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Original Article

Risk factors of new symptomatic vertebral compression fractures after percutaneous vertebroplasty

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Abstract: *Background:* Percutaneous vertebroplasty (PVP) is an effective procedure to relieve pain caused by osteoporotic vertebral compression fractures (VCFs). New VCF is a common complication of the vertebroplasty. Many scholars have focused on new VCFs after PVP, but the risk factors of new VCFs have not been fully revealed. Therefore, the incidence and the risk factors of new VCFs were investigated in the study. *Methods:* From July 2010 to September 2014, 112 patients who underwent PVP at 141 levels for osteoporotic VCFs were retrospectively analyzed. Potential risk factors, such as age, gender, bone mineral density (BMD), intradiscal leakage, injected cement volume, and numbers of fractures and thoracolumbar junction fractures were evaluated. *Results:* 22 patients (19.6%) had subsequent symptomatic new VCFs at the last follow-up. The incidence of new fractures in 3-months, 1-year and 2-years was 31.8% (6 cases), 40.9% (9 cases), and 77.3% (17 cases) respectively. Among the risk factors, only the BMD showed a significant relationship to new VCFs (univariate analysis, P = 0.001; multivariate analysis, P = 0.003). None of other factors showed a statistically significant effect by multivariate analysis. *Conclusion:* The most important risk factor affecting new VCFs is osteoporosis. The incidence of new symptomatic VCFs after PVP is higher in osteoporotic patients with lower BMD.

Keywords: Vertebroplasty, osteoporotic vertebral compression fracture, risk factors, BMD, percutaneous vertebroplasty

Introduction

The incidence of osteoporosis has been rising quickly among the growing aging population. Osteoporotic vertebral compression fractures (VCFs) occur in 20% of people over age 70 [1]. Percutaneous vertebroplasty (PVP) as a minimally invasive vertebral augmentation technique, is an efficient procedure to treat painful osteoporotic VCFs [2]. PVP not only immediately stabilizes the fractured vertebral body, but also enhances loading capacity and relieves pain. However, complications such as new VCFs also have been reported in patients undergone PVP [2].

The incidence of new VCFs varies from 5.5 to 52.0%. There is still controversy about whether new VCFs are generated by the natural progression of osteoporosis or caused by a consequence of augmentation. Rho et al [3] reported that bone mineral density (BMD) and bone cement leakage were risk factors for the development of new VCFs after PVP. However, Ren et al [4] reputed that BMD and bone cement leakage were not significantly associated with new fractures following PVP. Accordingly, risk factors include age, sex, amount of bone cement injected, bone cement leakage, and number of initial symptomatic fractures treated were also considered.

The purpose of this study is to quantify symptomatic new VCFs and to reveal the risk factors for new symptomatic VCFs in patients who underwent PVP.

Methods

Patients

From July 2010 to September 2014, 112 patients (88 females and 24 males; mean age 73.5, aged 54-91), who were treated with PVP for VCFs at our institution were retrospectively

Table 1. Characteristics of patient group

Parameters	Values
No of patients, n	112
Mean age (range, years)	73.5 (54-91)
Sex	
Male	24
Female	88
Number of initial fractures	
1 level	86
2 level	23
3 level	3
Cement leakage into disk	22
BMD (T-score)	-3.1 ± 1.0
Amount of bone cement (mL)	4.1 ± 1.2
Location of vertebrae	
T-L junction	92
Non-T-L junction	20
New VCFs	22

enrolled in this study. The study protocol was approved by Institutional Review Board of the First Affiliated Hospital of Jinan University. All patients provided written informed consent.

Inclusion and exclusion criteria

The inclusion criteria were primary osteoporosis with pain or local tenderness consistent with imaging findings, initial treatment by PVP, no clear history of trauma, and at least 2-year follow-up period after the procedure. The exclusion criteria were loss to the last follow-up and the presence of pathologic compression fractures (metastasis, multiple myeloma). A total of 112 patients (141 vertebrae) met the above criteria and were enrolled in the study.

Vertebroplasty technique

All the vertebroplasty procedures were performed at the Department of Spinal Surgery under sterile conditions with a C-arm fluoroscopic guidance. With the patient in a prone position, local anesthesia (1% lidocaine) was administered over the skin, subcutaneous tissues, muscular tissues, and periosteum of the targeted pedicle. To achieve fracture reduction in some cases, patients were positioned in slight hyperextension with pillows inserted under the chest and pelvis. A 2.5 mm needle was inserted to the anterior third of the vertebral body under biplane fluoroscopic guidance. Polymethylmethacrylate (PMMA) bone cement was injected with a satisfied distribution. Injection was immediately terminated when bone cement dispersion to the posterior one-fourth of the vertebral body on the lateral projection or cement leakage was founded. When necessary, pedicle puncture injection of bone cement was performed on the other side. Patients were bed restricted for 24 hours after PVP. All patients were provided with calcium Vitamin D3 supplementation and bisphosphonates after the procedure.

Comparison parameters

Two spine surgeons (Z.L. and J.D.) evaluated independently the pre- and postoperative radiographs in early follow-up. First, the presence or absence of intradiscal cement leakage was recorded. Cement leakage was defined by the presence of any cement leakage beyond the endplate and into the disc. The possible relationships between cement leakage and the occurrence of adjacent new vertebral fracture after PVP were evaluated. The followed parameters were also evaluated for possible relationships with the occurrence of adjacent new vertebral fracture. Data regarding age, sex, BMD (T-score), amount of bone cement, number of initial symptomatic fractures (levels treated) were collected. The level of fracture was divided into T-L junction (T11-L2) and non-T-L junction.

Statistical analysis

All statistical analysis was processed using SPSS 20.0 software (SPSS, Chicago, IL, USA). Univariate and multivariate binary logistic regression analyses were used to assess a possible relationship between a new vertebral fracture and the following factors: age, sex, BMD, amount of bone cement, cement leakage into the disk and number of initial symptomatic fractures. Data were presented as the mean ± SD. $P < 0.05$ was considered statistically significant.

Results

General data of patients

One hundred and twelve patients, accounting for a total of 141 VCFs, met the inclusion criteria. 86 had 1-level fractures, 23 had 2-level

Table 2. Summary of clinical features of 22 patients with new symptomatic VCFs

No	Sex	Age (years)	BMD (T-score)	Amount of bone cement (mL)	Cement leakage into disk	Initial VCFs	New VCFs	New VCFs occurrence time (months)	Treatment
1	F	80	3.2	4	(-)	T11	T12	43	n.a.
2	F	87	2.6	3/3	(-)	T12/L1	T8	1	n.a.
3	M	72	3.9	2	(+)	L1	L4	15	PVP
4	F	64	4.8	4	(+)	T12	L4	58	n.a.
5	M	71	2.6	4.5	(+)	T9	T8	9	n.a.
6	F	78	2.8	4/3.6	(-)	T11/L1	T11	3	n.a.
7	F	85	3.4	3/3.5	(+)	T12/L1/L3	T11	8	n.a.
8	F	83	3.3	2.5	(-)	T8	T7	14	PVP
9	F	84	3.2	4	(+)	L1	T12	1	n.a.
10	F	73	3.1	5/5	(+)	L2/L3	T12	50	n.a.
11	F	61	4.4	3	(-)	L1	T7/8/11/12	5	PVP
12	F	75	3.4	4/5	(-)	T12/L2		1	n.a.
13	F	68	3	3.6/4	(-)	T11/L1	T12	22	PVP
14	F	68	4.6	2.5/2.5/2.5	(-)	T12/L1/L2	T11	1	n.a.
15	F	71	6.1	4	(+)	T11	L3	27	PVP
16	F	77	3.2	3.6	(-)	T7	L1	19	PVP
17	F	65	2.4	4	(-)	T12	L3/L4	1	PVP
18	F	79	2.6	5	(-)	L2	L3	5	PVP
19	M	84	5.6	4.5	(+)	L1	T12	16	n.a.
20	F	77	4.5	3.5	(+)	T12	T10	25	n.a.
21	M	82	3.8	3.5	(-)	T11	L1	20	PVP
22	F	67	2.9	4	(+)	L3/L4	L4	1	n.a.

n.a. not applicable.

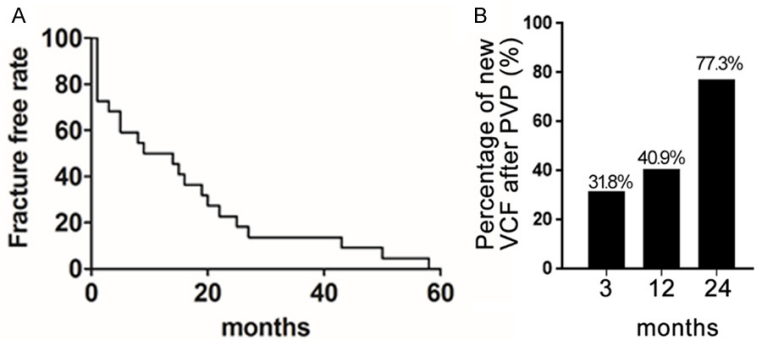

Figure 1. The incident time of new fractures after vertebroplasty by the Kaplan-Meier survival analysis. A. The analytic curve showing patients showed incident free of new fractures after vertebroplasty were included for Kaplan-Meier survival analysis. B. Statistical data presentes the selected time point of percentage of new VCF after PVP.

fractures, and 3 had 3- level fractures. There were 88 females and 24 male patients. The mean age was 73.5 (range 54-91, **Table 1**). No major complication such as cardiovascular events or pulmonary embolism was recorded.

Data analysis

The mean number of initially treated VCFs was 1.26 (range 1-3). There were 22 (19.6%) patients showing new VCFs during the follow-up period (**Table 1**). **Table 2** showed the clinical features of the 22 patients. 13 patients were treated with conservative management. The other 9 patients underwent secondary vertebroplasty for new VCFs (**Table 2**). The incidence of new fractures in 3-months, 1-year and 2-years was 31.8% (6 cases), 40.9% (9 cases), and 77.3% (17 cases) respectively (**Table 2**). Of the 22 patients with new fractures, nearly 50% of the new VCFs occurred within 9 months after PVP, over 70% of the new VCFs within 24 months after PVP (**Figure 1**).

The BMD T-score was -3.7 in patients with new VCFs and -2.9 in patients without new VCFs. 10 patients had cement leakage into the disk with new VCFs and 13 patients had cement leakage into the disk without new VCFs. BMD, number of initial fractures and cement leakage into the

Table 3. Characteristics of patients with and patients without new VCFs (mean ± SD)

Variable	Patients with new VCF (n = 22)	Patients without new VCF (n = 90)	*P* value Univariate	Multivariate
Age (years)	76.4 ± 7.3	72.9 ± 8.3	0.07	0.085
Sex (male/female)	4/18	20/70	0.679	0.999
BMD (T-score)	-3.7 ± 1.0	-2.9 ± 1.0	0.001*	0.003*
Number of initial fractures			0.012*	0.079
1 level	13	73		
≥ 2 levels	9	17		
Cement leakage into disk	10	13	0.03*	0.148
Amount of bone cement (mL)	3.8 ± 0.9	4.2 ± 1.2	0.125	0.159
Location of vertebrae			0.314	0.917
T-L junction	19	73		
Non-T-L junction	3	17		

*Statistical significance was defined as P < 0.05.

disc space between patients with or without VCF showed significant differences (P < 0.05) by univariate analysis. Age was older in the new VCFs group compared with the controls, but the difference was not statistically significant (P = 0.07). Only BMD was significantly associated with new VCFs after PVP determined by multivariate analysis (P < 0.01; **Table 3**).

Discussion

New VCF is a common complication of vertebroplasty that can cause renewed back pain, leading to disability, and compromised satisfaction after PVP [5]. The incidence of new VCFs ranges from 8% to 52% [6]. In our studies, the incidence of new fractures was 20%, which was consistent with other report [4]. We found the incidence of new fractures in 3-month, 1-year and 2-years was 31.8% (6 cases), 40.9% (9 cases), and 77.3% (17 cases) respectively. These results indicate that the occurrence of new fractures is usually developed in the first two years after the procedure.

In our study, lower BMD was the only risk factor of new VCFs after PVP according to multivariate logistic regression. Low BMD is supposed to be a risk factor for new VCFs in several studies [7, 8]. In our study, the average BMD was -2.9 in the control group, however, it decreased to only -3.7 in the new VCFs group, indicating that osteoporosis was an important risk factor of new VCFs. Uppin et al [9] indicated that patients with lower BMP were more likely to develop new VCF. Zou et al [10] also demonstrated that a lower BMD was risk factor of new VCF and vertebroplasty didn't increase the risk of new VCFs. Therefore, the most important risk factor for new VCFs maybe the osteoporosis itself.

Cement leakage was usually occurred after vertebroplasty, with a incidence varies from 5% to 80% [11]. Leakage may accelerate degenerative disk damage and increase the pressure in the intervertebral disks [12]. The increase in pressure and loading changes on adjacent levels after vertebroplasty, especially in patients with osteoporotic vertebrae, may lead to new VCFs [13]. Komemushi et al [14] reported that cement leakage into the disk increased the risk of new fracture. Cement leakage has been proposed as a predictive factor for vertebral fractures. In our study, cement leakage was a risk factor of new VCFs as shown by univariate analysis, however, no statistically significant differences in cement leakage were found by multivariate analysis, which is consistent with a previous report [4].

The number of initial symptomatic fractures is considered to be a risk factor for new fractures after PVP [4]. A previous study demonstrated that the number of VCFs at baseline was the only risk factor for new VCFs [15]. Voormolen et al [16] also indicated that the presence of more than two preexisting VCFs increased the risk of new fracture. However, some studies showed that the number of initial VCFs was not related with the emergence of new fractures after PVP [7]. In our studies, the presence ≥ 2 preexisting VCFs was a significant factor of new VCFs as

shown by univariate analysis, however, there was no statistically significant differences by multivariate analysis.

Delmas et al [17] found that the thoracolumbar location of the initial compression fracture was the only predictor of the risk for new VCFs after PVP. He indicated that range of motion of the spine was at the maximum lead to high incidence of new fractures at the thoracolumbar junction. However, we found no differences in the incidence of new VCFs between T-L levels and no T-L levels.

The optimal amount of injected bone cement is still controversial [5]. Previous studies indicate that large volume of cement injected will increase the pressure on the adjacent vertebrae and increase the risk of new VCFs. Chosa et al [18] reported that large volume cement injection increased the incidence of new fractures compared with small volume cement injection. However, other studies demonstrated that no correlation between cement volume and the occurrence of new VCFs [7]. In our study, the cement volume and new VCFs were not correlated as shown by univariate and multivariate analysis.

There are several limitations in our study. Firstly, this is a retrospective study. Only symptomatic new VCFs was identified as re-fracture, and the actual re-fracture rate maybe higher than the reported rate in our study. True incidence of new VCFs will be detected by MRI for each patient after vertebroplasty. Secondly, in our study, the sample size was relatively small. However, our study had strict inclusion and exclusion criteria with long-term follow-up periods, which led to a homogenous patient sample.

Disclosure of conflict of interest

None.

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