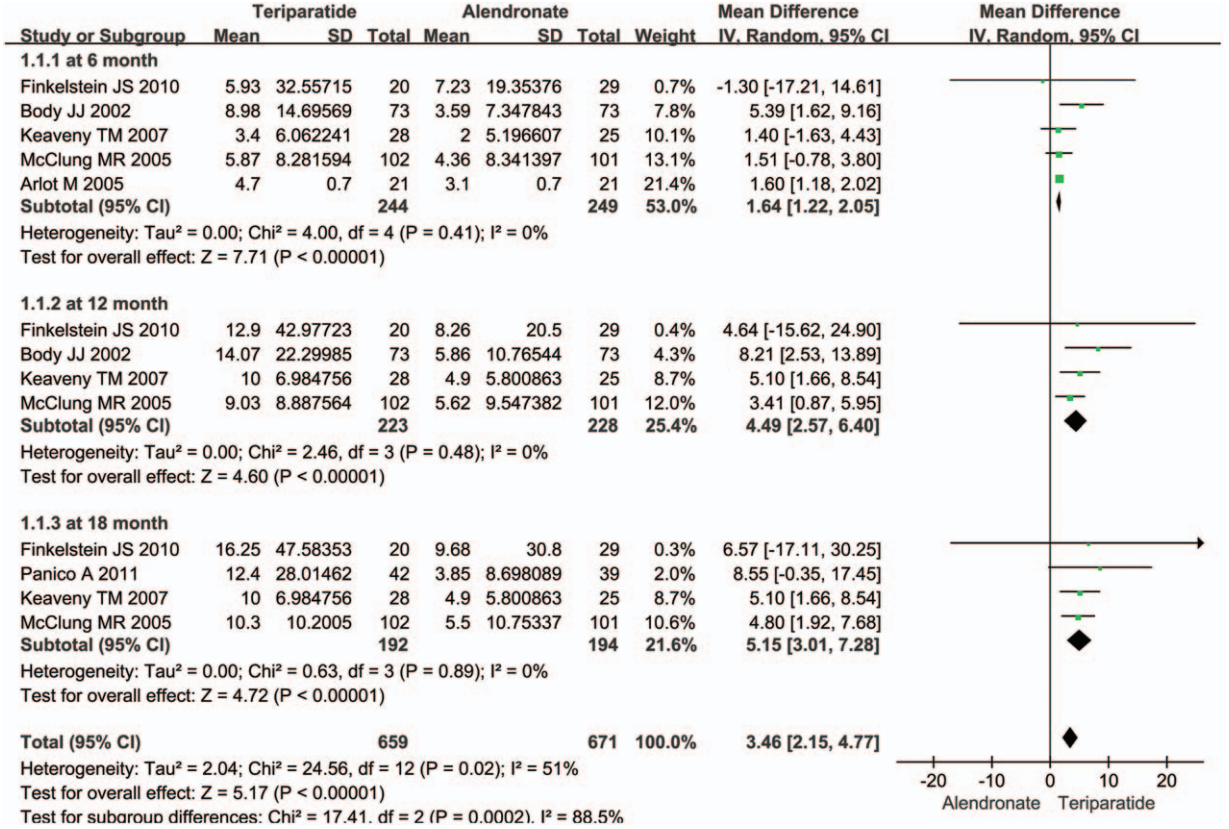

Figure 2. Teriparatide versus alendronate for lumbar spine BMD: Overall and subgroup analyses stratified by treatment duration. BMD = bone mineral density.

greater in postmenopausal osteoporosis patients administered teriparatide compared to those administered alendronate for 6 months (WMD: 1.64, 95% CI: 1.22–2.05, $P < .00001$; $I^2 = 0\%$; Fig. 2), 12 months (WMD: 4.49, 95% CI: 2.57–6.40, $P < .00001$; $I^2 = 0\%$; Fig. 2), and 18 months (WMD: 5.15, 95% CI: 3.01–7.28, $P < .00001$; $I^2 = 0\%$; Fig. 2); and indicated no significant difference in the percentage change in femoral neck BMD in postmenopausal osteoporosis patients administered teriparatide compared to those administered alendronate for 12 months (WMD = 1.71, 95% CI: −0.35 to 3.77 $P = .44$; $I^2 = 0\%$; Fig. 3) or 18 months (WMD = 1.69, 95% CI: −0.58 to 3.95 $P = .10$; $I^2 = 51\%$; Fig. 3).

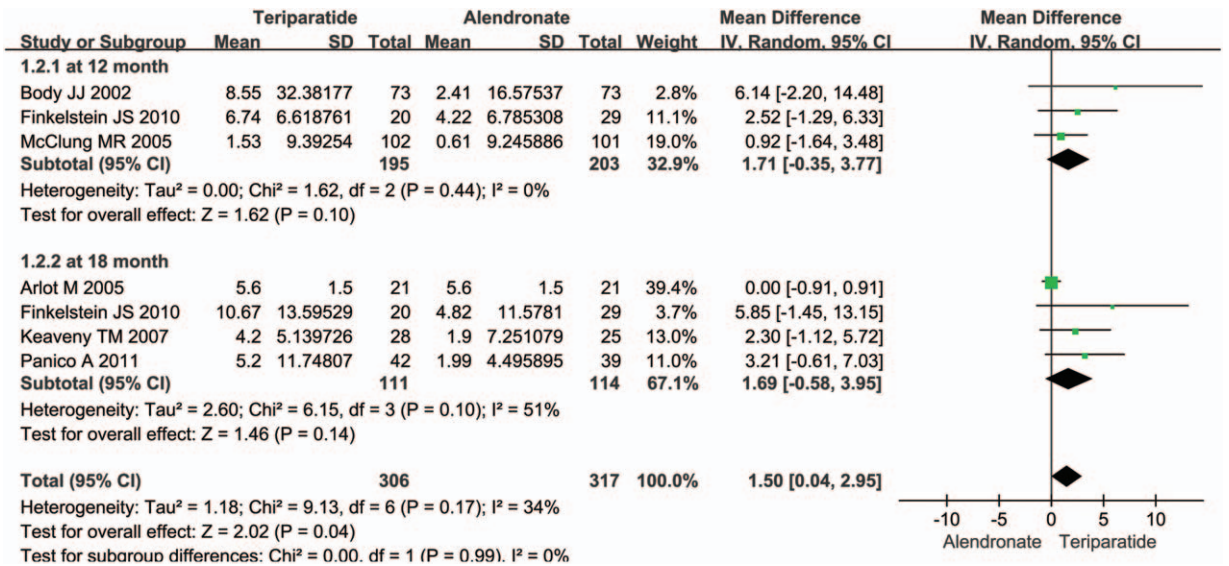

Figure 3. Teriparatide versus alendronate for femoral neck BMD: Overall and subgroup analyses stratified by treatment duration. BMD = bone mineral density.

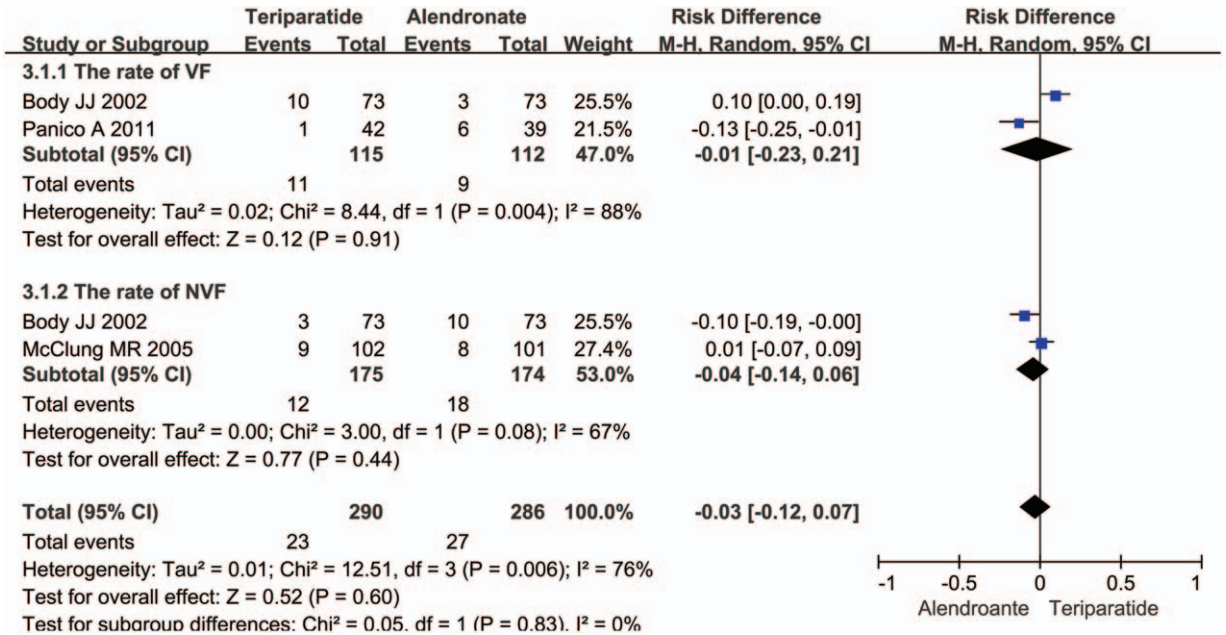

Figure 4. Teriparatide versus alendronate: Vertebral and nonvertebral fracture incidence.

Subgroup analyses stratified by teriparatide dose indicated that the percentage change in lumbar spine BMD was significantly greater in postmenopausal osteoporosis patients administered 20 μg teriparatide (WMD = 5.45; 95% CI: 2.83–8.07; $P < .0001$; $I^2 = 0\%$; Fig. 5A) and 40 μg teriparatide (WMD = 5.95; 95% CI: 3.02–7.62; $P < .0001$; $I^2 = 0\%$; Fig. 5A) compared to those administered 10 mg alendronate. There was no significant difference in the percentage change in femoral neck BMD in postmenopausal osteoporosis patients administered 20 μg teriparatide (WMD = 0.25; 95% CI: −0.58 to 1.09; $P = .56$; $I^2 = 30\%$; Fig. 5B) compared to those administered 10 mg alendronate; however, the difference in patients administered 40 μg teriparatide was significant (WMD = 3.33; 95% CI: 0.42–6.23; $P = .02$; $I^2 = 0\%$; Fig. 5B).

To confirm that our results are robust, we performed a sensitivity analysis, excluding 1 study at a time. Results showed that the overall findings of the meta-analysis were not affected by the inclusion/exclusion of any one particular study (Table 3).

3.6. Assessment of study quality

The level of evidence for each trial was graded as 3 to 5 according to the Jadad quality score. For publication bias, the shape of the funnel plot showed obvious asymmetry for trials investigating percentage change in lumbar spine BMD (Fig. 6A), but slight asymmetry for trials investigating percentage change in femoral neck BMD (Fig. 6B) and incidence of vertebral and nonvertebral fractures (Fig. 6C).

4. Discussion

This meta-analysis of 6 RCTs investigating the efficacy of teriparatide versus alendronate in postmenopausal osteoporosis patients showed that the percentage change in lumbar spine BMD was significantly greater in patients administered teriparatide for 6, 12, and 18 months compared to those administered alendronate. Subgroup analyses confirmed teriparatide efficacy was not duration or dose dependent. There was no significant difference in the percentage change in femoral neck BMD or the incidence of vertebral and/or nonvertebral fractures in patients administered teriparatide compared with alendronate.

Teriparatide is a once daily subcutaneous injection that is recommended for treatment of postmenopausal osteoporosis.[21] Our meta-analysis revealed that teriparatide increased lumbar spine BMD by 3.46% compared with alendronate. In accordance with our findings, previous meta-analyses have also shown that teriparatide versus placebo (calcium) can increase BMD in the spine and femoral neck of postmenopausal women with osteoporosis.[22–24] In contrast to our results, Shen et al[25] reported that PTH significantly increased femoral head BMD compared with bisphosphonates, and the effect was duration and dose-dependent. Furthermore, Neer et al[26] found that 20 μg teriparatide increased femoral neck BMD by 9.7% versus placebo. Although 10 mg of alendronate has proven efficacy for increasing lumbar spine and hip BMD after 2 to 3 years and 3 to 4 years of treatment, respectively, in postmenopausal osteoporosis versus placebo,[27] our data indicate teriparatide may be superior to alendronate for increasing lumbar spine BMD in postmenopausal osteoporosis.

The difference in the percentage increase in lumbar spine BMD resulting from teriparatide and alendronate treatment may be explained by their different mechanisms of action.[28,29] Teriparatide is a bone-forming agent, which increases biochemical markers of bone turnover. Previous reports show that teriparatide treatment increases markers of bone formation more rapidly and to a higher level than markers of bone resorption, suggesting an imbalance in bone turnover in favor of formation.[30,31] Furthermore, recombinant PTH may increase trabecular connectivity. By contrast, the majority of BMD increases observed with alendronate treatment result from increased mineralization of existing bone matrix.[28]

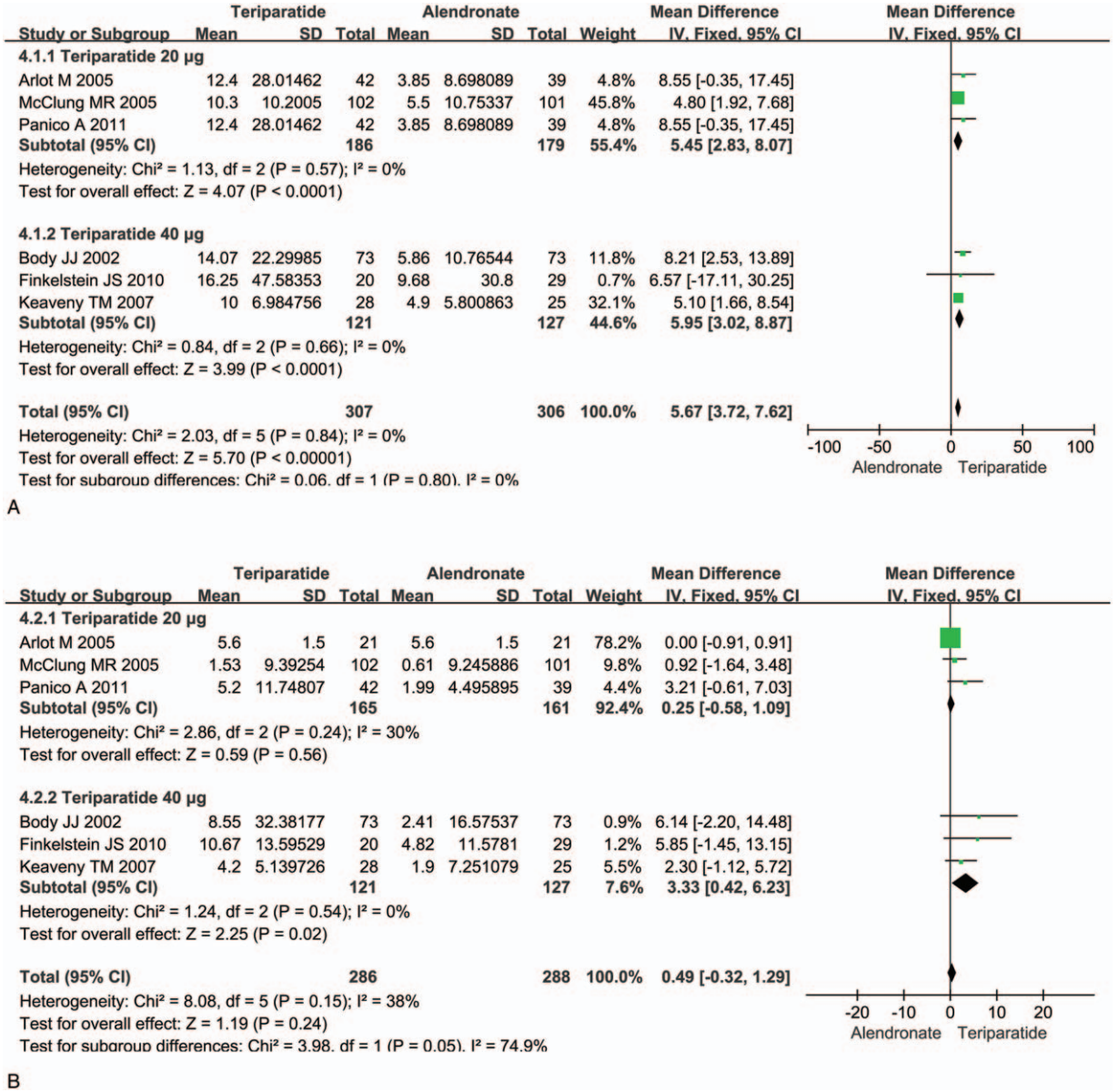

Figure 5. Teriparatide versus alendronate for lumbar spine BMD (A) and femoral neck BMD (B): Subgroup analyses stratified by dose of teriparatide. BMD = bone mineral density.

The effect of teriparatide and alendronate on the relative risk of fracture in postmenopausal osteoporosis patients is reported in several studies with varying magnitude. In accordance with our findings, Trevisani et al[32] found no significant difference in the incidence of vertebral or nonvertebral fractures in patients treated with teriparatide versus alendronate. However, the Fracture Prevention Trial showed that the incidence of new vertebral fractures and new nonvertebral fragility fractures was reduced in

Table 3

Sensitivity analyses excluding studies considered as contributing the most heterogeneity.

Outcome or subgroup	Studies	Excluded study	Heterogeneity			*P* (test for overall effect)
			χ^2	I^2, %	*P*	
1.1 Lumbar spine	6					
1.1.1 at 6 mo	4	McClung 2005	3.99	25	.26	.006
1.1.2 at 12 mo	3	Finkelstein 2010	2.46	19	.29	<.00001
1.1.3 at 18 mo	3	Excluded any one study		0		<.001
1.2 Femoral neck	5					
1.2.1 at 12 mo	2	Finkelstein 2010	1.37	27	.24	.35
1.2.2 at 18 mo	3	Arlot 2005	0.76	0	.68	.01

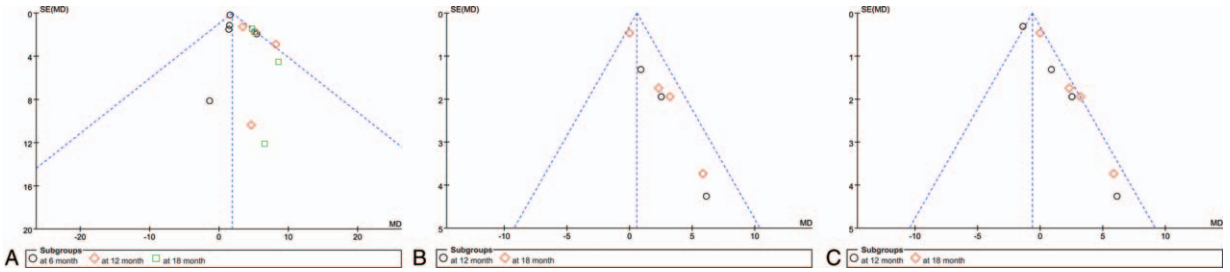

Figure 6. Funnel plots. (A) Lumbar spine BMD. (B) Femoral neck BMD. (C) Fracture incidence. BMD = bone mineral density, MD = mean difference, SE = standard error.

postmenopausal women treated with teriparatide compared with placebo.[26] Previous meta-analyses have shown that the incidence of vertebral or nonvertebral fractures was significantly reduced by alendronate in postmenopausal women without prevalent fractures and BMD levels below the World Health Organization threshold for osteoporosis compared with placebo.[27,33] The discrepancies between our findings and the results of previous studies may be explained by our small sample size.

Only 1 study investigating teriparatide versus alendronate in postmenopausal osteoporosis reported adverse events associated with treatment. Panico et al showed that the most-common reported adverse effects associated with teriparatide were back pain that worsened in the first month of treatment, nausea, and headache and dizziness. The most common adverse events associated with alendronate were abdominal pain, arthralgia, and dyspepsia; tolerability of alendroante was comparable to teriparatide.[18]

In Sweden, for postmenopausal women (mean age: 70 years, total hip T-score: −2.7 and 3.3 previous fractures), the cost per quality-adjusted life year (QALY) gained for teriparatide versus no treatment was estimated at €43,473.[34] In the United States, for women with no additional fracture risk factors, the cost per QALY gained for alendronate ranged from 70,000 to 332,000 dollars, depending on patient age and femoral neck bone density.[35] In Sweden, the cost-effectiveness ratios for teriparatide versus alendroante for postmenopausal osteoporosis cohorts with 1 or 2 fractures were €36,995 and €19,371 per QALY, respectively.[36] These data demonstrate that there are high-risk osteoporosis patient cohorts where use of teriparatide as a first-line agent is a cost-effective treatment option compared with alendronate.

4.1. Limitations of study

This study is associated with some limitations. First, some of the included data were extracted from figures, which may limit its accuracy. Second, the sample size of 6 included studies was small.

5. Conclusions

The results of this meta-analysis suggest that teriparatide may be superior to alendronate for increasing lumbar spine BMD in postmenopausal osteoporosis. The efficacy and safety of long-term teriparatide and alendronate treatment in postmenopausal osteoporosis should be further investigated in clinical trials.

References

[1] Kanis JA, Melton LJ, Christiansen C, et al. The diagnosis of osteoporosis. J Bone Miner Res 1994;9:1137–41.
[2] Report of a WHO Study GroupAssessment of fracture risk and its application to screening for postmenopausal osteoporosis. World Health Organ Tech Rep Ser 1994;843:1–29.
[3] van Staa TP, Leufkens HG, Cooper C. The epidemiology of corticosteroid-induced osteoporosis: a meta-analysis. Osteoporos Int 2002;13:777–87.
[4] Shaker JL, Lukert BP. Osteoporosis associated with excess glucocorticoids. Endocrinol Metab Clin North Am 2005;34:341–56.
[5] Chrischilles EA, Butler CD, Davis CS, et al. A model of lifetime osteoporosis impact. Arch Intern Med 1991;151:2026–32.
[6] Adami S, Brandi ML, Canonico PL, et al. Appropriate use of anabolic treatment for severe osteoporosis. Clin Cases Miner Bone Metab 2010;7:114–22.
[7] Lyritis GP, Georgoulas T, Zafeiris CP. Bone anabolic versus bone anticatabolic treatment of postmenopausal osteoporosis. Ann N Y Acad Sci 2010;1205:277–83.
[8] Rogers MJ. New insights into the molecular mechanisms of action of bisphosphonates. Curr Pharm Des 2003;9:2643–58.
[9] Giuliani N, Pedrazzoni M, Negri G, et al. Bisphosphonates stimulate formation of osteoblast precursors and mineralized nodules in murine and human bone marrow cultures in vitro and promote early osteoblastogenesis in young and aged mice in vivo. Bone 1998;22:455–61.
[10] Plotkin LI, Weinstein RS, Parfitt AM, et al. Prevention of osteocyte and osteoblast apoptosis by bisphosphonates and calcitonin. J Clin Invest 1999;104:1363–74.
[11] Adachi JD, Saag KG, Delmas PD, et al. Two-year effects of alendronate on bone mineral density and vertebral fracture in patients receiving glucocorticoids: a randomized, double-blind, placebo-controlled extension trial. Arthritis Rheum 2001;44:202–11.
[12] Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary. Control Clin Trials 1996;17:1–2.
[13] Body JJ, Gaich GA, Scheele WH, et al. A randomized double-blind trial to compare the efficacy of teriparatide [recombinant human parathyroid hormone (1-34)] with alendronate in postmenopausal women with osteoporosis. J Clin Endocrinol Metab 2002;87:4528–35.
[14] Arlot M, Meunier PJ, Boivin G, et al. Differential effects of teriparatide and alendronate on bone remodeling in postmenopausal women assessed by histomorphometric parameters. J Bone Miner Res 2005;20:1244–53.
[15] McClung MR, San MJ, Miller PD, et al. Opposite bone remodeling effects of teriparatide and alendronate in increasing bone mass. Arch Intern Med 2005;165:1762–8.
[16] Keaveny TM, Donley DW, Hoffmann PF, et al. Effects of teriparatide and alendronate on vertebral strength as assessed by finite element modeling of QCT scans in women with osteoporosis. J Bone Miner Res 2007;22:149–57.
[17] Finkelstein JS, Wyland JJ, Lee H, et al. Effects of teriparatide, alendronate, or both in women with postmenopausal osteoporosis. J Clin Endocrinol Metab 2010;95:1838–45.
[18] Panico A, Lupoli GA, Marciello F, et al. Teriparatide vs. alendronate as a treatment for osteoporosis: changes in biochemical markers of bone turnover, BMD and quality of life. Med Sci Monit 2011;17:CR442–8.
[19] Schnitzer T, Bone HG, Crepaldi G, et al. Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis. Alendronate Once-Weekly Study Group. Aging (Milano) 2000;12:1–2.
[20] Simon JA, Lewiecki EM, Smith ME, et al. Patient preference for once-weekly alendronate 70 mg versus once-daily alendronate 10 mg: a multicenter, randomized, open-label, crossover study. Clin Ther 2002;24:1871–86.

[21] Management of osteoporosis in postmenopausal women: 2010 position statement of the North American Menopause Society. Menopause 2010;17:25–54.
[22] Stevenson M, Jones ML, De Nigris E, et al. A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. Health Technol Assess 2005;9:1–60.
[23] Han SL, Wan SL. Effect of teriparatide on bone mineral density and fracture in postmenopausal osteoporosis: meta-analysis of randomised controlled trials. Int J Clin Pract 2012;66:199–209.
[24] Song J, Jin Z, Chang F, et al. Single and combined use of human parathyroid hormone (PTH) (1-34) on areal bone mineral density (aBMD) in postmenopausal women with osteoporosis: evidence based on 9 RCTs. Med Sci Monit 2014;20:2624–32.
[25] Shen L, Xie X, Su Y, et al. Parathyroid hormone versus bisphosphonate treatment on bone mineral density in osteoporosis therapy: a meta-analysis of randomized controlled trials. PLoS ONE 2011;6:e26267.
[26] Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1–34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 2001;344:1434–41.
[27] Cranney A, Wells G, Willan A, et al. Meta-analyses of therapies for postmenopausal osteoporosis. II. Meta-analysis of alendronate for the treatment of postmenopausal women. Endocr Rev 2002;23:508–16.
[28] Boivin GY, Chavassieux PM, Santora AC, et al. Alendronate increases bone strength by increasing the mean degree of mineralization of bone tissue in osteoporotic women. Bone 2000;27:687–94.
[29] Greenspan SL, Bone HG, Ettinger MP, et al. Effect of recombinant human parathyroid hormone (1-84) on vertebral fracture and bone mineral density in postmenopausal women with osteoporosis: a randomized trial. Ann Intern Med 2007;146:326–39.
[30] Chen P, Satterwhite JH, Licata AA, et al. Early changes in biochemical markers of bone formation predict BMD response to teriparatide in postmenopausal women with osteoporosis. J Bone Miner Res 2005;20:962–70.
[31] Dobnig H, Sipos A, Jiang Y, et al. Early changes in biochemical markers of bone formation correlate with improvements in bone structure during teriparatide therapy. J Clin Endocrinol Metab 2005;90:3970–7.
[32] Trevisani VF, Riera R, Imoto AM, et al. Teriparatide (recombinant human parathyroid hormone 1-34) in postmenopausal women with osteoporosis: systematic review. Sao Paulo Med J 2008;126:279–84.
[33] Karpf DB, Shapiro DR, Seeman E, et al. Prevention of nonvertebral fractures by alendronate. A meta-analysis. Alendronate Osteoporosis Treatment Study Groups. JAMA 1997;277:1159–64.
[34] Borgström F, Ström O, Marin F, et al. Cost effectiveness of teriparatide and PTH(1-84) in the treatment of postmenopausal osteoporosis. J Med Econ 2010;13:381–92.
[35] Schousboe JT, Nyman JA, Kane RL, et al. Cost-effectiveness of alendronate therapy for osteopenic postmenopausal women. Ann Intern Med 2005;142:734–41.
[36] Murphy DR, Smolen LJ, Klein TM, et al. The cost effectiveness of teriparatide as a first-line treatment for glucocorticoid-induced and postmenopausal osteoporosis patients in Sweden. BMC Musculoskelet Disord 2012;13:213.