The Risk of New Osteoporotic Vertebral Compression Fractures in the Year after Percutaneous Vertebroplasty

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PURPOSE: To prospectively assess the incidence, location, and possible causative mechanisms of new vertebral compression fractures (VCFs) in 66 symptomatic patients with osteoporotic VCFs treated with percutaneous vertebroplasty (PV) and to study the relation between new VCFs and back pain symptoms.

MATERIALS AND METHODS: Sixty-six patients with 102 painful symptomatic VCFs were treated with PV. All patients had baseline total spinal magnetic resonance (MR) imaging. Follow-up MR imaging was performed at 3, 6, and 12 months to locate new VCFs. Visual analog scales for pain and pain medication consumption were used to assess clinical outcomes. The following characteristics were compared in patients with new VCFs after PV versus patients without new VCFs: patient age, sex, presence of secondary osteoporosis, bone mineral density, number of preexisting VCFs, shape and grade of VCFs, type of bone cement used for PV, volume of injected cement, and cement leakage in intervertebral disc spaces.

RESULTS: Sixteen of 66 patients had 26 new VCFs during 1 year of follow-up after PV. Most new VCFs occurred within 3 months of PV, half of new VCFs appeared in levels adjacent to treated levels, and half of the new VCFs were symptomatic. The presence of more than two preexisting VCFs was the only independent risk factor for the development of a new VCF.

CONCLUSIONS: New VCFs occurred after PV in 24% of patients. Half of new VCFs occurred in levels adjacent to treated levels and half were symptomatic. The presence of more than two preexisting VCFs was the only independent risk factor for the development of a new VCF.

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Abbreviations: PV = percutaneous vertebroplasty, VAS = visual analog scale, VCF = vertebral compression fracture

PERCUTANEOUS vertebroplasty (PV) is the percutaneous stabilization of a compressed vertebral fracture with the injection of polymethylmethacrylate. The main goal of PV is to reduce or eliminate pain caused by vertebral compression fractures (VCFs). Although patients with primary or secondary osteolytic vertebral tumors were initially treated with this procedure, the main target population for PV is patients with painful, therapy-resistant VCFs caused by osteoporosis. A major concern after PV in patients with osteoporosis is the occurrence of new VCFs in the nontreated vertebral bodies at other levels. Some authors believe new VCFs after PV are caused by the augmented stiffness of the treated vertebrae related to the amount of injected cement or by cement leakage in the adjacent vertebral disc space (1–7). Others have stated that the ongoing osteoporosis induces new VCFs (8–11).

In this study, we prospectively assessed the incidence, location, and possible causative mechanisms of new VCFs in 66 patients treated with PV after osteoporotic VCF by magnetic resonance (MR) imaging follow-up. We also studied the relation between new VCFs and back pain symptoms.

PATIENTS AND METHODS

Patients

Between March 2002 and March 2004, 77 consecutive patients under-

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went PV of painful osteoporotic VCFs in our hospital. Eleven patients were excluded from the study. One patient died of unrelated disease within 2 months. Ten patients refused 3-month and/or 6-month follow-up MR imaging and were excluded from the study. The remaining 66 patients had 6-month follow-up MR imaging after PV and constitute the current study population. PV was performed only if conservative treatment had failed and back pain still existed after at least 6 weeks. Other causes of back pain were excluded by means of anamnesis, physical examination, and MR imaging.

All patients had total spine MR imaging before PV. Preprocedural MR imaging sequences consisted of sagittal T1-weighted, T2 turbo spin-echo weighted, and short τ inversion recovery sequences and additional transverse T2 turbo spin-echo weighted images at the level of the VCF. Only patients with VCF with a minimum of 15% height loss compared with the dorsal wall height of the vertebral body and presence of bone marrow edema of the collapsed vertebral body were included for treatment. Before treatment, all patients underwent bone mineral densitometry. Before the procedure, institutional review board approval and patient informed consent were obtained.

Procedure

PV was performed under local anesthesia in a biplane angiography suite (Integris BN 3000 Neuro; Philips Medical Systems, Best, The Netherlands). Polymethylmethacrylate bone cement was injected under continuous fluoroscopic imaging guidance. Various bone cements were used: Simplex-P (Howmedica, Limerick, Ireland), Palacos LV-40 (Schering-Plough Europe, Brussels, Belgium), Osteopal V (Biomet Merck, Ried b. Kerzers, Switzerland), and Osteo-Firm (William Cook Europe, Bjaeverskov, Denmark). In each treated VCF, the amount of injected cement per vertebral body was noted. Immediately after the procedure, computed tomography with multiplanar reconstructions of treated levels was performed to identify possible extra cement leakage or other local complications that might not have been noted on fluoroscopy. Intervertebral disc leakage into upper or lower disk space in relation to the treated level was assessed.

Imaging Follow-up

After PV, total spine MR imaging scans were scheduled at 3, 6, and 12 months. Follow-up MR imaging consisted of sagittal T1-weighted and short τ inversion recovery sequence images and additional transverse T2 turbo spin-echo weighted images of treated vertebrae and new VCFs if present.

Preprocedural and postprocedural total spinal MR images were compared to identify new VCFs. Regardless of the presence of clinical symptoms, we considered new VCFs to be present when postprocedural MR images showed more than 15% compression of the vertebral body and bone marrow edema at a level other than the treated vertebra. The presence, number, and level of new VCFs were recorded. Development of new VCFs between two directly adjacent treated VCFs was noted separately.

Clinical Follow-up

Before PV treatment and at every MR imaging follow-up visit, patients were asked to fill out a visual analog score (VAS) for pain and pain medication use. The VAS consisted of a 10-point scale ranging from 0 indicating no pain to 10 indicating the most severe pain ever in the patient's life (12). Treatment was considered successful if the follow-up VAS score was at least 50% lower than the initial VAS score. The follow-up pain questionnaire was also used to distinguish symptomatic from asymptomatic new VCFs. A new VCF was considered asymptomatic if the patient had no or minor back pain, a follow-up VAS score less than 50% of the initial VAS score, and no need for extra pain medication.

Statistical Analysis

The decrease in VAS score of patients with osteoporotic VCFs before and after PV was tested with the Wilcoxon paired-sample test.

The following patient characteristics were compared in patients with new VCFs versus patients without VCFs: age, sex, presence of secondary osteoporosis, and bone mineral density. In secondary osteoporosis, bone loss is associated with an identifiable medical condition in which treatment with steroid drugs is required. The following imaging characteristics were compared between groups: the number of preexisting VCFs, vertebral shape (wedge, biconcave, or crush), and grade of VCF (mild, moderate, and severe). The shape and grade of every treated VCF was scored according to the semiquantitative visual grading of vertebral deformities (13). The shape of VCF was classified on the basis of reduction in anterior height (ie, wedged), middle height (ie, biconcave), or posterior height (ie, crush). The grade of VCF was classified on the basis of the percentage of reduction: 15%–25% (mild), 26%–40% (moderate), and more than 40% (severe). Shape and grade of treated VCFs were determined by two radiologists on a consensus basis.

The following technical characteristics were compared between groups: type of bone cement used, volume of injected cement, and occurrence of cement leakage into adjacent intervertebral disc space(s). Corresponding 95% confidence limits were calculated with confidence interval estimation (14).

Differences in baseline characteristics between patients with and without new VCFs were compared with the χ^2 test for categoric variables and an unpaired t test for continuous variables. The independent effect of baseline characteristics on the occurrence of new VCFs was estimated with logistic regression analysis by calculating odds ratios and corresponding 95% CIs.

RESULTS

The 66 patients treated with PV had a total of 228 preexisting VCFs with a median of three VCFs per patient (range, 1–10). Of these 228 VCFs, 102 showed bone marrow edema on MR imaging and were subsequently treated with PV in 68 sessions. Two patients were treated in two PV sessions.

There were no technical failures and there was no procedural morbidity. Injected bone cements included Simplex-P, Palacos LV-40, Osteopal V, and Osteo-Firm in 15, 28, 29, and 30 VCFs, respectively. All 66 patients had 3-month and 6-month MR imaging

Table 1
Characteristics of Total Patient Group ($N = 66$)

Characteristic	Value
Mean age ± SD, y (range)	70 ± 10(46–88)
Female sex (%)	50 (76)
Mean bone mineral density ± SD*	−2.92 ± 1.2
Secondary osteoporosis	11 (17)
Total number of preexisting VCFs	228
Median preexisting VCFs per patient	3
1	12 (18)
2	20 (30)
≥3	34 (52)
Total number of VCFs treated by PV	102
Shape of treated VCF	
Wedge	39 (38)
Biconcave	61 (60)
Crush	2 (2)
Grade of treated VCFs	
Mild	18 (18)
Moderate	43 (42)
Severe	41 (40)
Mean cement volume ± SD, mL (range)	2.8 ± 0.9 (1–5)
Mean initial VAS ± SD	8.8 (1.3)
Median VAS	9.0
Pain medication	
None	7 (11)
Paracetamol/NSAID	27 (41)
Morphine	32 (48)
Patients with new VCFs	16 (24)
Patients without new VCFs	50 (76)

* T-score.
Note.—Values in parentheses are percentages unless specified otherwise. NSAID = nonsteroidal antiinflammatory drug.

follow-up and 46 patients (70%) had 12-month MR imaging follow-up. **Table 1** summarizes the characteristics of the total group of patients at the time of PV.

Postprocedural median VAS scores were significantly lower than initial VAS scores at all points in time, and patients needed less pain medication in follow-up after treatment with PV ($P < .001$; **Figs 1, 2**).

In 16 of 66 patients (24%; 95% CI, 15%–36%), 26 new osteoporotic VCFs occurred. **Table 2** summarizes the number and characteristics of all new VCFs at different follow-up periods. Multiple new VCFs at different time intervals arose in seven patients: five patients developed two new VCFs each, one patient developed three new VCFs, and one patient developed four new VCFs.

Of the 26 new VCFs, 16 appeared within 3 months, with 11 of these 16 at adjacent levels. Eight of these 16 new VCFs were symptomatic. On MR imaging at 6 months and 12 months, new VCFs were less frequently observed, less symptomatic, and located at levels distant from the initially treated level. Of the 26 new VCFs, 10 were treated by PV, two were conservatively treated, and 14 needed no therapy because they were asymptomatic.

Most initially treated VCFs and new VCFs were located at the thoracolumbar junction (vertebrae T10 through L2). No one specific initially treated vertebral level was associated more often with new VCFs or with adjacent new VCFs (**Table 3**).

A comparison of patient, imaging, and technical characteristics in patients with and without new VCFs on follow-up are listed in **Table 4**. There were no differences in age, sex, secondary osteoporosis, or bone mineral density. Eleven patients (17%) had steroid-induced osteoporotic VCFs, of whom two patients developed new VCFs. There was no difference in the shape or grade of vertebral deformities of initially treated VCFs.

The number of preexisting VCF differed between patients with and without new VCFs, and in the multivariate analysis, the number of preexisting VCFs remained the only predictor of new VCFs. With three or more preexisting VCFs, the risk of developing a new VCF was significantly higher (odds ratio, 3.8; 95% CI, 1.1–13.5) compared with patients with one or two preexisting VCFs. There was no difference in mean injected cement volume and type of bone cement used.

Of the 102 treated VCFs, cement leakage to adjacent intervertebral disc space occurred in 31 cases (30%). Of the 14 new VCFs that arose adjacent to the treated VCF, one (7%) occurred in relation to cement leakage to the adjacent disc space.

In the subgroup of five eligible patients in whom two VCFs were treated with PV with an intact level left untreated in between, two new VCFs occurred (40%) in these initially intact adjacent vertebral bodies. Both new VCFs were asymptomatic.

DISCUSSION

Nearly 25% of patients developed one or more new VCFs in the 1 year of follow-up after treatment of painful osteoporotic VCFs with PV. The majority of these new VCFs occurred within 3 months after PV. In the first 3 months, most new VCFs were located at adjacent levels, whereas later in follow-up, more distant levels were involved. Almost half of new VCFs were symptomatic. Presence of more than two preexisting VCFs was the only predictor in the development of new VCFs. Age, sex, presence of secondary osteoporosis, bone mineral density, vertebral shape, grade of VCF, type of bone cement used, volume of injected cement, and cement leakage in the intervertebral disc space did not influence the occurrence of new VCFs after PV.

The incidence of new VCFs after PV was reported to range from 8% to 52% in several studies (9–11,15) (**Table 5**). However, most of these studies were not prospectively designed, and additional radiologic examinations were performed in symptomatic patients only. The studies with the largest numbers of patients showed the lowest incidences but were retrospectively designed (11,15). The results of our study are almost identical to the inci-

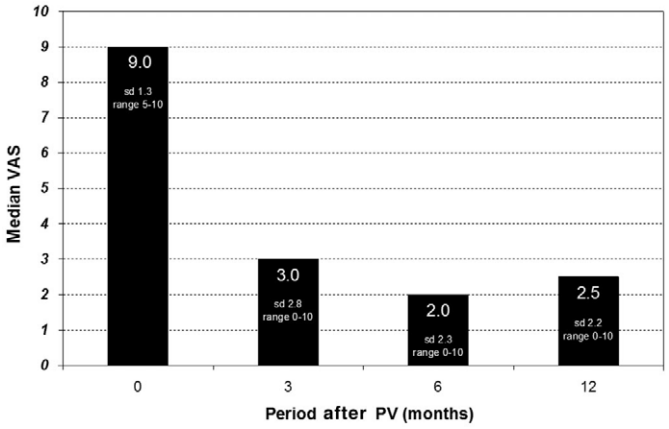

Figure 1. VAS for pain immediately before the procedure and at each follow-up interval after PV.

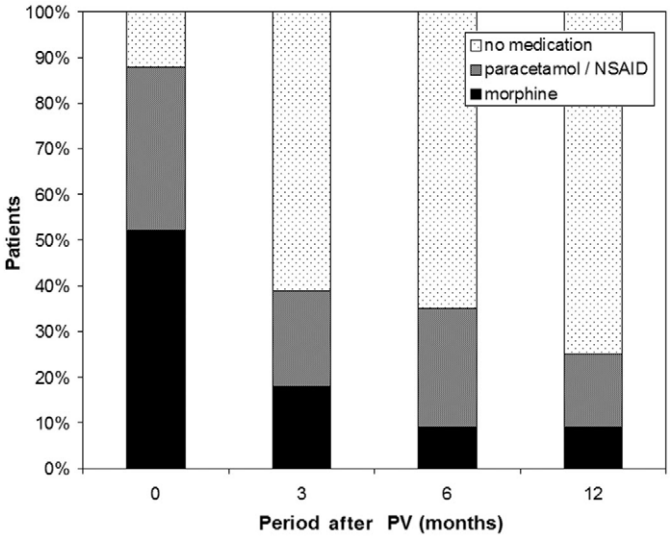

Figure 2. Use of pain medication immediately before the procedure and at each follow-up interval after PV (NSAID = nonsteroidal antiinflammatory drug).

Table 2
New VCFs at Different Follow-up Periods after PV

Months after PV	Patients with New VCFs	No. of New VCFs	Symptomatic VCFs	Adjacent VCFs
3	12	16 (62)	8 (50)	11 (69)
6	5	6 (23)	2 (33)	2 (33)
12	3	4 (15)	2 (50)	1 (25)
Total	16	26 (100)	12 (46)	14 (54)

Note.—Values in parentheses are percentages.

Table 3
Thoracolumbar Spine Level Distribution of Initially Treated Osteoporotic VCFs by PV and New VCFs after PV

Spine Level	Initially Treated VCFs (n = 102)	New VCFs (n = 26)	Adjacent New VCFs (n = 14)	Symptomatic New VCFs (n = 12)
T5	1	1	–	–
T6	3	1	–	–
T7	6	1	1	1
T8	7	1	–	1
T9	2	1	1	1
T10	5	4	2	1
T11	11	–	–	–
T12	19	3	2	2
L1	19	3	3	2
L2	18	1	1	1
L3	3	5	3	1
L4	5	3	–	2
L5	3	2	1	–

dence found in one other prospective study (10). However, the number of patients in this analysis was small. The incidence of new osteoporotic VCFs within 1 year in patients conservatively treated after an osteoporotic VCF is approximately 20% (16,17). With the presence of two or more preexisting VCFs, the incidence increases to 24% (17). The incidence of new VCFs after PV seems to be in the range of the incidence of new VCFs in the natural course of osteoporosis (16–22).

Within 3 months after PV, the majority of new VCFs occurred in levels adjacent to treated levels, as was also observed by others (9,11,15). Studies of spinal biomechanics indicate that the stiffness of augmented vertebrae can be 36 times greater than normal spinal cancellous bone (4). The increase in pressure and weight-bearing changes on adjacent intervertebral discs after PV, and the indirect increase in pressure on adjacent untreated vertebral bodies, especially in patients with osteoporotic vertebrae, can cause new adjacent VCFs (1–5,7). Our study showed no relation between specific treated vertebral level and the occurrence of new adjacent or distant VCFs. We also found that VCFs mostly occur at vertebral levels T10 through L2 in untreated and treated patients. This is in concordance with the results of a study by Kim et al (15). Another explanation of the occurrence of new VCFs in the vicinity of treated VCFs after PV may be that the increased daily activities as back pain decreases after PV cause additional stress on the vertebral bodies (11).

Table 4
Comparison of Characteristics of Patients with and without New VCFs after PV

	Patients with New VCFs (n = 16)	Patients without New VCFs (n = 50)	P Value
Median age, y (range)	70 (56–87)	70 (46–88)	.7
Female sex	11 (69)	39 (78)	.5
Mean bone mineral density ± SD*	−3.0 ± 1.2	−2.9 ± 0.9	.7
Secondary osteoporosis	2 (13)	9 (18)	.6
Median number of preexisting VCFs	5	2	.04
1	0 (0)	102 (100)	
2	20 (20)	82 (80)	
≥3	36 (35)	66 (65)	
Shape of treated VCF			.5
Wedge	51 (50)	66 (65)	
Biconcave	51 (50)	36 (35)	
Crush	0	0	
Grade of treated VCF			.7
Mild	13 (13)	20 (20)	
Moderate	51 (50)	41 (40)	
Severe	38 (37)	41 (40)	
Mean cement volume ± SD, mL (range)	2.7 ± 1.0 (1–4)	2.8 ± 0.7 (1–5)	.8
Cement leakage intervertebral discs spaces (%)	1 (7)	30 (93)	.7
Type of bone cement used (%)			.8
Simplex P	4 (27)	11 (73)	
Palacos LV	7 (25)	21 (75)	
Osteopal V	7 (24)	22 (76)	
Osteo-Firm	8 (27)	22 (73)	

* T-score.
Note.—Values in parentheses are percentages unless specified otherwise.

Table 5
Incidence of New Osteoporotic VCFs after PV Treatment in the Literature (6,9,10,11,15)

Study (Reference)	No. of Patients	Follow-up Period (y)	Incidence of new VCFs	Method of VCF Assessment
Grados et al, 2000 (9)	25	1–7	52	VAS and radiography once in 1997
Perez-Higueras et al, 2002 (10)	13	5	23	Prospective: pain questionnaire
Uppin et al, 2003 (11)	177	1–2	12	Retrospective
Kim et al, 2004 (15)	106	1–3	8	Retrospective: MR in symptomatic patients
Lin et al, 2004 (6)	38	1	36	Prospective: MR in symptomatic patients
Present study	66	1	24	Prospective: pain questionnaire and MR at 3, 6, and 12 months after PV

Development of new VCFs between two directly adjacent treated VCFs was examined separately. In two of five patients treated with PV of two VCFs with an untreated intact adjacent vertebral level between them, a new VCF occurred in this initially intact adjacent vertebral level. With this small number of patients, no definitive conclusions can be drawn regarding the influence of PV treatment on new VCFs in intact levels between treated levels. However, because both new VCFs after PV were asymptomatic and three eligible patients did not develop a new VCF, prophylactic treatment with PV of initially intact vertebral levels between adjacent treated levels is not indicated.

Apart from the possible influence on location of occurrence of new VCFs after PV, some authors (1–7,9,15) have suggested that the changed weight-bearing effects and increased vertebral stiffness resulting from PV is the major contributing factor in development of new VCFs after PV, independent of the effect of the underlying osteoporosis. Volume of injected bone cement has been suggested as a causative risk factor (3,5,6). In our study, no difference in volume of injected cement was observed in patients with or without a new VCF after PV. Moreover, the mean volume of cement used was much lower in our study than in another study with a lower incidence of new VCFs (11). We also found no relation between cement leakage and the occurrence of new adjacent VCFs as suggested in other studies (6).

Another possible causative mechanism in the development of new VCFs after PV could be the influence of the ongoing osteoporosis independent of PV treatment. In patients with osteoporotic VCFs not treated with PV, the presence of more and/or more severe

preexisting osteoporotic VCFs resulted in higher incidences of new VCFs (17–22). Specific possible osteoporotic risk factors in our study such as bone mineral density T-scores, presence of primary or secondary osteoporosis, and severity of preexisting VCFs were comparable in patients with and without new VCFs after PV. The only predictor of occurrence of new VCFs after PV was the presence of more than two preexisting VCFs.

The majority of osteoporotic VCFs cause only minor local back pain symptoms and generally heal within 4–8 weeks with evident reduction in back pain (17,23–25). After PV, we observed minor or nonexistent back pain symptoms in approximately half of new VCFs, which is in concordance with the natural history of osteoporotic new VCFs in the first year after initial vertebral fracture (25). We are aware of no other prospective studies of pain symptoms in patients with new VCFs after PV.

Because our data on new VCFs in patients treated with PV are comparable to the reported incidences of new VCF in untreated patients with osteoporosis, PV does not seem to change the natural history of the disease. This implies that screening of patients after PV for new VCFs is not indicated. Only patients with three or more preexisting VCFs should be informed of the increased risk of development of new VCFs in the future.

In conclusion, new VCFs occurred after PV in 24% of patients. Half of new VCFs occurred in levels adjacent to treated levels and half were symptomatic. The presence of more than two preexisting VCFs was the only independent risk factor for the development of new VCFs.

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