Retrospective Study

Effect of the Location of Endplate Cement Extravasation on Adjacent Level Fracture in Osteoporotic Patients Undergoing Vertebroplasty and Kyphoplasty

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Background: The most widely researched risk/complication following vertebroplasty (VP) or kyphoplasty (KP) is that of adjacent level fracture (ALF). Current literature results regarding the effect of intradiscal extravasation of cement on the risk of ALF is conflicting with about half of the studies concluding there is no added risk with endplate extravasation and half of the studies reporting opposite conclusions.

Objective: The purpose of the study is to further stratify the data to determine whether specifically the location and extent of endplate cement extravasation more strongly affect ALF risk in osteoporotic patients following either VP or balloon KP.

Study Design: Retrospective cohort study.

Setting: University teaching hospital

Methods: One hundred and fifty-six cemented levels in 80 patients, treated at a single center between 2008 and 2012 were reviewed. Age, gender, T-score, body mass index, and osteoporosis type (primary or secondary) were recorded. An ALF was defined as a fracture: 1) in a non-cemented vertebra; 2) adjacent to a cemented level; and 3) not due to trauma or malignancy. Location of the cement extravasation (anterior, middle, or posterior third of the vertebral body) and extravasation extent (percentage of the intervertebral disc height occupied by the bolus) were measured. A logistic modeling strategy permitted examining the association between the location and extent of extravasation and the odds of ALF.

Results: ALF occurred in 14 of the 52 patients (27%) and 20 of the 98 levels (20.4%) remaining after exclusions. Odds of ALF were 5.9 times higher (95% CI: 1.6 to 21.2, P = 0.008) with extravasation when compared to no leakage. Odds of ALF in a given patient were 22.6 times higher (95% CI: 3.0 to 170.9, P = 0.003) with anterior extravasation when compared to no leakage. Leakage in the middle or posterior thirds and extent of extravasation were not associated with ALF.

Limitations: Limitations of the study include the retrospective study design and small sample size as well as the retrospective implementation of follow-up criteria posing risk of selection bias.

Conclusions: Cement endplate extravasation isolated to the anterior third of the vertebral body is associated with is significantly higher odds of ALF after VP or KP in patients with osteoporosis.

Key words: Adjacent vertebral fracture, intradiscal leak, osteoporotic compression

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Percutaneous vertebroplasty (VP) is a technique in which cement (polymethylmethacrylate [PMMA]) is used for the percutaneous augmentation of vertebral body compression fractures (VCF). Since the introduction in 1984 (1-2), percutaneous cement augmentation has gained popularity attributable to the early positive results and relatively low risk of the procedure (3-7). With the advent of balloon kyphoplasty (KP) in the late 1990s, the utility and potential benefit of cement augmentation was expanded to include the theoretical benefit of height restoration and improved cement control (8-10)). As the number of cement augmentation procedures continued to rise, a notable increase in subsequent fracture of the adjacent non-cemented vertebral bodies was noted by some operators. This risk of adjacent level fracture (ALF) has been extensively researched and dominates the current literature on the topic of cement augmentation complications (11-22). The cause of ALF is debated; some authors suggesting ALF is a consequence of a general increased risk of re-fracture in osteoporotic patients who have sustained previous fracture, while others propose qualities innate to the PMMA may be the cause (11,23-24). ALF risk has also been shown to increase based on independent risk factors such as low bone density or T-score (12-15), secondary osteoporosis (16-17) kyphotic angulation (14), vertebral body height restoration (14,20), increased cement volume (21), and location of the fracture at the thoracolumbar junction (12,13,15,22). The most scrutinized independent risk of ALF is that of intradiscal cement extravasation. The current literature is conflicting as to the effect of intradiscal cement extravasation on the risk of ALF in osteoporotic patients. About half of the existing studies show an increased risk of ALF with intradiscal extravasation (12,15,18-20), while the other half concludes there is no increased risk of ALF with intradiscal extravasation (13,25-29). We contend that the current literature has reported conflicting and contradictory results because it has failed to take into account the location and extent of endplate extravasation.

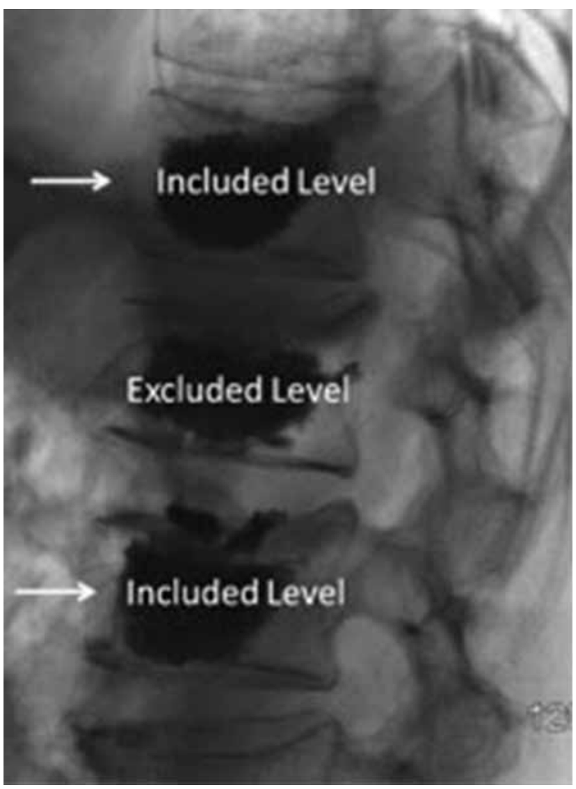

Fig. 1. *Example of excluded central vertebral body level. In this case 3 levels were cemented. The central level was excluded given that the adjacent 2 vertebral bodies were reinforced and no longer susceptible to fracture. The superior and inferior most levels (arrows) were included.*

The purpose of our study is to determine whether the location and the extent of endplate extravasation affect ALF risk in osteoporotic patients following either VP or balloon KP.

Methods

Study Design and Patient Selection

This is a retrospective cohort study in which a total of 156 VP and KP procedures in 80 patients performed at a single center between June 2008 and July 2012 were retrospectively reviewed, following approval by the Intuitional Review Board.

Cemented levels in patients with VCF secondary to osteoporosis were selected for the study. Patients with ALF were included in the study regardless of the length of follow-up. In patients who did not return with an ALF, a 6 month follow-up required for inclusion, as greater than 80% of ALFs have been shown to occur within the first 6 months following VP (7,30-32). Only those treated levels adjacent to a non-cemented level were included (Fig. 1).

Patients receiving percutaneous treatment for pathologic or traumatic fracture and patients who did not fracture and had a follow-up of less than 6 months were excluded from the study. Additionally, any treated level between 2 adjacent treated levels was excluded.

For example, in cases where 3 consecutive levels were treated, the middle level was excluded from the data given that the 2 adjacent treated levels were no longer susceptible to fracture (Fig. 1).

Vertebroplasty and Kyphoplasty Technique

Patients were selected for percutaneous cement augmentation based on the presence of VCF and associated back pain. Fracture acuity was confirmed by 1.5T or 3T magnetic resonance imaging (MRI) fluid sensitive sequence (TE: 30 – 60, TR: 3500 – 4200, TI: 150 – 220) demonstrating edema in the fractured vertebral body. In a small fraction of the study population, fracture acuity was confirmed by close radiographic follow-up with conventional anterio-posterior (AP) and lateral spine radiographs demonstrating short interval development of VCF.

All VP and KP procedures were performed in a single center using a Siemens Axiom Artis bi-plane fluoroscopy unit. Various vendors' equipment was used for VP and balloon augmentation over the study period (Stryker Interventional Spine, Kalamazoo, MI; Carefusion, San Diego, CA; Medtronic, Minneapolis, MN). Cement augmentation technique involved placement of either unipedicular or bipedicular 8 – 13G access trocars into the affected vertebral body. If balloon augmentation was performed, 10 – 20mm balloons were placed via the indwelling trocars and inflated up to a maximum of 400 psi. Regardless of vendor, moderate to high viscosity PMMA was administered via manual injection (52% of levels performed with high viscosity cement). Preprocedural assessment of fracture morphology, acuity of fracture, and degree of compression were factors used to determine whether VP or balloon augmentation was performed (66% KP and 33% VP).

Data Collection

The presence or absence of intradiscal cement extravasation and the morphology of the extravasated cement bolus were analyzed in each included level. Intradiscal cement extravasation was defined as any cement bolus that extended beyond the superior or inferior endplate into the intervertebral disc space. Cement extravasation into the venous system or through the anterior or posterior vertebral body was not considered intradiscal extravasation. When intradiscal cement extravasation was confirmed, the morphology of the extravasated bolus was further analyzed to include the extent of extravasation, defined as the percentage of the craniocaudal intradiscal space occupied by the extravasated bolus, and location of extravasation, defined as anterior, middle, or posterior third of the endplate. A simplistic method was implemented to determine the extent of disc extravasation, which involved measuring the height of extravasated bolus and dividing by the height of the intervertebral disc space at that location to gain a percentage (Fig. 2). This simplistic method was used to in order to replicate a reasonable intraprocedural method of calculation that could be easily applied to clinical practice.

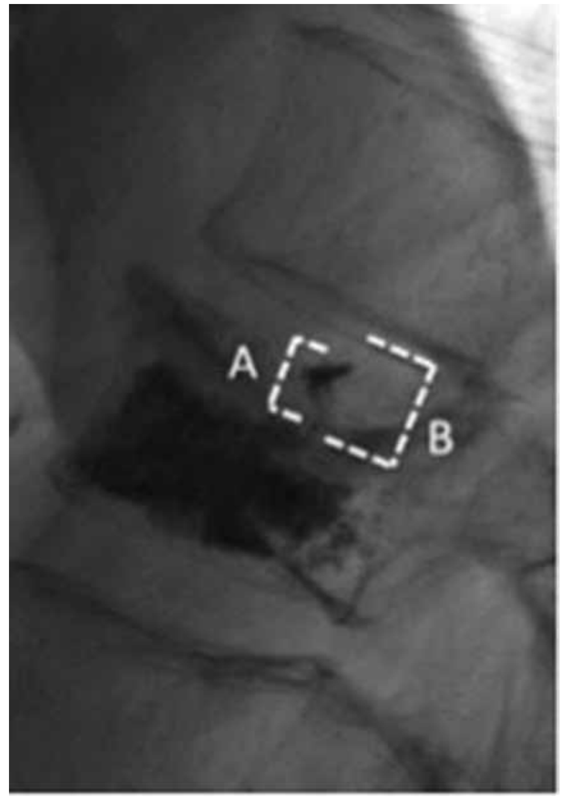

Fig. 2. *Measurement technique for the assessment of extent of intradiscal extravasation on lateral procedural fluoroscopic image of the lumbar spine. The height of the cement bolus (A) was divided by the height of the intervertebral disc space (B) to gain a percentage.*

To determine the location of cement extravasation, the vertebral body was divided into thirds along the anteroposterior axis. The thirds were logically defined as anterior, middle, and posterior based on the respective location along the superior or inferior endplate (Fig. 3).

After the vertebral body was radiographically segmented into anterior, middle, and posterior thirds, the

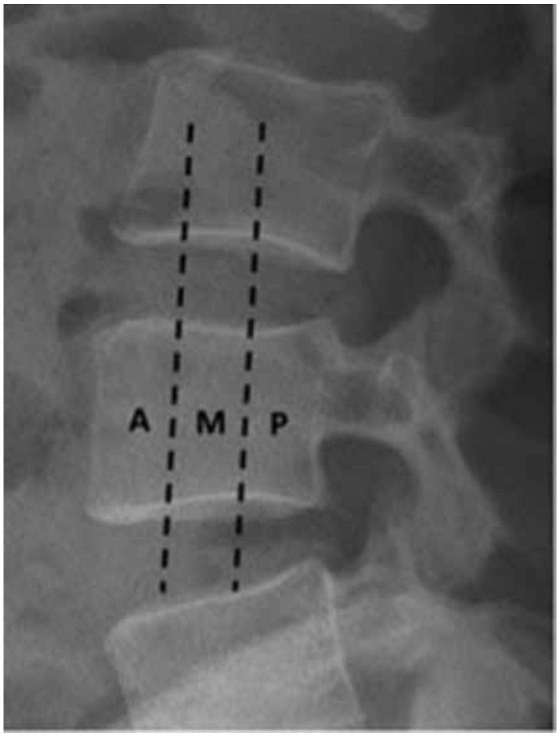

Fig. 3. *Lateral radiograph of the lumbar spine. Measurement technique for the determination of endplate extravasation location. The vertebral body was split into equal thirds defined as anterior (A), middle (M), and posterior (P).*

primary location of the cement extravasation relative to the delineated thirds was documented. In the event that the cement bolus occupied greater than one third, or extended beyond the delineated third, the segment with the greatest volume of cement bolus was noted as the primary location (Fig. 4).

Data were collected irrespective of the cementation technique; this is to say VP and KP patients were not analyzed independently. The reasoning for which was as follows: Our study focuses on the effect of disc extravasation on the adjacent vertebral bodies and not the means by which the cement entered the disc space. The method of cement administration (VP vs KP) was therefore considered inconsequential.

Statistical Methods

We calculated descriptive statistics for patient demographics, disease characteristics, and surgical outcomes. We fit separate logistic regression models to test the association of location of extravasation and extent of extravasation with the risk of ALF. In each model, ALF was the outcome. The first model included the presence of extravasation as the only predictor. The second model included anterior location and combined middle and posterior location of extravasation as predictors. The third model included the extent of extravasation as the only predictor. In all models, we used a random

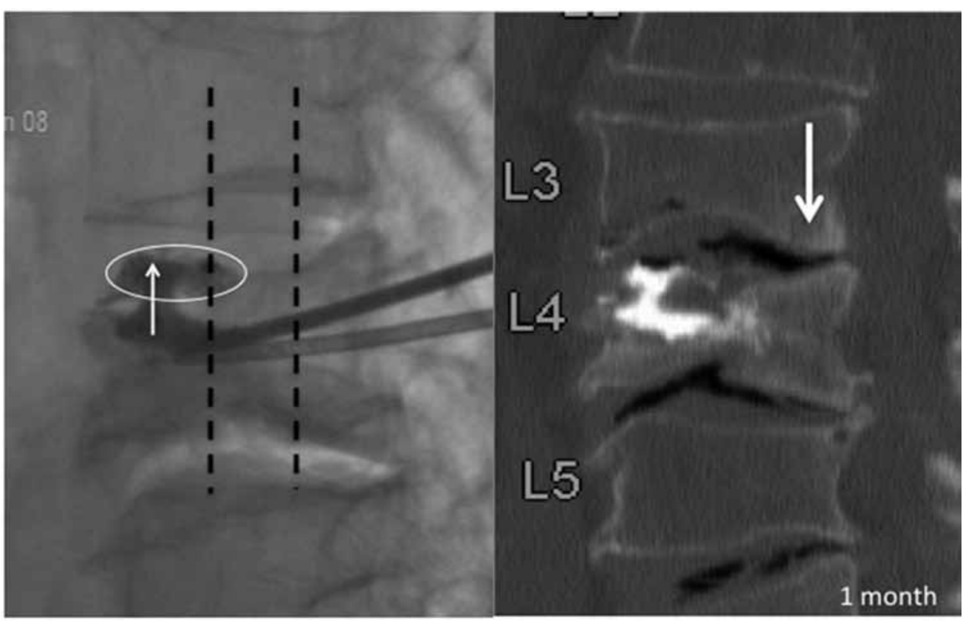

Fig. 4. *An 68-year-old male with secondary osteoporosis due to panhypopituitarism returning for evaluation of new onset back pain following L4 vertebroplasty. Left image demonstrates primarily anterior third extravasation with some extension to the middle third of the intervertebral disc (circle). Right image shows a new adjacent inferior endplate L3 fracture at one month follow-up (arrow).*

intercept for patients to account for correlation among treated levels within a single patient. We next fit separate logistic regression models to test the association of patient demographics and disease characteristics with ALF. For each model, the outcome was the presence of at least one ALF among repairs performed for the patient, with age, gender, t-score, BMI, or osteoporosis type as the only predictor. For each model, odds ratios, 95% confidence intervals, and P-values were produced. To control for multiple comparisons, we used an alpha spending approach. Hypothesis tests for extravasation were performed at 0.04/3 = 0.013, and associations between patient characteristics and fracture were tested at 0.01/5 = 0.002.

Results

A total of 156 VP and KP procedures in 80 patients were reviewed. Thirty-one levels in 20 patients were excluded based on the pathologic nature of fracture (multiple myeloma, solid osseous metastases, and trauma). An additional 11 levels (8 patients) were excluded due to insufficient follow-up. Of the remaining 114 treated levels (52 patients), only those levels adjacent to susceptible non-cemented vertebral bodies, 98 levels, were analyzed.

Demographic and medical information including age, gender, body mass index (BMI), T-score for bone density, and osteoporosis type (primary or secondary) were recorded for each patient, and procedure type (VP or KP) was recorded for each treated level. At post-surgical assessment, outcomes including presence of ALF, location of cement extravasation, and extent of extravasation were recorded.

A fracture was considered to be an ALF if: 1) it occurred in an untreated vertebra; 2) it was adjacent to a treated level; and 3) the fracture was not pathologic or due to trauma. Cement extravasation location was defined as occurring in either the anterior, middle, or posterior third of the vertebral body. Extent of the intradiscal leak was defined as the percentage of the intervertebral disc height occupied by the extravasated cement bolus.

After excluding levels not at risk for ALF, a total of 98 levels in 52 patients were analyzed. Patient demographics and medical characteristics appear in Table 1.

ALFs occurred in 20 levels (21% of total levels) within 14 patients (27% of all patients). Nine of the 20 ALF cases occurred following intradiscal extravasation (45%). For levels with extravasation, Table 2 summarizes the surgical procedure, location, and extent of extravasation, and the presence or absence of ALF.

The odds of ALF were 5.9 times higher (95% CI: 1.6 to 21.2, P = 0.008) in a patient with extravasation compared to the same patient with no leakage.

Twenty of the 98 treated levels were noted to have intradiscal extravasation: 8 occurring in the anterior third, 9 occurring in the middle third, and 3 in the posterior third. Of the levels in which anterior third extravasation was present (8 levels), 6 were shown to have ALF on follow-up exam. Three levels with primarily middle third extravasation (9 total) went on to have ALF. None of the 3 levels with posterior extravasation were shown to have ALF on follow-up exam. ALFs following cement extravasation involved the most directly opposed adjacent level endplate in all but one patient as detailed in Table 3. Pictorial case examples are provided in Figs. 5-7.

Table 1. *Patient demographics and medical characteristics.*

	All Patients (N=52)	Patients with at least one adjacent level fracture (N=14)	Patients with no adjacent level fractures (N=38)
Age	68.85 ± 11.47	68.79 ± 12.49	68.87 ± 11.24
Body mass index	26.61 ± 5.52	28.36 ± 6.36	25.94 ± 5.11
T-score	-2.43 ± 0.86	-2.24 ± 1.06	-2.52 ± 0.76
Gender			
Male	17 (33%)	4 (29%)	13 (34%)
Female	35 (67%)	10 (71%)	25 (66%)
Osteoporosis Type			
Primary	35 (67%)	9 (64%)	26 (68%)
Secondary	16 (31%)	5 (36%)	11 (29%)
Unknown	1 (2%)	0 (0%)	1 (3%)
Average Number of Repairs	1.88 ± 1.25	2.36 ± 1.60	1.71 ± 1.06
Average Number of Adjacent Level Fractures	0.38 ± 0.75	1.43 ± 0.76	N/A

Table 2. *Extravasation characteristics*.

	All Levels with extravasation (N=20)	Levels with extravasation and adjacent level fracture (N=9)	Levels with extravasation and no adjacent level fracture (N=11)
Extent of Extravasation	55.25% ± 25.30%	51.89% ± 24.12%	58.00% ± 27.05%
Location of Extravasation			
Anterior	8 (40%)	6 (67%)	2 (18%)
Middle	9 (45%)	3 (33%)	6 (55%)
Posterior	3 (15%)	0 (0%)	3 (27%)
Procedure			
Kyphoplasty	14 (66%)	6 (67%)	8 (73%)
Vertebroplasty	6 (34%)	3 (33%)	3 (27%)

Table 3. *Treated levels with extravasation and adjacent level fracture.*

	Level treated	Location of extravasation relative to the endplate	Level and location of adjacent level fracture
1	L4	Anterior superior	L3 inferior endplate
2	T12	Middle superior	T11 inferior endplate
3	L1	Middle inferior	L2 inferior endplate
4	L3	Anterior superior	L2 inferior endplate
5	T11	Anterior superior	T10 inferior endplate
6	L1	Anterior superior	T12 inferior endplate
7	L2	Anterior inferior	L3 superior endplate
8	T6	Middle inferior	T7 superior endplate
9	T8	Anterior superior	T7 inferior endplate

The odds of ALF were 22.6 times higher (95% CI: 3.0 to 170.9, P = 0.003) in a patient with anterior extravasation compared to the same patient with no leakage. Leakage in the middle or posterior third did not impact the odds of fracture (OR = 2.4, 95% CI: 0.45 to 12.7, P = 0.30). Increasing extent of extravasation was not significantly associated with ALF (OR for extent increase of 25 percentage points = 1.8, 95% CI: 1.09 to 1.26, P = 0.024).

No associations were observed between ALF risk and gender (OR women vs. men = 1.3, 95% CI: 0.34 to 5.0, P = 0.70), age (OR for one year increase in age = 1.0, 95% CI: 0.95 to 1.1, P = 0.98), BMI (OR for one unit increase in BMI = 1.1, 95% CI: 0.96 to 1.2, P = 0.18), osteoporosis type (OR for secondary vs. primary = 1.3, 95% CI: 0.36 to 4.8, P = 0.68), or T-score (OR for one unit increase in T-score = 1.5, 95% CI: 0.61 to 3.6, P = 0.39.

Discussion

VP and balloon KP have been shown to be safe and effective for the management of painful osteoporotic VCFs; however, complications do occur. The most widely researched risk/complication following VP or KP is that of ALF. Current literature reports ALFs occurring at rates from 6.5% to 51% (6,7,14,16,26-28,31-33), a range that encompasses the 21% ALF rate found in our study. The occurrence of intradiscal extravasation is variable based on operator technique. We found extravasation occurred in 20% of treated levels, which is in keeping with range of percentages reported in the literature (4,7,12,14,25).

Of particular interest is the relationship of intradiscal cement leak and the occurrence of ALF. This association has been studied in increasingly greater detail in the past several years, but conclusions in the literature regarding this relationship remain varied. Physiologic studies have shown that the presence of cement both within the vertebral body and within the intervertebral disc space decreases disc compliance and increases load transfer and stress to the adjacent levels, potentially increasing risk of fracture (35,36).

We found cement disc extravasation, in general, was associated with a 5.9 times higher risk of ALF, concurrent with the results reported by Nieuwenhuijse et

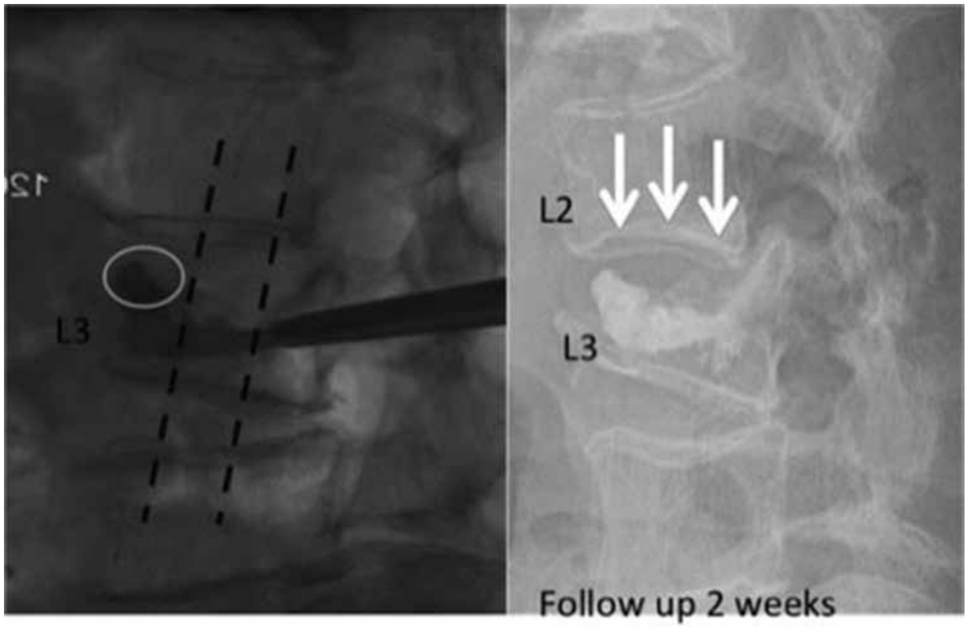

Fig. 5. *An 87-year-old osteoporotic female with increasing back pain 2 weeks following balloon kyphoplasty. Left image demonstrates intraprocedural image from L3 vertebroplasty with a bolus of cement extravasated into the anterior intervertebral disc space (circle). Right image demonstrates inferior endplate compression fracture of the adjacent L2 vertebral body at 2 week follow-up (arrows).*

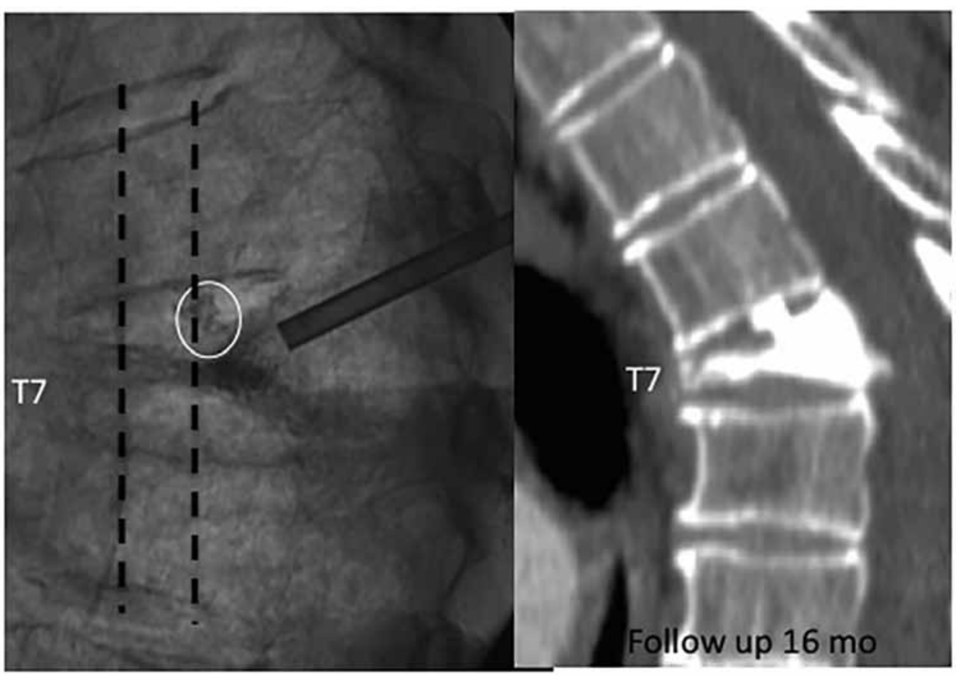

Fig. 6. *A 79-year-old female with primary osteoporosis and T7 compression fracture. Left image demonstrates posterior extravasation of cement during kyphoplasty (circle). Right images illustrate an intact adjacent T6 level at 16 month follow-up.*

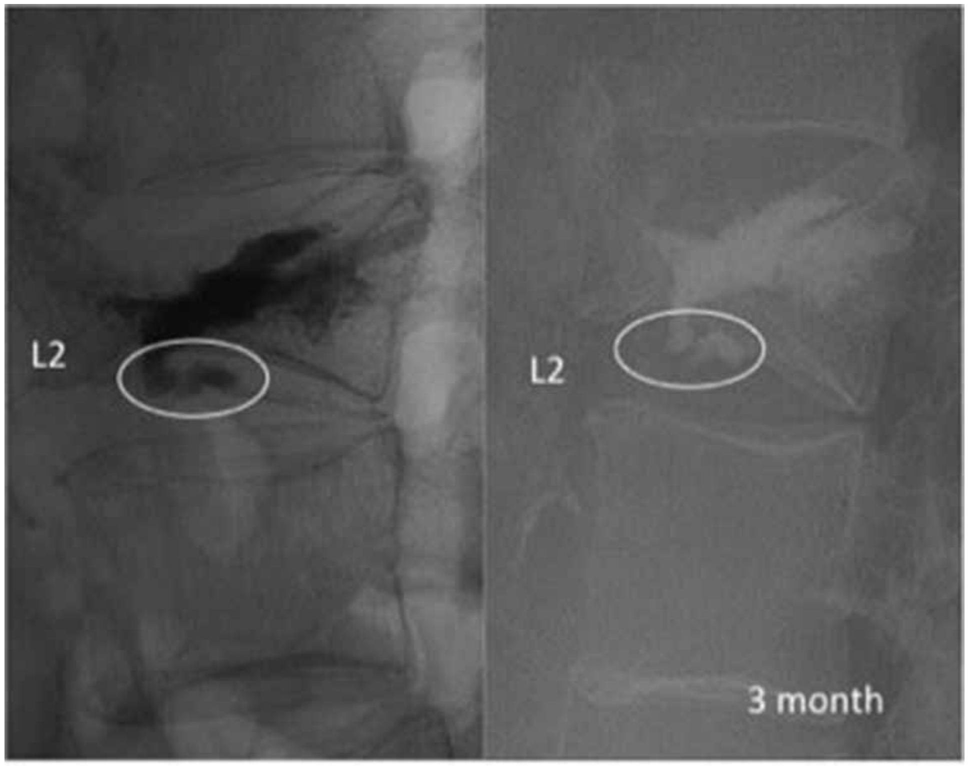

Fig. 7. A 79-year-old female with primary osteoporosis and L2 compression fracture. Left image depicts middle third inferior endplate extravasation during vertebroplasty (circle). Right image demonstrates an intact adjacent L3 vertebral body at 6 month follow-up.

al (12), and supported by the findings in half of the current literature on the topic (15,18-19). Nieuwenhuijse et al (12), who published the only prospective study on the topic, concluded that the presence intradiscal cement extravasation following cement augmentation was a strong risk factor for the occurrence of ALF, yielding a hazard ratio of 5.47.

Contradicting results are equally prevalent in the literature, raising questions as to the validity of the aforementioned conclusions. In a retrospective study of 424 cement augmentation patients, Khola et al (27) found no statistical difference in ALF rates in patients with and without intradiscal extravasation and concluded that intradiscal extravasation was not a risk factor for ALF. Syed et al (29), Lu et al (13), and Lee et al (28) reached similar conclusions in retrospective studies of 308, 155, and 188 cement augmentation patients, respectively.

In our study, we further assessed the morphology of the intradiscal cement bolus, specifically the antero-posterior location of the cement bolus and extent of the cement bolus into the intervertebral disc space as independent risk factors. We found a significant, 22 times, increased risk of ALF in those patients with intradiscal extravasation to the anterior third of the intervertebral disc space and little to no increased risk of fracture in those patients with the extravasated bolus isolated to the middle or posterior third of the disc space. We suggest that the increased risk of ALF in patients with intradiscal extravasation in the anterior third may occur as a product of the increased physiologic leverage effect across the anterior intervertebral disc space relative to the posterior or middle disc space. When extravasation is located in the anterior third of the disc, the anterior endplate of the adjacent level is susceptible to increased impaction forces against the solid PMMA cement bolus as a result of the inherent increased movement across the anterior spine. Patients with anterior extravasation would therefore be more likely to sustain subsequent ALF. The middle and posterior extravasations by contrast, do not inflict the same impaction force on the adjacent endplate due to the added stability and restricted leverage motion applied by the posterior elements. Middle and posterior disc extravasation thus would have less risk of ALF.

The results of our study may explain the contradictory conclusions in the current literature. Previous studies investigating intradiscal extravasation as a risk of ALF have classified the extravasation using a binary outcome model whereby extravasation was documented as either present or absent, irrespective of the location. It can be assumed that when assessing extravasation as a whole, a statistically significant odds ratio would be highly variable depending on the dominant site of extravasation in that specific population and under a specific vertebral augmentation technique. Those cases with more anterior extravasation would likely show an increased risk of ALF and those with more middle and posterior extravasations would likely show no elevated risk of ALF.

With regard to the extent (%) of intradiscal extravasation, we found no statistically significant increase risk of ALF. This being said, the P-value of 0.024 of our data lies at the cusp of our alpha-spending significance limit of 0.02, and with a more sophisticated evaluation of intradiscal volume and a larger patient population, we feel this independent factor may in fact prove to be significant.

While our results demonstrate no association between age, gender, BMI, T-score, and secondary osteoporosis and ALF risk, these relationships have been proposed and supported in the literature. Decreasing bone mineral density (T-score) has been associated with ALF in both prospective and retrospective analyses (10,11). Harrop et al (14) suggests that differences in the quality of bone mineral density in patients with secondary (medically induced) osteoporosis versus primary (estrogen related) osteoporosis may increase risk of subsequent fracture. Additional factors associated with increased fracture risk that were not directly assessed in our study include location of the fracture at the thoracolumbar junction (10,11,13,20), kyphotic angulation (14), vertebral body height restoration (12,18), and increased cement volume (19).

Our study has several limitations beyond the retrospective nature of the study and small sample size. Given the retrospective implementation of our follow-up criteria, our study was at risk for selection bias. For example, patients with no ALFs may be less likely to follow-up. This being said, follow-up of VP and KP patients was generally not an issue given the regimented spine and endocrinology clinical follow-up established by our institution. Also, our data was collected on patients who underwent VP and KP in a single center with specific operator dependent technique. Heterogeneity in cementation technique was therefore not addressed in our study. The final limiting by-product of the retrospective nature was that much of the secondary information, in particular the T-scores and BMI, was not available on all patients thus further weakening the study power with regard to these factors.

Conclusion

Odds of ALF following VP and KP in osteoporotic patients was significantly higher following cement extravasation in the anterior third of the disc space. Overall patients with intradiscal cement extravasation had significant increased risk of ALF compared with patients without extravasation.

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