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#### Clinical Article

# Clinical Outcomes after Percutaneous Vertebroplasty for Pathologic Compression Fractures in Osteolytic Metastatic Spinal Disease

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**Objective**: Percutaneous vertebroplasty (VP) can provide immediate stabilization in pathologic fractures of spinal tumors. However, long term follow-up data in cases of pathologic fractures are lacking. The authors report follow-up results of VP in 185 pathologic fractures of 102 spinal tumor patients.

**Methods**: Percutaneous VP was performed at 185 vertebral bodies of 102 patients from 2001 to 2007. Retrospective analysis was done with medical records and radiological data. The change of visual analogue score (VAS), vertebral body (VB) height and kyphotic angle were measured preoperatively and on postoperative one day and at 3, 6, and 12 months.

**Results** : The patients were composed of metastatic spine tumors (81%) and multiple myeloma (19%). Involved spinal segments were between T6 and L5. Mean follow-up period was 12.2 months. VAS for back pain was 8.24 preoperatively, 3.59 (postoperative one day), 4.08 (three months) and 5.22 (one year). VB compression ratio changed from 21.33% preoperatively to 13.82% (postoperative one day), 14.36% (three month), and 16.04% (one year). Kyphotic angle changed from 15.35° preoperatively to 12.03° (postoperative one day), 13.64° (three month), and 15.61° (one year).

**Conclusion :** Immediate pain relief was definite after VP in pathologic compression fracture of osteolytic spinal disease. Although VAS was slightly increased on one year follow-up, VP effect was maintained without significant change. These results indicate that VP could be a safe and effective procedure as a palliative treatment of the spinal tumor patients.

KEY WORDS : Vertebral compression fractures · Percutaneous vertebroplasty · Spinal metastasis · Multiple myeloma.

# INTRODUCTION

Vertebroplasty (VP) with polymethylmethacrylate (PM-MA) was first introduced as a technique for the treatment of vertebral hemangiomas in 1987<sup>7</sup>). Since that time, it has become a valuable therapeutic option in the management of axial back pain caused by osteoporotic fractures, metastasis and multiple myeloma<sup>2,3,5,11,12,18</sup>.

Destructive vertebral lesions are a common source of morbidity in patients with metastatic disease and multiple myeloma. Vertebral compression fractures cause considerable morbidity including back pain, decreased mobility, neurological complications, kyphoscoliosis, and risk of adjacent fractures. The resulting spinal deformity can lead to decreased lung capacity, reduced physical and social functioning, depression, a loss of independence, and malnutrition caused by early satiety<sup>19)</sup>. Therefore, compression fractures that cause severe back pain have a number of deleterious effects on the patient and may lead to impairment of functioning and decline of quality of life.

In metastatic spine tumors, the primary treatment is radiation therapy (RT). RT provides local tumor control, significant pain relief, but limited spinal stabilization. However, in cases of spinal pathologic compression fractures, immediate spinal stabilization is required. Non-operative treatments including bed rest and external orthotics can partially stabilize the weakened spinal column. VP can be performed as a complement to radiotherapy to provide immediate vertebral stabilization. It is a minimally invasive percutaneous procedure that is performed with the patient under light sedation and local anesthesia<sup>6,12)</sup>. Only a few studies report on the long-term outcome of VP in the treatment of meta-

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static lesions of the spine. The objective of this study was to assess the efficacy and the long-term outcome of VP in the treatment of painful compression fractures in spinal tumor patients.

# MATERIALS AND METHODS

# **Patient population**

A retrospective analysis was done on 102 patients with vertebral compression fractures because of metastatic tumors (83 patients) or hematological malignancies (19 patients). These patients underwent VP at 185 different levels in the Korea Cancer Center Hospital between March 2001 and November 2007. There were 60 men and 42 women, whose median age was 55 years (range 22-82 years). All patients underwent plain radiography and most of them MR imaging of the spine. In some cases, CT scanning and radionucleotide bone scanning were checked instead of MRI.

Indications for VP were; 1) pathologic compression fractures of bone metastasis or hematological malignancies on imaging, 2) back pain without neurological deficit, and 3) intractable pain unresponsive to conservative treatment (consisting of analgesic medication, bed rest, and in some cases external brace therapy).

Contraindications include; 1) epidural compression of the neural elements; failure to localize symptomatic level; 2) significant medical contraindications such as uncorrected coagulopathy, 3) local infection at the planned injection site, and 4) intolerance to being positioned prone.

The pain score, vertebral body (VB) height and kyphotic angle were analyzed preoperative, postoperatively and at 3, 6, and 12 months. The visual analog scale (VAS) was used to measure pain status. The VAS ranged from 0 to 10, with 0 for no pain and 10 for intolerable pain.

We also compared three parameters between VP plus RT group and non-RT group. Comparison was made between total patients group with multiple myeloma patients group.

#### **Operative technique**

Vertebroplasty was performed under fluoroscopic guidance (C-arm) in the neurointerventional angiography suite or in the operation rooms. The procedure was usually performed after the injection of a local anesthetic or epidural anesthesia. The needle entry site was localized over the pedicle in the anteroposterior plane. Unilateral transpedicular approach was used in most of patients. In cases in which pedicles were not visualized on fluoroscopy because of tumor involvement, the extrapedicular approach was performed. The needle tip was positioned as near to anterior margin of vertebral body as possible. Venogram was not performed. The cement injection process was monitored continuously under fluoroscopic control in the lateral plane. The injection was stopped when the PMMA reached the posterior margin of the vertebral body. If the PMMA did not pass the midline to other side of the vertebral body, a second puncture was done from the other pedicle.

# Assessment of restored height and kyphosis correction by vertebroplasty

Loss of VB height and degree of kyphosis were measured on lateral radiographs by calipers in the digital system. Anterior height and posterior height were measured in the fractured VB. Compression ratio of the fractured VB was recorded as a percentage of subtraction anterior VB height from posterior VB height and posterior VB height of the fractured VB. Kyphotic angle was obtained by connecting the intersections of the VB diagonals between the inferior endplate of the vertebra above the fractured VB and the superior endplate of the vertebra below the fractured VB<sup>9</sup> (Fig. 1).

## Statistical analysis

The statistical analysis was performed on a personal computer running commercially available software (version 12.0 for Windows; SPSS, Inc., Chicago, IL, USA). A probability



**Fig. 1.** Assessment of sagittal alignment, VB compression ratio=(B-A)/B×100. Kyphotic angle=C (modified Cobb method).

Table '	1. '	Tumor	type
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Primary malignancy	No. of cases
Breast	24
Multiple myeloma	19
Lung	16
Liver	10
Rectum	6
Unknown origin	5
stomach	4
Colon	4
Cervix	2
Others	12
Total	102

value of 0.05 or less was considered significant. Values are given as mean±standard deviation.

# RESULTS

#### Patient characteristics

The most common primary tumor type was breast cancer (24 out of 102; Table 1). The fractures occurred between T6 and L5. The fracture distribution was shown in Fig. 2. The most commonly involved levels are between T12 and L5. Fifty-nine patients (58%) had undergone spinal radio-therapy. The length of follow-up review was calculated from the date of procedure to the most recent clinic visit or death (Fig. 3). Mean follow-up period was 12.2 months (range 1-82 months).

## VAS change

The numbers of patients available for VAS evaluation at each follow-up interval were 102 at one day, 78 (76%) at 3 months, 49 (48%) at 6 months and 44 (43%) at one year. The preoperative VAS was 8.24±0.81, and it was reduced

to  $3.59\pm1.46$  at postoperative one day (*p*=0.0001) (Fig. 4). All patients exhibited excellent improvement of pain within the first 24 hours. On follow-up, VAS increased slightly to  $4.08\pm1.92$  at postoperative 3 months and to  $5.22\pm2.6$  at postoperative one year (*p*=0.0001).

# Compression ratio and kyphotic angle change

The numbers of patients available for radiographic evaluation at each follow-up interval were 63 (62%) at one day; 36 (35%) at 3 months; 30 (29%) at 6 months; and 23 (23%) at one year. The preoperative mean compression ratio was 21.33±16.35%, and it decreased to 13.82±12.16% at one day after surgery. At 3 months, 6 months, and one year follow-up, it was 14.36±11.57%, 15.96±10.72%, and 16.04±10.82 respectively.

There was significant difference between preoperative compression ratio and postoperative compression ratio at one day, 3 months, and 6 months (p<0.05) (Fig. 5). However, there was no statistical difference between preoperative compression ratio and postoperative compression ratio at one year.

The preoperative mean kyphotic angle was  $15.35\pm10.03^{\circ}$  (range 5-25°), and was corrected to  $12.03\pm9.86^{\circ}$  (range 2-22°) at postoperative one day. At 3 months, 6 months, it was  $13.64\pm10.85^{\circ}$  (range 3-24°) and  $14.16\pm11.10^{\circ}$  (range 3-25°), respectively. There was significant statistical difference between preoperative kyphotic angle and postoperative kyphotic angle at one day, 3 months, 6 months, and 1 year (*p*<0.05)(Fig. 6).







Fig. 3. Preoperative magnetic resonance (MR) image scan and serial radiographs in a 48-year-old woman treated with vertebroplasty (VP) suffering from metastasis of breast cancer (L3, 4, 5). A : Preoperative sagittal non-enhanced MR image of a L4 compression fracture with L3, 4, 5 metastasis. B : Preoperative lateral X-ray; 10% of L4 vertebral body (VB) compression ratio and 23° of kyphotic angle (VAS : 9). C : Postoperative one day X-ray; 6% of L4 VB compression ratio and 18° of kyphotic angle (VAS : 2). D : Postoperative 3 months X-ray; 11% of L4 VB compression ratio and 19° of kyphotic angle (VAS : 3). E : Postoperative 6 months X-ray; 18% of L4 VB compression ratio, 24° of kyphotic angle and new L2 VB compression fracture (VAS : 7). F : Postoperative one year X-ray (VAS : 2). VAS : visual analogue score.

# RT group vs. non-RT group

Fifty-nine patients (58%) among 102 patients who underwent VP received spinal RT. A comparison between RT group and non-RT group was presented in Fig. 7. Preoperative VAS was 8.13±0.84 in RT group and 8.37±0.75



**Fig. 4.** Visual analog scale (VAS) change (pre- vertebroplasty (VP) and post-VP). Data are expressed as mean±standard deviation. The differences between the VAS scores prior to VP and at one day, 3, 6, and 12 months are statistically significant, respectively (p=0.0001). \*p<0.05 in comparison to preoperatively. n : number of follow-up patients.



**Fig. 5.** Changes of vertebral body compression ratio after vertebroplasty. Data are expressed as mean±standard deviation. The differences between vertebral body compression ratio prior to vertebroplasty and at one day, 3, and 6 months are statistically significant (at one day, 3 months p=0.0001, at 6 months p=0.036, at one year p=0.303). \*p<0.05 in comparison to preoperatively. n : number of follow-up patients.



**Fig. 6.** Changes of kyphotic angle after vertebroplasty. Data are expressed as mean±standard deviation. The differences between vertebral body compression ratio prior to vertebroplasty and at one day, 3, 6, and 12 months are statistically significant (at one day, 3, 6 months p=0.0001, at one year p=0.044). \*p<0.05 in comparison to preoperatively. n : number of follow-up patients.

in non-RT group. Postoperatively, both groups of patients experienced significant reduction in pain; the median VAS decreased to 3 in both groups. The differences between preoperative VAS and postoperative VAS at one day, 3 months, 6 months, and one year were statistically significant in both groups, respectively (p < 0.05). VAS was shown a little lower in RT group than in non-RT group on one year follow-up. However, there were no significant difference between RT group and non-RT group (p>0.05). In RT group, the preoperative mean compression ratio was 22.58±17.17%, and it was decreased to 15.41±15.07% at one day after VP (p < 0.05). At 3 months, 6 months follow-up, it was  $15.94 \pm$ 14.59%, 17.17±3.38%, respectively (p<0.05). In non-RT group, the preoperative mean compression ratio was 21.28± 16.82%, and it was decreased to 13.40±10.53% at one day after VP (p < 0.05). At 3 months, 6 months, and one year follow-up, it was 14.61±10.86%, 16.64±9.15%, and 16.18 $\pm$ 9.62%. respectively (p>0.05). In RT group, the



**Fig. 7.** Change of visual analog scale, vertebral body (VB) compression ratio, and kyphotic angle after vertebroplasty (VP) between RT group and non-RT group. There was no statistical difference between RT and non-RT, RT : radiation therapy. A : Change of pain score after VP, B : Change of VB compression ratio after VP, C : Change of kyphotic angle after VP. n : number of follow-up patients (RT/non-RT).





**Fig. 8.** Change of visual analog scale after vertebroplasty (total patients vs. multiple myeloma). n=number of follow-up patients (total group/ multiple myeloma).

preoperative mean kyphotic angle was  $15.77\pm10.19^{\circ}$ , and was corrected to  $12.21\pm9.40^{\circ}$  at one day after VP (p<0.05). At 3 months, 6 months, angle was  $12.97\pm9.94^{\circ}$ ,  $13.66\pm10.03^{\circ}$ , respectively (p<0.05). In non-RT group, the preoperative mean kyphotic angle was  $14.95\pm10.01^{\circ}$ , and was corrected to  $11.87\pm10.44^{\circ}$  at one day after VP (p>0.05). At 3 months, 6 months, and one year angle was  $13.78\pm11.97^{\circ}$ ,  $14.08\pm12.57^{\circ}$ , and  $16.75\pm15.31^{\circ}$ , respectively (p>0.05). When the change of compression ratio and kyphotic angle in RT group was compared with those of non-RT group, there was no significant difference between them.

## Multiple myeloma

In multiple myeloma patients (n=19), the preoperative VAS was  $8\pm0.86$ , and it was reduced to  $3.23\pm1.09$  at postoperative one day (p<0.05)(Fig. 8). In the one year follow-up, VAS increased slightly to  $3.53\pm1.33$  at 3 months postoperatively and to  $5.07\pm2.36$  at one year (p<0.05). When the change of VAS in multiple myeloma patients was compared to that of total patients, the trend of change was similar. However, VAS of multiple myeloma patients was slightly lower than that of total group at each corresponding time point. There was no statistical difference between preoperative compression ratio, kyphotic angle and postoperative compression ratio, kyphotic angle at 3 months, 6 months, and 1 year (p>0.05).

## Complication

Leakage of cement outside of the vertebral body was noted in 32 of 185 injected vertebrae (17%). Leaks were in the epidural space (13 cases), in the adjacent disks (13 cases) and in the venous plexus (6 cases). But, none of the patients developed any clinical or neurological symptoms. No other complications were observed with the procedure.

# DISCUSSION

Compression fractures caused by metastases and myeloma

often result in intractable back pain in these patients. The presence of a pathologic fracture secondary to vertebral destruction, or the development of spinal instability from such a fracture, may be the origin of pain. The release of chemical mediators, the increased pressure within the bone, microfractures, the stretching of periosteum, reactive muscle spasm, nerve root infiltration and compression of nerves by the collapse of vertebrae are the possible mechanisms of malignant bone pain<sup>13,20</sup>.

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Non-operative treatments for painful spinal metastasis consist of bed rest, external bracing, RT and analgesics. RT provides an effective symptomatic treatment for local bone pain. Tumor shrinkage and inhibition of the release of chemical pain mediators are the main mechanisms by which RT probably acts. The analgesic effect of RT can be complete or almost complete in 70% of cases. However, RT does not correct spinal instability, and its efficacy is delayed. Symptomatic relief from RT generally requires 4-12 weeks and may be related to reossification. Unlike the delayed effects of RT, VP provides immediate strengthening of the anterior column, which may limit painful VB fracture<sup>8,10,14,16,17</sup>.

Various theories have been suggested on pain relief effect after VP. It is likely that a component of the VP-related analgesia is secondary to immobilization of microfractures and reduction of mechanical forces<sup>3)</sup>. The destruction of nerve endings caused by the cytotoxic, mechanical, and vascular effects of PMMA as well as the thermal effects of polymerization, however, may also play a role in pain relief<sup>3,4,20)</sup>. Furthermore, it has been proposed that PMMA has an antitumoral effect, which may explain the rarity of local recurrence after VP. This effect may be the result of the cytotoxicity, thermal effects, and ischemia produced by PMMA<sup>4,20)</sup>.

In other studies of VP in metastatic spinal disease, Cortet et al.<sup>1)</sup> performed VP in 37 patients, 29 with metastases and 8 with multiple myeloma. They have reported a decrease in pain within 48 hours of VP in 97% of their 37 patients with osteolytic metastases or multiple myeloma; pain was completely absent in 13.5%, significantly reduced in 55%, and moderately reduced in 30%. Beneficial effects were seen in 89% at 3 months and 75% after 6 months. Their complication rate was 2 to 3%.

Fourney et al.<sup>5)</sup> reported on the treatment of tumorous lesions with VP and kyphoplasty in patients undergoing 65 vertebroplasties and 32 balloon kyphoplasties. They have reported complete pain relief after 49 procedures (84%), and no change after five procedures (9%). The median preand postoperative VAS scores were 7 and 2, respectively (p<0.001). Pain reduction remained significant at each follow-up interval through one year (p=0.02). The mean percentage of restored vertebral body height was 42±21%. Mean improvement in local kyphosis was 4.1±3.72°.

Pflugmacher et al.<sup>15)</sup> reported on the treatment of 31 patients with 64 balloon kyphoplasty procedures in pathologic VB fractures. The median pain scores (VAS) decreased significantly (p<0.05) from pre- (8.8) to post-treatment (3.1). During one year follow-up, balloon kyphoplasty stabilized vertebral height and prevented further kyphotic deformity. These results are in concordance with our result, which demonstrated significant change of VAS after VP.

Pain relief is believed to be the result of stabilizing the fracture with PMMA. All patients had significant improvement in VAS score. In our study, at one year follow-up, we noticed a slight increase VAS from 4.08 at 3 months postoperatively to 5.22 at one year. The increase of VAS in the one year follow-up may be due to disease progression. We also observed statistically significant improvements in height restoration as measured by vertebral body compression ratio. Similarly, the kyphotic deformity significantly improved. The mean volume of injected PMMA was 3.63 cm<sup>3</sup> (range 1-5 cm<sup>3</sup>). The VAS did not correlate with the amount of injected cement. With regard to the effect of RT, VAS was shown a little lower in RT group than in non-RT group on follow up at one year. Although not statistically significant, RT further decreased pain during one year follow-up. This finding indicates that RT provides additional stabilization of fractured vertebral body and resultant pain relief is maintained on long term follow-up.

# CONCLUSION

VP is an effective, minimally invasive procedure for the stabilization of pathological vertebral fractures caused by osteolytic lesions of vertebral bodies. Although more data are needed to evaluate the use of VP for the treatment of malignant compression fractures, the evidence is compelling that VP can be used safely in the treatment of metastatic lesions of the VB in patients who were previously considered poor surgical candidates because of limited life expectancy. Although pain relief on one year follow-up was not as good as on immediate follow-up, VP effect was shown to be somewhat maintained. Our results indicate that VP could be a safe and effective procedure as a palliative treatment of the spinal tumor patients.

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