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Original Article

Comparative Analysis of Romosozumab Versus Vertebroplasty With Denosumab: Efficacy, Safety, and Secondary Bone Mineral Density Outcomes

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See the commentary on "Comparative Analysis of Romosozumab Versus Vertebroplasty With denosumab: Efficacy, Safety, and Secondary Bone Mineral Density Outcomes" via https://doi.org/10.14245/ns.2550298.149.

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Objective: This study aimed to compare the efficacy and safety of romosozumab, a bone anabolic agent, versus vertebroplasty, a conventional surgical intervention, in treating osteoporotic vertebral compression fractures (OVCFs).
Methods: A retrospective analysis included 86 thoracic/lumbar compression fracture patients from 2014 to 2022 at a medical center. Forty-two patients received romosozumab (monthly injections for 1 year) followed by 1 year of denosumab, while 44 underwent vertebroplasty followed by denosumab injections biannually for 2 years. Outcomes were assessed using the Numerical Rating Scale (NRS) for pain, bone mineral density (BMD), vertebral compression ratio, and Cobb angle over 12 months.
Results: At 12 months, the romosozumab group showed a greater reduction in NRS scores (4.90 ± 1.01 vs. 4.27 ± 1.34, p = 0.015) and a higher increase in lumbar BMD (0.8 ± 0.5 vs. 0.5 ± 0.3, p = 0.000) compared to the vertebroplasty group. There were no significant differences in changes in hip total BMD and femur neck BMD (p = 0.190, p = 0.167, respectively). Radiographic assessments showed no significant differences in vertebral compression ratio (14.7% vs. 14.8%; p = 0.960) or Cobb angle (4.2° vs. 4.9°; p = 0.302). The incidence of major osteoporotic fractures was lower in the romosozumab group (7.1% vs. 25.0%, p = 0.051), with similar rates of cardiovascular events in both groups (4.8% vs. 9.1%, p = 0.716).
Conclusion: Romosozumab has demonstrated superior pain reduction and lumbar BMD improvement compared to vertebroplasty at 12 months, with no significant differences in radiographic outcomes or adverse events, suggesting it as an alternative to vertebroplasty for OVCF.

Keywords: Osteoporotic vertebral compression fractures, Romosozumab, Vertebroplasty, Bone mineral density, Major osteoporotic fractures, Adverse events

INTRODUCTION

Osteoporotic vertebral compression fractures (OVCFs) are among the most common sites for osteoporotic fractures globally, with an overall prevalence rate of approximately 20% in both men and women.[1] These fractures occur in 30%–50% of individuals over the age of 50.[2] Beyond the high prevalence, the risk of subsequent vertebral fractures is 3 times higher after the first

fracture and can increase up to 23 times after the third fracture.[3,4] In addition, OVCF not only pose a risk of neurological deterioration in patients but also significantly increase medical care costs, making them a critical area of concern and the focus of numerous studies.[5]

Recently, anabolic osteoporosis medications have been widely used to increase bone mineral density (BMD) and reduce fracture risk. Among these, Romosozumab (Evenity, Amgen, Thousand Oaks, CA, USA), proven through the FRActure study in postmenopausal woMen with ostEoporosis (FRAME),[6] Active-Controlled Fracture Study in Postmenopausal Women With Osteoporosis at High Risk (ARCH),[7] and Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation (BRIDGE)[8] trials, has been recognized as a superior anabolic agent compared to other drugs. Additionally, romosozumab has been shown to reduce the incidence of new vertebral fractures through its bone-forming effects.[9]

There was significant initial enthusiasm for the use of vertebroplasty and kyphoplasty following their introduction.[10,11] However, some randomized controlled trials (RCTs) and studies have raised doubts about the efficacy of vertebroplasty, and some reviews have even strongly recommended against its use.[12-14] Furthermore, recent studies have suggested that another bone anabolic agent, teriparatide, may provide superior outcomes compared to VP.[15-17] However, there is still a paucity of research regarding the use of romosozumab, which is recognized for its greater potency in promoting cancellous bone healing—the principal mechanism of recovery in OVCF—as compared with teriparatide.[18-24]

In this study, we first assessed the degree of back pain by measuring the Numerical Rating Scale (NRS) at the time of vertebral fracture, as well as at 1 month and 12 months posttreatment. Secondly, we compared radiographic outcomes by evaluating the compression ratio and Cobb angle on lateral x-rays at the time of fracture and 12 months posttreatment, and analyzed BMD.

MATERIALS AND METHODS

1. Study Participants

This retrospective study included thoracic and lumbar compression fracture outpatients at a single medical center hospital from January 2014 to July 2022, with a follow-up period of at least 2 years. All procedures performed in this study involving human participants were in accordance with the ethical standards and were approved by the Institutional Review Board (IRB) of the Hallym University Sacred hospital (IRB number: 2024-07-027-001). Additionally, all procedures were conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. Patients included in this study were those diagnosed with acute compression fractures, defined as presenting with acute pain within 2 weeks of onset and magnetic resonance imaging findings consistent with acute compression fractures, such as bone marrow edema (T1 low signal and fat suppression T2 high signal). The romosozumab group received monthly injections of 210 mg for 1 year, totaling 12 doses, followed by a switch to denosumab for maintenance. Patients in the romosozumab group underwent bed rest for 2 weeks, after which they were instructed to begin ambulation while wearing an lumbosacral orthosis brace for fractures at L3–5 and a thoracolumbosacral orthosis brace for fractures at T4–L2. The vertebroplasty group received denosumab (Prolia, Amgen, Thousand Oaks, CA, USA), 60 mg as a subcutaneous injection every 6 months for 2-year postsurgery. Patient allocation to the treatment groups was determined by evolving treatment protocols over time. From 2014 to 2019, vertebroplasty was the common treatment for acute OVCFs. Patients underwent 2 weeks of bed rest following diagnosis, after which a follow-up visit was conducted, and vertebroplasty was performed for those reporting persistent pain and expressing their intent for additional intervention. Beginning in 2019, romosozumab was incorporated into clinical practice as part of updated treatment protocols. All eligible patients, except those with contraindications such as a history of cerebrovascular accident, received romosozumab regardless of age, surgical preference, or comorbidities.

Vertebroplasty was performed under fluoroscopic guidance using polymethylmethacrylate cement to stabilize the fracture site. Cement volumes of 2–3 mL for thoracic vertebrae and 3–5 mL for lumbar vertebrae were injected, with the goal of maximizing cement volume. Injection was immediately halted if any leakage toward surrounding vasculature or nerves was observed. Exclusion criteria were: (1) previous fusion surgery, (2) pathological fractures, (3) metabolic or bone diseases, (4) neurological deficits. Major osteoporotic fractures were defined as fractures of the vertebrae (spine), proximal femur (hip), and distal forearm (wrist) within 2 years,[25] and cardiovascular diseases were defined as coronary artery disease, myocardial infarction (MI), and stroke within 2 years.

2. Parameters Measurements

All patients underwent dual-energy x-ray absorptiometry to measure BMD at the time of fracture and at the outpatient fol-

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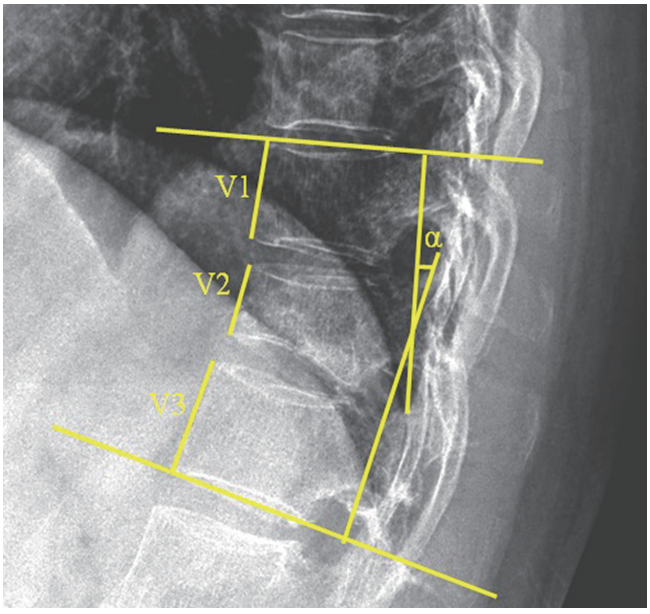

Fig. 1. The vertebral compression ratio was defined by measuring the ratio of the anterior height of the upper (V1), lower (V3), and fractured (V2) vertebral levels: [(V1+V3)/2–V2]/[(V1+V3)/2]. The Cobb angle (α) was defined as the angle between the superior endplate of the upper adjacent vertebra and the inferior endplate of the lower adjacent vertebra.

low-up 1 year later. Osteoporosis was defined according to the traditional criteria as a T score of ≤ -2.5 at the lumbar spine, total hip, or femoral neck. Radiologically, the decrease in lumbar body height and the resulting kyphotic changes were measured using 2 methods on plain radiographs taken in the standing position at baseline and 12 months: vertebral compression ratio and Cobb angle (Fig. 1). The NRS was used to measure patient-reported outcomes at baseline, 1 month, and 12 months. While the injections were administered for 2 years, the main outcomes of the study—radiographic parameters, NRS, and BMD—were based on the outcomes observed at the 1-year follow-up. However, cardiovascular events and major osteoporotic fractures were assessed over the entire 2-year follow-up period.

3. Statistical Analysis

We used the statistical software R ver. 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria) for the analysis. Paired T-tests and the Wilcoxon test were conducted to evaluate changes in BMD after 12 months and changes in NRS among baseline, 1 month and 12 months within each group. In addition, T-test and Mann-Whitney U-test were used to compare the delta (Δ) values of the vertebral compression ratio and Cobb angle between the 2 groups. The odds ratio for major osteoporotic fractures was analyzed using analysis of covariance (ANCOVA), adjusted for BMD values.

Table 1. Base characteristics in patients with 2 groups

Characteristic	Romosozumab (n = 42)	Vertebroplasty (n = 44)	p-value
Age (yr)	78.6 ± 7.8	79.2 ± 5.7	0.682
Male sex	3 (7.1)	8 (18.2)	0.227
BMI (kg/m^2)	23.1 ± 3.3	21.9 ± 3.2	0.111
Level			0.920
T4–10	5 (11.9)	6 (13.6)	
T11–L2	26 (61.9)	28 (63.6)	
L3–5	11 (26.2)	10 (22.7)	
Thyroid disease	3 (7.1)	3 (6.8)	> 0.999
CKD	3 (7.1)	1 (2.3)	0.576
Creatinine	0.9 ± 0.7	0.7 ± 0.2	0.137
Baseline NRS	7.3 ± 0.6	7.1 ± 0.8	0.338
Baseline BMD			
Lumbar BMD	-2.9 ± 0.8	-3.1 ± 0.9	0.209
Femur neck BMD	-2.5 ± 0.8	-2.6 ± 0.9	0.502
Vertebral compression ratio (%)	26.8 ± 16.3	21.5 ± 12.1	0.094
Cobb angle (°)	2.3 ± 19.6	0.2 ± 16.1	0.587

Values are presented as mean ± standard deviation or number (%).
BMI, body mass index; CKD, chronic kidney disease; NRS, numerical rating scale; BMD, bone mineral density.

RESULTS

1. Patient Demographics

A total of 86 patients met the inclusion criteria, with 42 in the romosozumab group and 44 in the vertebroplasty group, and their demographic and baseline clinical characteristics were compared (Table 1). The mean age was 78.6 ± 7.8 years in the romosozumab group and 79.2 ± 5.7 years in the vertebroplasty group (p = 0.682). The mean body mass index was slightly higher in the romosozumab group (23.1 ± 3.3 kg/m^2) compared to the vertebroplasty group (21.9 ± 3.2 kg/m^2), but this difference was not significant (p = 0.111). The average time elapsed from the onset of the compression fracture to the initial outpatient visit was 7.5 ± 3.2 days in the vertebroplasty group and 6.9 ± 4.5 days in the romosozumab group (p = 0.479). The distribution of vertebral fracture levels was similar across both groups, with no significant differences (p = 0.920). There were minimal differences in the prevalence of thyroid disease (7.1% vs. 6.8%, p = 1.000) and chronic kidney disease (CKD) (7.1% vs. 2.3%, p = 0.576) between

the groups. Lumbar BMD was slightly lower in the vertebroplasty group (-3.1 ± 0.9) compared to the romosozumab group (-2.9 ± 0.8), but this difference was not significant (p = 0.209). Femur neck BMD values were also comparable between the groups (-2.5 ± 0.8 vs. -2.6 ± 0.9, p = 0.502). The vertebral compression ratio and Cobb angle showed no significant differences between the groups (p = 0.094 and p = 0.587, respectively).

Of the 119 patients who initially started romosozumab therapy, 42 (35.3%) completed the full 12 injections over 1 year and met the 2-year follow-up criteria. The remaining 64.7% of patients, who did not complete the full protocol, received an average of 2.9 injections.

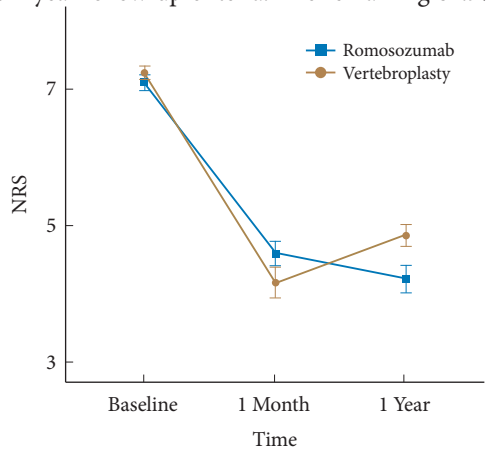

Fig. 2. Change in Numerical Rating Scale (NRS) over 1 year for patients treated with romosozumab and vertebroplasty. The figure represents the mean reduction (Δ) in NRS scores from baseline at 1 month and 12 months. The NRS score reduction at 1 month was 4.21 ± 1.42 in the romosozumab group and 4.64 ± 1.22 in the vertebroplasty group (p = 0.145). At 12 months, the NRS score reduction was 4.90 ± 1.01 in the romosozumab group and 4.27 ± 1.34 in the vertebroplasty group (p = 0.015).

2. Comparison of Change in NRS, BMD Score, and Radiological Outcomes

The NRS scores were assessed at the 1-month and 12-month intervals following the initiation of treatment (Fig. 2). After 1 month, the reduction in NRS scores was 4.21 ± 1.42 in the romosozumab group and 4.64 ± 1.22 in the vertebroplasty group, with no statistically significant difference observed between the groups (p = 0.145). At 12 months, the NRS scores decreased by 4.90 ± 1.01 in the romosozumab group and 4.27 ± 1.34 in the vertebroplasty group, with the romosozumab group showing a significantly greater reduction (p = 0.015).

To evaluate the effects of treatment over a 12-month period, changes in BMD were analyzed in 2 groups (Fig. 3). The change in lumbar BMD (Δ) after 12 months was found to be significantly greater in the romosozumab group, increasing by 0.8 ± 0.5 compared to 0.5 ± 0.3 in the vertebroplasty group (p = 0.000). In contrast, changes in femur total BMD were similar between the 2 groups, with both showing an increase of 0.1 ± 0.2, resulting in no statistically significant difference (p = 0.190). Similarly, the change in femur neck BMD was 0.1 ± 0.2 in the romosozumab group and 0.0 ± 0.2 in the vertebroplasty group, with showing no significant difference (p = 0.167). These findings suggest that romosozumab resulted in a more substantial improvement in lumbar BMD, whereas the effects on femur BMD were similar between the 2 treatment groups.

Radiological outcomes were assessed by evaluating changes in vertebral compression ratios and Cobb angles over a 12-month

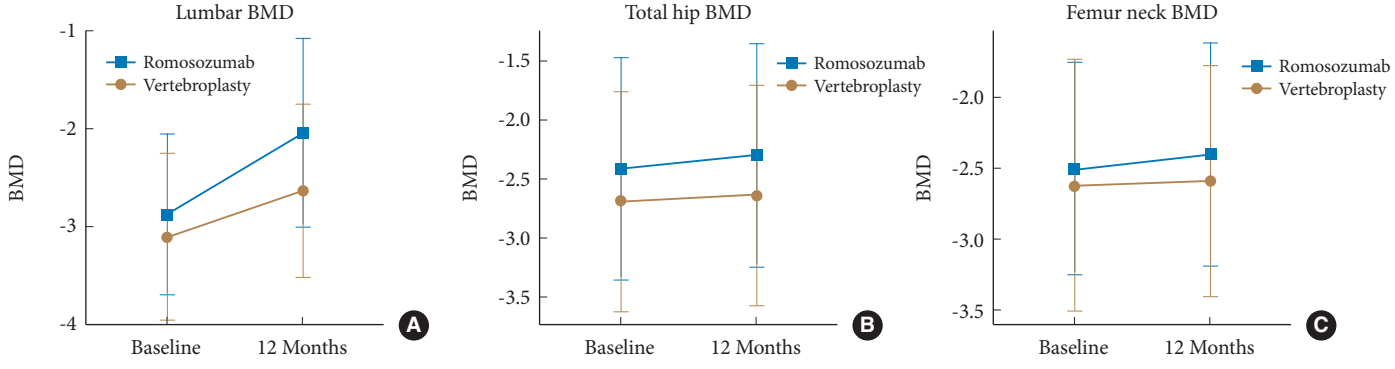

Fig. 3. Change in bone mineral density (BMD) over one year for patients treated with romosozumab alone and vertebroplasty. The change in lumbar BMD (A) score (Δ) after 12 months decreased by 0.8 ± 0.5 in the romosozumab group and by 0.5 ± 0.3 in the vertebroplasty group (p = 0.000). However, the change in total hip BMD (B) score (Δ) after 12 months was 0.1 ± 0.2 in the romosozumab group and 0.1 ± 0.2 in the vertebroplasty group (p = 0.190), while the change in femur neck BMD (C) score (Δ) after 12 months was 0.1 ± 0.2 in the romosozumab group and 0.0 ± 0.2 in the vertebroplasty group (p = 0.167).

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period (Table 2, Fig. 4). The mean change in vertebral compression ratio increased by 14.7% ± 8.1% in the romosozumab group and by 14.8% ± 8.6% in the vertebroplasty group, with no statistically significant difference between the 2 groups (p = 0.960). Furthermore, the change in Cobb angle was 4.2° ± 1.8° in the romosozumab group and 4.9° ± 3.7° in the vertebroplasty group, also showing no significant difference (p = 0.302).

3. Adverse Event, Major Osteoporotic Fracture in 2-Year Follow-up, Senile Osteoporosis

During the 2-year follow-up period, a comparative analysis was conducted to evaluate the incidence of major osteoporotic fractures and cardiovascular events, including stroke and coronary artery disease, between the romosozumab and vertebroplasty groups (Table 3).

In the vertebroplasty group, 4 out of 44 patients (9.1%) experienced cardiovascular events. These events included non-ST-elevation myocardial infarction (NSTEMI) occurring 22 months post-procedure, right anterior cerebral artery (ACA) territory small multiple infarcts at 18 months, left ACA territory small infarcts at 18 months, and a small pontine infarct at 20 months, all managed conservatively. In the romosozumab group, 2 out of 42 patients (4.8%) experienced cardiovascular events. One case involved ST-elevation myocardial infarction (STEMI) occurring 3 months after completing the 12 injections, requiring percutaneous coronary intervention (PCI), while the other case presented with right ACA and middle cerebral artery (MCA) territory small multiple infarcts 6 months after the injections, managed conservatively. The incidence rates between the 2 groups were not statistically significant (p = 0.716).

The adjusted odds ratio for major osteoporotic fractures, determined using ANCOVA to control for confounding factors, was 3.155 (0.773–12.884). Additionally, the incidence of cardiovascular disease was 4.8% in the romosozumab group and 9.1% in the vertebroplasty group (p = 0.716), indicating no statistically significant difference between the 2 groups. A noninferiority study was conducted by dividing the romosozumab-treated group into 2 subgroups (Table 4): those aged 80 years and older

Table 2. Comparison of delta values (differences from baseline) for compression ratio (%) and Cobb angle (°) between romosozumab and vertebroplasty groups over 1 year

Variable	Romosozumab (Δmean ± SD)	Vertebroplasty (Δmean ± SD)	p-value
Compression ratio (%)	14.7 ± 8.1	14.8 ± 8.6	0.960
Cobb angle (°)	4.2 ± 1.8	4.9 ± 3.7	0.302

SD, standard deviation.

Table 3. Comparison of major osteoporotic fractures and cardiovascular disease incidence between romosozumab and vertebroplasty groups over 2 years

Variable	Romosozumab (n = 42)	Vertebroplasty (n = 44)	p-value
Major osteoporotic fracture			0.051
Occur, n (%)	3 (7.1)	11 (25.0)	
Odds ratio (95% CI)	4.333 (1.114–16.853)		0.034
Cardiovascular disease			0.716
Occur, n (%)	2 (4.8)	4 (9.1)	

CI, confidence interval.

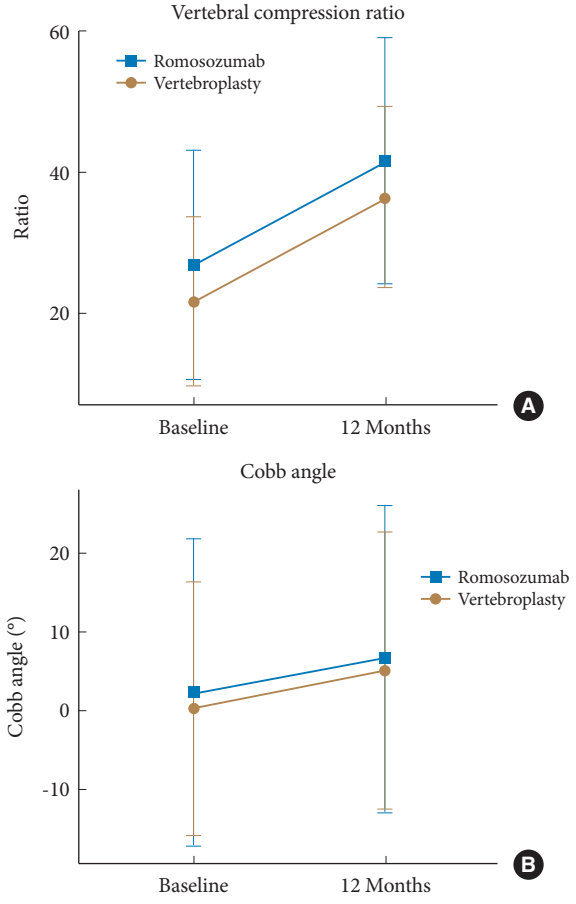

Fig. 4. Changes in original values of vertebral compression ratio and Cobb angle over 1 year for patients treated with romosozumab and vertebroplasty. (A) The change in vertebral compression ratio (Δ) after 12 months increased by 14.7% ± 8.1% in the romosozumab group and by 14.8% ± 8.6% in the vertebroplasty group (p = 0.960). (B) In addition, the change in Cobb angle (Δ) after 12 months was 4.2° ± 1.8° in the romosozumab group and 4.9° ± 3.7° in the vertebroplasty group (p = 0.302).

Table 4. Baseline characteristics and changes in BMD and NRS over 1 year between senile and nonsenile groups in patients treated with romosozumab

Variable	Senile (n = 22)	Nonsenile (n = 20)	p-value
Age (yr)	84.5 ± 3.9	72.1 ± 5.4	< 0.001
Male sex	2 (9.1)	1 (5.0)	> 0.999
BMI (kg/m^2)	22.9 ± 3.3	23.2 ± 3.3	0.762
Level			0.068
T4–10	4 (18.2)	1 (5.0)	
T11–L2	10 (45.5)	16 (80.0)	
L3–5	8 (36.4)	3 (15.0)	
Thyroid disease	3 (13.6)	0 (0)	0.265
CKD	3 (13.6)	0 (0)	0.265
Baseline NRS	7.3 ± 0.7	7.3 ± 0.6	0.892
Baseline BMD			
Lumbar BMD	-2.8 ± 0.8	-2.9 ± 0.8	0.637
Femur neck BMD	-2.8 ± 0.6	-2.7 ± 0.8	0.510
Vertebral compression ratio (%)	24.4 ± 14.1	29.4 ± 18.3	0.321
Cobb angle (°)	1.7 ± 16.2	2.9 ± 23.2	0.843

Values are presented as mean ± standard deviation or number (%).
BMD, bone mineral density; NRS, numerical rating scale; BMI, body mass index; CKD, chronic kidney disease.

(senile) and those under 80 years (nonsenile). Upon comparing the baseline characteristics of the senile and nonsenile groups, no significant differences were observed. The results demonstrated no statistically significant differences between the senile and nonsenile groups in terms of BMD changes at the lumbar spine, total hip, or femur neck, nor in the changes in NRS scores after 1 month and 1 year (Table 5).

DISCUSSION

Previous studies have predominantly focused on demonstrating that bone anabolic agents for osteoporosis are more efficacious than antiresorptive agents, with few significant differences in adverse events. These studies primarily compare the increase in BMD between different medications and the incidence of vertebral refractures, excluding patients with recent fractures. However, our study differs from previous research by not only comparing the increase in BMD and radiological parameters, but also by demonstrating the potential of romosozumab as a viable alternative to vertebroplasty and its effectiveness in reducing the recurrence of major osteoporotic fractures over a 2-year period. Furthermore, we found no significant differences in the incidence of various adverse effects, and these findings may suggest a new paradigm for the treatment of OVCFs in the future.

Table 5. One-year changes in BMD and NRS in senile and nonsenile groups treated with romosozumab

Variable	Senile (n = 22)	Nonsenile (n = 20)	p-value
Lumbar BMD 1-yr change	0.79 ± 0.58	0.90 ± 0.36	0.403
Total hip BMD 1-yr change	0.09 ± 0.18	0.13 ± 0.22	0.531
Femur neck BMD 1-yr change	0.09 ± 0.23	0.12 ± 0.25	0.701
1-Mo NRS change	3.90 ± 1.50	4.50 ± 1.30	0.147
1-Yr NRS change	4.70 ± 1.10	5.20 ± 0.90	0.134

Values are presented as mean ± standard deviation.
BMD, bone mineral density; NRS, numerical rating scale.

Up until decades ago, interventions for osteoporosis predominantly focused on osteoclasts to inhibit bone remodeling, as demonstrated by bisphosphonates and the RANKL inhibitor denosumab. In contrast, the parathyroid hormone (PTH) analogue teriparatide, and later, the PTH-related protein analogue abaloparatide, have been utilized to stimulate osteogenic effects, accompanied by varying degrees of increased bone turnover. In contrast, targeting sclerostin with a monoclonal antibody, such as romosozumab, significantly enhances bone formation, primarily through modeling-based mechanisms, while simultaneously reducing bone resorption.

The superior efficacy of romosozumab and its safety was studied in 3 large, international, RCTs. The FRAME[6] and ARCH[7] studies were conducted on postmenopausal women, while the BRIDGE[8] study was conducted on men with osteoporosis. FRAME trial, which involved 7,180 postmenopausal women with osteoporosis, demonstrated that one year of romosozumab treatment led to increases in BMD of 13.3% in the spine and 6.8% in the hip from baseline. Our study demonstrated that, after 1 year of romosozumab administration, spine BMD increased by 28.8% from baseline, while the vertebroplasty group showed a 15.3% increase (p = 0.000). Additionally, similar to FRAME study, total hip BMD increased by 4.5% in the romosozumab group and by 1.9% in the control group (p = 0.202). In the FRAME study, clinical fractures at 1 year occurred in 1.6% of patients in the romosozumab group versus 9.5% in the placebo group, indicating a 36% reduction in fracture risk (p = 0.008). Similarly, our study found a 7.1% incidence of major osteoporotic fractures in the romosozumab group compared to 25% in the vertebroplasty group at 2 years (p = 0.051).

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In the ARCH trial, which involved 4,093 postmenopausal women with severe osteoporosis, treatment with romosozumab or alendronate for one year showed that Romosozumab significantly outperformed alendronate. Specifically, romosozumab increased BMD by approximately 2.5 times at the spine and 2 times at the hip within the first year, and reduced vertebral fracture risk by 37% at one year and by 48% at 2 years compared to alendronate. In addition, the BRIDGE trial, which was conducted on 245 men aged 55 to 90 years, demonstrated that a 12-month treatment with romosozumab resulted in significant increases in spine and hip BMD compared to placebo and was well tolerated in men with osteoporosis. Our studies have yielded results that align with those of several prominent studies, while also demonstrating efficacy in the elderly population. These findings indicate that romosozumab may be effective not only in treating postmenopausal osteoporosis but also in managing osteoporosis in the elderly.

Previous studies have predominantly emphasized the advantages of vertebroplasty, particularly its capacity to provide rapid pain relief and facilitate early ambulation, while maintaining an acceptably low complication rate.[26-28] However, a recent retrospective analysis, utilizing the ACS-NSQIP (American College of Surgeons-National Surgical Quality Improvement Program) database with 1,932 patients, reported a higher-than-expected overall complication rate of 8.6%, with minor complications, major complications, and mortality rates of 2.7%, 4.9%, and 2.1%, respectively, which represents a level of risk that could be considered clinically concerning.[29] Moreover, some studies have long elucidated the limitations and potential complications of vertebroplasty, with an increasing body of literature questioning the extent of its efficacy.[12,13]

The results derived from the ARCH study raised concerns regarding the association between romosozumab and cardiovascular risk. According to the U.S. Food and Drug Administration, romosozumab should not be initiated in patients who have experienced a MI or stroke within the past year. The pathogenesis linking sclerostin inhibition or sustained low levels of sclerostin with elevated cardiovascular risk remains unclear, and no underlying mechanisms have been identified in preclinical or genetic studies.[30] Some study that the expression of sclerostin in calcified blood vessels may represent a secondary effect of the ossification process, wherein vascular smooth muscle cells are transformed into an osteoblast or osteocyte phenotype.[31] Other researchers have proposed that sclerostin upregulation functions as an inhibitor of vascular calcification in certain animal models.[32,33] Thus, the inhibition of sclerostin by romosozumab could result in increased vascular calcification.

In our study, patients with a history of cardiovascular disease within the past year were excluded from treatment. After 2 years follow-up of romosozumab administration, the incidence of cardiovascular events was 4.8% versus 9.1% ($p = 0.716$), showing no significant difference. This finding contrasts with the results of the ARCH study, which reported a higher incidence of cardiovascular events in the romosozumab group compared to the alendronate group (50 vs. 38 at 12 months).[7] However, the previous and larger placebo-controlled FRAME trial showed no such risk, consistent with our results.[6] This discrepancy could be attributed to the protective effects of alendronate, as suggested by some studies that bisphosphonates may lower the risk of cardiovascular mortality and decrease mortality in various patient groups by reducing arterial wall calcification.[34] While more studies and reports are needed following the use of romosozumab, the current cardiovascular safety profile appears to be trending favorably.[35]

It has been shown that while the bone-forming effects of romosozumab diminish over time, its antiresorptive effects persist.[36,37] The exact mechanisms underlying the reduction in bone formation are not fully understood, but they are likely related to mechanostatic responses in the bone that lead to the overexpression of counter-regulatory molecules, such as Dickkopf-related protein 1, which inhibit Wnt signaling and, consequently, osteoblast differentiation.[38] Due to this early attenuation phenomenon, we decided on a regimen that involves switching to denosumab after 12 monthly doses of romosozumab.

This study had some limitations that should be considered. First, the low adherence rate of 35.3% for completing the full 12 injections may have introduced potential bias. As a retrospective analysis, it was challenging to determine whether the 64.7% of patients lost to follow-up discontinued treatment due to pain improvement, the high cost of the medication (as it is not covered by insurance in most cases), or other reasons. Furthermore, smoking and alcohol consumption rates, known high-risk factors for pseudarthrosis formation, could not be assessed in this outpatient-based study. As a result, it was not possible to evaluate whether other confounding variables contributed to pseudarthrosis formation in the 2 groups. Additionally, the study utilized only plain x-rays without dynamic imaging, which may have led to an underestimation of the frequency of intravertebral clefts and pseudarthrosis. Moreover, due to the limited availability of cases with BMD follow-up extending to 24 months, only 12-month BMD and x-ray follow-ups were conducted. In South Korea, the out-of-pocket medical expenses for vertebro-

plasty followed by 1 year of denosumab treatment are approximately comparable to the cost of 12 doses of romosozumab over 1 year, both ranging from around $1,500 to $2,500. In this study, romosozumab showed comparable results to vertebroplasty in terms of radiological changes and NRS improvement at 1 year, with additional benefits such as reducing the risk of major osteoporotic fractures and achieving greater lumbar BMD gain. However, with a small sample size and patients limited to those with acute OVCFs treated at a single medical center, the generalizability of these findings is limited. Further prospective and multicenter studies are needed to validate these results. Nevertheless, Romosozumab likely provides significant advantages for patients who prefer to avoid invasive procedures, particularly elderly individuals, those with CKD, or those at high medical risk.

CONCLUSION

While vertebroplasty provides more effective relief for acute pain within the first month, romosozumab has demonstrated superior outcomes in NRS scores after 1 year. No significant differences were observed between the 2 groups in radiographic and clinical outcomes, including Cobb angle and compression ratio, after 1 year. Furthermore, romosozumab has shown a greater increase in lumbar BMD and has proven effective in reducing the risk of major osteoporotic fractures, as well as in the management of both postmenopausal and senile osteoporosis.

NOTES

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