

# Risk Factors for Subsequent Fracture after Osteoporotic Vertebral Compression Fracture

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**Objective:** Percutaneous vertebroplasty is an effective treatment that relieves pain caused by vertebral compression fracture. However, vertebroplasty may increase the risk for subsequent vertebral compression fracture. The purpose of this study is to evaluate the incidence of and risk factors for subsequent fracture after vertebroplasty.

**Methods:** A retrospective analysis was performed for 112 patients who were diagnosed with a first osteoporotic compression fracture at a single level and underwent vertebroplasty at that level. Possible risk factors for subsequent fracture, such as age, sex, bone mineral density (BMD), location of treated vertebrae, pattern of cement distribution, cement volume, presence of intradiscal cement leakage, and direction of cement leakage, were analyzed.

**Results:** During the follow-up period, 18 new subsequent vertebral fractures developed (16.1%). Subsequent fractures were more common in osteoporotic patients (T-score  $\leq -2.5$ ) ( $p=0.034$ ,  $r=0.208$ ). Intravertebral cement volume  $\geq 3.5$  cc were also associated with a significantly higher risk of fracture ( $p=0.012$ ,  $r=0.238$ ).

**Conclusion:** Low BMD and volume of intravertebral cement were the factors most strongly associated with subsequent fracture after percutaneous vertebroplasty. (Korean J Neurotrauma 2013;9:120-124)

**KEY WORDS:** Osteoporotic compression fracture · Bone mineral density · Cement volume.

## Introduction

Percutaneous vertebroplasty (PVP) is considered an effective treatment method for relieving the pain of osteoporotic vertebral compression fractures (VCFs). Although vertebroplasty is relatively safe and has a low complication rate, however, subsequent fracture after vertebroplasty is not uncommon. A possible increase in risk of new VCF after augmentation is of concern, especially in osteoporotic patients. Furthermore, there is no standard parameter for variables such as optimal cement volume, proper cement injection site, and optimal pattern of cement distribution. Factors that may induce subsequent fracture are also uncertain.

The purpose of this study was to evaluate the incidence of and risk factors for subsequent fracture after vertebroplasty.

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## Materials and Methods

### Patient selection

Between January 1, 2007, and December 31, 2009, a total of 296 patients underwent vertebroplasty at our department. All VCFs were confirmed by magnetic resonance (MR) imaging. Patients followed up for a minimum of 6 months were included for analysis. We selected 112 patients with primary fracture (first-time fracture) at a single level who received vertebroplasty at that level (Table 1). We also excluded pathologic fractures (metastases and multiple myeloma). Symptomatic subsequent VCFs were diagnosed using plain radiographs and MRI.

### Procedure

All vertebroplasty procedures were performed in an operating room under C-arm guidance. In most cases, an 11-gauge needle was inserted through the routine unipedicular approach. A 13-gauge needle was used in the mid-thoracic level. Bone cement was injected under fluoroscopic control. The procedure was terminated if cement leakage occurred or if the cement reached the posterior quar-

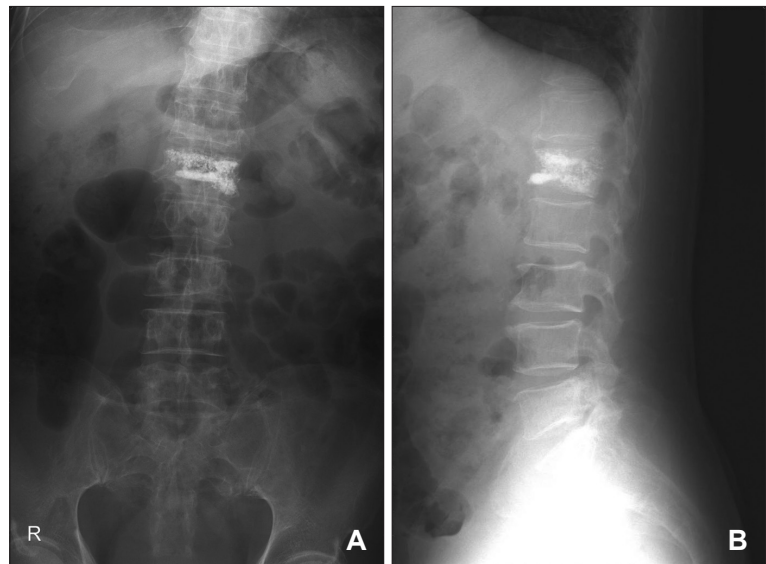
ter of the vertebral body. If the injected cement did not cross the midline, the same procedure was repeated through the contralateral pedicle. Patients were encouraged to ambulate 4 hours after the vertebroplasty.

**TABLE 1.** The demographics of the patients

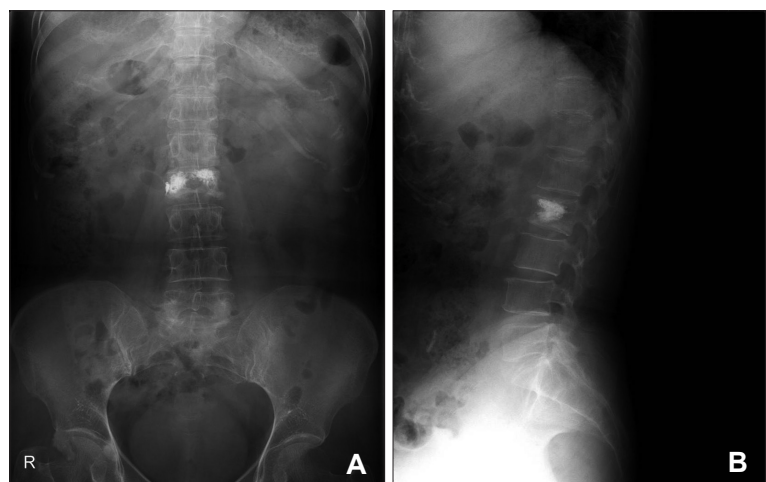
Number of cases (n)	
Sex	
Male	60
Female	52
Mean ages (years)	76.0 (range 61–92)
Level of initial compression fracture	
Thoracolumbar (T12-L2)	84
Above T12	12
Below L2	16
Total	112

### Comparison parameters

Age, sex, bone mineral density (BMD), location of treated vertebrae, pattern of cement distribution, volume of intravertebral cement, presence of intradiscal cement leakage, and direction of cement leakage were assessed in relation to subsequent vertebral fracture. Averaged T-scores from L1 to L4 were used for BMD assessment. Vertebral levels from T12 to L2 were classified as the thoracolumbar junction. The optimal volume of cement was is not clear. Therefore, in our study, we divided patients according to the volume of cement used: greater than or less than 3.5 cc. In cases in which a bipedicular approach was used, the volume of cement was calculated as the sum of both sides. According to the pattern of cement distribution, cases were divided into two groups as follows: cases in which the cement was evenly distributed in the vertebral body (Figure 1) and cases with a partially augmented vertebral body (Figure 2).



**FIGURE 1.** Postoperative anteroposterior (A) and lateral (B) plain X-ray show evenly distributed cement in vertebral body.



**FIGURE 2.** Postoperative anteroposterior (A) and lateral (B) plain X-ray show partially augmented cement in vertebral body.

Incidental fractures were designated as either adjacent or non-adjacent to the vertebral level being treated with vertebroplasty. Subsequent fractures were also classified as adjacent or non-adjacent. Refracture, additional compression at vertebroplasty level, was not assessed in our study due to ambiguity between continued decrease in vertebral height and an additional VCF.

### Statistical analysis

All statistical analyses were performed using SPSS ver. 10.0 (SPSS Inc., Chicago, IL). Correlation analysis (Pearson) and Fisher's exact test were used for statistical analysis. A *p*-value of less than 0.05 was considered statistically significant.

## Results

The mean age of patients was 76.0 years (range, 61–92 years). There were 60 men and 52 women. No major complications occurred during the procedure. The mean follow-up period was 15.4 months (range, 6–48 months). Eighteen subsequent fractures occurred during the follow-up period. Among them, 6 were adjacent VCFs and 12 were non-adjacent VCFs. The mean interval between the first fracture and an adjacent fracture was 10.8 months (range,

6–24 months), whereas the mean interval between a first fracture and a non-adjacent fracture was 16.5 months (range, 1–26 months). Thus, adjacent fractures tended to occur sooner than non-adjacent fractures, but non-adjacent fractures were more common. The relationship between subsequent VCFs and these factors is shown in Table 2.

### Sex

Our patients consisted of 60 men and 52 women. Subsequent fractures occurred in 7 men (11.7%) and 11 women (21.2%). Although subsequent fractures were more common in women, the difference was not statistically significant (*p*=0.135, 0.173, *r*=−0.133).

### Age

We classified patients according to age; 106 patients were aged 65 years and over, the other 6 less than 65 years. Seventeen subsequent fractures occurred in patients aged 65 years and over (16.0%) and 1 in a patient less than 65 years (16.7%). The difference was not statistically significant (*p*=0.660, 0.484, *r*=0.067).

### Bone mineral density

Eighty-five patients had T-scores below −2.5, and 27 had scores above −2.5. Seventeen subsequent fractures occurred

**TABLE 2.** The relation of factors and subsequent fractures after percutaneous vertebroplasty

	Subsequent fracture (n=18)	Non-subsequent fracture (n=94)	<i>p</i> -value (Fisher's exact test)	<i>p</i> -value (Pearson)	Correlation coefficient (r-value)
Sex			0.135	0.173	−0.133
Men	7	53			
Women	11	41			
Age			0.660	0.484	0.067
More than 65	17	89			
Less than 65	1	5			
BMD (mean T-score)			0.034	0.028	0.208
≤−2.5	17	68			
>−2.5	1	26			
Level of treated vertebrae			0.269	0.377	−0.084
Thoracolumbar (T12-L2)	12	72			
Above T12 or below L2	3	25			
Pattern of cement distribution			0.476	0.701	−0.037
Evenly distribution	14	69			
Partially augmentation	4	25			
Cement volume			0.012	0.014	0.238
More than 3.5 cc	15	49			
Less than 3.5 cc	3	45			
Intradiscal cement leakage			0.331	0.478	0.068
Presence	5	24			
Absence	13	88			

BMD: bone mineral density

in osteoporotic patients (20.0%) and 1 occurred in a non-osteoporotic patient (3.7%). Low BMD was significantly related to subsequent fracture after vertebroplasty ( $p=0.034$ ,  $r=0.208$ ).

#### Location of initial VCF

Initial VCFs occurred at the thoracolumbar region (T12-L2) in 84 patients, and 12 subsequent fractures were in this region (14.3%). Subsequent fractures occurred more frequently in lower lumbar vertebrae (21.4%), but the difference was not statistically significant ( $p=0.269$ ,  $0.377$ ,  $r=-0.084$ ).

#### Pattern of cement distribution

Cement was distributed evenly in 83 patients, and 14 subsequent fractures occurred in these patients (16.9%). The cement was partially augmented in the vertebral bodies of 29 patients, and 4 subsequent fractures developed in these patients (13.8%). The occurrence of subsequent fracture was not statistically different in these groups ( $p=0.476$ ,  $0.701$ ,  $r=-0.037$ ).

#### Cement volume

Of 48 patients in whom the cement volume was less than 3.5 cc, 3 (6.3%) developed subsequent fractures. Of 64 patients in whom the cement volume was greater than 3.5 cc, 15 (23.4%) developed subsequent fractures, a statistically significant difference ( $p=0.012$ ,  $0.014$ ,  $r=0.238$ ).

#### Cement leakage

Intradiscal cement leakage occurred in 24 patients (21.4%). Among them, 18 patients had cement leakage into the upper disc space, and 4 patients had leakage into the lower disc space. Subsequent fractures occurred in 5 patients in whom cement leakage occurred into the disc space. Subsequent fractures occurred more commonly in cases with intradiscal cement leakage (20.8% vs. 14.8%), but the difference was not statistically significant ( $p=0.331$ ,  $0.478$ ,  $r=0.068$ ).

## Discussion

Cement leakage after vertebroplasty is not uncommon, but most of the leakage is not clinically significant. Subsequent VCFs mean unexpected following new VCF after VCF, commonly occur after percutaneous vertebroplasty. Subsequent VCFs are classified as adjacent fracture, non-adjacent fracture, and refracture. The incidence of subsequent VCF is about 12% to 52%.<sup>1,3,12</sup> Subsequent VCFs may lead to continued back pain and severe kyphotic deformi-

ty. The relationship between vertebroplasty and subsequent fractures is still uncertain. Risk of new VCFs is greater in patients who undergo vertebroplasty/kypoplasty than in patients with prior VCFs who do not undergo the procedure.<sup>11</sup> However, it is difficult to draw strong conclusions about the causal relationship between vertebroplasty and subsequent fractures based on a review of the literature.<sup>9,18</sup>

Significant restoration of anterior vertebral height increases the risk of subsequent fracture in cemented vertebrae.<sup>5</sup> Subsequent VCFs occur more frequently and sooner in adjacent vertebrae than in nonadjacent vertebrae.<sup>6,17,18</sup> Our study also showed that adjacent fractures occurred sooner than non-adjacent fractures. In another study, adjacent fractures were more common than non-adjacent fractures,<sup>17</sup> however, this was not the case in our study.

The mechanisms of subsequent fractures varied. A direct pillar effect (a difference in strength) may provoke an adjacent fracture, and a dynamic hammer effect (a difference in segmental mobility) may lead to a non-adjacent fracture.<sup>11</sup> Ma et al.<sup>19</sup> performed an extensive review of the literature and stated that there are three strong risk factors for new VCFs: lower BMD, intradiscal cement leakage, and vertebral height restoration. Yoo et al.<sup>21</sup> confirmed that these three factors were related to new VCFs after vertebroplasty. Although another study did not find a correlation between recurrent fracture and BMD,<sup>19</sup> our study did find a significant correlation between lower BMD and subsequent fracture.

A thoracolumbar location of the initial VCF has been found to correlate with adjacent vertebral fracture.<sup>3,7</sup> However, in our study, a thoracolumbar location of the initial VCF was less commonly associated with subsequent fractures than was a thoracic or lumbar location.

Evenly distributed cement augmentation restores the biomechanical properties of vertebrae.<sup>15</sup> The distribution of cement augmentation, whether either even or focal, was not related to subsequent fracture in our study.

Cranial vertebrae are most likely to fracture at the adjacent level, whereas thoracic vertebrae are least likely to fracture at the adjacent level.<sup>7</sup> About one-fifth of osteoporotic women with VCF treated with vertebroplasty have a subsequent fracture within 1 year.<sup>16</sup> In our study, only one patient with a VCF at T11 developed an adjacent fracture (1/12, 8.33%).

Large fill volumes may not be the most biochemically optimal configuration and only a small amount of bone cement (3.5 cc or 14% of vertebral volume fraction) was necessary to restore stiffness to predamage levels.<sup>4</sup> Another study showed that approximately 3.5 cc of bone cement largely restored normal stress distribution in fractured and

adjacent vertebral bodies and that 7 cc of bone cement was required to restore motion segment stiffness and load-shearing between the vertebral bodies and neural arch.<sup>8)</sup> The other study showed that stiffness and strength are weakly correlated with the percentage fill volume of cement injected during vertebroplasty.<sup>10)</sup> Therefore, the standard intravertebral cement volume was determined to be 3.5 cc. Intravertebral cement volume of more than 3.5 cc of was significantly associated with subsequent fractures in our study.

Additional vertebroplasties for new fractures exert analgesic effects similar to those of the initial procedure. However, the second treatment for new adjacent fractures frequently causes more subsequent new fractures than those second treatment for non-adjacent fractures.<sup>20)</sup>

In cases involving adjacent fractures, lower body mass index and intradiscal cement leakage were significant predictive factors for fracture.<sup>1,22)</sup> The most important risk factors affecting new VCFs were osteoporosis and intervertebral discal cement leakage.<sup>12-14)</sup> In particular, large volumes ( $\geq 1$  cc) of intradiscal leakage should be avoided.<sup>13)</sup> However, the importance of intradiscal leakage in subsequent VCF is debatable.<sup>2,3)</sup> Our study showed no correlation between subsequent VCF and intradiscal leakage. No subsequent fractures occurred in cases where the cement leaked into the lower disc space, likely because a relatively smaller volume of cement leaked into the lower disc space than into the upper disc space.

The limitations of our study are that the follow-up periods were relatively short and that refractures were excluded.

## Conclusion

Low BMD and more than 3.5 cc of intravertebral cement volume were the factors most strongly associated with subsequent fractures after PVP. Therefore, patients with lower BMD and those in whom intravertebral cement volume exceeds 3.5 cc may need more careful follow-up after PVP.

■ The authors have no financial conflicts of interest.

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