Predictive factors for subsequent vertebral fracture after percutaneous vertebroplasty

YONG AHN, M.D., JUNE HO LEE, M.D., HO-YEON LEE, M.D., PH.D., SANG-HO LEE, M.D., PH.D., AND SANG-HYUN KEEM, M.D.

Department of Neurosurgery, Wooridul Spine Hospital, Seoul, Korea

Object. The purpose of this study was to evaluate the predictive factors for subsequent vertebral fracture occurring after percutaneous vertebroplasty (PVP) at the neighboring levels (adjacent vs nonadjacent levels).

Methods. The medical records of 508 consecutive patients treated with PVP between January 2000 and December 2002 were retrospectively reviewed. A total of 45 patients with 49 painful vertebral fractures occurring after PVP was identified based on clinical and radiological findings. New vertebral fractures, developing at any of the 3 consecutive vertebral bodies (VBs) above or below the previously treated level, were the focus of the study. The patients were divided into 3 groups: an adjacent-level fracture group, nonadjacent-level fracture group, and a control group composed of 50 randomly selected patients in whom there was no evidence of a new fracture. Clinical, imaging, and procedure-related factors for each group were statistically analyzed.

Results. In 31 patients 35 VBs were classified as adjacent-level fractures, and in 14 patients 14 VBs were classified as nonadjacent-level fractures. After further vertebroplasty, the overall pain intensity and satisfaction rate in patients with post-PVP fractures were similar to those in the control group. In cases involving adjacent fractures, lower body mass index and intradiscal cement leakage were the significant predictive factors of fracture. In contrast, lower mobility of the index segment was related to nonadjacent-level fracture.

Conclusions. According to the authors’ results, the mechanisms of subsequent fracture at adjacent and nonadjacent vertebrae are different. A direct pillar effect (that is, the difference in strength caused by cement augmentation) may provoke an adjacent-level fracture, whereas a dynamic hammer effect (the difference in segmental mobility) may lead to a nonadjacent fracture. (DOI: 10.3171/SPI/2008/9/8/129)

KEY WORDS • osteoporosis • predictive factor • surgery-related vertebral fracture • vertebroplasty

Percutaneous vertebroplasty has been regarded as an effective management option for various vertebral compression fractures, but the development of post-PVP vertebral fracture is a not uncommon sequela and an additional vertebroplasty is frequently required. The incidence of subsequent vertebral fracture has been regarded as an effective management option for various vertebral fractures, but the development of post-PVP vertebral fracture is a not uncommon sequela and an additional vertebroplasty is frequently required. The incidence of subsequent vertebral fracture varies from 12 to 52% according to the literature.10,17,25,28,29 It is uncertain whether the vertebroplasty itself is the cause of subsequent vertebral fractures. Although many authors have reported the condition as a new fracture after vertebroplasty, there are also studies explaining the risk of subsequent fracture as a natural phenomenon of the disease.1,18,19 Unfortunately, no valid study has been conducted to contend with this issue.27 To prevent or reduce the occurrence of fracture after PVP, knowledge of the risk factors for subsequent fracture is essential. It has been reported that adjacent vertebrae are the most common site of subsequent fractures (incidence 41–67%).5,12,28,29 Some biomechanical and clinical studies have demonstrated the mechanism and causative factors of adjacent-vertebral fracture.3,4,6 The authors of these studies have named the phenomenon the “pillar” effect or “stress-riser” effect and have attributed this phenomenon to intradiscal cement leakage or maximum filling of cement as the predictive factors. However, these are only procedure-related factors, and the patient’s constitution or spinal geometry has not been taken into consideration. Moreover, there was no adequate explanation regarding the mechanism, nor were the prediction rules set for nonadjacent neighboring-segment fracture after vertebroplasty.

Abbreviations used in this paper: BMD = bone mineral density; BMI = body mass index; PMMA = polymethylmethacrylate; PVP = percutaneous vertebroplasty; ROM = range of motion; SD = standard deviation; VAS = visual analog scale; VB = vertebral body.
The objective of this study was to evaluate the predictive factors for neighboring-segment fracture after vertebroplasty, taking into account each patient’s constitution, spinal geometry, and the procedure-related factors. We also tried to ascertain the possible mechanism of these subsequent fractures and to explain how the mechanism differed between adjacent and nonadjacent fractures.

**Methods**

**Study Design and Patient Selection**

We examined our computerized database to identify all patients who had undergone PVP at our hospital from January 2000 to December 2002. Acute or subacute osteoporotic vertebral compression fractures were the sole pathological entity, and cases involving traumatic fractures or malignancies were excluded from this study. The medical records of 508 consecutively treated patients were retrospectively reviewed. From the database, we selected cases in which the patients had undergone additional vertebroplasty to treat a painful vertebral fracture after initial PVP. The inclusion criteria for the new fracture were as follows: 1) relapse of pain after initial vertebroplasty, after an obvious pain-free interval; 2) evidence of new VB fracture on both MR imaging and radiography, occurring within any of the 3 consecutive VBs above or below the previously treated level; and 3) additional vertebroplasty required to relieve painful symptoms due to a subsequent fracture. Cases involving a painless, minor fracture and/or same-segment fracture were excluded from the study. The patients were divided into 3 groups: those with adjacent-level fractures (Fig. 1), those with nonadjacent-level fractures (Fig. 2), and those comprising a control group. We carefully reviewed the clinical and imaging records to rule out any evidence of vertebral fracture occurring after PVP during the follow-up period. There were 50 control patients randomly selected from a database of cases in which there was no evidence of subsequent vertebral fracture after initial PVP. The absence of subsequent vertebral fracture was defined in 2 ways: 1) no pain relapse after initial PVP and 2) no findings of subsequent fracture on follow-up radiographs. These findings were further confirmed by telephone interview or patient’s visit to the outpatient office.

**Procedural Detail**

The PVP was performed using the technique described by Jensen et al. The patient was placed prone on the radiolucent table. A fluoroscopically guided uni- or bilateral transpedicular approach was performed with an 11-gauge bone biopsy needle (Hyun Medical). The ideal needle placement was at the anterior third of the body. The PMMA (Simplex P; Stryker Howmedica) was mixed with barium sulfate powder (Biotrace, Bryan) and tobramycin. The mixed bone cement was injected by using 1-ml syringes under fluoroscopic guidance. The end point was when the cement reached the posterior quarter of the VB or when significant leakage occurred.

**Comparison Parameters**

Data regarding parameters such as age, sex, height, body weight, BMI, and BMD were obtained from clinical records. The BMI is calculated as weight in kilograms divided by the square of the height in meters (kg/m²); the lumbar spine bone density and the femur bone density were measured by dual-energy x-ray absorptiometry. Spinal geometric properties such as the location of the fracture, type of the fracture, local kyphosis, and sagittal-plane ROM were measured using preoperative radiographs (Fig. 3). Simple lateral radiographs with the patient in a neutral posture were performed to evaluate the spinal sagittal and coronal planes.

![Fig. 1. Radiographic and MR imaging examples of an adjacent-segment fracture after initial PVP in a 68-year-old woman with an L-2 vertebral compression fracture. A: Prevertebroplasty images showing L-2 compression fracture (white arrow). B: Radiograph acquired immediately after L-2 vertebroplasty showing intradiscal cement leakage (white arrow) with intact adjacent vertebrae. C: Images obtained 4 weeks after vertebroplasty (white arrow) demonstrating new compression fracture at L-1 (black arrow).](image-url)
position and during flexion and extension were available in all cases. Local kyphosis across the fractured vertebra was calculated using the Cobb angle measurement on standing lateral radiographs.\(^{20}\) Kyphosis was defined as the angle between the lines parallel to the superior endplate of the vertebra 1 level above the fractured vertebra and the inferior endplate of the vertebra 1 level below the fractured vertebra. The sagittal-plane ROM was measured on the flexion/extension lateral radiograph to evaluate segmental mobility. The adjacent ROM was defined as the sagittal-plane rotation angle between the fractured vertebra and adjacent vertebra, and the overall ROM was defined as the total sagittal rotation angle of the adjacent 4 contiguous intervertebral segments. In most patients, the upper and/or lower 4 consecutive segments were measurable as the longest vertebral segments from the index vertebra on the lateral radiographs. The mean relative mobility was defined as the ratio between the adjacent ROM and the overall ROM (adjacent ROM/overall ROM). Procedure-related parameters were also analyzed. Any cement leakage beyond the endplate and into the disc was checked on the immediate postoperative lateral radiograph. However, contact of the injected cement with either VB endplate was not regarded as intradiscal leakage. The volume of PMMA injected into the treated segment and the bilaterality of approach were also documented.

Outcome Evaluation

Pain intensity was rated using a 10-point VAS. Satisfaction rate was also assessed at the final follow-up. Each patient was asked the following question: “What is your level of satisfaction regarding the surgical procedure performed?” The patient could choose between 3 different assessments of satisfaction: very satisfied, moderately satisfied, or not satisfied. The overall satisfaction rate included patients who were very satisfied or moderately satisfied. Analysis of variance, the Kruskal–Wallis test, and the chi-square test were used to compare the study groups. Data were presented as the mean ± SD. A binary logistic regression analysis was then used to determine if the individual factors were independently associated with the subsequent vertebral fracture. The level of statistical significance was \(p < 0.05\).

Results

Demographics and Clinical Outcome

There were 50 patients (55 vertebrae) in the control group in whom there was no evidence of subsequent vertebral fracture, whereas there were 31 patients with 35 affected vertebrae in the adjacent fracture group and 14 patients with 14 affected vertebrae in the nonadjacent fracture group. Of the 49 new VB fractures, 35 (71.4\%) developed at the adjacent level. The mean ages of patients in the control, adjacent fracture, and nonadjacent fracture groups were 69.6, 69.5, and 69.1 years, respectively. The mean VAS score decreased from 7.3 to 3.8 in the control group, from 7.8 to 3.5 in the adjacent fracture group, and from 8.9 to 3.2 in the nonadjacent fracture group. The overall satisfaction rate in each group was 88, 83.9, and 85.7\%, respectively. No statistically significant differences were found in age, sex, preoperative and final VAS, or the overall satisfaction rate among the groups (Table 1).

Constitutional Factors

Among the constitutional factors, the mean BMI and the mean body weight were highest in patients with nonadjacent-level fractures, followed by those in the control group; they were lowest in patients with adjacent-level fractures.
In particular, the mean BMI of patients in the adjacent fracture group was 22.3 kg/m², which was significantly lower than those in the other groups (p < 0.05). On the other hand, the mean body weight of patients in the nonadjacent fracture group was 60 kg, significantly higher than that in the other groups (p < 0.05). However, the BMDs were not significantly different among the groups. The mean spinal BMD (T- and Z-scores) calculated in the adjacent fracture group was relatively lower and that in the nonadjacent fracture group was higher than that in the control group, but the difference was not statistically significant (Table 2).

### Spinal Geometry

As for the spinal geometry, the degree of local kyphosis and the level of the fracture was not different among the groups, although the degree of local kyphosis in the adjacent-level fracture group was somewhat higher than that in the other groups. The incidence of fracture occurrence at the thoracolumbar junction (T11–L2) tended to be higher both in the nonadjacent fracture group (71.4%) and the adjacent fracture group (67.6%) compared with the control group (59.4%), but the difference was not significant. The mean adjacent ROM in the nonadjacent fracture group (1.9°) tended to be lower than that in the adjacent fracture group (3.5°) or the control group (3.6°), but the difference was not significant (p = 0.22). However, the mean relative mobility in the nonadjacent fracture group (0.2) was significantly lower than that in the adjacent fracture (0.4) or of the control (0.6) group (p = 0.027) (Table 3).

**TABLE 1**

Demographic and clinical data obtained in patients who underwent PVP and sustained an adjacent-segment or remote-segment fracture*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group</th>
<th>Adjacent</th>
<th>Nonadjacent</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>50</td>
<td>31</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>no. of vertebrae</td>
<td>55</td>
<td>35</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>mean age (yrs)</td>
<td>69.6</td>
<td>69.5</td>
<td>69.1</td>
<td>0.949†</td>
</tr>
<tr>
<td>M/F ratio</td>
<td>4:46</td>
<td>5:26</td>
<td>2:12</td>
<td>0.430‡</td>
</tr>
<tr>
<td>mean VAS pain score</td>
<td>7.3 ± 2.1</td>
<td>7.8 ± 2</td>
<td>8.9 ± 1.1</td>
<td>0.1†</td>
</tr>
<tr>
<td>preop</td>
<td>3.8 ± 1.9</td>
<td>3.5 ± 1.8</td>
<td>3.2 ± 0.9</td>
<td>0.521†</td>
</tr>
<tr>
<td>postop</td>
<td>88</td>
<td>83.9</td>
<td>85.7</td>
<td>0.918‡</td>
</tr>
<tr>
<td>overall satisfaction rate (%)</td>
<td>9</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>very satisfied</td>
<td>35</td>
<td>22</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>mod satisfied</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

* mod = moderately.
† Comparison made using analysis of variance (ANOVA).
‡ Comparison made using the chi-square test.
§ Mean values are presented ± SD.
Subsequent fracture after vertebroplasty

**TABLE 2**
Comparison of groups by constitutional factors*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group</th>
<th>Adjacent</th>
<th>Nonadjacent</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>spinal BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-score</td>
<td>−3.2 ± 1.0</td>
<td>−3.3 ± 1.1</td>
<td>−2.9 ± 1.2</td>
<td>0.504</td>
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<tr>
<td>Z-score</td>
<td>−1.1 ± 0.9</td>
<td>−1.4 ± 1.0</td>
<td>−0.9 ± 1.0</td>
<td>0.234</td>
</tr>
<tr>
<td>femur BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-score</td>
<td>−3.5 ± 0.9</td>
<td>−3.4 ± 1.1</td>
<td>−3.4 ± 0.8</td>
<td>0.877</td>
</tr>
<tr>
<td>Z-score</td>
<td>−1.5 ± 0.9</td>
<td>−1.4 ± 1.0</td>
<td>−1.3 ± 0.7</td>
<td>0.786</td>
</tr>
<tr>
<td>weight (kg)</td>
<td>54.9 ± 8.5</td>
<td>52.5 ± 7.5</td>
<td>60.1 ± 10.7</td>
<td>0.021</td>
</tr>
<tr>
<td>height (cm)</td>
<td>151.6 ± 7.5</td>
<td>153.3 ± 7.9</td>
<td>156.2 ± 8.3</td>
<td>0.145</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.8 ± 3.1</td>
<td>22.3 ± 2.6</td>
<td>24.6 ± 3.3</td>
<td>0.023</td>
</tr>
</tbody>
</table>

* Values are presented as mean ± SD, where appropriate.
† Comparison made using ANOVA.

**Procedures-Related Factors**

As for the procedure-related factors, the mean volume of PMMA injected per VB in the adjacent fracture group (6.4 ml) was larger than that in the nonadjacent fracture group (5.1 ml) or control group (5.8 ml), but the variation was not significant (p = 0.96). However, intradiscal PMMA leakage was strongly related to the development of an adjacent-segment fracture. The rate of intradiscal cement leakage in the adjacent fracture group was 54.3%, which was significantly higher than that in the other groups (21.4 and 20.8% for the nonadjacent and control groups, respectively) (p = 0.004) (Table 4). The method of approach (bi- or unilateral) showed no significant intergroup difference.

**Multivariate Analysis for Subsequent Vertebral Fracture**

In patients with an adjacent-level fracture, both lower BMI (p = 0.013) and presence of intradiscal cement leakage (p = 0.002) were significant. In patients with a nonadjacent-segment fracture, relative mobility (p = 0.024) was the most important predictive factor. After multivariate analysis, a higher body weight (p = 0.728) was not significantly associated with a nonadjacent-level fracture.

**Discussion**

For patients with a painful osteoporotic compression fracture, vertebroplasty is widely accepted as a minimally invasive treatment modality, but an unexpected subsequent or additional postoperative fracture may ensue and require further interventions. The causal relationship between the procedure and the subsequent fracture is unclear, and there are 2 issues that remain debatable. The first question is whether the vertebroplasty itself causes subsequent fractures. Some authors have explained the occurrence of a subsequent fracture as a progression of the underlying disease, where others have suggested that the cement augmentation and increased physical activity after vertebroplasty may have played a role. However, the adjacent vertebra is regarded as the most common site where a subsequent fracture develops. However, there is no predictive rule for the nonadjacent vertebral fracture. Both of these issues, especially the latter, had to be thoroughly addressed in the current study, and therefore we evaluated the risk factors for the nonadjacent fracture group as well as for the adjacent fracture group.

In general, it has been believed that the patients with a low BMI and low body weight are at higher risk of recurrent fracture of the spine or the hip, but there have been few reports on the effect of constitutional factors on the development of subsequent spinal fracture after vertebroplasty. As the result of univariate analysis in our study, BMI and body weight were found to be the major constitutional factors affecting postprocedural vertebral fracture. Slenderly built patients with osteoporotic bone and lower BMI ran the risk of sustaining an adjacent-level fracture after vertebroplasty, whereas relatively heavier patients with osteoporotic bone ran the risk of sustaining a nonadjacent-level fracture. The multivariate analysis demonstrated that the adjacent-segment fracture was closely related to lower BMI, whereas the nonadjacent-level fracture was not related to any constitutional factors. This finding suggests that the mechanism of the subsequent fracture might be different according to contiguous or noncontiguous relationship of the lesion to the initially treated level. The reason for this phenomenon is unclear. We postulate that lower BMI may be associated with weaker vertebra, which is then subject to the direct pillar effect of adjacent vertebral augmentation.

The degree of osteoporosis may be a potential predictor for subsequent fracture, but there was no intergroup difference in the mean BMD in our study population. The BMD may be affected by degenerative changes or...
osteoarthropathy. Thus, when the weak vertebra is associated with spinal degenerative osteoarthropathy, a high BMD does not necessarily indicate stronger bones, and the risk of vertebral fracture is not diminished. Shiraki et al. have reported that BMD was significantly related to BMI, and the incidence of vertebral fracture was negatively correlated with BMI in elderly women. According to our results, we also postulate that BMI is a better indicator of subsequent vertebral fracture than BMD. In our study, the characteristics of segmental mobility differed among the groups. The mean relative mobility of the adjacent segment was significantly lower in patients with nonadjacent-level fractures. In other words, if the adjacent segment is relatively rigid, the possibility of subsequent fracture is higher for a remote segment than it is for the adjacent segment. When the adjacent segment is relatively rigid or less mobile, the axial loading from daily activities of living or the effect of cement augmentation may affect the more mobile remote segment. The higher mobility gradient may produce a hammerlike effect on the remote vertebra, causing a subsequent fracture. We postulate that increased physical activity after the vertebroplasty may promote this phenomenon.

Besides segmental mobility, another possible geometrical factor is local kyphosis. Theoretically, kyphotic alignment may exaggerate the hammer effect, causing a subsequent fracture, but in our study the degree of local kyphosis or the level of the vertebra was not significantly related to the subsequent fracture.

Over the past few years, many convincing studies have been undertaken on the subject of cement volume and cement leakage. In previous studies the authors have reported that intradiscal cement leakage might increase the stress to the adjacent vertebra and cause a new fracture. These findings concur with results of our current study, because we also found that intradiscal PMMA leakage during the initial vertebroplasty was the main cause of adjacent-level fracture. As for the injected cement volume, theoretically, maximum filling with a large amount of cement may increase the stress to the adjacent vertebra and occasionally may cause a subsequent fracture. There is some controversy about this theory according to various centers of research. Many authors have commented on this phenomenon. Others, however, have reported that the cement volume was not related to the outcome. In our series, the volume of PMMA was not significantly related to a subsequent vertebral fracture.

In summary, the significant predictive factors for the post-PVP development of adjacent-level fracture were lower BMI and the presence of intradiscal cement leakage. The factor associated with subsequent nonadjacent-level fracture was lower mobility of the index segment causing a mobility gradient. Based on the present results, we postulate that the mechanisms of subsequent fracture are different for adjacent- and nonadjacent-segment fracture conditions. The mechanism for adjacent fractures can be explained by the direct pillar effect (Fig. 4). Cement augmentation of a very weak bone with intradiscal PMMA leakage may increase the strength gradient, leading to an adjacent fracture. In contrast, the mechanism of a nonadjacent fracture can be explained by the dynamic hammer effect (Fig. 5). If the adjacent segment is already rigid, the pillar effect is not prominent through the adjacent segment. In that case, the augmentation strength may affect a mobile remote segment. The mobility gradient between a rigid adjacent segment and a relatively mobile remote segment may cause a subsequent fracture.

There may be some contradictory factors, because our...
study was performed retrospectively. Moreover, the study included only patients who underwent repeated intervention, not those patients with subsequent fracture only treated with conservative management. Therefore, the true prevalence of subsequent fracture could not be calculated. However, our study also has considerable validity. The patients of each study group were compared under strict inclusion criteria, and the cases were selected from a relatively large patient population (508 consecutive patients). In our study, postoperative factors such as the type of medical treatment or the level of physical activity after the procedure were not considered. Increased physical activity after the vertebroplasty may cause subsequent fractures. However, we mainly focused on preoperative or procedure-related factors in our study. The risk of postoperative activity-related subsequent fracture may be one of the interesting issues for future studies to consider. Finally, there is a further question that needs to be addressed. The consistency of the injected cement material may be important. Baroud et al. have suggested that the use of softer cement material may be helpful in preventing a subsequent vertebral fracture. However, we could not evaluate the effect of cement softness because the same kind of bone cement was used in all the patients. We believe it will be very important for a future study to examine the effects of bone cements with varying strength and hardness.

Conclusions

The risk factors and mechanisms of subsequent fracture at adjacent and nonadjacent vertebrae are different. A strength gradient caused by bone cement augmentation may provoke a subsequent adjacent fracture (direct pillar effect), whereas a mobility gradient between neighboring segments may cause a subsequent nonadjacent fracture (dynamic hammer effect).

Acknowledgments

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Address correspondence to: Yong Ahn, M.D., Department of Neurosurgery, Wooridul Spine Hospital, 47-4 Chungdam-dong, Gangnam-gu, Seoul 135-100, South Korea. email: ns-ay@hanmail.net.