CLINICAL ARTICLE

Efficacy of Recombinant Human Parathyroid Hormone versus Vertebral Augmentation Procedure on Patients with Acute Osteoporotic Vertebral Compression Fracture

Pengguo Gou, MD1, Zhihui Zhao, MD2, Chen Yu, MD1, Xuefeng Hou, MD1, Gang Gao, MD1, Ting Zhang, MD1, Feng Chang, MD1

1Department of Orthopedic Surgery, The Fifth Affiliated Hospital of Shanxi Medical University, Taiyuan, Shanxi and 2Department of Orthopedic Surgery, The Tianjin 4th Centre Hospital, Tianjin, Tianjin, China

Objective: Although widely used in clinical practice, vertebral augmentation procedure (VAP) for osteoporotic vertebral compression fracture (OVCF) is not supported. Recently, the effect of recombinant human parathyroid hormone (1–34) (rhPTH) has been paid great attention for its efficacy in anti-osteoporosis and bone union. This study aims to explore the outcome of rhPTH on acute OVCF and compare it with VAP to clarify its therapeutic advantages.

Methods: The retrospective study comprised 71 acute OVCF patients from January 2015 to March 2020: 22 received rhPTH treatment (rhPTH group) and 49 underwent VAP (VAP group). The rhPTH group was 15 women and seven men with an average of 76.18 years, and the VAP group were 35 women and 14 men with an average of 73.63 years. The thoracic/lumbar vertebrae were 14/8 in the rhPTH group and 29/20 in the VAP group. The average follow-up period was 14.05 months in the rhPTH group and 13.82 months in the VAP group. The two groups were assessed regarding the visual analog score (VAS), Oswestry Disability Index (ODI), OVCF bone union, bone mineral density (BMD), kyphotic angle (KA), anterior and posterior border height (ABH and PBH, respectively), adverse events and the health-related quality of life assessed by short form-36 health survey scores (SF-36). Categorical variables were analyzed by chi-square test and continuous variables between groups were analyzed by independent samples t-test or Mann–Whitney U test according to the normality.

Results: During the follow-up, the VAS was significantly lower in the rhPTH group than in the VAP group at month 3 (0.39 ± 0.6 vs 0.68 ± 0.651) (p = 0.047), month 6 (0.45 ± 0.60 vs 2.18 ± 1.22) (p < 0.001), and month 12 (0.45 ± 0.60 vs 2.43 ± 1.49) (p < 0.001). At month 12, the ODI was significantly lower in the rhPTH group (18.59 ± 3.33% than in the VAP group (28.93 ± 16.71%) (p < 0.001). Bone bridge was detected on sagittal computed tomography images of all fractured vertebrae in the rhPTH group. The BMD was significantly higher in the rhPTH group (87.66 ± 5.91 Hounsfield units [HU]) than in the VAP group (68.15 ± 11.32HU) (p < 0.001). There were no significant differences in the changes in KA, ABH, and PBH between groups (all p > 0.05). The incidence of new OVCF was significantly lower in the rhPTH group than in the VAP group (p = 0.042). All scores of SF-36 were significantly higher in the rhPTH group than in the VAP group (all p < 0.05).

Conclusion: In acute OVCF patients, rhPTH was better than VAP in increasing spinal BMD to promote OVCF healing, reduce new OVCF, and improve back pain, physical ability, and health-related quality of life.

Key words: fracture healing; osteoporosis; parathyroid hormone; procedures; spine

Address for correspondence Pengguo Gou, Department of Orthopedic Surgery, The Fifth Affiliated Hospital of Shanxi Medical University, Yingze District, Taiyuan, Shanxi 030012, China Tel: +8613934790616, Email: 763146351@qq.com; Feng Chang, Department of Orthopedic Surgery, The Fifth Affiliated Hospital of Shanxi Medical University, Yingze District, Taiyuan, Shanxi 030012, China Tel: +8613935174932, Email: cfmedmail@163.com

Received 15 May 2022; accepted 26 July 2022

© 2022 THE AUTHORS. ORTHOPAEDIC SURGERY PUBLISHED BY TIANJIN HOSPITAL AND JOHN WILEY & SONS AUSTRALIA, LTD.

Orthopaedic Surgery 2022;14:2510-2518 • DOI: 10.1111/os.13470

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.
**Introduction**

Osteoporotic vertebral compression fracture (OVCF) is the most common fragility fracture, accounting for almost 50% of all osteoporotic fractures. The estimated incidence in individuals >50 years of age was 307-100,000 per year based on a German study. Symptomatic OVCF patients commonly suffer from significant and long-lasting back pain, substantially impacting patients' health-related quality of life (HRQoL). In addition to increased morbidity and mortality, OVCF imposes a significant economic burden on the public health systems worldwide and patient families.

Traditional conservative treatment, including pain medication, bed rest, and bracing, is an option for symptomatic OVCF. However, approximately 30%-40% of patients still experience severe back pain following the healing of OVCF. The progressive vertebral collapse was not rare after conservative treatment. In addition, not all OVCF healed following this treatment. Once nonunion occurs, patients may suffer from intractable back pain and neurological deficits, leading to a further reduced HRQoL and increased mortality.

Vertebral augmentation procedure (VAP) was widely applied to stabilize the fractured vertebrae to relieve back pain immediately, considering the drawbacks of conservative treatment. However, recent high- to moderate-quality evidence indicates that VAP does not offer significant clinical benefits compared with the sham procedure. One challenge was that VAP treatment only targeted the restoration of stability of the fractured vertebrae and did not improve vertebral bone mineral density (BMD) to decrease the fracture risk of the treated or non-treated vertebrae. Another challenge is that VAP is not suitable for patients with surgical contraindications.

Recombinant human parathyroid hormone (rhPTH), the only anabolic drug in all anti-osteoporosis agents, has been widely employed for osteoporosis with a therapeutic effect following rhPTH treatment in patients with acute OVCF was limited. Therefore, our study aimed to: (i) explore the outcome of rhPTH on acute OVCF as to the back pain, physical ability, fracture union, changes in BMD, kyphotic angle (KA), vertebral height, adverse events and HRQoL; and (ii) compare with VAP to illustrate the treatment advantages of rhPTH.

**Materials and Methods**

**Patients**

This study retrospectively reviewed the medical records of acute OVCF patients receiving rhPTH or VAP treatment between January 2015 and March 2020 to compare the clinical efficacy. The study was approved by the Institutional Review Board of the Fifth Affiliated Hospital of Shanxi Medical University (approval No. 2022-199).

**Inclusion and Exclusion Criteria**

Inclusion criteria: (i) age 60-90 years; (ii) acute OVCF (>2 weeks) from low energy trauma (fall from a standing height or less); (iii) patients suffering from severe back pain; (iv) only underwent either rhPTH or VAP treatment.

Exclusion criteria: (i) history of taking drugs affecting bone metabolism; (ii) vertebral infections or tumor; (iii) history of spinal surgery; (iv) OVCF with spinal cord dysfunction; (v) endplate Modic changes.

Finally, 22 patients who received rhPTH treatment (rhPTH group) and 49 patients who underwent VAP (VAP group) were included in this study. All the patients' data were collected and measured by two experienced orthopaedic surgeons. Both readers were blinded to all the clinical and imaging data.

**Radiological Diagnosis**

Magnetic resonance imaging (MRI) was performed and used for OVCF diagnosis, on which the bone marrow signals displayed hypointensity on T1-weighted and hyperintensity on T2-weighted and fat-suppressed sequences. Given that T10-L2 vertebra levels are the most common fracture site, CT values of L4 ≤ 80 Hounsfield unit (HU) were applied to the osteoporosis diagnosis.

**Treatment Method**

Patients in the rhPTH group received once daily rhPTH administered by 20μg subcutaneous injection in the morning for at least 6 months in the rhPTH group. Commonly, patients received rhPTH treatment within their community, not requiring hospitalization. Patients in the VAP group were administered VAP treatment in the VAP group. No patients in both groups were administered analgesics following the treatment. Calcium (1.2g/day) and vitamin D (800 IU/day) were administrated in both groups.

**Clinical Outcomes Assessment**

The visual analog score (VAS) was used to evaluate each patient's back pain at baseline, month 1, 3, 6, and 12 following treatment. The Oswestry Disability Index (ODI) was employed to assess each patient's physical ability at baseline and month 12.
Fracture Union Assessment
Bone healing of OVCF was defined as the recovery of bone continuity detected on sagittal CT sections at month 4 following treatment, in which the formation of a bone bridge connected the upper and lower endplates. Sagittal CT images of the fractured vertebrae were quantitatively assessed with ImageJ (https://imagej.nih.gov/ij/) with a HU ratio of 200–1000 to evaluate bone bridge after rhPTH treatment. The region of interest (ROI) was drawn according to the vertebral outline after importing the image. Bone tissue within the ROI was detected by setting the CT values of 200–1000 HU and was marked in red. The red region connecting the upper and lower endplates indicated the bone bridge (Fig. 1). Bone union assessment of the cemented vertebrae was not performed in the VAP group because the assessment of the bone bridge was affected by high-density bone cement.

KA and Vertebral Height Assessment
The KA, anterior and posterior border height (ABH and PBH) of the fractured vertebrae were analyzed on the lateral X-rays. The KA of the fractured vertebrae was measured using the angle of the endplate line. The loss rate of vertebral height and the increment in KA were reviewed at baseline and month 12, respectively. The loss rate of vertebral height (%) = [(vertebral height)_baseline - (vertebral height)_month 12 × 2] × 100/ [(upper vertebral height + lower vertebral height)].

BMD Evaluation
The CT value of L4 quantified on sagittal CT images was used to evaluate the spinal BMD at baseline and month 12.

Adverse Events Evaluation
During follow-up, the adverse events were recorded, including new OVCF and such serious adverse events affecting the continuation of treatment as severe gastrointestinal disorders, major adverse cardiac events, and severe dizziness.

HRQoL Assessment
The Short Form-36 Health Survey (SF-36) was employed for evaluating each patient’s HRQoL at baseline and month 12. The SF-36 is composed of the physical component summary (PCS) scores (physical functioning [PF], role physical [RP], bodily pain [BP], and general health [GH]) and mental component summary (MCS) scores (social functioning [SF], mental health [MH], role physical [RE], and vitality [VT]).

Power Calculation
Based on our pilot experiment, we assumed a normal distribution and VAS standard deviation (SD) of 1.50. With a two-sided \( \alpha = 0.05 \), a minimum sample size of 11 patients in each group gave a power of 0.9 to detect a mean difference of 1.50.

Statistical Analyses
Data analysis were performed by SPSS version 21 (SPSS Inc.). Results were presented as mean ± SD. Interclass correlation coefficients (ICC) were analyzed to assess the extents of agreement of quantitative variables collected from the two readers. The average values of quantitative variables from the two readers were used for further analyses. Categorical variables were analyzed using the chi-square tests. Independent samples T-test or Mann-Whitney U test were performed according to data normality. A paired t-test and Wilcoxon signed-rank test were performed to compare intragroup differences according to the data normality. Statistical significance was set at \( p < 0.05 \).

Result

Demographic Data
The demographic data between groups, including gender, age, the interval from injury to MRI study, location of OVCF, the period from OVCF to initial treatment, and

Fig. 1. Fracture union assessed by ImageJ after rhPTH treatment. The original sagittal CT image of L2 (A, arrowhead). The region of interest is drawn according to the L2 outline (B, yellow line). Bone bridge connecting the upper and lower endplates is detected by setting the CT values of 200–1000 HU (C, red color region), indicating bone healing. HU, Hounsfield unit.
follow-up period, indicated no statistical differences (all \( p > 0.05 \)). (Table 1).

**Repeatability of Quantitative Variables**

The inter-observer agreements for quantitative variables between reader 1 and reader 2 were excellent. Table 2 shows all the results of inter-observer agreements for all quantitative variables both in the rhPTH and VAP groups (all \( p < 0.001 \)).

**Clinical Outcomes**

No significant differences in VAS were found between the rhPTH and VAP groups at baseline (7.91 ± 0.68 vs 7.80 ± 0.68) (\( p = 0.568 \)) and month 1 (2.68 ± 0.72 vs 2.92 ± 0.89) (\( p = 0.332 \)). However, the VAS was significantly lower in the rhPTH group than the VAP group at month 3 (0.39 ± 0.61 vs 0.68 ± 0.65) (\( p = 0.047 \)), month 6 (0.45 ± 0.60 vs 2.18 ± 1.22) (\( p < 0.001 \)), and month 12 (0.45 ± 0.60 vs 2.43 ± 1.49) (\( p < 0.001 \)) (Fig. 2).

No significant differences in ODI were found between the rhPTH (79.49 ± 12.05%) and the VAP group (83.67 ± 6.75%) at baseline (\( p = 0.219 \)). At month 12, however, the ODI in the rhPTH group (18.59 ± 3.33%) was significantly lower than the VAP group (28.93 ± 16.71%) (\( p < 0.001 \)) (Fig. 2).

From baseline to month 12, the decrement in VAS was significantly higher in the rhPTH group (7.45 ± 0.86) than in the VAP group (5.33 ± 1.74) (\( p < 0.001 \)). The decrement

---

**TABLE 1 Patients’ demographic data**

|                           | rhPTH group (\( n = 22 \)) | VAP group (\( n = 49 \)) | Test statistic | \( p \)-value |
|---------------------------|----------------------------|---------------------------|----------------|----------------|
| Gender (female/male)      | 15/7                       | 35/14                     | 0.077          | 0.783          |
| Age (years)               | 76.18 ± 5.43               | 73.63 ± 5.78              | 0.583          | 0.085          |
| Interval from injury to MRI study (days) | 4.55 ± 4.04               | 5.10 ± 4.01               | 0.080          | 0.591          |
| Location of OVCF (thoracic/lumbar) | 14/8                      | 29/20                     | 0.556          | 0.727          |
| Period from OVCF to initial treatment (days) | 6.59 ± 4.22               | 7.94 ± 4.23               | 0.039          | 0.218          |
| Follow-up period (months) | 14.05 ± 1.13               | 13.82 ± 1.20              | 0.394          | 0.452          |

**TABLE 2 Repeatability and intra-observer agreement of quantitative variables**

|                           | rhPTH group | VAP group | ICC | 95% CI          | \( p \)-value | ICC | 95% CI          | \( p \)-value |
|---------------------------|-------------|-----------|-----|-----------------|--------------|-----|-----------------|--------------|
| VAS Baseline              | 0.782       | 0.782     | 0.320-0.836 | <0.001        | 0.859       | 0.859-0.851     | <0.001        |
| Month 1                   | 0.947       | 0.947     | 0.766-0.955 | <0.001        | 0.893       | 0.679-0.885     | <0.001        |
| Month 3                   | 0.892       | 0.892     | 0.59-0.916  | <0.001        | 0.913       | 0.736-0.908     | <0.001        |
| Month 6                   | 0.922       | 0.922     | 0.674-0.934 | <0.001        | 0.961       | 0.872-0.957     | <0.001        |
| Month 12                  | 0.888       | 0.888     | 0.579-0.910 | <0.001        | 0.899       | 0.691-0.890     | <0.001        |
| ODI Baseline              | 0.897       | 0.897     | 0.603-0.916 | <0.001        | 0.856       | 0.598-0.852     | <0.001        |
| Month 12                  | 0.809       | 0.809     | 0.380-0.856 | <0.001        | 0.965       | 0.884-0.961     | <0.001        |
| KA Baseline               | 0.923       | 0.923     | 0.697-0.941 | <0.001        | 0.867       | 0.624-0.863     | <0.001        |
| ABH Baseline              | 0.871       | 0.871     | 0.424-0.885 | <0.001        | 0.865       | 0.617-0.859     | <0.001        |
| PBH Baseline              | 0.898       | 0.898     | 0.616-0.922 | <0.001        | 0.931       | 0.784-0.926     | <0.001        |
| MCBS Baseline             | 0.916       | 0.916     | 0.673-0.935 | <0.001        | 0.896       | 0.689-0.889     | <0.001        |
| BMD Baseline              | 0.866       | 0.866     | 0.524-0.898 | <0.001        | 0.847       | 0.554-0.834     | <0.001        |
| Month 12                  | 0.812       | 0.812     | 0.387-0.860 | <0.001        | 0.823       | 0.526-0.820     | <0.001        |
| PCS Baseline              | 0.962       | 0.962     | 0.839-0.970 | <0.001        | 0.897       | 0.688-0.888     | <0.001        |
| Month 12                  | 0.815       | 0.815     | 0.393-0.860 | <0.001        | 0.823       | 0.515-0.814     | <0.001        |
| MCS Baseline              | 0.910       | 0.910     | 0.651-0.929 | <0.001        | 0.811       | 0.481-0.800     | <0.001        |
| PCS Baseline              | 0.965       | 0.965     | 0.850-0.972 | <0.001        | 0.925       | 0.767-0.919     | <0.001        |
| Month 12                  | 0.899       | 0.899     | 0.591-0.915 | <0.001        | 0.894       | 0.686-0.888     | <0.001        |

Abbreviations: ABH, anterior border height; BMD, bone mineral density; ICC, interclass correlation coefficients; CI, confidence intervals; KA, kyphotic angle; MCS, mental component summary; ODI, Oswestry Disability Index; PBH, posterior border height; PCS, physical component summary; VAS, visual analog score.
in ODI was significantly higher in the rhPTH group (60.91 ± 11.67) than in the VAP group (54.74 ± 17.47) \((p = 0.026)\).

**Fracture Union of OVCF**

Sagittal CT images analyzed by ImageJ confirmed the radiographic fracture union in all affected vertebrae at month 4 following rhPTH treatment.

**KA, ABH, and PBH**

Figure 3A showed no differences in KA between rhPTH and VAP groups (16.50 ± 2.87° vs 16.43 ± 3.76°) from baseline \((p = 0.138)\) to month 12 (17.68 ± 2.55° vs 16.96 ± 3.93°) \((p = 0.115)\). From baseline to month 12, no differences were observed in the KA increment in the rhPTH (1.18 ± 0.85°) and VAP groups (0.49 ± 2.74°) \((p = 0.056)\) (Fig. 3B).

There were no significant differences in ABH between the rhPTH and VAP groups at baseline (1.45 ± 0.32 vs 1.53 ± 0.35) \((p = 0.344)\) and month 12 (1.19 ± 0.29 vs 1.27 ± 0.32) \((p = 0.360)\), nor in PBH between groups at baseline (2.18 ± 0.23 vs 2.23 ± 0.23) \((p = 0.313)\) and month 12 (2.17 ± 0.23 vs 2.22 ± 0.23) \((p = 0.293)\) (Fig. 4A).

From baseline to month 12, no significant differences were found between the rhPTH (11.05 ± 4.78%) and VAP groups (11.20 ± 4.50%) \((p = 0.895)\), nor the loss rate of PBH between the rhPTH (0.41 ± 1.33%) and VAP group (0.37 ± 1.25%) \((p = 0.897)\) (Fig. 4B). Figure 5 shows typical cases of changes in KA, ABH, and PBH following rhPTH and VAP treatments.

**BMD**

At baseline, no differences in spinal BMD assessed by L4 CT value were found between rhPTH (63.95 ± 6.93HU) and VAP groups (67.17 ± 11.55 HU) \((p = 0.173)\). The value in the rhPTH group (87.66 ± 5.91HU) was significantly higher than the VAP group (68.15 ± 11.32HU) at month 12 \((p < 0.001)\). The CT value of L4 increased markedly in the rhPTH group from baseline to month 12 \((p < 0.001)\) but not in the VAP group \((p = 0.212)\) (Fig. 6).
From baseline to month 12, significant differences were found in the BMD increment in the rhPTH (23.71 ± 6.12HU) and VAP groups (0.98 ± 5.43HU) \((p < 0.001)\).

Adverse Events
No serious adverse events occurred in either of the groups. No new OVCF occurred in the rhPTH group. However, eight patients experienced new OVCF following VAP. The new OVCF rate was higher in patients receiving VAP \((p = 0.042)\).

SF-36
No significant differences in the SF-36, including eight subscale scores, MCS and PCS scores, were found between groups at baseline (all \(p > 0.05\)). At month 12, the SF-36 in the rhPTH group was significantly higher than in the VAP group (all \(p < 0.05\)). (Table 3).

From baseline to month 12, all the increment of subscale scores, MCS and PCS scores in the rhPTH group were significantly higher than in the VAP group (all \(p < 0.05\)).

Discussion
By the end of the follow-up period in the present study, the VAS and ODI were better in the rhPTH group than in the VAP group. CT images confirmed the OVCF union in all patients in the rhPTH group. No significant differences in the changes in such imaging parameters as KA, ABH, and PBH were found between the two groups. The spinal BMD assessed by the CT value of L4 was higher in the rhPTH group than in the VAP group. The number of new OVCF was

**Fig. 4** (A) No significant differences in the ABH and PBH were found between groups at baseline or month 12.
(B) There were no significant differences in the loss rates of ABH and PBH between groups from baseline to month 12, respectively. ABH, anterior border height; PBH, posterior border height

**Fig. 5** (A, B) The KA, ABH, and PBH in a 65-year-old female with acute L2 OVCF changes from \(7^\circ\), 2.40, and 2.6 cm before treatment (A) to \(9^\circ\), 2.25, and 2.6 cm following rhPTH at month 12 (B). (C, D) The KA, ABH, and PBH in a 67-year-old female with fresh T12 OVCF changes from \(12^\circ\), 2.00, and 2.50 cm before treatment (C) to \(13^\circ\), 1.85, and 2.50 cm after VAP treatment at month 12 (D). ABH, anterior border height; KA, kyphosis angle; PBH, posterior border height
fewer in the rhPTH group than in the VAP group. The HRQoL assessed by the SF-36 was higher in the rhPTH group than in the VAP. All the results collected confirmed that rhPTH was better than VAP in improving back pain and physical ability, promoting fracture union, increasing the spinal BMD to decrease the incidence of new OVCF and improving the HRQoL.

**Challenges of VAP Treatment**

VAP can significantly and quickly reduce back pain by restoring the stability of the fractured vertebra. Recently, however, high- to moderate-quality evidence indicated that VAP offered no clinical benefits compared with the sham procedure and did not recommend VAP to treat acute or subacute OVCF.

OVCF is the most severe complication of systemic osteoporosis, and the reduction of vertebral refracture risk should be one of the outcomes of OVCF treatment. Attention should be paid to treating both local fracture and systemic low bone mass. Hence, the OVCF and osteoporosis treatment to prevent new OVCF is vital in clinical practice.

However, the bone cement injected into the fractured...
vertebra could not exert the effects either in boosting OVCF union or improving the whole spinal BMD. In contrast, the fracture risk increased significantly following VAP both in the cemented vertebra and adjacent vertebrae. Given the disadvantages of VAP, orthopaedic surgeons have been exploring effective treatments for acute OVCF.

**Advantage of rhPTH for OVCF**

In our study, the VAS significantly decreased in the rhPTH group compared with the VAP group during the follow-up. By the end of the follow-up, the back pain and physical ability in the rhPTH group assessed by VAS and ODI were better than those in the VAP group.

The effects of rhPTH treatment on bone healing at various fracture sites have been described in the literature. Different from previous studies, sagittal CT images were used to quantitatively assess the union of OVCF. Our study indicated that the bone bridge connecting the upper and lower endplates was detected on sagittal CT images of all the fractured vertebrae, confirming the enhancing effect of rhPTH on the bone union of OVCF.

Piazzolla et al. reported the bone union of OVCF related to the improved VAS and ODI. Unlike the mechanisms of VAP, rhPTH treatment gradually restored the continuity of fractured vertebrae. The gradually improved VAS and ODI showed that boosting OVCF healing following rhPTH treatment could exert more reliable clinical outcomes than VAP treatment during the entire follow-up period.

There had been reports that VAP treatment could prevent progressive kyphosis and vertebral height loss. At month 12, both KA and increment of KA were similar in both groups in our study. However, no changes in KA could fully demonstrate the loss of vertebral height following treatment. So, we further evaluated the changes in ABH and PBH of the OVCF vertebra. We found no statistical difference in the changes in ABH and PBH between groups at month 12. All measurements indicated that rhPTH treatment exerted a preventive effect on vertebral height loss.

Mikula et al. confirmed that rhPTH treatment could increase lumbar BMD assessed by routine CT. Our study's CT quantitative assessment of BMD was a better method than dual-energy X-ray absorptiometry. The increased BMD of L4 was observed in the rhPTH group compared with no changes in the values in the VAP group.

According to Lindsay, a new OVCF will occur again in approximately 20% of females within a year. The OVCF risk could be reduced by 40%–70% following rhPTH treatment. Compared with VAP, improved BMD, a surrogate determinant of increased vertebral strength, may relate to lower OVCF risk in our study. By the end of the follow-up, the rhPTH group had a lower rate of new OVCF than the VAP group.

OVCF was related to a negative impact on the HRQoL. Chen et al. reported that rhPTH treatment showed better clinical outcomes with significantly improved HRQoL. Although SF-36 improved by the end of follow-up, the scores were higher in the rhPTH group than in the VAP group.

Compared with VAP, one advantage was rhPTH treatment with no hospital treatment required, reducing healthcare costs. Combining the improved clinical outcomes, bone union signs, ameliorated osteoporosis, and lower rates of new OVCF, rhPTH treatment could be an effective alternative to VAP for OVCF.

**Limitations**

Our study showed the clinical outcomes of rhPTH for acute OVCF, especially in boosting OVCF union. However, multicentric randomized trials are necessary for future studies. Although vital for early treatment, we only focused on patients with acute OVCF in this study. Further studies are needed to assess the clinical efficacy of rhPTH on subacute and chronic OVCF. High-density bone cement within the vertebral bodies affects the evaluation of bone bridge. We did not evaluate the fracture union of the affected vertebrae in the VAP group, which is another limitation. Additionally, the subsequent anti-osteoporosis therapy with other anti-osteoporotic medications should also be considered in the future.

**Conclusion**

For acute OVCF patients, rhPTH could significantly increase bone mineral density to promote the radiographic union of the fractured vertebrae and reduce new OVCF. More importantly, it was superior to VAP in alleviating back pain and improving physical ability and health-related quality of life, with no requirements for hospitalization.

**Author’s Contribution**

Pengguo Gou and Feng Chang conceived and designed the study. Pengguo Gou, Zhihui Zhao, and Chen Yu wrote the manuscript. Ting Zhang and Gang Gao performed the experiments. Xuefeng Hou performed the data analyses. All authors read and approved the final manuscript. Pengguo Gou and Feng Chang contributed equally to this manuscript. Pengguo Gou, Zhihui Zhao, and Chen Yu contributed equally to this manuscript.

**Conflicts of Interest**

All the authors declare no conflict of interest.

References

1. Bailie G, Cauley JA, Luckey MM, et al. Worldwide prevalence and incidence of osteoporotic vertebral fractures. Osteoporos Int. 2017;28: 1531–42.

2. Hernlund E, Svedbom A, Ivergard M, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and...
the European Federation of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos. 2013;8:136.

3. Schouboe JT. Epidemiology of vertebral fractures. J Clin Densitom. 2016;19:8–22.

4. Zeytnoglu M, Jain RK, Vokes TJ. Vertebral fracture assessment: enhancing the diagnosis, prevention, and treatment of osteoporosis. Bone. 2017;104:54–65.

5. Borgstrom F, Olafsson G, Strom O, et al. The impact of different health dimensions on overall quality of life related to kyphoplasty and non-surgical management. Osteoporos Int. 2013;24:1991–9.

6. Si L, Winzenberg TM, de Graan J, Palmer AJ. A systematic review and meta-analysis of utility-based quality of life for osteoporosis-related conditions. Osteoporos Int. 2014;25:1987–97.

7. Jung HK, Park YS, Seo HY, Lee JC, An KC, Kim JH, et al. Quality of life in patients with osteoporotic vertebral compression fractures. J Bone Metab. 2017;24:187–96.

8. Bluc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA. 2009;301:513–21.

9. Ruiz-Adame M, Correa M. A systematic review of the indirect and social costs studies in fragility fractures. Osteoporos Int. 2020;31:1205–16.

10. Ameis A, Randhawa K, Yu H, Coté P, Haldeman S, Chou R, et al. The global spine care initiative: a review of reviews and recommendations for the non-invasive management of acute osteoporotic vertebral compression fracture pain in low- and middle-income communities. Eur Spine J. 2018;27:861–9.

11. Klazen CA, Verhaar HJ, Loehne PN, et al. Clinical course of pain in acute osteoporotic vertebral compression fractures. J Vasc Interv Radiol. 2010;21:1405–9.

12. Vennmans A, Klazen CA, Longe PN, et al. Natural history of pain in patients with conservatively treated osteoporotic vertebral compression fractures: results from VERTOS II. J Neurosurg Spine. 2012;33:519–21.

13. Lim J, Choi S-W, Yoon JY, Kwon HJ, Kim SH, Koh HS. (K) post-traumatic delayed vertebral collapse: Kummell’s disease. J Korean Neurosurg Soc. 2018;61:1–9.

14. Eddin AA, Ong KL, Lau E, Kurtz SM. Morbidity and mortality after vertebral fractures: comparison of vertebral augmentation and nonoperative Management in the Medicare Population. Spine. 1976;20:1501–5.

15. Clark W, Bird P, Gonski P, Diamond TH, Smedley P, McNeil HP, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOR): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2016;388:1408–16.

16. Buchbinder R, Buisja L. Why we should stop performing vertebroplasties for osteoporotic spinal fractures. Intern Med J. 2019;49:1367–71.

17. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 2018;4:CD006349.

18. Lin WC, Lee YC, Lee CH, Kuo YL, Cheng YF, Lui CC, et al. Fractures in cemented vertebrae after percutaneous vertebroplasty: a retrospective analysis. Eur Spine J. 2008;17:592–9.

19. Zhao Y, Xue R, Shi N, Xue Y, Zong Y, Lin W, et al. Aggravation of spinal deformity following new osteoporotic vertebral compression fracture prevented by teriparatide in patients with surgical contraindications. Osteoporos Int. 2016;27:3309–17.

20. Hayashi T, Maeda T, Masuda M, Ueta T, Shiba K. Morphology of the injured posterior wall causing spinal canal encroachment in osteoporotic vertebral compression fractures. Spine. 2016;41:3712–9.

21. Lim J, Choi S-W, Youm JY, Kwon HJ, Kim SH, Koh HS. (K) post-traumatic delayed vertebral collapse: Kummell’s disease. J Korean Neurosurg Soc. 2018;61:1–9.

22. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 2018;4:CD006349.

23. Lim J, Choi S-W, Youm JY, Kwon HJ, Kim SH, Koh HS. (K) post-traumatic delayed vertebral collapse: Kummell’s disease. J Korean Neurosurg Soc. 2018;61:1–9.

24. Eddin AA, Ong KL, Lau E, Kurtz SM. Morbidity and mortality after vertebral fractures: comparison of vertebral augmentation and nonoperative Management in the Medicare Population. Spine. 1976;20:1501–5.

25. Clark W, Bird P, Gonski P, Diamond TH, Smedley P, McNeil HP, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOR): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2016;388:1408–16.

26. Buchbinder R, Buisja L. Why we should stop performing vertebroplasties for osteoporotic spinal fractures. Intern Med J. 2019;49:1367–71.

27. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 2018;4:CD006349.

28. Lin WC, Lee YC, Lee CH, Kuo YL, Cheng YF, Lui CC, et al. Fractures in cemented vertebrae after percutaneous vertebroplasty: a retrospective analysis. Eur Spine J. 2008;17:592–9.

29. Zhao Y, Xue R, Shi N, Xue Y, Zong Y, Lin W, et al. Aggravation of spinal deformity following new osteoporotic vertebral compression fracture prevented by teriparatide in patients with surgical contraindications. Osteoporos Int. 2016;27:3309–17.

30. Hayashi T, Maeda T, Masuda M, Ueta T, Shiba K. Morphology of the injured posterior wall causing spinal canal encroachment in osteoporotic vertebral compression fractures. Spine. 2016;41:3712–9.

31. Lim J, Choi S-W, Youm JY, Kwon HJ, Kim SH, Koh HS. (K) post-traumatic delayed vertebral collapse: Kummell’s disease. J Korean Neurosurg Soc. 2018;61:1–9.

32. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 2018;4:CD006349.