Percutaneous Vertebroplasty: Relationship between Vertebral Body Bone Marrow Edema Pattern on MR Images and Initial Clinical Response[1]

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Purpose: To prospectively investigate the relationship between initial clinical response and bone marrow edema pattern on preprocedural magnetic resonance (MR) images in vertebral bodies selected for percutaneous vertebroplasty (PVP).

Materials and Methods: Institutional review board approval and written informed consent were obtained. PVP was performed for osteoporotic compression fractures in 80 consecutive patients (mean age, 72.4 years; range, 44–85 years; 67 women and 14 men; 157 vertebrae). Patients were divided into three groups according to the proportion of the vertebra in which the bone marrow edema pattern was observed on sagittal MR images: group 1, 50% or more of the vertebra; group 2, less than 50%; group 3, no edema pattern observed. By using Wilcoxon rank sum test, Fisher exact test, and Wilcoxon signed rank test, groups were examined for differences in treatment efficacy, which was defined as the difference between preprocedural and postprocedural pain as assessed by means of visual analog scale (VAS) score at 1–3 days after PVP.

Results: Forty-four patients were assigned to group 1, 14 to group 2, and 22 to group 3. No significant difference was seen between the groups with respect to age, sex, number of treated vertebrae, or preprocedural VAS score. In group 1, VAS score decreased from 7.5 before the procedure to 2.9 after (improvement of 4.6). In group 2, the score decreased from 6.8 to 3.1 (improvement of 3.7). In group 3, the score decreased from 7.0 to 4.3 (improvement of 2.7). Improvement was significantly greater in group 1 than in group 3 ($P < .005$).

Conclusion: PVP resulted in significantly greater clinical improvement in patients with an extensive bone marrow edema pattern than in those without this pattern.

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Percutaneous vertebroplasty (PVP) is widely accepted as a useful treatment for back pain that results from osteoporotic compression fractures (1–5). However, in patients with multiple compression fractures and in those with chronic fracture, determining which vertebra to treat is frequently difficult. In such patients, the treatment location is commonly determined from findings at imaging, which includes magnetic resonance (MR) imaging, bone scintigraphy, and computed tomography (CT) (1,5). MR imaging provides information on anatomic vertebral collapse and the loss of normal signal intensity from the vertebral bone marrow space. Loss of normal signal intensity, which indicates the presence of bone marrow edema, is useful in determining the vertebra that is to be treated (5). However, to the best of our knowledge, no study results have been published that examine the relationship between bone marrow edema and clinical response. Hence, the purpose of our study was to prospectively investigate the relationship between the initial clinical response and the bone marrow edema pattern on preprocedural MR images in vertebral bodies selected for treatment by means of PVP.

Materials and Methods

This study was approved by the institutional review board (Kansai Medical University). All patients provided written informed consent. For each patient, a folder was prospectively created that contained images, including radiographs, MR images, and CT scans. Preprocedural clinical information and data regarding PVP procedures for each patient were entered into a personal computer and were managed by using Excel (version 2003; Microsoft, Redmond, Wash). Furthermore, MR images were transferred to a workstation (GE Medical Systems, Milwaukee, Wis) and were viewed by using this workstation.

Patients

This study was performed between February and December 2003 and consisted of 89 consecutive patients (179 vertebrae) who were scheduled to undergo PVP for vertebral compression fractures that resulted from osteoporosis. The indication for PVP was back pain caused by vertebral body compression fracture, with pain on percussion of the vertebral spinous process. In cases with multiple compression fractures, in which percussion pain of the spinous process was unclear, a physical examination was performed by using fluoroscopy. Patients with back pain attributed to myelopathy or radiculopathy resulting from stenosis of the vertebral canal or narrowing of the intervertebral foramen were excluded.

Before the PVP procedure, physical examination, neurologic examination, electrocardiography, respiratory function tests (forced vital capacity and forced expiratory volume during 1.0 second), and laboratory investigations (evaluation of red blood count, white blood cell count, platelet count, prothrombin time, and C-reactive protein level) were performed. The following diagnostic imaging studies were also performed: anterior and lateral radiography of the thoracic and lumbar vertebrae; MR imaging of the vertebrae, including the vertebra affected by the compression fracture (performed within 1 week of the procedure); and CT. In six of 89 patients, MR images showed fluid collection in the fractured vertebra; because this was considered to be the cause of the back pain, these patients were excluded from the study. Three patients were excluded because vertebral body signal intensity changes could not be evaluated owing to artifacts caused by patient movement during MR imaging. A total of 80 patients (mean age, 72.4 years; range, 44–85 years; 67 women and 14 men) and 157 vertebrae (62 thoracic, 95 lumbar) were therefore included in the study.

MR Imaging Protocol

MR imaging examinations were performed at 1.5 T (Signa; GE Medical Systems) according to the standard protocol at our institution. T1-weighted and fat-suppressed T2-weighted MR images were obtained in the sagittal plane. Each series was obtained with a quadrature thoracolumbar spine coil. The following imaging sequences were used: *(a)* a sagittal T1-weighted spin-echo sequence, with 666.7/12.3 (repetition time msec/echo time msec), section thickness of 3.7 mm, and field of view of 300 × 300 mm; and *(b)* a sagittal T2-weighted spin-echo sequence, with 4000/96.4, fat suppression, section thickness of 3.7 mm, and field of view of 300 × 300 mm.

Analysis of MR Images and Patient Classification

The MR images were evaluated by two neuroradiologists (K.I. and N.O., with 16 and 11 years of experience interpreting spinal MR images, respectively). The neuroradiologists were aware that the patients were being evaluated for PVP. However, they were unaware of the specific information, such as the location of back pain, the results of the neurologic examination, and other clinical data (including the patient's history), and these neuroradiologists reached a consensus for each case. Regions exhibiting the bone marrow edema pattern were defined as those

Advance in Knowledge

- PVP resulted in a significantly greater ($P < .005$) clinical response in patients with a bone marrow edema pattern that involved an extensive area on MR images than in those without a bone marrow edema pattern.

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Abbreviations:
PMMA = polymethylmethacrylate
PVP = percutaneous vertebroplasty
VAS = visual analog scale

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that exhibited signal intensity lower than that of fatty bone marrow on T1-weighted MR images and signal intensity higher than that of fatty bone marrow on fat-suppressed T2-weighted MR images. If the region exhibited conflicting findings on these two types of images, a region of extensive signal intensity change was defined as a region of bone marrow edema pattern.

Vertebral bodies were classified into three groups according to the proportion of the vertebral body affected by the bone marrow edema pattern, as seen in the sagittal plane. In other words, all sagittal MR images that depicted the vertebral bodies were analyzed, and three images that showed the right side, center, and left side of the vertebral bodies were selected. The three sagittal images were midline and at the levels of the left and right pedicles. The area ratio of bone marrow edema pattern was then determined on each image. If the distribution of this pattern differed on the right, central, and left sagittal MR images, the image with the broadest distribution was used for classification purposes. Classification criteria were as follows: type 1, vertebrae in which bone marrow edema pattern was present in 50% or more of the vertebral body; type 2, vertebrae in which this pattern was present in less than 50% of the vertebral body; and type 3, vertebrae with no bone marrow edema pattern.

Furthermore, on the basis of this classification system, patients were divided into the following three groups: Group 1 consisted of patients in whom the bone marrow edema pattern was present in 50% or more of the vertebral body (patients with at least one type 1 vertebral body), group 2 consisted of patients in whom the bone marrow edema pattern was present in less than 50% of the vertebral body (patients with no type 1 vertebral bodies, but at least one type 2 vertebral body), and group 3 consisted of patients with no bone marrow edema pattern (patients with only type 3 vertebral bodies). Patients with differing proportions of bone marrow edema pattern in multiple vertebrae selected for treatment were classified according to the vertebra with the highest proportion of edema pattern.

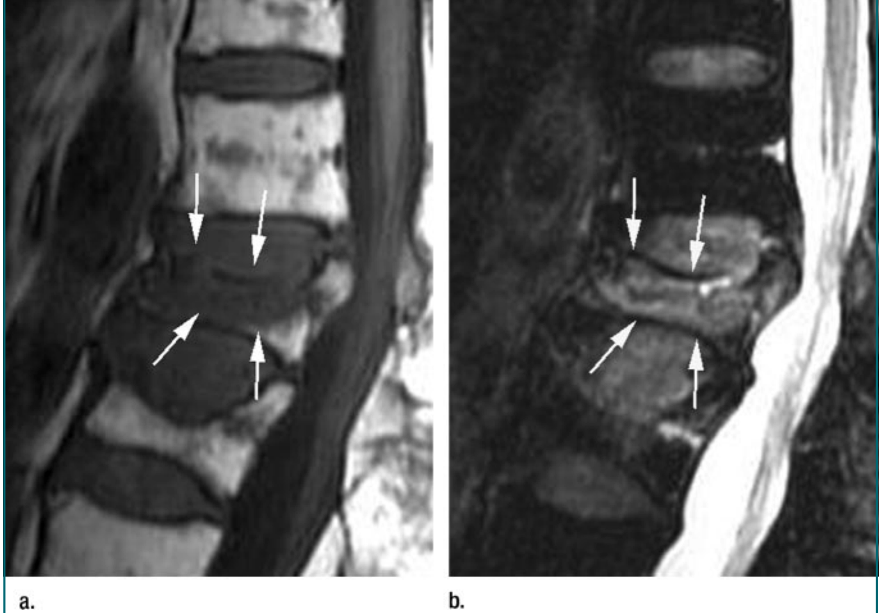
PVP Procedure

All procedures were performed either by one of the authors (N.T.), who had 5 years of experience in PVP, or by a fellowship trainee under the supervision of this author.

PVP was performed with the use of combined CT and fluoroscopic guidance (Advantex LCA and ACT; GE Medical Systems). Thirty minutes before the procedure, 10 mg morphine hydrochloride (Sankyo, Tokyo, Japan), 0.5 mg atropine sulfate (Tanabe, Osaka, Japan), and 25 mg hydroxyzine hydrochloride (Pfizer Japan, Tokyo, Japan) were administered intramuscularly. Local anesthesia was induced with 10 mL of 1% lidocaine (AstraZeneca, Osaka, Japan) administered from the skin to the periosteum of the pedicle by using a 22-gauge Cathelin needle (Terumo Europe, Leuven, Belgium) with use of fluoroscopic guidance. After orientation of the puncture needle was confirmed at CT and was aligned with the Cathelin needle, a 13-gauge bone biopsy needle (Osteo-Site Murphy M2; Cook, Bloomington, Ind) was advanced into the pedicle of the vertebral arch. CT was repeated and, after the orientation of the biopsy needle was confirmed, the visualization modality was changed to lateral fluoroscopy and the bone biopsy needle was advanced to the anterior one-third of the vertebral body close to the midline.

Intraosseous venography was performed with 1–5 mL of iopamidol (Iopamiron 300; Schering Japan, Osaka, Japan) to confirm that the needle was not positioned within a direct venous anastomosis to the central or epidural veins. Subsequently, 20 grams of methylmethacrylate powder (Osteobond copolymer bone cement; Zimmer, Warsaw, Ind) was mixed with 5 grams of barium sulfate powder (Horii Pharmaceutical, Osaka, Japan) that had been sterilized with dry heat to increase its opacity. Ten milliliters of liquid methylmethacrylate monomer was added to the powder, and the mixture was blended to a toothpaste-like consistency

Figure 1



a. b.

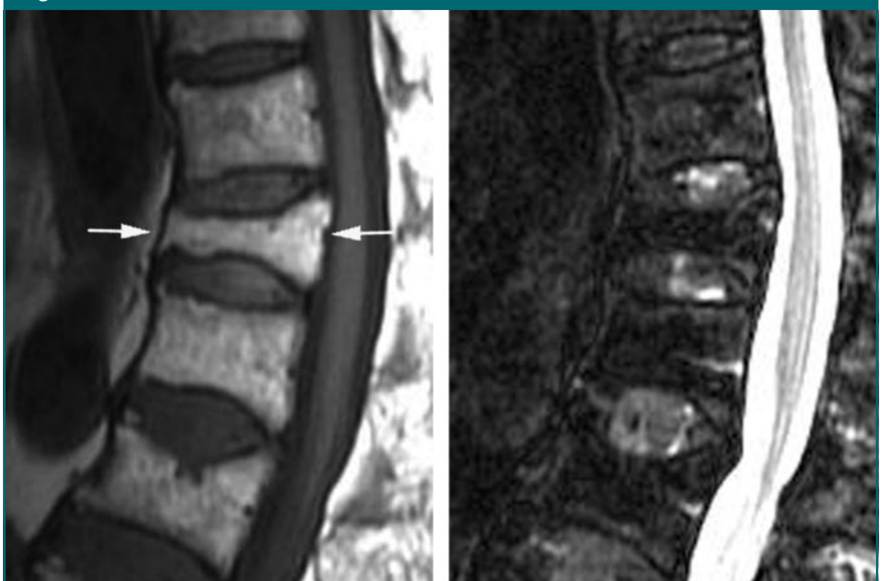
Figure 1: Sagittal **(a)** T1-weighted (666.7/12.3) and **(b)** fat-suppressed T2-weighted (4000/96.4) MR images of osteoporotic compression fracture of L1 vertebral body with extensive bone marrow edema pattern in a 76-year-old man. All regions of the vertebral body show low signal intensity (arrows) in **a** and high signal intensity (arrows) in **b** (group 1).

Figure 2

a. b.

Figure 2: Sagittal **(a)** T1-weighted (666.7/12.3) and **(b)** fat-suppressed T2-weighted (4000/96.4) MR images of osteoporotic compression fracture of L4 and L5 vertebral bodies with considerable bone marrow edema pattern in a 74-year-old woman. Regions of low signal intensity (arrows) are present in the anterosuperior portion of L4 and L5 in **a** and occupy less than 50% of the vertebrae. Regions of high signal intensity (arrows) are seen in the anterosuperior portion of L4 and L5 in **b**. The high signal intensity regions occupied less than 50% of the vertebrae (group 2).

Figure 3



a. b.

Figure 3: Sagittal **(a)** T1-weighted (666.7/12.3) and **(b)** fat-suppressed T2-weighted (4000/96.4) MR images of osteoporotic compression fracture of T12 vertebral body without bone marrow edema pattern (arrows) in a 76-year-old man. A reduction in vertebral body height and a compression fracture are seen in T12, but signal intensity is equal to that in the vertebra below on both images (group 3).

to produce polymethylmethacrylate (PMMA). By using 1-mL syringes, the PMMA was injected with lateral fluoroscopic guidance. PMMA injection was terminated when adequate filling of the vertebral body was achieved or if leakage occurred. If leakage occurred, the needle was repositioned, and additional PMMA was injected to fill the remaining part of the vertebral body. The needle was then removed, and all patients were observed in the supine position for 2 hours.

Outcome Evaluation and Postprocedural Management

Pain level was evaluated with a visual analog scale (VAS) of 0–10; a score of 0 represented no pain, and a score of 10 indicated severe pain. Severity of preprocedural pain was assessed by either the attending physician or the physician who was scheduled to perform PVP and was evaluated on the day before or the day of PVP. Severity of postprocedural pain was assessed by either the attending physician or the physician who performed PVP and was evaluated between 1 day and 3 days after the procedure. According to the procedures at our institution, patients undergoing PVP were admitted and, once the procedures were completed, the patients were returned to their ward and instructed to rest in the supine position for 2 hours. While the patients were allowed to move after that, most patients were sleeping because of the effects of the medication administered before PVP. Therefore, the severity of pain after PVP was not assessed on the day of the procedure. The patients were evaluated with respect to the degree of pain reduction: less than 25%, 25%–49%, and 50% or more.

Statistical Analysis

The degree of VAS score improvement in each patient was calculated by subtracting the postprocedural VAS score from the preprocedural VAS score. Intergroup differences in the degree of VAS score improvement were statistically assessed. Furthermore, in each patient, the degree of pain reduction was calculated by dividing the degree of VAS score improvement by the preprocedural score.

Among the three patient groups (groups 1, 2, and 3), age, volume of cement injected per vertebra, number of treated vertebrae, preprocedural VAS score, postprocedural VAS score, and degree of VAS score improvement were compared and analyzed by using the Wilcoxon rank sum test, while the Fisher exact test was used to analyze sex differences. The Wilcoxon signed rank test was used to compare preprocedural and postprocedural VAS scores among the three groups. These statistical analyses were conducted by using StatView (version 5.0 for Windows; SAS Institute, Cary, NC), and P values of less than .05 were considered to indicate a statistically significant difference.

Results

Sixty vertebrae were classified as type 1, 28 as type 2, and 69 as type 3. Forty-four patients were accordingly assigned to group 1 (Fig 1), 14 were assigned to group 2 (Fig 2), and 22 were assigned to group 3 (Fig 3). The Fisher exact test showed a statistically significant difference in the distribution of patients between groups 1 and 3 on the basis of sex ($P = .043$). The Wilcoxon rank sum test indicated no significant difference between the three groups with respect to age, volume of cement injected per vertebra, or preprocedural VAS score. However, a statistically significant difference was seen between groups 2 and 3 with respect to the number of treated vertebrae ($P = .021$; Table 1). A statistically significant difference was evident between groups 1 and 3 with respect to postprocedural VAS score ($P = .037$), and significant differences were seen between preprocedural and postprocedural VAS scores in all three groups ($P < .001$ in group 1, $P < .004$ in group 2, and $P < .001$ in group 3).

VAS score improvement, defined as the pre- to postprocedural difference (preprocedural minus postprocedural VAS score), was 4.6 ± 2.7 (mean pain score ± standard deviation) in group 1, 3.7 ± 3.1 in group 2, and 2.8 ± 1.9 in group 3; the difference between groups 1 and 3 was statistically significant ($P < .005$; Table 2).

Pain reduction (Table 3) of at least 50% was achieved in 30 (68%) of 44 patients in group 1, eight (57%) of 14 patients in group 2, and nine (41%) of 22 patients in group 3. Pain relief of 25%–49% was achieved in seven (16%) of 44 patients in group 1, three (21%) of 14 patients in group 2, and eight (36%) of 22 patients in group 3. Less than 25% reduction in pain was achieved in seven (16%) of 44 patients in group 1, three (21%) of 14 patients in group 2, and five (23%) of 22 patients in group 3.

Table 1

Summary of Patient Data

Parameter	Group 1	Group 2	Group 3
No. of patients	44	14	22
Age (y)*	72.9 ± 6.9	70.8 ± 6.9	72.7 ± 8.3
Women/men	36/8†	10/4	21/1†
No. of treated vertebrae*	2.0 ± 0.8	1.5 ± 0.8‡	2.3 ± 0.9‡
Volume of PMMA injected (mL)*	4.1 ± 1.7	4.4 ± 2.2	3.6 ± 1.2

Note.—Unless indicated, data are numbers of patients. Group 1 = bone marrow edema pattern present in 50% or more of vertebral body, group 2 = present in less than 50% of vertebral body, and group 3 = no bone marrow edema pattern.

* Data are mean ± standard deviation.

† Statistically significant difference ($P = .043$).

‡ Statistically significant difference ($P = .021$).

Table 2

Summary of VAS Score Results

Parameter	Group 1	Group 2	Group 3
Preprocedural VAS score	7.5 ± 1.9	6.8 ± 2.0	7.0 ± 2.2
Postprocedural VAS score	2.9 ± 2.8	3.1 ± 2.5	4.3 ± 2.4
VAS score improvement	4.6 ± 2.7*	3.7 ± 3.1	2.8 ± 1.9*

Note.—Data are mean ± standard deviation.

* Statistically significant difference ($P < .005$).

Table 3

Change in Pain Severity after PVP

	VAS Score Improvement*			
Group	≥50%	25%–49%	<25%	Mean Rate (%)
1 ($n = 44$)	30 (68)	7 (16)	7 (16)	61.63
2 ($n = 14$)	8 (57)	3 (21)	3 (21)	50.00
3 ($n = 22$)	9 (41)	8 (36)	5 (23)	46.21

Note.—Except where noted, data are number of patients, and numbers in parentheses are percentages.

* Improvement rate = (preprocedural VAS score − postprocedural VAS score)/preprocedural VAS score.

Discussion

Our results suggest that the more extensive the bone marrow edema pattern is in the treated vertebra, the greater the pain relief provided by PVP will be. This finding supports the idea that the presence of bone marrow edema is useful for selecting the vertebra to be treated (5). However, no significant difference