

# Risk Factors of New Adjacent Compression Fracture after Percutaneous Vertebroplasty: Effectiveness of Bisphosphonate in Osteoporotic or Osteopenic Elderly Patients

Dae-Hyun Seo, MD<sup>1</sup>, Si-Hyuck Oh, MD<sup>1</sup>, Kyeong-Wook Yoon, MD<sup>1</sup>,  
Jung-Ho Ko, MD, PhD<sup>1</sup>, Young-Jin Kim, MD, PhD<sup>1</sup>, and Jee Young Lee, MD<sup>2</sup>

<sup>1</sup>Departments of Neurosurgery, <sup>2</sup>Radiology, Dankook University College of Medicine, Cheonan, Korea

**Objective:** The purpose of this study is to investigate the incidence of new compression and to analyze factors that influence the fractures in adjacent levels after percutaneous vertebroplasty (PVP).

**Methods:** This retrospective study examined 206 patients who had undergone PVP for single level osteoporotic or osteopenic compression fractures during the last seven years in our department. After PVP, the patients were observed for at least over one year, and 29 patients showed new additional compression fractures in adjacent levels. One hundred seventy seven patients who did not show additional compression fractures were analyzed as the control group. Statistical comparisons were performed between the groups, in terms of age, gender, bone mineral density, whether bisphosphonate (BPP) was treated, preoperative kyphosis, preoperative wedge angle, change in wedge angle, amount of bone cement, existence of intradiscal bone cement leakage, and initial fracture levels.

**Results:** The statistically significant factors that influence new compression fractures in adjacent levels after PVP were as follows: being female, initial thoracolumbar junction fracture, preoperative large kyphotic, preoperative large wedge angle, change in wedge angle, administration of BPP in osteopenia group, and intradiscal cement leakage.

**Conclusion:** This study identified many factors that influence newly developed compression fractures in adjacent levels after PVP. Interestingly, the administration of BPP in osteopenia group had positive influence on new fractures in this study. Therefore, we recommend early administration of BPP to patients with osteopenia. (Korean J Neurotrauma 2014;10(2):86-91)

**KEY WORDS:** Spinal fractures · Fractures compression · Adjacent vertebral fractures · Diphosphonates · Risk factors · Vertebroplasty.

## Introduction

Percutaneous vertebroplasty (PVP) is a surgical procedure that is effectively used to relieve the pain for osteoporotic compression fractures. According to previous studies, approximately 80% to 90% of the patients who had undergone PVP showed pain relief effects that were statistically

significant.<sup>14)</sup> The mechanism of pain relief was known to be caused by the stabilization of vertebral body, the loss of micro-movements in fractured sites, and the effectiveness of neuroblocking by chemical and thermal responses of polymethyl methacrylate (PMMA).

Since the late 1990s when PVP has been widely used in Korea, some complications have been reported. As for the acute complications, pneumothorax, rib fractures, and the local compression of nerve roots and spinal cords due to the leakage of PMMA were reported and for the worst case, pulmonary thromboembolism has also been reported.<sup>2)</sup> The subacute or chronic complications include new compression fractures in the adjacent levels, which occur in about 10% to 20% of the total patients.<sup>14)</sup> However, the risk factors that cause new compression fractures have not been re-

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**Address for correspondence:** Young-Jin Kim, MD, PhD  
Department of Neurosurgery, Dankook University College of Medicine, 119 Dandae-ro, Dongnam-gu, Cheonan 330-714, Korea  
Tel: +82-41-550-3979, Fax: +82-41-552-6870  
E-mail: spine1225@naver.com

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searched frequently.

This study investigated on the incidence and risk factors of fractures in adjacent levels after PVP, and the analyses were used to determine whether bisphosphonate (BPP) has actual preventive effects on new compression fractures in adjacent levels.

## Materials and Methods

This study was conducted on 206 patients who had undergone PVP due to persistence of pain after two weeks of conservative treatment, after single-level osteopenic or osteoporotic compression fracture, in our department between January 2006 and December 2012. The follow-up observations were performed on the 206 patients for over 12 months. The pathological fractures (due to cancer, infection, inflammatory disease, and high energy trauma, etc.) and fractures in multiple levels were excluded.

We determined the following as the risk factors that influenced adjacent levels: age, gender, bone mineral density (BMD), whether treated with BPP, preoperative kyphosis, preoperative wedge angle, change in wedge angle, amount of bone cement, existence of intradiscal cement leakage, and initial fractures levels.

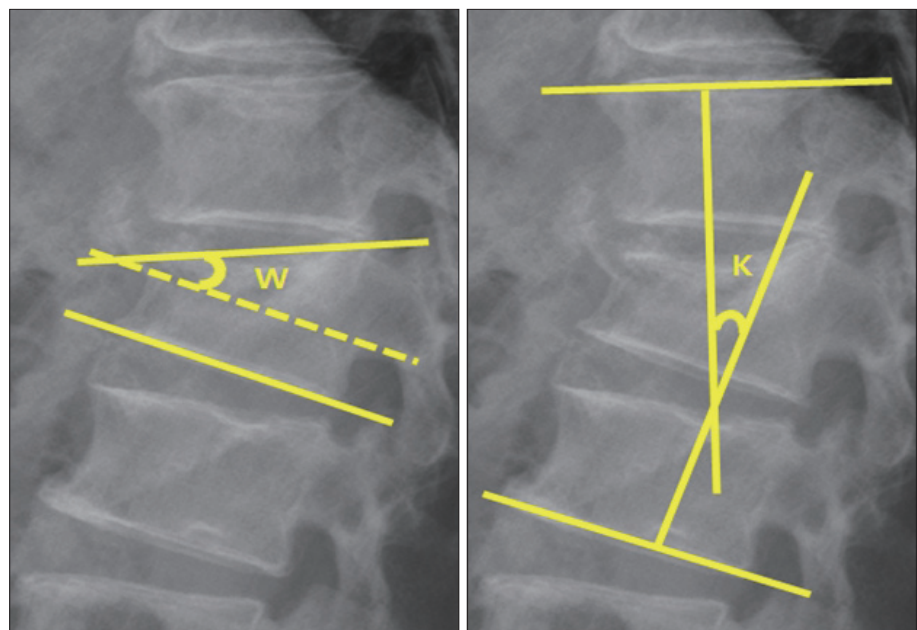
The diagnosis of compression fractures were determined by X-ray and magnetic resonance image. The diagnostic criteria were the loss of vertebral height on X-ray, decreased signals on T1 weighted images, increased signals on T2 weighted images, and increased signals on short tau inversion recovery images.

The BMD was measured for all patients who developed initial compression fractures by dual-energy X-ray absorptiometry technique (DXA; Hologic QDR 2000, Hologic Inc., Waltham, MA, USA). The osteoporosis was defined as  $T\text{-score} \leq -2.5$  and osteopenia was defined as  $-2.0 \leq T\text{-score} < -1.0$ . The wedge angle was obtained using the angle gap between the upper and lower epiphyseal plates in the initial fracture body. The change in wedge angle change was obtained using the interval angle between preoperative and postoperative angles. The kyphotic angle was obtained using the angle gap between the upper epiphyseal plates on the upper adjacent body and the lower epiphyseal plates on the lower adjacent body (Figure 1).

This procedure was performed under local anesthesia. For the image amplification devices, Monoplane (Philips Integris Allura 15/12 Cath Lab, Philips Medical Systems, Best, the Netherlands) was used between 2006 and 2008, and Artis zee Biplane system (Siemens, Erlangen, Germany) was used between 2009 and 2012.

Before injecting PMMA, venography was performed to prevent the injection of cement into veins and to identify the possible direction of cement leakage. The PMMA was injected through one-side pedicle, and the amount of PMMA was adjusted according to the degree of fractures in each patient. After the surgery, patients who were diagnosed with osteopenia or osteoporosis were recommended to take BPP and adopt a diet plan including calcium, vitamin D and heliotherapy.

We compared the fracture group that developed new fractures in adjacent levels and the non-fracture group that did



**FIGURE 1.** The method of estimating wedge angle and kyphotic angle (W: wedge angle, K: kyphotic angle).

not develop new fractures in adjacent levels. The age, gender, BMD, administration of BPP, preoperative kyphosis, preoperative wedge angle, change in wedge angle, amount of bone cement, existence of intradiscal cement leakage, and initial fractures levels were examined in the two groups. We used Fisher's exact tests, independent *t*-tests, and SPSS 21.0 (SPSS Inc., Chicago, IL, USA) to statistically analyze the data. The statistically significant level was set at  $p < 0.05$ .

## Results

Two hundred six patients had undergone PVP after the initial compression fracture. They had mean age of 70.5 years [mean standard deviation (SD) ± 11.7], 12.2° (mean SD ± 8.31) of initial kyphotic angle, 7.59° (mean SD ± 4.8) of initial wedge angle, 3.5° (mean SD ± 4.8) of change in wedge angle, and -2.3 (mean SD ± 1.0) of BMD. The amount of PMMA was estimated at an average of 4.3 mL (mean SD ±

**TABLE 1.** Clinical and demographic data for total patients

	Mean value (%)
Age (years)	70.5
Sex (male:female)	78:128
Initial fracture level, n (%)	
Thoracic	52 (25.2)
T-L junction	41 (19.9)
Lumbar	113 (54.9)
BMD (spine)(T-score)	-2.3
Preoperative kyphotic angle	12.2°
Preoperative wedge angle	7.59°
Wedge angle change	3.5°
Injected volume (mL)	4.3
Bisphosphonate	78 (37.9%)

n: number, BMD: bone mineral density, T-L: thoracolumbar

1.4). The BPP was applied to 78 patients (37.9%)(Table 1).

### Risk factors that affect new adjacent compression fractures after PVP

The total patients were divided into new compression fracture group and non-fracture group, in adjacent levels after PVP. Among the total of 206 patients, 29 patients (14.1%) developed new compression fractures in adjacent levels within 12 months. There was no statistically significant difference in patients' age and amount of PMMA between the fracture and non-fracture groups (Table 2). On the other hand, in terms of gender, fracture group had a larger number of females with statistical significance ( $p = 0.004$ ). In correlation between the previous compression fracture levels and the incidence of additional fractures, the incidence of new compression fractures were more frequent in thoracolumbar junction level than in other levels (thoracic vertebrae and lumbar vertebra)( $p = 0.000$ ). In comparing two groups, the fracture group's average BMD had T-score of -2.80 (mean SD -1.5--4.8) and the non-fracture group's BMD had T-score of -2.38 (mean SD -0.1--4.5). This showed that BMD was lower in the fracture group with statistical significance ( $p = 0.045$ ).

The preoperative kyphotic angle and wedge angle were compared between the two groups. For the initial kyphotic angles, the average angles were shown to be 12.69° (mean SD 0.3--42.4) in the non-fracture group and 9.20° (mean SD 0.2--23.9) in the fracture group. For the initial wedge angles, the average angles were measured to be 10.94° (mean SD 4--31.4) in the fracture group and 6.77° (mean SD 4--26.4) in the non-fracture group. Both the initial kyphotic angles and wedge angles exhibited larger angles in the fracture group than in the non-fracture group ( $p = 0.036$ ,  $p = 0.000$ ).

**TABLE 2.** Clinical and demographic data for the two study group

Characteristics	Fracture group (n=29)	Non-fracture group (n=177)	p-value
Age (years)	72.45	70.16	>0.05
Sex ratio (male:female)	4:25	74:103	0.004
Initial fracture level, n (%)			<0.001
Thoracic	1 (3.5)	51 (28.8)	
T-L junction	19 (65.5)	22 (12.4)	
Lumbar	9 (31.0)	104 (58.8)	
Use of bisphosphonate, n (%)	9 (31)	69 (39)	>0.05
Intradiscal leakage, n (%)	7 (24.1)	12 (6.8)	0.011
Injected volume (mL)	4.7	4.1	>0.05
Mean BMD (T-score)	-2.80	-2.38	0.045
Mean initial kyphotic angle	9.20	12.69	0.036
Mean initial wedge angle	10.94	6.77	<0.001
Wedge angle change	6.9	1.3	0.032

n: number, BMD: bone mineral density, T-L: thoracolumbar

**TABLE 3.** Association bisphosphonate with new-onset fracture in osteopenia group

	Bisphosphonate prescribed	Bisphosphonate non-prescribed	<i>p</i> value
Non-fracture	41 (97.6%)	67 (84.8%)	
Fracture	1 (2.4%)	12 (15.2%)	
Total	42 (100%)	79 (100%)	0.033

**TABLE 4.** Association bisphosphonate with new-onset fracture in osteoporosis group

	Bisphosphonate prescribed	Bisphosphonate non-prescribed	<i>p</i> value
Non-fracture	28 (77.8%)	41 (83.7%)	
Fracture	8 (22.2%)	8 (16.3%)	
Total	36	49	>0.05

The change in wedge angle was also larger in the fracture group ( $p=0.032$ ). The leakage of PMMA in the disc space was discovered in 24.1% of the fracture group and in 6.8% of the non-fracture group. This clearly confirmed that the leakage of PMMA was larger in the fracture group ( $p=0.011$ ). However, the injected volume was not different between the two groups ( $p>0.05$ ). There was no statistically significant differences in terms of the relations between the administration of BPP and the additional new fractures ( $p>0.005$ ).

#### Effectiveness of administration of BPP

All patients were advised to take BPP for active treatment of osteoporosis, and follow-up study was conducted. In comparing fracture group with non-fracture group, the relationship between the administration of BPP and the occurrence of fractures in adjacent levels had no statistically significant differences in all patients (Table 2). However, there was a difference in effectiveness of BPP administration between the osteoporosis group and the osteopenia group. There were 121 osteopenia patients, and among them, 42 patients (34.7%) took BPP, and 79 patients (65.3%) did not take BPP. For the comparison of the relationship between medication of BPP and additional new compression fractures, the medicated group showed lower rate of additional new compression fractures than the non-medicated group, with statistical significance ( $p=0.033$ )(Table 3).

On the other hand, the osteoporosis group showed no statistical significance in the relations between the administration of BPP and the additional new compression fractures ( $p>0.05$ )(Table 4).

## Discussion

The PVP is characterized by surgical convenience such

as the use of local anesthesia, short procedure time, and less invasive technique. Therefore, it is relatively safe on elderly patients and on patients with high risk of general anesthesia. However, PVP is not completely free of complications. Only a few studies on new adjacent compression fractures after operation have continued since the 2000s.<sup>13)</sup>

The incidence of new compression fractures was reported to range from 15% to 22% within one year after surgery. In this study, it was determined to be at 14.1%. The present study shows a lower incidence of additional new compression fractures than that of the existing studies. This is because we used Monoplane and Biplane device, instead of C-type image amplification devices which were used in most of the previous studies. These equipments increased surgical accuracy during PVP by allowing the simultaneous identification of anterior-posterior and lateral view, and complications such as leakage of PMMA could be reduced.<sup>6)</sup>

There are three leading factors that make PVP to cause new adjacent compression fractures. First, PMMA is hardened to stiffness after injection into the fractured body, and it has higher intensity than the normal cancellous bones.<sup>5)</sup> This causes PMMA to have different stiffness from the surrounding vertebral body. This stress increasing effect induces compression fractures. In particular, Grados et al.<sup>3)</sup> reported that the vertebral body injected with PMMA showed a higher level of risk for fractures (odds ratio 2.27, 95% confidence interval 1.1–4.5) than the vertebral body that was not injected with PMMA. The vertical compression force on overall vertebrae is shifted to the other side after the injection of PMMA, and this increases vertical pressures in the adjacent levels.

Secondly, Uppin et al.<sup>15)</sup> reported that the relief of pain immediately after the surgery encouraged physical activities of patients, and this subsequently increased the risk of new compression fractures in the adjacent levels.

Thirdly, Ross et al.<sup>10)</sup> noted that the osteoporosis patients have three to four times higher levels of risk for the occurrence of additional new compression fractures than the healthy individuals. The PVP not only leads to simple fractures in the adjacent levels, but also promotes degenerative changes in the adjacent levels. Therefore, preoperative screening tests on the patients for osteoporosis and postoperative treatments play an important role for their prognosis.<sup>12)</sup>

While large-scale and multi-centered studies have been actively conducted regarding the BPP and its preventive effects of fractures, it has not been researched in the severe osteoporosis group. However, this study reveals tendency that the use of BPP has preventive effects on new compres-

sion fractures in adjacent levels of osteopenia patients.

We hypothesized that osteoporosis patients who already had fractures with seriously lowered T-score, were highly unlikely to maintain the bone strength, because they had serious loss of bone density. For this reason, the administration of BPP which inhibits reabsorption by working on osteoclasts has no effect on severe osteoporotic patients. To establish our hypothesis, we divided the patients into two groups, the osteopenia group (bone density was not yet seriously lowered) and the osteoporosis group (already diagnosed with osteoporosis due to reduced levels of bone density), and compared their incidences of additional new compression fractures in adjacent levels.

The patients among the in high risk group, who had undergone PVP were advised to take BPP. Seventy eight patients took BPP and 128 patients did not take it. Nine patients in the medicated group and 20 patients in the non-medicated group developed new additional compression fractures in adjacent levels. This comparison did not show a large gap in the incidence of new compression fractures between the medicated and non-medicated groups (Table 2).

However, the administration of BPP in osteopenia group was found to have preventive effects on the additional new compression fractures ( $p=0.003$ )(Table 3). This result showed that the efficacy of BPP could differ depending on the severity of bone density. In other words, the effects of BPP were negligible in patients with the severe loss of bone density. This could be understood by the action mechanism of BPP, which operates through suppression reabsorption by working on osteoclast. This does not affect the formation of bones. Therefore, if it is continuously used under the condition in which the bone mass is not sufficient, this is reported to rather negatively influence the metabolism of bones. This is also related to our present studies. The effects of BPP on patients with the severe loss of bone strength are likely to be negligible. For these patients, teriparatide (recombinant form of parathyroid hormone) may have some effect for bone formation.<sup>11)</sup> Relatively, patients who still have sufficient amount of bone mass and bone density may have benefited from BPP.

Some studies are being conducted regarding the risk factors to prevent new compression fractures in adjacent levels after PVP. In particular, its correlation with BMD has been researched frequently. In this study, BMD of the fracture group was lower at a statistically significant level. This result confirmed the importance of preventive treatment on new compression fractures after the initial osteoporotic compression fractures.<sup>8)</sup>

Other factors that can influence compression fractures

after PVP are preoperative kyphotic angle and wedge angle on X-ray images. In this study, both preoperative kyphotic angle and wedge angle were found to influence new compression fractures, with statistical significance. In most studies, preoperative kyphotic angle has been reported to have no relationship with additional fractures, but changes in kyphotic and wedge angle before and after the surgery have been found to influence the outcome. As Lin et al.<sup>6)</sup> noted, this study also found that the wedge angle was associated with prognosis even with an initial angle. This is because a larger wedge angle leads to a greater concentration of axial compression force on one side.<sup>7,9)</sup>

An additional factor that can influence new compression fractures is cement leakage on disc space. It was reported that cement leakage occurs in vertebral body through the weakest tension point, and increases the compression stress in the leaked area, and ergonomically weakens the adjacent vertebral endplates.<sup>1,4)</sup> Similar to other studies, the postoperative outcome in our study was determined to be influenced by cement leakage. Therefore, the level and pattern of fractures should be accurately identified before surgery, and an appropriate amount of cement should be injected during the surgery by using a suitable technique.

This study examined the risk factors on new compression fractures in adjacent levels, which could occur after PVP in the patient with initial compression fracture. In determining the prognosis of patients, the adjustable factors depend on the skills of technique of the physicians and the preventive medication for osteopenia group. However, this study has some limitations. First, this was conducted in a retrospective manner, and had a limited number of subjects. In addition, there were no data about the onset times and symptoms of additional new compression fractures.

## Conclusion

This study confirmed that PVP has clear effects on the relief of acute pain in compression fractures, but the incidence of new compression fractures in adjacent levels after surgery is about 14.1%, which is not low. The influential factors on new compression fractures in adjacent levels after PVP, include gender, BMD, kyphotic angle, wedge angle, intradiscal leakage, and previous compression fracture levels. In particular, osteopenia patients were observed to benefit from preventive effects of BPP on new compression fractures. Therefore, we would like to recommend early administration of BPP to patients with osteopenia.

■ The authors have no financial conflicts of interest.



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