

## Clinical Article

# Enhancing Box Sign : Enhancement Pattern of Acute Osteoporotic Compression Fracture

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**Objective** : Although gadolinium enhancement of compression fractures is well known, the enhancement pattern of the acute stage of a fracture is not completely understood. Here, we investigated the enhancement pattern of acute vertebral compression fractures (VCFs).

**Methods** : We conducted a retrospective study of patients with acute osteoporotic VCFs admitted to hospital between January 2004 and December 2005. The demographic details, stage of the fracture, management data, and results were analyzed. There were nine men and 22 women, and the mean age was 71 years (range, 53-92 years). According to the onset of pain, patients were divided into the following four groups : Group I (less than 3 days), Group II (4-7 days), Group III (8-14 days), and Group IV (14-30 days).

**Results** : All patients had central low-signal intensity of the nonenhancing part of vertebral bodies on T1 images. Enhancing box sign (EBS) was seen 7 days of VCF development. After 7 days of onset (Groups III and IV), patch or Kummell's enhancements occurred. EBS has been statistically correlated with stage of compression fracture (Pearson's correlation = -0.774). However, EBS had no statistically significant correlation with prognosis in our study (Pearson's correlation = 0.059).

**Conclusion** : EBS represents a characteristic sign 7 days of VCF development.

**KEY WORDS** : Compression fracture · Magnetic resonance imaging · Gadolinium.

## INTRODUCTION

Osteoporotic vertebral compression fracture (VCF) is a common clinical problem among elderly patients. Radiological studies report that the prevalence of VCF is 26% in women older than 50 years of age<sup>13,18</sup>. In addition, VCF is associated with pain, impaired physical performance, and a high mortality rate<sup>11,20</sup>.

It is important that acute VCF should be diagnosed and treated before the development of complications or mortality. Furthermore, the wide application of percutaneous vertebroplasty (VP) in the treatment of VCF emphasizes the importance of diagnosis. It is often difficult to determine the level of acute VCF in many patients with VCF,

and MRI is used widely for this purpose<sup>3</sup>. However, few studies on the enhancement patterns of acute VCF have been conducted, except for the differentiation of acute VCF from malignant compression fracture.

The purpose of this study was to investigate the enhancement patterns of acute VCF.

## MATERIALS AND METHODS

### Patient population

The authors conducted a retrospective study of patients with osteoporotic VCF admitted to hospital between January 2004 and December 2005.

The inclusion criteria were benign osteoporotic VCF in patients who underwent routine MRI and an enhancement study within one month of developing symptoms. Patients with severe trauma (e.g., because of a car accident) or other etiology were excluded from the study. MRI was performed within 1-30 days (mean, 9 days) after onset of symptoms.

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Thirty-one patients were enrolled the inclusion criteria. There were nine men and 22 women, whose ages ranged from 53 to 92 years with a mean age of 71 years.

According to the onset of pain from MRI study, patients were divided into the following four groups : Group I (less than 3 days), Group II (4-7 days), Group III (8-14 days), and Group IV (14-30 days).

All patients underwent VP or kyphoplasty. The prognosis of patients was rated by the MacNab grade at discharge.

### MRI and review

MRI was performed with a 1.5-T imager with a spine coil (Syn-spine; Philips Medical Systems, Eindhoven, Netherland). Routine MRI sequencing included T1-weighted imaging, fat-suppressed T2-weighted imaging, and fat-suppressed gadolinium-enhanced T1-weighted imaging.

MRI was reviewed by a musculoskeletal radiologist and a neurosurgeon specializing in spinal surgery by mutual agreement.

The signal intensity and enhancement patterns of the compressed vertebrae were evaluated. The signal intensity of vertebral bodies was considered hypointense, isointense, or hyperintense compared with the signal intensity of normal vertebrae on T1- and T2-weighted images. The most extensively enhanced plane of sagittal fat-suppressed enhanced T1-weighted imaging was used for the evaluation.

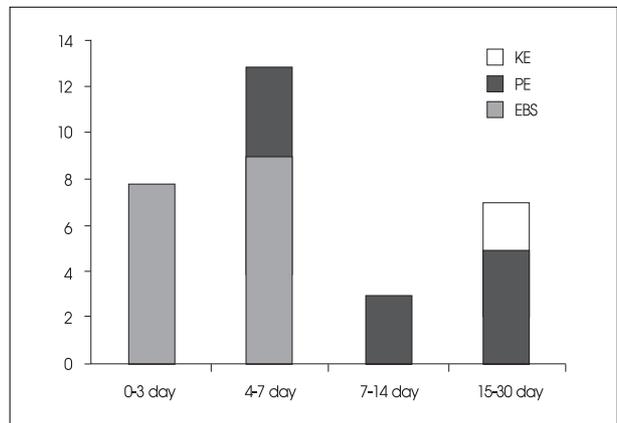
The enhancing pattern was classified as follows : enhancing box sign (EBS), diffuse patch enhancement (PE), and Kummell's enhancement (KE). EBS was defined as a central nonenhanced region encircled by a coarse enhanced rim. Vertebrae with EBS had a nonenhanced part when the enhanced rim reached the endplate. PE was defined as a diffuse enhancement without a central non-enhancing part. KE exhibited a well-marginated enhancement with a central nonenhancing lesion. KE had minimal enhancement subjacent to the fluid cavity whereas EBS had irregular enhancement adjacent to edema<sup>20</sup>. Examples are shown in Fig. 1.

### Statistical analysis

The enhancing patterns were analyzed according to the patient's age, sex, and onset of back pain. Statistical analysis was performed using SPSS for Windows (SPSS Inc, Chicago, IL, USA). Categorical variables were compared using Pearson's correlation (PC). The statement of correlation was considered significant at the 0.01 level (two-tailed).



**Fig. 1.** Classification of the enhancement pattern of vertebral compression fracture on sagittal fat-suppressed T1-weighted imaging. A : Enhancing box sign, B : patch enhancement, C : Kummell's enhancement.



**Fig. 2.** The enhancement pattern of acute vertebral compression fracture according to the onset of pain. KE : Kummell's enhancement, PE : patch enhancement, EBS : Enhancing box sign.

## RESULTS

Eight patients were assigned to Group I, 13 patients were assigned to Group II, three patients were assigned to Group III, and seven patients were assigned to Group IV. Seventeen patients had EBS, 12 had PE, and two had KE. EBS occurred in eight patients in Group I and nine patients in Group II (Fig. 2). EBS statistically correlated with the stage of the compression fracture ( $PC = -0.774$ ). All patients with EBS had a central low-signal intensity of the nonenhancing part of vertebral bodies on T1 images. The PE pattern was seen in four of 17 patients in Group II, all three patients in Group III, and in five of seven patients in Group IV. All patients in Group IV presented with KE.

Ten of 31 patients had no previous event before development of VCF. Others had a history of minor trauma, such as falling over, weight bearing or strain. A significant association was found between presence of trauma history and the occurrence of EBS ( $PC = -0.483$ ). Other parameters such as age and sex had no statistically significant association with EBS.

For postoperative pain reduction of MacNab grade, in Group I, five of eight patients had excellent outcomes. The

remaining three patients had good outcomes. In Group II, 10 of 13 patients had excellent outcomes and the remaining three patients had good outcomes. In Group III, two patients had an excellent outcome and one patient had a good outcome. In Group IV, five of seven patients had excellent outcomes, one had a good outcome, and the remaining patient had a fair outcome.

For enhancement pattern, 12 of 17 patients with EBS had excellent outcomes and the remaining patients had good outcomes. For patch enhancement, eight of 12 patients had excellent outcomes, three of 12 patients had good outcomes and one patient had a fair outcome. All patients with KE had excellent outcomes.

## DISCUSSION

Determination of acute VCF is a common problem in the neurosurgical field. Acute VCF is commonly determined from several findings, which include tenderness, plain radiography, bone scintigraphy, computed tomography (CT) and MRI. Plain radiographs and physical examination have failed to detect acute VCF in the patients with multiple VCFs<sup>11</sup>. Bone scans have the limitation of the diagnosis of acute VCF because of prolonged tracer uptake, which can take as long as 12 months<sup>22</sup>. Because MRI has the advantage of detecting acute VCF as well as ruling out other pathologies such as pathologic fracture, disc herniation, and spinal stenosis<sup>22</sup>. MRI is applied for precise diagnosis of acute VCF.

Acute VCF has a low signal compared with the high signal normally seen in the marrow fat on sagittal T1-weighted sequences in normal vertebrae on MRI<sup>7,9-11,20</sup>. Some authors report that low signal intensity on sagittal T1 represents edema and is related to prognosis<sup>11,21</sup>. However, McArdle et al.<sup>12</sup> state that T1-weighted images of VCF had normal signals from day 1 through to day 4 and decreased to become a low signal after day 6. In addition, a healing fracture of chronic VCF or heterogeneous fatty marrow can produce a decreased signal on T1-weighted sequences<sup>2,9,14</sup>. Furthermore, hemorrhage, which is an important finding in acute and subacute VCF, may appear as a high signal on T1-weighted images<sup>9,14</sup>. Various reports show that T2-weighted images of the VCF after less than one month have low<sup>2,20</sup> or high signal intensities<sup>20</sup>.

First, these heterogeneous findings of MRI stem from the arbitrary clinical definition of ACF. Cuenod et al.<sup>6</sup> reported that "acute" indicated pain for less than 2 months that involved the segment of the back with the vertebral collapse. The cutoff of 2 months was chosen because, in their clinical experience, most cases of osteoporotic vertebral

collapse remain painful for 4-8 weeks after onset<sup>6</sup>. Others selected 2 weeks or 3 months for definition of acute VCF<sup>5,10,19</sup>. Second, heterogeneous findings are related to sequential change of edema or hemorrhage of fractured vertebral body. To reduce the bias from definition, VCFs in our study was divided according to the stage of hemorrhage and edema of MRI<sup>17</sup>, not by clinical or by arbitrary decision. In addition, contrast enhancement study was selected for precise diagnosis of acute VCF. Because many authors describe that extensive enhancement is an important sign of acute VCF<sup>20,22</sup>, we focused on the characteristics of enhancement patterns of acute VCF.

In our study, EBS was seen only 7 days before acute VCF. Chen et al.<sup>4</sup> described that an increase in vascularity at the fractured site is seen in the acute phase of VCF. Moore et al.<sup>15</sup> reported that acute compressive mechanical stresses were transferred to the endplates, resulting in an acute increase of endplate vascularity that disappeared in the chronic stage. EBS represents an immediate increase of vascularity in the endplate in patients with VCF. Conversely, if EBS is related to acute mechanical stress, patients with a history of trauma could have more EBS with statistical significance. Cuenod et al.<sup>6</sup> reported that eight (16%) of 50 patients with acute VCF had similar EBS and EBS was not encountered in malignant compression fractures in their reports. EBS represents a characteristic sign of acute VCF 7 days before onset.

After 7 days of onset (Groups III and IV) PE or KE occurred. Many authors reported Kummell disease as vertebral cleft, fluid sign or intravertebral vacuum<sup>1,7,8,16,20</sup>. Although KE could be considered to have a similar enhancement pattern to EBS, KE reveals a sharply marginated enhancement around the vacuum cleft or fluid because the unhealed fracture or fluid has no adjacent inflammatory change and is distinctly divided from the enhancing wall<sup>7,20</sup>. In addition, Dupuy et al.<sup>8</sup> report that KE has characteristic smooth-marginated fluid collection. In contrast, EBS has an irregular rim enhancement surrounding the compact core of edema or hemorrhage without fluid collection. Therefore, it is easy to differentiate KE from EBS. Baur et al. reported that fluid sign was detected in 21 (40%) of 52 osteoporotic VCF<sup>1</sup>. They revealed that fluid sign was not seen in bandlike bone marrow edema and developed after bone marrow necrosis by osteoclast and osteoblast. They exhibited that fluid sign have a tendency of older stage of acute VCF<sup>1</sup>. KE was identified as enhancing pattern of Kummell disease and represented older stage of VCF as compared with EBS.

Our study was concerned with changes in CE pattern of acute VCF according to time sequence, rather than inten-

sity or area of the enhancement. Uemura et al.<sup>22)</sup> reported that extensive CE predicted better pain relief after PVP. (PC = 0.059). Although patients with EBS had excellent or good recovery from pain of MacNab grade, a significant association was not found between EBS and the MacNab grade in our study (PC = 0.059). However, the sagittal enhancing MRI revealed on sequential information of acute VCF. EBS represents a characteristic sign within 7 days of VCF development. Additionally, classification according to the stage of hemorrhage and edema of MRI revealed more physiologic and consistent result.

There are several limitations to the present study. First, this study was a retrospective review. The fracture date was reviewed from patients' recall of onset of pain. In addition, we excluded VCFs that were over one month old because patients could not recall the precise date of onset. Second, we could have some selection bias, because all patients received PVP.

## CONCLUSION

The sagittal enhancing MRI reveals on sequential information of acute VCF. EBS represents a characteristic sign within 7 days of VCF development. It was associated with acute mechanical stresses transferred to the endplates.

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## References

- Baur A, Stabler A, Arbogast S, Duerr HR, Bard R, Reiser M : Acute osteoporotic and neoplastic vertebral compression fractures : fluid sign at MR imaging. *Radiology* 225 : 730-735, 2002
- Baur A, Stabler A, Bruning R, Bard R, Krodell A, Reiser M, et al. : Diffusion-weighted MR imaging of bone marrow : differentiation of benign versus pathologic compression fractures. *Radiology* 207 : 349-356, 1998
- Brown DB, Glaiberman CB, Gilula LA, Shimony JS : Correlation between preprocedural MRI findings and clinical outcomes in the treatment of chronic symptomatic vertebral compression fractures with percutaneous vertebroplasty. *AJR Am J Roentgenol* 184 : 1951-1955, 2005
- Chen WT, Shih TT, Chen RC, Lo HY, Chou CT, Lee JM, et al. : Blood perfusion of vertebral lesions evaluated with gadolinium-enhanced dynamic MRI : in comparison with compression fracture and metastasis. *J Magn Reson Imaging* 15 : 308-314, 2002
- Chen WT, Shih TT, Chen RC, Lo SY, Chou CT, Lee JM, et al. : Vertebral bone marrow perfusion evaluated with dynamic contrast-enhanced MR imaging : significance of aging and sex. *Radiology* 220 : 213-218, 2001
- Cuenod CA, Laredo JD, Chevret S, Hamze B, Naouri JF, Chapaux X, et al. : Acute vertebral collapse due to osteoporosis or malignancy : appearance on unenhanced and gadolinium-enhanced MR images. *Radiology* 199 : 541-549, 1996
- Do HM : Magnetic resonance imaging in the evaluation of patients for percutaneous vertebroplasty. *Top Magn Reson Imaging* 11 : 235-244, 2000
- Dupuy DE, Palmer WE, Rosenthal DI : Vertebral fluid collection associated with vertebral collapse. *AJR Am J Roentgenol* 167 : 1535-1538, 1996
- Frager D, Elkin C, Swerdlow M, Bloch S : Subacute osteoporotic compression fracture : misleading magnetic resonance appearance. *Skeletal Radiol* 17 : 123-126, 1988
- Jung HS, Jee WH, McCauley TR, Ha KY, Choi KH : Discrimination of metastatic from acute osteoporotic compression spinal fractures with MR imaging. *Radiographics* 23 : 179-187, 2003
- Mathis JM, Barr JD, Belkoff SM, Barr MS, Jensen ME, Deramond H : Percutaneous vertebroplasty : a developing standard of care for vertebral compression fractures. *AJNR Am J Neuroradiol* 22 : 373-381, 2001
- McArdle CB, Crofford MJ, Mirfakhraee M, Amparo EG, Calhoun JS : Surface coil MR of spinal trauma : preliminary experience. *AJNR Am J Neuroradiol* 7 : 885-893, 1986
- Melton LJ 3rd, Kan SH, Frye MA, Wahner HW, O'Fallon WM, Riggs BL : Epidemiology of vertebral compression fracture. *Am J Epidemiol* 129 : 1000-1011, 1989
- Modic MT, Masaryk TJ, Weinstein MA : Magnetic resonance imaging of the spine. *Magn Reson Annu* : 37-54, 1986
- Moore RJ, Osti OL, Vernon-Roberts B, Fraser RD : Changes in endplate vascularity after an outer anulus tear in the sheep. *Spine* 17 : 874-878, 1992
- Oka M, Matsusako M, Kobayashi N, Uemura A, Numaguchi Y : Intravertebral cleft sign on fat-suppressed contrast-enhanced MR : correlation with cement distribution pattern on percutaneous vertebroplasty. *Acad Radiol* 12 : 992-999, 2005
- Osborn AG : *Diagnostic neuroradiology*. St. Louis : Mosby, 1994
- Silverman SL : The clinical consequences of vertebral compression fracture. *Bone* 13 Suppl 2 : S27- S31, 1992
- Singh A, Wetherington CA, Gilula LA : Percutaneous vertebroplasty in osteoporotic compression fracture with epidural hematoma. *AJR Am J Roentgenol* 186 : 909-910, 2006
- Stallmeyer MJ, Zoarski GH, Obuchowski AM : Optimizing patient selection in percutaneous vertebroplasty. *J Vasc Interv Radiol* 14 : 683-696, 2003
- Tanigawa N, Komemushi A, Kariya S, Kojima H, Shomura Y, Ikeda K, et al. : Percutaneous vertebroplasty : relationship between vertebral body bone marrow edema pattern on MR images and initial clinical response. *Radiology* 239 : 195-200, 2006
- Uemura A, Kobayashi N, Numaguchi Y, Fuwa S, Saida Y : Pre-procedural MR imaging for percutaneous vertebroplasty : special interest in contrast enhancement. *Radiat Med* 25 : 325-328, 2007