

Retrospective Evaluation

Risk Factors for the Occurrence of Insufficient Cement Distribution in the Fractured Area after Percutaneous Vertebroplasty in Osteoporotic Vertebral Compression Fractures

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Background: Insufficient cement distribution (ICD) in the fractured area has been advocated to be responsible for unsatisfied pain relief after percutaneous vertebroplasty (PVP) for osteoporotic vertebral compression fractures (OVCFs). However, little is known about risk factors for the occurrence of ICD.

Objective: The present study aimed to identify independent risk factors of the emergence of ICD.

Study Design: A retrospective cohort study.

Setting: Department of spinal surgery, an affiliated hospital of a medical university.

Methods: Patients who underwent PVP for single-level OVCF from January 2012 to September 2014 and met this study's inclusion criteria were retrospectively reviewed. Associations of ICD with co-variables (age, gender, bone mass density with a T-score, amount of injected cement, cement leakage, fracture level, fracture age, fracture severity grade, and location of the fractured area) and the influence of ICD on pain relief were analyzed.

Results: A total of 225 patients were included. ICD was found in 26 (11.6%) patients. Fractured area located in the superior portion of the index vertebra was significantly associated with occurrence of ICD. No further significant associations between the studied co-variables and emergence of ICD were seen in the adjusted analysis. In addition, patients with ICD had significantly higher immediate postoperative visual analog scale scores of back pain compared with those with sufficient cement distribution in the fractured area.

Limitation: Location of the fractured area and cement distribution in the fractured area could not be evaluated quantitatively.

Conclusions: The incidence of ICD is higher in patients with the fractured area located in the superior portion of the index vertebra and ICD might be responsible for unsatisfied pain relief after PVP for OVCFs.

Key words: Percutaneous vertebroplasty, insufficient cement distribution, fractured area, risk factor, osteoporosis, vertebral compression fracture, spine, unsatisfied pain relief, cement augmentation

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Osteoporotic vertebral compression fractures (OVCFs) are very common in the elderly, with an estimated 1.4 million new fractures occurring every year worldwide (1). OVCFs may cause pain, limited physical function, decreased quality of life, and increased mortality (2-4). In cases with persistent pain, OVCFs have been traditionally treated with bed rest, analgesics, braces, and physical therapy (5,6). However, such treatments are only partially effective, and about one third of patients have been reported to suffer from persistent pain and progressive functional limitation (7,8).

Since the introduction of percutaneous vertebroplasty (PVP) by Galibert et al in 1987 (9), this minimally invasive therapy has gained popularity as a stabilizing treatment for symptomatic OVCFs that are refractory to conservative management (10). Despite patients typically presented with rapid and durable pain relief and often regaining lost function (7,11), unrelieved pain after PVP has been reported and insufficient cement distribution (ICD) in the unstable fractured area of the index vertebra might explain this observation (12-14). However, few studies are available concerning the reasons why ICD could happen.

Therefore, it seems logical to assume that the identification of the risk factors related to the occurrence of ICD would help to minimize the incidence of ICD, which could ultimately optimize the results of our treatment. Thus, the purpose of this study was to identify independent risk factors for the emergence of ICD following PVP in patients with OVCFs.

METHODS

Patients

The medical records of patients who underwent PVP for painful vertebral compression fractures between January 2012 and September 2014 at our institution were retrospectively reviewed. Protocol of this study was approved by the ethics committee of our hospital and written informed consent was obtained from each patient. The inclusion criteria were single-level symptomatic OVCF treated with PVP, available preoperative magnetic resonance imaging (MRI) and postoperative computed tomography (CT) scan. The exclusion criteria were non-osteoporotic vertebral compression fractures or compression fractures secondary to other factors, such as pathologic fractures due to metastasis or symptomatic hemangioma; unavailable preoperative MRI and postoperative CT scan; and multiple-level PVP patients.

PVP

All of PVP procedures were performed by 3 experienced spinal surgeons with standard training in PVP techniques. Patients were carefully positioned in a prone position with an extended posture on a radiolucent operating table. PVP was performed under local anesthesia (1% lidocaine) in all cases. A bilateral transpedicle approach was used for all patients. According to Jensen et al's technique (15), under fluoroscopic C-arm guidance, 11 to 13 gauge bone biopsy needles were inserted parallel to the superior and inferior edges of the pedicle, or in a slightly descending course through the pedicle. The stylet was removed from the trocar when the needle tip was optimally positioned, after which bone cement, which was thicker than a toothpaste-like consistency, was inserted into the vertebral body. The bone cement was prepared by combining polymethylmethacrylate powder with sterile barium sulfate for opacification, followed by the addition of liquid monomer (Tianjin Synthetic Material Research Institute, Tianjin, China). The cement injection process was monitored continuously under C-arm fluoroscope in the lateral plane. Injection was temporarily halted when initial cement leakage, without any discomfort to the patients, was noted and terminated on the re-occurrence of cement leakage or when bone cement reached the posterior quarter of the vertebral body to avoid cement leakage into spinal canal or neural foramina. In general, bone cement was injected until there was a satisfactory distribution judged by the operators. Patients were on enforced bed rest for a few hours and treated with calcium and vitamin D supplements for anti-osteoporosis after PVP.

Data Collection

Data were collected on age, gender, preoperative and immediate postoperative visual analog scale (VAS) score for back pain, bone mass density (BMD) with a T-score, amount of injected cement, cement leakage, fracture level, fracture age, fracture severity grade, location of the fractured area, and cement distribution in the fractured area. Two independent spinal surgeons were involved in the radiographic evaluation. When there was disagreement between them, a consensus meeting was held.

Age, gender, preoperative and immediate postoperative VAS for back pain, BMD T-score, amount of injected cement, fracture level, and fracture age were recorded in reviewing medical records of the patients. VAS was routinely used to record the degree of back

pain felt by all patients before surgery and on the second day after surgery. The measures were recoded before analgesic drug therapy. The BMD T-scores were measured using dual-energy x-ray absorptiometry (QDR4500, Hologic, Bedford, USA), and L2-L4 vertebra were selected for these measurements. Cement leakage, defined as the presence of any extravertebral cement, was assessed on the postoperative CT scan of the treated levels. Fracture level of T1-T10, T11-L2, and L3-L5 were defined as thoracic, thoracolumbar, and lumbar segments, respectively. Fracture age was defined as the time between the onset of new back pain related to a radiological confirmed fracture and admission into hospital. Fracture severity grade was characterized according to the semiquantitative classification of Genant et al (16), in which the diminished vertebral height was in the severity range from mild to moderate to severe, or 20% to 25%, 26% to 40%, and more than 40%, respectively, of height reduction. Location of the fractured area was defined as the line-shape area with hypo-intensity in MRI T1-weighted, T2-weighted, short-tau-inversion-recovery sequences and increased density in CT imaging indicating impaction of the fractured area and classified into 3 types including superior, middle, and inferior with the fractured area in the corresponding parts of the index vertebra observed in the sagittal images (Fig. 1). Patients with unclear MRI or extremely irregular fractured area that involved 2 or 3 parts of the index vertebra were also excluded from this study.

For the purpose of this study, patients were divided into those who obtained sufficient cement distribution in the fractured area (Sufficient Group) and those who did not obtain sufficient cement distribution in the fractured area (Insufficient Group). Sufficient cement distribution in the fractured area was defined as cement distribution in more than half of the fractured area observed on postoperative CT scan of the treated levels (Fig. 2). On the contrary, ICD was defined as cement distribution in less than half of the fractured area (Fig. 3).

Statistical Analysis

Quantitative variables were described using means and standard deviations, whereas frequencies were reported for qualitative variables. Univariate analysis was used to assess clinical outcome of preoperative and immediate postoperative VAS for back pain within and between the 2 groups and risk factors (age, gender, BMD T-score, amount of injected cement, cement leakage, fracture level, fracture age, fracture severity grade, and location of fractured area) associated with

the emergence of ICD between the 2 groups. Continuous data were compared using the student t test and Mann-Whitney test or Wilcoxon signed-ranks test when data were non normality or heteroscedasticity, whereas discontinuous data were analyzed using the Chi-squared test or Fisher exact test and Mann-Whitney test when data were ordinal. In addition, a multivariate stepwise logistic regression analysis was performed to identify which independent factors helped to predict the occurrence of ICD, with adjustments made for other potential confounding factors. These statistical tests were 2-tailed and a $P < 0.05$ was considered to be significant. Corresponding 95% confidence limits (CIs) were calculated with confidence interval estimation. Statistical analysis was conducted using SPSS statistical package, version 13.0 (SPSS Inc., Chicago, IL).

RESULTS

A total of 225 cases were finally included in this study. The associated clinical and radiographic features were described in Table 1. ICD was found in 26 (11.6%) patients. The postoperative back pain score in both groups was significantly lower in comparison to preoperative back pain score ($P < 0.001$). The immediate postoperative VAS for back pain, however, was significantly higher in the Insufficient Group than in the Sufficient Group ($P < 0.001$) while no statistical differences in preoperative VAS for back pain between the 2 groups were identified ($P = 0.525$) (Table 1).

Non-adjusted comparisons using univariate analysis between patients with and without sufficient cement distribution in the fractured area showed that there were no significant differences between the 2 groups regarding age, gender, BMD T-score, amount of injected cement, cement leakage, fracture level, fracture age, and fracture severity grade ($P > 0.05$) except location of the fractured area ($P = 0.028$) (Table 1).

Multivariate stepwise logistic regression analysis also indicated that age, gender, BMD T-score, amount of injected cement, cement leakage, fracture level, fracture age, and fracture severity grade were not significantly associated with the occurrence of ICD ($P > 0.05$). Only location of the fractured area was revealed to be significantly associated with the emergence of ICD ($P = 0.040$). According to dummy variable analysis of the model, patients with the fractured area located in the superior portion of the index vertebra had a 4.8-times (95%CI 1.1 – 21.7, $P = 0.041$) higher likelihood for occurrence of ICD than those with the fractured area being in the inferior portion, but no statistical

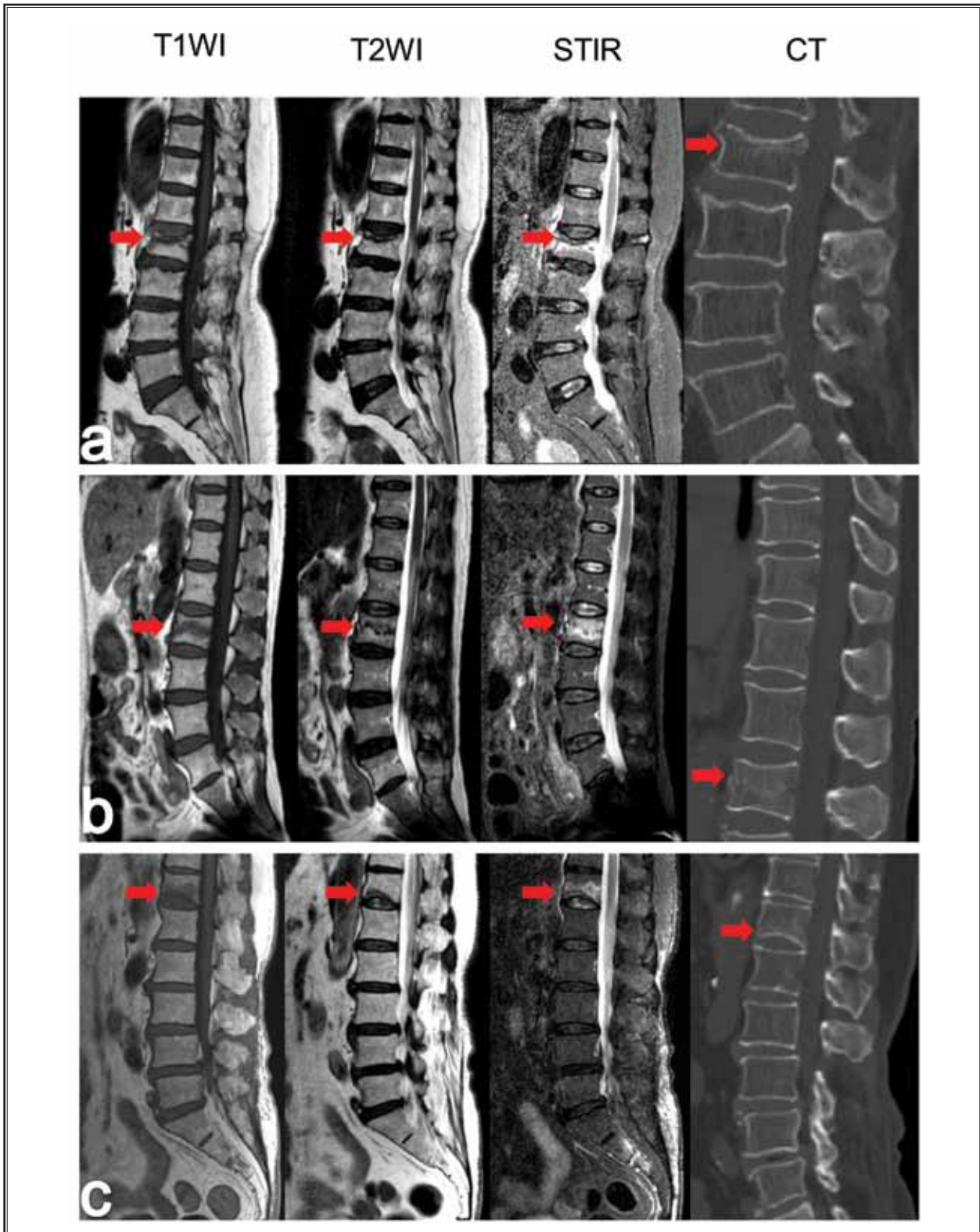


Fig. 1. Preoperative MR and CT images show the fractured area located in the superior (a), middle (b), and inferior (c) portion of L2, L2, and T12 OVCFs (red arrow).

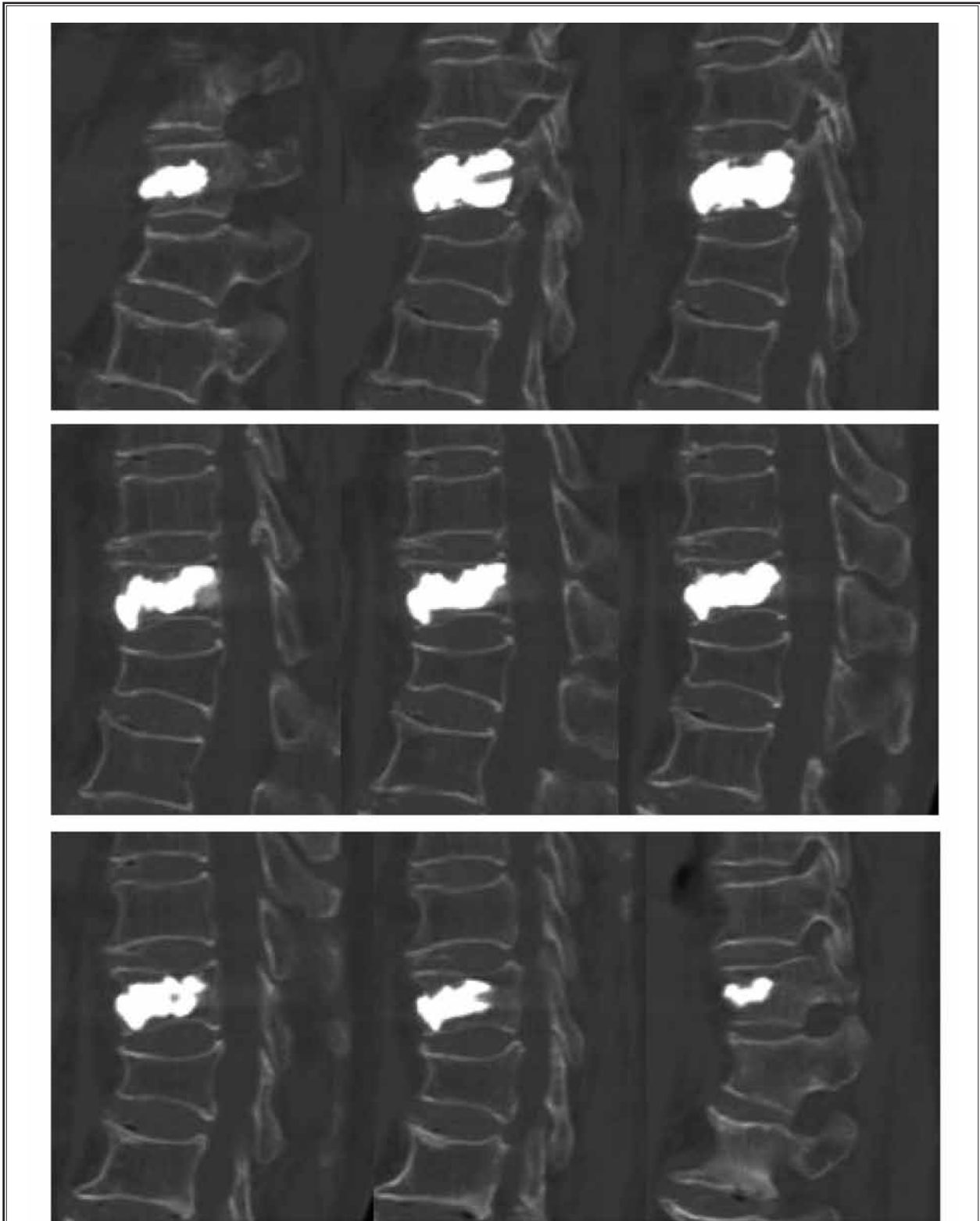


Fig. 2. Postoperative CT images of T11 augmented vertebra from left to right show sufficient cement distribution in the fractured area.

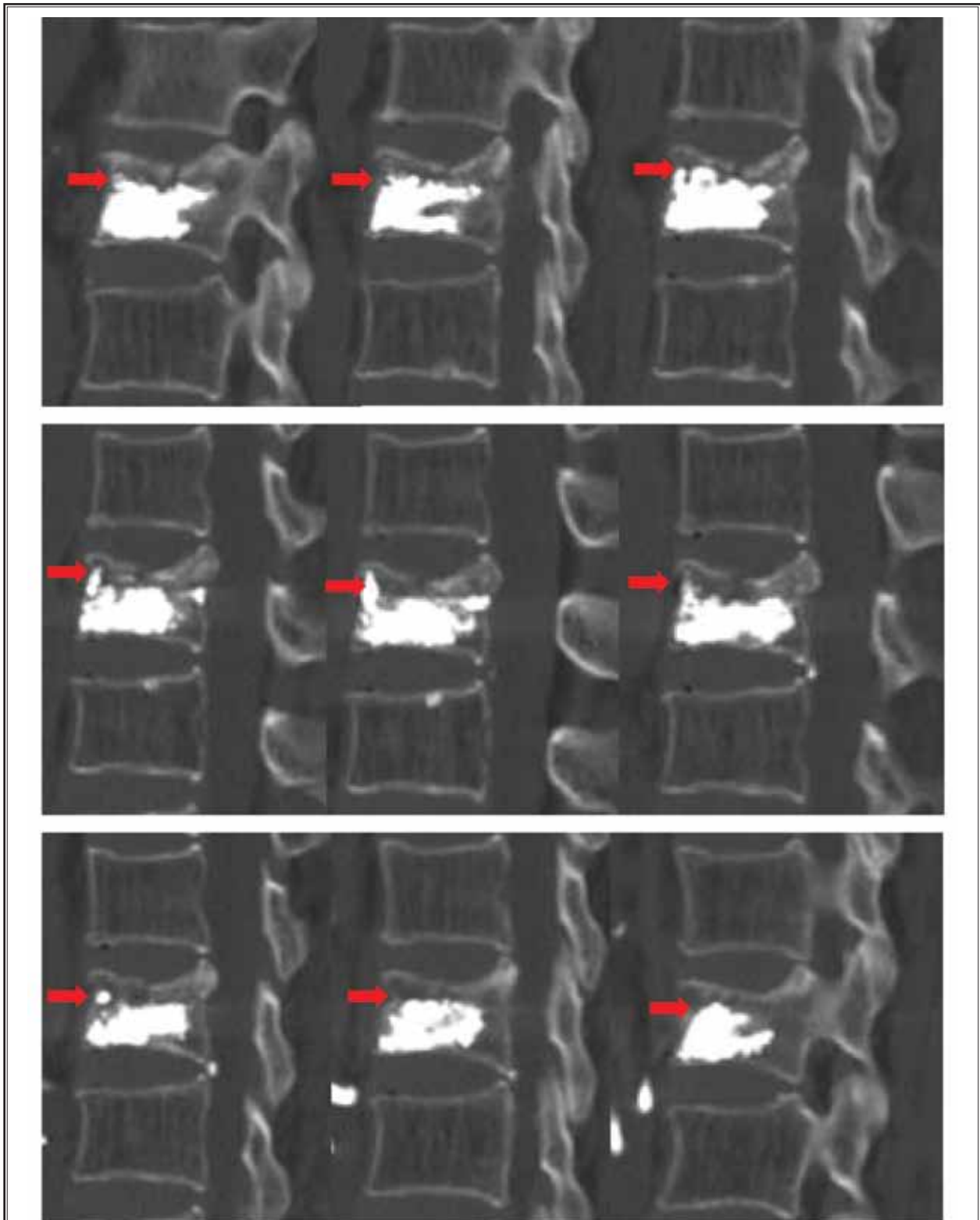


Fig. 3. Postoperative CT images of L2 augmented vertebra from left to right show insufficient cement distribution in the fractured area (red arrow).

Risk Factors for the Occurrence of Insufficient Cement Distribution

Table 1. Results of univariate analysis for demographic and clinical characteristics of the patients with sufficient and insufficient cement distribution in the fractured area.

	Cement distribution in the fractured area		Total (n = 225)	Comparison (P value)
	Insufficient (n = 26)	Sufficient (n = 199)		
Age (years)	73.4 ± 6.9	73.9 ± 10.0	73.8 ± 9.7	0.504
Gender (male/female)	6/20	28/171	34/191	0.245
BMD (T-score)	-4.1 ± 0.8	-4.0 ± -0.8	-4.0 ± 0.8	0.285
Amount of injected cement (mL)	5.4 ± 1.6	5.0 ± 1.6	5.1 ± 1.6	0.232
Cement leakage (yes/no)	15/11	81/118	96/129	0.100
Fracture level (thoracic/thoracolumbar/lumbar)	2/19/5	44/121/34	46/140/39	0.228
Fracture age (months)	1.7 ± 0.6	1.8 ± 0.7	1.8 ± 0.7	0.825
Fracture severity grade (mild/moderate/severe)	14/11/1	99/65/35	113/76/36	0.350
Location of the fractured area (superior/middle/inferior)	18/6/2	84/70/45	102/76/47	0.028*
Preoperative VAS	7.6 ± 0.6	7.5 ± 0.8	7.5 ± 0.8	0.525
Immediate postoperative VAS	4.6 ± 0.7	2.1 ± 0.9	2.4 ± 1.2	< 0.001*

*Statistically significant

Table 2. Results of multivariate stepwise logistic regression analysis for occurrence of insufficient cement distribution in the fractured area.

	OR	95%CI	P value
Location of the fractured area			0.040*
Middle versus inferior	1.9	0.4 – 10.0	0.433
Superior versus inferior	4.8	1.1 – 21.7	0.041*

*Statistically significant

differences could be found between patients with the fractured area being in the inferior portion and those with the fractured area located in the middle portion ($P = 0.433$) (Table 2).

Discussion

Use of PVP as an alternative treatment for some OVCFs refractory to conservative management is controversial, primarily due to 2 previous independent level 1 trials, both of which found that patients randomized to PVP did not experience decreased pain or disability relative to patients in the placebo arm (17,18). Furthermore, although these 2 studies have been criticized for a variety of reasons, the American Academy of Orthopedic Surgeons believed that these 2 studies did have sufficient power to detect the minimal clinically important difference in pain, and clinical practice guideline issued by the American Academy of Orthopedic Surgeons strongly recommended against PVP for symptomatic OVCFs (19). Despite these controversies, increased use of PVP for managing OVCFs has been the

trend, likely owing to individual physician experience on the efficacy of PVP, some guidelines recommending PVP (7,11), as well as numerous and ever-increasing research studies showing its benefits (20-24).

To the best of our knowledge, this is the first study conducted to identify the risk factors for the occurrence of ICD following PVP in patients with OVCFs. In addition to osteoporosis as fracture etiology, we restricted the analysis to patients with a single-level fracture and typical location of the fractured area for creating a uniform cohort and simplifying interpretation of the results. Our current study found that the location of the fractured area was revealed to be an independent risk factor for predicting the emergence of ICD. To be specific, ICD was inclined to happen in patients with the fractured area located in the superior portion of the index vertebra. Additionally, patients with ICD were found to experience a lower degree of back pain relief compared with those with sufficient cement distribution in the fractured area.

Stabilization of the fractured area and restora-

tion of vertebral strength are the most acceptable mechanisms for pain relief after PVP in treatment of OVCFs for the reason that back pain caused by OVCFs is mostly likely to be related to periosteal nerves aggravated by micromotion at the fractured area (25). This hypothesis has been supported by biomechanical studies, which indicated that PVP generally restored or increased vertebral strength and stiffness relative to pre-fracture values and likely provided stabilization of the vertebral body so as to prevent micromotion of the fractured area (26-28). In our present study, based on cement distribution in the fractured area observed in postoperative CT scan, the cohort was categorized into Sufficient Group, consisting of those with sufficient cement distribution in the fractured area, and Insufficient Group, composed of those with ICD, and a higher degree of pain relief was found in the Sufficient Group than in the Insufficient Group. Additionally, incidence of sufficient cement distribution in the fractured area was found to be as high as 88.4%, which was similar to the reported success rate of 89% – 93% in PVP for OVCFs (7). These findings, to some extent, support the biomechanical results for explanation of mechanisms of pain relief after PVP for OVCFs from a clinical aspect, which is consistent with studies conducted by He et al (12), Yang et al (13), and Chui et al (14). Despite unsatisfactory results in the Insufficient Group, patients in this group still experienced some degree of pain relief, which might be explained by partial restoration of vertebral stiffness and strength or thermal (29,30), chemical (31), or placebo effects (17,18).

If the increased stiffness yields stabilization of micromotion in the fractured area, the most important factor for pain reduction is advocated to be the spatial distribution in the fractured area and amount of injected cement is believed to be the second influencing factor (32). Therefore, location of the fractured area and amount of injected cement were considered in our present study. Fracture level and fracture severity grade were also included to eliminate the effect of variants in the size of vertebral bodies on the amount of injected cement caused by these 2 factors. Both univariate and multivariate analyses showed no significant relationship between the amount of injected cement, fracture level, fracture severity grade, and occurrence of ICD, which is in agreement with perspective held by He et al (12). However, significant association of location of the fractured area with occurrence of ICD was found and ICD tended to happen in patients with the fractured area located in the superior portion of the index

vertebra. In our view, this is mainly due to Jensen et al's technique (15) we adopted in performing PVP, in which the needle advances routinely towards anterior inferior part of the index vertebra and cement is relatively difficult to diffuse into the fractured area located in the superior part that is comparatively far away from the needle placement when the recommended amount of cement is injected.

Cement leakage has been referred as a possible risk factor of ICD considering that it might hinder injecting the planned amount of bone cement (14). In fact, this speculation is reasonable because some operators argued that injection of bone cement should be terminated as soon as any cement leakage was noted (33). However, a significant relationship between cement leakage and occurrence of ICD could not be detected in our study, although the incidence of cement leakage was higher in the Insufficient Group than in the Sufficient Group. The reason we speculate is that cement injection was temporarily halted when initial cement leakage without any discomfort to the patients was noted and terminated on recurrence of cement leakage in our cases. Furthermore, a certain amount of cement could be considered to be injected in the contralateral side. Obviously, compared with immediate termination on initial cement leakage, the operations we performed should decrease the incidence of ICD.

Limitations

Firstly, we could not quantitatively and accurately locate the fractured area because almost all the fractured areas were irregular, although we have excluded cases with unclear MRI and extremely irregular fractured areas that involved 2 or 3 parts of the index vertebra. Secondly, definition of sufficient/insufficient cement distribution in the fractured area was only based on observations on postoperative CT instead of accurate measurements as we think measurements of the irregular shape of cement distribution might be impossible. The above factors might have effects on our results, which could not be cancelled out in this study. Furthermore, some other influencing factors that are not taken into consideration in this study might exist. Even so, we believe that a significant association of the occurrence of ICD with the location of the fractured area does exist. In addition, although we consider that the difference in immediate postoperative VAS for back pain could be attributed to cement distribution in the fractured area, there are other variables that could confound the results, such as degree of kyphosis cor-

rection, thoracolumbar fascia injury, fracture morphology, etc. It would be desirable that would be further studies on the influencing factors of pain relief after PVP for OVCFs by multivariate analysis to eliminate the confounding variables.

CONCLUSION

Location of the fractured area is an independent risk factor for the occurrence of ICD and patients with the fractured area located in the superior portion of the index vertebra have a higher incidence of ICD after

PVP for OVCFs. Age, gender, BMD T-score, amount of injected cement, cement leakage, fracture level, fracture age, and fracture severity grade do not increase the risk of occurrence of ICD. In addition, ICD might be responsible for the unrelieved pain after PVP for OVCFs. We should pay attention to cement distribution in the fractured area and make some modifications of the PVP technique by making needles travel relatively close to the fractured area located in the superior portion of the index vertebra when performing PVP for OVCFs.

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