Fractures following percutaneous vertebral augmentation: The procedure or the underlying disease?

Hirva Bakeri, Pamela Taxel

ABSTRACT

Introduction: We report cases of three patients who had vertebral compression fractures (VCFs) that occurred temporally close to and at levels adjacent to prior percutaneous vertebral augmentation (PVA) of vertebral fractures. Our objective is to evaluate the association between PVA and new/adjacent-level vertebral fractures. Case Series: Case 1 presented to our Osteoporosis (OP) Clinic with a previous diagnosis of OP, briefly on alendronate. Following this, she had a compression fracture (CF) at L3 followed by balloon kyphoplasty (BK). She was then on teriparatide for two years. Following this, over a span of several months, she had CFs (T8-L2) requiring BK, with seven of those fractures within six months. Case 2 presented for evaluation in the setting of CFs. She had never received antiresorptive therapy. She underwent BK at T12 and L1, and was noted to have a new T11 fracture 3-4 weeks later. Case 3 presented with a prior history of CF at T12 treated with BK, followed by new vertebral fractures at T11 and L1 also treated with BK, and finally CF at T10, which was also treated with BK. Conclusion: These cases illustrate that new fractures may occur sooner and at adjacent levels following PVA, demonstrating a possible association between the two. Given the mixed data regarding this, we would like to emphasize the need for clinicians to complete a thorough OP work-up and discuss the risks and benefits of these procedures with patients.

Keywords: Kyphoplasty, Osteoporosis, Vertebral compression fractures

INTRODUCTION

Osteoporosis is a systemic disorder that compromises bone strength and leads to an increased risk for fractures. Osteoporotic vertebral compression fractures (OVCFs) are the primary complication associated with OP and the major source of morbidity and health care costs [1]. Osteoporotic vertebral compression fractures can cause increased spinal kyphosis, and persistent back pain that leads to significant functional deterioration, impaired mobility, decreased pulmonary function, and poor quality of life [2, 3]. Conservative treatments of painful compression fractures include bed rest, analgesia, muscle relaxants, bracing, and physical therapy [4]. However, patients who do not respond to conservative measures may be offered PVA which includes percutaneous vertebroplasty (PVP) or BK despite mixed data regarding their efficacy, safety, and potential harm to patients.
Percutaneous vertebroplasty is a minimally invasive procedure, in which bone cement, polymethylmethacrylate (PMMA), is injected into fractured vertebrae via a percutaneous procedure in order to strengthen it [5]. Kyphoplasty was developed from the vertebroplasty concept. It involves an additional step of introducing a balloon via the vertebral pedicle into the vertebral body, where it is inflated to create a cavity into which the bone cement is injected, thus also restoring vertebral height and reducing the risk of increasing spinal kyphosis [1, 2]. These new minimally invasive techniques can quickly relieve pain, partially restore vertebral height, provide biomechanical stability, shorten recovery time, improve function, and eliminate the need for extended nursing and rehabilitation, thereby reducing health care costs [4].

However, there are also significant risks involved with these procedures including fractures of already stabilized vertebrae to fractures of adjacent segment vertebrae, persistent pain, cement leakage, and spinal cord compression requiring immediate decompression [6, 7]. We present three cases in which compression fracture at several adjacent vertebral levels occurred soon after initial PVA procedure, raising concern that the procedure itself is implicated in the development of new VCFs. Bone density and lab data on these patients are presented in Table 1.

### CASE SERIES

#### Case 1

A 63-year-old female was seen in our Osteoporosis Clinic in 2016 with a history of OP diagnosed by bone mineral density (BMD) in 2006, with a lumbar-spine T-score of −3.2. She had a remote history of Graves' disease with radioactive iodine therapy, and had been on thyroid hormone replacement with normal levels. She underwent complete evaluation in our Osteoporosis Clinic, which showed no evidence of secondary etiology of her OP. She had no other significant risk factors or family history of OP. Initial treatment included hormone replacement therapy (HRT) as well as alendronate, which was discontinued within weeks due to heartburn. In 2011, she suffered an initial compression fracture at L3 after lifting a heavy object and underwent BK. Following this, she was treated with teriparatide from 2011 to 2013 with HRT continued simultaneously until 2013, when both were discontinued and not followed by any further antiresorptive treatment. In 2015, upon evaluation due to increased back pain, she was noted to have compression fractures at L1 and T12, and underwent BK at these levels. There was no history of trauma or falls. Two months later, she once again had back pain without associated trauma and was noted to have new compression fractures at L2, T10, and T11, and once again underwent BK at these levels. She was treated with raloxifene for several

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-spine BMD (g/cm²)</td>
<td>0.655*</td>
<td>1.069</td>
<td>0.710</td>
</tr>
<tr>
<td>L-spine T-score</td>
<td>−3.7</td>
<td>−1.1</td>
<td>−2.5</td>
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<tr>
<td>T-hip BMD (g/cm²)</td>
<td>0.675</td>
<td>0.742</td>
<td>0.802</td>
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<tr>
<td>T-hip T-score</td>
<td>−2.2</td>
<td>−2.1</td>
<td>−1.6</td>
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<tr>
<td>25-OH Vitamin D (nl: 20–65 ng/mL)</td>
<td>50</td>
<td>33</td>
<td>48</td>
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<tr>
<td>BSAP (PM nl: 5.6–29 mcg/L)</td>
<td>12.2 (mcg/L)</td>
<td>19.9 mcg/L</td>
<td>8 (U/L)</td>
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<tr>
<td>Total calcium (nl: 8.9–10.4 mg/dL)</td>
<td>10.1</td>
<td>9.7</td>
<td>9</td>
</tr>
<tr>
<td>Urine NTx (nl: 26–124 nM BCE/mM creatinine)</td>
<td>27</td>
<td>53</td>
<td>21</td>
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<tr>
<td>Urine calcium/creatinine (nl: 10–320)</td>
<td>168</td>
<td>235</td>
<td>74</td>
</tr>
<tr>
<td>Albumin (nl: 3.8–5.3 g/dL)</td>
<td>4.5</td>
<td>4.4</td>
<td>3.6</td>
</tr>
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**Abbreviations:** nl: normal; BSAP: Bone specific alkaline phosphatase; PM: postmenopausal; NTx: Cross-linked N-telopeptide of type I collagen; BCE: Bone collagen equivalent

*L-spine 12/15: L4 only (due to prior PVA at L1-3).*
months, the only medication she would consent to, but it was discontinued for unclear reasons. Several months later she suffered further compression fractures at T8 and T9, and, once again, underwent BK for a total of eight vertebral levels (T10–L3), with seven fractures within six months. She initiated treatment with risedronate after this last procedure, but did not tolerate it due to severe muscle and joint aches. Since 2017, she has been on low-dose HRT with estradiol.

Case 2

An 81-year-old female was seen in our Osteoporosis Clinic for evaluation of her bone health in the setting of compression fractures, and long-standing low back pain due to spinal stenosis. In December 2017, she had a fall backward on her bathroom floor but reported no significant pain at that time. However, she was hospitalized in January 2018 with flu and pneumonia with increased cough. After that hospitalization, she had significant worsening of her back pain, and was found to have T12 and L1 VCFs. She was seen in the Osteoporosis Clinic for evaluation, and secondary work-up was negative for malignancy and other secondary etiologies for OP. She had never received antiresorptive therapy. She was noted to have inadequate calcium intake; however, had no other risk factors or family history of OP. Calcium and Vitamin D regimens were improved, with the plan to start therapy, as she met criteria for severe OP in the setting of two compression fractures of the spine. Although cautioned against it, she underwent BK several months later due to lack of pain control with conservative treatment. She did not have any perioperative or intraoperative complications. However, 3–4 weeks later she experienced sudden onset of severe-knifelike pain in her low back and was found to have a T11 inferior endplate fracture. Her pain ultimately subsided with conservative pain management within 4–5 weeks, and she is currently receiving abaloparatide anabolic therapy.

Case 3

The patient is a 79-year-old female who was first seen in consultation at the Osteoporosis Clinic in 2008 because of decline in bone density. She had a history of degenerative arthritis with joint replacements at the left hip and bilateral knees. She had a remote history of fracture of her tibia and fibula, as well as an L3 vertebral fracture after vertebroplasty in 2004. She also had a history of lumbar fusion L3–L5 completed in 2008. She had been previously tried oral bisphosphonates, but these were discontinued due to significant gastritis. She did not have any risk factors or known family history of OP. After our evaluation, she had a single intravenous (IV) Reclast infusion, but she was noted to have flu-like symptoms and significant swelling of her hands and refused further infusions. She remained off any antiresorptive therapy and did clinically well until May 2012, when she tripped in her bathroom and sustained a fall. She was noted to have a compression fracture at T12. This was initially followed by conservative treatment with rehabilitation and pain management. The patient was seen by a neurosurgeon and then had initial kyphoplasty in July 2012 with mild pain relief. One month later, due to increase in pain, X-rays were completed which revealed new vertebral fractures, and she had kyphoplasty done at T11 and L1 in August 2012. One month later, she was found to have another fracture followed by kyphoplasty at T10 in September 2012. In October 2012, she was noted to have PVA at L3.

DISCUSSION

Osteoporotic VCFs, a common occurrence in the elderly, can cause severe back pain, functional limitation, and spinal deformity. These patients can be managed through conservative measures, such as analgesia, lumbar bracing, and physical therapy [8]. Patients with severe intractable pain, who have failed conservative measures, may be considered for PVA [2]. However, it should be noted that these procedures should not be considered without a thorough OP evaluation, and complete discussion regarding nonpharmacological and pharmacological therapies for this underlying disorder.

We present three cases of VCFs that occurred temporally close and at levels adjacent to initial and/or prior PVA treatment of vertebral fractures. These new fractures occurred within 1–3 months after initial vertebroplasty or kyphoplasty procedures. Thus, we postulate that the incident procedure was the cause of the subsequent vertebral fractures.

Although more than 3000 articles have been published on vertebral augmentation, there remains debate over its effectiveness [1] and adverse events related to it [9]. The literature is inconclusive regarding the increased incidence of new adjacent vertebral fractures, with the rates widely varying for both PVP (8–52%) and BK (3–29%) [6]. Some studies have shown that patients who received PVA treatments have higher likelihood of suffering from refractures, and that these recurrent fractures may occur sooner in these patients as compared to those who received conservative treatment [10]. On the other hand, some believe that the development of new fractures is a natural process associated with OP, and that it is not affected by PVA treatment [10]. In support of that argument, in 2001 Lindsay et al. [11] carried out a study of 381 postmenopausal women with incident vertebral fractures, and reported that the incidence of a new vertebral fracture within the subsequent year of fracture was 19.2%. However, location of fracture level related to initial fracture was not reported in that study.

Theoretical and experimental models have demonstrated that vertebrae treated with PMMA are stiffer and less compliant than the fractured vertebrae. This increased stiffness induces a load shift that increases the risk of fracture in the adjacent vertebrae.
and may place the remainder of the axial skeleton at greater risk of collapse [2, 12]. However, in contrast, some studies have shown that the endplate deformation of fractured vertebrae under compressive load and the stress concentration in the posterior annulus is reduced after PVA, restoring the nuclear pressure in adjacent intervertebral discs, and thus potentially decreasing the risk of recurrent fractures by restoring the normal load sharing [13, 14].

In a retrospective study with 271 patients who underwent PVP with a mean follow-up interval of 25.6 months, Lo et al. [4] evaluated surgical outcomes in relation to variables including age, gender, BMD, the numbers of prior vertebroplasty procedures, cement volume, postoperative kyphotic angle, the vertebral level, and kyphotic changes. They found that 6.16% of all treated vertebra developed associated new vertebral fractures. They noted that there were 55.6% new fractures found at the adjacent level to previous vertebroplasty, and the T12–L1 levels had the highest incidence (61.11%, 11 of 18) of developing new fracture after vertebroplasty. They also found that cranial vertebrae were most likely to fracture at the adjacent level, whereas thoracic vertebrae were least likely to fracture at the adjacent level. They did not find any statistically significant association with the additional risk factors.

In another retrospective study, Civelek et al. [6] analyzed 171 patients treated with BK and followed them for 41.04 ± 21.78 months. New, symptomatic VCFs were recorded after the procedure. They also evaluated variables including age, sex, amount of cement injected, initial kyphotic angle (KA), change of KA after BK, severity of OP, and percentage of height restoration of the vertebral body. They found that sex and initial KA were significantly associated with adjacent fractures; females and higher preoperative KA were at higher risk of new VCFs. The severity of OP was not associated with new VCFs. Balloon kyphoplasty alone was not associated with incidence of subsequent VCFs.

In 2015, Xie et al. [10] completed a meta-analysis of randomized controlled trials (RCTs) comparing PVA and conservative treatment for incidence of new vertebral fractures, particularly related to adjacent vertebrae following treatment. They analyzed seven RCT studies including 871 patients, out of which 436 received PVA treatment and the rest received conservative treatment. They found that the number of new vertebral fractures was not significantly different between the two groups, even at 24 months after treatment. However, a limitation of this study was the different follow-up times between the various RCTs, ranging from three months to two years. In order to account for this, they further divided them into two subgroups of short-term follow-up (three months or less) and long-term follow-up (more than one year). Further analysis of these subgroups confirmed that, when compared to conservative treatment, PVA did not significantly increase the overall incidence of new vertebral fractures.

Interestingly, in a prospective study by Yi et al. [15], following PV and BK versus conservative therapy for 49 months, the investigators noted that new compression fractures occurred sooner after cement injection than in the conservative group, and more often in adjacent levels than the conservative group. However, overall there was similar incidence of recompression in the procedure groups versus the conservatively treated group. The authors do not report whether OP treatment was initiated in any of the groups.

Given the lack of consensus in the field, the American Society for Bone and Mineral Research (ASBMR) charged a task force to address key questions regarding the efficacy and safety of vertebral augmentation. This was accomplished by completing a systematic review of the existing literature and meta-analyses of outcomes. The review included RCTs and quasi-randomized trials that enrolled adults with acute nontraumatic vertebral fractures, aged >40 years. They directly compared PVP or BK with other treatment comparator groups (e.g., placebo, sham procedure, conservative management, PVP, BK, or pharmacologic treatment). Risk of bias was assessed according to the Cochrane risk of bias tool [7].

Analyzing five randomized placebo-controlled trials, they found no clear evidence regarding whether or not PVP increases risk of incident or radiographic VCFs due to a low number of events and the potential for bias in previous studies. Similarly, it is uncertain whether BK increases risk of incident or radiographic VCFs, due to a lack of high-quality evidence [7].

CONCLUSION

There are mixed data regarding whether there is an increased incidence of new or adjacent VCF following PVP and BK due to methodology and bias in studies and meta-analyses. While there may be short-term advantages of PVA associated with improved pain control and quality of life compared to conservative therapy, our three cases suggest that early and adjacent new fractures following PVA may occur. Given the mixed evidence regarding the efficacy of these procedures, as well as potential adverse events related to it, clinicians involved in the treatment of patients with OP are obligated to fully discuss and weigh the risks and benefits of these procedures whenever possible before patients undergo them. Further, OP evaluation and treatment underscore appropriate care of this population.

REFERENCES

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Author Contributions
Hirva Bakeri – Acquisition of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved
Pamela Taxel – Conception of the work, Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written consent was not obtained from the patients as IRB does not require written consents for case series up to 3 patients and all our patients were de-identified. We can obtain written consents, if required.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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