Vertebral Compression Fracture Treatment with Vertebroplasty and Kyphoplasty: Experience in 407 Patients with 1,156 Fractures in a Tertiary Cancer Center

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Abstract

**Background.** Painful vertebral compression fractures (VCFs), whether pathologic or osteoporotic, are a source of morbidity in cancer patients. At our tertiary cancer center, over the past decade we have used vertebroplasty (VP) and kyphoplasty (KP) to treat painful VCFs. More data are needed on the treatment of VCFs in cancer patients with these techniques.

**Methods.** We retrospectively reviewed the medical records of cancer patients with painful VCFs that had been treated at our institution between January 1, 2001 and May 31, 2008. Information was collected on demographic and clinical characteristics, features of the fractures, procedural details, and complications. Pre- and post-procedural pain and related symptoms were assessed using a subset of patients who had responded to the Brief Pain Inventory and the Edmonton Symptom Assessment Scale.

**Results.** A total of 407 cancer patients had 1,156 fractures that had been treated with VP or KP during 536 surgical procedures. Patients had an average of 2.8 fractures (range, 1–10). The majority of patients had pathologic fractures due to multiple myeloma (43%) or osteoporotic fractures (35%). Most fractures occurred in the thoracolumbar region. Adjacent-level fractures occurred in 18% of patients. Surgery provided significant relief from pain and several related symptoms. Symptomatic, serious complications requiring open surgery occurred in two cases (<0.01%) in our series.

**Conclusions.** Our single-center experience revealed that a large number of cancer patients suffer from painful VCFs. The use of VP or KP in treating painful VCFs in cancer patients has good efficacy and an acceptably low complication rate.

Key Words. Kyphoplasty; Vertebroplasty; Vertebral Compression Fracture; Osteoporosis; Spinal Metastasis; Spine Fractures; Spine Interventional Procedures

Introduction

Many cancer patients suffer morbidity due to skeletal metastasis, pain, and vertebral compression fractures (VCFs). Skeletal complications are very common in multiple myeloma, regardless of stage, and in metastatic breast, prostate, and other solid tumors. Extradural metastases account for approximately 95% of secondary spinal tumors. Two-thirds of the primary sources of metastatic neoplasms to the spinal axis are carcinomas of the breast, lung, and prostate; renal cell carcinoma and myeloma together account for about 10% of spinal metastases [1].

Many patients with systemic cancer develop skeletal metastases, most commonly in the spine. Spinal metastases are present in 40% of patients who die of
cancer. Symptomatic spinal metastases occur in approximately 5–10% of cancer patients at some time during the course of their disease. These symptomatic spinal metastases most often involve the thoracic spine (70% of cases) and less frequently the lumbar segments (20%) and cervical segments (10%) [2]. Thus, each year more than 50,000 cancer patients in the United States could be expected to have symptomatic vertebral metastases [3].

Spinal metastases can lead to debilitating pain and weakness that cause marked deterioration in quality of life. Vertebroplasty (VP) and kyphoplasty (KP) are two techniques used to treat painful VCFs. VP is the percutaneous injection of a vertebral body with bone cement, generally polymethylmethacrylate (PMMA). PMMA has been used in orthopedics since the late 1960s [4]. Percutaneous VP was first reported by a French group in 1987 for the treatment of painful hemangiomas [5]. Since then, the indications for VP have expanded to include osteoporotic compression fractures and painful vertebral metastasis [6,7] (Table 1). KP is a modification of VP; it involves the percutaneous placement of balloons (called “tamps”) into the vertebral body with an inflation/deflation sequence to create a cavity prior to PMMA injection. Percutaneous KP may restore vertebral body height and reduce the kyphotic angulation of the compression fracture prior to injection [8].

Ideal candidates for PV or PK have activity-related axial pain corresponding to the level of a recent compression fracture. In a retrospective study of 740 levels treated with VP and/or KP, the pain outcome was the same regardless of the fracture etiology (osteoporosis vs pathologic) [9]. PV and KP are minimally invasive procedures that provide significant pain relief after percutaneous vertebral augmentation in patients with pathologic fractures [10,11].

At our tertiary care center, we have pushed “relative” contraindications in cancer patients without increasing morbidity, even in cases of very advanced cancers [12,13].

### Table 1 Overview of guidelines for the use of percutaneous vertebroplasty from the Society of Interventional Radiologists [29] and the Cardiovascular and Interventional Radiological Society of Europe [25]

#### Indications
1. Painful osteoporotic VCF refractory to 3 weeks of analgesic therapy
2. Painful vertebrae due to benign or malignant primary or secondary bone tumors
3. Painful VCF with osteonecrosis (Kummel’s disease)
4. Reinforcement of vertebral body prior to surgical procedure*
5. Chronic traumatic VCF with nonunion*

#### Absolute contraindications
1. Asymptomatic VCF
2. Patient improving on medical therapy
3. Ongoing infection
4. Prophylaxis in osteoporotic patient
5. Uncorrectable coagulopathy
6. Myelopathy due to retropulsion of bone/canal compromise
7. Allergy to PMMA or opacification agent

#### Relative contraindications
1. Radicular pain
2. VCF >70% height loss*
3. Severe spinal stenosis, asymptomatic retropulsion of bony fragment
4. Tumor extension into canal/epidural space
5. Lack of surgical backup*

* Recent updates [25]. PMMA = polymethylmethacrylate; VCF = vertebral compression fracture.

Adjacent-Level Fractures

VCFs that arise after VP or KP may occur at adjacent levels or remote to the treated “vertebroplastied” level. Friiborg et al. first noted a slight increase in adjacent-level fractures after VP or KP with long-term follow-up [14]. The rate of any new fractures varies from 7% to 20% over 1 year of follow-up, with refracturing occurring early on at the adjacent levels [15]. These findings suggest a local unfavorable biomechanical situation in some patients who suffer adjacent-level fracturing, and an ongoing disease process (usually osteoporosis) in patients who sustain remote fracturing. Also, certain patient populations may be at higher risk for future fractures, such as those with osteoporosis, those with previous vertebral fracture, and organ transplant recipients [16,17]. In those studies, the outcome of pain relief following VP or KP for adjacent-level fractures is similar for those after the initial procedure [18].

Vertebroplasty vs Kyphoplasty

Both VP and KP effectively reduce pain associated with VCFs and have low complication rates. Although clinicians tend to favor one procedure over another regardless of the clinical circumstances, a recent small study of osteoporotic VCFs found no significant difference by procedure in outcomes at 6 months [19]. No specific head-to-head comparison trials have been done in the cancer setting [20]. At our cancer center, we currently favor KP for patients who have a collapse of more than 20% of vertebral height and a fracture age of less than 3 months, with the hopes of restoring vertebral height and maintaining functional anatomy. Deramond et al. stated that KP may be preferable over VP for patients with severe or multiple wedge deformity that had developed in the preceding 3 weeks, but this suggestion is speculative until direct comparison trials can be performed [21]. The advantages of each procedure are listed in Table 2.
Methods

Medical Records Review

After receiving approval from the Institutional Review Board of The University of Texas MD Anderson Cancer Center, we initiated a comprehensive electronic database search of institutional records to identify cancer patients who had been treated with PV or PK at the center between January 1, 2001 and May 31, 2008, a period spanning 7.5 years. We reviewed the medical records to collect information on a patient’s demographic characteristics, clinical diagnosis, surgical procedures (VP, KP, or both), vertebral fracture location and type (pathologic or osteoporotic, existing or new, and if new, adjacent or remote), previous cancer treatments, and complications. Prior to their VP or KP, patients had rated their pain using the Brief Pain Inventory and reported the severity of related symptoms using the Edmonton Symptom Assessment Scale. A Health Insurance Portability and Accountability Act (HIPAA)-compliant database was created for our study with FILEMAKER PRO software (version 9; FileMaker, Inc., Santa Clara, CA, USA).

Patient Surveys

We also conducted a responder analysis to assess the difference in scores for pain and related symptoms among patients who had this documented prior to procedure and at a follow-up visit within 2 months of VP and/or KP. Patients without a documented visit within this time frame were excluded from the responder analysis. Pain and symptom data were unavailable for 237 patients (58%), and thus those patients were excluded from symptom analysis.

The Brief Pain Inventory [Cleeland, 1989; Cleeland, 1990; Cleeland, 1991; Cleeland & Ryan, 1994] [22] asks patients to rate the severity of their pain at its worst and at its least for the preceding week, usually, and at the time the questionnaire is being administered. Each item is rated on an 11-point scale, where 0 is “no pain” and 10 is “pain as bad as you can imagine.”

The Edmonton Symptom Assessment System has been validated and is frequently used in clinical care [23]. Each of nine symptoms (fatigue, nausea, depression, anxiety, drowsiness, mental clarity, shortness of breath, poor appetite, and insomnia) is rated on an 11-point scale, with 0 being “none” and 10 being “worst.” In addition, the overall sense of well-being was assessed also using an 11-point scale, with 0 being “best” and 10 being “worst.”

Statistical Analyses

Summary statistics were used to describe the patient cohort. Frequency distributions, cross tabulations, proportions, means, standard deviations (SDs), and ranges were computed for demographic and clinical variables. Descriptive statistics were used for pain and related symptom variables. We used a one-sample t-test to determine whether there was a significant reduction in the scores for pain and related symptoms between the first and second surveys. Statistical analysis was conducted using Statistical Package of the Social Sciences (SPSS) software (version 17.0; IBM Corp., Somers, NY, USA). The criterion for statistical significance was set at a two-tailed alpha level of 0.05.

Results

We identified 407 patients who had undergone a total of 536 procedures to repair 1,156 fractures. Some patients had more than one fracture repaired at the time of the procedure, and some patients had undergone repeated, discrete procedures.

Demographic and Clinical Characteristics

The patient sample was evenly split among males (48%) and females (52%). The average age was 62.9 years. Pathologic fractures due to multiple myeloma comprised 43% of our cases. Osteoporotic fractures comprised 35% of cases and were followed by pathologic fractures due to lung cancer (9%), breast cancer (8%), and lymphoma (5%). Before undergoing PV or PK, 75% of the patients had received chemotherapy and 47% radiotherapy (16% of the latter had received directed spinal radiation).

Procedures and Fractures

Of the 536 spinal procedures that had been performed, 262 were VPs only, 156 were KPs only, 111 were combined VP/KPs (i.e., a different technique had been applied at different spinal levels during the same surgery), and 7 were sacroplasties.

Three hundred seven patients (75%) had undergone a single procedure to treat a total of 649 fractures (Table 3). The number of patients decreased and the average number of fractures treated increased as the number of procedures increased from one to four per patient. For patients who had had two, three, or four treatments, the procedures had occurred at discrete times, usually for new fractures, although a small number had been

<table>
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<th>Table 2</th>
<th>Comparison of vertebroplasty and kyphoplasty features [21,35,40]</th>
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<tr>
<td><strong>Vertebroplasty</strong></td>
<td><strong>Kyphoplasty</strong></td>
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<tr>
<td>Less expensive</td>
<td>More anatomic correction of spinal deformity</td>
</tr>
<tr>
<td>Faster for both the surgeon and patient</td>
<td>Greater height restoration in fractures &lt;3 months old</td>
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<tr>
<td>Indicated for fractures &gt;3 months old</td>
<td>Indicated for patients with extensive kyphosis</td>
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<tr>
<td>Less PMMA extravasation</td>
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PMMA = polymethylmethacrylate.
"staged-sequential" procedures for patients who had incurred a large number of fractures. A single patient had undergone five procedures to treat six fractures.

There was an average of 2.8 fractures treated per patient (range, 1–10). One hundred twenty-five patients (31%) had incurred a single compression fracture. L1 (N = 154; 13.3%) and T12 (N = 149; 12.9%) were the most common fracture sites (Figure 1).

**New and Adjacent-Level Fractures**

Of the 407 patients who had been treated for a total of 1,156 fractures, 100 patients (24%) had experienced 259 new fractures (i.e., fractures subsequent to a previous procedure). The new fractures accounted for 22% of the total number of fractures.

Of the new fractures, 119 (46%) had occurred at a level adjacent to previously cemented fractures. Fifty of the 78 patients who had undergone two procedures, and all of the patients who had undergone three, four, or five procedures, had been treated for adjacent-level fractures. Thus, of the total cohort, 72 (18%) had experienced this type of fracture.

Sixty-one percent of the patients who had developed new fractures had had pathologic fractures. Sixty-one percent of those, in turn, had occurred at adjacent levels.

**Assessment of Pain and Related Symptoms**

Pain and symptom data were unavailable for 237 patients (58%), and thus those patients were excluded from symptom analysis. This was the only exclusion criteria and largely speaks to the tertiary cancer center population with many out-of-town patients without local follow-up. Pain and symptom scores were available for 170 of the 407 patients (42%) for a follow-up period of up to 60 days (mean, 25 days [SD = 13.9]; range, 2–59 days). The pain score dropped significantly between the first and second visits (95% confidence interval: 0.99, 1.85; \( P < 0.001 \)) by an average of 1.4 points (SD = 2.8) (Table 4). Nineteen percent of the respondents reported an increase in pain, 22% no change, and 59% less pain. Between the first and second visits, the mean Edmonton Symptom Assessment System scores for related symptoms decreased significantly for fatigue (1.14, \( P < 0.001 \)), depression (1.03, \( P < 0.001 \)),

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<th>Table 3</th>
<th>Number of discrete surgical procedures and fractures treated</th>
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<tr>
<td>Number of procedures undergone</td>
<td>Number (%) of patients who had undergone X procedures</td>
</tr>
<tr>
<td>1</td>
<td>307 (75)</td>
</tr>
<tr>
<td>2</td>
<td>78 (19)</td>
</tr>
<tr>
<td>3</td>
<td>16 (4)</td>
</tr>
<tr>
<td>4</td>
<td>5 (1)</td>
</tr>
<tr>
<td>5</td>
<td>1 (1)</td>
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<tr>
<td>Total: 407 (100)</td>
<td>Total: 1,156</td>
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<th>Table 4</th>
<th>Mean reduction in pain and other symptoms and the associated 95% confidence interval</th>
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<tbody>
<tr>
<td>Symptom</td>
<td>No. of patients</td>
</tr>
<tr>
<td>---------</td>
<td>----------------</td>
</tr>
<tr>
<td>Pain</td>
<td>170</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>133</td>
</tr>
<tr>
<td>Anxiety</td>
<td>136</td>
</tr>
<tr>
<td>Depression</td>
<td>136</td>
</tr>
<tr>
<td>Difficulty thinking clearly</td>
<td>134</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>132</td>
</tr>
<tr>
<td>Fatigue</td>
<td>148</td>
</tr>
<tr>
<td>Insomnia</td>
<td>131</td>
</tr>
<tr>
<td>Nausea</td>
<td>133</td>
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SD = standard deviation.
P < 0.001), anxiety (1.02, P < 0.001), drowsiness (1.02, P < 0.001), and difficulty thinking clearly (0.63, P < 0.006) (Table 4). Shortness of breath, insomnia, and nausea were not significantly reduced.

Complications

Complications (including cement extrusion) had not been noted in the medical records for 400 of the 536 procedures (75%) (Figure 2). The vast majority of the complications were asymptomatic cement extrusions. Of the 134 complications that had been noted, paravertebral cement spread was the most prevalent (38.8%, N = 52) and was followed by intradiscal extrusion (28.4%, N = 38), venous extrusion (23.9%, N = 32), epidural extrusion (3.7%, N = 5), and others (5.2%; N = 7). Some of the complications were a combination of these but were too few to show. The combinations are so small that they are not shown—all combinations not shown comprised 0.7%. We grouped the procedures into three procedural groups, those who had simultaneous VP and KP during one procedure at different levels (KP/VP), those having only VP or KP during the procedure. Significant differences in procedural complications were seen between these groups. There were more complications associated with the combination KP/VP than either KP alone (35% vs 19%, P < 0.003) or VP alone (35% vs 24%, P < 0.02). No significant difference was observed for the KP alone vs VP alone comparison (19% vs 24%, P < 0.27).

Of the 111 combination procedures (KP/VP), there were no significant differences in the proportion of procedures of vertebral level for those who had complication (34% [one level of each] vs 40% [multiple], P < 0.56). There were no significant differences in the proportion of levels that is pathologic for those who had complication (34% [no pathologic fracture] vs 54% [with pathologic], P < 0.17) (Figure 2).

Of the seven non-extrusion complications, symptomatic epidural extravasation was experienced by four patients, two of whom required open-surgery decompression for mild weakness that resulted in symptomatic resolution. Mildly increased pain and radicular symptoms were noted for two patients, who did well with conservative management. A final patient with significant comorbidities, including morbid obesity and diabetes, developed vertebral body infection that was subsequently treated successfully.

Discussion

At the MD Anderson Cancer Center, we follow the standards for the safe practice of VP and KP in treating painful vertebral compression fractures that have been published by the Society of Interventional Radiologists (SIR) in 2003 and recently updated by the Cardiovascular and Interventional Radiological Society of Europe [24,25]. We have pushed the “relative” contraindications in our patient population and have performed cement augmentation for patients with vertebra plana and retroplused fragments [12]. Prior to the procedure (VP/KP), the patient should not be using any anticoagulants and the coagulation profile should be normal. Platelet count should be at least 50,000 at the time of the procedure, although no data exist for identifying a clear cut-off count. There may be instances when the risk–benefit ratio favors these procedures in patients with lower platelet counts, and possible platelet transfusion prior to the procedure.

VP and KP require the clinician to be trained in spinal anatomy, fluoroscopic imaging, and the use of these techniques in performing interventional procedures. At our cancer center, VP and KP are performed in a sterile operating room suite that will allow fluoroscopic imaging of the spine, and cement injection is halted when it reaches the posterior one-third of the vertebral body. To minimize PMMA leakage, the use of high viscosity cement and a relatively small volume injection is recommended [11,26,27].

Our decision making for VP and KP involves multidisciplinary care conferences among clinicians from departments of pain medicine, radiation oncology, neurosurgery, and neuroradiology. We also implement an algorithm for KP when there is an increased concern for cement extravasation, neurologic compromise, or recent multilevel fractures with kyphosis.

Complications from VP and KP are rare but can be serious. The exact incidence of complications is unknown. Our data revealed a complication rate of 24%, with a
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majority of them occurring with augmentation of a pathologic fracture. Most case series report asymptomatic PMMA extravasation rates of 10–15% [8,28]. Our higher rate is not surprising given the large number of pathologic fractures that had been treated. SIR categorizes complications for these techniques as minor or major. Minor complications require no therapy and having no consequence, such as PMMA extravasation into the disc. Major complications require therapy, including an unplanned increase in the level of care needed, or ongoing care. Most case series report major complications to be <1%, except for cases with neoplastic involvement of the vertebrae, for which the rate is <5% [29]. The major complication rate in our cohort was far below 1%, even though it was a population of cancer patients. We did not find any statistical difference in complication rate by fracture type (pathologic vs non-pathologic), procedure type (KP alone vs VP alone), or number of levels treated. We did see a higher complication rate in the combination cases (KP/VP), perhaps denoting cases with more complexity in some way.

PMMA can flow out of the vertebral body posteriorly into the spinal canal or neural foramina or anteriorly into the paraspinous veins, with systemic consequences. There are also case reports of nerve root and spinal cord compression from extravertebral PMMA [30,31]. Infectious complications are rare, but a few reports of osteomyelitis requiring corpectomy exist [32]. Meticulous attention to sterile technique is warranted, including preoperative intravenous antibiotic administration. In our study cohort, one serious post-operative infection had occurred but was attributable to patient characteristics rather than the procedure.

Despite the low complication rates and frequently successful patient outcomes, recent reviews and editorials have called for a more critical evaluation of VP and KP. Garfin et al. acknowledged that there is a 95% improvement in pain and significant improvement in function following these procedures, but because both procedures are technically demanding with the potential for significant complications, they recommended further efficacy and safety studies [33]. Einhorn called for careful monitoring of outcomes and minimal training standards [34]. Watts et al. asserted that controlled multi-center trials are needed to determine the short- and long-term safety of these procedures [35]; Jarvik and Deyo called for randomized controlled trials or some type of control cohort to compare long-term outcomes carefully [36]; and Birkmeyer recommended randomized clinical trials because of the lack of sufficient evidence via case series to prove safety, efficacy, and cost-effectiveness [37].

Our retrospective analysis showed that 59% of respondents reported decreased pain, which is a rate lower than what is seen in the current available literature [38,39].

However, this follow-up information was available for only 42% of the patients in our cohort. This is a major weakness of our retrospective analysis confounding our ability to quantify the pain relief data accurately. Many of our out-of-town patients that do well post-procedurally will not return to the pain center for a follow-up visit, and usually patients who have pain due to other cancer-related sources will return to the pain center for further evaluation and treatment. Thus, the retrospective analysis has considerable limitations for gathering accurate pain relief data.

A recently published prospective RCT (the CAFÉ trial) comparing KP with conservative treatment in cancer patients with painful VCFs found significant improvement in pain scores, performance status, quality of life measures and medication use at a 1-month time point. The mean reduction in pain scores was 3.8, and the responder rate-number meeting a threshold of 70 on the Karnofsky index was 74% vs 38% in the conservative treatment arm [39].

Other studies are needed to compare in a randomized fashion PV and PK in various disease states. Early studies are under way to evaluate biologic materials for spinal injection in place of acrylic (i.e., PMMA). The role of local tumor ablation with or without PK or PV also needs study and clarification. Despite the need for more research, these two spinal procedures have shown great promise for treating painful VCFs due to a variety of pathologic states. With careful patient selection, adequate training, and attention to detail during the procedure, serious complications are rare.

Conclusions

We reported the experience of performing PV and PK in our tertiary cancer hospital over a span of 7.5 years. We actively use these techniques in the context of multidisciplinary assessment and multimodal treatment strategies. Many vertebral fractures were related to multiple myeloma, osteoporosis, and metastatic tumor. Our safety record is very good: the rate of serious complications is <1%. The efficacy of pain control after surgery was difficult to interpret because of the retrospective nature of the study, but we found 59% of the evaluable patients reported less pain after surgery. In summary, we view PV and PK as valuable adjunctive therapies for cancer patients with painful VCFs of all etiologies. Our complication rate is low and the efficacy level is acceptable.

References


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