Retrospective Study

Earlier Vertebroplasty for Osteoporotic Thoracolumbar Compression Fracture May Minimize the Subsequent Development of Adjacent Fractures: A Retrospective Study

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Background: Percutaneous vertebroplasty (PVP) is widely used to treat osteoporotic vertebral compression fractures (OVCFs). The influence of timing (early vs. late) of PVP on the development of adjacent vertebral fractures (AVF) has rarely been discussed.

Objective: This study aimed to compare the incidence of AVF among patients who received early PVP (≤ 30 days after symptom onset, EPVP) or late PVP (> 30 days after symptom onset, LPVP) in the thoracolumbar region (T10 to L2) after a 1-year follow up.

Study Design: A retrospective cohort study.

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

Methods: Patients who had single-level, T-score ≤ -2.5 of lumbar bone mineral density (BMD), primary OVCF in the thoracolumbar region (T10 to L2) and who received PVP between July 2012 and June 2014 were included in the study. They were divided into early PVP and late PVP groups according to the interval between symptom onset and treatment. The risk factors associated with subsequent AVFs were analyzed.

Results: Of the 225 patients reviewed, 124 met the criteria and were followed for a minimum of 1 year. Eleven patients (14.1%) in the EPVP group (n = 78) and 18 patients (39.1%) in the LPVP group (n = 46) experienced an AVF during the first year following vertebroplasty. Outcomes were significantly better in patients with higher bone mineral density, lower cement volume, and without cement leakage ($P < 0.01$). Cox regression indicated an increase risk for AVF for LPVP, with an adjusted hazard ratio of 6.08 (95% confidence interval: 2.50–14.81).

Limitation: The incidence of AVFs could be over estimated due to this being a retrospective study with a small case number and lack of either biomechanical study of intra-vertebral cement distribution by times to support the result.

Conclusions: Compared with later interventions, PVP performed within 30 days after fracture development may be associated with a lower risk of adjacent fractures in the thoracolumbar region.

Key words: Percutaneous vertebroplasty, osteoporosis, osteoporotic vertebral compression fracture, adjacent vertebral fracture

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Percutaneous vertebroplasty (PVP) is currently widely used to treat osteoporotic vertebral compression fractures (OVCF). The related cement augmentation procedure is associated with reduced mortality (1,2) and lower re-admission rates in the elderly following OVCF (3).

However, the possibility of an increased risk of adjacent vertebral fracture (AVF) has been reported. This typically develops within a month following surgery (4) and the fractures are often located in the thoracolumbar region (5,6). Previous biomechanical studies suggest that cement augmentation may increase the rate of AVFs due to increased stress in the adjacent levels after PVP (7), recent prospective studies have reported that the incidence of AVFs is similar or even lower when cement augmentation is used to treat acute OVCF (8,9). Presently kyphoplasty is more favorable than vertebroplasty because of the advantages of greater vertebral height reduction and possible lower incidence of adjacent fractures. But vertebroplasty is believed to be more cost-effective in treating OVCF-related pain and, in some hospitals, is still the main method of treatment for osteoporotic compression fractures due to its efficacy for pain relief as well as lower costs when compared to kyphoplasty (10,11).

Previous studies with regards to AVFs following PVP used different follow-up periods and did not evaluate the timing of the PVP intervention. In this study, we analyzed the AVFs that occurred after PVP for treatment of a single-level fracture in the thoracolumbar region. This study focused on the timing of the PVP, as well as the occurrence of AVFs, and analyzed patient characteristics, radiographic findings, and cement leakage to identify the risk factors associated with their clinical outcomes.

Methods

Patient Eligibility

All patients treated with single-level vertebroplasty at a hospital in Taiwan from June 2012 to July 2014 were retrospectively reviewed. A total of 225 patients who experienced single-level OVCF and who received PVP were reviewed. Approval was obtained from the institutional review board and the ethics committee of the Buddhist Dalin Tzuchi Hospital, Taiwan (No. B10502021). The inclusion criterias were primary OVCFs and a lumbar bone mineral density (BMD) T-Score ≤ -2.5. In our institute, all patients with OVCF were advised to receive conservative treatment with brace protection and analgesia at their first visit. PVP was offered for those who presented with their pain score ≥ 7 at 2 weeks, and for patients with persistent back pain with pain score ≥ 5 at one month. All patients had a preoperative spinal x-ray including an anteroposterior view, a lateral view, and magnetic resonance imaging (MRI) for diagnosis of OVCF. Preoperatively, lumbar bone mineral density (BMD) measurement was obtained with dual-energy x-ray absorptiometry (Hologic Discovery, WI, Bedford, MA, USA), and the corresponding T-score was calculated. Each patient's body mass index (BMI) was also calculated.

Twelve patients with a history of proven malignancy, 5 patients who were bedridden because of medical disease, 2 regular steroid users, and 1 chronic renal failure patient receiving hemodialysis were excluded. Four patients with a history of spinal instrumentation and fusion were also excluded. Forty patients did not complete the 1-year follow-up. These included 10 patients who died and 30 who were lost to follow-up. One hundred and thirty of the remaining 161 cases experienced OVCF in the thoracolumbar region between T10 and L2. Two of these patients later underwent an instrumentation procedure because of cement leakage and persistent back pain; they and 1 patient with infection were excluded from this study. Three patients received cement augmentation at the same level within 3 months of the initial procedure and were also excluded from this study. In total, 124 cases with disease located in the thoracolumbar region were included (T10 to L2) and analyzed to identify the risk factors associated with the development of AVFs (Fig. 1).

Vertebroplasty Procedure

Before surgery, the patient was placed on a radiolucent table in the prone position with a pillow over the chest to keep the thoracolumbar spine in a hyperextended position to maintain reduction. An 11-gauge needle was advanced to the site of the fracture under fluoroscopic guidance after local anesthesia (1% lidocaine) was administered. The needle tip was placed over the anterior third of the vertebral body, and bone cement (Simplex P Bone Cement; Stryker, Kalamazoo, MI, USA) was injected in the doughy phase using 1-mL syringes. A unilateral approach was used in most cases; however, if the bone cement did not distribute though the midline of the vertebral body, the surgeon used a contralateral side approach. The injection was terminated if the bone cement dispersed to the posterior one-fourth of the vertebral body on the lateral projection

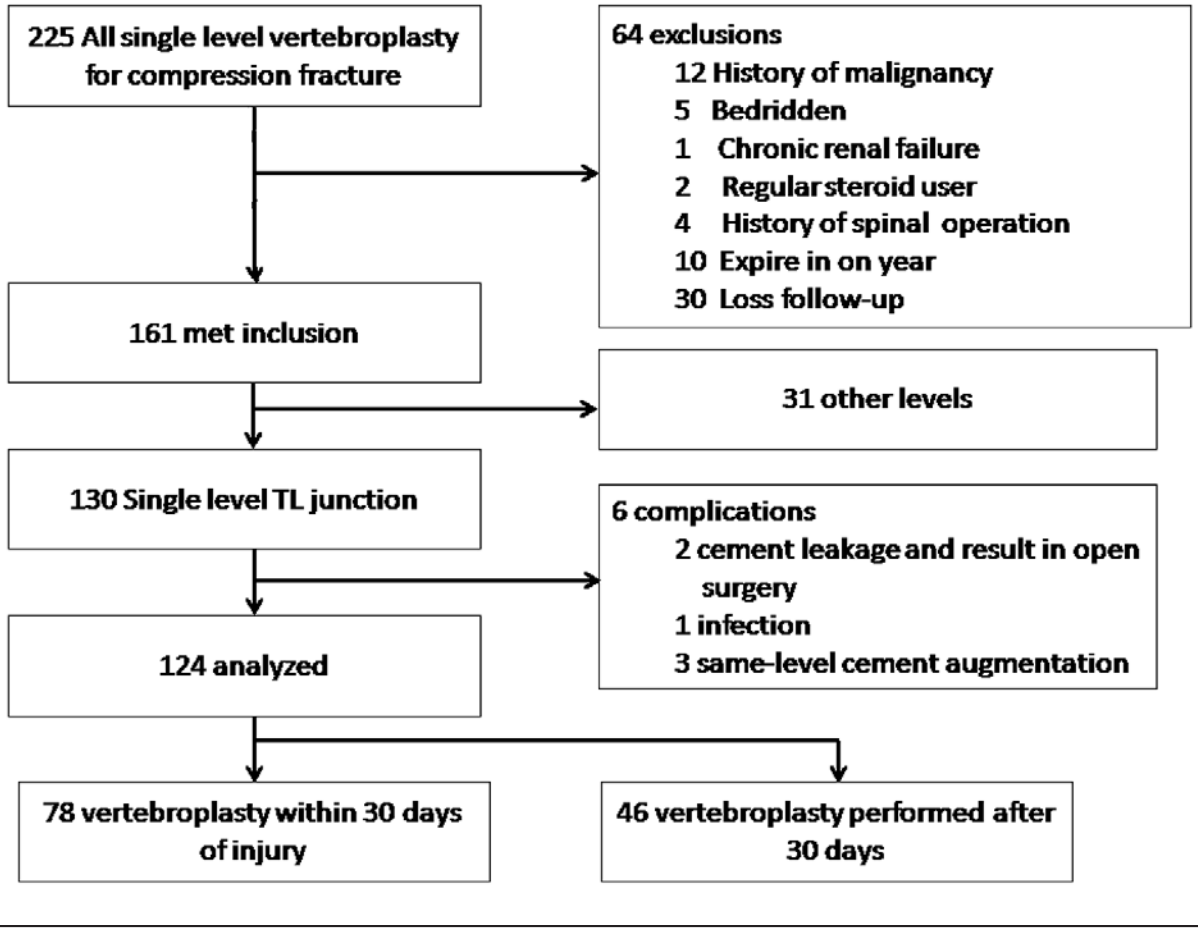

Fig. 1. *Flow chart of the study.*

or in cases of cement leakage. After needle removal, bed rest was enforced for 30 minutes, after which the patient was allowed to ambulate. After the operation, all patients were treated with calcium supplementation and bisphosphonates.

Parameters Observed

Collected and recorded data included patient's age, gender, BMI, BMD (T-score), preoperative and immediate postoperative visual analog scale (VAS) of pain, fracture level, the amount of bone cement injected, and the time when the fracture happened. This information enabled calculation of the interval between symptom onset and PVP. For patients whose fractures occurred more than 3 months before the PVP, the time was recorded as > 90 days.

X-ray Measurements

X-rays were reviewed and measurments of cement leakage into the disk, preoperative angles, postoperative wedge angles, and the postoperative T–L Cobb angles were taken and recorded. All radiographs were stored in Digital Imaging and Communications in Medicine (DICOM) format and reviewed using the PACS v. 3.0.11.4 BN2 (Infinitt, Phillipsburg, NJ, USA). The vertebral wedge angles were measured on both preoperative and postoperative x-rays. The angle was defined and measured at the lower endplate of the upper vertebra and the upper endplate of the lower vertebra at the fracture site on a neutral lateral x-ray film (Figs. 2a, b). The Cobb angle was measured as the angle between the upper endplate of T10 and the lower endplate of L2 on postoperative lateral x-ray (Fig. 3). These

radiological findings were interpreted and recorded by 2 independent expert reviewers who were blinded to the BMD results and the final results were an average of the data recorded by these 2 reviewers.

Criteria for Adjacent Vertebral Fracture (AVF)

An AVF was defined as the recurrence of back pain in the absence of intervening major trauma. X-ray examinations of these patients showed wedging changes in VCFs and MRI examinations showed vertebral marrow edema by reading low and high signal intensity on T1- and high signal on T2-weighted examinations of the areas adjacent to the level where the previous PVP took place. The time when the AVFs occurred was defined as the time between the operation and confirmation of a new fracture by x-ray or MRI examination following the occurrence of new back pain.

Statistical Analysis

All data collected were entered into SPSS v. 22 (SPSS Inc., Chicago, IL, USA) for further analysis.

PVP performed within 30 days after symptom onset was defined as early PVP (EPVP), whereas PVP performed 30 days later was defined as late PVP (LPVP). Demographic data between the 2 groups were compared using the t-test and the Chi Square test. One-year postoperative rates of freedom from AVFs between the 2 groups were also calculated using the Kaplan–Meier method and were tested with the log-rank test. We employed a Cox proportional hazards regression analysis to compute the adjusted hazards ratio (AHR) and the corresponding 95% confidence interval (CI) for AVFs between them after taking into consideration the baseline variables, including gender, age, BMD, BMI, cement volume, presence or absence of cement leakage, and x-ray parameters including preoperative and postoperative wedge angles and post-PVP Cobb angles.

Results

The median age of these 124 patients was 76.9 years (range, 50-94 years), and 108 of the patients were women (87.1%). Fifty-eight patients (46.8%) experienced VCF at the L1 level, 21 (16.9%) at L2, 33 (26.6%) at T12, 9 (7.3%) at T11, and 3 (2.4%) at T10. Among these patients, 29 (23.4 %) experienced an AVF during the first year following the initial surgery.

Characteristics of patients with EPVP were compared to those of LPVP and then charted (Table 1). There were no significant differences between the 2 groups with regards to age, BMD and BMI. But the levels of preoperative VAS and the immediate postoperative VAS levels appeared to be higher in the EPVP group than in the LPVP group (Both with *P*-values < 0.05) (Table 1).

Multivariate Cox regression analysis revealed that lower BMD, higher cement volume, female gender, and disc cement leakage were statistically significant risk factors for an AVF. LPVP was associated with a poorer outcome regarding AVF and was associated with an AHR of 6.08 (95% CI 2.50–14.81) compared to EPVP (Fig.

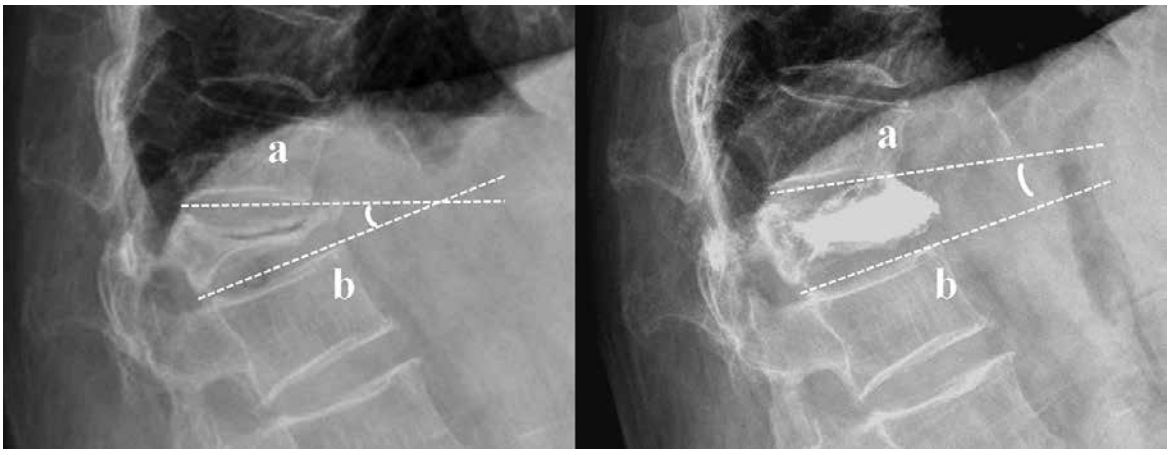

Fig. 2. *A preoperative wedge angle and b postoperative wedge angle were based on the lower end plate of the upper vertebral body (dotted line a) and the upper end plate of the lower vertebral body (dotted line b).*

4). All the radiologic parameters were not significantly associated with the risk of AVFs (Table 2).

We compared the radiographic findings in these 2 groups and found that the preoperative local wedging angle was smaller in the EPVP group (–15.4 ± 8.1 vs. –19.4 ± 9.7 degrees, $P = 0.016$). The cement volume and the postoperative angle were not significantly different between the 2 groups (Table 3).

Discussion

Cement augmentation procedures, including PVP or kyphoplasty, are now widely accepted for the treatment of OVCFs. These procedures reduce pain, improve patients' quality of life, and reduce the mortality of the geriatric population and were used for treatment of both acute and chronic vertebral fractures (13-15). However, an adjacent-level fracture may be accelerated by vertebroplasty and commonly occurs at the thoracolumbar junction (4,6).

On the basis of different inclusion criteria, studies have reported the risk of an adjacent fracture after PVP may increase with a lower BMD (6,16-18), greater age (16,19), female gender, and cement leakage to disc (19,20), intervertebral vacuum (16), lower BMI (21), increased preoperative segmental kyphosis (22), greater anterior height restoration rate (18), the distribution of cement within the fracture (23) and a larger number of fractures (17,23-25).

Since there is a general consensus that the specific biomechanical anatomy of the transition zone (26) of spine leads to a higher risk of AVF at TL junction and a lower BMD may increase the risk of AVF, we limited our analysis to cases with a lower BMD that involved the thoracolumbar region (T10 to L2) and single-level fractures. We focused on the incidence of AVFs within 1 year after the initial surgery.

The timing of the PVP intervention is controversial. Early intervention to treat acute fractures, e.g., within 2 weeks of the symptom onset, may lead to unnecessary surgery (27), whereas late intervention may compromise the results (28). Because of these discordant opinions about interventions to treat PVP, patients may undergo PVP procedures at different times.

We examined the influence of time sequences and found that the incidence of AVF was higher when PVP was performed later.

The mechanisms of adjacent fractures are still under debate. Some believe that an AVF is related to increased stiffness after cement augmentation, which

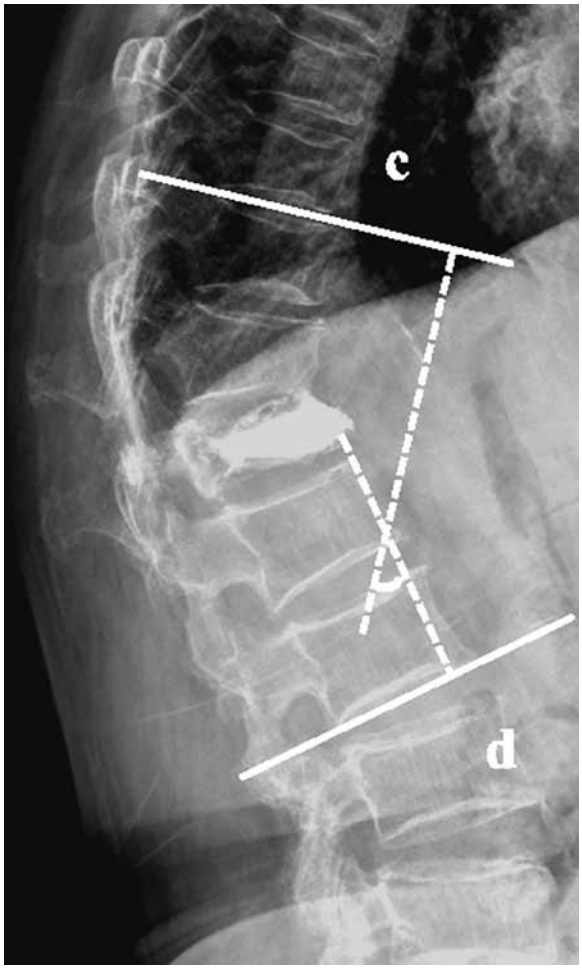

Fig. 3. *The Cobb angle was obtained as the angle between the upper endplate of T10 and the lower endplate of L2 on postoperative lateral x-ray.*

Table 1. *Demographic data: Early vs. late percutaneous vertebroplasties (PVP).*

	Early PVP (n = 78) Mean ± SD	Late PVP (n = 46) Mean ± SD	*P*
Age	77.3 (±7.85)	76.422 (± 6.36)	0.521
BMI	23.91 (± 4.20)	23.72 (± 3.75)	0.805
BMD	–3.16 (± 1.05)	–3.07 (± 0.88)	0.609
Preoperation VAS	8.2 ± 1.1	6.5 ± 1.0	< 0.001
Postoperation VAS	3.6 ± 0.5	3.3 ± 0.6	0.005

Early PVP = patient received percutaneous vertebroplasty within 30 days after symptom onset, late PVP = patient received percutaneous vertebroplasty > 30 days after symptom onset, BMI = body mass index, BMD = bone mineral density, VAS = visual analog scale of pain

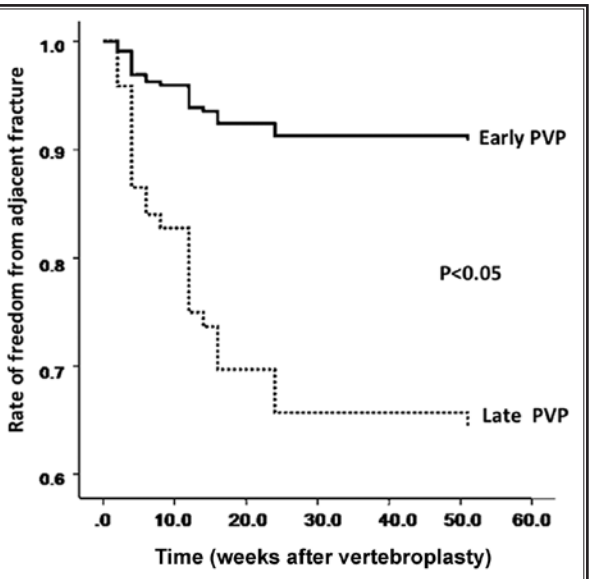

Fig. 4. *Kaplan–Meier curve of incidences of adjacent fractures in the early and late percutaneous vertebroplasty groups.*

Table 2. *Patient characteristics and 1-year hazard ratios (HR) and 95 % confidence intervals (CI) for risk of adjacent fracture.*

	HR	95.0% CI	*P*
Late PVP	6.083	2.498–14.298	< 0.001
BMD	0.469	0.273–0.805	0.006
BMI	0.934	0.827–1.054	0.269
Female gender	4.517	1.427–14.298	0.010
Age	1.058	0.994–1.127	0.077
Disc leakage	4.902	2.115–11.362	< 0.001
Cement volume	1.548	1.249–1.918	< 0.001
Preoperation wedge angle	1.003	0.954–1.055	0.907
Postoperation wedge angle	0.980	0.917–1.047	0.543
Thoracolumbar kyphotic angle	0.985	0.955–1.016	0.342

PVP = percutaneous vertebroplasty, BMD = bone mineral density, BMI = body mass index

Table 3. *Comparison of the results of early vs. late percutaneous vertebroplasties (PVP).*

	Early PVP (n = 78) Mean ± SD	Late PVP (n = 46) Mean ± SD	*P**
Cement volume	5.0050 (± 1.73)	4.7850 (± 2.06)	0.526
Preoperation angle	-15.4400 (± 8.12)	-19.4100 (± 9.66)	0.016
Postoperation angle	-10.4600 (± 7.97)	-12.8700 (± 8.04)	0.108
Kyphosis angle	25.7200 (± 11.82)	25.3900 (± 14.16)	0.891
Restored angle	5.1795 (± 5.68)	6.5870 (± 8.00)	0.298

SD = standard deviation. *By t-test

may bring more stress to adjacent levels (7). However, some authors (29) believe that PVP does not increase the rate of new VCF compared to conservative treatment. In fact, Farrokhi et al (30) reported less adjacent VCF in a PVP group compared to a conservatively treated group.

However, as fractures age during conservative treatment waiting time, the vertebral height may collapse more and motion at the fracture site during activities might also lead to further bone loss over the fracture site approaching the end plate. In vertebroplasty, without internal support device or reduction like kyphoplasty, reduction of vertebral height through posture reduction only may be inadequate and the cement distribution in the bone could be altered.

Biomechanically, hard callus formation for bony fracture in adult takes 3~6 weeks (31). We believe that as early as 1 month after vertebral fracture, the kyphosis deformity could be fixed and cannot be reduced by simply performing vertebroplasty. On the other hand, the intra-vertebral new callus formation may also lead to sclerotic changes of the bone and may show an intra-vertebral vacuum on x-rays. The intra-vertebral cracks and sclerotic changes may also create barriers between the cement and trabecular bone preventing firm integration. This contributes to different cement distribution patterns. In this study, we defined vertebroplasty performed in 30 days as the early PVP groups and vertebroplasty performed after 30 days as the late PVP groups. We found that the 1-year incidence of AVFs was lower in the EPVP group. Several factors probably contributed to these results. Firstly, the integration of the bone–cement interface may be better in the EPVP group. After waiting a period of time, the repeated trauma of normal activity may introduce stress between the fracture interface and the native bone, which can create a void effect over the fracture site. This increases the cement volume needed to fill the defect. This void effect has been shown to lower the intergradient effect between bone and cement (32) and increases the incidence of new VCF (23). At the same time, increased cement volume fractures were also found to increase adjacent fractures (33). In acute cases, the dispersed fill pattern and load-bearing properties of the bioactive composite may also result in fewer subsequent fractures (23,34). Secondly, repeated compressive loading over the fracture site can lead to bone loss near the end plate. The extension of bone cement to the disc level was reported to contribute to adjacent fractures (35), and this can easily be seen in the LPVP groups (Fig. 5). Thirdly, cement augmentation is believed to further

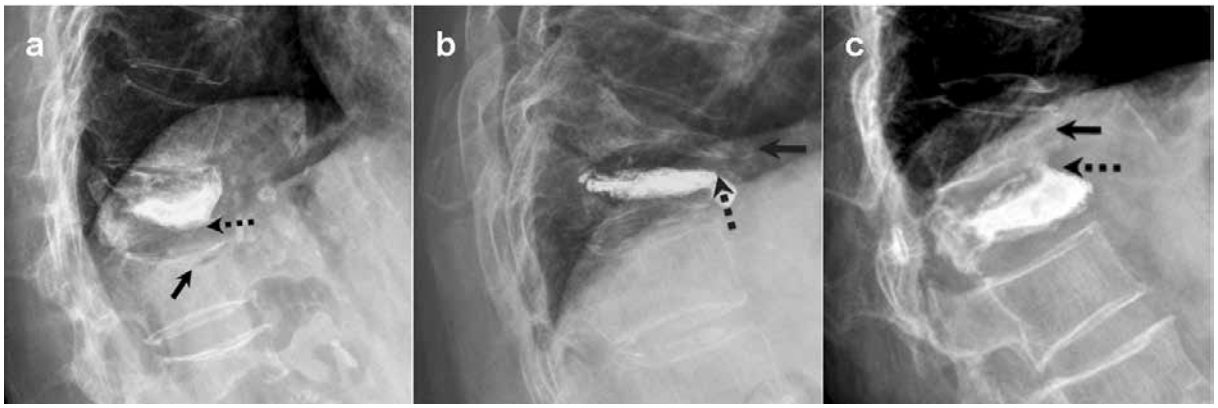

Fig. 5. *Extension of bone cement to disc level (dotted-line arrow) and adjacent fracture (solid-line arrow) in a) 1 week after surgery in a 73-year-old female patient with an L1 vertebral compression fracture who received percutaneous vertebroplasty on day 60 after symptom onset due to lifting and b) 4 week after surgery in a 79-year-old female patient with a T12 OVCF who received percutaneous vertebroplasty more than 2 months after fracture c) 2 weeks after surgery in a 78-year-old female patient with T12 OVCF who received percutaneous vertebroplasty more than 2 months after fracture.*

lower both the failure load and the stiffness of the end plate (36) and the anterior wedge deformities of the vertebral body may start with endplate damage (37,38). We believe that a prolonged waiting time before repair may also lead to end plate injury during normal activity; thus, after vertebroplasty has been performed, the incidence of AVF may accelerate. Lastly, studies has shown that inactivity-induced loss of muscle mass is most rapid during the initials weeks of inactivity (39-41). And this may have a negative impact on back muscle and reduced muscle tone protecting the osteoporotic vertebral body from new compression fractures (42) in the LPVP group.

The reported incidence of AVF varies widely. The overall incidence of AVF was relatively higher in this study compared to recent studies (22,24,43). Several factors could contribute to the high incidence in our study. Firstly, our inclusion criteria, the thoracolumbar location (T10 to L2) and osteoporosis, were in itself risk factors for AVF. The average BMD in both the EPVP and the LPVP groups was less than -3.0. Secondly, is failure to maintain reduction even with a hyperextension position during PVP. This may result in residual post-operative local kyphosis in both early and late groups, which may increase the risk of AVF (8,24,44). Thirdly, subsequent fractures resulting from minor trauma could also be overlooked in this retrospective study.

None of the x-ray parameters contributed to the risk of adjacent fractures in our study. The overall residual kyphosis in both EPVP and LPVP groups may lead to the minimization of influence of kyphosis angle on the risk of AVF in regression mode. However, as our review demonstrated, the reported AVF rate was as high as 41.4%–55.6% in earlier reports and as low as 6.5%–8.9% in a recent controlled randomized study (43). We believe that the reported incidence of AVFs is higher in earlier reports because of the relatively conservative approach used to cement augmentation, and included a prolonged waiting time before surgical repair. If PVP is done within 1 month after symptom onset, the rate of AVFs should decrease, especially over the thoracolumbar region (T10 to L2).

Limitations

There are some limitations of this retrospective study. First, the case number is small and a great number of patients either died or were lost to follow-up. The actual incidence of AVFs could have been altered because of these factors. Second, this is a retrospective study and the indications for both early and late surgery were different, which could also cause a bias in patient selection. A prospective study with restricted indications for early and late PVP might be necessary. Third, the real changes in the vertebral body and the gradient from cement to bony structures in chronic and acute cases cannot be fully understood on the basis of published reports, so further biomechanical study such as a finite element analysis or additional CT evaluation may be necessary.

Conclusions

Our study showed that although vertebroplasty is associated with AVFs, early vertebroplasty for VCF at the thoracolumbar junction is associated with fewer AVFs. Although PVP can effectively ease pain in any stages of OVCFs, PVP that is delayed more than 30 days may lead to increased kyphosis, more pain, and increased rates of subsequent AVFs. Accordingly, we believe that strategies in favor of earlier PVP after OVCF can be more effective. When PVP was performed late, efforts to prevent AVFs via preventive PVP should be considered.

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